Mathematical Biosciences and Engineering

http://www.aimspress.com/journal/MBE

Mathematical Biosciences and Engineering, 16(4): 2852–2874.
DOI: 10.3934/mbe.2019141
Received: 09 January 2019
Accepted: 20 March 2019
Published: 02 April 2019

Research article

The SIS model with diffusion of virus in the environment

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Abstract: In this paper, we propose an SIS-type reaction-diffusion equations, which contains both direct transmission and indirect transmission via free-living and spatially diffusive bacteria/virus in the contaminated environment, motivated by the dynamics of hospital infections. We establish the basic reproduction number R_0 which can act as threshold level to determine whether the disease persists or not. In particular, if $R_0 < 1$, then the disease-free equilibrium is globally asymptotically stable, whereas the system is uniformly persistent for $R_0 > 1$. For the spatially homogeneous system, we investigate the traveling wave solutions and obtain that there exists a critical wave speed, below which there has no traveling waves, above which the traveling wave solutions may exist for small diffusion coefficient by the geometric singular perturbation method. The finding implies that great spatial transmission leads to an increase in new infection, while large diffusion of bacteria/virus results in the new infection decline for spatially heterogeneous environment.

Keywords: spatial heterogeneity; diffusion; basic reproduction number; threshold dynamics; traveling wave solution

1. Introduction

It is known that some bacteria or virus, who can survive and remain viable out of hosts for certain time, have posed a great threat to the public health. For example, transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *Acinetobacter baumannii* (MRAB) were observed in an intensive care unit (ICU) of a hospital in China [1–5]. There is evidence showing that strains of MRSA or MRAB can remain viable on dust particles or skin scales for many weeks or months [6], and consequently are important causes of infection. Hence, investigating the effect of indirect transmission via free-living bacteria/virus in the disease evolution plays an important role in the control of hospital infection. Many mathematical models have been proposed to analyse the transmission dynamics of hospital infection [7–15]. Wang et al. [13] proposed a mathematical model including both direct and indirect transmission routes, and obtained that environmental contamination was a threat to hospital infection and free-living bacteria/virus in the environment could promote transmission and initiate infection even if an infection had died out among health-care workers and patients. However, free-living bacteria/virus can disperse in an ICU or the whole ward with air movement, which is neglected in most mathematical models. Thus, it remains challenging to accurately describe diffusion process of bacteria/virus and investigate the transmission dynamics of free-living bacteria/virus in the contaminated environment on disease infection, which provides the motivation for our study.

Many reaction-diffusion equations are formulated to investigate the roles of diffusion and spatial heterogeneity on the transmission of diseases [16–25]. The classic susceptible-infected-susceptible (SIS) reaction-diffusion disease system with spatial heterogeneity was investigated by Allen et al. [16]. Then the model was extended to include periodic coefficients [21, 24] or heterogeneous environments diffusion rate [25, 26] or advection rate [27–29] or a linear source term [30] or various incidence [17, 22, 31]. Meanwhile, there are a number of within-host viral dynamic models which represent interactions of free virus particles and targeted cells [32, 33] and their mobility [34–42]. Some models introduced the random mobility for viruses [38], some let part parameters be location dependent [34], while other allowed all parameters be space dependent [37, 40]. In order to investigate the effect of spatial heterogeneity and distinct diffusion rates on the dynamics of the model, Wu and Zou [41] proposed a model which describes distinct dispersal rates for the susceptible and infected hosts, while keeping the virus unmove. These reaction-diffusion equations are formulated to model transmission dynamics of disease/virus either on population level or on individuals level. Little remains unclear for investigation of both between- and within-host dynamics.

The main purpose of this study is to consider the transmission dynamics at the population level and viral dynamics at the individual level motivated by hospital infection, and examine effect of diffusion of free-living bacteria/virus in the contaminated environment on transmission dynamics. We then propose the following reaction-diffusion equations with only bacteria/virus dispersing

$$\begin{cases} \frac{\partial S}{\partial t} = A - \beta(x)SI - \nu(x)SW - dS + \gamma I, & x \in \Omega,\ t > 0, \\ \frac{\partial I}{\partial t} = \beta(x)SI + \nu(x)SW - dI - \gamma I, & x \in \Omega,\ t > 0, \\ \frac{\partial W}{\partial t} = \nabla \cdot (D(x)\nabla W) + eI - cW, & x \in \Omega,\ t > 0, \end{cases} \tag{1.1}$$

where $S(x,t)$, $I(x,t)$ and $W(x,t)$ are the densities of susceptible patients, infectious patients and free bacteria/virus at position x at time t, respectively. A is the recruitment rate of susceptible patients, $\beta(x)$ is the disease transmission rate between the susceptible and the infected individuals, $\nu(x)$ is the disease transmission rate between the susceptible and the environmental virus, d is the natural death rate and γ is the recovery rate, $D(x)$ is the space dependent diffusion coefficient of bacteria/virus, e is the shading rate and c is rate of clearance, we assume all parameters are positive. We impose the Neumann boundary conditions and nonnegative initial conditions for model (1.1):

$$\frac{\partial W}{\partial n} = 0, \quad x \in \partial\Omega,\ t > 0, \tag{1.2}$$

$$(S(x,0), I(x,0), W(x,0)) = (S_0(x), I_0(x), W_0(x)) \geq, \not\equiv \mathbf{0}, \quad x \in \Omega. \tag{1.3}$$

We shall analyse the well-posedness and threshold dynamics of the proposed system. The basic reproduction number is established and proved to be a threshold value for disease persistence in section 2. In section 3, we prove the existence and non-existence of the traveling wave solutions. In section 4, numerical simulations shall be performed to study the influence of spatial heterogeneous and diffusion rate on the basic reproduction number. We then give a brief discussion in section 5.

2. Dynamics of the model

In this section, we analyse the well-posedness and the threshold dynamics of system (1.1)-(1.3).

2.1. Well-posedness of the system

Let $\mathbb{X} = C(\bar{\Omega}, \mathbb{R}^3)$ be the Banach space with the supremum norm $\|\cdot\|_{\mathbb{X}}$, $\mathbb{X}^+ = C(\bar{\Omega}, \mathbb{R}^3_+)$. Then $(\mathbb{X}, \mathbb{X}^+)$ is an ordered Banach space. Define $T_1(t)\varphi_1 = e^{-dt}\varphi_1$, $T_2(t)\varphi_2 = e^{-(d+\gamma)t}\varphi_2$, and let $T_3 : C(\bar{\Omega}, \mathbb{R}) \to C(\bar{\Omega}, \mathbb{R})$ be the C_0 semigroups associated with $\nabla \cdot (D(x)\nabla) - c$ subject to the Neumann boundary condition, namely,

$$(T_3(t)\varphi_3)(x) = \int_\Omega G(x, y, t)\varphi_3 \mathrm{d}y,$$

where $t \geq 0$, $\varphi = (\varphi_1, \varphi_2, \varphi_3) \in \mathbb{X}$, G is the Green function associated with $\nabla \cdot (D(x)\nabla) - c$ subject to the Neumann boundary condition. Then $T_3(t) : C(\bar{\Omega}, \mathbb{R}) \to C(\bar{\Omega}, \mathbb{R})$ is compact and strongly positive for each $t > 0$ by [43, Corollary7.2.3].

Define $F = (F_1, F_2, F_3) : \mathbb{X}^+ \to \mathbb{X}$ by

$$\begin{aligned}
F_1(\psi)(x) &= A - \beta(x)\psi_1\psi_2 - \nu(x)\psi_1\psi_3 + \gamma\psi_2, \\
F_2(\psi)(x) &= \beta(x)\psi_1\psi_2 + \nu(x)\psi_1\psi_3, \\
F_3(\psi)(x) &= e\psi_2,
\end{aligned}$$

where $\psi = (\psi_1, \psi_2, \psi_3) \in \mathbb{X}^+$. Then (1.1)-(1.3) can be rewritten as the following integral equation:

$$u(t) = T(t)\psi + \int_0^t T(t-s)F(u(s))\mathrm{d}s, \tag{2.1}$$

where $u(t) = (S(t), I(t), W(t))^T$, $T(t) = diag(T_1(t), T_2(t), T_3(t))$.

We observe that the subtangential conditions in [44, Corollary4] are satisfied. Then we get the following result.

Lemma 2.1. *For every initial value function* $\psi \in \mathbb{X}^+$*, system* (2.1) *has a unique noncontinuable solution* $u(\cdot, t, \psi) \in \mathbb{X}^+$ *on* $[0, \tau_\psi)$ *where* $0 < \tau_\psi \leq +\infty$*. Moreover, if* $\tau_\psi < +\infty$*, then* $\lim_{t\to\tau_\psi^-} \| u(t) \|_{\mathbb{X}} = \infty$.

Now, we will show the global existence and uniform boundedness of solutions of system (1.1)-(1.3).

Lemma 2.2. *For every initial value function* $\psi \in \mathbb{X}^+$*, system* (1.1)-(1.3) *has a unique solution* $u(\cdot, t, \psi) \in \mathbb{X}^+$ *on* $[0, \infty)$*, and solutions of* (1.1)-(1.3) *are uniformly bounded and ultimately bounded.*

Proof. Let $N(x, t) := S(x, t) + I(x, t)$. Then $N(x, t)$ satisfies

$$\frac{\partial N(x, t)}{\partial t} = A - dN, \ x \in \Omega, \ t > 0,$$

It then follows that $N(x,t)$ is uniformly bounded, and hence, $S(x,t)$, $I(x,t)$ are uniformly bounded. Again by the comparison principle, we know that $W(x,t)$ is uniformly bounded. It is easy to see that $\lim_{t\to\infty} N(x,t) = \frac{A}{d}$ uniformly for $x \in \bar{\Omega}$. Then there exist $0 < \varepsilon_0 \ll 1$ and $\bar{t} > 0$ such that

$$S(\cdot,t) + I(\cdot,t) = N(\cdot,t) \le (1+\varepsilon_0)\frac{A}{d},\ \forall t \ge \bar{t}.$$

Hence,

$$S(\cdot,t) \le (1+\varepsilon_0)\frac{A}{d},\quad I(\cdot,t) \le (1+\varepsilon_0)\frac{A}{d},\ \forall t \ge \bar{t}. \tag{2.2}$$

This implies that $S(\cdot,t)$ and $I(\cdot,t)$ are ultimately bounded(point dissipative).

From (2.2) and the third equation of (1.1), we obtain that

$$\begin{cases} \frac{\partial W}{\partial t} \le \nabla\cdot(D(x)\nabla W) + e(1+\varepsilon_0)\frac{A}{d} - cW, & x\in\Omega,\ t > \bar{t}, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega,\ t > \bar{t}. \end{cases}$$

It follows from the comparison principle and [45, Lemma1] that there exist a $\tilde{t} > \bar{t} > 0$ such that

$$W(x,t) \le (1+2\varepsilon_0)\frac{eA}{cd},\ \forall t \ge \tilde{t}. \tag{2.3}$$

Therefore, $W(x,t)$ is ultimately bounded. □

The following Lemma will play an important role in establishing the persistence of (1.1)-(1.3).

