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GLOBAL DYNAMICS OF A REACTION AND DIFFUSION MODEL FOR AN HTLV-I INFECTION WITH MITOTIC DIVISION OF ACTIVELY INFECTED CELLS *

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Abstract This paper is concerned with the global dynamics of a reaction and diffusion model for an HTLV-I infection with mitotic division of actively infected cells and CTL immune response. The well posedness of the proposed model is investigated. In the case of a bounded spatial domain, we establish the threshold dynamics in terms of the basic reproduction number $\mathcal{R}_0$ for the spatially heterogeneous model. Also, by means of different Lyapunov functions, the global asymptotic properties of the steady states for the spatially homogeneous model are studied. In the case of an unbounded spatial domain, there are no travelling wave solutions connecting the infection-free steady state with itself when $\mathcal{R}_0 < 1$. Finally, numerical simulations and conclusions are given.

Keywords HTLV-I infection model, CTL immune response, Threshold dynamics, Global stability, Travelling wave solutions.

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1. Introduction

Mathematical models combined with experimental measurements have been proved to be valuable in understanding the dynamics of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and human T-cell leukemia type-1 (HTLV-I) pathogenesis (see, for example [5, 38–40]). Analysis of mathematical models is also very helpful for the clinical treatment. In recent years, the dynamics of the HIV, HBV and HTLV-I models have received considerable attentions (see, for example [4, 13, 19, 32, 33, 38–40] and the references therein).

HTLV-I is a persistent human retrovirus that infects many individuals worldwide. HTLV-I infection is life-long and there is still no cure nor preventative vaccine for HTLV-I, and neither is there satisfactory treatment for HTLV-I-associated pathologies (see, for example [5, 32, 37]). In most virus infections, cytotoxic T lymphocytes (CTLs) plays an important role in antiviral defense by providing a cell-mediated response to specific foreign antigens associated with cells (see, for example, [7, 28, 33, 51]). Because of the importance in medicine, dynamical properties

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of HTLV-I models with immune response have been studied by many authors. Considering the mitotic division of actively infected cells and CTL immune response, [33] investigated the following HTLV-I infection model

$$\begin{cases} \dot{x}_s(t) = \xi - \mu_1 x_s(t) - \beta x_s(t) y(t), \\ \dot{u}(t) = \beta x_s(t) y(t) + r y(t) - (\tau + \mu_2) u(t), \\ \dot{y}(t) = \tau u(t) - \gamma y(t) z(t) - \mu_3 y(t), \\ \dot{z}(t) = v y(t) - \mu_4 z(t), \end{cases} \tag{1.1}$$

where $x_s(t)$, $u(t)$, $y(t)$, and $z(t)$ represent density of healthy $CD4^+$ helper T-cells, latently infected $CD4^+$ helper T-cells, actively infected $CD4^+$ helper T-cells, and HTLV-I-specific $CD8^+$ CTLs at time t, respectively. T cells are produced at a rate ξ, die at rate $\mu_1 x_s(t)$, and become latently infected cells at rate $\beta x_s(t) y(t)$. The constant μ_2 represents the death rate of latently infected $CD4^+$ T cells. The actively infected $CD4^+$ helper T-cells are produced at rate $\tau u(t)$, die at rate $\mu_3 y(t)$ and are removed at rate $\gamma y(t) z(t)$ by the CTL immune response. The constant τ is the rate of the latently infected cells translating to the actively infected cells. The actively infected cells by mitosis produce daughter cells and the daughter cells enter the latent period at the rate $r y(t)$. The CTL cells proliferate at rate $v y(t)$ by contacting with infected cells, and die at rate $\mu_4 z(t)$.

For the model (1.1), the global stabilities of the equilibria were discussed by [33]. It is traditionally assumed that the rate of infection in most HTLV-I models is bilinear according to the principle of mass action. Recently, various functional response functions have been studied in many mathematical models, such as the Holling-II, Beddington-DeAngelis functional response, and the Crowley-Martin functional response and so on (see, for example [10, 15, 18, 19, 22, 24, 26, 29, 44, 56, 58] and the references therein). In these functional response functions mentioned above, the incidence rate of the form $\beta x^p y^q$, where x and y are respectively the number of susceptible and infective individuals in the population, and β, p and q are positive constants, is the most common nonlinear incidence rate. In recent years, models with this incidence rate were considered by many authors (see, for example [15, 24, 29, 51] and the references therein). Epidemiological models with the incidence rate of the form $\beta x^p y^q$ show a much wider range of dynamical behaviors than to those with bilinear incidence rate βxy. These behaviors are mainly determined by parameters β, p and q. For such models, there may exist multiple attractive regions in phase space (see, for example, [29]). In some cases, periodic solutions may appear by Hopf bifurcation at some critical parameter value (see, for example, [15, 29]).

The model (1.1) which is governed by ordinary differential equations is implicitly assumed that cells are well mixed. However, there is another phenomenon that plays a crucial role in determining the dynamical behavior of the model (1.1), that is diffusion (see, for example [11, 12, 27, 34, 48, 50, 54, 56, 58] and the references therein). From [23], we know that T cells/macrophages must pass through the basement membrane and migrate into the central nervous system (CNS) parenchyma after trans-endothelial migration. Also, as argued by [6, 7, 28, 46], we have that $CD4^+$ (both healthy cells and infected cells) and $CD8^+$ CTLs can move and go from regions of high concentration to regions of low concentration. That is, the cells may disperse spatially and evolve in time. Both of these considerations involving diffusion process may cause different cell movements because of the different con-

centration levels of cells (see, for example, [11, 12, 27, 34, 48, 50, 54–56, 58] and the references therein).

