Analysis of a reaction-diffusion cholera epidemic model in a spatially heterogeneous environment

Wang, Jinliang

Xie, Fanglin

Kuniya, Toshikazu

(Citation)
Communications in Nonlinear Science and Numerical Simulation,80:104951

(Issue Date)
2020-01

(Resource Type)
journal article

(Version)
Accepted Manuscript

Analysis of a reaction-diffusion cholera epidemic model in a spatially heterogeneous environment

Jinliang Wang & Fanglin Xie
School of Mathematical Science,
Heilongjiang University, Harbin 150080, P.R. China

Toshikazu Kuniya*
Graduate School of System Informatics,
Kobe University, 1-1 Rokkodai-cho, Nada-ku, Kobe 657-8501, Japan

Abstract

In this paper, we derive and analyze a reaction-diffusion cholera model in bounded spatial domain with zero-flux boundary condition and general nonlinear incidence functions. The parameters in the model are space-dependent due to the spatial heterogeneity. By applying the theory of monotone dynamical systems and uniform persistence, we prove that the model admits the global threshold dynamics in terms of the basic reproduction number $\Re_0$, which is defined by the spectral radius of the next generation operator. When all model parameters are strictly positive constants, we study three types of nonlinear incidence functions to achieve the global stability results on the unique positive cholera-endemic steady state (CESS) whenever it exists. For all these examples, the sharp threshold property based on the basic reproduction number was completely established by using Lyapunov functional techniques under some realistic assumptions. Our numerical results reveal that when $\Re_0 > 1$, the convergence speed of the solution to the CESS becomes faster as the diffusion coefficient d becomes larger in the spatially homogeneous case. While in the spatially heterogeneous case, cholera can not be controlled by limiting the movement of host individuals, and the spatial heterogeneity does not always enhance the disease persistence.

Keywords: Diffusive cholera model, Spatial heterogeneity, Lyapunov functional, Basic reproduction number.

1 Introduction

Cholera is a severe water-borne infectious disease caused by the bacterium Vibrio cholerae. The complexity of cholera dynamics lies in the fact that both direct contact with infected individuals (e.g. hugging, shaking hands, and eating food prepared by dirty hands) and indirect

*Corresponding author. E-mail address: tkuniya@port.kobe-u.ac.jp

contact from the environment to people ingesting the contaminated water or food are involved. It can spread rapidly and lead to death within days if left untreated.

Mathematical models have played a central role in deeper understanding of cholera dynamics. Therefore, it is reasonable to incorporate pathogens in the environment (water) into the disease models, see for example, models with human transmission route (e.g. [1]), and models with both the environment-to-human and human-to-human transmission pathways (e.g. [2–6]). Taking into account various aspects related to epidemiological feature of cholera, such as hyperinfectivity [7], age-structure [8–10], multiple infection stages [11], multi-group structure [5,11], spatiotemporally heterogeneous environment [12], subsequent contributions have recently been proposed and analyzed. In the forms of mathematical models, all of these cholera models consist of many nonlinear ordinary differential equations or mixed system of ordinary and partial differential equations.

In a recent work, Shuai and van den Driessche [13] divided a population into subpopulations, and each subpopulation is further partitioned into three compartments: susceptible (S_i), infectious (I_i), and removed (R_i). Denote by W_i the number of pathogen shed by individuals in I_i. They formulated and studied the following multigroup cholera model incorporates both within-group and inter-group direct/indirect transmission:

$$\begin{cases} \dfrac{\mathrm{d}S_i}{\mathrm{d}t} = \Lambda_i - \displaystyle\sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\varphi_j(I_j) - \sum_{j=1}^{n} \lambda_{ij}\phi_i(S_i)\psi_j(W_j) - d_i S_i, \\ \dfrac{\mathrm{d}I_i}{\mathrm{d}t} = \displaystyle\sum_{j=1}^{n} \beta_{ij}\phi_i(S_i)\varphi_j(I_j) + \sum_{j=1}^{n} \lambda_{ij}\phi_i(S_i)\psi_j(W_j) - \mu_i I_i, \\ \dfrac{\mathrm{d}W_i}{\mathrm{d}t} = h_i(I_i) - \delta_i W_i, \ i = 1, 2, ..., n. \end{cases} \tag{1.1}$$

Here functions ϕ_i, φ_i, ψ_i and h_i are assumed to be differentiable, nonnegative, monotone nondecreasing and concave. β_{ij} and λ_{ij} are the direct and indirect transmission rates to S_i from I_j and W_j, respectively; Λ_i is the recruitment rate of susceptible individuals in the group i; d_i, μ_i, δ_i are the death or removal rate of each subpopulation in group i, respectively. The authors completely demonstrated the construction of Lyapunov functions for above model by appealing a matrix-theoretic method using the Perron eigenvector and a graph-theoretic method based on Kirchhoff's matrix tree theorem. In fact, in the above work, the spatial effect is described by the multi-group structure and each subpopulation shares the same epidemiological parameters. We see that in model (1.1), only infected individuals and pathogens can move in the habitat space, and the movement of susceptible individuals is ignored.

In reality, the spread of infectious diseases are significantly affected by the spatial heterogeneity, for example, spatial position, water resource availability and hygiene conditions. The movement of human hosts and dispersal of pathogens are also accepted as central role that affects the spatial spreading of disease, which also requires complex disease models. The following partial differential equation (PDE) cholera model was proposed by Wang and Wang [14], which includes the diffusion terms to describe the movement of human hosts and bacteria in a spatially heterogeneous environment:

$$\begin{cases} \frac{\partial S}{\partial t} = D_1\Delta S + \Lambda - Sf_1(I) - Sf_2(W) - dS_i + \sigma R, \ x \in [0,1], \\ \frac{\partial I}{\partial t} = D_2\Delta I + Sf_1(I) + Sf_2(W) - (d+\gamma)I, \ x \in [0,1], \\ \frac{\partial R}{\partial t} = D_3\Delta R + \gamma I - (d+\sigma)R, \ x \in [0,1], \\ \frac{\partial W}{\partial t} = D_4\Delta W + \xi I + h(W) - \delta W, \ x \in [0,1], \\ \frac{\partial S}{\partial x} = \frac{\partial I}{\partial x} = \frac{\partial R}{\partial x} = \frac{\partial W}{\partial x} = 0, x = 0, 1. \end{cases} \tag{1.2}$$

Here, human population and the bacteria are assumed to undergo a diffusion process, which is described by the diffusion terms $D_1\Delta S$, $D_2\Delta I$, $D_3\Delta R$ and $D_4\Delta W$. $D_i > 0$ $(1 \leq i \leq 4)$ are the diffusion coefficients of S, I, R and W, respectively. The functions $f_1(I)$ and $f_2(W)$ represent the direct and indirect transmission rates, respectively. The function $h(W)$ represents the intrinsic growth of the bacteria due to the fact that the vibrios can independently persist in the environment. d and δ are the natural death rate of humans and bacteria, respectively. γ is the recovery rate, σ is the immunity loss rate and ξ is the shedding rate of bacteria. Wang and Wang [14] assumed that the habitat in (1.2) is one-dimensional and bounded, and investigated how diffusive spatial spread affect the disease spread. They obtained that incorporating diffusive spatial spread does not produce a Turing instability in some extent.

However, a habitat should be not necessarily one-dimensional, and this motivates us to consider a PDE cholera model in a general bounded spatial domain. This constitutes one motivation of this paper. Our second motivation comes from the fact that the diffusion coefficients as well as several parameters of disease transmission rates involving space can be typically space dependent, instead of constants, due to the spatial heterogeneity (see recent publications [15–19]). The above two important factors related to PDE cholera model seem to have received little attention. Our goal in this paper is to investigate the effect of spatial heterogeneity and general nonlinear incidence functions on the dynamics of diffusive cholera models. To make things not too complicated, we omit the intrinsic growth of the bacteria, and consider the solution dynamics with zero-flux boundary condition. With these considerations, we consider the following diffusive cholera model:

$$\begin{cases} S_t = \nabla \cdot [d_1(x)\nabla S] + \lambda(x) - f_1(x,S,I) - f_2(x,S,P) - \mu(x)S, & x \in \Omega,\ t>0, \\ I_t = \nabla \cdot [d_2(x)\nabla I] + f_1(x,S,I) + f_2(x,S,P) - [\mu(x)+\gamma(x)]\, I, & x \in \Omega,\ t>0, \\ P_t = \nabla \cdot [d_3(x)\nabla P] + m(x)I - \eta(x)P, & x \in \Omega,\ t>0, \\ S(x,0) = S_0(x),\ I(x,0) = I_0(x),\ P(x,0) = P_0(x), & x \in \overline{\Omega}, \end{cases} \tag{1.3}$$

with

$$\frac{\partial S}{\partial \mathbf{n}} = \frac{\partial I}{\partial \mathbf{n}} = \frac{\partial P}{\partial \mathbf{n}} = 0, \quad x \in \partial\Omega,\ t>0. \tag{1.4}$$

Here $S(x,t)$ and $I(x,t)$ stand for the density of susceptible and infected individuals at location x and time t, respectively, while $P(x,t)$ stands for the concentration of the cholera bacteria in the water source at location x and time t; $d_1(x)$, $d_2(x)$ and $d_3(x)$ are diffusion functions measuring the mobility of susceptible and infected individuals and cholera at location x, respectively; $\lambda(x)$ is the recruitment rate of susceptible individuals; $\mu(x)$ is the natural death rate of susceptible individuals and infected individuals; $\gamma(x)$ is the removal rate of infected individuals; $m(x)$ is the shedding rate of cholera bacteria from infected individuals; $\eta(x)$ is the natural death rate of cholera bacteria; $f_1(x,S,I)$ and $f_2(x,S,P)$ are general nonlinear incidence functions corresponding to the direct infection transmission between susceptible and infected individuals and the indirect infection transmission between susceptible individuals and cholera bacteria, respectively; Ω is a habitat; $\mathbf{n}$ is the outward normal vector on $\partial\Omega$; ∇ is the gradient operator. Throughout this paper, we make the following assumptions.

(A1) Ω is a bounded domain in $\mathbb{R}^n$, $n \in \mathbb{N}$ with sufficiently smooth boundary $\partial\Omega$.

(A2) $d_1(\cdot), d_2(\cdot), d_3(\cdot), \lambda(\cdot), \mu(\cdot), \gamma(\cdot), m(\cdot), \eta(\cdot) \in C^2(\overline{\Omega})$ and they are strictly positive and uniformly bounded on $\overline{\Omega}$.

(A3) $f_1(x,S,I) > 0$ and $f_2(x,S,P) > 0$ for all $x \in \overline{\Omega}$ and $S, I, P > 0$. $f_1(x,S,0) = f_1(x,0,I) = f_2(x,S,0) = f_2(x,0,P) = 0$ for all $x \in \overline{\Omega}$ and $S, I, P \geq 0$.

(A4) $f_1(x,S,I)$ and $f_2(x,S,P)$ are twice continuously differentiable with respect to $(x,S,I) \in \overline{\Omega} \times \mathbb{R}_+ \times \mathbb{R}_+$ and $(x,S,P) \in \overline{\Omega} \times \mathbb{R}_+ \times \mathbb{R}_+$, respectively.

The organization of this paper is as follows. In Section 2, we show the existence and uniqueness of the global classical solution of system (1.3)-(1.4). We further show that the boundedness of the solution and the existence of a continuous semiflow. In Section 3, we define the basic reproduction number $\Re_0$ for system (1.3)-(1.4) by the sprectral radius of the next generation operator. In Section 4, under some additional assumptions on the functions f_1 and f_2, we investigate the threshold dynamics of system (1.3)-(1.4): the cholera-free steady state (CFSS) is globally asymptotically stable if $\Re_0 < 1$, whereas the system (1.3)-(1.4) is uniformly strongly persistent if $\Re_0 > 1$. In Section 5, we consider the spatially homogeneous case. Under the assumptions of positivity, monotonicity and concavity on the nonlinear incidence functions, we show that if $\Re_0 > 1$, then the unique cholera-endemic steady state (CESS) exists and it is globally asymptotically stable. Specifically, we consider three special cases of the nonlinear incidence functions. The proofs will be performed by using Lyapunov functional techniques. In Section 6, we perform numerical simulation that supports our theoretical results. We numerically show that the diffusion coefficient affects to the convergence speed of the solution to the steady state, cholera can not be controlled by limiting the movement of host individuals, and the spatial heterogeneity does not always enhance the disease persistence. Finally, Section 7 is devoted to the discussion.

2 Well-posedness of the problem

This section is devoted to prove that system (1.3)-(1.4) has a unique global classical solution. Let us define the following differential operators:

$$
\begin{aligned}
&A_i^0\varphi := \nabla\cdot\left[d_i(\cdot)\nabla\varphi\right],\\
&D(A_i^0) := \left\{\varphi\in C^2(\Omega)\cap C^1(\overline{\Omega}) : A_i^0\varphi\in C(\overline{\Omega}),\ \ \frac{\partial\varphi}{\partial\mathbf{n}} = 0,\ x\in\partial\Omega\right\},\quad i=1,2,3.
\end{aligned}
$$

From [20, Chapter 7], we see that for $i = 1,2,3$, the closure A_i of A_i^0 generates a C_0-semigroup $\{T_i(t)\}_{t\geq 0}$ such that $u_i(t) = T_i(t)\varphi$ is the solution of $u_i'(t) = A_i u_i(t)$, $t > 0$ with $u_i(0) = \varphi \in D(A_i)$, where

$$
D(A_i) := \left\{\varphi\in C(\overline{\Omega}) : \lim_{t\to+0}\frac{(T_i(t)-I_d)\varphi}{t}\ \text{exists}\right\}.
$$

Here I_d denotes the identity operator. Let us define the following nonlinear operators on $\overline{\Omega}\times\mathbb{R}^3$:

$$
\begin{cases}
F_1(x,\mathbf{r}) := \lambda(x) - f_1(x,r_1,r_2) - f_2(x,r_1,r_3) - \mu(x)r_1,\\
F_2(x,\mathbf{r}) := f_1(x,r_1,r_2) + f_2(x,r_1,r_3) - \left[\mu(x)+\gamma(x)\right]r_2, \qquad x\in\overline{\Omega},\quad \mathbf{r}=(r_1,r_2,r_3)\in\mathbb{R}^3.\\
F_3(x,\mathbf{r}) := m(x)r_2 - \eta(x)r_3,
\end{cases}
$$

Let $\mathbb{X}_i := C(\overline{\Omega})$, $i = 1,2,3$ and let

$$
\begin{aligned}
&A := \prod_{i=1}^3 A_i,\quad D(A) := \prod_{i=1}^3 D(A_i),\quad T(t) := \prod_{i=1}^3 T_i(t),\quad t\geq 0,\\
&F(x,\mathbf{r}) := (F_1(x,\mathbf{r}),F_2(x,\mathbf{r}),F_3(x,\mathbf{r}))\quad (x,\mathbf{r})\in\overline{\Omega}\times\mathbb{R}^3,\quad \mathbb{X} := \prod_{i=1}^3\mathbb{X}_i,
\end{aligned}
$$

where $\mathbb{X}$ is equipped with the following norm:

$$
\|\psi\|_{\mathbb{X}} := \max\{\sup_{x\in\overline{\Omega}}|\psi_1(x)|,\ \sup_{x\in\overline{\Omega}}|\psi_2(x)|,\ \sup_{x\in\overline{\Omega}}|\psi_3(x)|\},\quad \psi = (\psi_1,\psi_2,\psi_3)\in\mathbb{X}.
$$

We can then rewrite system (1.3)-(1.4) as the following abstract form in $\mathbb{X}$:

$$u_t(t) = Au(t) + \mathcal{F}(u(t)), \quad t > 0, \quad u(0) = \phi \in D(A) \subset \mathbb{X}, \tag{2.1}$$

where $u(t) = (S(\cdot,t), I(\cdot,t), P(\cdot,t)) \in \mathbb{X}$, $t > 0$, $\phi = (S_0(\cdot), I_0(\cdot), P_0(\cdot)) \in \mathbb{X}$ and

$$\mathcal{F}(\psi)(x) := F(x, \psi(x)), \quad x \in \overline{\Omega}, \quad \psi \in \mathbb{X}.$$

From (2.1), a mild solution can be obtained as a continuous solution of the following integral equation,

$$u(t) = T(t)\phi + \int_0^t T(t-s)\mathcal{F}(u(s))\mathrm{d}s, \quad t > 0, \quad u(0) = \phi \in \mathbb{X}.$$

Let $\mathbb{X}^+$ be the positive cone of $\mathbb{X}$. By using [20, Corollary 7.3.2], we prove the following proposition on the existence of the unique classical solution in $\mathbb{X}^+$.

