SUFFICIENT CONDITIONS FOR GLOBAL DYNAMICS OF A VIRAL INFECTION MODEL WITH NONLINEAR DIFFUSION

WEI WANG∗
College of Mathematics and Systems Science
Shandong University of Science and Technology
Qingdao 266590, China

WANBIAO MA
Department of Applied Mathematics, School of Mathematics and Physics
University of Science and Technology Beijing
Beijing 100083, China

XIULAN LAI
Institute for Mathematical Sciences, Renmin University of China
Beijing 100872, China

(Communicated by Yang Kuang)

Abstract. In this paper, we study the global dynamics of a viral infection model with spatial heterogeneity and nonlinear diffusion. For the spatially heterogeneous case, we first derive some properties of the basic reproduction number $R_0$. Then for the auxiliary system with quasilinear diffusion, we establish the comparison principle under some appropriate conditions. Some sufficient conditions are derived to ensure the global stability of the virus-free steady state. We also show the existence of the positive non-constant steady state and the persistence of virus. For the spatially homogeneous case, we show that $R_0$ is the only determinant of the global dynamics when the derivative of the function $g$ with respect to $V$ (the rate of change of infected cells for the repulsion effect) is small enough. Our simulation results reveal that pyroptosis and Beddington-DeAngelis functional response function play a crucial role in the controlling of the spreading speed of virus, which are some new phenomena not presented in the existing literature.

1. Introduction. Reaction-diffusion equation models have been developed from the cellular level to discuss the influence of spatial mobility of cells and viral infection dynamics (see, e.g. [8, 9, 13, 15, 18, 19, 20, 24, 27]). However, to the best of our knowledge, very little has been known and undertaken on threshold dynamics for viral infection dynamics from the genetic level. In [24], we proposed

2020 Mathematics Subject Classification. Primary: 34D20, 35C07; Secondary: 35Q92, 92D3.

Key words and phrases. Nonlinear diffusion, spatial heterogeneity, quasilinearly parabolic system, basic reproduction number, global dynamics.

This work is supported by the NNSF of China (11901360) to W. Wang and supported by the National Key R-D Program of China (No. 2017YFF0207401) and the NNSF of China (No. 11971055) W. Ma.

∗ Corresponding author: Wei Wang.
Table 1. Summary of model parameters.

| Parameters | Descriptions |
|------------|--------------|
| $\xi (x)$ | Generation of uninfected cells |
| $\beta (x)$ | Infection rate |
| $q (x)$ | Pyroptosis effect of inflammatory cytokines on uninfected cells |
| $\alpha_1 (x)$ | Death rate due to pyroptosis |
| $\alpha_2 (x)$ | Production rate of inflammatory cytokines |
| $k (x)$ | Production rate of virus |
| $d_U (x)$ | Death rate of uninfected cells |
| $d_V (x)$ | Death rate of infected cells |
| $d_M (x)$ | Death rate of inflammatory cytokines |
| $d_\omega (x)$ | Death rate of virus |
| $D_0$ | Diffusion rate of cells (uninfected cells and infected cells) |
| $D_1$ | Diffusion rate of inflammatory cytokines |
| $D_2$ | Diffusion rate of virus |
| $a$ | Rate of the inhibitory effect on virus |
| $b$ | Rate of the inhibitory effect on inflammatory cytokines |

A reaction-diffusion equation model from the genetic level to describe caspase-1-mediated pyroptosis by inflammatory cytokines released from infected cells, which is governed by a set of partial differential equations:

$$
\begin{align*}
\frac{\partial U(t, x)}{\partial t} &= D_0 \Delta U + \xi (x) - \frac{\beta (x) U(t, x) \omega(t, x)}{1 + \omega(t, x)} - d_U U(t, x) - q(x) U(t, x) M(t, x), \\
\frac{\partial V(t, x)}{\partial t} &= D_0 \Delta V + \int_{\Gamma} \frac{\beta (y) U(y, t - \tau) \omega(y, t - \tau) dy}{1 + \omega(y, t - \tau)} - d_V V(t, x), \\
\frac{\partial M(t, x)}{\partial t} &= D_1 \Delta M + \alpha_2 (x) V(t, x) - d_M M(t, x), \\
\frac{\partial \omega(t, x)}{\partial t} &= D_2 \Delta \omega + k(x) V(t, x) - d_\omega \omega(t, x),
\end{align*}
$$

where $U(t, x), V(t, x), M(t, x)$ and $\omega(t, x)$ are the concentrations of uninfected cells, infected cells, inflammatory cytokines and virus at time $t$ and location $x$, respectively. The detailed biological meanings for model (1) can be found in Table 1. In [24], we derived the threshold-type result in terms of the basic reproduction number for the spatially heterogeneous case in a bounded domain. We also studied traveling wave phenomena for the spatially homogeneous case in an unbounded domain.

In model (1), the saturation response $\beta (x) U \omega / (1 + \omega)$, is adopted. It is widely known that the Beddington-DeAngelis functional response is similar to the saturation response, which was introduced by Beddington [3] and DeAngelis [4]. However, Beddington-DeAngelis functional response has an extra term $a_2 U$ in the denominator modeling mutual interference among uninfected cells, which is defined by

$$
\frac{\beta (x) U \omega}{1 + a_1 \omega + a_2 U},
$$

where $a_1, a_2 \geq 0$ are constants. Similar to [7, 25], we also incorporate Beddington-DeAngelis functional response function into viral infection dynamical models. This constitutes one of main motivations of the present study.
Recently, Doceul et al reported that vaccinia virus can spread much faster than its free diffusion, which is also found in some other kinds of virus [6]. The spread of viruses can be promoted by the high concentration of infected cells [6]. A new mechanism which is called the repulsion of superinfecting virions by infected cells was proposed to explain this interesting phenomenon [6]. In order to explain this interesting phenomenon, Lai and Zou proposed the following reaction-diffusion system with repulsion effect [8]:

\[
\begin{aligned}
\frac{\partial U(t, x)}{\partial t} &= D_0 \Delta U + \xi(x) - \beta(x)U(t, x)\omega(t, x) - d_U U(t, x), \\
\frac{\partial V(t, x)}{\partial t} &= D_0 \Delta V + \beta(x)U(t, x)\omega(t, x) - d_V V(t, x), \\
\frac{\partial \omega(t, x)}{\partial t} &= \nabla \cdot (D_\omega(V)\nabla \omega) + k(x)V(t, x) - d_\omega \omega(t, x).
\end{aligned}
\]

In model (2), the flux of viruses relies not only on the concentration gradient, but also on the concentration of infected cells. Namely,

\[
\vec{J}_\omega = D_\omega(V)(-\nabla \omega),
\]

where \(D_\omega(V)\) was an increasing function of infected cells, which was assumed to be

\[
D_\omega(V) = D_2 + g(V),
\]

where \(D_2\) is the free diffusion rate of virus and \(g \in C^2(R_+, R_+)\), \(g(0) = 0\) and is an increasing function of \(V\) [8]. In model (2), the well-posedness of solutions, the basic reproduction number and the linear stabilities of steady states were discussed. From the numerical simulations, it has been found that the repulsion effect can promote the asymptotic spreading speed of virus. However, the global stability analysis of model (2) is not given due to a technical difficulty. Recently, in [9], Li and Ma performed theoretical analysis for the global stability analysis of model (2). These results inspire us to incorporate repulsion effect into more general viral infection dynamical models both mathematically and biologically. This is another motivation of this study.

To make things not too complicated (as the nonlinear diffusion which is described by repulsion effect, it has already made the global analysis very challenging), we neglect the nonlocal time delay in model (1). With these considerations, we study the global dynamics of the following reaction-diffusion system:

\[
\begin{aligned}
\frac{\partial U(t, x)}{\partial t} &= D_0 \Delta U + \xi(x) - \beta(x)U(t, x)(1 + a_1 \omega(t, x) + a_2 U(t, x)) + \frac{1 + b M(t, x)}{1 + b M(t, x)} - d_U U(t, x), \\
\frac{\partial V(t, x)}{\partial t} &= D_0 \Delta V + \beta(x)U(t, x)(1 + a_1 \omega(t, x) + a_2 U(t, x)) - (d_V + \alpha_1) V(t, x), \\
\frac{\partial M(t, x)}{\partial t} &= D_1 \Delta M + \alpha_2 V(t, x) - d_M M(t, x), \\
\frac{\partial \omega(t, x)}{\partial t} &= \nabla \cdot (D_\omega(V)\nabla \omega) + k(x)V(t, x) - d_\omega \omega(t, x),
\end{aligned}
\]

with zero-flux boundary conditions

\[
\frac{\partial U(t, x)}{\partial \nu} = \frac{\partial V(t, x)}{\partial \nu} = \frac{\partial M(t, x)}{\partial \nu} = \frac{\partial \omega(t, x)}{\partial \nu} = 0, \quad x \in \partial \Omega, \quad t > 0,
\]
where \( \nu \) is the outward normal to \( \partial \Omega \). For the initial conditions, we assume
\[
U(x, 0) = U_0(x) > 0, \quad V(x, 0) = V_0(x) \geq 0,
M(x, 0) = M_0(x) \geq 0, \quad \omega(x, 0) = \omega_0(x) \geq 0.
\] (5)

Our main results on the global dynamics of model (3) on a bounded domain include:

- Some properties of \( R_0 \) are derived.
- For the auxiliary system with quasilinear diffusion, we establish the comparison principle.
- Virus-free steady state of model (3) is globally asymptotically stable when conditions (8) and (11) hold.
- We show the existence of positive non-constant steady state and the persistence of virus when conditions (8) and (16) hold.
- For the spatially homogeneous case, we show that \( R_0 \) is the only determinant of the global dynamics when the derivative of the function \( g \) with respect to \( V \) is small enough.