Since the pioneering work of [41], the existence of travelling wave solutions in reaction-diffusion models has drawn much attentions. The model with reaction terms satisfying the quasi-monotonicity or exponential quasi-monotonicity conditions was considered, and a monotone iteration scheme was established by [49]. Then the method of Schauder's fixed point theorem is employed to prove the existence of travelling wavefronts to the model with quasi-monotonicity [35]. However, the reaction terms for many models may not satisfy either the quasi-monotonicity or the exponential quasi-monotonicity conditions. Therefore, it is a very interesting problem to investigate the existence of travelling wave solutions for models with non-quasi-monotonic reaction terms. Recently, the existence of travelling wave solutions of a class of delayed models with two equations is investigated by employing the Schauder's fixed point theorem, in which non-linear reaction terms satisfy the partial quasi-monotonicity (PQM) and partial exponential quasi-monotonicity (see, for example, [17, 30]). Further, the existence of travelling wave solutions of the delayed models with three equations for virus infection dynamical models are investigated in which the non-linear reaction terms satisfy the partial quasi-monotonicity (PQM) (see, for example, [12, 58]). Some further developments can be found in [12, 34, 50, 55, 56, 58, 60].

Taking into account the inhomogeneous distribution of cells in different spatial locations within a domain $\Omega \subseteq \mathbb{R}^N (N \geq 1)$ with smooth boundary $\partial\Omega$ at any given time, a diffusive HTLV-I infection model with mitotic division of actively infected cells, CTL immune response and nonlinear incidence is proposed

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D_1 \Delta x_s + \xi(x) - \mu_1 x_s(x,t) - \beta(x) x_s^q(x,t) y^p(x,t), \\ \dfrac{\partial u(x,t)}{\partial t} = D_1 \Delta u + \beta(x) x_s^q(x,t) y^p(x,t) + r(x) y(x,t) - (\tau(x) + \mu_2) u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} = D_1 \Delta y + \tau(x) u(x,t) - \gamma(x) y(x,t) z(x,t) - \mu_3 y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} = D_2 \Delta z + v(x) y(x,t) - \mu_4 z(x,t). \end{cases} \tag{1.2}$$

The model (1.2) is based on some assumptions. Firstly, we assume the within-host environment is spatially heterogenous. That is, we assume that $\xi(x)$, $\beta(x)$, $r(x)$, $\tau(x)$, $\gamma(x)$, and $v(x)$ may depend on the spatial location x. We further assume that these functions are positive, continuous and bounded in x on $\overline{\Omega}$ assuming

$$\begin{aligned} &\overline{\xi} = \max_{x\in\overline{\Omega}} \xi(x), \ \overline{\beta} = \max_{x\in\overline{\Omega}} \beta(x), \ \overline{r} = \max_{x\in\overline{\Omega}} r(x), \ \overline{v} = \max_{x\in\overline{\Omega}} v(x), \\ &\overline{\gamma} = \max_{x\in\overline{\Omega}} \gamma(x), \ \overline{\tau} = \max_{x\in\overline{\Omega}} \tau(x), \ \underline{\xi} = \min_{x\in\overline{\Omega}} \xi(x). \end{aligned}$$

Secondly, we assume that healthy $CD4^+$ helper T-cells, latently infected $CD4^+$ helper T-cells, and actively infected $CD4^+$ helper T-cells can move (see, for example, [6,7,23,28,46]) and follow the Fickian diffusion with the same diffusion rate D_1 (see, for example [34]), meaning that the fluxes of these cells are proportional to their concentration gradient and go from regions of high concentration to regions of low concentration.

Thirdly, we also assume that HTLV-I-specific $CD8^+$ CTLs can move (see, for example, [6, 7, 28, 46]), following the Fickian diffusion with diffusion rate D_2. Note that movement of $CD4^+$ T cells may be slow comparing with $CD8^+$ CTLs, that is, $D_1 \leq D_2$.

If $p \neq 1$ and $q \neq 1$, then the existence of the steady states of the model (1.2) seems very intricate. For the sake of simplicity, in this paper, we assume $p = 1$ and $q > 0$ (see, for example [51]). That is, we consider the following diffusive HTLV-I infection model with mitotic division of actively infected cells, CTL immune response and nonlinear incidence

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D_1 \Delta x_s + \xi(x) - \mu_1 x_s(x,t) - \beta(x) x_s^q(x,t) y(x,t), \\ \dfrac{\partial u(x,t)}{\partial t} = D_1 \Delta u + \beta(x) x_s^q(x,t) y(x,t) + r(x) y(x,t) - (\tau(x) + \mu_2) u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} = D_1 \Delta y + \tau(x) u(x,t) - \gamma(x) y(x,t) z(x,t) - \mu_3 y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} = D_2 \Delta z + v(x) y(x,t) - \mu_4 z(x,t), \end{cases} \tag{1.3}$$

for $t > 0,\ x \in \Omega$, with the Neumann boundary conditions

$$\frac{\partial x_s(x,t)}{\partial n} = \frac{\partial u(x,t)}{\partial n} = \frac{\partial y(x,t)}{\partial n} = \frac{\partial z(x,t)}{\partial n} = 0, \qquad t > 0,\ x \in \partial\Omega, \tag{1.4}$$

and the initial conditions

$$\begin{aligned} &x_s(x,0) = x_{s0}(x) > 0,\ u(x,0) = u_0(x) \geq 0, \\ &y(x,0) = y_0(x) \geq 0,\ z(x,0) = z_0(x) \geq 0, \qquad x \in \overline{\Omega}. \end{aligned} \tag{1.5}$$