Lemma 2.3. *Suppose $u(x,t,\psi)$ is a solution of system* (1.1)-(1.3). *Then for any $\psi \in \mathbb{X}^+$, $S(x,t,\psi) > 0, I(x,t,\psi) > 0,\ W(x,t,\psi) > 0, \forall x \in \bar{\Omega}, t > 0$. Furthermore, $\liminf_{t\to\infty} S(x,t,\psi) \ge m(x)$, where $m(x)$ is a strictly positive function on $\bar{\Omega}$.*

Proof. We prove $I(x,t,\psi) > 0$ by contradiction, suppose there exist $\hat{x} \in \bar{\Omega}$ and $\hat{t} > 0$ such that $I(x,t) > 0$ on $\Omega \times (0,\hat{t})$ and $I(\hat{x},\hat{t}) = 0$ and $\frac{\partial I(\hat{x},\hat{t})}{\partial t} < 0$. Then from the third equation of (1.1), we know that W satisfies the following inequality:

$$\begin{cases} \frac{\partial W}{\partial t} \ge \nabla\cdot(D(x)\nabla W) - cW, & x\in\Omega,\ t \in (0,\hat{t}], \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega,\ t \in (0,\hat{t}]. \end{cases}$$

It follows from the strong maximum principle [46, p.172,Theorem4] and the Hopf boundary lemma [46, p.170,Theorem3] that $W(x,t) \ge 0$ on $\Omega \times [0,\hat{t}]$. Then from the second equation of (1.1), we get $\frac{\partial I(\hat{x},\hat{t})}{\partial t} \ge 0$, a contradiction. Thus, $I(x,t) > 0$ for $\forall x \in \bar{\Omega}, t > 0$. We can use the above equation again and the strong maximum principle and the Hopf boundary lemma to obtain the positivity of W. Then from the first equation of (1.1), we can easily get that $S(x,t,\psi) > 0, \forall x \in \bar{\Omega}, t > 0$, for any $\psi \in \mathbb{X}^+$. Denote $M := (1+\varepsilon_0)\frac{A}{d},\ \hat{M} := (1+2\varepsilon_0)\frac{eA}{cd}$. From (2.2) and (2.3), it follows that $I(\cdot,t) \le M,\ W(\cdot,t) \le \hat{M}, \forall t \ge \tilde{t}$. Again from the first equation of (1.1), we obtain that

$$\frac{\partial S}{\partial t} \ge A - (\beta(x)M + \nu(x)\hat{M} + d)S,\ x \in \bar{\Omega},\ t > \tilde{t}.$$

By [24, Theorem2.2.1] and the comparison principle, we obtain that

$$\liminf_{t\to\infty} S(x,t,\psi) \ge \frac{A}{\beta(x)M + \nu(x)\hat{M} + d},\ \forall x \in \bar{\Omega}.$$

□

Now, we will establish the existence of the global attractor of system (1.1)-(1.3). To this end, we first define the solution semiflow $\Psi_t : \mathbb{X}^+ \to \mathbb{X}^+$ associated with (1.1)-(1.3) by

$$\Psi_t(\psi) = u(\cdot, t, \psi),\ \forall t \geq 0,$$

where $u(\cdot, t, \psi)$ is the solution of (1.1)-(1.3) with $u(\cdot, 0, \psi) = \psi \in \mathbb{X}^+$. Noting that (2.2) and (2.3) hold, we let

$$U = \{(S, I, W) \in \mathbb{R}^3_+ : 0 \leq S + I \leq M,\ 0 \leq W \leq \hat{M}\}.$$

Then $\Psi_t(\psi) \in U,\ \forall t \geq \tilde{t},\ \psi \in \mathbb{X}^+$.

Obviously, M and $\hat{M}$ are upper solutions of systems

$$\frac{\partial N(x,t)}{\partial t} = A - dN,\ x \in \Omega,\ t > 0.$$

and

$$\begin{cases} \frac{\partial W}{\partial t} = \nabla \cdot (D(x)\nabla W) + eA/d - cW, & x \in \Omega,\ t > 0, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega,\ t > 0, \end{cases}$$

respectively. Then by the comparison principle, U is positively invariant for Ψ_t, namely, for $\forall t \geq 0,\ \psi \in U,\ \Psi_t(\psi) \in U$.

Note that the solution semiflow Ψ_t is not compact due to the lack of diffusion terms for the first two equations in system (1.1). In order to solve this problem, we introduce the Kuratowski measure of noncompactness κ(see [47]), which is described as

$$\kappa(\mathcal{D}) := \inf\{r : \mathcal{D} \text{ has a finite cover of diameter } r\}$$

for any bounded set $\mathcal{D}$. We set $\kappa(\mathcal{D}) = \infty$ whenever $\mathcal{D}$ is unbounded. It is easy to see that $\mathcal{D}$ is precompact(i.e., $\bar{\mathcal{D}}$ is compact) if and only if $\kappa(\mathcal{D}) = 0$.

For convenience, we let

$$\begin{aligned} f_1(x, S, I, W) &= A - \beta(x)SI - \nu(x)SW - dS + \gamma I, \\ f_2(x, S, I, W) &= \beta(x)SI + \nu(x)SW - dI - \gamma I, \\ f_3(x, I, W) &= eI - cW. \end{aligned}$$

Then (1.1)-(1.3) can be rewritten as follows

$$\begin{cases} \frac{\partial S}{\partial t} = f_1(x, S, I, W), & x \in \Omega,\ t > 0, \\ \frac{\partial I}{\partial t} = f_2(x, S, I, W), & x \in \Omega,\ t > 0, \\ \frac{\partial W}{\partial t} = \nabla \cdot (D(x)\nabla W) + f_3(x, I, W), & x \in \Omega,\ t > 0, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega,\ t > 0, \\ (S(x,0), I(x,0), W(x,0)) = (S_0(x), I_0(x), W_0(x)) \geq \mathbf{0}, & x \in \Omega. \end{cases}$$

For $\mathbf{u} = (S, I)$, $w = W$, we impose the following assumption: there exists a constant $\hat{r} > 0$ such that

$$\mathbf{x}^T \left[\frac{\partial \mathbf{f}(x, \mathbf{u}, w)}{\partial \mathbf{u}}\right] \mathbf{x} \leq -\hat{r}\mathbf{x}^T\mathbf{x},\ \forall \mathbf{x} \in \mathbb{R}^2,\ x \in \Omega,\ (\mathbf{u}, w) \in U, \tag{2.4}$$

where $\mathbf{f}(x, \mathbf{u}, w) := (f_1(x, S, I, W), f_2(x, S, I, W))$. It is easy to see that (2.4) is equivalent with the following inequality.

$$\mathbf{x}\begin{pmatrix} -\beta(x)I - \nu(x)W - d & -\beta(x)S + \gamma \\ \beta(x)I + \nu(x)W & \beta(x)S - d - \gamma \end{pmatrix}\mathbf{x} \leq -\hat{r}\mathbf{x}^T\mathbf{x},\ \forall \mathbf{x} \in \mathbb{R}^2,\ x \in \Omega,\ (\mathbf{u}, w) \in U.$$

Lemma 2.4. *Let* (2.4) *hold. Then* Ψ_t *is* κ*-contracting in the sense that*

$$\lim_{t\to\infty} \kappa(\Psi_t \mathcal{D}) = 0$$

for any bounded set $\mathcal{D} \in \mathbb{X}^+$*, where* κ *is the Kuratowski measure of noncompactness as defined above.*

Proof. By the similar method as in [48, Lemma 4.1], we can prove that Ψ_t is asymptotically compact on $\mathcal{D}$ in the sense that for any sequences $\psi_n \in \mathcal{D}$ and $t_n \to \infty$, there exist subsequences ψ_{n_k} and $t_{n_k} \to \infty$ such that $\Psi_{t_{n_k}}(\psi_{n_k})$ converges in $C(\bar{\Omega}, \mathbb{R}^3)$ as $k \to \infty$. Then it follows from [49, Lemma23.1(2)] that the omega-limit set of $\mathcal{D} : \omega(\mathcal{D})$, is nonempty, compact, invariant in $\mathbb{X}^+$ and $\omega(\mathcal{D})$ attracts $\mathcal{D}$. In view of [50, Lemma 2.1(b)], we obtain that

$$\kappa(\Psi_t(\mathcal{D})) \leq \kappa(\omega(\mathcal{D})) + \delta(\Psi_t(\mathcal{D}), \omega(\mathcal{D})) = \delta(\Psi_t(\mathcal{D}), \omega(\mathcal{D})) \to 0 \text{ as } t \to \infty.$$

□

By Lemma 2.2, Ψ_t is point dissipative on $\mathbb{X}^+$ and the positive orbits of compact subsets of $\mathbb{X}^+$ for Ψ_t are bounded. By Lemma 2.4, $\lim_{t\to\infty} \kappa(\Psi_t \mathcal{D}) = 0$ for each subset $\mathcal{D}$ of $\mathbb{X}^+$. Then by [50, Theorem2.6], we have the following results.

Theorem 2.5. *Suppose* (2.4) *hold. Then* Ψ_t *has a global attractor on* $\mathbb{X}^+$.

2.2. Threshold dynamics of the system

In the following, we investigate the basic reproduction number and the threshold dynamics for the system (1.1)-(1.3). We easily know that the system (1.1)-(1.3) admits a disease-free equilibrium $E_0 = (\bar{S}, 0, 0)$, where $\bar{S} = \frac{A}{d}$. Let $R(x) := \frac{\beta(x)\bar{S}}{d+\gamma}$, which represent the local basic reproduction number for infected-to-susceptible infection at position $x \in \Omega$. We make the assumption that for all $x \in \Omega$, $R(x) < 1$, which means the infection can not be endemic only by infected-to-susceptible infection. Linearizing the system at E_0 gives the following equations:

$$\begin{cases} \frac{\partial u_2}{\partial t} = (\beta(x)\bar{S} - d - \gamma)u_2 + \nu(x)\bar{S}u_3, & x \in \Omega, t > 0, \\ \frac{\partial u_3}{\partial t} = \nabla \cdot (D(x)\nabla u_3) + eu_2 - cu_3, & x \in \Omega,\ t > 0, \\ \frac{\partial u_3}{\partial n} = 0, & x \in \partial\Omega,\ t > 0. \end{cases} \tag{2.5}$$

Let $Q(t)$ be the solution semiflows on $C(\bar{\Omega}, \mathbb{R}^2)$ associated with the linear system (2.5). It is easy to see that $Q(t)$ is a positive C_0-semigroup on $C(\bar{\Omega}, \mathbb{R}^2)$, and its generator B can be written as

$$B = \begin{pmatrix} \beta(x)\bar{S} - d - \gamma & \nu(x)\bar{S} \\ e & \nabla \cdot (D(x)\nabla) - c \end{pmatrix}.$$

Note that B is a closed and resolvent-positive operator.