2. Some notations. Throughout this paper, let \( R^n_+ \) be the positive cone in \( R^n \), i.e.,
\[
R^n_+ = \{(a_1, a_2, \cdots, a_n)^T \in R^n \mid a_i \geq 0, \ i = 1, 2 \cdots n\}.
\]

\( W^{m,p}(\Omega, R^n) \) for \( m \geq 1 \) and \( 1 < p \leq +\infty \) denotes the Sobolev space of \( R^n \)-valued functions with norm \( \|\cdot\|_{m,p} \). Let \( L^p(\Omega) \) (\( 1 \leq p \leq +\infty \)) denote the usual Lebesgue space in a bounded domain \( \Omega \subset R^n \) with norm
\[
\|\cdot\|_p = \left( \int_\Omega |\cdot|^p \, dx \right)^{\frac{1}{p}}
\]
for \( 1 \leq p < +\infty \) and \( \|\cdot\|_\infty = \text{ess sup}_{x \in \Omega} |\cdot| \). When \( p \in (n, +\infty) \), then
\[
W^{1,p}(\Omega, R^n) \hookrightarrow C(\Omega, R^n)
\]
which is the space of \( R^n \)-valued continuous functions.

Set
\[
X^n_+ := W^{1,p}(\Omega, R^n),
\]
then \( X^n_+ \) is the positive cone of \( X^n \), i.e.,
\[
X^n_+ = W^{1,p}(\Omega, R^n_+).
\]
Then \( X^n_+ \) deduces a partial order and \( (X^n, X^n_+) \) is a strongly ordered space. We assume that \( p > n \), and \( n \) is a positive integer; \( \text{Int}(\Omega) \) is the interior of \( \Omega \).

3. Basic reproduction number. Rewrite model (3) as
\[
\begin{cases}
\phi_t + A(\phi)\phi = F(x, \phi), \ x \in \phi, \ t > 0, \\
\mathcal{H}\phi = 0, \ x \in \partial \Omega, \ t > 0,
\end{cases}
\]
where
\[
(A(\phi))_{j,k} = -\partial_j (a_{j,k}(\phi) \partial_k \phi), \quad \mathcal{H}\phi = \frac{\partial \phi}{\partial \nu},
\]
and \( a_{j,k} = a(\phi) \delta_{j,k} (1 \leq j, k \leq 4) \), and
\[
a(\phi) = \begin{pmatrix}
D_0 & 0 & 0 & 0 \\
0 & D_0 & 0 & 0 \\
0 & 0 & D_1 & 0 \\
0 & 0 & 0 & D_{\omega}(\phi_2)
\end{pmatrix},
\]
for $\phi = (\phi_1, \phi_2, \phi_3, \phi_4) \in X^4_\delta$. Here $\delta_{j,k}$ is the Kronecker delta function, and

$$F(x, \phi) = \begin{pmatrix}
\xi(x) - \frac{\beta(x)U_\omega}{1 + a_1^2 + a_2U} - d_UU - \frac{q(x)U_\omega}{1 + bM}
\frac{\beta(x)U_\omega}{1 + a_1^2 + a_2U} - (d_V + \alpha_1)V
\alpha_2(x)V - d_M M
\frac{k(x)V - d_\omega \omega}{4}
\end{pmatrix},$$

for $\phi = (U, V, M, \omega)$.

Clearly, $a(\phi) \in C^2(R^4_+ \cup R^4_0)$, where we identified $L(R^4_0)$ with the space of $4 \times 4$ real matrices. Furthermore, the boundary value problem is normally elliptic [2]. Hence, we get the following result.

**Theorem 3.1.** For every initial value $(U_0, V_0, M_0, \omega_0) \in X^4_\delta$, model (3) has a unique solution which satisfies

$$(U, V, M, \omega) \in C([0, +\infty), X^4_\delta) \cap C^{1,2}((0, +\infty) \times \Omega, R^4).$$

Furthermore, there is a constant $\zeta$ such that

$$0 < U(t, x) < \zeta, \quad 0 \leq V(t, x), \quad M(t, x), \quad \omega(t, x) < \zeta$$

for all $(t, x) \in [0, +\infty) \times \Omega$.

**Proof.** By [2, Theorems 14.4 and 14.6] or [1, Theorem 1], it follows that model (3) admits a unique classical solution $(U, V, M, \omega)$ defined on $[0, \delta_0) \times \Omega$ such that

$$(U, V, M, \omega) \in C((0, \delta_0), X^4_\delta) \cap C^{2,1}((0, \delta_0) \times \Omega, R^4),$$

where $\delta_0 > 0$ is the maximal interval of existence of the solution of model (3). From [2, Theorem 15.1], the nonnegativity of the solution of model (3) can be obtained. To show $\delta_0 = +\infty$, motivated by [1], we only need to prove that the solution of model (3) is bounded.

Denote $W = U + V$, it follows that

$$\frac{\partial W}{\partial t} = D_0 \Delta (U + V) + \xi(x) - \frac{q(x)U(t, x)M(t, x)}{1 + bM(t, x)} - d_UU - (d_V + \alpha_1)V \leq D_0 \Delta W + \bar{\xi} - gW,$$

where $\bar{\xi} = \max_{x \in \Omega} \xi(x)$ and $g = \min\{d_U, d_V + \alpha_1\}$.

In view of [10], $\bar{\xi}/g$ is the globally attractive steady state for the scalar parabolic equations

$$\begin{cases}
\frac{\partial W}{\partial t} = D_0 \Delta W + \bar{\xi} - gW, & x \in \Omega, \ t > 0,
\frac{\partial W}{\partial \nu} = 0, & x \in \partial \Omega, \ t > 0.
\end{cases}$$

According to the parabolic comparison theorem [16, Theorem 7.3.4], it can be shown that $U + V$ is bounded. Since $U$ and $V$ are nonnegative, $U(t, x)$ and $V(t, x)$ of model (3) are bounded, namely, $0 \leq U(t, x) \leq U_M$ and $0 \leq V(t, x) \leq V_M$, where $U_M$ and $V_M$ are positive constants.

From the third equation of model (3), we have

$$\frac{\partial M}{\partial t} \leq D_1 \Delta M + \overline{\alpha}_2 V_M - d_M M,$$

hence $M$ is bounded, namely, $0 \leq M(t, x) \leq M_M$, where $M_M$ is a positive constant.
Let $\kappa = \max_{x \in \Omega} k(x)$ and $\omega_M = \frac{\kappa V_M}{d_\omega}$. For any $V$, the operator $F$ is defined

$$F \omega = \omega_t - \nabla \cdot (D_\omega(V) \nabla \omega) - k(x)V + d_\omega \omega.$$ 

We know that $F \omega = 0$. On the other hand, we find

$$F \omega_M = d_\omega \omega_M - k(x)V \geq d_\omega \omega_M - \kappa V_M = \kappa V_M - \kappa V_M = 0 = F \omega.$$ 

On the boundary, $\frac{\partial \omega_M}{\partial \nu} = 0$ holds. Hence, $\omega = \omega_M$ is an upper solution of the forth equation in model (3). The comparison principle [16, Theorem 7.3.4] indicates that $0 \leq \omega(t, x) \leq \omega_M$. Thus, the solution $(U, V, M, \omega)$ of model (3) is bounded. By [1], this implies $\delta_0 = +\infty$, meaning that the solution of model (3) exists globally. The proof is complete.

\textbf{Lemma 3.2.} Let $\Phi(t) : X_+^4 \to X_+^4$ be the solution semiflow associated with model (3) in the sense that

$$\Phi(t) \varphi = (U(t, \cdot, \cdot, \cdot), V(t, \cdot, \cdot, \cdot), M(t, \cdot, \cdot, \cdot), \omega(t, \cdot, \cdot, \cdot)), \quad \forall \ t \geq 0, \ \varphi \in X_+^4,$$

where $(U(t, x, \cdot, \cdot), V(t, x, \cdot, \cdot), M(t, x, \cdot, \cdot), \omega(t, x, \cdot, \cdot))$ is the solution of model (3). Then $\Phi(t)$ admits a global attractor in $X_+^4$.

\textbf{Proof.} We first show the compactness of $\Phi(t)$ on $X_+^4$. Since $D_0 > 0$ and $D_1 > 0$, it is well known that the first three components $U(t, x), V(t, x)$ and $M(t, x)$ of model (3) are compact. To verify the compactness of the forth component $\omega(t, x)$ of model (3), we assume that $\Gamma(t, x, y, D(t, x))$ is the Green function associated with the following linear parabolic equation

$$\begin{cases}
\frac{\partial z}{\partial t} = \nabla \cdot (D(t, x) \nabla z), \ x \in \Omega, \ t > 0, \\
\frac{\partial z}{\partial \nu} = 0, \ x \in \partial \Omega, \ t > 0,
\end{cases}$$

where

$$D(t, x) = D_\omega(V) = D_2 + g(V) \leq D_2 + g(\zeta) = M,$$

and $\Gamma(t, x, y, D(t, x))$ is a twice continuously differentiable function of $x$. From model (3), we have

$$\omega(t, x; \varphi) = e^{-d_\omega t} \int_\Omega \Gamma(t, x, y, D(t, x)) \varphi_4(y)dy$$

$$+ \int_0^t e^{-d_\omega (t-s)} \int_\Omega \Gamma(t, x, y, D(t, x))k(y)V(t-s, y)dyds, \ \varphi_4 \in X_+.$$ 