In the model (1.3), $x_s(x,t)$, $u(x,t)$, $y(x,t)$ and $z(x,t)$ represent density of healthy $CD4^+$ helper T-cells, latently infected $CD4^+$ helper T-cells, actively infected $CD4^+$ helper T-cells, and HTLV-I-specific $CD8^+$ CTLs at location x and time t, respectively. Δ is the Laplacian operator. Other parameters are the same as the model (1.1) in [33]. $\frac{\partial}{\partial n}$ denotes the outward normal derivative on $\partial\Omega$, and the Neumann boundary conditions imply that the cell populations do not move across the boundary $\partial\Omega$.

The purpose of this paper is to investigate threshold dynamics for the spatially heterogeneous model and the global stabilities of the two classes of steady states for the spatially homogeneous model in the case of a bounded spatial domain. Furthermore, we are also interested in the nonexistence of travelling wave solutions when $\mathcal{R}_0 < 1$ in the case of an unbounded spatial domain.

This paper is organized as follows. In Section 2, we discuss well posedness of the model (1.3). In the case of a bounded spatial domain, we establish the basic reproduction number $\mathcal{R}_0$ and investigate the threshold dynamics. By means of different Lyapunov functions, the global asymptotic properties of the steady states are obtained in Section 3. In Section 4, the non-existence of travelling wave solutions which connects the infection-free steady state E_0 with itself of the model (1.3) when $\mathcal{R}_0 < 1$ is discussed. In Section 5, numerical simulations and conclusions are given. We also investigate the existence of travelling wave solutions connecting the infection free steady state E_0 and the chronic-infection steady state E^* by numerical simulations.

2. Spatially heterogeneous model

In this section, we investigate the well posedness of the model (1.3) and establish the basic reproduction number $\mathcal{R}_0$. Further, we study the threshold dynamics in terms of $\mathcal{R}_0$ for the spatially heterogeneous model, assuming a bounded spatial domain $\Omega \subseteq \mathbb{R}^N$.

2.1. Well posedness of the model

In this section, we use the method similar to [34] study the well posedness of the model (1.3) (see, also [55]). As usual, we denote the following positive cone in $\mathbb{R}^4$ by $\mathbb{R}^4_+$, i.e.,

$$\mathbb{R}^4_+ = \{U = (x_s, u, y, z)^T \in \mathbb{R}^4 \mid x_s \geq 0, u \geq 0, y \geq 0, z \geq 0\}.$$

Let $p > 4$ so that the space $W^{1,p}(\Omega, \mathbb{R}^4)$ is continuously embedded in the continuous function space $C(\Omega, \mathbb{R}^4)$ (see, for example [1]). Since x_s, u, y and z are populations, we only need to consider the following phase space

$$X_+ = \{U \in W^{1,p}(\Omega, \mathbb{R}^4) \mid U(\overline{\Omega}) \subset \mathbb{R}^4_+ \text{ and } \partial U/\partial n = 0 \text{ on } \partial\Omega\}.$$

Obviously, the model (1.3) can be rewritten as the following abstract quasi-linear parabolic model

$$\begin{aligned} &U_t + \mathcal{A}(U)U = \mathcal{F}(x, U), \ x \in \Omega, \ t > 0, \\ &\mathcal{B}U = 0, \ x \in \partial\Omega, \ t > 0, \end{aligned}$$

where

$$\mathcal{A}(U)U = -\sum_{j,k} \partial_j(a_{j,k}\partial_k U), \ \mathcal{B}U = \frac{\partial U}{\partial n},$$

and $a_{j,k} = a\delta_{j,k}$, $1 \leq j, k \leq 4$,

$$a = \begin{pmatrix} D_1 & 0 & 0 & 0 \\ 0 & D_1 & 0 & 0 \\ 0 & 0 & D_1 & 0 \\ 0 & 0 & 0 & D_2 \end{pmatrix},$$

here $\delta_{j,k}$ is the Kronecker delta function, and

$$\begin{aligned} \mathcal{F}(x, U) = \Big(&\xi(x) - \mu_1 x_s - \beta(x) x_s^q y, \ \beta(x) x_s^q y + r(x) y - (\tau(x) + \mu_2) u, \\ &\tau(x) u - \gamma(x) y z - \mu_3 y, \ v(x) y - \mu_4 z\Big)^T, \end{aligned}$$

for $U = (x_s, u, y, z)$. Clearly, we know that $a \in C^2(L(\mathbb{R}^4_+))$, where we identified $L(\mathbb{R}^4_+)$ with the space of 4×4 real matrices. Furthermore, the boundary value problem is normally elliptic (see, for example [3]). For the global existence and nonnegativity of solutions of the model (1.3), we have the following theorem.

Theorem 2.1. *Assuming that $\overline{r} < \mu$, for every initial value (x_{s0}, u_0, y_0, z_0), the model (1.3) has a unique solution defined on $[0, +\infty) \times \overline{\Omega}$, such that*

$$(x_s, u, y, z) \in C\Big([0, +\infty), X_+\Big) \cap C^{2,1}\Big([0, +\infty) \times \overline{\Omega}, \mathbb{R}^4\Big).$$

Moreover, the solution of the model (1.3) satisfies $x_s(x,t) \geq 0$, $u(x,t) \geq 0$, $y(x,t) \geq 0$ and $z(x,t) \geq 0$, for all $(t,x) \in [0, +\infty) \times \overline{\Omega}$, where $\mu = \min\{\mu_1, \mu_2, \mu_3\}$.