Proposition 2.1. *Suppose that (A1)-(A4) hold. For each $\phi \in \mathbb{X}^+$, system (1.3)-(1.4) has the unique classical solution $u(t) = u(t,\phi) \in \mathbb{X}^+$ defined on $[0,\sigma)$, where $\sigma = \sigma(\phi) \leq +\infty$. $u(t)$ is continuously differentiable and satisfies (2.1) on $(0,\sigma)$. If $\sigma < +\infty$, then $\|u(t)\|_{\mathbb{X}} \to +\infty$ as $t \to \sigma - 0$.*

Proof. By [20, Corollary 7.3.2], it suffices to show that $F_i(x, \mathbf{r}) \geq 0$ for all $i = 1,2,3$, $x \in \overline{\Omega}$ and $\mathbf{r} \in \mathbb{R}^3_+$ such that $r_i = 0$. This is obvious from assumptions (A2) and (A3). This completes the proof. □

We now prove the following theorem on the existence and uniqueness of the global classical solution of system (1.3)-(1.4).

Theorem 2.1. *Suppose that (A1)-(A4) hold. For each $\phi \in \mathbb{X}^+$, system (1.3)-(1.4) has the unique global classical solution $u(t) = u(t,\phi) \in \mathbb{X}^+$ such that $u(t) \in D(A)$ on $(0,+\infty)$ and $u(0) = \phi$.*

Proof. By Proposition 2.1, it suffices to show that $\sigma = \sigma(\phi) = +\infty$ for any $\phi \in \mathbb{X}^+$. On the contrary, suppose that $\sigma < +\infty$. By the first equation in (1.3) and assumptions (A2)-(A3), we have

$$S_t \leq \nabla \cdot [d_1(x)\nabla S] + \lambda^+ - \mu^- S, \quad x \in \Omega, \ t > 0,$$

where $\lambda^+ := \max_{x\in\overline{\Omega}} \lambda(x) \in (0,+\infty)$ and $\mu^- := \min_{x\in\overline{\Omega}} \mu(x) \in (0,+\infty)$. By the comparison principle and the similar arguments as in [21, Proof of Theorem 1], we see that there exists a positive constant $M_1 > 0$ such that

$$0 \leq S(x,t) \leq M_1, \quad t \in [0,\sigma), \ x \in \overline{\Omega}.$$

Thus, S does not blow up at $t = \sigma$. Suppose that $f_1(\tilde{x}, S(\cdot,t), I(\cdot,t)) + f_2(\tilde{x}, S(\cdot,t), P(\cdot,t)) \to +\infty$ as $t \to \sigma - 0$ for some $\tilde{x} \in \Omega$. We then have from the first equation in (1.3) that $S_t(\tilde{x},t) \to -\infty$

as $t \to \sigma - 0$. This implies that $S(\tilde{x}, t) < 0$ in the neighborhood of σ, which contradicts to the positivity of S. Hence, $f_1(x, S(\cdot,t), I(\cdot,t)) + f_2(x, S(\cdot,t), P(\cdot,t)) < +\infty$ for all $x \in \Omega$ and $t \in [0, \sigma)$. By the second equation in (1.3) and assumption (A2), we have

$$I_t \leq \nabla \cdot [d_2(x)\nabla I] + f^+ - \left(\mu^- + \gamma^-\right) I, \quad x \in \Omega, \ t > 0,$$

where

$$f^+ := \sup_{(x,t)\in\Omega\times[0,\sigma)} [f_1(x, S(x,t), I(x,t)) + f_2(x, S(x,t), P(x,t))] < +\infty,$$

and $\gamma^- := \min_{x\in\overline{\Omega}} \gamma(x) \in (0, +\infty)$. Similar to the above argument, we see that there exists a positive constant $M_2 > 0$ such that

$$0 \leq I(x,t) \leq M_2, \quad t \in [0, \sigma), \ x \in \overline{\Omega}.$$

Thus, I also does not blow up at $t = \sigma$. By the third equation in (1.3) and assumption (A2), we have

$$P_t \leq \nabla \cdot [d_3(x)\nabla P] + m^+ M_2 - \eta^- P, \quad x \in \Omega, \ t > 0,$$

where $m^+ := \max_{x\in\overline{\Omega}} m(x) \in (0, +\infty)$ and $\eta^- := \min_{x\in\overline{\Omega}} \eta(x) \in (0, +\infty)$. Similar to the above argument, we see that there exists a positive constant $M_3 > 0$ such that

$$0 \leq P(x,t) \leq M_3, \quad t \in [0, \sigma), \ x \in \overline{\Omega}.$$

Thus, P also does not blow up at $t = \sigma$ and this is a contradiction. Consequently, $\sigma = +\infty$ and the proof is complete. □

In a similar way of the proof of Theorem 2.1, we obtain the following corollary on the boundedness of the solution.

Corollary 2.1. *Suppose that (A1)-(A4) hold. For each solution $u(t) = (S(\cdot,t), I(\cdot,t), P(\cdot,t))$, $t \geq 0$ of system (1.3)-(1.4) with initial condition $\phi \in \mathbb{X}^+$, there exist positive constants $M_1, M_2, M_3 > 0$ such that*

$$0 \leq S(x,t) \leq M_1, \quad 0 \leq I(x,t) \leq M_2, \quad 0 \leq P(x,t) \leq M_3$$

holds for all $x \in \overline{\Omega}$ and $t \geq 0$.

Proof. The proof is done by replacing σ in the proof of Theorem 2.1 by $+\infty$. □

Moreover, by Theorem 2.1 and [20, Theorem 7.3.1], we obtain the following corollary on the existence of a continuous semiflow.

Corollary 2.2. *Suppose that (A1)-(A4) hold. For each $\phi \in \mathbb{X}^+$, system (1.3)-(1.4) generates a semiflow $\{\Psi(t)\}_{t\geq 0} : \mathbb{X}^+ \to \mathbb{X}^+$ defined by $\Psi(t)\phi := u(t, \phi)$, $t \geq 0$. For any closed and bounded subset $B \in \mathbb{X}^+$ and $t > 0$, $\Psi(t)B$ has compact closure in $\mathbb{X}^+$.*

Proof. The assertion directly follows from Theorem 2.1 and (d)-(e) of [20, Theorem 7.3.1]. □

3 Basic reproduction number

In this section, we define the basic reproduction number $\Re_0$ for system (1.3)-(1.4). The cholera-free steady state (CFSS) of system (1.3)-(1.4) is given by $Q^0 := (S^0(\cdot), 0, 0) \in \mathbb{X}^+$, where $S^0(x)$ satisfies

$$0 = \nabla \cdot \left[d(x)\nabla S^0\right] + \lambda(x) - \mu(x)S^0, \quad x \in \Omega, \qquad \frac{\partial S^0}{\partial \mathbf{n}} = 0, \quad x \in \partial\Omega.$$

By a similar argument as in [22, Section 2.2] or [21, Section 2.1], we see that there always exists the unique CFSS such that $S^0(x) > 0$ on $\overline{\Omega}$. Linearizing the equations of I and P in system (1.3)-(1.4) around CFSS, we obtain the following equations:

$$\begin{cases} I_t = \nabla \cdot [d_2(x)\nabla I] + \dfrac{\partial f_1(x, S^0, 0)}{\partial I} I + \dfrac{\partial f_2(x, S^0, 0)}{\partial P} P - [\mu(x) + \gamma(x)]\, I, & x \in \Omega,\ t > 0, \\ P_t = \nabla \cdot [d_3(x)\nabla P] + m(x)I - \eta(x)P, & x \in \Omega,\ t > 0, \\ \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x \in \partial\Omega,\ t > 0. \end{cases} \tag{3.1}$$

We now make the following additional assumption:

(A5) $\partial f_1(x, S^0, 0)/\partial I > 0$ and $\partial f_2(x, S^0, 0)/\partial P > 0$ for all $x \in \overline{\Omega}$.

Under assumption (A5), the linear system (3.1) is cooperative and irreducible. Substituting $I(x,t) = e^{\kappa t}\varphi(x), P(x,t) = e^{\kappa t}\psi(x)$ into (3.1) and dividing each equation by $e^{\kappa t}$, we obtain the following eigenvalue problem:

$$\begin{cases} \kappa\varphi = \nabla \cdot [d_2(x)\nabla \varphi] + \dfrac{\partial f_1(x, S^0, 0)}{\partial I} \varphi + \dfrac{\partial f_2(x, S^0, 0)}{\partial P} \psi - [\mu(x) + \gamma(x)]\, \varphi, & x \in \Omega, \\ \kappa\psi = \nabla \cdot [d_3(x)\nabla \psi] + m(x)\varphi - \eta(x)\psi, & x \in \Omega, \\ \dfrac{\partial \varphi}{\partial \mathbf{n}} = \dfrac{\partial \psi}{\partial \mathbf{n}} = 0, & x \in \partial\Omega. \end{cases} \tag{3.2}$$

Let $\mathbb{Y} := C(\overline{\Omega}) \times C(\overline{\Omega})$ and let $\mathbb{Y}^+$ be the positive cone of $\mathbb{Y}$. By using the Krein-Rutman theorem as in [20, Proof of Theorem 7.6.1], we can prove the following lemma:

Lemma 3.1. *Suppose that (A1)-(A5) hold. There exists a principal eigenvalue κ_0 of problem (3.2) associated with a strictly positive eigenvector $(\varphi_0, \psi_0) \in \mathbb{Y}^+$.*

Proof. Since the linear system (3.1) is cooperative and irreducible, we can see as in [20, Proof of Theorem 7.5.1] that it generates a compact and strongly positive semigroup $\{\mathcal{S}(t)\}_{t\geq 0} : \mathbb{Y}^+ \to \mathbb{Y}^+$, generated by a linear operator L. Then, as shown in [20, Proof of Theorem 7.6.1], there exists a $\mu_0 \in \mathbb{R}$ such that the resolvent operator $B := (\mu I_d - L)^{-1}$ is compact and strongly positive for all $\mu > \mu_0$. By the Krein-Rutman theorem (see, e.g., [23, Theorem 3.2]), the spectral radius $r(B)$ is a positive eigenvalue of operator B associated with a strictly positive eigenvector $w_0 := (\varphi_0, \psi_0) \in \mathbb{Y}^+$. Let $\kappa_0 := \mu - 1/r(B)$. We then have $Lw_0 = \kappa_0 w_0$, and thus, $\mathcal{S}(t)w_0 = \mathrm{e}^{\kappa_0 t} w_0$, $t \geq 0$. Hence, we see that κ_0 is the principal eigenvalue of problem (3.2) associated with the eigenvector $w_0 = (\varphi_0, \psi_0)$. This completes the proof. □

Following the definition in [24], we define the basic reproduction number [25] by the spectral radius $\Re_0 := r(\mathcal{K})$, where $\mathcal{K}$ is the next generation operator on $\mathbb{Y}$ defined by

$$\mathcal{K}\psi(x) := \int_0^{+\infty} \Phi(x)\mathcal{T}(t)\psi \mathrm{d}t, \quad x \in \overline{\Omega}, \quad \psi = \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix} \in \mathbb{Y}.$$

Here, $\Phi(x)$, $x \in \overline{\Omega}$ is a matrix-valued function defined by

$$\Phi(x) := \begin{pmatrix} \dfrac{\partial f_1(x, S^0, 0)}{\partial I} & \dfrac{\partial f_2(x, S^0, 0)}{\partial P} \\ m(x) & 0 \end{pmatrix}, \quad x \in \overline{\Omega},$$

and $\{\mathcal{T}(t)\}_{t\geq 0} : \mathbb{Y} \to \mathbb{Y}$ is the solution semigroup associated with the following linear system:

$$\begin{cases} I_t = \nabla \cdot [d_2(x)\nabla I] - [\mu(x) + \gamma(x)]\, I, & x \in \Omega,\ t > 0, \\ P_t = \nabla \cdot [d_3(x)\nabla P] - \eta(x)P, & x \in \Omega,\ t > 0, \\ \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x \in \partial\Omega,\ t > 0. \end{cases}$$

Using [26, Theorem 3.5], we prove the following proposition.

Proposition 3.1. *Suppose that (A1)-(A5) hold.* $\Re_0 - 1$ *has the same sign as* κ_0.

Proof. Let us define the following matrix-valued function:

$$\mathcal{B}(x) := \begin{pmatrix} \nabla \cdot [d_2(x)\nabla] - [\mu(x) + \gamma(x)] & 0 \\ 0 & \nabla \cdot [d_3(x)\nabla] - \eta(x) \end{pmatrix}, \quad x \in \overline{\Omega}.$$

We then see that $\mathcal{B}$ is resolvent-positive and $s(\mathcal{B}) < 0$, where $s(\cdot)$ denotes the spectral bound of an operator. Moreover, by the arguments in the proof of Lemma 3.1, we see that $L = \Phi + \mathcal{B}$ is resolvent-positive, and thus, it follows from [26, Theorem 3.5] that $\kappa_0 = s(L) = s(\Phi + \mathcal{B})$ has the same sign as $r(\Phi(-\mathcal{B})^{-1}) - 1$. Since $\mathcal{K} = \Phi(-\mathcal{B})^{-1}$ and $\Re_0 = r(\mathcal{K})$, we complete the proof. □

Let us define the following sets.

$$\begin{aligned} \mathbb{X}_0 &:= \left\{\psi = (\psi_1, \psi_2, \psi_3) \in \mathbb{X}^+ : \psi_2(\cdot) \not\equiv 0 \text{ and } \psi_3(\cdot) \not\equiv 0\right\}, \\ \partial\mathbb{X} &:= \left\{\psi = (\psi_1, \psi_2, \psi_3) \in \mathbb{X}^+ : \text{either } \psi_2(\cdot) \equiv 0 \text{ or } \psi_3(\cdot) \equiv 0\right\}. \end{aligned} \tag{3.3}$$

Note that $\mathbb{X}_0 \cup \partial\mathbb{X} = \mathbb{X}^+$ and $\mathbb{X}_0 \cap \partial\mathbb{X} = \emptyset$. Before going to the next section, we give the following useful lemma, which gives the strict positivity of the solution of system (1.3)-(1.4):

Lemma 3.2. *Suppose that (A1)-(A4) hold. Let* $\Psi(t)\phi = (S(\cdot,t), I(\cdot,t), P(\cdot,t))$, $t \geq 0$ *be the solution semiflow for system (1.3)-(1.4) with* $\phi \in \mathbb{X}_0$. *Then,* $I(x,t) > 0$ *and* $P(x,t) > 0$ *for all* $t > 0$ *and* $x \in \overline{\Omega}$.