Let $u_i(x,t) = e^{\lambda t}\phi_i(x),\ i = 2,3$ in (2.5), we obtain the following eigenvalue problem:

$$\begin{cases}(\beta(x)\bar{S} - d - \gamma)\phi_2 + \nu(x)\bar{S}\phi_3 = \lambda\phi_2, & x \in \Omega,\\ \nabla \cdot (D(x)\nabla\phi_3) + e\phi_2 - c\phi_3 = \lambda\phi_3, & x \in \Omega,\\ \frac{\partial\phi_3}{\partial n} = 0, & x \in \partial\Omega.\end{cases} \tag{2.6}$$

Lemma 2.6. *Suppose $s(B)$ is the spectral bound of B, then $s(B)$ is the principal eigenvalue of* (2.6) *with a positive eigenfunction.*

Proof. Define an one-parameter family of linear operators $L_\lambda = \nabla \cdot (D(x)\nabla) - c + \frac{e\nu(x)\bar{S}}{\lambda - \beta(x)\bar{S} + d + \gamma}$, $\forall \lambda > \underline{\beta}\bar{S} - d - \gamma$, where $\underline{\beta} = \min_{x\in\bar{\Omega}} \beta(x)$. Let $C = e \cdot \min_{x\in\bar{\Omega}} \nu(x) \cdot \bar{S} > 0$, and let λ_1 be the principal eigenvalue of the elliptic eigenvalue problem:

$$\begin{cases}\nabla \cdot (D(x)\nabla\phi) - c\phi = \lambda\phi, & x \in \Omega,\\ \frac{\partial\phi}{\partial n} = 0, & x \in \partial\Omega,\end{cases}$$

with a positive eigenfunction ϕ^*. Set

$$\lambda_0 := \frac{\lambda_1 + \underline{\beta}\bar{S} - d - \gamma + \sqrt{\left(\underline{\beta}\bar{S} - d - \gamma - \lambda_1\right)^2 + 4C}}{2}.$$

Since $C > 0$, we have $\lambda_0 > \underline{\beta}\bar{S} - d - \gamma$. It then follows that

$$\begin{aligned} L_{\lambda_0}\phi^* &= \nabla \cdot (D(x)\nabla\phi^*) - c\phi^* + \frac{e\nu(x)\bar{S}}{\lambda_0 - \beta(x)\bar{S} + d + \gamma}\phi^* \\ &\geq \lambda_1\phi^* + \frac{C}{\lambda_0 - \underline{\beta}\bar{S} + d + \gamma}\phi^* \\ &= \lambda_0\phi^*. \end{aligned}$$

Thus, $e^{\lambda_0 t}\phi^*(x)$ is a subsolution of the integral form of the linear system $u_t = L_{\lambda_0}u$. By [23, Theorem 2.3(i)], we know that problem (2.6) has an eigenvalue with geometric multiplicity one and a positive eigenfunction. □

Let $\Phi(t)$ be the solution semiflow on $C(\bar{\Omega}, \mathbb{R}^2)$ associated with the following system

$$\begin{cases}\frac{\partial P_2}{\partial t} = -(d + \gamma)P_2, & x \in \Omega,\ t > 0,\\ \frac{\partial P_3}{\partial t} = \nabla \cdot (D(x)\nabla P_3) + eP_2 - cP_3, & x \in \Omega,\ t > 0,\\ \frac{\partial P_3}{\partial n} = 0, & x \in \partial\Omega,\ t > 0.\end{cases}$$

Define

$$F(x) := \begin{pmatrix} \beta(x)\bar{S} & \nu(x)\bar{S} \\ 0 & 0 \end{pmatrix}.$$

Suppose the distribution of initial infection described by $\psi(x) := (\psi_2(x), \psi_3(x))$. Then $\Phi(t)\psi$ is the distribution of those infective members under the influence of mobility, mortality, and transform. Thus the distribution of new infections at time t is $F(x)\Phi(t)\psi(x)$.

Denote the total distribution of new infections as

$$L(\psi)(x) := \int_0^\infty F(x)\Phi(t)\psi(x)\mathrm{d}t.$$

Following the idea of next generation operators, we define the spectral radius of L as the following

$$R_0 := \rho(L).$$

By the general results in [23, Theorem3.1], we easily know the following lemma.

Lemma 2.7. *$R_0 - 1$ has the same sign as $s(B)$.*

Lemma 2.8. *Let $R_0 > 1$ and (2.4) hold, then the disease-free equilibrium E_0 is a uniform weak repeller in the sense that for any sufficiently small positive constant ϵ_0*

$$\limsup_{t\to\infty} \| \Psi_t(\psi) - (\bar{S}, 0, 0) \| \geq \epsilon_0, \ \forall \psi \in \mathbb{X}^+.$$

Proof. Suppose by contradiction that there exists a $\psi_0 \in \mathbb{X}^+$ such that

$$\limsup_{t\to\infty} \| \Psi_t(\psi_0) - (\bar{S}, 0, 0) \| < \epsilon_0.$$

Then there exists a $t_1 > 0$ such that $S(x, t, \psi_0) > \bar{S} - \epsilon_0, \ \forall t \geq t_1, \ x \in \bar{\Omega}$. Thus we get that

$$\begin{cases} \frac{\partial I}{\partial t} \geq \beta(x)I(\bar{S} - \epsilon_0) + \nu(x)W(\bar{S} - \epsilon_0) - (d+\gamma)I, & x \in \Omega, \ t \geq t_1, \\ \frac{\partial W}{\partial t} \geq \nabla \cdot (D(x)\nabla W) + eI - cW, & x \in \Omega, \ t \geq t_1, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega, \ t \geq t_1. \end{cases} \tag{2.7}$$

By Lemma 2.3, we have $I(x, t, \psi_0) > 0, \ W(x, t, \psi_0) > 0, \ \forall x \in \bar{\Omega}, \ t > t_1$, there exists $\delta_0 > 0$ such that $(I(x, t, \psi_0), W(x, t, \psi_0)) \geq \delta_0 \tilde{\psi}$, where $\tilde{\psi}$ is the corresponding eigenfunction of eigenvalue $s(\tilde{B})$ of (2.6), where $\tilde{B}$ is

$$\tilde{B} = \begin{pmatrix} \beta(x)(\bar{S} - \epsilon_0) - d - \gamma & \nu(x)(\bar{S} - \epsilon_0) \\ e & \nabla \cdot (D(x)\nabla) - c \end{pmatrix}.$$

Note that $\delta_0 e^{s(\tilde{B})(t-t_1)}\tilde{\psi}$ is a solution of the following system:

$$\begin{cases} \frac{\partial I}{\partial t} = \beta(x)I(\bar{S} - \epsilon_0) + \nu(x)W(\bar{S} - \epsilon_0) - (d+\gamma)I, & x \in \Omega, \ t \geq t_1, \\ \frac{\partial W}{\partial t} = \nabla \cdot (D(x)\nabla W) + eI - cW, & x \in \Omega, \ t \geq t_1, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega, \ t \geq t_1. \end{cases}$$

It then follows from (2.7) and the comparison principle that

$$(I(x, t, \psi_0), W(x, t, \psi_0)) \geq \delta_0 e^{s(\tilde{B})(t-t_1)}\tilde{\psi}, \ \forall x \in \bar{\Omega}, \ t \geq t_1.$$

Since $R_0 > 1$, by Lemma 2.7, we know that $s(B) > 0$, it follows from [51, Lemma4.5] that $s(\tilde{B}) > 0$. Hence, $I(x, t, \psi_0)$ and $W(x, t, \psi_0)$ are unbounded, a contradiction. □

The following result implies that R_0 can act as the threshold value for disease persistence.

Theorem 2.9. *Suppose* (2.4) *is true. Then the following statements are valid:*

(i) *If* $R_0 < 1$*, then the disease-free steady state* E_0 *is globally asymptotically stable;*
(ii) *If* $R_0 > 1$*, then there exists a constant* $\sigma > 0$ *such that any positive solution of* (1.1)-(1.3) *with* $S_0(x) \not\equiv 0,\ I_0(x) \not\equiv 0,\ W_0(x) \not\equiv 0$ *satisfies*

$$\liminf_{t\to\infty} S(x,t) \geq \sigma,\ \liminf_{t\to\infty} I(x,t) \geq \sigma,\ \liminf_{t\to\infty} W(x,t) \geq \sigma$$

uniformly for all $x \in \bar{\Omega}$*, and system* (1.1)-(1.3) *has at least one positive equilibrium.*

Proof. (i) The locally asymptotically stability of E_0 follows from [23, Theorem3.1], we only need to prove that E_0 is globally attractive. From Lemma 2.2, we know that

$$S(x,t) \leq M,\ I(x,t) \leq M,\ W(x,t) \leq \hat{M}, \forall x \in \bar{\Omega},\ t \geq \tilde{t}.$$

Then we have the following system:

$$\begin{cases} \frac{\partial I}{\partial t} \leq \beta(x)MI + \nu(x)MW - (d+\gamma)I, & x \in \Omega,\ t \geq \tilde{t}, \\ \frac{\partial W}{\partial t} = \nabla \cdot (D(x)\nabla W) + eI - cW, & x \in \Omega,\ t \geq \tilde{t}, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega,\ t \geq \tilde{t}. \end{cases} \tag{2.8}$$

By Lemma 2.6, there exists a positive eigenfunction $\hat{\phi} := (\hat{\phi}_2, \hat{\phi}_3)$ corresponding to $s(\hat{B})$, where

$$\hat{B} = \begin{pmatrix} \beta(x)M - d - \gamma & \nu(x)M \\ e & \nabla \cdot (D(x)\nabla) - c \end{pmatrix}.$$

For any given $\psi \in \mathbb{X}^+$, there exists a constant $\alpha > 0$ such that $(I(x,\tilde{t},\psi), W(x,\tilde{t},\psi)) \leq \alpha\hat{\phi}(x),\ \forall x \in \bar{\Omega}$. Since the following linear system

$$\begin{cases} \frac{\partial I}{\partial t} = \beta(x)MI + \nu(x)MW - (d+\gamma)I, & x \in \Omega,\ t \geq \tilde{t}, \\ \frac{\partial W}{\partial t} = \nabla \cdot (D(x)\nabla W) + eI - cW, & x \in \Omega,\ t \geq \tilde{t}, \\ \frac{\partial W}{\partial n} = 0, & x \in \partial\Omega,\ t \geq \tilde{t} \end{cases} \tag{2.9}$$

has a solution $\alpha e^{s(\hat{B})(t-\tilde{t})}\hat{\phi}(x),\ t \geq \tilde{t}$. By the comparison principle, we obtain that

$$(I(x,t,\psi), W(x,t,\psi)) \leq \alpha e^{s(\hat{B})(t-\tilde{t})}\hat{\phi}(x),\ t \geq \tilde{t}.$$

Since $R_0 < 1$, it follows from Lemma 2.7 that $s(B) < 0$, then by the continuity of the principal eigenvalue, we get that $s(\hat{B}) < 0$. Thus, $\lim_{t\to\infty}(I(x,t,\psi), W(x,t,\psi)) = \mathbf{0}$ uniformly for $x \in \bar{\Omega}$. Therefore the asymptotic equation of S is as follows

$$\frac{\partial S(x,t)}{\partial t} = A - dS.$$

We obtain that $\lim_{t\to\infty} S(x,t,\psi) = \bar{S}$ uniformly for $x \in \bar{\Omega}$ by the theory for asymptotically autonomous semiflows [52, Corollary 4.3]. Therefore the disease-free equilibrium $(\bar{S}, 0, 0)$ is globally attractive in $\mathbb{X}^+$.