Proof. Note that the model (1.3) is normally elliptic and triangular. According to [3, Theorem 14.4 and Theorem 14.6] or [2, Theorem 1], the model (1.3) has a unique classical solution (x_s, u, y, z) defined on $[0, \eta_0) \times \overline{\Omega}$ such that

$$(x_s, u, y, z) \in C\Big([0, \eta_0),\ X_+\Big) \cap C^{2,1}\Big([0, \eta_0) \times \overline{\Omega},\ \mathbb{R}^4\Big),$$

where $\eta_0 > 0$ is the maximal interval of existence of the solution of the model (1.3). From [3, Theorem 15.1], we know that the solution of the model (1.3) is nonnegative. In order to show that $\eta_0 = +\infty$, motivated by [2, Theorem 5.2], it suffices to prove that the solution of the model (1.3) is bounded.

Next, we need to show that any nonnegative solution $(x_s(x,t), u(x,t), y(x,t), z(x,t))$ of the model (1.3) lies in a certain bounded region.

Let $W = x_s + u + y$. Adding the first three equations of the model (1.3) yields

$$\frac{\partial W(x,t)}{\partial t} \leq D_1 \Delta W + \overline{\xi} - (\mu - \overline{r})W.$$

By [31, Lemma 1], we know that $\frac{\overline{\xi}}{\mu - \overline{r}}$ is the globally attractive steady state for the scalar parabolic equations

$$\begin{aligned} &\frac{\partial W(x,t)}{\partial t} = D\Delta W + \overline{\xi} - (\mu - \overline{r})W, \quad x \in \Omega,\ t > 0, \\ &\frac{\partial W}{\partial n} = 0, \quad x \in \partial\Omega,\ t > 0. \end{aligned}$$

From [42, Theorem 7.3.4], we know that $x_s + u + y$ is bounded. Combined with the nonnegativity of x_s, u, and y, we obtain that $x_s(x,t)$, $u(x,t)$ and $y(x,t)$ of the model (1.3) are bounded. We assume $0 \leq x_s(x,t) \leq X_M$, $0 \leq u(x,t) \leq U_M$ and $0 \leq y(x,t) \leq Y_M$.

Here we assume $\overline{r} < \mu$ which corresponds to the producing rate of $CD4^+$ T cells being lower than the rate of removal due to natural death [33]. Thus, it ensures that the quantity on the right-hand side of the inequality is always positive.

From the last equation of the model (1.3), we have

$$\begin{aligned} \frac{\partial z(x,t)}{\partial t} &= D_2 \Delta z + v(x) y(x,t) - \mu_4 z(x,t) \\ &\leq D_2 \Delta z + Y_M \overline{v} - \mu_4 z(x,t), \end{aligned}$$

which implies that $z(x,t)$ of the model (1.3) is bounded assuming that $0 \leq z(x,t) \leq Z_M$. We completes the proof. □

2.2. Basic reproduction number

In this subsection, we establish the basic reproduction number $\mathcal{R}_0$ for the reaction-diffusion equation with spatially heterogenous for the model (1.3).

Letting $\mathbb{X} = C(\overline{\Omega},\ \mathbb{R}^4)$ be the Banach space of continuous functions with supremum norm $\|\cdot\|_{\mathbb{X}}$. We also denote the positive cone as $\mathbb{X}_+ = C(\overline{\Omega},\ \mathbb{R}^4_+)$. It is easy to see that $\mathbb{X}_+$ induces a partial order, making $(\mathbb{X},\ \mathbb{X}_+)$ strongly ordered space. Again, we denote $\mathbb{Y} := C(\overline{\Omega},\ \mathbb{R})$ and $\mathbb{Y}_+ = C(\overline{\Omega},\ \mathbb{R}_+)$.

To this end, we firstly show that the model (1.3) has a unique infection-free steady state. Letting $u(x,t) = 0$, $y(x,t) = 0$ and $z(x,t) = 0$ in the $x_s(x,t)$ equation in the model (1.3), we easily obtain that

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D_1 \Delta x_s(x,t) + \xi(x) - \mu_1 x_s(x,t),\ x \in \Omega,\ t > 0, \\ \dfrac{\partial x_s(x,t)}{\partial n} = 0,\ x \in \partial\Omega,\ t > 0. \end{cases} \tag{2.1}$$

From [31, Lemma 1], we easily obtain that the model (2.1) has a unique positive steady state $\widehat{x_s}(x)$, which is globally attractive in $C(\overline{\Omega}, \mathbb{R})$. Thus, the model (1.3) has a unique infection-free steady state $E_0 = (\widehat{x_s}(x), 0, 0, 0)$.