For any $x_1, x_2 \in \Omega$ with $x_1 < x_2$, we get

$$| \omega(t, x_1; \varphi) - \omega(t, x_2; \varphi) |$$

$$\leq \int_\Omega | \Gamma_x(t, \eta, y, D(t, \eta)) || \varphi_4(y) | dy | x_1 - x_2 |$$

$$+ \int_0^t e^{-d_\omega (t-s)} \int_\Omega | \Gamma_x(t, \eta, y, D(t, \eta)) || k(y)V(t-s, y) | dyds | x_1 - x_2 |,$$

where $\eta \in (x_1, x_2)$. Since $D(t, x), \varphi_4(x)$ and $k(x)$ are continuous and bounded uniformly for $t \in [0, +\infty)$ and $x \in \bar{\Omega}$, there is a positive constant $\kappa$ satisfying

$$| \omega(t, x_1; \varphi) - \omega(t, x_2; \varphi) | \leq \kappa | x_1 - x_2 |.$$
Thus, for any \( \varepsilon > 0 \), there exists \( \delta = \varepsilon / \kappa \) such that when \( |x_1 - x_2| \leq \delta, \forall x_1, x_2 \in \Omega \), we get
\[
| \omega(t, x_1; \varphi) - \omega(t, x_2; \varphi) | \leq \varepsilon,
\]
which indicates that \( \omega(t, x; \varphi) \) is equicontinuous on \( \Omega \). Note that Theorem 3.1 shows that \( \omega(t, x) \) is uniformly bounded for \( t \) and \( x \). Hence, \( \omega(t, x; \varphi) \) is compact. Furthermore, from the proof of Theorem 3.1, we have that \( \Phi(t) \) is point dissipative on \( X^+ \), and forward orbits of bounded subsets of \( X^+ \) for \( \Phi(t) \) are bounded. Thus, \( \Phi(t) \) admits a global attractor in \( X^+ \). The proof is complete. \( \square \)

The following lemma implies the existence of virus-free steady state, which is from [24].

**Lemma 3.3.** Model (3) admits a unique virus-free steady state \( E_0 = \left( \hat{U}(x), 0, 0 \right) \). Furthermore, if \( \xi(x) \) is a constant \( \xi \) for all \( x \in \Omega \), then \( \hat{U}(x) = \frac{\xi}{d_V} \).

For any \( \varphi = (\varphi_2, \varphi_4) \in X^1 \times X^1 \) and each \( t \geq 0, N(t)\varphi(x) = (N_2(t)\varphi_2(x), N_4(t)\varphi_4(x)) \), where \( N_2(t) \) and \( N_4(t) : X^1 \to X^1 \) are the strongly continuous semigroups associated with \( D_0\Delta - (d_V + \alpha_1) \) and \( D_2\Delta - d_\omega \), subject to (4), respectively. Namely,
\[
[N_2(t)\varphi_2](x) = e^{-(d_V + \alpha_1)t} \int_{\Omega} \Gamma(t, x, y, D_0)\varphi_2(y)dy
\]
and
\[
[N_4(t)\varphi_4](x) = e^{-d_\omega t} \int_{\Omega} \Gamma(t, x, y, D_2)\varphi_4(y)dy,
\]
where \( \Gamma(t, x, y, D_0) \) and \( \Gamma(t, x, y, D_2) \) are the Green functions associated with \( D_0\Delta \) and \( D_2\Delta \) subject to (4), respectively. Thus, \( M(t) \) is a positive \( C_0 - \)semigroup.

Below, as in [5, 21], we define the basic reproduction number of model (3). To this end, we define the positive linear operator by
\[
C(\varphi)(x) = (C_2(\varphi)(x), C_4(\varphi)(x)), \ \forall \varphi = (\varphi_2, \varphi_4) \in X^1 \times X^1, \ x \in \Omega,
\]
where
\[
C_2(\phi)(x) = \frac{\beta(x)\hat{U}(x)}{1 + a_2\hat{U}(x)} \varphi_4(x), \ \ C_4(\phi)(x) = k(x)\varphi_2(x).
\]
Then the basic reproduction number is defined by the spectral radius of the following operator
\[
\mathcal{L}(\varphi) = \int_0^{+\infty} C(N(t)\varphi)dt = C \int_0^{+\infty} (N(t)\varphi)dt,
\]
that is,
\[
R_0 = r(\mathcal{L}).
\]

**Lemma 3.4.** The following properties of \( R_0 \) hold:

(i)
\[
R_0 \leq \max_{x \in \Omega} \sqrt{\frac{\beta(x)\hat{U}(x)k(x)}{(1 + a_2\hat{U}(x))(d_V + \alpha_1)d_\omega}}.
\]

(ii)
\[
R_0 \geq \min_{x \in \Omega} \sqrt{\frac{\beta(x)\hat{U}(x)k(x)}{(1 + a_2\hat{U}(x))(d_V + \alpha_1)d_\omega}}.
\]
Proof. For \( \forall \varphi \in X^2 \), one gets
\[
L(\varphi) = \begin{pmatrix}
\beta(x)\hat{U}(x) + \infty \\
1 + a_2\hat{U}(x)
\end{pmatrix}
+ \infty
\int_0^\infty e^{-d_\omega t} \int_\Omega \Gamma(t, x, y, D_2)\varphi_4(y)dydt = \mu \varphi_2,
\]
and
\[
k(x) \int_0^\infty e^{-(dV + \alpha_1)t} \int_\Omega \Gamma(t, x, y, D_0)\varphi_2(y)dydt = \mu \varphi_4,
\]
which implies that
\[
K(\varphi_2) = \mu^2 \varphi_2,
\]
where
\[
K(\varphi_2)(x) = \beta(x)\hat{U}(x) + \infty
\int_0^\infty e^{-d_\omega t} \int_\Omega \Gamma(t, x, y, D_2)\varphi_4(y)dydt,
\]
with
\[
\varphi_4(y) = k(y) \int_0^\infty e^{-(dV + \alpha_1)t} \int_\Omega \Gamma(t, y, z, D_0)\varphi_2(z)dzdt.
\]
It is easy to see that \( K \) is linear, compact and strongly positive. Hence, \( \dim\mathcal{N}(\mu^2I - K) < +\infty \). Thus, we have
\[
\dim\mathcal{N}(\mu I - L) \leq \dim\mathcal{N}(\mu^2I - K) < +\infty.
\]
By using the same proof as that of [23, Theorem 3.1], it follows that \( \mu I - L \) is semi-Fredholm for all \( \mu > 0 \), and
\[
r(K) = (r(L))^2 = B_0^2.
\]
Furthermore, by applying the fact that, for \( x \in \Omega, \ t > 0, \ D_0 > 0, \ D_2 > 0, \)
\[
\int_\Omega \Gamma(t, x, y, D_0)dy = 1,
\]
and
\[
\int_\Omega \Gamma(t, x, y, D_2)dy = 1,
\]
we get
\[
\|K(\varphi_2)\| \leq \frac{\beta\hat{U}k}{(1 + a_2\hat{U})(dV + \alpha_1)d_\omega} \|\varphi_2\|.
\]
It is well-known that
\[
r(K) \leq \|K\| \leq \frac{\beta\hat{U}k}{(1 + a_2\hat{U})(dV + \alpha_1)d_\omega}.
\]
Hence, we have

\[ R_0 \leq \sqrt{\frac{\beta \tilde{U} \tilde{k}}{(1 + a_2 \tilde{U}) (d_V + \alpha_1) d_\omega}}, \]

where \( \tilde{U} = \max_{x \in \Omega} \tilde{U}(x), \beta = \max_{x \in \Omega} \beta(x) \) and \( k = \max_{x \in \Omega} k(x) \).

On the other hand, if we take \( c = (c_2, c_4) \in R^2 \), then we have

\[
(\mu I - \mathcal{L})(\pi) = \begin{pmatrix}
\mu & -\frac{\beta(x) \tilde{U}(x)}{1 + a_2 \tilde{U}(x)} d_\omega \\
-k(x) & \mu
\end{pmatrix} \begin{pmatrix}
c_2 \\
c_4
\end{pmatrix}, \quad x \in \Omega,
\]

which implies that, if

\[
\mu < \min_{x \in \Omega} \sqrt{\frac{\beta(x) \tilde{U}(x) k(x)}{(1 + a_2 \tilde{U}(x)) (d_V + \alpha_1) d_\omega}},
\]

then \( \mu \) cannot in the spectrum of the linear and compact operator \( \mathcal{L} \). Thus, one gets

\[
r(\mathcal{L}) \geq \min_{x \in \Omega} \sqrt{\frac{\beta(x) \tilde{U}(x) k(x)}{(1 + a_2 \tilde{U}(x)) (d_V + \alpha_1) d_\omega}}.
\]

Then

\[
R_0 \geq \min_{x \in \Omega} \sqrt{\frac{\beta(x) \tilde{U}(x) k(x)}{(1 + a_2 \tilde{U}(x)) (d_V + \alpha_1) d_\omega}}.
\]

Similarly, if

\[
\mu > \max_{x \in \Omega} \sqrt{\frac{\beta(x) \tilde{U}(x) k(x)}{(1 + a_2 \tilde{U}(x)) (d_V + \alpha_1) d_\omega}},
\]

then \( \mu \) cannot in the spectrum of the linear and compact operator \( \mathcal{L} \). Thus, one gets

\[
r(\mathcal{L}) \leq \max_{x \in \Omega} \sqrt{\frac{\beta(x) \tilde{U}(x) k(x)}{(1 + a_2 \tilde{U}(x)) (d_V + \alpha_1) d_\omega}}.
\]

Then

\[
R_0 \leq \max_{x \in \Omega} \sqrt{\frac{\beta(x) \tilde{U}(x) k(x)}{(1 + a_2 \tilde{U}(x)) (d_V + \alpha_1) d_\omega}}.
\]