(ii) Let $\mathbb{X}_0 = \{\psi = (S, I, W) \in \mathbb{X}^+ : I(\cdot) \not\equiv 0 \text{ and } W(\cdot) \not\equiv 0\}$, and $\partial\mathbb{X}_0 = \{\psi = (S, I, W) \in \mathbb{X}^+ : I(\cdot) \equiv 0 \text{ or } W(\cdot) \equiv 0\}$. It follows from Lemma 2.3 that for any $\psi \in \mathbb{X}_0$, we have

$$I(x, t, \psi) > 0,\ W(x, t, \psi) > 0,\ \forall x \in \bar{\Omega},\ t > 0.$$

This implies that $\Psi_t(\mathbb{X}_0) \subseteq \mathbb{X}_0,\ \forall t \geq 0$. Set $M_\partial = \{\psi \in \partial\mathbb{X}_0 : \Psi_t(\psi) \in \partial\mathbb{X}_0,\ \forall t \geq 0\}$, and let $\omega(\psi)$ be the omega limit set of the forward obit $O^+(\psi) = \{\Psi_t(\psi) : t \geq 0\}$.

claim : $\omega(\psi) = \{(\bar{S}, 0, 0)\}, \forall \psi \in M_\partial$.

Since $\psi \in M_\partial$, then $\Psi_t(\psi) \in \partial\mathbb{X}_0,\ \forall t \geq 0$. Thus, $I(\cdot, t, \psi) \equiv 0$ or $W(\cdot, t, \psi) \equiv 0,\ \forall t \geq 0$. Suppose $W(\cdot, t, \psi) \equiv 0,\ \forall t \geq 0$, we get $I(\cdot, t, \psi) \equiv 0,\ \forall t \geq 0$ by the third equation of (1.1). Then we obtain that $\lim_{t\to\infty} S(x, t, \psi) = \bar{S}$ uniformly for $x \in \bar{\Omega}$ by the first equation of (1.1). If there exists a $t_2 \geq 0$ such that $W(x, t_2, \psi) \not\equiv 0$, then $W(x, t, \psi) > 0,\ \forall x \in \bar{\Omega},\ t \geq t_2$ by Lemma 2.3. Hence, $I(\cdot, t, \psi) \equiv 0,\ \forall t > t_2$. It follows from the third equation of (1.1) that $\lim_{t\to\infty} W(x, t, \psi) = 0$ uniformly for $x \in \bar{\Omega}$. Then we get that $\lim_{t\to\infty} S(x, t, \psi) = \bar{S}$ uniformly for $x \in \bar{\Omega}$ by the first equation of (1.1). Therefore, $\omega(\psi) = \{(\bar{S}, 0, 0)\}, \forall \psi \in M_\partial$.

Define a continuous function $h : \mathbb{X}^+ \to [0, \infty)$ by

$$h(\psi) := \min\{\min_{x\in\bar{\Omega}} \psi_2(x),\ \min_{x\in\bar{\Omega}} \psi_3(x)\},\ \forall \psi \in \mathbb{X}^+.$$

By Lemma 2.3, $h^{-1}(0, \infty) \subseteq \mathbb{X}_0$, and h has the property that if $h(\psi) > 0$ or $h(\psi) = 0,\ \psi \in \mathbb{X}_0$, then $h(\Psi_t(\psi)) > 0,\ \forall t > 0$. Thus, h is a generalized distance function for the semiflow $\Psi_t : \mathbb{X}^+ \to \mathbb{X}^+$(see [53]). It follows from the above discussion and Lemma 2.8 that any forward obit of Ψ_t in M_∂ converges to E_0, and $W^s(E_0) \cap \mathbb{X}_0 = \emptyset$, where $W^s(E_0)$ is the stable subset of E_0. Further, E_0 is an isolated invariant set in $\mathbb{X}^+$ and there is no cycle in M_∂ from $\{E_0\}$ to $\{E_0\}$. By [53, Theorem3], there exists an $\hat{\sigma} > 0$ such that $\min_{\psi\in\omega(\psi)} h(\psi) > \hat{\sigma},\ \forall \psi \in \mathbb{X}_0$, which induces that

$$\liminf_{t\to\infty} I(x, t) \geq \hat{\sigma},\ \liminf_{t\to\infty} W(x, t) \geq \hat{\sigma},\ \forall \psi \in \mathbb{X}_0.$$

From Lemma 2.3, there exists an $0 < \sigma \leq \hat{\sigma}$ such that

$$\liminf_{t\to\infty} S(x, t) \geq \sigma,\ \liminf_{t\to\infty} I(x, t) \geq \sigma,\ \liminf_{t\to\infty} W(x, t) \geq \sigma,\ \forall \psi \in \mathbb{X}_0.$$

Therefore, the uniformly persistence is obtained.

It follows from [50, Theorem3.7] that $\Psi_t : \mathbb{X}_0 \to \mathbb{X}_0$ has a global attractor A_0. By [50, Theorem4.7], Ψ_t has an equilibrium in $\mathbb{X}_0$. Moreover, Lemma 2.3 implies that the equilibrium is positive. □

3. Traveling wave solutions

In this section, we will establish the existence and non-existence of traveling waves of the following homogeneous system

$$\begin{cases} \frac{\partial S}{\partial t} = A - \beta S I - \nu S W - dS + \gamma I, & x \in (-\infty, \infty),\ t > 0, \\ \frac{\partial I}{\partial t} = \beta S I + \nu S W - dI - \gamma I, & x \in (-\infty, \infty),\ t > 0, \\ \frac{\partial W}{\partial t} = D\Delta W + eI - cW, & x \in (-\infty, \infty),\ t > 0, \end{cases} \tag{3.1}$$

where all coefficients are positive constants. Note that here we consider the spreading speed and traveling waves for system (3.1) in an infinite spatial domain $(-\infty, \infty)$. It is actually not reasonable for the realistic problem, but rather a mathematical requirement to study traveling waves. The reaction-diffusion epidemic model in a spatially homogeneous habitat with the Neumann boundary condition admits the same basic reproduction number as its ODE counterpart by [23, Theorem 3.4], then we can get the basic reproduction number $\bar{R}_0 = \frac{\beta\bar{S}+(e/c)\nu\bar{S}}{d+\gamma}$ with $\bar{S} = \frac{A}{d}$. It is clear that when $\bar{R}_0 > 1$, system (3.1) has two steady-state solutions, $E_0 = (\bar{S}, 0, 0)$ and $E_1 = (S^*, I^*, W^*)$, where

$$S^* = \frac{c(d+\gamma)}{c\beta + e\nu}, \quad I^* = \frac{c(d+\gamma)(\bar{R}_0 - 1)}{c\beta + e\nu}, \quad W^* = \frac{e(d+\gamma)(\bar{R}_0 - 1)}{c\beta + e\nu}.$$

We assume that the solution has the form $S(x,t) = p(x+at)$, $I(x,t) = q(x+at)$, $W(x,t) = u(x+at)$, where the functions p, q, u are functions of the variable $s = x + at$ and the wave speed parameter a is positive. Then the system (3.1) becomes

$$\begin{cases} ap' &= A - \beta pq - \nu pu - dp + \gamma q, \\ aq' &= \beta pq + \nu pu - dq - \gamma q, \\ au' &= Du'' + eq - cu, \end{cases} \tag{3.2}$$

here prime represents differentiation with respect to the variable s. For the ecological purpose, we need that the traveling waves p, q and u be nonnegative and satisfy the boundary conditions:

$$(p(-\infty), q(-\infty), u(-\infty)) = \left(\frac{A}{d}, 0, 0\right),$$

$$(p(+\infty), q(+\infty), u(+\infty)) = (p^*, q^*, u^*), \tag{3.3}$$

where $p^* = S^*, q^* = I^*, u^* = W^*$.

Denote $u' = v$. Then system (3.2) becomes

$$\begin{cases} ap' &= A - \beta pq - \nu pu - dp + \gamma q, \\ aq' &= \beta pq + \nu pu - dq - \gamma q, \\ u' &= v, \\ Dv' &= av - eq + cu. \end{cases} \tag{3.4}$$

If $\bar{R}_0 > 1$, then system (3.4) has two equilibria

$$\hat{E}_0 = (\bar{S}, 0, 0, 0), \quad \hat{E}_1 = (p^*, q^*, u^*, 0).$$

If there exists a heteroclinic orbit connecting these two critical points, then the traveling wave solutions of the original system exists. We calculate the Jacobian matrix of system (3.4) at $\hat{E}_0$, and the characteristic equation is as follows:

$$(\lambda + \frac{d}{a})(\lambda^3 + C_1\lambda^2 + C_2\lambda + C_3) = 0, \tag{3.5}$$

where $C_1 = \frac{(-\beta\bar{S}+d+\gamma)D-a^2}{aD}$, $C_2 = \frac{\beta\bar{S}-d-\gamma-c}{D}$, $C_3 = \frac{e\nu\bar{S}+c\beta\bar{S}-cd-c\gamma}{aD}$.