Proof. The assertion directly follows from the inequalities

$$\begin{cases} I_t \geq \nabla \cdot [d_2(x)\nabla I] - [\mu(x) + \gamma(x)]\, I, & x \in \Omega,\ t > 0, \\ P_t \geq \nabla \cdot [d_3(x)\nabla P] - \eta(x)P, & x \in \Omega,\ t > 0, \\ \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x \in \partial\Omega,\ t > 0, \end{cases}$$

and the strong maximum principle (see, e.g., [27, Chapter 3]). This completes the proof. □

4 Threshold dynamics

In this section, we study the global asymptotic behavior of system (1.3)-(1.4) in connection with the basic reproduction number $\Re_0$. Motivated by [28], we make the following additional assumptions:

(A6) $f_1(x, S, I)$ and $f_2(x, S, P)$ are monotone non-decreasiong with respect to $S \geq 0$ for all $x \in \overline{\Omega}$ and $I, P \geq 0$.

(A7) The following inequalities hold for all $x \in \overline{\Omega}$ and $I, P \geq 0$:

$$f_1(x, S^0, I) \leq \frac{\partial f_1(x, S^0, 0)}{\partial I} I \quad \text{and} \quad f_2(x, S^0, P) \leq \frac{\partial f_2(x, S^0, 0)}{\partial P} P.$$

We now prove the following theorem on the global asymptotic stability of the CFSS:

Theorem 4.1. *Suppose that (A1)-(A7) hold. If* $\Re_0 < 1$, *then the CFSS* $Q^0 = (S^0, 0, 0) \in \mathbb{X}^+$ *of system (1.3)-(1.4) is globally asymptotically stable.*

Proof. It follows from the first equation of (1.3) that

$$S_t \leq \nabla \cdot [d_1(x)\nabla S] + \lambda(x) - \mu(x)S, \quad x \in \Omega, \quad t > 0.$$

We then see from the comparison principle and the argument in [22, Section 2.2] or [21, Lemma 1] that $\limsup_{t\to+\infty} S(x,t) \leq S^0(x)$ for all $x \in \overline{\Omega}$. Hence, without loss of generality, we can assume that $S(x,t) \leq S^0(x)$ for all $x \in \overline{\Omega}$ and $t \geq 0$. By assumptions (A6) and (A7), we have

$$\begin{cases} I_t \leq \nabla \cdot [d_2(x)\nabla I] + \dfrac{\partial f_1(x, S^0, 0)}{\partial I} I + \dfrac{\partial f_2(x, S^0, 0)}{\partial P} P - [\mu(x) + \gamma(x)]\, I, & x \in \Omega,\ t > 0, \\ P_t = \nabla \cdot [d_3(x)\nabla P] + m(x)I - \eta(x)P, & x \in \Omega,\ t > 0, \\ \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x \in \partial\Omega,\ t > 0. \end{cases} \tag{4.1}$$

Thus, we see that the solution of (3.1) is an upper solution. Let $(\overline{I}(\cdot,t), \overline{P}(\cdot,t)) \in \mathbb{Y}^+$, $t \geq 0$ be the solution of (3.1) with initial condition $\overline{I}(x,0) = M\varphi_0(x)$ and $\overline{P}(x,0) = M\psi_0(x)$, $x \in \overline{\Omega}$, where $M > 0$ is a sufficiently large constant and $(\varphi_0, \psi_0) \in \mathbb{Y}^+$ is the strictly positive eigenvector of problem (3.2) associated with eigenvalue κ_0. Since (φ_0, ψ_0) is strictly positive, we can assume without loss of generality that M is so large that $\overline{I}(x,0) \geq I_0(x)$ and $\overline{P}(x,0) \geq P_0(x)$ for all $x \in \overline{\Omega}$. By the comparison principle, we have that $I(x,t) \leq \overline{I}(x,t) = M\mathrm{e}^{\kappa_0 t}\varphi_0(x)$ and $P(x,t) \leq \overline{P}(x,t) = M\mathrm{e}^{\kappa_0 t}\psi_0(x)$ for all $x \in \overline{\Omega}$ and $t \geq 0$. By Proposition 3.1, $\kappa_0 < 0$, and thus, $I \to 0$ and $P \to 0$ as $t \to +\infty$. There then exists for arbitrary small $0 < \epsilon_1 \ll \min_{x\in\overline{\Omega}} \lambda(x)$, a large $T_1 > 0$ such that $f_1(x,S,I) + f_2(x,S,P) \leq f_1(x,S^0,I) + f_2(x,S^0,P) \leq \epsilon_1$ for all $x \in \overline{\Omega}$ and $t > T_1$. We then have from the first equation of (1.3) that

$$S_t \geq \nabla \cdot [d_1(x)\nabla S] + \lambda(x) - \epsilon_1 - \mu(x), \quad x \in \Omega, \quad t > T_1.$$

Similar to the above argument, we have that

$$S^0_{\epsilon_1}(x) \leq \liminf_{t\to+\infty} S(x,t) \leq \limsup_{t\to+\infty} S(x,t) \leq S^0(x), \quad x \in \overline{\Omega},$$

where $S^0_{\epsilon_1}(x)$ satisfies

$$0 = \nabla \cdot \left[d(x)\nabla S^0_{\epsilon_1}\right] + \lambda(x) - \epsilon_1 - \mu(x)S^0_{\epsilon_1}, \quad x \in \Omega, \qquad \frac{\partial S^0_{\epsilon_1}}{\partial \mathbf{n}} = 0, \quad x \in \partial\Omega.$$

Since ϵ_1 is arbitrary and $S^0_{\epsilon_1} \to S^0$ as $\epsilon_1 \to 0$, we obtain that $S \to S^0$ as $t \to +\infty$. This completes the proof. □

We next study the uniform persistence of system (1.3)-(1.4) for $\Re_0 > 1$. For $\epsilon > 0$, let us define $\Re_\epsilon := r(\mathcal{K}_\epsilon)$, where

$$\mathcal{K}_\epsilon := \int_0^{+\infty} \Phi_\epsilon(x)\mathcal{T}(t)\psi \mathrm{d}t, \quad x \in \overline{\Omega}, \quad \psi = \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix} \in \mathbb{Y}$$

and

$$\Phi_\epsilon(x) := \begin{pmatrix} \dfrac{\partial f_1(x, S^0 - \epsilon, \epsilon)}{\partial I} & \dfrac{\partial f_2(x, S^0 - \epsilon, \epsilon)}{\partial P} \\ m(x) & 0 \end{pmatrix}, \quad x \in \overline{\Omega}.$$

By the continuity, if $\Re_0 > 1$, then there exists a sufficiently small $\epsilon > 0$ such that $\Re_\epsilon > 1$ and

$$\frac{\partial f_1(x, S^0 - \epsilon, \epsilon)}{\partial I} > 0 \text{ and } \frac{\partial f_2(x, S^0 - \epsilon, \epsilon)}{\partial P} > 0 \text{ for all } x \in \overline{\Omega}.$$

In what follows, we fix such an $\epsilon > 0$ for $\Re_0 > 1$. By a similar argument as in Proposition 3.1, we see that the following eigenvalue problem has a positive eigenvalue $\kappa_\epsilon > 0$ associated with a strictly positive eigenvector $(\varphi_\epsilon, \psi_\epsilon) \in \mathbb{Y}^+$:

$$\begin{cases} \kappa\varphi = \nabla \cdot [d_2(x)\nabla\varphi] + \dfrac{\partial f_1(x, S^0-\epsilon, \epsilon)}{\partial I}\varphi + \dfrac{\partial f_2(x, S^0-\epsilon, \epsilon)}{\partial P}\psi - [\mu(x)+\gamma(x)]\,\varphi, & x \in \Omega, \\ \kappa\psi = \nabla \cdot [d_3(x)\nabla\psi] + m(x)\varphi - \eta(x)\psi, & x \in \Omega, \\ \dfrac{\partial\varphi}{\partial \mathbf{n}} = \dfrac{\partial\psi}{\partial \mathbf{n}} = 0, & x \in \partial\Omega. \end{cases} \tag{4.2}$$

We now make the following additional assumption:

(A8) The following inequalities hold for all $x \in \overline{\Omega}$, $S \geq S^0 - \epsilon$ and $0 \leq I, P \leq \epsilon$:

$$f_1(x, S, I) \geq \frac{\partial f_1(x, S^0-\epsilon, \epsilon)}{\partial I} I \quad \text{and} \quad f_2(x, S, P) \geq \frac{\partial f_2(x, S^0-\epsilon, \epsilon)}{\partial P} P.$$

For instance, we can easily check that the bilinear incidence rate $f(\cdot, x, y) = \beta xy$, $\beta > 0$ and the saturated incidence rate $f(\cdot, x, y) = \beta xy/(1+\alpha y)$, $\alpha, \beta > 0$ satisfy this assumption. Under these settings, we now prove the following lemma on the uniform weak persistence of system (1.3)-(1.4) in norm $\|\cdot\|_{\mathbb{X}}$:

Lemma 4.1. *Suppose that (A1)-(A8) hold. Suppose that $\Re_0 > 1$ and let $\epsilon > 0$ be a sufficiently small constant as stated above. Then, the CFSS $Q^0 = (S^0, 0, 0) \in \mathbb{X}^+$ is a uniform weak repeller. That is, for the solution semiflow $\Psi(t)\phi = (S(\cdot,t), I(\cdot,t), P(\cdot,t))$, $t \geq 0$ with $\phi = (S_0(\cdot), I_0(\cdot), P_0(\cdot))$, we have*

$$\limsup_{t\to+\infty} \left\|\Psi(t)\phi - Q^0\right\|_{\mathbb{X}} \geq \epsilon, \tag{4.3}$$

provided $\phi \in \mathbb{X}_0 = \{\psi = (\psi_1, \psi_2, \psi_3) \in \mathbb{X}^+ : \psi_2(\cdot) \not\equiv 0 \text{ and } \psi_3(\cdot) \not\equiv 0\}$.

Proof. Suppose on the contrary that (4.3) does not hold. We then have that there exists a $T > 0$ such that $S(t,x) \geq S^0(x) - \epsilon$ and $I(t,x), P(t,x) \leq \epsilon$ for all $x \in \overline{\Omega}$ and $t \geq T$. Under assumption (A8), we have

$$\begin{cases} I_t \geq \nabla \cdot [d_2(x)\nabla I] + \dfrac{\partial f_1(x, S^0-\epsilon, \epsilon)}{\partial I} I + \dfrac{\partial f_2(x, S^0-\epsilon, \epsilon)}{\partial P} P - [\mu(x)+\gamma(x)]\, I, & x \in \Omega,\ t > T, \\ P_t = \nabla \cdot [d_3(x)\nabla P] + m(x)I - \eta(x)P, & x \in \Omega,\ t > T, \\ \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x \in \partial\Omega,\ t > T. \end{cases}$$

By Lemma 3.2, we see that $I(x,T) > 0$ and $P(x,T) > 0$ for all $x \in \overline{\Omega}$. Since $\varphi_\epsilon(x)$ and $\psi_\epsilon(x)$ are strictly positive on $\overline{\Omega}$, there exists a sufficiently small constant $\zeta > 0$ such that $I(x,T) \geq \zeta e^{\kappa_\epsilon T}\varphi_\epsilon(x)$ and $P(x,t) \geq \zeta e^{\kappa_\epsilon T}\psi_\epsilon(x)$ for all $x \in \overline{\Omega}$. Let $(\underline{I}(\cdot,t), \underline{P}(\cdot,t)) \in \mathbb{Y}^+$, $t \geq 0$ be the solution of the following auxiliary system with initial condition $\underline{I}(x,T) = \zeta e^{\kappa_\epsilon T}\varphi_\epsilon(x)$ and $\underline{P}(x,t) = \zeta e^{\kappa_\epsilon T}\psi_\epsilon(x)$, $x \in \overline{\Omega}$:

$$\begin{cases} I_t = \nabla \cdot [d_2(x)\nabla I] + \dfrac{\partial f_1(x, S^0-\epsilon,\epsilon)}{\partial I} I + \dfrac{\partial f_2(x, S^0-\epsilon,\epsilon)}{\partial P} P - [\mu(x)+\gamma(x)]\, I, & x\in\Omega,\ t>T, \\ P_t = \nabla\cdot[d_3(x)\nabla P] + m(x) I - \eta(x) P, & x\in\Omega,\ t>T, \\ \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x\in\partial\Omega,\ t>T. \end{cases}$$

By the comparison theorem, we have that $I(x,t) \geq \underline{I}(x,t) = \zeta e^{\kappa_\epsilon t}\varphi_\epsilon(x)$ and $P(x,t) \geq \underline{P}(x,t) = \zeta e^{\kappa_\epsilon t}\psi_\epsilon(x)$ for all $x \in \overline{\Omega}$ and $t \geq T$. Since $\kappa_\epsilon > 0$ for $\Re_0 > 1$ as stated above, we have that $I(x,t) \to +\infty$ and $P(x,t) \to +\infty$ as $t \to +\infty$ for all $x \in \overline{\Omega}$, which contradicts to Corollary 2.1. This completes the proof. □

To prove the uniform strong persistence of system (1.3)-(1.4) for $\Re_0 > 1$, we make the following additional assumption:

(A9) There exist strictly positive continuous functions $g_1(x)$ and $g_2(x)$ such that

$$f_1(x, S^0, I) \leq g_1(x) \text{ and } f_2(x, S^0, P) \leq g_2(x), \quad x \in \overline{\Omega},\ I, P \geq 0.$$

For instance, the saturated incidence rate satisfies this assumption. Note that this assumption excludes the bilinear incidence rate (see [21] for the previous results in the case of bilinear incidence rate). Under (A9), we prove the following theorem on the uniform strong persistence of the disease in system (1.3)-(1.4):

Theorem 4.2. *Suppose that (A1)-(A9) hold. If $\Re_0 > 1$, then there exists a constant $\epsilon_0 > 0$ such that*

$$\liminf_{t\to+\infty} I(t,x) \geq \epsilon_0, \quad \liminf_{t\to+\infty} P(t,x) \geq \epsilon_0,$$

provided $\phi \in \tilde{\mathbb{X}}_0$, where $\tilde{\mathbb{X}}_0 := \{\psi = (\psi_1,\psi_2,\psi_3) \in \mathbb{X}^+ : \text{either } \psi_2(\cdot) \not\equiv 0 \text{ or } \psi_3(\cdot) \not\equiv 0\} \subset \mathbb{X}_0$.

Proof. We first prove the existence of a global attractor in $\mathbb{X}^+$. By the argument in the proof of Theorem 4.1, we see that $\limsup_{t\to+\infty} S(x,t) \leq S^0(x)$ for all $x \in \overline{\Omega}$. By (A6) and (A9) and the second equation of (1.3), we have

$$I_t \leq \nabla\cdot[d_2(x)\nabla I] + g_1(x) + g_2(x) - [\mu(x)+\gamma(x)]\, I, \quad x\in\Omega, \quad t>0.$$

Hence, as in the argument in the proof of Theorem 4.1, we see that there exists a strictly positive function $I^0(x)$, $x \in \overline{\Omega}$ such that $\limsup_{t\to+\infty} I(x,t) \leq I^0(x)$ for all $x \in \overline{\Omega}$. Then, for any $\tilde{\epsilon} > 0$, there exists a sufficiently large $\tilde{t} > 0$ such that

$$R_t \leq \nabla\cdot[d_3(x)\nabla R] + m(x)\left[I^0(x) + \tilde{\epsilon}\right] - \eta(x) P, \quad x\in\Omega, \quad t>\tilde{t}.$$

We then see as above that there exists a strictly positive function $R^0(x)$, $x \in \overline{\Omega}$ such that $\limsup_{t\to+\infty} R(x,t) \le R^0(x)$ for all $x \in \overline{\Omega}$. Thus, we see that the solution semiflow $\Psi(t)$, $t \ge 0$ is point dissipative (note that $S^0(\cdot)$, $I^0(\cdot)$ and $R^0(\cdot)$ are independent from the choice of initial condition ϕ). Since the compactness of the semiflow $\Psi(t)$, $t \ge 0$ follows from Corollary 2.2, we see from [29, Theorem 3.4.8] that $\Psi(t)$, $t \ge 0$ has a global attractor in $\mathbb{X}^+$.