Linearizing the model (1.3) at E_0, we obtain the following linearized model

$$\begin{cases} \dfrac{\partial u_1}{\partial t} = D_1 \Delta u_1 - \mu_1 u_1 - \beta(x) \widehat{x_s}^{\,q}(x) u_3, \\ \dfrac{\partial u_2}{\partial t} = D_1 \Delta u_2 + \Big(\beta(x) \widehat{x_s}^{\,q}(x) + r(x)\Big) u_3 - \Big(\mu_2 + \tau(x)\Big) u_2, \\ \dfrac{\partial u_3}{\partial t} = D_1 \Delta u_3 + \tau(x) u_2 - \mu_3 u_3, \\ \dfrac{\partial u_4}{\partial t} = D_2 \Delta u_4 + v(x) u_3 - \mu_4 u_4, \end{cases} \tag{2.2}$$

satisfying the following boundary conditions

$$\frac{\partial u_1}{\partial n} = \frac{\partial u_2}{\partial n} = \frac{\partial u_3}{\partial n} = \frac{\partial u_4}{\partial n} = 0, \qquad \forall x \in \partial\Omega,\ t > 0.$$

From the model (2.2), we easily observe that the equations u_2 and u_3 are independent from the equations u_1 and u_4. Obviously, we know that these two equations constitute a cooperative system. Substituting $u_2(x,t) = e^{\lambda t}\varphi_1(x)$ and $u_3(x,t) = e^{\lambda t}\varphi_2(x)$ into equations of u_2 and u_3 of the model (2.2), we get the following eigenvalue problem

$$\begin{aligned} &\lambda\varphi_1(x) = D_1 \Delta \varphi_1(x) + \Big(\beta(x) \widehat{x_s}^{\,q}(x) + r(x)\Big)\varphi_2(x) - \Big(\tau(x) + \mu_2\Big)\varphi_1(x), \\ &\lambda\varphi_2(x) = D_1 \Delta \varphi_2(x) + \tau(x)\varphi_1(x) - \mu_3\varphi_2(x), \end{aligned} \tag{2.3}$$

$$\frac{\partial \varphi_1(x)}{\partial n} = \frac{\partial \varphi_2(x)}{\partial n} = 0, \qquad \forall x \in \partial\Omega,\ t > 0,\ \varphi = (\varphi_1, \varphi_2) \in \mathbb{Y} \times \mathbb{Y}.$$

According to [42, Theorem 7.6.1], we easily get the following Lemma.

Lemma 2.1. *The eigenvalue problem (2.3) has a principal eigenvalue* $\lambda_0\Big(D_1, \widehat{x_s}(x)\Big)$ *with a strictly positive eigenvector.*

Assuming that for each $t \geq 0$, $\mathcal{T}_1(t)$ and $\mathcal{T}_2(t)$ are the strongly continuous semigroups associated with $D_1\Delta - \Big(\tau(x) + \mu_2\Big)$ and $D_1\Delta - \mu_3$ subject to Neumann boundary conditions, respectively, that is,

$$[\mathcal{T}_1(t)\phi](x) = \int_\Omega \Gamma(x, y, t, D_1)\phi(y)dy$$

and

$$[\mathcal{T}_2(t)\phi](x) = e^{-\mu_3 t}\int_\Omega \Gamma(x, y, t, D_1)\phi(y)dy$$

for any $\phi_1,\ \phi_2 \in \mathbb{Y}$, $t \geq 0$. Here $\Gamma(x, y, t, D_1)$ represents the Green function associated with $D_1\Delta$ subject to homogenous Neumann boundary conditions. Therefore, it can be known that $\mathcal{T}_i(t) : \mathbb{Y} \to \mathbb{Y},\ i = 1, 2$ is strongly positive and compact for each $t > 0$ ([42, Corollary 7.2.3]). Thus, we obtain that $\mathcal{T}(t) = \Big(\mathcal{T}_1(t), \mathcal{T}_2(t)\Big)$ is a positive C_0- semigroup.

According to [45, 52], we obtain the basic reproduction number of the model (1.3) (see, also [31]). To this end, we define a positive linear operator as follows

$$\mathcal{S}(\phi)(x) = \Big(\mathcal{S}_1(\phi)(x), \mathcal{S}_2(\phi)(x)\Big), \qquad \forall \phi = (\phi_1, \phi_2) \in \mathbb{Y} \times \mathbb{Y},\ x \in \overline{\Omega},$$

where

$$\mathcal{S}_1(\phi)(x) = \Big(\beta(x)\widehat{x_s}^q(x) + r(x)\Big)\phi_2(x), \qquad \mathcal{S}_2(\phi)(x) = \tau(x)\phi_1(x).$$

In order to establish the basic reproduction number for the spatially heterogeneous model (1.3), we assume that there are no infected cells (both latently infected and actively infected) initially. In other words, the model (1.3) is near E_0. Let $(\phi_1(x), \phi_2(x))$ be the spatial distribution of initial latently infected cells and actively infected cells at $t = 0$. According to the model (1.3), we obtain that, as time evolves, those distributions can reach $\Big([\mathcal{T}_1(t)\phi_1](x),\ [\mathcal{T}_2(t)\phi_2](x)\Big)$ at time t. Therefore, the total distribution of new latently infected cells can have the following form

$$\Big[\int_0^{+\infty} \mathcal{S}_1(\mathcal{T}(t)\phi)dt\Big](x) = \int_0^{+\infty} \Big(\beta(x)\widehat{x_s}^q(x) + r(x)\Big)[\mathcal{T}_2(t)\phi_2](x)dt.$$

Similarly, the total distribution of new actively infected cells have the following form

$$\Big[\int_0^{+\infty} \mathcal{S}_2(\mathcal{T}(t)\phi)dt\Big](x) = \int_0^{+\infty} \tau(x)[\mathcal{T}_1(t)\phi_1](x)dt.$$

Hence, we obtain that

$$\mathcal{L}(\phi) = \int_0^{+\infty} \mathcal{S}\Big(\mathcal{T}(t)\phi\Big)dt = \mathcal{S}\int_0^{+\infty} \Big(\mathcal{T}(t)\phi\Big)dt.$$

Here $\mathcal{L}$ represents the next infection operator. Biologically, the next infection operator maps the initial distribution ϕ of initial latently infected cells and actively

infected cells to the total distribution of new latently infected cells and actively infected cells produced during the infection period.