Denote

$$P(\lambda) := \lambda^3 + C_1\lambda^2 + C_2\lambda + C_3 = 0. \tag{3.6}$$

Since $\bar{R}_0 > 1$, namely, $C_3 > 0$, then we can easily know that (3.6) has a negative root. It follows from Hurwitz criterion that (3.6) has two roots with positive real parts. In order to determine the conditions under which these two roots are positive real numbers, we consider

$$P_1(\lambda) := \frac{P'(\lambda)}{3} = \lambda^2 + \frac{2C_1}{3}\lambda + \frac{C_2}{3}. \tag{3.7}$$

If $\beta\bar{S} < d + \gamma + c$, then $P'(\lambda) = 0$ has a unique positive root

$$\lambda_* = \frac{1}{3Da}\left(D\beta\bar{S} - D(d+\gamma) + a^2 + \sqrt{(D\beta\bar{S} - Dd - D\gamma + a^2)^2 - 3Da^2(\beta\bar{S} - d - \gamma - c)}\right).$$

Since $P(0) > 0$, then (3.6) has two different positive real roots if and only if

$$P(\lambda_*) < 0, \tag{3.8}$$

and has two conjugate complex roots with positive real parts if $P(\lambda_*) > 0$.

We now transform the condition (3.8) into the relation of the parameters a. We find conditions under which $P(\lambda_*) = 0$ and $P'(\lambda_*) = 0$. Set

$$P(\lambda) = P_1(\lambda)Q_1(\lambda) + R_1(\lambda), \quad P_1(\lambda) = R_1(\lambda)Q_2(\lambda) + R_2(a),$$

where $Q_1(\lambda)$ and $R_1(\lambda)$ are the quotient and remainder of $P(\lambda)$ divided by $P_1(\lambda)$, $Q_2(\lambda)$ and R_2 are the quotient and remainder of $P_1(\lambda)$ divided by $R_1(\lambda)$, respectively. By direct calculations, we see that the sign of $-R_2(a)$ is determined by

$$P_2(a) := b_0a^6 + b_1a^4 + b_2a^2 + b_3,$$

where

$$\begin{aligned}
b_0 &= (c - \beta\bar{S} + d + \gamma)^2 + 4(ev\bar{S} + c\beta\bar{S} - cd - c\gamma) > 0,\\
b_1 &= 2D[(c - \beta\bar{S} + d + \gamma)^3 + c(c - \beta\bar{S} + d + \gamma)^2 + 3(c - \beta\bar{S} + d + \gamma)(ev\bar{S} + c\beta\bar{S} - cd - c\gamma)\\
&+ 6c(ev\bar{S} + c\beta\bar{S} - cd - c\gamma)],\\
b_2 &= D^2(\beta\bar{S} - d - \gamma)^2(c - \beta\bar{S} + d + \gamma)^2\\
&+ 18D^2(\beta\bar{S} - d - \gamma)(c - \beta\bar{S} + d + \gamma)(ev\bar{S} + c\beta\bar{S} - cd - c\gamma)\\
&+ 12D^2(\beta\bar{S} - d - \gamma)^2(ev\bar{S} + c\beta\bar{S} - cd - c\gamma) - 27D^2(ev\bar{S} + c\beta\bar{S} - cd - c\gamma)^2,\\
b_3 &= 4D^3(\beta\bar{S} - d - \gamma)^3(ev\bar{S} + c\beta\bar{S} - cd - c\gamma).
\end{aligned}$$

Lemma 3.1. *Assume $\beta\bar{S} < d + \gamma$. Then there exists a constant $a^* > 0$ such that $P_2(a^*) = 0$ and*

(i) *if $0 < a < a^*$,* (3.6) *has a negative real root and two conjugate complex roots with positive real parts;*
(ii) *if $a = a^*$,* (3.6) *has a negative real root and a positive real multiple root;*
(iii) *if $a > a^*$,* (3.6) *has a negative real root and two different positive real roots.*

Proof. Since $\beta\bar{S} < d + \gamma$, we can obtain that $b_0 > 0, b_1 > 0, b_3 < 0$. By the Descarte's rule of signs, we know that there is a unique $a^* > 0$ such that $P_2(a^*) = 0$, and we have

$$P_2(a)\begin{cases} < 0, & 0 < a < a^*, \\ = 0, & a = a^*, \\ > 0, & a > a^*. \end{cases}$$

We can prove that $P(\lambda_*) = 0$ and $P'(\lambda_*) = 0$ when $a = a^*$. Since $P(\lambda)$ is a decreasing function of a, then we can easily obtain the conclusion. □

Note that if $0 < a < a^*$, the characteristic equation (3.5) has two negative real roots and two conjugate complex roots with positive real parts. Then there exists a two-dimensional unstable manifold based at $\hat{E}_0$ and the critical point $\hat{E}_0$ is a spiral point on the unstable manifold. Therefore, a trajectory approaching $\hat{E}_0$ must have $u(s) < 0$ for some s. This contradicts with the non-negativity of the traveling waves. Naturally, we have the following results.

Theorem 3.2. *Suppose $\beta A < d(d + \gamma)$ and $\bar{R}_0 > 1$. Then for any $0 < a < a^*$, system* (3.2) *has no traveling wave solutions* $(p(x + at), q(x + at), u(x + at))$ *satisfying boundary conditions* (3.3).

In the following, we consider the existence of traveling waves for $a \geq a^*$ and $0 < D \ll 1$. we investigate the existence of traveling waves for (3.1) by the geometric singular perturbation method [54]. To this end, we first show the global stability of the two steady-state solutions $E_0(\bar{S}, 0, 0)$ and $E_1(S^*, I^*, W^*)$ of the following system:

$$\begin{cases} \frac{dS}{dt} = A - \beta SI - \nu SW - dS + \gamma I, \\ \frac{dI}{dt} = \beta SI + \nu SW - dI - \gamma I, \\ \frac{dW}{dt} = eI - cW. \end{cases} \tag{3.9}$$

Lemma 3.3. *If $\bar{R}_0 < 1$, then the solution E_0 of* (3.9) *is globally asymptotically stable and if $\bar{R}_0 > 1$, then the solution E_1 of* (3.9) *is globally asymptotically stable.*

Proof. It is easy to see that E_0 is locally asymptotically stable by the characteristic equation and Hurwitz criterion. From the proof of the local stability of E_0 we know that $s(\bar{B}) < 0 \Leftrightarrow \bar{R}_0 < 1$ by [55], where

$$\bar{B} = \begin{pmatrix} \beta A/d - d - \gamma & \nu A/d \\ e & -c \end{pmatrix}.$$

We then use the same method as Theorem 2.9 to prove that E_0 is globally attractive. From the first two equations in system (3.9), we know that for any $\varepsilon > 0$, there exist $t_3 > 0$, such that $S(t) + I(t) := N(t) \leq A/d + \varepsilon,\ t \geq t_3$. Then we have the following system:

$$\begin{cases} \frac{dI}{dt} \leq \beta(A/d + \varepsilon)I + \nu(A/d + \varepsilon)W - (d + \gamma)I, & t \geq t_3, \\ \frac{dW}{dt} = eI - cW, & t \geq t_3. \end{cases}$$

Consider the following auxiliary system

$$\begin{cases} \frac{dI}{dt} = \beta(A/d + \varepsilon)I + \nu(A/d + \varepsilon)W - (d + \gamma)I, & t \geq t_3, \\ \frac{dW}{dt} = eI - cW, & t \geq t_3. \end{cases}$$

Define

$$\bar{B}(\varepsilon) = \begin{pmatrix} \beta(A/d + \varepsilon) - d - \gamma & \nu(A/d + \varepsilon) \\ e & -c \end{pmatrix}.$$

If $\bar{R}_0 < 1$, then $s(\bar{B}) < 0$. It follows from the continuity of the principal eigenvalue that for sufficiently small $\varepsilon > 0$, $s(\bar{B}(\varepsilon)) < 0$, then by the above auxiliary system and the comparison principle, $\lim_{t\to\infty}(I(t), W(t)) = \mathbf{0}$. Therefore the asymptotic equation of S is as follows

$$\frac{dS(t)}{dt} = A - dS.$$

We then get that $\lim_{t\to\infty} S(t) = \bar{S}$. Therefore the disease-free equilibrium $(\bar{S}, 0, 0)$ is globally attractive.

We next prove the global stability of E_1. Linearizing (3.9) at (S^*, I^*, W^*) and we obtain the following equation

$$\begin{cases} \frac{dS}{dt} = (-\beta I^* - \nu W^* - d)S + (\gamma - \beta S^*)I - \nu S^* W, \\ \frac{dI}{dt} = (\beta I^* + \nu W^*)S + (\beta S^* - d - \gamma)I + \nu S^* W, \\ \frac{dW}{dt} = eI - cW. \end{cases}$$

Then the characteristic equation is as follows

$$\lambda^3 + A_1\lambda^2 + A_2\lambda + A_3 = 0, \tag{3.10}$$

where

$$\begin{aligned} A_1 &= \beta I^* - \beta S^* + \nu W^* + 2d + \gamma + c, \\ A_2 &= (c+d)(\beta I^* - \beta S^* + \nu W^* + 2d + \gamma) - e\nu S^* - d^2, \\ A_3 &= cd(\beta I^* - \beta S^* + \nu W^* + d + \gamma) - de\nu S^*. \end{aligned}$$

Substitute S^*, I^*, W^* by $\frac{c(d+\gamma)}{c\beta+e\nu}$, $\frac{c(d+\gamma)(\bar{R}_0-1)}{c\beta+e\nu}$, $\frac{e(d+\gamma)(\bar{R}_0-1)}{c\beta+e\nu}$, respectively, then we get

$$\begin{aligned} A_1 &= (d+\gamma)(\bar{R}_0 - 1) + d + c + \frac{e\nu(d+\gamma)}{c\beta + e\nu}, \\ A_3 &= cd(d+\gamma)(\bar{R}_0 - 1), \\ A_1A_2 - A_3 &= \left[(d+\gamma)(\bar{R}_0 - 1) + d + c + \frac{e\nu(d+\gamma)}{c\beta+e\nu}\right]\left[(c+d)(d+\gamma)(\bar{R}_0-1) + \frac{de\nu(d+\gamma)}{c\beta+e\nu}\right] \\ &+ cd\left[c + d + \frac{e\nu(d+\gamma)}{c\beta+e\nu}\right]. \end{aligned}$$

$A_1 > 0$, $A_3 > 0$, $A_1A_2 - A_3 > 0$, since $\bar{R}_0 > 1$. By Hurwitz criterion, it is easy to see that all eigenvalues of (3.10) have negative real parts. Thus the solution E_1 of (3.9) is locally asymptotically stable.