We next prove that $\cup_{\phi\in M_\partial}\omega(\phi) = \{Q^0\}$, where $M_\partial := \{\phi \in \partial\mathbb{X} : \Psi(t)\phi \in \partial\mathbb{X} \text{ for all } t \ge 0\}$ and $\omega(\phi) := \cap_{t\ge0}\overline{\cup_{s\ge t}\{\Psi(s)\phi\}}$ is the omega limit set. Let $\phi \in M_\partial$. We see from (3.3) that either $I(\cdot,t) \equiv 0$ or $P(\cdot,t) \equiv 0$ for each $t \ge 0$. By (A2) and (A3), it is easy to see that $S(x,t) > 0$ for all $x \in \overline{\Omega}$ and $t > 0$. If $I(\cdot,t^*) \equiv 0$ and $P(\cdot,t^*) \not\equiv 0$ for some $t^* \ge 0$, then it follows from the third equation of (1.3) and the strong maximum principle as in the proof of Lemma 3.2 that $P(x,t) > 0$ for all $x \in \overline{\Omega}$ and $t > t^*$. Then, $I(\cdot,t) \equiv 0$ and $I_t(\cdot,t) = f_2(\cdot,S,P) > 0$ for all $t > t^*$, which is a contradiction. If $I(\cdot,t^*) \not\equiv 0$ and $P(\cdot,t^*) \equiv 0$ for some $t^* \ge 0$, then we have in a similar way that $P(\cdot,t) \equiv 0$ and $P_t(\cdot,t) = m(\cdot)I(\cdot,t) > 0$ for all $t > t^*$, which is a contradiction. Thus, we have that $I(\cdot,t) \equiv 0$ and $P(\cdot,t) \equiv 0$ for all $t \ge 0$. We then have from the first equation of (1.3) that $S_t = \nabla\cdot[d_1(x)\nabla S] + \lambda(x) - \mu(x)S$, $x \in \Omega$, $t > 0$. Thus, as in the proof of Theorem 4.1, we see that $S \to S^0$ as $t \to +\infty$. This implies that $\cup_{\phi\in M_\partial}\omega(\phi) = \{Q^0\}$.

As in [22, Proof of Theorem 2.5] or [21, Proof of Theorem 3], we define the generalized distance function $\rho : \mathbb{X}^+ \to [0,+\infty)$ as follows:

$$\rho(\psi) := \min\left\{\min_{x\in\overline{\Omega}}\psi_2(x),\ \min_{x\in\overline{\Omega}}\psi_3(x)\right\}, \quad \psi = (\psi_1,\psi_2,\psi_3) \in \mathbb{X}^+.$$

It is easy to see from the above argument that $\rho^{-1}(0,+\infty) \subset \mathbb{X}_0$ and $W^s(Q^0)\cap\rho^{-1}(0,+\infty) = \emptyset$, where $W^s(Q^0) := \{\phi \in \mathbb{X}^+ : \lim_{t\to+\infty}\|\Psi(t)\phi - Q^0\|_{\mathbb{X}} = 0\}$ denotes the stable set of Q^0. Moreover, it is easy to see that Q^0 does not form any cycle in ∂X_0 and it is isolated in $\mathbb{X}$. Thus, by [30, Theorem 3], we can conclude that there exists an $\epsilon_0 > 0$ such that $\min_{\phi\in\mathbb{X}_0}\left\{\min_{\psi\in\omega(\phi)}\rho(\psi)\right\} \ge \epsilon_0$. This implies that

$$\liminf_{t\to+\infty} I(t,x) \ge \epsilon_0, \quad \liminf_{t\to+\infty} P(t,x) \ge \epsilon_0,$$

provided $\phi \in \mathbb{X}_0$. It is easy to see from the strictly positivity of $m(\cdot)$ and $f_2(\cdot,S,P)$ for $S,P > 0$ that $\Psi(t)\phi \in \mathbb{X}_0$ for all $t > 0$ if $\phi \in \tilde{\mathbb{X}}_0$. This completes the proof. □

For example, under assumptions (A1) and (A2) on other parameters, we can check that the following functions f_1 and f_2 satisfy assumptions (A3)-(A9), for $x \in \overline{\Omega}$ and $S, I, P \ge 0$,

$$\text{(i)} \quad (f_1(x,S,I), f_2(x,S,P)) = \left(\frac{\beta_1(x)SI}{1+\alpha_1(x)I}, \frac{\beta_2(x)SP}{1+\alpha_2(x)P}\right), \tag{4.4}$$

$$\text{(ii)} \quad (f_1(x,S,I), f_2(x,S,P)) = \left(\beta_1(x)S\ln\left(1+\frac{I}{1+\alpha_1(x)I}\right), \beta_2(x)S\ln\left(1+\frac{P}{1+\alpha_2(x)P}\right)\right),$$

$$\text{(iii)} \quad (f_1(x,S,I), f_2(x,S,P)) = \left(\beta_1(x)S\frac{\arctan(\alpha_1(x)I)}{\alpha_1(x)}, \beta_2(x)S\frac{\arctan(\alpha_2(x)P)}{\alpha_2(x)}\right),$$

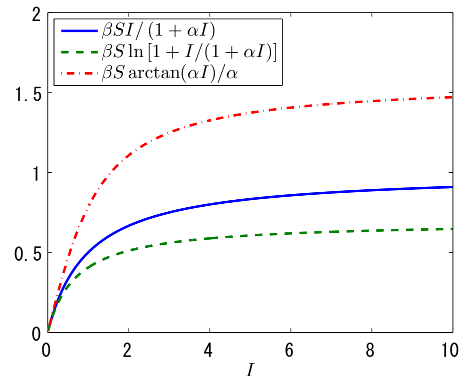


Fig. 1.An example of functions in (4.4) (i)-(iii), where $\alpha = \beta = S = 1$ and $0 \leq I \leq 10$.

where $\alpha_i(\cdot), \beta_i(\cdot) \in C^2(\overline{\Omega})$, $i = 1, 2$ are strictly positive and uniformly bounded on $\overline{\Omega}$. Note that these functions have the monotonicity with respect to S, I and P, the concavity with respect to I and P and the saturation effect with respect to I and P (see Fig. 1).

5 The spatially homogeneous case

In this section, we are concerned with cases study when the parameters are all strictly positive constants. We will get the global stability results on unique positive steady state whenever it exists by using Lyapunov functions. Denote by $Q^* := (\bar{S}, \bar{I}, \bar{P})$ the constant steady state throughout this section.

In what follows, we make the following assumptions.

(B1) Ω is a bounded domain in $\mathbb{R}^n$, $n \in \mathbb{N}$ with sufficiently smooth boundary $\partial\Omega$.

(B2) d_1, d_2, d_3, λ, μ, γ, m and η are independent of the variable x and strictly positive constants.

It is easy to see that (B1) and (B2) are equivalent to (A1) and (A2) in the spatially homogeneous case, respectively.

5.1 Nonlinear incidence functions with $f_1(S, I)$ and $f_2(S, P)$

In this subsection, we still use general nonlinear incidence functions $f_1(S, I)$ and $f_2(S, P)$ to present the direct infection transmission between susceptible and infected individuals and the indirect infection transmission between susceptible individuals and cholera bacteria, respectively.

The model to be studied takes the following form:

$$\begin{cases} \dfrac{\partial S}{\partial t} = d_1\Delta S + \lambda - f_1(S,I) - f_2(S,P) - \mu S, & x\in\Omega,\ t>0,\\ \dfrac{\partial I}{\partial t} = d_2\Delta I + f_1(S,I) + f_2(S,P) - (\mu+\gamma)I, & x\in\Omega,\ t>0,\\ \dfrac{\partial P}{\partial t} = d_3\Delta P + mI - \eta P, & x\in\Omega,\ t>0,\\ S(x,0)=S_0(x),\quad I(x,0)=I_0(x),\quad P(x,0)=P_0(x), & x\in\overline{\Omega},\\ \dfrac{\partial S}{\partial \mathbf{n}} = \dfrac{\partial I}{\partial \mathbf{n}} = \dfrac{\partial P}{\partial \mathbf{n}} = 0, & x\in\partial\Omega,\quad t>0. \end{cases} \tag{5.1}$$

For the sake of simplicity, motivated by [28, Corollary 5.1], we make the following assumptions on $f_1(S,I)$ and $f_2(S,P)$.

(B3) $f_1(S,I) > 0$ and $f_2(S,P) > 0$ for all $S,I,P>0$. $f_1(S,0) = f_1(0,I) = f_2(S,0) = f_2(0,P) = 0$ for all $S,I,P\ge 0$.

(B4) $f_1(S,I)$ and $f_2(S,P)$ are twice continuously differentiable with respect to $(S,I)\in\mathbb{R}\times\mathbb{R}$ and $(S,P)\in\mathbb{R}\times\mathbb{R}$, respectively. $\partial^2 f_1(S,I)/\partial I^2 \le 0$ and $\partial^2 f_2(S,P)/\partial P^2 \le 0$ for all $S,I,P\ge 0$.

(B5) $\partial f_1(S,I)/\partial S \ge 0$, $\partial f_2(S,P)/\partial S \ge 0$, $\partial f_1(S,I)/\partial I \ge 0$ and $\partial f_2(S,I)/\partial P \ge 0$ for all $S,I,P\ge 0$.

It is easy to see that (B3)-(B5) imply (A3)-(A6) in the spatially homogeneous case. Note that they further imply (A7) and (A8) in the specially homogeneous case. In fact, by the second order Taylor expansion,

$$\begin{aligned} 0 = f_1(S,0) =& f_1(S,I) + \frac{\partial f_1(S,I)}{\partial I}(0-I) + \frac{\partial^2 f_1(S,\xi)}{\partial I^2}I^2 \\ \le& f_1(S,I) - \frac{\partial f_1(S,I)}{\partial I}I, \quad S,I\ge 0, \end{aligned} \tag{5.2}$$

where $\xi\in\mathbb{R}$ is a number such that $|\xi|<|I|$. Hence, if $S\ge S^0-\epsilon$ and $0\le I\le\epsilon$, then

$$f_1(S,I) \ge \frac{\partial f_1(S,I)}{\partial I}I \ge \frac{\partial f_1(S^0-\epsilon,\epsilon)}{\partial I}I.$$

We can obtain a similar inequality for $f_2(S,P)$. Thus, (A8) holds. Moreover, since

$$\frac{\partial}{\partial I}\left(\frac{f_1(S,I)}{I}\right) = \frac{1}{I^2}\left(\frac{\partial f_1(S,I)}{\partial I}I - f_1(S,I)\right), \quad S,I\ge 0,$$

the above inequality (5.2) implies that $f_1(S,I)/I$ is monotone non-increasing with respect to I. Hence, we have

$$\frac{f_1(S^0,I)}{I} \le \lim_{I\to 0}\frac{f_1(S^0,I)}{I} = \frac{\partial f_1(S^0,0)}{\partial I},$$

and thus,

$$f_1(S^0, I) \le \frac{\partial f_1(S^0, 0)}{\partial I} I.$$

We can obtain a similar inequality for $f_2(S^0, P)$. Thus, (A7) holds.

Clearly, system (5.1) has the CFSS $Q^0 = (S^0, 0, 0)$, where $S^0 = \lambda/\mu$. Following the arguments in Section 3, the next generation operator $\mathcal{K}$ is given by

$$\mathcal{K}\psi = \int_0^{+\infty} \Phi \mathcal{T}(t)\psi \mathrm{d}t, \quad \psi = \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix} \in \mathbb{Y}, \tag{5.3}$$

where

$$\Phi = \begin{pmatrix} \dfrac{\partial f_1(S^0, 0)}{\partial I} & \dfrac{\partial f_2(S^0, 0)}{\partial P} \\ m & 0 \end{pmatrix},$$

$$\mathcal{T}(t)\psi = \begin{pmatrix} \mathrm{e}^{-(\mu+\gamma)t} \displaystyle\int_\Omega \Gamma_2(t, \cdot, y)\psi_1(y)\mathrm{d}y & 0 \\ 0 & \mathrm{e}^{-\eta t} \displaystyle\int_\Omega \Gamma_3(t, \cdot, y)\psi_2(y)\mathrm{d}y \end{pmatrix}, \quad \psi = \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix} \in \mathbb{Y}.$$

Here $\Gamma_i(t, x, y)$, $t > 0$, $x, y \in \Omega$, $i = 2, 3$ denotes the Green's functions associated with $d_i\Delta$, $i = 2, 3$ subject to the Neumann boundary condition. Let $\varphi_i := \int_\Omega \psi_i(x)\mathrm{d}x$, $i = 1, 2$. We then have by integrating both sides of (5.3) that

$$\mathcal{K}\begin{pmatrix} \varphi_1 \\ \varphi_2 \end{pmatrix} = \begin{pmatrix} \dfrac{\partial f_1(S^0, 0)}{\partial I} & \dfrac{\partial f_2(S^0, 0)}{\partial P} \\ m & 0 \end{pmatrix} \begin{pmatrix} \dfrac{1}{\mu+\gamma} & 0 \\ 0 & \dfrac{1}{\eta} \end{pmatrix} \begin{pmatrix} \varphi_1 \\ \varphi_2 \end{pmatrix}.$$

Thus, $\Re_0^{(5.1)} = r(\mathcal{K})$ is explicitly given as follows:

$$\Re_0^{(5.1)} = \frac{1}{2}\left[\frac{\partial f_1(S^0, 0)}{\partial I} \frac{1}{\mu+\gamma} + \sqrt{\left(\frac{\partial f_1(S^0, 0)}{\partial I} \frac{1}{\mu+\gamma} \right)^2 + 4\frac{\partial f_2(S^0, 0)}{\partial P} \frac{m}{\eta(\mu+\gamma)}} \right]. \tag{5.4}$$

By Theorem 4.1, we immediately obtain the following theorem.

Theorem 5.1. *Suppose that (B1)-(B5) hold. If $\Re_0^{(5.1)} < 1$, then the CFSS $Q^0 = (S^0, 0, 0) = (\lambda/\mu, 0, 0) \in \mathbb{X}^+$ of system (5.1) is globally asymptotically stable.*

Proof. As stated above, (B1)-(B5) imply (A1)-(A7). Thus, the assertion directly follows from Theorem 4.1. □

Next, we focus on the constant positive cholera-endemic steady state (CESS) of system (5.1). We denote it by $Q^* := (\bar{S}, \bar{I}, \bar{P}) \in \mathbb{X}^+$, if it exists, it should satisfy the following equations:

$$\begin{cases} 0 = \lambda - f_1(\bar{S}, \bar{I}) - f_2(\bar{S}, \bar{P}) - \mu\bar{S}, \\ 0 = f_1(\bar{S}, \bar{I}) + f_2(\bar{S}, \bar{P}) - (\mu+\gamma)\bar{I}, \\ 0 = m\bar{I} - \eta\bar{P}. \end{cases} \tag{5.5}$$

The following lemma concerns with the existence of the CESS, Q^*.