In view of [9,47,52], we define the spectral radius of $\mathcal{L}$ as the basic reproduction number of the model (1.3), that is,

$$\mathcal{R}_0 = r(\mathcal{L}).$$

By the results in [45] (see, also [53, Theorem 3.1 (i)]), we obtain the following lemma.

Lemma 2.2. *$\mathcal{R}_0 - 1$ has the same sign as λ_0.*

Since the parameters depend on the location x, we cannot give the explicit formula for $\mathcal{R}_0 = r(\mathcal{L})$. For simplicity, here, we assume that all the parameters of the model (1.3) are constants. In the special case, the explicit formula for $\mathcal{R}_0$ can be actually derived. Indeed, applying [53, Theorem 3.4] (see also, [31, Lemma 5]), we easily obtain the following theorem.

Theorem 2.2. *Assume that $\xi(x)$, $\beta(x)$, $r(x)$, $\tau(x)$, $\gamma(x)$, and $v(x)$ are positive constants, so that $\widehat{x_s}(x) = \frac{\xi}{\mu_1} \triangleq x_H$. Then*

$$\mathcal{R}_0 = \sqrt{\frac{\tau(\beta x_H^q + r)}{(\tau + \mu_2)\mu_3}}.$$

We cannot give the explicit formula for the basic reproduction number $\mathcal{R}_0$ if at least one of the parameters are spatially dependent. In this case, numerical simulation becomes a natural choice (see, for example [34,53]). It is worth noting that the diffusion coefficients have no effects on the basic reproduction number $\mathcal{R}_0$ for the case of spatially homogeneous model. We employ numerical simulations to investigate the influence of diffusion coefficients for the basic reproduction number $\mathcal{R}_0$ in the case of the spatially heterogeneous model. For simplicity, we assume $\Omega = (0, 1)$. Then we have

$$\Gamma(x, y, t, D) = 1 + 2\sum_{n=1}^{\infty} e^{-Dn^2\pi^2 t}\cos(n\pi x)\cos(n\pi y).$$

Note that $\mathcal{L}$ is a compact and positive linear operator on $\mathbb{X} = C([0, 1],\ \mathbb{R}^2)$. Therefore, we employ the orthogonal projection method to simulate the basic reproduction number $\mathcal{R}_0$ by computing the eigenvalues of compact linear operators [8]. Let

$$\xi = 10^5,\ \beta(x) = 3{\times}10^{-9}x^2,\ r = 0.1,\ \tau = 0.3,\ \mu_1 = 0.1,\ \mu_2 = 0.2,\ \mu_3 = 0.4,\ \gamma = 450.$$

From the numerical simulation, we find that $\mathcal{R}_0$ is a decreasing function of D_1 (see, Figure 1). Further, we find that $\mathcal{R}_0 = 1$ when $D_1 \approx 0.03$.

2.3. Threshold dynamics in a bounded spatial domain

In this subsection, we establish the threshold-type result in terms of $\mathcal{R}_0$ in a bounded spatial domain. To this end, we need the following Lemmas. In the following, we also assume $\overline{r} < \mu$.

Lemma 2.3. *For any $\phi = (\phi_1, \phi_2, \phi_3, \phi_4) \in \mathbb{X}_+$, the solution semiflow $\Phi(t) = U(t, \cdot, \phi) :\ \mathbb{X}_+ \to \mathbb{X}_+$ has a compact global attractor for $t > 0$.*

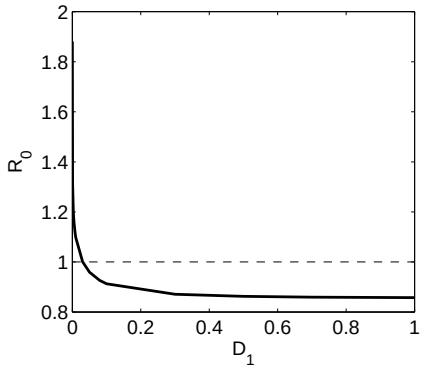

Figure 1. Basic reproduction number $\mathcal{R}_0$ is a decreasing function of D_1.

Proof. From the analysis of Theorem 2.1, we obtain that

$$\frac{\partial W(x,t)}{\partial t} \leq D_1 \Delta W + \overline{\xi} - (\mu - \overline{r})W.$$

Then, the comparison principle implies there exists $t_1(\phi) > 0$ such that $x_s(x,t) \leq \frac{2\overline{\xi}}{\mu-\overline{r}} =: B_1$, $u(x,t) \leq \frac{2\overline{\xi}}{\mu-\overline{r}} =: B_1$ and $y(x,t) \leq \frac{2\overline{\xi}}{\mu-\overline{r}} =: B_1$ for $t > t_1$.

From the forth equation of the model (1.3), we obtain that

$$\frac{\partial z(x,t)}{\partial t} \leq D_1 \Delta z + \overline{v} B_1 - \mu_4 z(x,t).$$

Again, the comparison principle implies there exists $t_2(\phi) > 0$ such that $z(x,t) \leq \frac{2\overline{v}B_1}{\mu_4} =: B_2$ for $t > t_2$.