Denote $N(t) := S(t) + I(t)$. Then $N(t)$ satisfies

$$\frac{dN(t)}{dt} = A - dN, \quad t > 0.$$

The solution of the above equation is $N(t) = \frac{A}{d} + (N(0) - \frac{A}{d})e^{-dt}$. Thus, equation (3.9) can be written as follows

$$\begin{cases} \frac{dI}{dt} = \beta(N-I)I + \nu(N-I)W - dI - \gamma I, \\ \frac{dW}{dt} = eI - cW. \end{cases}$$

The limit system of the above equation is

$$\begin{cases} \frac{dI}{dt} = \beta(\frac{A}{d} - I)I + \nu(\frac{A}{d} - I)W - dI - \gamma I := \tilde{f}_1, \\ \frac{dW}{dt} = eI - cW := \tilde{f}_2. \end{cases} \tag{3.11}$$

Note that equation (3.11) has two equilibrium $\hat{E}_0(0,0)$ and $\hat{E}_1(I^*, W^*)$ when $\bar{R}_0 > 1$, and the local stability of the two equilibrium is clear. Next, we will show $\hat{E}_1(I^*, W^*)$ is globally stable. Take Dulac function $K(I,W) = \frac{1}{IW}$, then $\frac{\partial(K\tilde{f}_1)}{\partial I} + \frac{\partial(K\tilde{f}_2)}{\partial W} = -\frac{\beta}{W} - \frac{\nu A/d}{I^2} - \frac{e}{W^2} < 0$. By the Bendixson-Dulac criterion, (3.11) has no limit cycles. Therefore, $\hat{E}_1(I^*, W^*)$ is globally asymptotically stable. From the limit equation theory [52, Theorem1.2, 1.3], we know that E_1 of (3.9) is globally asymptotically stable for $\bar{R}_0 > 1$.

□

Note that for sufficiently small $D > 0$, system (3.4) is a singularly perturbed system. Let $s = D\xi$. Then system (3.4) becomes

$$\begin{cases} a\dot{p} &= D(A - \beta pq - \nu pu - dp + \gamma q), \\ a\dot{q} &= D(\beta pq + \nu pu - dq - \gamma q), \\ \dot{u} &= Dv, \\ \dot{v} &= av - eq + cu, \end{cases} \tag{3.12}$$

where dots represent differentiation with respect to ξ. In fact, systems (3.4) and (3.12) are equivalent for $D > 0$, the different time-scales produce two different limiting systems. Letting $D \to 0$ in (3.4), we can get

$$\begin{cases} ap' &= A - \beta pq - \nu pu - dp + \gamma q, \\ aq' &= \beta pq + \nu pu - dq - \gamma q, \\ u' &= v, \\ 0 &= av - eq + cu. \end{cases} \tag{3.13}$$

Thus, the flow of system (3.13) is confined to the set

$$\mathcal{M} = \{(p,q,u,v) \in \mathbb{R}^4 : v = \frac{eq - cu}{a}\},$$

and its dynamics are only determined by the first three equations. On the other hand, taking $D \to 0$ in (3.12), we have

$$\begin{cases} a\dot{p} &= 0, \\ a\dot{q} &= 0, \\ \dot{u} &= 0, \\ \dot{v} &= av - eq + cu. \end{cases} \tag{3.14}$$

Any points in $\mathcal{M}$ are the equilibria of system (3.14). In general, system (3.4) is known as the slow system, because the time-scale s is slow, and (3.12) is referred to as the fast system, v is called the fast variable. $\mathcal{M}$ is the slow manifold. Since the eigenvalues of the linearization of the fast system (3.12) restrict to $\mathcal{M}$ are $0, 0, 0, a$, respectively. Thus $\mathcal{M}$ is normally hyperbolic. According to Fenichel's Invariant Manifold Theorem [56], there exists a three-dimensional locally invariant manifold

$$\tilde{\mathcal{M}} = \{(p, q, u, v) \in \mathbb{R}^4 : v = \frac{eq - cu}{a} + Dg(p, q, u; D)\},$$

for $0 \leq D \leq D_1$, and $D_1 > 0$ is a small constant, g is a smooth function and satisfy $g(\bar{S}, 0, 0; D) = 0$. Returning back to slow time, we get the dynamics on $\tilde{\mathcal{M}}$ are

$$\begin{cases} p' &= \frac{A-\beta pq-\nu pu-dp+\gamma q}{a}, \\ q' &= \frac{\beta pq+\nu pu-dq-\gamma q}{a}, \\ u' &= \frac{eq-cu}{a} + Dg(p, q, u; D). \end{cases} \tag{3.15}$$

When $D = 0$, the flow on $\mathcal{M}$ is

$$\begin{cases} p' &= \frac{A-\beta pq-\nu pu-dp+\gamma q}{a}, \\ q' &= \frac{\beta pq+\nu pu-dq-\gamma q}{a}, \\ u' &= \frac{eq-cu}{a}. \end{cases} \tag{3.16}$$

Since (3.16) and (3.9) are essentially equal, then E_0 is unstable and E_1 is globally asymptotically stable when $\bar{R}_0 > 1$ by Lemma 3.3. Moreover, the eigenvalues of the linearization of (3.16) at E_0 are

$$\begin{aligned} \lambda_1 &= -d/a, \\ \lambda_2 &= -\left(c - \beta\bar{S} + d + \gamma + \sqrt{(c - \beta\bar{S} + d + \gamma)^2 + 4(c\beta\bar{S} - cd - c\gamma + e\nu\bar{S})}\right)/(2a), \\ \lambda_3 &= -\left(c - \beta\bar{S} + d + \gamma - \sqrt{(c - \beta\bar{S} + d + \gamma)^2 + 4(c\beta\bar{S} - cd - c\gamma + e\nu\bar{S})}\right)/(2a). \end{aligned}$$

Since $a \geq a^*$, λ_3 is the unique eigenvalue with positive real part. By [57, Theorem6.1], there exists a one-dimensional unstable manifold based on E_0. Because E_1 is globally stable, the positive branch of the one-dimensional unstable manifold of E_0 for system (3.16), $\mathcal{N}^U(E_0)$, connects to E_1, that is to say, there exists a heteroclinic orbit connecting E_0 and E_1 for system (3.16). Obviously, the manifolds $\mathcal{N}^U(E_0)$ and $\mathcal{N}^S(E_1)$ intersect transversally along the heteroclinic orbit. In the following, we prove that for small $D > 0$, this intersection will persist. To this end, we show that for small $D > 0$, the equilibrium E_1 of system (3.15) is locally asymptotically stable.

Lemma 3.4. *For system* (3.15)*, suppose* $\beta A < d(d + \gamma)$ *and* $\bar{R}_0 > 1$*. Then for any* $a \geq a^*$*, there exists* $D_0 > 0$ *such that* E_1 *is locally asymptotically stable if* $0 < D < D_0$.

Proof. Let $g_1(D) = \frac{\partial g}{\partial p}(E_1)$, $g_2(D) = \frac{\partial g}{\partial q}(E_1)$, $g_3(D) = \frac{\partial g}{\partial u}(E_1)$. Linearizing (3.15) at E_1, we obtain the characteristic equation

$$\lambda^3 + A_1(D)\lambda^2 + A_2(D)\lambda + A_3(D) = 0, \tag{3.17}$$

where

$$\begin{aligned} A_1(D) &= \frac{1}{a}[\beta q^* - \beta p^* + \nu u^* + 2d + \gamma + c - aDg_3(D)], \\ A_2(D) &= \frac{1}{a^2}[(\beta q^* - \beta p^* + \nu u^* + 2d + \gamma)(d + c - aDg_3(D)) - \nu p^*(e + aDg_2(D)) + \nu p^* aDg_1(D) - d^2], \\ A_3(D) &= \frac{1}{a^3}[d(\beta q^* - \beta p^* + \nu u^* + d + \gamma)(c - aDg_3(D)) - d(e\nu p^* + \nu p^* aDg_2(D)) + d\nu p^* aDg_1(D)]. \end{aligned}$$

For any $a \geq a^*$, there exists $\tilde{a} \geq 0$ such that $a = a^* + \tilde{a}$, and let

$$\begin{aligned} &H_1(D, \tilde{a}) = A_1(D, a = a^* + \tilde{a}), \quad H_2(D, \tilde{a}) = A_3(D, a = a^* + \tilde{a}), \\ &H_3(D, \tilde{a}) = A_1(D, a = a^* + \tilde{a})A_2(D, a = a^* + \tilde{a}) - A_3(D, a = a^* + \tilde{a}). \end{aligned}$$

Then we have

$$\begin{aligned} H_1(0, \tilde{a}) &= \frac{1}{a^*+\tilde{a}}\left[(d+\gamma)(\bar{R}_0 - 1) + d + c + \frac{ev(d+\gamma)}{c\beta+ev}\right] > 0, \\ H_2(0, \tilde{a}) &= \frac{1}{(a^*+\tilde{a})^3}\left[cd(d+\gamma)(\bar{R}_0 - 1)\right] > 0, \\ H_3(0, \tilde{a}) &= \frac{1}{(a^*+\tilde{a})^3}\left[(d+\gamma)(\bar{R}_0 - 1) + d + c + \frac{ev(d+\gamma)}{c\beta+ev}\right]\left[(c+d)(d+\gamma)(\bar{R}_0 - 1) + \frac{dev(d+\gamma)}{c\beta+ev}\right] \\ &\quad + \frac{1}{(a^*+\tilde{a})^3}cd\left[c + d + \frac{ev(d+\gamma)}{c\beta+ev}\right] > 0. \end{aligned}$$

Since $H_i(0, \tilde{a}) > 0$, $i = 1, 2, 3$, for any $0 \leq \tilde{a}$, there exists $\hat{D}(\tilde{a}) > 0$ such that $H_i(D, \tilde{a}) > 0$ for any $0 < D < \hat{D}(\tilde{a})$. Let $D_2 = \inf\{\hat{D}(\tilde{a}) | 0 \leq \tilde{a}\}$ and $D_0 = \min\{D_1, D_2\}$. Then $A_1(D) > 0, A_3(D) > 0, A_1(D)A_2(D) - A_3(D) > 0$ for $0 < D < D_0$ and $a^* \leq a$. By Hurwitz criterion, all eigenvalues of (3.17) have negative real parts. Thus, E_1 is locally asymptotically stable. □

Now, by [54, Theorem3.1], we can get the following results

Theorem 3.5. *Suppose* $\beta A < d(d+\gamma)$ *and* $\bar{R}_0 > 1$*, then there exist* $D_0 > 0$ *such that for any* $0 < D < D_0$*, system* (3.2) *has a traveling wave solutions* $(p(x+at), q(x+at), u(x+at))$ *satisfying boundary conditions* (3.3) *for any* $a \geq a^*$.

4. Numerical simulation

In this section, we use the numerical method to explore the influence of spatial heterogeneous transmission and diffusion coefficients on the basic reproduction number R_0.