Lemma 5.1. *Suppose that (B1)-(B5) hold. If $\Re_0^{(5.1)} > 1$, then there exists at least one CESS $Q^* = (\bar{S}, \bar{I}, \bar{P}) \in \mathbb{X}^+$ of system (5.1).*

Proof. By the third equation of (5.5), we have $\bar{P} = m\bar{I}/\eta$. Thus, (5.5) can be rewritten as follows.

$$\begin{cases} 0 = \lambda - g(\bar{S}, \bar{I}) - \mu \bar{S}, \\ 0 = g(\bar{S}, \bar{I}) - (\mu + \gamma)\bar{I}, \end{cases} \tag{5.6}$$

where $g(\bar{S}, \bar{I}) = f_1(\bar{S}, \bar{I}) + f_2(\bar{S}, m\bar{I}/\eta)$. Similar to the argument in [28, Proof of Theorem 3.1], we then see that the CESS Q^* exists if

$$\Re_0^1 := \lim_{I \to 0} \frac{g(S^0, I)}{g(\bar{S}, I)} = \frac{\partial g(S^0, 0)}{\partial I} \frac{1}{\mu + \gamma} = \frac{\partial f_1(S^0, 0)}{\partial I} \frac{1}{\mu + \gamma} + \frac{\partial f_2(S^0, 0)}{\partial P} \frac{m}{\eta(\mu + \gamma)} > 1. \tag{5.7}$$

If $\partial f_1(S^0, 0)/\partial I(\mu + \gamma)^{-1} \geq 2$, then both of $\Re_0^{(5.1)}$ and $\Re_0^1$ are greater than 1 and the CESS Q^* exists. If $\partial f_1(S^0, 0)/\partial I(\mu + \gamma)^{-1} < 2$, then we see by a simple calculation that $\Re_0^{(5.1)} > 1$ is equivalent to $\Re_0^1 > 1$. Thus, the CESS Q^* exists. This completes the proof. □

As shown in the above proof, we can regard $\Re_0^1$ as the threshold value instead of $\Re_0^{(5.1)}$. Finally, we aim to establish global stability results for CESS Q^* by using Lyapunov functional. To this end, we need the following additional assumption.

(B6) The following inequality holds for all $S, P \geq 0$:

$$\left(\frac{f_2(\bar{S}, \bar{P})}{f_2(S, \bar{P})} - \frac{f_1(\bar{S}, \bar{I})}{f_1(S, \bar{I})} \right) \left(1 - \frac{f_2(S, P)}{f_2(\bar{S}, \bar{P})} \right) \leq 0. \tag{5.8}$$

Note that (B6) is satisfied if the nonlinear incidence functions have separable forms as in Section 5.2. The following theorem concerns with the global asymptotic stability of the CESS.

Theorem 5.2. *Suppose that (B1)-(B6) hold. If $\Re_0^1 > 1$, then the CESS $Q^* = \left(\bar{S}, \bar{I}, \bar{P}\right) \in \mathbb{X}^+$ of system (5.1) with initial condition $\phi \in \mathbb{X}_0$ is globally asymptotically stable.*

Proof. We define

$$\mathcal{L}_1 \left[S, I, P\right](t) := \int_\Omega \mathcal{U}_1 \left[S, I, P\right](x, t) \mathrm{d}x,$$

where

$$\mathcal{U}_1 \left[S, I, P\right](x, t) := \ S - \bar{S} - \int_{\bar{S}}^{S} \frac{f_1(\bar{S}, \bar{I})}{f_1(z, \bar{I})} dz + \bar{I} g\left(\frac{I}{\bar{I}}\right) + \frac{f_2(\bar{S}, \bar{P})}{m\bar{I}} g\left(\frac{P}{\bar{P}}\right).$$

The partial derivative of $\mathcal{U}_1 \left[S, I, P\right]$ with respect to t satisfies

$$\frac{\partial \mathcal{U}_1}{\partial t} = \left(1 - \frac{f_1(\bar{S}, \bar{I})}{f_1(S, \bar{I})}\right) \frac{\partial S}{\partial t} + \left(1 - \frac{\bar{I}}{I}\right) \frac{\partial I}{\partial t} + \frac{f_2(\bar{S}, \bar{P})}{m\bar{I}} \left(1 - \frac{\bar{P}}{P}\right) \frac{\partial P}{\partial t}.$$

Directly computing the derivative of $\mathcal{L}_1$ gives

$$\begin{aligned}\frac{\partial \mathcal{L}_1}{\partial t} = & \int_\Omega \left\{ \left(1 - \frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})}\right) d_1 \triangle S + \left(1 - \frac{\bar{I}}{I}\right) d_2 \triangle I + \frac{f_2(\bar{S},\bar{P})}{m\bar{I}} \left(1 - \frac{\bar{P}}{P}\right) d_3 \triangle P \right\} \mathrm{d}x \\ & + \int_\Omega G_1(t,x,S,I,P) \mathrm{d}x,\end{aligned}$$

where

$$\begin{aligned}G_1(t,x,S,I,P) = & \mu\bar{S}\left(1 - \frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})}\right)\left(1 - \frac{S}{\bar{S}}\right) \\ & + f_1(\bar{S},\bar{I})\left(1 - \frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})} + \frac{f_1(S,I)}{f_1(S,\bar{I})} - \frac{\bar{I}f_1(S,I)}{If_1(\bar{S},\bar{I})} + 1 - \frac{I}{\bar{I}}\right) \\ & + f_2(\bar{S},\bar{P})\left(1 - \frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})} + \frac{f_1(\bar{S},\bar{I})f_2(S,P)}{f_1(S,\bar{I})f_2(\bar{S},\bar{P})} - \frac{\bar{I}f_2(S,P)}{If_2(\bar{S},\bar{P})} + 1 - \frac{I}{\bar{I}}\right) \\ & + f_2(\bar{S},\bar{P})\left(\frac{I}{\bar{I}} - \frac{I\bar{P}}{\bar{I}P} - \frac{P}{\bar{P}} + 1\right) \\ = & \mu\bar{S}\left(1 - \frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})}\right)\left(1 - \frac{S}{\bar{S}}\right) \\ & + f_1(\bar{S},\bar{I})\left(3 - \frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})} - \frac{\bar{I}f_1(S,I)}{If_1(\bar{S},\bar{I})} - \frac{If_1(S,\bar{I})}{\bar{I}f_1(S,I)}\right) \\ & + f_1(\bar{S},\bar{I})\left(-1 + \frac{f_1(S,I)}{f_1(S,\bar{I})} - \frac{I}{\bar{I}} + \frac{If_1(S,\bar{I})}{\bar{I}f_1(S,I)}\right) \\ & + f_2(\bar{S},\bar{P})\left(4 - \frac{f_2(\bar{S},\bar{P})}{f_2(S,\bar{P})} - \frac{\bar{I}f_2(S,P)}{If_2(\bar{S},\bar{P})} - \frac{I\bar{P}}{\bar{I}P} - \frac{Pf_2(S,\bar{P})}{\bar{P}f_2(S,P)}\right) \\ & + f_2(\bar{S},\bar{P})\left(-1 + \frac{f_2(S,P)}{f_2(S,\bar{P})} - \frac{P}{\bar{P}} + \frac{Pf_2(S,\bar{P})}{\bar{P}f_2(S,P)}\right) \\ & + f_2(\bar{S},\bar{P})\left(-\frac{f_1(\bar{S},\bar{I})}{f_1(S,\bar{I})} + \frac{f_1(\bar{S},\bar{I})f_2(S,P)}{f_1(S,\bar{I})f_2(\bar{S},\bar{P})} - \frac{f_2(S,P)}{f_2(S,\bar{P})} + \frac{f_2(\bar{S},\bar{P})}{f_2(S,\bar{P})}\right).\end{aligned}$$

Using the arithmetic-geometric mean and the monotonicity of the function $f_1(S,I)$ with respect to S (see assumption (B5)), we have

$$
\begin{aligned}
G_1(t,x,S,I,P) \le f_1(\bar S,\bar I)\Big(&-1+\frac{f_1(S,I)}{f_1(S,\bar I)}-\frac{I}{\bar I}+\frac{If_1(S,\bar I)}{\bar I f_1(S,I)}\Big)\\
&+f_2(\bar S,\bar P)\Big(-1+\frac{f_2(S,P)}{f_2(S,\bar P)}-\frac{P}{\bar P}+\frac{Pf_2(S,\bar P)}{\bar P f_2(S,P)}\Big)\\
&+f_2(\bar S,\bar P)\Big(-\frac{f_1(\bar S,\bar I)}{f_1(S,\bar I)}+\frac{f_1(\bar S,\bar I)f_2(S,P)}{f_1(S,\bar I)f_2(\bar S,\bar P)}-\frac{f_2(S,P)}{f_2(S,\bar P)}+\frac{f_2(\bar S,\bar P)}{f_2(S,\bar P)}\Big)\\
=\ & f_1(\bar S,\bar I)\Big(\frac{I}{\bar I}-\frac{f_1(S,I)}{f_1(S,\bar I)}\Big)\Big(\frac{f_1(S,\bar I)}{f_1(S,I)}-1\Big)\\
&+f_2(\bar S,\bar P)\Big(\frac{P}{\bar P}-\frac{f_2(S,P)}{f_2(S,\bar P)}\Big)\Big(\frac{f_2(S,\bar P)}{f_2(S,P)}-1\Big)\\
&+f_2(\bar S,\bar P)\Big(\frac{f_2(\bar S,\bar P)}{f_2(S,\bar P)}-\frac{f_1(\bar S,\bar I)}{f_1(S,\bar I)}\Big)\Big(1-\frac{f_2(S,P)}{f_2(\bar S,\bar P)}\Big).
\end{aligned}
$$

Under the assumption (B4), we can conclude that $I/\bar I \le f_1(S,I)/f_1(S,\bar I) \le 1$ for $0 < I \le \bar I$, and $1 \le f_1(S,I)/f_1(S,\bar I) \le I/\bar I$ for $I > \bar I$. In a similar way, we can obtain similar inequalities for $f_2(S,P)$. Further from assumption (B6), we have the following inequality.

$$
\begin{aligned}
\frac{\partial \mathcal{L}_1}{\partial t} \le &\Big(1-\frac{f_1(\bar S,\bar I)}{f_1(S,\bar I)}\Big)d_1\triangle S+\Big(1-\frac{\bar I}{I}\Big)d_2\triangle I+\frac{f_2(\bar S,\bar P)}{m\bar I}\Big(1-\frac{\bar P}{P}\Big)d_3\triangle P\Big\}\mathrm{d}x\\
= &-\Big[d_1 f_1(\bar S,\bar I)\int_\Omega \frac{\frac{\partial f_1(S,\bar I)}{\partial S}|\nabla S|^2}{(f_1(S,\bar I))^2}\mathrm{d}x+d_2\bar I\int_\Omega\frac{|\nabla I|^2}{I^2}\mathrm{d}x+d_3\frac{f_2(\bar S,\bar P)\bar P}{m\bar I}\int_\Omega\frac{|\nabla P|^2}{P^2}\mathrm{d}x\Big]\le 0.
\end{aligned}
$$

Therefore, $\mathcal{L}_1$ is a Lyapunov function for the system (5.1). Obviously, $\partial\mathcal{L}_1/\partial t = 0$ if and only if $(S,I,P) = (\bar S,\bar I,\bar P)$.

By using some standard arguments, we can see that

$$(S(x,t), I(x,t), P(x,t)) \to (\bar S,\bar I,\bar P) \text{ in } [L^2(\Omega)]^2, \text{ as } t\to\infty.$$

Recall that $\|S(\cdot,t)\|_{L^\infty}$, $\|I(\cdot,t)\|_{L^\infty}$ and $\|P(\cdot,t)\|_{L^\infty}$ are bounded due to Theorem 2.1. Hence by [31, Theorem A2], for some positive constant C_0, we have

$$\|S(\cdot,t)\|_{C^2(\bar\Omega)}+\|I(\cdot,t)\|_{C^2(\bar\Omega)}+\|P(\cdot,t)\|_{C^2(\bar\Omega)}\le C_0.$$

Hence, the Sobolev embedding theorem allows one to claim

$$(S(x,t), I(x,t), P(x,t)) \to (\bar S,\bar I,\bar P) \text{ in } [L^\infty(\Omega)]^2, \text{ as } t\to\infty.$$

We can use LaSalle's invariance principle to show that the system (5.1) admits a connected global attractor on $\mathbb{X}^+$ and

$$\lim_{t\to\infty}(S(\cdot,t), I(\cdot,t), P(\cdot,t)) = \left(\bar S,\bar I,\bar P\right).$$

That is, Q^* is globally asymptotically stable for (5.1). This completes the proof. □

5.2 Nonlinear incidence functions with $\phi(S)\varphi(I)$ and $\phi(S)\psi(P)$

In this subsection, we consider nonlinear incidence functions with $\phi(S)\varphi(I)$ and $\phi(S)\psi(P)$ that is commonly used in previous literature [13, 28, 32, 33].

Under the assumptions (B1) and (B2), we consider the following model.

$$\begin{cases} \dfrac{\partial S}{\partial t} = d_1\Delta S + \lambda - \phi(S)\varphi(I) - \phi(S)\psi(P) - \mu S, & x \in \Omega,\ t > 0, \\ \dfrac{\partial I}{\partial t} = d_2\Delta I + \phi(S)\varphi(I) + \phi(S)\psi(P) - (\mu+\gamma)I, & x \in \Omega,\ t > 0, \\ \dfrac{\partial P}{\partial t} = d_3\Delta P + mI - \eta P, & x \in \Omega,\ t > 0, \end{cases} \tag{5.9}$$

with the same initial and boundary conditions as in model (5.1). We further give the additional assumptions on $\phi(S)$ and $\varphi(I)$.

(B3') All nonnegative functions $\phi(\cdot), \varphi(\cdot)$ and $\psi(\cdot)$ only vanish at 0.

(B4') $\phi(\cdot), \varphi(\cdot)$ and $\psi(\cdot)$ are monotone non-decreasing with respect to $S, I, P \geq 0$.

(B5') $\partial^2\varphi(I)/\partial I^2 \leq 0$ and $\partial^2\psi(P)/\partial P^2 \leq 0$ for all $I, P \geq 0$.

Clearly, system (5.9) has the CFSS $Q^0 = (S^0, 0, 0)$, where $S^0 = \lambda/\mu$. Similar arguments as in subsection 5.1, we define

$$\Re_0^{(5.9)} = \frac{1}{2}\left[\phi(S^0)\frac{\partial\varphi(0)}{\partial I}\frac{1}{\mu+\gamma} + \sqrt{\left(\phi(S^0)\frac{\partial\varphi(0)}{\partial I}\frac{1}{\mu+\gamma}\right)^2 + 4\phi(S^0)\frac{\partial\psi(0)}{\partial P}\frac{m}{\eta(\mu+\gamma)}}\right]. \tag{5.10}$$

We set

$$\Re_0^2 = \phi(S^0)\frac{\partial\varphi(0)}{\partial I}\frac{1}{\mu+\gamma} + \phi(S^0)\frac{\partial\psi(0)}{\partial P}\frac{m}{\eta(\mu+\gamma)}.$$

Note that $\Re_0^2 > 1$ is equivalent to $\Re_0^{(5.9)} > 1$. We have the following result.