Furthermore, the solution semiflow $\Phi(t) = U(t,\cdot,\phi) : \mathbb{X}_+ \to \mathbb{X}_+$ is point dissipative. Then it suffices to prove that the solution semiflow is compact. In view of [48, Theorem 2.2.6], we can get that $\Phi(t)$ is compact for any $t > 0$. Thus, from [14, Theorem 3.4.8], it can be concluded that $\Phi(t) = U(t,\cdot,\phi)$ has a compact global attractor in $\mathbb{X}_+$ for $t > 0$. □

Lemma 2.4. *Let $U(t,\cdot,\phi)$ be the solution of the model (1.3) with $U(0,\cdot,\phi) = \phi \in \mathbb{X}_+$, then we have*

(i) If there exists some $t_0 > 0$ such that $u(t_0,\cdot,\phi) \not\equiv 0$, $y(t_0,\cdot,\phi) \not\equiv 0$ and $z(t_0,\cdot,\phi) \not\equiv 0$, then $u(t,\cdot,\phi) > 0$, $y(t,\cdot,\phi) > 0$, and $z(t,\cdot,\phi) > 0$ for all $t > t_0$, $x \in \overline{\Omega}$.

(ii) It holds that $x_s(t,\cdot,\phi) > 0$ for any $t > 0$, $x \in \overline{\Omega}$, $q \geq 1$, and

$$\liminf_{t\to\infty} x_s(t,\cdot,\phi) \geq \frac{\underline{\xi}}{\mu_1 + \overline{\beta} B_1^q}$$

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

Proof. From the model (1.3), we easily obtain that

$$\begin{cases} \dfrac{\partial u(x,t)}{\partial t} \geq D_1\Delta u - (\tau(x)+\mu_2)u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} \geq D_1\Delta y - (\gamma(x)z(x,t)+\mu_3)y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} \geq D_2\Delta z - \mu_4 z(x,t), \\ \dfrac{\partial u(x,t)}{\partial n} = \dfrac{\partial y(x,t)}{\partial n} = \dfrac{\partial z(x,t)}{\partial n} = 0,\ x \in \partial\Omega. \end{cases}$$

If $u(t_0,\cdot,\phi) \not\equiv 0$, $y(t_0,\cdot,\phi) \not\equiv 0$ and $z(t_0,\cdot,\phi) \not\equiv 0$, the comparison principle implies that $u(t,\cdot,\phi) > 0$, $y(t,\cdot,\phi) > 0$, and $z(t,\cdot,\phi) > 0$ for $t > t_0$, $x \in \overline{\Omega}$, that is, the conclusion (i) holds.

From the model (1.3), we easily obtain that

$$\begin{aligned} \frac{\partial x_s(x,t)}{\partial t} &= D_1\Delta x_s + \xi(x) - \mu_1 x_s(x,t) - \beta(x)x_s^q(x,t)y(x,t), \\ &\geq D_1\Delta x_s + \underline{\xi} - (\mu_1 + \overline{\beta}B_1 x_s^{q-1})x_s. \end{aligned}$$

In order to show the conclusion (ii), there are two cases to be discussed.

If $q = 1$, we obtain that $x_s(t,\cdot,\phi) \geq v(t,\cdot,\phi) > 0$ for $t > 0$, $x \in \overline{\Omega}$ and

$$\liminf_{t\to\infty} x_s(t,\cdot,\phi) \geq \frac{\underline{\xi}}{\overline{\beta}B_1 + \mu_1}$$

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

If $q > 1$, we obtain that $x_s(t,\cdot,\phi) \geq v(t,\cdot,\phi) > 0$ for $t > 0$, $x \in \overline{\Omega}$ and

$$\liminf_{t\to\infty} x_s(t,\cdot,\phi) \geq \frac{\underline{\xi}}{\mu_1 + \overline{\beta}B_1^q}$$

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

From the analysis above, we obtain that $x_s(t,\cdot,\phi) \geq v(t,\cdot,\phi) > 0$ for $t > 0$, $x \in \overline{\Omega}$ and

$$\liminf_{t\to\infty} x_s(t,\cdot,\phi) \geq \frac{\underline{\xi}}{\mu_1 + \overline{\beta}B_1^q}$$

for any $q \geq 1$, uniformly for $x \in \overline{\Omega}$. We complete the proof. □

In order to establish the uniform persistence of the model (1.3), we need to show the following Lemma.

Lemma 2.5. *If $\mathcal{R}_0 > 1$, then there exists $\tau_1 > 0$ such that for any $\phi \in \mathbb{X}_+$ with $\phi_2 \not\equiv 0$ and $\phi_3 \not\equiv 0$ the solution $U(t,\cdot,\phi)$ of the model (1.3) satisfying*

$$\limsup_{t\to\infty} \parallel U(t,\cdot,\phi) - (\widehat{x_s}(x),0,0,0) \parallel_{\mathbb{X}_+} \geq \tau_1.$$