Let μ_1 be the unique positive eigenvalue of the following eigenvalue problem

$$\begin{cases} -\nabla \cdot (D(x)\nabla\varphi) + c\varphi = \mu \frac{ev(x)\bar{S}}{d+\gamma-\beta(x)\bar{S}}\varphi, & x \in \Omega, \\ \frac{\partial\varphi}{\partial n} = 0, & x \in \partial\Omega, \end{cases}$$

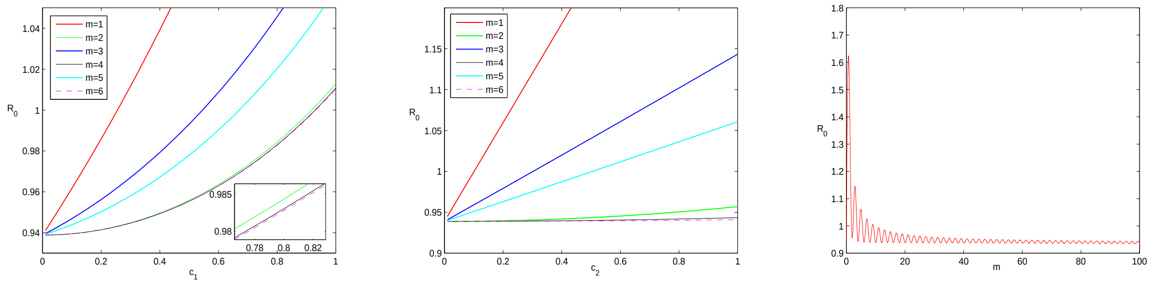
with a strictly positive eigenfunction, where $\bar{S} = A/d$. Then it follows from [23, Theorem3.2, 3.3] that $R_0 = 1/\mu_1$. We can get the variational characterization of R_0 [16, Lemma2.3] as:

$$R_0 = \sup_{\varphi \in H^1(\Omega), \varphi \neq 0} \left\{ \frac{1}{\int_\Omega (D(x)|\nabla\varphi|^2 + c\varphi(x)^2)dx} \int_\Omega \frac{ev(x)\bar{S}}{d+\gamma-\beta(x)\bar{S}}\varphi(x)^2 dx \right\}.$$

We observe that when all parameters are constant, R_0 gives $R_0 = \frac{ev\bar{S}}{c(d+\gamma-\beta\bar{S})}$, which has the same threshold property as $\bar{R}_0$, defined in section 3 for homogeneous system.

We initially investigate the effect of spatially heterogeneous transmission on R_0. We numerically compute R_0 via the above eigenvalue problem. Let $\beta(x) = \beta_0(1 + c_1\sin(m\pi x))$ with $0 \leq c_1 < 1$ or $v(x) = v_0(1 + c_2\sin(m\pi x))$ with $0 \leq c_2 < 1$, and keep other parameters as homogeneous values [13], where $A = 0.86$, $e = 470$, $\beta_0 = 0.0105$, $v_0 = 0.000004$, and we take $c = 0.07$, $d = 0.0056$, $\gamma = 6$, $D = 0.137$. Figure 1 indicates that R_0 is an increasing function of c_1 (or c_2) for various parameter

m, which implies that spatially heterogenous transmission can increase the risk of disease infection and lead to more new infections. It is interesting to note that the effect of m on the basic reproduction number R_0 is not monotonic, but great value of parameter m leads to R_0 decline roughly. It indicates that frequent variation of heterogeneity of transmissions is harmful for disease transmission.



(a) (b) (c)

Figure 1. The influence of spatial heterogeneous transmission on R_0. Parameters: $A = 0.86$, $e = 470$, $c = 0.07$, $d = 0.0056$, $\gamma = 6, D = 0.137, x \in (0, 1)$. (a) $\beta(x) = 0.0105(1 + c_1 \sin(m\pi x))$, $\nu = 0.000004$. (b) $\beta = 0.0105$, $\nu(x) = 0.000004(1 + c_2 \sin(m\pi x))$. (c) $\beta = 0.0105$, $\nu(x) = 0.000004(1 + \sin(m\pi x))$.

To investigate the effect of different diffusion coefficient on R_0, we choose diffusion coefficient as $D(x) = D_0(1 + c_3 \sin(\pi x))$, and let D_0 and c_3 $(0 \leq c_3 < 1)$ vary. It follows from Figure 2(a)-(b) that R_0 keeps constant as D_0 or c_3 varies, given spatially homogenous transmission rates. It implies that no matter what the diffusion rate is, diffusion does not influence the R_0 for spatially homogeneous transmission rates. Whereas, the basic reproduction number R_0 is decreasing with respect to D_0 and c_3(see Figure 2(c)-(d)) when transmission rates are spatially dependent, which indicates that increasing diffusion rate of bacteria/virus can reduce the new infections for spatially heterogeneous transmission rates. It may suggest us that for the case of hospital infection, frequent ventilation is beneficial for controlling of infection.

5. Conclusions and discussion

It is known that many models either on population level or individual level have been proposed to investigate effect of diffusion of disease infection [16, 18, 41, 58], however few combines the epidemic dynamics on population level with dynamics of diffusive bacteria/virus on individual level in one model. Motivated by the dynamics of hospital infections [13], we formulated an SIS-type reaction-diffusion equations, which contains both direct transmission and indirect transmission via free-living and spatially moving bacteria/virus in the contaminated environment. It is worth noting that our proposed model extends the existing reaction-diffusion models by including extra term and heterogeneous diffusive coefficient on the basis of realistic transmission dynamics mainly induced by free-living bacteria [1, 2, 7, 32]. In fact, our model can be simplified to a model, which is similar to a viral dynamic model [40] which includes both virus-to-cell and cell-to-cell transmission. Wang et al. [40] investigated the global stability of disease-free equilibrium and endemic equilibrium in heterogeneous and homogeneous environment by constructing the Lyapunov functional, respectively. Notice that this extra term (i.e., recovery term) brings much difficulty to prove the existence of the traveling wave solutions for small diffusion coefficient, since it is hard to find suitable Lyapunov functional.

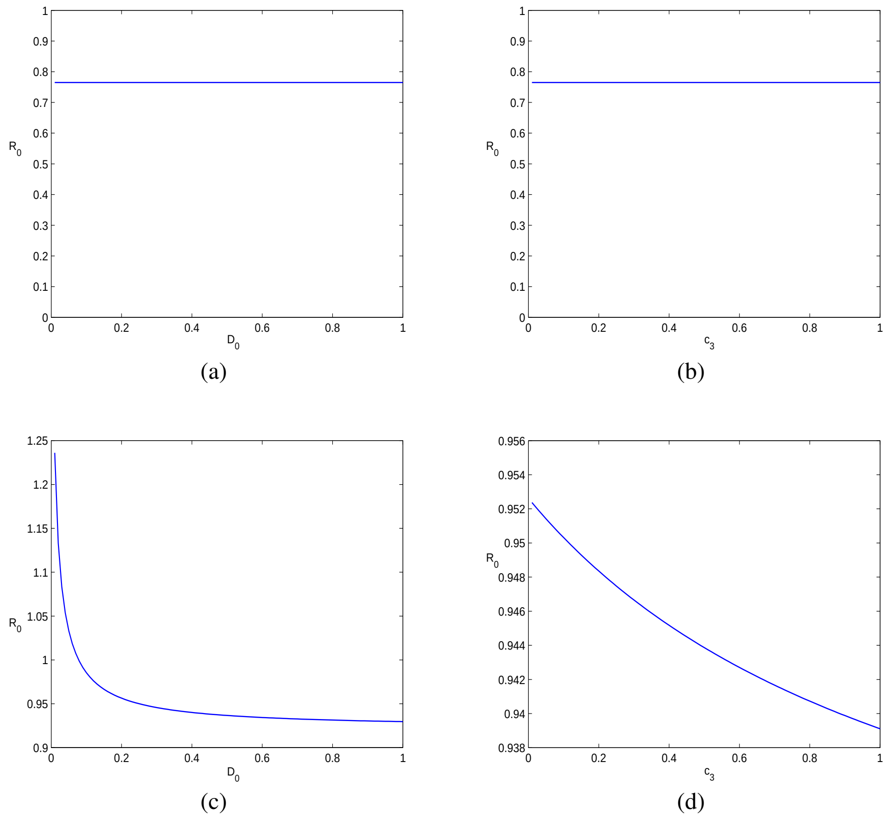


Figure 2. The influence of different diffusion coefficient on R_0. Parameters: $A = 0.86,\ e = 470,\ c = 0.07,\ d = 0.0056,\ \gamma = 7,\ D_0 = 0.137, x \in (0, 1)$. (a) $\beta = 0.0105,\ \nu = 0.000004,\ D(x) = D_0(1+\sin(\pi x))$. (b) $\beta = 0.0105,\ \nu = 0.000004,\ D(x) = D_0(1+c_3 \sin(\pi x))$. (c) $\beta(x) = 0.0105(1 + \cos(\pi x)),\ \nu(x) = 0.000004(1 + \cos(\pi x)),\ D(x) = D_0(1 + \sin(\pi x))$. (d) $\beta(x) = 0.0105(1 + \cos(\pi x)),\ \nu(x) = 0.000004(1 + \cos(\pi x)),\ D(x) = D_0(1 + c_3 \sin(\pi x))$.

We initially studied the globally existence of the solution and proved that the system has a global attractor, then we established the basic reproduction number R_0, which governs whether the disease persists or not. In particular, we obtained that if $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable, while if $R_0 > 1$, the system is uniformly persistent. We also investigated the existence and non-existence of the traveling wave solutions for the spatially homogeneous system. We proved that there exists a critical wave speed below which there is no traveling waves, above which the traveling wave solutions may exist for small diffusion coefficient by the geometric singular perturbation method (see Theorem 3.5). Actually the sum of susceptible and infected in our model converges to A/d, we can utilize this property to effectively reduce the dimensionality of the proposed system. Consequently, we can investigate the dynamic behaviours for the reduced system and then get the corresponding results for the original system by using the theory of asymptotically autonomous semiflows [52] and the theory of chain transitive sets [24]. Numerical results imply that great spatial transmission leads to an increase in new infection, while great diffusion of bacteria/virus results in the new infection decline for spatially heterogeneous environment. This may suggest us a control strategy for control of hospital infection, which is, frequent ventilation, and consequently increasing diffusion of bacteria/virus, is beneficial for reducing new hospital infections.

Acknowledgement

The work was supported by the National Natural Science Foundation of China (NSFC, 11631012(YX), 11571273(YX)).

Conflict of interest

The authors declare there is no conflict of interest.