Lemma 5.2. *Suppose that (B1)-(B2) and (B3')-(B5') hold. If $\Re_0^2 < 1$, then the CFSS $Q^0 = (S^0, 0, 0) = (\lambda/\mu, 0, 0) \in \mathbb{X}^+$ of system (5.9) is globally asymptotically stable; If $\Re_0 > 1$, then there exists at least one CESS $Q^* = (\bar{S}, \bar{I}, \bar{P}) \in \mathbb{X}^+$ of system (5.9).*

Theorem 5.3. *Suppose that (B1)-(B2) and (B3')-(B5') hold. If $\Re_0^2 > 1$, then the CESS $Q^* = \big(\bar{S}, \bar{I}, \bar{P}\big) \in \mathbb{X}^+$ of system (5.9) with initial condition $\phi \in \mathbb{X}_0$ is globally asymptotically stable.*

Proof. Note that the steady state of the system (5.9) satisfies the following equations:

$$\begin{cases} \lambda = \phi(\bar{S})\varphi(\bar{I}) + \phi(\bar{S})\psi(\bar{P}) + \mu\bar{S}, \\ (\mu+\gamma)\bar{I} = \phi(\bar{S})\varphi(\bar{I}) + \phi(\bar{S})\psi(\bar{P}), \\ m\bar{I} = \eta\bar{P}. \end{cases} \tag{5.11}$$

We define

$$\mathcal{L}_2\left[S,I,P\right](t) := \int_\Omega \mathcal{U}_2\left[S,I,P\right](x,t)\mathrm{d}x,$$

where

$$\mathcal{U}_2\left[S,I,P\right](x,t) := \int_{\bar{S}}^{S} \frac{\phi(z)-\phi(\bar{S})}{\phi(z)}\mathrm{d}z + \bar{I}g\left(\frac{I}{\bar{I}}\right) + \frac{\phi(\bar{S})\psi(\bar{P})}{m\bar{I}}g\left(\frac{P}{\bar{P}}\right).$$

The partial derivative of $\mathcal{U}_2\left[S,I,P\right]$ with respect to t satisfies

$$\frac{\partial \mathcal{U}_2}{\partial t} = \left(1-\frac{\phi(\bar{S})}{\phi(S)}\right)\frac{\partial S}{\partial t} + \left(1-\frac{\bar{I}}{I}\right)\frac{\partial I}{\partial t} + \frac{\phi(\bar{S})\psi(\bar{P})}{m\bar{I}}\left(1-\frac{\bar{P}}{P}\right)\frac{\partial P}{\partial t}.$$

Directly computing the derivative of $\mathcal{L}_2$ gives

$$\begin{aligned}\frac{\partial \mathcal{L}_2}{\partial t} = &\int_\Omega \left\{\left(1-\frac{\phi(\bar{S})}{\phi(S)}\right)d_1\triangle S + \left(1-\frac{\bar{I}}{I}\right)d_2\triangle I + \frac{\phi(\bar{S})\psi(\bar{P})}{m\bar{I}}\left(1-\frac{\bar{P}}{P}\right)d_3\triangle P\right\}\mathrm{d}x\\ &+\int_\Omega G_2(t,x,S,I,P)\mathrm{d}x,\end{aligned}$$

where

$$\begin{aligned}G_2(t,x,S,I,P) = {} & \mu\bar{S}\left(1-\frac{\phi(\bar{S})}{\phi(S)}\right)\left(1-\frac{S}{\bar{S}}\right)\\ &+\phi(\bar{S})\varphi(\bar{I})\left(1-\frac{\phi(\bar{S})}{\phi(S)}+\frac{\varphi(I)}{\varphi(\bar{I})}-\frac{\bar{I}\phi(S)\varphi(I)}{I\phi(\bar{S})\varphi(\bar{I})}+1-\frac{I}{\bar{I}}\right)\\ &+\phi(\bar{S})\psi(\bar{P})\left(1-\frac{\phi(\bar{S})}{\phi(S)}+\frac{\psi(P)}{\psi(\bar{P})}-\frac{\bar{I}\phi(S)\psi(P)}{I\phi(\bar{S})\psi(\bar{P})}+1-\frac{I}{\bar{I}}\right)\\ &+\phi(\bar{S})\psi(\bar{P})\left(\frac{I}{\bar{I}}-\frac{I\bar{P}}{\bar{I}P}-\frac{P}{\bar{P}}+1\right)\\ = {} & \mu\bar{S}\left(1-\frac{\phi(\bar{S})}{\phi(S)}\right)\left(1-\frac{S}{\bar{S}}\right)\\ &+\phi(\bar{S})\varphi(\bar{I})\left(3-\frac{\phi(\bar{S})}{\phi(S)}-\frac{\bar{I}\phi(S)\varphi(I)}{I\phi(\bar{S})\varphi(\bar{I})}-\frac{I\varphi(\bar{I})}{\bar{I}\varphi(I)}\right)\\ &+\phi(\bar{S})\varphi(\bar{I})\left(-1+\frac{\varphi(I)}{\varphi(\bar{I})}-\frac{I}{\bar{I}}+\frac{I\varphi(\bar{I})}{\bar{I}\varphi(I)}\right)\\ &+\phi(\bar{S})\psi(\bar{P})\left(4-\frac{\phi(\bar{S})}{\phi(S)}-\frac{\bar{I}\phi(S)\psi(P)}{I\phi(\bar{S})\psi(\bar{P})}-\frac{I\bar{P}}{\bar{I}P}-\frac{P\psi(\bar{P})}{\bar{P}\psi(P)}\right)\\ &+\phi(\bar{S})\psi(\bar{P})\left(-1+\frac{\psi(P)}{\psi(\bar{P})}-\frac{P}{\bar{P}}+\frac{P\psi(\bar{P})}{\bar{P}\psi(P)}\right).\end{aligned}$$

Using the arithmetic-geometric mean and the monotonicity of the function $\phi(S)$ with respect to

S (see assumption (B4')), we have

$$\begin{aligned} G_2(t,x,S,I,P) &\leq \phi(\bar{S})\varphi(\bar{I})\Big(-1 + \frac{\varphi(I)}{\varphi(\bar{I})} - \frac{I}{\bar{I}} + \frac{I\varphi(\bar{I})}{\bar{I}\varphi(I)}\Big) \\ &\quad + \phi(\bar{S})\psi(\bar{P})\Big(-1 + \frac{\psi(P)}{\psi(\bar{P})} - \frac{P}{\bar{P}} + \frac{P\psi(\bar{P})}{\bar{P}\psi(P)}\Big) \\ &= \phi(\bar{S})\varphi(\bar{I})\Big(\frac{I}{\bar{I}} - \frac{\varphi(I)}{\varphi(\bar{I})}\Big)\Big(\frac{\varphi(\bar{I})}{\varphi(I)} - 1\Big) \\ &\quad + \phi(\bar{S})\psi(\bar{P})\Big(\frac{P}{\bar{P}} - \frac{\psi(P)}{\psi(\bar{P})}\Big)\Big(\frac{\psi(\bar{P})}{\psi(P)} - 1\Big). \end{aligned}$$

From the concavity of the functions $\varphi(I)$ and $\psi(P)$ with respect to I and P (see assumption (B5')), we have

$$\Big(\frac{I}{\bar{I}} - \frac{\varphi(I)}{\varphi(\bar{I})}\Big)\Big(\frac{\varphi(\bar{I})}{\varphi(I)} - 1\Big) \leq 0, \text{ and } \Big(\frac{P}{\bar{P}} - \frac{\psi(P)}{\psi(\bar{P})}\Big)\Big(\frac{\psi(\bar{P})}{\psi(P)} - 1\Big).$$

It follows that

$$\begin{aligned} \frac{\partial \mathcal{L}_2}{\partial t} &\leq \Big(1 - \frac{\phi(\bar{S})}{\phi(S)}\Big)d_1\triangle S + \Big(1 - \frac{\bar{I}}{I}\Big)d_2\triangle I + \frac{\phi(\bar{S})\psi(\bar{P})}{m\bar{I}}\Big(1 - \frac{\bar{P}}{P}\Big)d_3\triangle P\Big\}\mathrm{d}x \\ &= -\Big[d_1\phi(\bar{S})\int_\Omega \frac{\frac{\partial\phi(S)}{\partial S}|\nabla S|^2}{\phi(S)^2}\mathrm{d}x + d_2\bar{I}\int_\Omega \frac{|\nabla I|^2}{I^2}\mathrm{d}x + d_3\frac{\phi(\bar{S})\psi(\bar{P})\bar{P}}{m\bar{I}}\int_\Omega \frac{|\nabla P|^2}{P^2}\mathrm{d}x\Big] \leq 0. \end{aligned}$$

Therefore, $\mathcal{L}_2$ is a Lyapunov function for the system (5.9). Similar arguments as in subsection 5.1, $\partial\mathcal{L}_2/\partial t = 0$ if and only if $(S,I,P) = (\bar{S},\bar{I},\bar{P})$. We can use LaSalle's invariance principle to show that the system (5.9) admits a connected global attractor on $\mathbb{X}^+$ and

$$\lim_{t\to\infty}(S(\cdot,t), I(\cdot,t), P(\cdot,t)) = \left(\bar{S},\bar{I},\bar{P}\right).$$

That is, Q^* is globally asymptotically stable for (5.9). This completes the proof. □

Remark 5.1. *Note that the left expression in (5.8) becomes zero and thus (B6) automatically holds in nonlinear incidence functions with $\phi(S)\varphi(I)$ and $\phi(S)\psi(P)$.*

5.3 Nonlinear incidence functions with $\beta_1 SI$ and $\beta_2 SP$

In this subsection, we study the following model.

$$\begin{cases} \dfrac{\partial S}{\partial t} = d_1\Delta S + \lambda - \beta_1 SI - \beta_2 SP - \mu S, & x\in\Omega,\ t>0, \\ \dfrac{\partial I}{\partial t} = d_2\Delta I + \beta_1 SI + \beta_2 SP - (\mu+\gamma)I, & x\in\Omega,\ t>0, \\ \dfrac{\partial P}{\partial t} = d_3\Delta P + mI - \eta P, & x\in\Omega,\ t>0, \end{cases} \tag{5.12}$$

with the same initial and boundary conditions as in model (5.1). Clearly, system (5.12) has the CFSS $Q^0=(S^0,0,0)$, where $S^0=\lambda/\mu$. The basic reproduction number is given by

$$\Re_0^{(5.12)}=\frac{1}{2}\left[\frac{\beta_1 S^0}{\mu+\gamma}+\sqrt{\left(\frac{\beta_1 S^0}{\mu+\gamma}\right)^2+4\frac{m}{\eta}\frac{\beta_2 S^0}{\mu+\gamma}}\right]. \tag{5.13}$$

As in the previous subsections, we see that $\Re_0^{(5.12)}>1$ if and only if $\Re_0^3>1$, where

$$\Re_0^3=\frac{\beta_1 S^0}{\mu+\gamma}+\frac{\beta_2 S^0 m}{\eta(\mu+\gamma)}. \tag{5.14}$$

If $\Re_0^3>1$, then the unique Q^* takes the following form

$$Q^*=\left(\frac{\mu+\gamma}{\beta_1+\beta_2 m/\eta},\frac{\mu}{\beta_1+\beta_2 m/\eta}(\Re_0^3-1),\frac{m\mu}{\eta(\beta_1+\beta_2 m/\eta)}(\Re_0^3-1)\right).$$

Lemma 5.3. *If $\Re_0^3<1$, the CFSS $Q^0=(S^0,0,0)=(\lambda/\mu,0,0)\in\mathbb{X}^+$ of system (5.12) is globally asymptotically stable; If $\Re_0^3>1$, then there exists at least one CESS $Q^*=(\bar S,\bar I,\bar P)\in\mathbb{X}^+$ of system (5.12).*

Theorem 5.4. *If $\Re_0^3>1$, then the CESS $Q^*=\left(\bar S,\bar I,\bar P\right)\in\mathbb{X}^+$ of system (5.12) with initial condition $\phi\in\mathbb{X}_0$ is globally asymptotically stable.*

Proof. We define

$$\mathcal{L}_3\left[S,I,P\right](t):=\int_\Omega \mathcal{U}_3\left[S,I,P\right](x,t)\mathrm{d}x,$$

where

$$\mathcal{U}_3\left[S,I,P\right](x,t):=\ \bar S g\left(\frac{S}{\bar S}\right)+\bar I g\left(\frac{I}{\bar I}\right)+\frac{\beta_2\bar S\bar P}{m\bar I}g\left(\frac{P}{\bar P}\right).$$

The partial derivative of $\mathcal{U}_3\left[S,I,P\right]$ with respect to t satisfies

$$\frac{\partial\mathcal{U}_3}{\partial t}=\left(1-\frac{\bar S}{S}\right)\frac{\partial S}{\partial t}+\left(1-\frac{\bar I}{I}\right)\frac{\partial I}{\partial t}+\frac{\beta_2\bar S\bar P}{m\bar I}\left(1-\frac{\bar P}{P}\right)\frac{\partial P}{\partial t}.$$

Directly computing the derivative of $\mathcal{L}_3$ gives

$$\begin{aligned}\frac{\partial\mathcal{L}_3}{\partial t}=&\int_\Omega\left\{\left(1-\frac{\bar S}{S}\right)d\triangle S+\left(1-\frac{\bar I}{I}\right)d\triangle I+\frac{\beta_2\bar S\bar P}{m\bar I}\left(1-\frac{\bar P}{P}\right)d\triangle P\right\}\mathrm{d}x\\&+\int_\Omega G_1(t,x,S,I,P)\mathrm{d}x,\end{aligned}$$

where

$$
\begin{aligned}
G_1(t,x,S,I,P) =&\ \mu\bar{S}\left(2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+\beta_1\bar{S}\bar{I}\left(1-\frac{\bar{S}}{S}+\frac{I}{\bar{I}}-\frac{S}{\bar{S}}+1-\frac{I}{\bar{I}}\right)\\
&+\beta_2\bar{S}\bar{P}\left(1-\frac{\bar{S}}{S}+\frac{P}{\bar{P}}-\frac{\bar{I}SP}{I\bar{S}\bar{P}}+1-\frac{I}{\bar{I}}\right)\\
&+\beta_2\bar{S}\bar{P}\left(\frac{I}{\bar{I}}-\frac{\bar{P}I}{P\bar{I}}-\frac{P}{\bar{P}}+1\right)\\
=&\left(\mu\bar{S}+\beta_1\bar{S}\bar{I}\right)\left(2-\frac{\bar{S}}{S}-\frac{S}{\bar{S}}\right)+\beta_2\bar{S}\bar{P}\left(3-\frac{\bar{S}}{S}-\frac{\bar{I}SP}{I\bar{S}\bar{P}}-\frac{\bar{P}I}{P\bar{I}}\right).
\end{aligned}
$$

Using the arithmetic-geometric mean, the following inequality holds,

$$
\begin{aligned}
\frac{\partial\mathcal{L}_1}{\partial t} \le&\ \int_\Omega\left\{\left(1-\frac{\bar{S}}{S}\right)d\triangle S+\left(1-\frac{\bar{I}}{I}\right)d\triangle I+\frac{\beta_2\bar{S}\bar{P}}{m\bar{I}}\left(1-\frac{\bar{P}}{P}\right)d\triangle P\right\}\mathrm{d}x\\
=&\ -d\left[\bar{S}\int_\Omega\frac{|\nabla S|^2}{S^2}\mathrm{d}x+\bar{I}\int_\Omega\frac{|\nabla I|^2}{I^2}\mathrm{d}x+\frac{\beta_2\bar{S}(\bar{P})^2}{m\bar{I}}\int_\Omega\frac{|\nabla P|^2}{P^2}\mathrm{d}x\right]\le 0.
\end{aligned}
$$