The proof is complete. \( \square \)
Linearizing model (3) at $E_0$ yields
\[
\begin{align*}
\frac{\partial E_1}{\partial t} &= D_0 \Delta E_1 - d_V E_1 - q(x)\hat{U}(x)E_3 - \frac{\beta(x)\hat{U}(x)}{1 + a_2 \hat{U}(x)}E_4, \ x \in \Omega, \ t > 0, \\
\frac{\partial E_2}{\partial t} &= D_0 \Delta E_2 + \frac{\beta(x)\hat{U}(x)}{1 + a_2 \hat{U}(x)}E_4 - (d_V + \alpha_1)E_2, \ x \in \Omega, \ t > 0, \\
\frac{\partial E_3}{\partial t} &= D_1 \Delta E_3 + \alpha_2(x)E_2 - d_M E_3, \ x \in \Omega, \ t > 0, \\
\frac{\partial E_4}{\partial t} &= D_2 \Delta E_4 + k(x)E_2 - d_\omega E_4, \ x \in \Omega, \ t > 0, \\
\frac{\partial E_1}{\partial \nu} &= \frac{\partial E_2}{\partial \nu} = \frac{\partial E_3}{\partial \nu} = \frac{\partial E_4}{\partial \nu} = 0, & \forall x \in \partial \Omega, \ t > 0.
\end{align*}
\]

Substituting $E_2(t, x) = e^M \varphi_2(x)$ and $E_4(t, x) = e^M \varphi_4(x)$ into equations of $E_2$ and $E_4$, for $(\varphi_2, \varphi_4) \in X_1 \times X_1$, we obtain the following eigenvalue problem
\[
\begin{align*}
\lambda \varphi_2(x) &= D_0 \Delta \varphi_2(x) + \frac{\beta(x)\hat{U}(x)}{1 + a_2 \hat{U}(x)} \varphi_4(x) - (d_V + \alpha_1) \varphi_2(x), \\
\lambda \varphi_4(x) &= D_2 \Delta \varphi_4(x) + k(x)\varphi_2(x) - d_\omega \varphi_4(x), \\
\frac{\partial \varphi_2(x)}{\partial \nu} &= \frac{\partial \varphi_4(x)}{\partial \nu} = 0, & \forall x \in \partial \Omega, \ t > 0.
\end{align*}
\]

In view of [16, Theorem 7.6.1], the following result holds.

**Lemma 3.5.** The eigenvalue problem (6) admits a principal eigenvalue $\lambda_0$ with a strictly positive eigenvector.

The following result can be verified by using [22, Theorem 3.1 (i)].

**Lemma 3.6.** $R_0 - 1$ has the same sign as $\lambda_0$.

4. **Comparison principle for an auxiliary system.** In order to discuss the global dynamics of model (3), we show that the following quasilinearity parabolic auxiliary system
\[
\begin{align*}
\frac{\partial V}{\partial t} &= D_0 \Delta V + \frac{\beta(x)\hat{U}(x)}{1 + a_2 \hat{U}(x)} \omega - (d_V + \alpha_1) V, \\
\frac{\partial M}{\partial t} &= D_1 \Delta M + \alpha_2(x) V - d_M M, \\
\frac{\partial \omega}{\partial t} &= \nabla \cdot (D_\omega(V)\nabla \omega) + k(x) V - d_\omega \omega, \\
\frac{\partial V}{\partial \nu} &= \frac{\partial M}{\partial \nu} = \frac{\partial \omega}{\partial \nu} = 0, & \forall x \in \partial \Omega, \ t > 0,
\end{align*}
\]
satisfies the comparison principle under appropriate conditions. The global existence, nonnegativity, uniqueness, and boundedness of solutions for model (7) can be shown by using the similar method as the proof of Theorem 3.1. As Theorem 3.1, we assume that there exists a constant $\zeta$ such that
\[
0 \leq V(t, x), M(t, x), \omega(t, x) \leq \zeta.
\]

We now state the comparison principle, which plays a crucial role on the discussions of global dynamics for model (3). Our method is inspired by Li and Ma [9, Theorem 3.1].
Theorem 4.1. Assume that there is a constant \( B \) such that for all solutions of model (3), there holds
\[
\|g'(V)\nabla \omega\|_\infty \leq B, \text{ for all } V, \omega \in X \text{ with } V, \omega \in [0, \zeta]. \tag{8}
\]

Let \( z_1(t, x; \varphi) = (V_1, M_1, \omega_1) \) and \( z_2(t, x; \varphi) = (V_2, M_2, \omega_2) \) be the solution of model (7) with initial data \( \varphi, \psi \in X \). If \( \varphi(x) \geq \psi(x) \) for all \( x \in \Omega \), it follows that \( z_1(t, x; \varphi) \geq z_2(t, x; \psi) \) for all \( x \in \Omega \) and \( t \geq 0 \).

Proof. Substituting \( z_1(t, x; \varphi) \) and \( z_2(t, x; \psi) \) into model (7), respectively, then subtracting one system from another, it follows that
\[
\begin{cases}
\frac{\partial(V_1 - V_2)}{\partial t} = D_0 \Delta (V_1 - V_2) + \frac{\beta(x)\bar{U}(x)}{1 + \alpha g\bar{U}(x)}(\omega_1 - \omega_2) - (d_V + \alpha_1)(V_1 - V_2), \\
\frac{\partial(M_1 - M_2)}{\partial t} = D_1 \Delta (M_1 - M_2) + \alpha_2(x)(V_1 - V_2) - d_M(M_1 - M_2), \\
\frac{\partial(\omega_1 - \omega_2)}{\partial t} = \nabla \cdot (D_2 \nabla(\omega_1 - \omega_2) + g(V_1)\nabla\omega_1 - g(V_2)\nabla\omega_2) + k(x)(V_1 - V_2) \\
\frac{\partial(V_1 - V_2)}{\partial \nu} = \frac{\partial(M_1 - M_2)}{\partial \nu} = \frac{\partial(\omega_1 - \omega_2)}{\partial \nu} = 0, \forall x \in \partial \Omega,\ t > 0.
\end{cases}
\tag{9}
\]

For convenience, we assume that \( g(x)y = f(x, y), \hat{a} = V_2, \hat{b} = \nabla\omega_2, \hat{h} = V_1 - V_2 \) and \( \hat{k} = \nabla\omega_1 - \nabla\omega_2 \). It follows from Taylor’s expression for the term \( g(V_1)\nabla\omega_1 - g(V_2)\nabla\omega_2 \) that
\[
g(V_1)\nabla\omega_1 - g(V_2)\nabla\omega_2 = f \left( \hat{a} + \hat{h}, \hat{b} + \hat{k} \right) - f \left( \hat{a}, \hat{b} \right)
\]
\[
= f_x \left( \hat{a} + \rho \hat{h}, \hat{b} + \rho \hat{k} \right) \hat{h} + f_y \left( \hat{a} + \rho \hat{h}, \hat{b} + \rho \hat{k} \right) \hat{k}
\]
\[
= g' \left( \hat{a} + \rho \hat{h} \right) \left( \hat{b} + \rho \hat{k} \right) \hat{h} + g \left( \hat{a} + \rho \hat{h} \right) \hat{k}
\]
\[
= g'(V_2 + \rho(V_1 - V_2))(\nabla\omega_1 + \rho(\nabla\omega_1 - \nabla\omega_2))(V_1 - V_2) + g(V_2 + \rho(V_1 - V_2))(\nabla\omega_1 - \nabla\omega_2)
\]
\[
= g'(\rho V_1 + (1 - \rho)V_2)\nabla(\rho\omega_1 + (1 - \rho)\omega_2)(V_1 - V_2) + g(\rho V_1 + (1 - \rho)V_2)\nabla(\omega_1 - \omega_2),
\]
where \( \rho \in (0, 1) \). Here, the Taylor’s expression for the term \( g(V_1)\nabla\omega_1 - g(V_2)\nabla\omega_2 \) can also be found in [9]. We set
\[
a(t, x) = g'(\rho V_1 + (1 - \rho)V_2)\nabla(\rho\omega_1 + (1 - \rho)\omega_2),
\]
and
\[
b(t, x) = g(\rho V_1 + (1 - \rho)V_2).
\]

According to Theorem 3.1 and the condition (8), \( a(t, x) \) and \( b(t, x) \) are bounded uniformly for \( t \geq 0 \) and \( x \in \Omega \). Let \( P_1 = V_1 - V_2, P_2 = M_1 - M_2, P_3 = \omega_1 - \omega_2 \).
Then we have
\[
\begin{cases}
\frac{\partial P_1}{\partial t} = D_0 \Delta P_1 + \frac{\beta(x)\hat{U}(x)}{1 + a_2 U(x)} P_3 - (d_V + \alpha_1)P_1, \\
\frac{\partial P_2}{\partial t} = D_1 \Delta P_2 + \alpha_2(x)P_1 - d_M P_2, \\
\frac{\partial P_3}{\partial t} = \nabla \cdot ((D_2 + b(t, x))\nabla P_3 + a(t, x)P_3) + k(x)P_1 - d_\omega P_3, \\
\frac{\partial P_3}{\partial \nu} = \frac{\partial P_2}{\partial \nu} = \frac{\partial P_3}{\partial \nu} = 0, \forall x \in \partial \Omega, \ t > 0.
\end{cases}
\] (10)

Since \(D_0, D_1 > 0\) as well as \(P_1(0, x) \geq 0, \ P_2(0, x) \geq 0\) and \(P_3(0, x) \geq 0\), it follows from [2, Theorems 14.4 and 14.6] that model (10) has a unique classical solution
\[(P_1(t, x), P_2(t, x), P_3(t, x))\]
defined on \([0, \tau) \times \Omega\) such that
\[(P_1, P_2, P_3) \in C([0, \tau), X^3) \cap C^{3,1}((0, \tau) \times \overline{\Omega}, R^3),\]
where \(\tau > 0\) is the maximal interval of existence of the solution of model (10). In view of [2, Theorem 15.1], the nonnegativity of the solution of model (10) can be obtained. Since \(z_1, z_2\) and \(z_3\) are uniformly bounded, so are \(P_1, P_2\) and \(P_3\). Thus, we have \(\tau = +\infty\) [2, Theorem 15.3]. The proof is complete.