References

1. J. M. Boyce, G. Potter-Bynoe, C. Chenevert, et al., Environmental contamination due to methicillin-resistant Staphylococcus aureus: possible infection control implications, *Infect. Control Hosp. Epidemiol.*, **18** (1997), 622–627.
2. J. M. Boyce, Environmental contamination makes an important contribution to hospital infection, *J. Hosp. Infect.*, **65** (2007), 50–54.
3. S. J. Dancer, Importance of the environment in meticillin-resistant Staphylococcus aureus acquisition: the case for hospital cleaning, *Lancet Infect. Dis.*, **8** (2008), 101–113.
4. S. J. Dancer, The role of environmental cleaning in the control of hospital acquired infection, *J. Hosp. Infect.*, **73** (2009), 378–385.
5. D. J. Weber and W. A. Rutala, Role of environmental contamination in the transmission of vancomycin-resistant enterococci, *Infect. Control Hosp. Epidemiol.*, **18** (1997), 306–309.
6. A. Rampling, S. Wiseman, L. Davis, et al., Evidence that hospital hygiene is important in the control of methicillin-resistant Staphylococcus aureus, *J. Hosp. Infect.*, **49** (2001), 109–116.
7. D. J. Austin, M. J. Bonten, R. A. Weinstein, et al., Vancomycin-resistant enterococci in intensive-care hospital settings:transmission dynamics, persistence, and the impact of infection control programs, *Proc. Natl. Acad. Sci.*, **96** (1999), 6908–6913.
8. B. S. Cooper, G. F. Medley and G. M. Scott, Preliminary analysis of the transmission dynamics of nosocomial infections:stochastic and management effects, *J. Hosp. Infect.*, **43** (1999), 131–147.
9. H. Grundmann, S. Hori, B. Winter, et al., Risk factors for the transmission of methicillin-resistant Staphylococcus aureusin an adult intensive care unit:fitting a model to the data, *J. Infect. Dis.*, **185** (2002), 481–488.
10. J. Raboud, R. Saskin, A. Simor, et al., Modeling transmission of methicillin-resistant Staphylococcus aureusamong patients admitted to a hospital, *Infect. Control Hosp. Epidemiol.*, **26** (2005), 607–615.
11. V. Sebille and A. J. Valleron, A computer simulation model for the spread of nosocomial infections caused by multidrug-resistant pathogens, *Comput. Biomed. Res.*, **30** (1997), 307–322.

12. V. Sebille, S. Chevret and A. J. Valleron, Modeling the spread of resistant nosocomial pathogens in an intensive-care unit, *Infect. Control Hosp. Epidemiol.*, **18** (1997), 84–92.

13. X. Wang, Y. Xiao, J. Wang, et al., A mathematical model of effects of environmental contamination and presence of volunteers on hospital infections in China, *J. Theor. Biol.*, **293** (2012), 161–173.

14. X. Wang, Y. Xiao, J. Wang, et al., Stochastic disease dynamics of a hospital infection model, *Math. Biosci.*, **241** (2013), 115–124.

15. X. Wang, Y. Chen, W. Zhao, et al., A data-driven mathematical model of multi-drug resistant Acinetobacter baumannii transmission in an intensive care unit, *Sci. Rep.*, **5** (2015), 9478.

16. L. J. S. Allen, B. M. Bolker, Y. Lou, et al., Asymptotic profiles of the steady states for an SIS epidemic reaction-diffusion model, *Discrete Contin. Dyn. Syst. Ser. A*, **21** (2008), 1–20.

17. K. Deng and Y. Wu, Dynamics of a susceptible-infected-susceptible epidemic reaction diffusion model, *Proc. Roy. Soc. Edinburgh Sect. A*, **146** (2016), 929–946.

18. R. Peng, Asymptotic profiles of the positive steady state for an SIS epidemic reaction-diffusion model. Part I, *J. Diff. Equ.*, **247** (2009), 1096–1119.

19. R. Peng and S. Liu, Global stability of the steady states of an SIS epidemic reaction-diffusion model, *Nonlinear Anal.*, **71** (2009), 239–247.

20. R. Peng and F. Yi, Asymptotic profile of the positive steady state for an SIS epidemic reaction-diffusion model: effects of epidemic risk and population movement, *Phys. D*, **259** (2013), 8–25.

21. R. Peng and X.-Q. Zhao, A reaction-diffusion SIS epidemic model in a time-periodic environment, *Nonlinearity*, **25** (2012), 1451–1471.

22. Y. Wu and X. Zou, Asymptotic profiles of steady states for a diffusive SIS epidemic model with mass action infection mechanism, *J. Diff. Equ.*, **261** (2016), 4424–4447.

23. W. Wang and X.-Q. Zhao, Basic reproduction numbers for reaction-diffusion epidemic models, *SIAM J. Appl. Dyn. Syst.*, **11** (2012), 1652–1673.

24. X.-Q. Zhao, *Dynamical Systems in Population Biology*, Springer, New York, 2017.

25. L. Zhang, Z. C. Wang and X.-Q. Zhao, Threshold dynamics of a time periodic reaction-diffusion epidemic model with latent period, *J. Diff. Equ.*, **258** (2015), 3011–3036.

26. L. Zhang and Z.C. Wang, A time-periodic reaction-diffusion epidemic model with infection period, *Z. Angew. Math. Phys.*, **67** (2016), 117, 14 pp.

27. R. Cui and Y. Lou, A spatial SIS model in advective heterogeneous environments, *J. Diff. Equ.*, **261** (2016), 3305–3343.

28. R. Cui, K. Y. Lam and Y. Lou, Dynamics and asymptotic profiles of steady states of an epidemic model in advective environments, *J. Diff. Equ.*, **263** (2017), 2343–2373.

29. K. Kuto, H. Matsuzawa and R. Peng, Concentration profile of the endemic equilibria of a reaction-diffusion-advection SIS epidemic model, *Calc. Var.*, **56** (2017), 1–28.

30. H. Li, R. Peng and F.-B. Wang, Vary total population enhances disease persistence: qualitative analysis on a diffusive SIS epidemic model, *J. Diff. Equ.*, **262** (2017), 885–913.

31. H. Li, R. Peng and Z.-A. Wang, On a diffusive susceptible-infected-susceptible epidemic model with mass action mechanism and birth-death effect: analysis, simulations, and comparison with other mechanisms, *SIAM J. Appl. Math.*, **78** (2018), 2129–2153.

32. S. Bonhoeffer, R. M. May, G. M. Shaw, et al., Virus dynamics and drug therapy, *Proc. Natl. Acad. Sci.*, **94** (1997), 6971–6976.

33. M. A. Nowak, S. Bonhoeffer, A. M. Hill, et al., Viral dynamics in hepatitis B virus infection, *Proc. Natl. Acad. Sci.*, **93** (1996), 4398–4402.

34. C. M. Brauner, D. Jolly, L. Lorenzi, et al., Heterogeneous viral environment in a HIV spatial model, *Discrete Contin. Dyn. Syst. Ser. B*, **15** (2011), 545–572.

35. H. Pourbashash, S. S. Pilyugin, P. De Leenheer, et al., Global analysis of within host virus models with cell-to-cell viral transmission, *Discrete Contin. Dyn. Syst. Ser. B*, **19** (2014), 3341–3357.

36. X. Ren, Y. Tian, L. Liu, et al., A reaction-diffusion within-host HIV model with cell-to-cell transmission, *J. Math. Biol.*, **76** (2018), 1–42.

37. F. Wang, Y. Huang and X. Zou, Global dynamics of a PDE in-host viral model, *Appl. Anal.*, **93** (2014), 2312–2329.

38. K. Wang and W. Wang, Propagation of HBV with spatial dependence, *Math. Biosci.*, **210** (2007), 78–95.

39. K. Wang, W. Wang and S. Song, Dynamics of an HBV model with diffusion and delay, *J. Theor. Biol.*, **253** (2008), 36–44.

40. J. Wang, J. Yang and T. Kuniya, Dynamics of a PDE viral infection model incorporating cell-to-cell transmission, *J. Math. Anal. Appl.*, **444** (2016), 1542–1564.

41. Y. Wu and X. Zou, Dynamics and profiles of a diffusive host-pathogen system with distinct dispersal rates, *J. Diff. Equ.*, **264** (2018), 4989–5024.

42. Y. Yang, J. Zhou, X. Ma, et al., Nonstandard finite difference scheme for a diffusive within-host virus dynamics model with both virus-to-cell and cell-to-cell transmissions, *Comput. Math. Appl.*, **72** (2016), 1013–1020.

43. H. L. Smith, *Monotone Dynamical Systems: An Introduction to the Theory of Competitive and Cooperative Systems*, *Math. Surveys Monogr.*, **41** (1995). http://b-ok.cc/book/2625388/3a5dac

44. R. Martin and H. L. Smith, Abstract functional differential equations and reaction-diffusion systems, *Trans. AMS.*, **321** (1990), 1–44.

45. Y. Lou and X.-Q. Zhao, A reaction-diffusion malaria model with incubation period in the vector population, *J. Math. Biol.*, **62** (2011), 543–568.

46. M. H. Protter and H. F. Weinberger, *Maximum Principles in Differential Equations*, Springer-Verlag, New York, 1984.

47. K. Deimling, *Nonlinear Functional Analysis*, Springer-Verlag, Berlin, 1985.

48. S. B. Hsu, F. B. Wang and X.-Q. Zhao, Dynamics of a periodically pulsed bio-reactor model with a hydraulic storage zone, *J. Dyn. Differ. Equ.*, **23** (2011), 817–842.

49. G. R. Sell and Y. You, *Dynamics of Evolutionary Equations*, Springer-Verlag, New York, 2002.

50. P. Magal and X.-Q. Zhao, Global attractors and steady states for uniformly persistent dynamical systems, *SIAM. J. Math. Anal.*, **37** (2005), 251–275.

51. S. B. Hsu, F. B. Wang and X.-Q. Zhao, Global dynamics of zooplankton and harmful algae in flowing habitats, *J. Diff. Equ.*, **255** (2013), 265–297.

52. H. R. Thieme, Convergence results and a Poincar -Bendixson trichotomy for asymptotically autonomous differential equations, *J. Math. Biol.*, **30** (1992), 755–763.

53. H. L. Smith and X-Q. Zhao, Robust persistence for semidynamical systems, *Nonlinear Anal.*, **47** (2001), 6169–6179.

54. P. Szmolyan, Transversal heteroclinic and homoclinic orbits in singular perturbation problems, *J. Diff. Equ.*, **92** (1991), 252–281.

55. W. Wang and X.-Q. Zhao, An epidemic model in a patchy environment, *Math. Biosci.*, **190** (2004), 97–112.

56. N. Fenichel, Geometric singular perturbation theory for ordinary differential equations, *J. Diff. Equ.*, **31** (1979), 53–98.

57. P. Hartman, *Ordinary Differential Equations*, Wiley and Sons, Baltimore, 1973. `http://b-ok.cc/book/981126/b95a4b`

58. X. Lai and X. Zou, Repulsion Effect on Superinfecting Virions by Infected Cells, *Bull. Math. Biol.*, **76** (2014), 2806–2833.

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