Therefore, $\mathcal{L}_3$ is a Lyapunov function for the system (5.12). Similar arguments as in subsection 5.1, $\partial\mathcal{L}_3/\partial t = 0$ if and only if $(S,I,P)=(\bar{S},\bar{I},\bar{P})$. We can use LaSalle's invariance principle to show that the system (5.12) admits a connected global attractor on $\mathbb{X}^+$ and

$$
\lim_{t\to\infty}\left(S(\cdot,t),I(\cdot,t),P(\cdot,t)\right)=\left(\bar{S},\bar{I},\bar{P}\right).
$$

That is, Q^* is globally asymptotically stable for (5.12). This completes the proof. □

Remark 5.2. *Note that all assumptions on nonlinear incidence functions are satisfied with bilinear incidence function. In fact, incidence functions that are commonly used in the literature satisfy assumptions in subsection 5.1 and 5.2, including, for example, saturating incidence for the direct or indirect transmission.*

Remark 5.3. *We set some assumptions on nonlinear incidence functions in subsection 5.1 and 5.2. The main reason lies in that these assumption must ensure that the existence of endemic equilibrium. On the other hand, these condition are all sufficient condition to establish global stability results, under which oscillations are excluded.*

Remark 5.4. *Note that if we let $(S(x,t),I(x,t),P(x,t))$ represent the concentrations of healthy cells (CD4 T cells), infected cells and virions at time t in location x, respectively, then model (5.12) is the one studied in [21] except for the diffusion parameters, which studied a diffusive within-host HIV model with virus-to-cell and cell-to-cell transmission mechanism. The global* *stability of unique positive constant steady state is proved by using the similar Lyapunov functional. Further, if diffusion parameters are all spatially homogeneous, then section 3 studied in [21] remains hold for our model (5.12), that is, the conditions of existence and nonexistence of the traveling wave solutions are also needed for (5.12).*

6 Numerical simulation

In this section, we perform numerical simulation that supports our theoretical results. For the sake of simplicity, we restrict our attention to the spacially 1-dimensional case: $\Omega \subset \mathbb{R}$. In what follows, we fix the following parameters.

$$\begin{cases} \lambda = 1\ [N], \quad \mu = 1\ [T^{-1}], \quad \gamma = 10\ [T^{-1}], \quad m = 10\ [N^{-1}T^{-1}], \quad \eta = 20\ [T^{-1}], \quad \Omega = (0, 20), \\ d := d_1 = d_2 = d_3 > 0, \\ S_0(x) = 1 - I_0(x), \quad I_0(x) = 0.01\mathrm{e}^{-(x-10)^2}, \quad P_0(x) = 0, \quad x \in [0, 20]. \end{cases} \tag{6.1}$$

where N and T denote the unit population and the unit time, respectively. It is obvious that assumptions (A1) and (A2) are satisfied. Although these parameters are not based on any obserbed data, a rough biological justification is as follows: the total population λ/μ is normalized as 1; the average infectious period $1/\gamma$ is 1/10 times shorter than the average life span $1/\mu$; $m = 10$ number of cholera bacteria are produced by one infective population per unit of time; the average life span $1/\eta$ of bacteria is 1/20 times shorter than the average life span of human. We further assume the saturated incidence functions:

$$f_1(x, S, I) = \frac{\beta_1(x)SI}{1+I}, \quad f_2(x, S, P) = \frac{\beta_2(x)SP}{1+P}, \tag{6.2}$$

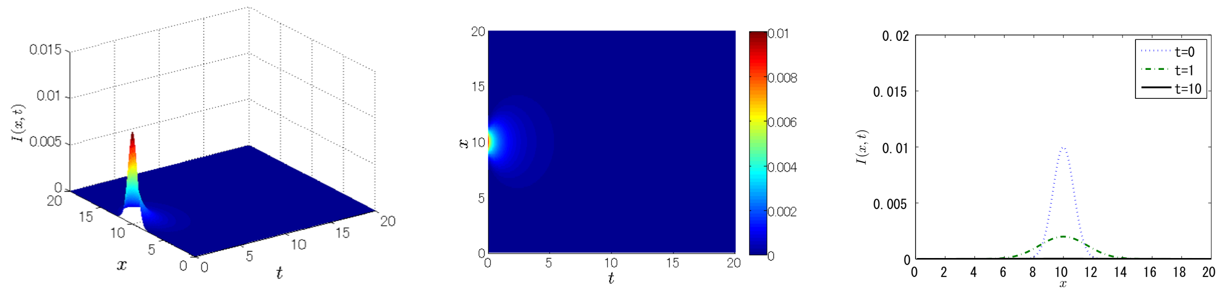
where $\beta_i(\cdot) \in C^2(\overline{\Omega})$, $i = 1, 2$ are strictly positive and uniformly bounded on $\overline{\Omega}$. As stated in (4.4), assumptions (A3)-(A9) are satisfied in this case.

6.1 The spatially homogeneous case

First, we consider the spatially homogeneous case: $\beta_i(x) \equiv \beta_i > 0$, $i = 1, 2$. We can easily check that all assumptions needed in the previous section are satisfied. $\Re_0$ can be computed by (5.13).

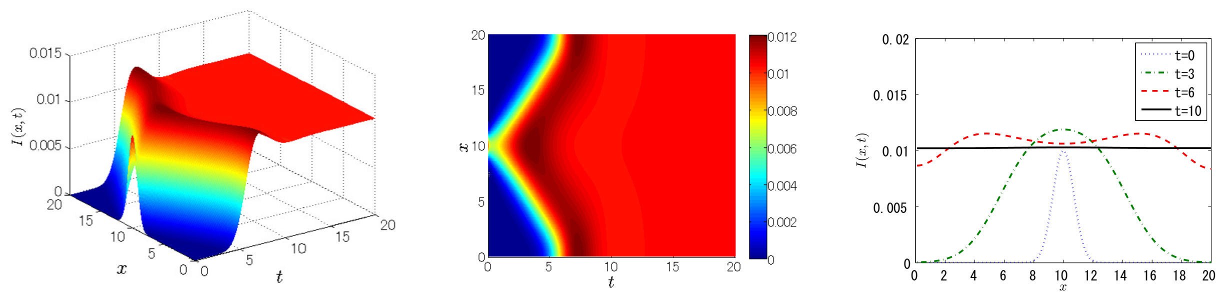
For $(d, \beta_1, \beta_2) = (1, 3, 15)$, we obtain $\Re_0 \approx 0.9733 < 1$. Thus, we see from Theorem 5.1 that the CFSS $Q^0 = (S^0, 0, 0) = (1, 0, 0) \in \mathbb{X}^+$ is globally asymptotically stable. In fact, we can observe in Fig. 2 that the density of infected individuals $I(x, t)$ converges to zero as time evolves.

For $(d, \beta_1, \beta_2) = (1, 5, 15)$, we obtain $\Re_0 \approx 1.0837 > 1$. Thus, we see from Theorem 5.2 that the CESS $Q^* = \left(\bar{S}, \bar{I}, \bar{P}\right) \in \mathbb{X}^+$ is globally asymptotically stable. In fact, we can observe in Fig.



(a) (b) (c)

Fig. 2.Time evolution of $I(x,t)$ of system (5.1) with (6.1)-(6.2) for $(d,\beta_1,\beta_2)=(1,3,15)$ ($\Re_0\approx 0.9733<1$).



(a) (b) (c)

Fig. 3.Time evolution of $I(x,t)$ of system (5.1) with (6.1)-(6.2) for $(d,\beta_1,\beta_2)=(1,5,15)$ ($\Re_0\approx 1.0837>1$).

3 that the density of infected individuals $I(x,t)$ converges to a positive constant distribution as time evolves.

As shown in Section 5, the constant CESS $Q^*=(\bar{S},\bar{I},\bar{P})$ and the basic reproduction number $\Re_0$ are independent from the diffusion coefficients. Fig. 4 shows that the diffusion coefficient d only affects the convergence speed of the solution to the CESS. More specifically, the convergence speed becomes larger as the diffusion coefficient d becomes larger (see Fig. 4).

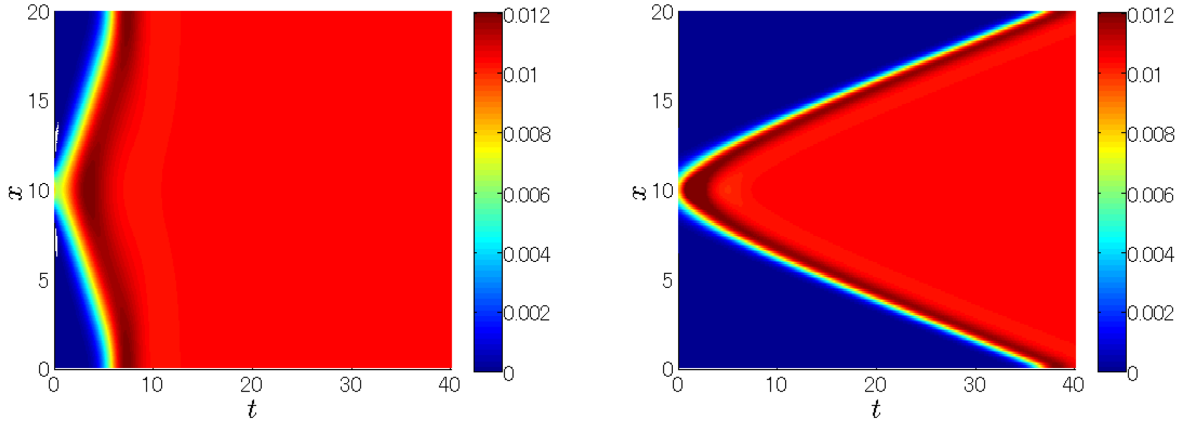
6.2 The spatially heterogeneous case

Next, we consider the spatially heterogeneous case. We assume (6.1) and (6.2) with

$$\beta_1(x)=\beta_1\left(1+0.05\sin\frac{13\pi x}{20}\right),\quad \beta_2(x)=\beta_2\left(1+0.05\sin\frac{13\pi x}{20}\right),\quad x\in[0,20], \tag{6.3}$$

where $\beta_1>0$ and $\beta_2>0$ are positive constants. It is easy to check that all assumptions needed in the previous sections are satisfied. In this case, the next generation operator $\mathcal{K}$ is given by, for $\psi=(\psi_1,\psi_2)\in\mathbb{Y}$ and $x\in[0,20]$,

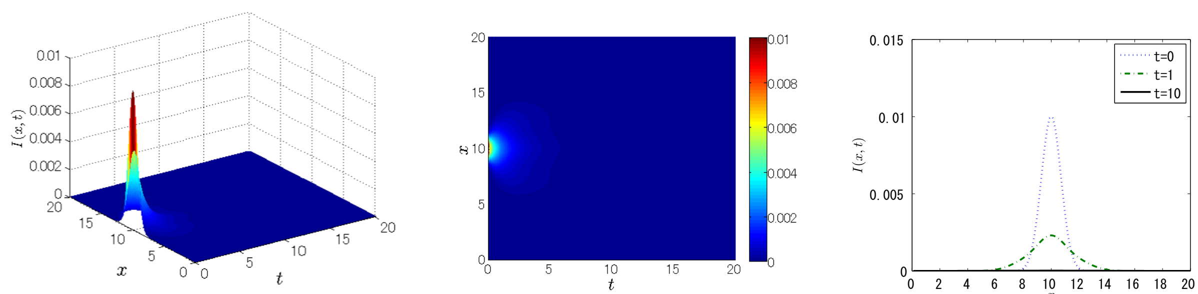
$$\mathcal{K}\psi(x)=\int_0^{+\infty}\int_0^{20}\begin{pmatrix}\beta_1(x) & \beta_2(x)\\ m(x) & 0\end{pmatrix}\begin{pmatrix}\Gamma(t,x,y)\mathrm{e}^{-(\mu+\gamma)t} & 0\\ 0 & \Gamma(t,x,y)\mathrm{e}^{-\eta t}\end{pmatrix}\begin{pmatrix}\psi_1(y)\\ \psi_2(y)\end{pmatrix}\mathrm{d}y\,\mathrm{d}t,$$



(a) $d = 1$.

(b) $d = 0.01$.

Fig. 4.Time evolution of $I(x,t)$ of system (5.1) with (6.1)-(6.2) for $(\beta_1, \beta_2) = (5, 15)$ ($\Re_0 \approx 1.0837 > 1$). (a) $d = 1$; (b) $d = 0.01$.



(a)

(b)

(c)

Fig. 5.Time evolution of $I(x,t)$ of system (1.3)-(1.4) with (6.1)-(6.3) for $(d, \beta_1, \beta_2) = (1, 3, 15)$ ($\Re_0 \approx 0.9789 < 1$).

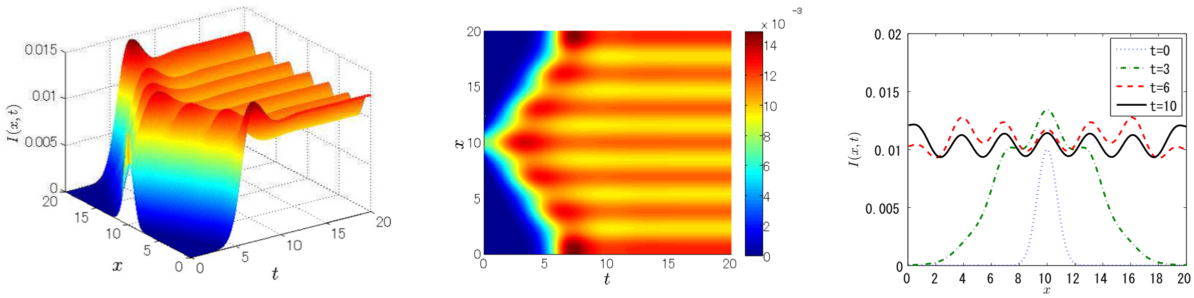
where

$$\Gamma(t,x,y) = \frac{1}{20} + \frac{1}{10}\sum_{n=1}^{+\infty} \cos\frac{n\pi x}{20}\cos\frac{n\pi y}{20} \mathrm{e}^{-d\left(\frac{n\pi}{20}\right)^2 t}, \quad t > 0, \quad x, y \in [0, 20]. \tag{6.4}$$

In what follows, for the computation of $\Re_0 = r(\mathcal{K})$, we employ the Fredholm discretization method to the integral operator $\mathcal{K}$ as in [34, Section 3.1.2].

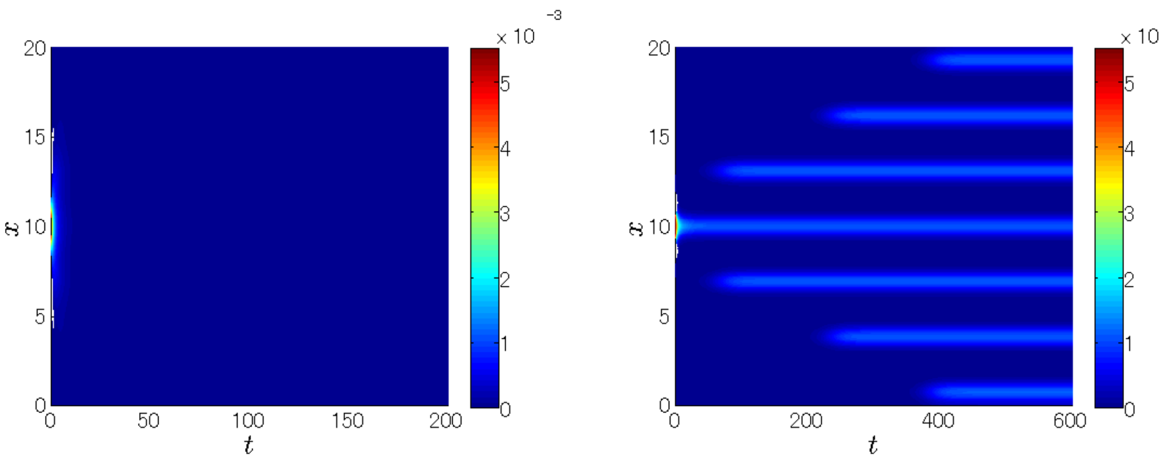
For $(d, \beta_1, \beta_2) = (1, 3, 15)$, we obtain $\Re_0 \approx 0.9789 < 1$. Thus, we see from Theorem 4.1 that the CFSS $Q^0 = (S^0, 0, 0) = (1, 0, 0) \in \mathbb{X}^+$ is globally asymptotically stable. In fact, we can observe in Fig. 5 that the density of infected individuals $I(x,t)$ converges to zero as time evolves.