5. Global dynamics. In this section, we discuss the global dynamics of model (3) by starting with the following lemma.

**Lemma 5.1.** Let \((U(t, x), V(t, x), M(t, x), \omega(t, x))\) be the solution of model (3). Assume that the condition (8) holds. Then the following two statements hold:

(i) \(U(t, x) > 0\) for \((t, x) \in [0, +\infty) \times \overline{\Omega}\).

(ii) If there is some \(t_0 > 0\) such that \(V(t_0, \cdot, \varphi) \not\equiv 0, \ M(t_0, \cdot, \varphi) \not\equiv 0\) and \(\omega(t_0, \cdot, \varphi) \not\equiv 0\), then \(V(t, \cdot, \varphi) > 0, \ M(t, \cdot, \varphi) > 0\) and \(\omega(t, \cdot, \varphi) > 0\) for all \(t > t_0\), \(x \in \overline{\Omega}\).

**Proof.** From model (3), one gets
\[
\begin{cases}
\frac{\partial U}{\partial t} \geq D_0 \Delta U - \left( d_U + \frac{q(x)}{b} + \frac{\beta(x)}{a_1} \right) U, \ x \in \Omega, \ t > 0, \\
\frac{\partial U}{\partial \nu} = 0, \ x \in \partial \Omega, \ t > 0, \\
U(0, x) = U_0(x) > 0, \ x \in \Omega.
\end{cases}
\]
By the standard comparison argument, one gets \(U(t, x; \varphi) > 0, \ x \in \overline{\Omega}, \ t \geq 0\), which indicates that (i) holds.

From model (3), we have
\[
\begin{cases}
\frac{\partial V}{\partial t} \geq D_0 \Delta V - (d_V + \alpha_1)V, \ x \in \Omega, \ t > 0, \\
\frac{\partial M}{\partial t} \geq D_1 \Delta M - d_M V, \ x \in \Omega, \ t > 0, \\
\frac{\partial \omega}{\partial t} \geq \nabla \cdot ((D_2 + g(V))\nabla \omega) - d_\omega \omega, \ x \in \Omega, \ t > 0, \\
\frac{\partial V}{\partial \nu} = \frac{\partial M}{\partial \nu} = \frac{\partial \omega}{\partial \nu} = 0, \ x \in \partial \Omega, \ t > 0, \\
V_0(x) \geq 0, \ M_0(x) \geq 0, \ \omega_0(x) \geq 0, \ x \in \Omega.
\end{cases}
\]
According to Theorem 4.1, (ii) holds. The proof is complete. \(\square\)
Lemma 5.2. Suppose that the condition (8) holds and
\[ \frac{\beta U_k}{1 + a_2 U} < (d_V + \alpha_1)d_\omega, \]  
then the steady state \((0, 0, 0)\) of model (7) with the initial data in \(X_3^+\) is globally asymptotically stable.

Proof. In view of Lemma 3.4, it follows that \(R_0 < 1\). It follows from Lemma 3.6 and \(R_0 < 1\) that the principal eigenvalue of model (6) satisfies \(\lambda_0 < 0\). Hence, the steady state \((0, 0, 0)\) of model (7) is locally stable. Next we show that \((0, 0, 0)\) of model (7) is globally attractive in \(X_3^+\).

From model (7), we have
\[
\begin{align*}
\frac{\partial z_1}{\partial t} &\leq D_0 \Delta z_1 + \frac{\beta U_k}{1 + a_2 U} z_3 - (d_V + \alpha_1)z_1, \ x \in \Omega, \ t > 0, \\
\frac{\partial z_2}{\partial t} &\leq D_1 \Delta z_2 + \beta z_1 - d_M z_2, \ x \in \Omega, \ t > 0, \\
\frac{\partial z_3}{\partial t} &\leq \nabla \cdot (D_{z_3}(z_1) \nabla z_3) + k z_1 - d_\omega z_3, \ x \in \Omega, \ t > 0, \\
\frac{\partial z_1}{\partial \nu} &= \frac{\partial z_2}{\partial \nu} = \frac{\partial z_3}{\partial \nu} = 0, \ \forall x \in \partial \Omega, \ t > 0.
\end{align*}
\]  
(12)

Since the equations for \(z_1\) and \(z_3\) are independent from the equation \(z_2\), we only consider the following system
\[
\begin{align*}
\frac{\partial \bar{z}_1}{\partial t} &= D_0 \Delta \bar{z}_1 + \frac{\beta U_k}{1 + a_2 U} \bar{z}_3 - (d_V + \alpha_1)\bar{z}_1, \ x \in \Omega, \ t > 0, \\
\frac{\partial \bar{z}_3}{\partial t} &= \nabla \cdot (D_{z_3}(\bar{z}_1) \nabla \bar{z}_3) + k \bar{z}_1 - d_\omega \bar{z}_3, \ x \in \Omega, \ t > 0, \\
\frac{\partial \bar{z}_1}{\partial \nu} &= \frac{\partial \bar{z}_3}{\partial \nu} = 0, \ \forall x \in \partial \Omega, \ t > 0.
\end{align*}
\]  
(13)

Application of Theorem 4.1 yields
\[ (z_1(t, x; \varphi), z_3(t, x; \varphi)) \leq (\bar{z}_1(t, x; \varphi), \bar{z}_3(t, x; \varphi)), \ \text{for} \ \varphi \leq \psi \ \text{in} \ X_2^+. \]

It is easy to see that the quadric equation
\[ (\mu + d_V + \alpha_1)(\mu + d_\omega) = \frac{\beta U_k}{1 + a_2 U} \]
has two negative roots. Assuming \(\mu\) is the larger one, i.e.,
\[ \mu = \frac{-(d_V + \alpha_1 + d_\omega) + \sqrt{(d_V + \alpha_1 + d_\omega)^2 + \frac{4\beta U_k}{1 + a_2 U}}}{2}. \]

Obviously, \(\mu + d_\omega > 0\) and \(\mu + d_V + \alpha_1 > 0\). We now define two functions as follows:
\[ \bar{z}_1(t, x) = K \frac{1}{\mu + d_V + \alpha_1} e^{\mu t}, \]
and
\[ \bar{z}_3(t, x) = Ke^{\mu t}, \]
where \(K > 0\) is an arbitrary constant.
For \( \varphi \in (\varphi_1, \varphi_3) \in X_+^2 \), we can find a sufficiently large number \( K \) satisfying
\[
\varphi = (\varphi_1, \varphi_3) \leq K \left( \frac{\beta U}{1 + a_2 U} \frac{1}{\mu + d_V + \alpha_1}, 1 \right) = K (\zeta_1(0, x), \zeta_3(0, x)) = \psi, \ x \in \Omega.
\]
Thus, one gets
\[
(z_1(t, x), z_3(t, x)) \leq K \left( \frac{\beta U}{1 + a_2 U} \frac{1}{\mu + d_V + \alpha_1} e^\mu, e^\mu \right),
\]
which leads to
\[
\lim_{t \to \infty} (z_1(t, x), z_3(t, x)) = (0, 0)
\]
uniformly for \( x \in \Omega \) in \( X_+^2 \). From model (7), we have that
\[
\lim_{t \to \infty} (z_1(t, x), z_2(t, x), z_3(t, x)) = (0, 0, 0)
\]
uniformly for \( x \in \Omega \) in \( X_+^3 \). The proof is complete.

**Theorem 5.3.** Assume that conditions (8) and (11) hold. Then \((\hat{U}(x), 0, 0, 0)\) of model (3) is globally asymptotically stable in \( X_+^4 \setminus \{0\} \).

**Proof.** From model (3), one gets
\[
\begin{cases}
\frac{\partial U}{\partial t} \leq D_0 \Delta U + \xi(x) - d_U U, \ x \in \Omega, \ t > 0, \\
\frac{\partial U}{\partial \nu} = 0, \ x \in \partial \Omega, \ t > 0, \\
U_0(x) > 0, \ \forall x \in \Omega.
\end{cases}
\]
We have that \( U(t, x) \leq \hat{U}(x) \) for all \( x \in \Omega, \ t \geq 0 \). From model (3), we have
\[
\begin{cases}
\frac{\partial V}{\partial t} \leq D_0 \Delta V + \frac{\beta(x) \hat{U}(x)}{1 + a_2 \hat{U}(x)} \omega - (d_V + \alpha_1)V, \ x \in \Omega, \ t > 0, \\
\frac{\partial M}{\partial t} = D_1 \Delta M + \alpha_2(x) V - d_M M, \ x \in \Omega, \ t > 0, \\
\frac{\partial \omega}{\partial t} = \nabla \cdot (D_\omega V \nabla \omega) + k(x) V - d_\omega \omega, \ x \in \Omega, \ t > 0, \\
\frac{\partial V}{\partial \nu} = \frac{\partial M}{\partial \nu} = \frac{\partial \omega}{\partial \nu} = 0, \ x \in \partial \Omega, \ t > 0.
\end{cases}
\]
It follows from Theorem 4.1 that
\[
(V(t, x; \varphi), M(t, x; \varphi), \omega(t, x; \varphi)) \leq (z_1(t, x; \psi), z_2(t, x; \psi), z_3(t, x; \psi))
\]
for \( \varphi \leq \psi \) in \( X_+^4 \), where \((z_1, z_2, z_3)\) is the solution of model (7). By Lemma 5.2, we have
\[
\lim_{t \to \infty} (V(t, x), M(t, x), \omega(t, x)) = (0, 0, 0)
\]
uniformly for \( x \in \Omega \).

Let \( \omega(U_0, V_0, M_0, \omega_0) \) be the omega-limit set of the orbit \( \Phi(t) \) with \((U_0, V_0, M_0, \omega_0) \in X_+^4 \). Since \( \Phi(t) \) is compact and continuous in \((t, x)\), there is a set \( \mathcal{S} \subset X_+^4 \) satisfying
\[
\omega(U_0, V_0, M_0, \omega_0) = \mathcal{S} \times \{(0, 0, 0)\}.
\]
For any given \( U_0 \in \mathcal{S} \), we get
\[
(U_0, 0, 0, 0) \in \omega(U_0, V_0, M_0, \omega_0) \subset X_+^4.
\]
It follows from [26, Lemma 1.2.1] that \( \omega(U_0, V_0, M_0, \omega_0) \) is compact, invariant and interval chain transitive set for \( \Phi(t) \). If \( U_0 \in X^4_+ \) with \( (U_0, 0, 0, 0) \in \omega(U_0, V_0, M_0, \omega_0) \), we have

\[
\Phi(t) \mid_{\omega(U_0, V_0, M_0, \omega_0)} (U_0, 0, 0, 0) = (Q(t)U_0, 0, 0, 0),
\]

where \( Q(t) \) is the solution semiflow for the following reaction-diffusion system

\[
\begin{align*}
\frac{\partial U}{\partial t} &= D_0 \Delta U + \xi(x) - d_U U, \; x \in \Omega, \; t > 0, \\
\frac{\partial U}{\partial \nu} &= 0, \; x \in \partial \Omega, \; t > 0.
\end{align*}
\]

Hence, \( S \) is a compact, invariant and internal chain transitive set for \( \Phi(x) \) where \( Q \) is a compact, invariant and internal chain transitive set for \( \Phi(x) \). It follows from the proof of Lemma 3.3 that model (15) admits a globally attractive solution \( \hat{U}(x) \) in \( X^4_+ \\setminus \{0\} \). Thus, \( \{\hat{U}(x)\} \) is an isolated invariant set in \( X^4_+ \\setminus \{0\} \) and no cycle connecting \( \{\hat{U}(x)\} \) to itself in \( X^4_+ \\setminus \{0\} \). It follows from [26, Theorem 1.2.2] that \( S = \hat{U}(x) \), and then

\[
\omega(U_0, V_0, M_0, \omega_0) = S \times \{(0, 0, 0)\} = \left\{ \left( \hat{U}(x), 0, 0, 0 \right) \right\},
\]

which indicates that \( \left( \hat{U}(x), 0, 0, 0 \right) \) is globally attractive for \( \Phi(t) \) in \( X^4_+ \).

In the following, we prove that \( \left( \hat{U}(x), 0, 0, 0 \right) \) is locally stable. From the condition (11) and Lemma 3.4, we get \( R_0 < 1 \). By Lemma 3.6, we have \( \lambda_0 < 0 \). It is well-known that the solution of model (3) satisfies

\[
\lim_{t \to \infty} (E_2(t, x), E_3(t, x), E_4(t, x)) = (0, 0, 0),
\]

and hence the first equation of model (3) is asymptotic to the following reaction-diffusion system

\[
\begin{align*}
\frac{\partial E_1}{\partial t} &= D_0 E_1 - d_U E_1, \; x \in \Omega, \; t > 0, \\
\frac{\partial E_1}{\partial \nu} &= 0, \; x \in \partial \Omega, \; t > 0.
\end{align*}
\]

Hence, one gets \( \lim_{t \to \infty} E_1(t, x) = 0 \). Through the argument similar to the above by using [26, Lemma 1.2.1 and Theorem 1.2.2], we have

\[
\lim_{t \to \infty} (E_1(t, x), E_2(t, x), E_3(t, x), E_4(t, x)) = (0, 0, 0, 0),
\]

and thus \( \left( \hat{U}(x), 0, 0, 0 \right) \) is locally stable. The proof is complete. \( \square \)

We now discuss the uniform persistence of model (3) when \( R_0 > 1 \). Define

\[
X^4_0 = \{(U, V, M, \omega) \in X^4_+: V(\cdot) \neq 0, \; M(\cdot) \neq 0 \; \text{and} \; \omega(\cdot) \neq 0 \}
\]

and

\[
\partial X^4_0 = X^4_+ \setminus X^4_0.
\]

**Theorem 5.4.** Suppose that the condition (8) is true and

\[
\frac{\hat{U}b_k}{1 + a_2 U} > (d_V + \alpha_1)d_\omega.
\]
Model (3) has at least one positive non-constant steady state \((U^*(x), V^*(x), M^*(x), \omega^*(x))\), \(x \in \Omega\). Furthermore, there is a positive constant \(\eta > 0\) such that each solutions
\[
(U(t, x), V(t, x), M(t, x), \omega(t, x))
\]
of model (3) with \((U(0, x), V(0, x), M(0, x), \omega(0, x)) \in X_0^4\) satisfying
\[
\lim_{t \to \infty} V(t, x) \geq \eta, \liminf_{t \to \infty} M(t, x) \geq \eta, \liminf_{t \to \infty} \omega(t, x) \geq \eta \quad \text{uniformly for } x \in \Omega.
\]

**Proof.** It follows from Lemma 3.4 that \(R_0 > 1\). Let
\[
M_0 = \{ l \in \partial X_0^4 : \Phi(t)l \in \partial X_0^4, \ t \geq 0 \},
\]
and \(\omega(l)\) be the omega limit set of the forward orbit \(\gamma^+(l) = \{ \Phi(t)l : t \geq 0 \}\).

**Claim 1:** \(\cup_{l \in M_0} \omega(l) \subset \{ E_0 \}, \text{ where } E_0 = \left( \tilde{U}(x), 0, 0, 0 \right)\), \(x \in \Omega\).

For any given \(l \in M_0\), we have \(\Phi(t)l \in \partial X_0^4, \ t \geq 0\). Hence, one gets \(V(t, \cdot; l) \equiv 0\), \(M(t, \cdot; l) \equiv 0\) or \(\omega(t, \cdot; l) \equiv 0\) for each \(t \geq 0\). If \(\omega(t, \cdot; l) \equiv 0, \forall t \geq 0\), we have \(V(t, \cdot; l) \equiv 0, \forall t \geq 0\). From model (3), we get \(\lim_{t \to \infty} M(t, x) = 0\) uniformly for \(x \in \Omega\). Then we obtain \(\lim_{t \to \infty} U(t, x) = \tilde{U}(x)\) uniformly for \(x \in \Omega\). If \(\omega(t, \cdot; l) \not\equiv 0\) for some \(t_1 \geq 0\), it follows that \(\omega(t, \cdot; l) > 0, \forall t \geq t_1\). Hence, one gets \(V(t, \cdot; l) \equiv 0\) or \(M(t, \cdot; l) \equiv 0\). For the case \(V(t, \cdot; l) \equiv 0\), we have \(\omega(t, \cdot; l) \equiv 0\). Then we have \(M(t, \cdot; l) \equiv 0\). Thus, the claim is true.

Since \(R_0 > 1\), it follows from Lemma 3.6 that \(\lambda_0 > 0\). Hence, there exists a sufficiently small number \(\sigma > 0\) satisfying
\[
\frac{(\tilde{U} - \sigma)\beta k}{1 + a_2(\tilde{U} - \sigma) + a_1 \sigma} > (d_V + \alpha_1)d_\omega,
\]
where \(\lambda_0^\sigma\) is the principle eigenvalue of the following eigenvalue problem
\[
\begin{cases}
\lambda_0^\sigma \varphi_2(x) = D_0 \Delta \varphi_2(x) + \frac{\beta(x)(\tilde{U}(x) - \sigma)}{1 + a_2(\tilde{U} - \sigma) + a_1 \sigma} \varphi_4(x) \\
\frac{-d_\omega + \alpha_1}{a_2} \varphi_2(x), x \in \Omega, \ t > 0,
\end{cases}
\]
\[
\lambda_0^\sigma \varphi_4(x) = D_2 \Delta \varphi_4(x) + k(x) \varphi_2(x) - d_\omega \phi_4(x), x \in \Omega, \ t > 0,
\]
\[
\frac{\partial \varphi_2}{\partial \nu} = \frac{\partial \varphi_4}{\partial \nu} = 0, \ x \in \partial \Omega, \ t > 0,
\]
with a strongly positive eigenfunction \((\tilde{\varphi}_2(x), \tilde{\varphi}_4(x))\).