For $(d, \beta_1, \beta_2) = (1, 5, 15)$, we obtain $\Re_0 \approx 1.0907 > 1$. Thus, we see from Theorem 4.2 that the disease in system (1.3)-(1.4) is uniformly persistent. In fact, we can observe in Fig. 6 that the density of infected individuals $I(x,t)$ is uniformly bounded below by a positive constant



(a) (b) (c)

Fig. 6.Time evolution of $I(x,t)$ of system (1.3)-(1.4) with (6.1)-(6.3) for $(d, \beta_1, \beta_2) = (1, 5, 15)$ ($\Re_0 \approx 1.0907 > 1$).



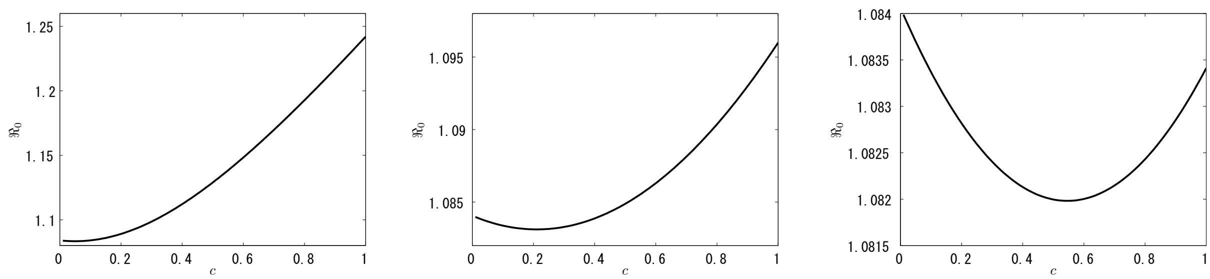
(a) $d = 1$. (b) $d = 0.01$.

Fig. 7.Time evolution of $I(x,t)$ of system (1.3)-(1.4) with (6.1)-(6.3) for $(\beta_1, \beta_2) = (3.2, 15)$. (a) $d = 1$ ($\Re_0 \approx 0.9897 < 1$); (b) $d = 0.01$ ($\Re_0 \approx 1.0078 > 1$).

for sufficiently large t. Moreover, we can see in the figure that $I(x,t)$ converges to a spatially heterogeneous CESS as time evlolves.

In contrast with the spatially homogeneous case, the basic reproduction number $\Re_0$ in this case depends on the diffusion coefficient d. We see from (6.4) and the Krein-Rutman theorem [23, Theorem 3.2] that $\Re_0$ is decreasing with respect to d. Thus, the CFSS Q^0 can lose its stability if the diffusion coefficient d is small. For instance, for $(d, \beta_1, \beta_2) = (1, 3.2, 15)$, we have $\Re_0 \approx 0.9897 < 1$, and thus, the CFSS Q^0 is globally asymptotically stable (Fig. 7 (a)). However, if we change the value of d from 1 to 0.01, then we have $\Re_0 \approx 1.0078 > 1$, and thus, the disease persists (Fig. 7 (b)).

Finally, we investigate the effect of the spatial heterogeneity on the basic reproduction number



(a) $k = 1$ (b) $k = 3$ (c) $k = 5$

Fig. 8.The basic reproduction number $\Re_0$ with (6.5) for $0 < c < 1$ and (a) $k = 1$, (b) $k = 3$ and (c) $k = 5$.

$\Re_0$. We use the following parameters.

$$\begin{cases} \lambda = 1, \quad \mu = 1, \quad \gamma = 10, \quad m = 10, \quad \eta = 20, \quad \Omega = (0,1), \\ d = d_1 = d_2 = d_3 = 1, \quad f_1(x,S,I) = \dfrac{\beta_1(x)SI}{1+I}, \quad f_2(x,S,P) = \dfrac{\beta_2(x)SP}{1+P}, \\ \beta_1(x) = 5\left(1 + c\cos k\pi x\right), \quad \beta_2(x) = 15\left(1 + c\cos k\pi x\right), \quad x \in [0,1], \end{cases} \tag{6.5}$$

where $0 < c < 1$ and $k \in \mathbb{N}$. The average values of $\beta_1(x)$ and $\beta_2(x)$ are $\int_0^1 \beta_1(x)\mathrm{d}x = 5$ and $\int_0^1 \beta_2(x)\mathrm{d}x = 15$, respectively. Thus, we can regard c as the intensity of the spatial heterogeneity (see also [22, Section 3.1]). For $k = 1$, we see from Fig. 8 (a) that $\Re_0$ is monotone increasing with respect to c. Thus, as claimed in [22], the spatial heterogeneity can enhance the disease spread in this case. However, for $k = 3$ and $k = 5$, we see from Fig. 8 (b)-(c) that $\Re_0$ is not monotone increasing with respect to c. Thus, as opposed to the suggestion in [22], the spatial heterogeneity does not always enhance the disease spread in these cases.

7 Discussion

It is widely known in current mathematical cholera studies that cholera transmission involves both direct (i.e. human-to-human) and indirect (i.e. environment-to-human) routes. Thus, multiple interactions among the human host, the pathogen, and the environment may affect the cholera transmission. In an effort to gain deeper understanding of cholera dynamics, we formulate and analyze a nonlinear reaction-diffusion model to capture the effect of movements of human hosts and bacteria in a spatially heterogeneous environment.

For this mathematical model, we define the basic reproduction number, $\Re_0$, which is characterized as the spectral radius of the next generation operator. Mathematical results reveal that $\Re_0 = 1$ serves a threshold. The disease will not die out if $\Re_0 < 1$ and the disease persist if $\Re_0 > 1$. Our results in Section 5 reveal some fundamental differences between three types of nonlinear incidence function in such spatial models when constructing Lyapunov functionals. Under certain assumptions, it is shown that if $\Re_0^1, \Re_0^2, \Re_0^3 < 1$, then the CFSS $Q^0 = (S^0, 0, 0) = (\lambda/\mu, 0, 0) \in \mathbb{X}^+$ of system (5.1), (5.9), (5.12) is globally asymptotically stable, respectively. Whereas if $\Re_0^1, \Re_0^2, \Re_0^3 > 1$, then the CESS $Q^* = (\bar{S}, \bar{I}, \bar{P}) \in \mathbb{X}^+$ of system (5.1), (5.9), (5.12) is globally asymptotically stable, respectively.

Our results are established on some nonlinear restricts on incidence function for the direct or indirect transmission. Assumptions (A1)-(A4) play a crucial role in proving that (1.3)-(1.4) has a unique global classical solution, so that (1.3)-(1.4) generates a semiflow $\{\Psi(t)\}_{t\geq 0} : \mathbb{X}^+ \to \mathbb{X}^+$ defined by $\Psi(t)\phi := u(t, \phi)$, $t \geq 0$. Under assumption (A5), the linear system (3.1) is cooperative and irreducible, which also ensures that eigenvalue problem (3.2) admits a principal eigenvalue κ_0, associated with a strictly positive eigenvector $(\varphi_0, \psi_0) \in \mathbb{Y}^+$ from the Krein-Rutman theorem. (A6)-(A8) demonstrate the monotonicity and concavity of the nonlinear incidence functions $f_1(\bar{S}, \bar{I})$ and $f_2(\bar{S}, \bar{P})$ with respect to $S, I, P \geq 0$, which play an important role in applying the comparison principle. Further, (A9) is devoted to proving that the solution semiflow $\Psi(t)$, $t \geq 0$ is point dissipative. Based on this, semiflow $\Psi(t)$ enjoys compactness (see Corollary 2.2) such that $\Psi(t)$, $t \geq 0$ has a global attractor in $\mathbb{X}^+$. It is easy to see that (B1)-(B5) implies (A1)-(A8) in the specially homogeneous case.

Our numerical results in subsection 6.1 reveal that CFSS Q^0 and CESS Q^* are globally asymptotically stable when basic reproduction number less and larger than 1, respectively. In Fig. 4, we found that the convergence speed becomes faster as the diffusion coefficient d becomes larger, although basic reproduction number $\Re_0$ are independent it. In subsection 6.2, we investigate the effect of spatial heterogeneity on disease dynamics. With strong contrast to subsection 6.1, basic reproduction number depends on the diffusion coefficient ($\Re_0$ is decreasing with respect to d). Thus, form Theorems 4.1 and 4.2, we can conclude that cholera can not be controlled by limiting the movement of host individuals. In Fig. 8 (a)-(c), we found that $\Re_0$ is not always monotone increasing with respect to c. Thus, as opposed to the suggestion in [22], the spatial heterogeneity does not always enhance the disease spread in these cases.

We argue that, however, bilinear incidence function does not satisfy the assumption (A9). In fact, individuals and cholera pathogen disperse at different rates, which further brings some new challenges due to the unboundedness of the bilinear incidence function. We leave it as future investigation.

Acknowledgements

The authors would like to thank the anonymous reviewers for their helpful comments to the previous version of our manuscript. J. Wang was supported by National Natural Science Foundation of China (No.11871179). T. Kuniya was supported by Japan Society for the Promotion of Science (No.15K17585 and No.19K14594).

References

[1] Neilan RLM, Schaefer E, Gaff H, Fister KR, Lenhart S. Modeling optimal intervention strategies for cholera. Bull Math Biol 2010:72:2004-2018.

[2] Codeço CT. Endemic and epidemic dynamics of cholera: The role of the aquatic reservoir. BMC Infectious Diseases 2001:1:1.

[3] Mukandavire Z, Liao S, Wang J, Gaff H, Smith DL, Morris JG. Estimating the reproductive numbers for the 2008–2009 cholera outbreaks in Zimbabwe. Proc Nat Acad Sci USA 2011:108:8767–8772.

[4] Posny D, Wang J, Mukandavire Z, Modnak C. Analyzing transmission dynamics of cholera with public health interventions. Math Biosci 2015:264:38–53.

[5] Tien JH, Earn DJD. Multiple transmission pathways and disease dynamics in a waterborne pathogen model. Bull Math Biol 2010:72:1506–1533.

[6] Yamazaki K, Wang X. Global well-posedness and asymptotic behavior of solutions to a reaction-convection-diffusion cholera epidemic model. Disc Cont Dyn Syst B 2016:21:1297–1316.

[7] Hartley DM, Morris JG, Smith DL. Hyperinfectivity: A critical element in the ability of V. cholerae to cause epidemics? PLOS Med 2006:3:63–69.

[8] Brauer F, Shuai Z, van den Driessche P. Dynamics of an age-of-infection cholera model. Math Biosci Eng 2013:10:1335–1349.

[9] Kokomo E, Emvudu Y. Mathematical analysis and numerical simulation of an age-structured model of cholera with vaccination and demographic movements. Nonlinear Anal RWA 2019:45:142–156.

[10] Wang J, Zhang R, Kuniya T. A note on dynamics of an age-of-infection cholera model. Math Biosci Eng 2016:13:227–247.

[11] Shuai Z, van den Driessche P. Global dynamics of cholera models with differential infectivity. Math Biosci 2013:234:118–126.

[12] Wang X, Zhao XQ, Wang J. A cholera epidemic model in a spatiotemporally heterogeneous environment. J Math Anal Appl 2018:468:893–912.

[13] Shuai Z, van den Driessche P. Global stability of infectious disease models using Lyapunov functions. SIAM J Appl Math 2013:73:1513–1532.

[14] Wang X, Wang J, Analysis of cholera epidemics with bacterial growth and spatial movement. J Biol Dyn 2015:9:233–261.

[15] Allen LJS, Bolker BM, Lou Y, Nevai AL. Asymptotic profiles of the steady states for an SIS epidemic reaction-diffusion model. Disc Cont Dyn Syst 2008:21:1–20.

[16] Li H, Peng R, Wang F. Varying total population enhances disease persistence: Qualitative analysis on a diffusive SIS epidemic model. J Diff Equat 2009:262:885–913.

[17] Wang FB, Shi J, Zou X. Dynamics of a host-pathogen system on a bounded spatial domain. Commun Pure Appl Anal 2015:14:2535–2560.

[18] Wu Y, Zou X. Asymptotic profiles of steady states for a diffusive SIS epidemic model with mass action infection mechanism. J Diff Equat 2016:261:4424–4447.

[19] Wu Y, Zou X. Dynamics and profiles of a diffusive host-pathogen system with distinct dispersal rates. J Diff Equat 2018:264:4989–5024.

[20] Smith HL. Monotone dynamical systems: an introduction to the theory of competitive and cooperative systems. American Mathematical Society; 1995.

[21] Ren X, Tian Y, Liu L, Liu X. A reaction-diffusion within-host HIV model with cell-to-cell transmission. J Math Biol 2018:76:1831–1872.

[22] Cai Y, Lian X, Peng Z, Wang W. Spatiotemporal transmission dynamics for influenza disease in a heterogeneous environment. Nonlinear Anal RWA 2019:46:178–194.

[23] Amann H. Fixed point equations and nonlinear eigenvalue problems in ordered Banach spaces. SIAM Rev 1976:18:620–709.

[24] Wang W, Zhao XQ. Basic reproduction numbers for reaction-diffusion epidemic models. SIAM J Appl Dyn Sys 2012:11:1652–1673.

[25] Diekmann O, Heesterbeek JAP, Metz JAJ. On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. J Math Biol 1990:28:365–382.

[26] Thieme HR. Spectral bound and reproduction number for infinite-dimensional population structure and time heterogeneity. SIAM J Appl Math 2009:70:188–211.

[27] Protter MH, Weinberger HF. Maximum principles in differential equations. New York: Springer-Verlag; 1984.

[28] Korobeinikov A. Global properties of infectious disease models with nonlinear incidence. Bull Math Biol 2007:69:1871–1886.

[29] Hale JK. Asymptotic behavior of dissipative systems. Providence: American Mathematical Society; 1989.

[30] Smith HL, Zhao XQ. Robust persistence for semidynamical systems. Nonlinear Anal TMA 2001:47:6169–6179.

[31] Brown KJ, Dunne PC, Gardner RA. A semilinear parabolic system arising in the theory of superconductivity. J Diff Equat 1981:40:232–252.

[32] Huang G, Takeuchi Y, Ma W, Wei D. Global stability for delay SIR and SEIR epidemic models with nonlinear incidence rate. Bull Math Biol 2010:72:1192–1207.

[33] Korobeinikov A, Maini PK. Non-linear incidence and stability of infectious disease models. Math Med Biol 2005:22:113–128.

[34] Chatelin F. The spectral approximation of linear operators with applications to the computation of eigenelements of differential and integral operators. SIAM Rev 1981:23:495–522.