**Claim 2:** \(E_0\) is a uniform weak repeller, i.e.,
\[
\limsup_{t \to \infty} \| \Phi(t)l - E_0 \| \geq \sigma \quad \text{for all } l \in X_0^4.
\]

By way of contradiction, we assume that there is \(l_0 \in X_0^4\) such that
\[
\limsup_{t \to \infty} \| \Phi(t)l_0 - E_0 \| < \sigma.
\]

Thus, there exists a \(t_1 > 0\) such that
\[
|U(t, \cdot) - \tilde{U}(x)| < \sigma, \omega(t, \cdot) < \sigma, \forall t \geq t_1.
\]
It follows from model (3) that
\[
\begin{align*}
\frac{\partial V}{\partial t} & \geq D_0 \Delta V + \frac{\beta(x) \left( \tilde{U}(x) - \sigma \right)}{1 + a_2 \left( \tilde{U}(x) - \sigma \right) + a_1 \sigma} \omega - (d_V + \alpha_1)V, \quad x \in \Omega, \quad t \geq t_1, \\
\frac{\partial \omega}{\partial t} & = D_2 \Delta \omega + g(V) \Delta \omega + g'(V) \nabla V \nabla \omega + k(x)V - d_\omega \omega, \quad x \in \Omega, \quad t \geq t_1,
\end{align*}
\]
\begin{equation}
\tag{18}
\frac{\partial V}{\partial \nu} = \frac{\partial \omega}{\partial \nu} = 0, \quad x \in \partial \Omega, \quad t \geq t_1.
\end{equation}

Applying Theorem 4.1 yields
\[
(V(t, x; l_0), \omega(t, x; l_0)) \geq (\overline{V}(t, x; \psi), \overline{\omega}(t, x; \psi))
\]
for \( l_0 \geq \psi, \ x \in \overline{\Omega}, \ t \geq t_1 \), where \( (\overline{V}(t, x), \overline{\omega}(t, x)) \) satisfies the following system
\[
\begin{align*}
\frac{\partial \overline{V}}{\partial t} & = D_0 \Delta \overline{V} + \frac{\beta(x) \left( \tilde{U}(x) - \sigma \right)}{1 + a_2 \left( \tilde{U}(x) - \sigma \right) + a_1 \sigma} \overline{\omega} - (d_V + \alpha_1)\overline{V}, \quad x \in \Omega, \quad t \geq t_1, \\
\frac{\partial \overline{\omega}}{\partial t} & = D_2 \Delta \overline{\omega} + g(\overline{V}) \Delta \overline{\omega} + g'(\overline{V}) \nabla \overline{V} \nabla \overline{\omega} + k(x)\overline{V} - d_\omega \overline{\omega}, \quad x \in \Omega, \quad t \geq t_1,
\end{align*}
\]
\begin{equation}
\tag{19}
\frac{\partial \overline{V}}{\partial \nu} = \frac{\partial \overline{\omega}}{\partial \nu} = 0, \quad x \in \partial \Omega, \quad t \geq t_1.
\end{equation}

By a simple computation, the quadratic equation
\[
(\mu + d_V + \alpha_1)(\mu + d_\omega) = \frac{\left( \tilde{U} - \sigma \right) \beta k}{1 + a_2 \left( \tilde{U} - \sigma \right) + a_1 \sigma}
\]
has a positive solution, which is
\[
\mu^+ = \frac{-(d_V + \alpha_1 + d_\omega) + \sqrt{(d_V + \alpha_1 - d_\omega)^2 + \frac{4\beta k}{1 + a_2 (\tilde{U} - \sigma) + a_1 \sigma}}}{2}.
\]

We now define two functions
\[
\overline{V}(t, x) = \varepsilon \frac{\mu^+ + d_\omega}{k} e^{\mu^+(t-t_1)}, \quad \overline{\omega}(t, x) = \varepsilon e^{\mu^+(t-t_1)},
\]
\begin{equation}
\tag{20}
\end{equation}
where \( \varepsilon > 0 \) is an arbitrary constant. Obviously, (20) is a solution of model (19).

By Lemma 5.1, one gets \( (V(t, x; l_0), \omega(t, x; l_0)) > 0, \ \forall (t, x) \in (0, +\infty) \times \overline{\Omega} \). We choose a sufficiently small number \( \varepsilon \) satisfying
\[
(V(t, x; l_0), \omega(t, x; l_0)) \geq \varepsilon \left( \frac{\mu^+ + d_\omega}{k}, 1 \right).
\]

Hence, we have
\[
(V(t, x; l_0), \omega(t, x; l_0)) \geq \varepsilon \left( \frac{\mu^+ + d_\omega}{k} e^{\mu^+(t-t_1)}, e^{\mu^+(t-t_1)} \right),
\]
for \( x \in \overline{\Omega}, \ t \geq t_1 \), which implies that \( V(t, x; l_0) \) and \( \omega(t, x; l_0) \) are unbounded. This contradiction implies that the assumption is not true. Thus, the claim holds.

Let us define a continuous function \( d : X_+^4 \to [0, +\infty) \) as follows:
\[
d(\varphi) = \min \left\{ \min_{x \in \overline{\Omega}} \varphi_2(x), \min_{x \in \overline{\Omega}} \varphi_3(x), \min_{x \in \overline{\Omega}} \varphi_4(x) \right\}, \ \forall \varphi \in X_+^4.
\]
Lemma 5.1 indicates that $d^{-1}(0, +∞) \subseteq X_0^4$ and $d(\Phi(t)\varphi) > 0$ for $t > 0$ if either $d(\varphi) = 0$ with $\varphi \in X_0^4$ or $d(\varphi) > 0$ [17].

The above two claims yield that any forward orbit of $\Phi(t)$ in $M_\beta$ converges to $E_0$. Moreover, $\{E_0\}$ is an isolated invariant set in $X_0^4$ and $W^s(\{E_0\}) \cap X_0^4 = ∅$, where $W^s(\{E_0\})$ is the stable set of $\{E_0\}$. Obviously, $\{E_0\}$ is acyclic on $M_\beta$. From Lemma 3.2 and [17, Theorem 3], it follows that there is a $\eta > 0$ such that

$$\min_{ξ∈Ω} d(ξ) > η, \quad ∀\varphi \in X_0^4,$$

which implies that

$$\liminf_{t→∞} V(t, x) ≥ η, \quad \liminf_{t→∞} M(t, x) ≥ η, \quad \liminf_{t→∞} \omega(t, x) ≥ η \text{ uniformly for } x ∈ \overline{Ω}.$$

We now illustrate the existence of positive non-constant steady state of model (3). From [11, Theorem 3.7 and Remark 3.10], we know that $\Phi(t) : X_0^4 → X_0^4$ admits a global attractor. Hence, by [11, Theorem 4.7], $\Phi(t)$ has a steady state $(U^*(x), V^*(x), M^*(x), \omega^*(x)) \in X_0^4$. It is easy to see that $U^*$ and $\omega^*$ satisfy the following system

\[
\begin{align*}
D_0 \Delta U^* + ξ(x) - d_U U^* - \frac{β(x)U^*ω^*}{1 + a_1U^* + a_2ω^*} - \frac{q(x)U^*M^*}{1 + bM^*} &= 0, \quad x ∈ Ω, \\
\frac{∂U^*}{∂ν} &= \frac{∂M^*}{∂ν} = \frac{∂ω^*}{∂ν} = 0, \quad x ∈ ∂Ω.
\end{align*}
\]

Assuming that $U^*$ gets a minimum $U^*(x) = 0$ at some point $x ∈ \overline{Ω}$, then $Δ\bar{U}(x) ≥ 0$. If $x ∈ \text{Int}(Ω)$, one gets

$$D_0 Δ\bar{U}(x) + ξ(x) = 0,$$

which leads to a contradiction. If $x ∈ ∂Ω$, by Hopf boundary lemma [14], then $\frac{∂U^*}{∂ν} < 0$, which also contradicts to (4). Thus, $U^*(x) > 0$. Similarly, we obtain $V^*(x) > 0$, $M^*(x) > 0$ and $ω^*(x) > 0$ for all $x ∈ \overline{Ω}$. The proof is complete. □

Let $β(x)$, $q(x)$ and $k(x)$ be positive constants $β$, $q$ and $k$, respectively. Then

$$\bar{U}(x) = \frac{ξ}{d_U}.$$

Then

$$R_0 = \sqrt{\frac{ξβk}{(dv + a_2ξ)(dv + α_1)d\omega}}.$$

Obviously, both conditions (11) and (16) are equivalent to $R_0 < 1$ and $R_0 > 1$, respectively. Hence, the following corollary can be directly derived from Theorems 5.3 and 5.4.

**Corollary 1.** Suppose that the condition (8) holds and $β(x)$, $q(x)$ and $k(x)$ are positive constants. Then the following two statements are valid:

(i) If $R_0 < 1$, $(\bar{U}(x), 0, 0, 0)$ of model (3) is globally asymptotically stable in $X_0^4 \setminus \{0\}$.

(ii) If $R_0 > 1$, model (3) has at least one positive non-constant steady state $(U^*(x), V^*(x), M^*(x), \omega^*(x)), x ∈ \overline{Ω}$. Furthermore, there is a positive constant $η > 0$ such that each solutions

$$(U(t, x), V(t, x), M(t, x), ω(t, x))$$

of model (3) with $(U(0, x), V(0, x), M(0, x), ω(0, x)) ∈ X_0^4$ satisfying

$$\liminf_{t→∞} V(t, x) ≥ η, \quad \liminf_{t→∞} M(t, x) ≥ η, \quad \liminf_{t→∞} ω(t, x) ≥ η \text{ uniformly for } x ∈ \overline{Ω}.$$
Remark 1. For the spatially homogeneous case where all parameters of model (3) are constants, both conditions (11) and (16) are equivalent to \( R_0 < 1 \) and \( R_0 > 1 \), respectively. For the spatially heterogeneous case, some sufficient conditions are needed for the comparison principle applicable to a quasilinearly parabolic auxiliary system. Hence, we only obtain some sufficient conditions for global dynamics of model (3) with nonlinear diffusion. Additionally, the condition (8) needs further improvement.

6. Biological implications. In this section, we discuss the influence of repulsion effect to the spreading speed of virus quantitatively when \( \Omega = R \). Since our focus is on the repulsion effect, we neglect the mobility of uninfected cells, infected cells and inflammatory cytokines. Namely, we consider the following reaction-diffusion system:

\[
\begin{align*}
\frac{\partial U(t, x)}{\partial t} &= \xi(x) - \frac{\beta(x)U(t, x)\omega(t, x)}{1 + a_1\omega(t, x) + a_2U(t, x)} - d_UU(t, x) - \frac{q(x)U(t, x)M(t, x)}{1 + bU(t, x)} , \\
\frac{\partial V(t, x)}{\partial t} &= \beta(x)U(t, x)\omega(t, x) - (d_V + \alpha_1)V(t, x) , \\
\frac{\partial M(t, x)}{\partial t} &= \alpha_2(x)V(t, x) - d_MM(t, x) , \\
\frac{\partial \omega(t, x)}{\partial t} &= \nabla \cdot (D_\omega(V)\nabla \omega) + k(x)V(t, x) - d_\omega \omega(t, x) .
\end{align*}
\]

Since \( D_\omega(V) \) is dependent on \( V \), it remains a challenging problem to solve it analytically. In what follows, we explore the repulsion effect for the spreading speed of virus numerically. We choose the function

\[ g(V) = g_0V, \quad (g_0 > 0), \]

to describe the repulsion effect. Obviously, the function \( g \) satisfies \( g(0) = 0 \), and is an increasing function of \( V \).

We choose the parameters as follows

\[ \xi = 10^7, \quad d_U = 0.1, \quad \beta = 9 \times 10^{-9}, \quad k = 500, \quad d_\omega = 5, \quad q = 0.0001, \alpha_1 = 0.01, \alpha_2 = 100, \quad d_M = 0.0001, \quad d_V = 0.1, \quad a_1 = 1 \times 10^{-8}, \quad a_2 = 1 \times 10^{-6}, \quad D_2 = 0.0001. \]

The initial functions are chosen as follows

\[ U_0(x) = 10^7, \quad V_0(x) = 0, \quad M_0(x) = 0, \quad \omega_0(x) = \begin{cases} 0 & \text{if } x < 0 \\ 100 & \text{if } x = 0 \\ 0 & \text{if } x > 0 \end{cases}. \]

The initial function \( \omega_0(x) \) indicates that 100 viruses are initially inoculated at \( x = 0 \). The asymptotic spreading speed can be estimated by using the method developed in [12]. More precisely, we assume that there exists some threshold value for virus \( \omega \). If the virus is below the threshold value, then the presence of the virus cannot be detected. We denote the location where the virus equals \( \omega \) as \( x(t) \). The asymptotic spreading speed is defined as

\[ c = \lim_{t \to +\infty} \frac{dx(t)}{dt}, \]

which describes the rate of increase of \( x(t) \) as \( t \) increases. Figure 1 (a) denotes the initial distribution of \( \omega_0(x) \). In Figure 1 (b), numerical results are plotted for \( g_0 = 0 \).
Figure 1. **a.** Initial distribution $\omega_0(x)$. **b.** Evolution of $\omega(t, x)$ from the initial distribution, where *dashed line (red)*: $g_0 = 0$, *solid line (black)*: $g_0 = 3.8 \times 10^{-8}$. **c.** The contour of **b.**

Figure 2. **a.** Evolution of $\omega(t, x)$ from the initial distribution, where *dashed line (red)*: $g_0 = 0$, *solid line (black)*: $g_0 = 3.8 \times 10^{-8}$. **b.** The contour of **a.**

(without repulsion effect) and $g_0 = 3.8 \times 10^{-8}$ (with repulsion effect). In Figure 1 (c), the inner triangle region represents the asymptotic spreading speed when the repulsion effect is neglected ($g_0 = 0$). The outer triangle region describes the asymptotic spreading speed when the repulsion effect is considered ($g_0 = 3.8 \times 10^{-8}$). From the numerical simulations, we observe that the repulsion effect can promote the asymptotic spreading speed of virus.
We now calculate the asymptotic spreading speed of virus quantitatively to verify the results. Letting $\omega = 0.1$, it follows from Figure 1 (c) that the spreading speed of virus approximately equals $c = 0.081$ in the absence of the repulsion effect ($g_0 = 0$), while the spreading speed of virus approximately equals $c = 0.335$ in the presence of the repulsion effect ($g_0 = 3.8 \times 10^{-8}$). Obviously, we observe that the repulsion effect can promote the asymptotic spreading speed.

If the death rate which is caused by pyroptosis is increased from $\alpha_1 = 0.01$ to $\alpha_1 = 0.08$, from Figure 2, we find that the spreading speed of virus approximately equals $c = 0.3 < 0.335$. In biology, pyroptosis can decrease the spreading speed of virus, which is a new phenomenon not presented in the existing literature.

If the constant $a_1$ is increased from $a_1 = 1 \times 10^{-8}$ to $a_1 = 3.8 \times 10^{-7}$, from Figure 3, we observe that the spreading speed of virus approximately equals $c = 0.192 < 0.335$. Similarly, if the constant $a_2$ is decreased from $a_2 = 1 \times 10^{-6}$ to $a_2 = 1 \times 10^{-7}$, from Figure 4, the spreading speed of virus approximately equals $c = 1.092 > 0.335$. This reveals that Beddington-DeAngelis functional response function plays a crucial role in the controlling of the spreading speed of virus.
Acknowledgments. We are grateful to the editor and anonymous referees for their careful reading and valuable comments which led to an improvement of our original manuscript.

REFERENCES

[1] H. Amann, Dynamical theory of quasilinear parabolic equations III: Global existence, Math. Z., 202 (1989), 219–250.
[2] H. Amann, Nonhomogeneous linear and quasilinear elliptic and parabolic boundary value problems, In: Function spaces, differential operators and nonlinear analysis, (Friedrichroda, 1992), vol 133. Teubner-Texte zur Mathematik. Teubner, Stuttgart, 1993, pp. 9–126.
[3] J. R. Beddington, Mutual interference between parasites or predators and its effect on searching efficiency, J. Animal Ecol., 44 (1975), 331–340.
[4] D. L. DeAngelis, R. A. Goldstein and R. V. O’Neill, A model for trophic interaction, Ecology, 56 (1975), 881–892.
[5] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, On the definition and the computation of the basic reproduction ratio $R_0$ in models of infectious disease in heterogeneous populations, J. Math. Biol., 28 (1990), 365–382.
[6] V. Doceul, M. Hollinshead, L. van der Linden and G. L. Smith, Repulsion of superinfecting virions: A mechanism for rapid virus spread, Science, 327 (2010), 873–876.
[7] G. Huang, W. Ma and T. Takeuchi, Global analysis for delay virus dynamics model with Beddington-DeAngelis functional response, Appl. Math. Lett., 24 (2011), 1199–1203.
[8] X. Lai and X. Zou, Repulsion effect on superinfecting virions by infected cells, Bull. Math. Biol., 76 (2014), 2806–2833.
[9] H. Li and M. Ma, Global dynamics of a virus infection model with repulsive effect, Discrete Contin. Dyn. Syst. Ser. B, 24 (2019), 4783–4797.
[10] 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.
[11] P. Magal and X.-Q. Zhao, Global attractors and steady states for uniformly persistent dynamical systems, SIAM J. Math. Anal., 37 (2005), 251–275.
[12] M. G. Neubert and I. M. Parker, Projecting rates of spread for invasive species, Risk Anal., 24 (2004), 817–831.
[13] S. Pankavich and C. Parkinson, Mathematical analysis of an in-host model of viral dynamics with spatial heterogeneity, Discrete Contin. Dyn. Syst. Ser. B, 21 (2016), 1237–1257.
[14] M. H. Protter and H. Weinberger, Maximum Principles in Differential Equations, Springer-Verlag, 1984.
[15] X. Ren, Y. Tian, L. Liu and X. Liu, A reaction-diffusion within-host HIV model with cell-to-cell transmission, J. Math. Biol., 76 (2018), 1831–1872.
[16] H. L. Smith, Monotone dynamical systems: An introduction to the theory of competitive and cooperative systems, Math Surveys Monogr, vol 41. American Mathematical Society, Providence, RI, 1995.
[17] H. L. Smith and X.-Q. Zhao, Robust persistence for semidynamical systems, Nonlinear Anal., 47 (2001), 6169–6179.
[18] S. Tang, Z. Teng and H. Miao, Global dynamics of a reaction-diffusion virus infection model with humoral immunity and nonlinear incidence, Comput. Math. Appl., 78 (2019), 786–806.
[19] F.-B. Wang, Y. Huang and X. Zou, Global dynamics of a PDE in-host viral model, Appl. Anal., 93 (2014), 2312–2329.
[20] W. Wang, W. Ma and Z. Feng, Complex dynamics of a time periodic nonlocal and time-delayed model of reaction-diffusion equations for modelling CD4+ T cells decline, J. Comput. Appl. Math., 367 (2020), 112430, 29 pp.
[21] W. Wang and X.-Q. Zhao, A nonlocal and time-delayed reaction-diffusion model of dengue transmission, SIAM J. Appl. Math., 71 (2011), 147–168.
[22] W. Wang and X.-Q. Zhao, Basic reproduction numbers for reaction-diffusion epidemic model, SIAM J. Appl. Dyn. Syst., 11 (2012), 1652–1673.
[23] W. Wang and X.-Q. Zhao, Spatial invasion threshold of lyme disease, SIAM J. Appl. Math., 75 (2015), 1142–1170.
[24] W. Wang and T. Zhang, Caspase-1-mediated pyroptosis of the predominance for driving CD4+ T cells death: A nonlocal spatial mathematical model, Bull. Math. Biol., 80 (2018), 540–582.
[25] Y. Zhang and Z. Xu, *Dynamics of a diffusive HBV model with delayed Beddington-DeAngelis response*, *Nonlinear Anal. RWA*, 15 (2014), 118–139.

[26] X.-Q. Zhao, *Dynamical Systems in Population Biology*, 2nd edn. CMS Books in Mathematics, Springer, Cham, 2017.

[27] G. Zhao and S. Ruan, *Spatial and temporal dynamics of a nonlocal viral infection model*, *SIAM J. Appl. Math.*, 78 (2018), 1954–1980.

Received January 2020; revised July 2020.

E-mail address: weiwang10437@sdust.edu.cn
E-mail address: wanbiao_ma@ustb.edu.cn
E-mail address: xiulanlai@ruc.edu.cn