Proof. For any given $\phi \in \mathbb{X}_+$ with $\phi_2 \not\equiv 0$ and $\phi_3 \not\equiv 0$, let

$$U(t,x,\phi) = \Big(x_s(t,x), u(x,t), y(t,x), z(t,x)\Big).$$

By the parabolic maximum principle and Lemma 2.4, from the model (1.3), we easily get

$$u(t,x)>0,\ y(t,x)>0,\ \forall t>0,\ x\in\overline{\Omega}. \tag{2.4}$$

Since $\mathcal{R}_0>1$, from Lemma 2.2, we easily get $\lambda_0>0$. Then for any given $\tau_1\in(0,\widehat{x_s}(x)]$, let $\lambda_0(\tau_1)$ be the principal eigenvalue of the following elliptic eigenvalue problem

$$\begin{aligned}
\lambda\varphi_1(x)&=D_1\Delta\varphi_1(x)+\Big(\beta(x)(\widehat{x_s}(x)-\tau_1)^q+r(x)\Big)\varphi_2(x)-\Big(\tau(x)+\mu_2\Big)\varphi_1(x),\\
\lambda\varphi_2(x)&=D_1\Delta\varphi_2(x)+\tau(x)\varphi_1(x)-\Big(\mu_3+\gamma(x)\tau_1\Big)\varphi_2(x),
\end{aligned}$$

$$\frac{\partial\varphi_1(x)}{\partial n}=\frac{\partial\varphi_2(x)}{\partial n}=0,\ \forall x\in\partial\Omega,\qquad t>0,\ \varphi=(\varphi_1,\varphi_2)\in\mathbb{Y}\times\mathbb{Y}.$$

It is easy to obtain $\lim\limits_{\tau_1\to0^+}\lambda_0(\tau_1)=\lambda_0$. Therefore, we can fix a sufficiently small number $\tau_1\in(0,\widehat{x_s}(x)]$ such that $\lambda_0(\tau_1)>0$. By contradiction, we assume that there exists some $\phi\in\mathbb{X}_+$ with $\phi_2\not\equiv0$ and $\phi_3\not\equiv0$ such that

$$\limsup_{t\to\infty}\parallel U(t,\cdot,\phi)-(\widehat{x_s}(x),0,0,0)\parallel_{\mathbb{X}_+}<\tau_1.$$

Then there exists a sufficiently large positive number T_1 such that

$$\widehat{x_s}(x)-\tau_1<x_s(x,t)<\widehat{x_s}(x)+\tau_1,\ y(x,t)<\tau_1,\ z(x,t)<\tau_1,\ \forall t\geq T_1,\ x\in\overline{\Omega}.$$

Therefore, for $\forall t\geq T_1,\ x\in\overline{\Omega}$, we obtain the following model

$$\begin{cases}
\dfrac{\partial u}{\partial t}\geq D_1\Delta u+\Big(\beta(x)(\widehat{x_s}(x)-\tau_1)^q+r(x)\Big)y-\Big(\mu_2+\tau(x)\Big)u,\\
\dfrac{\partial y}{\partial t}\geq D_1\Delta y+\tau(x)u-\Big(\mu_3+\gamma(x)\tau_1\Big)y,
\end{cases}$$

We easily see that $(v_2(x,t),\ v_3(x,t)):=e^{\lambda_0(\tau_1)t}\Big(\psi_1(x),\ \psi_2(x)\Big)$ satisfies the following linear model

$$\begin{cases}
\dfrac{\partial v_2}{\partial t}=D_1\Delta u_2+\Big(\beta(x)(\widehat{x_s}(x)-\tau_1)^q+r(x)\Big)v_3-\Big(\mu_2+\tau(x)\Big)v_2,\\
\dfrac{\partial v_3}{\partial t}=D_1\Delta v_3+\tau(x)v_2-\Big(\mu_3+\gamma(x)\tau_1\Big)v_3,\qquad t\geq T_1.
\end{cases}$$

Here, $\Big(\psi_1(x),\ \psi_2(x)\Big)$ be the positive eigenfunction associated with λ_0.

In view of (2.4) and the comparison principle, we can choose a sufficiently small number $\vartheta>0$ such that

$$\Big(u(x,t),\ y(x,t)\Big)\geq\vartheta\Big(v_2(x,t),\ v_3(x,t)\Big),\ \forall t\geq T_1,\ x\in\overline{\Omega}.$$

Since $\lambda_0(\tau_1)>0$, we obtain

$$\lim_{t\to+\infty}u(t,x)=\infty,\ \lim_{t\to+\infty}y(t,x)=\infty,$$

which is a contradiction. We complete the proof. □

Now we state the result of threshold dynamics as follows.

Theorem 2.3. *If $\mathcal{R}_0 < 1$, then the infection-free steady state E_0 is globally attractive in $\mathbb{X}_+$ for the model (1.3).*

If $\mathcal{R}_0 > 1$, then there exists $\zeta > 0$ such that any nonnegative solution $U(t,x,\phi)$ with $\phi_2 \not\equiv 0$ and $\phi_3 \not\equiv 0$ such that

$$\liminf_{t\to\infty} u(x,t) \geq \zeta, \ \liminf_{t\to\infty} y(x,t) \geq \zeta,$$

uniformly for all $x \in \overline{\Omega}$.

Proof. It is easy to see that $\lambda_0(\widehat{x_s}(x)) < 0$ when $\mathcal{R}_0 < 1$ by Lemma 2.2. Since

$$\lim_{\varepsilon\to 0} \lambda_0\Big(\widehat{x_s}(x)+\varepsilon\Big) = \lambda_0\Big(\widehat{x_s}(x)\Big) < 0,$$

there exists $\varepsilon_0 > 0$ sufficiently small such that $\lambda_0\Big(\widehat{x_s}(x)+\varepsilon_0\Big) < 0$. For fixed $\varepsilon_0 > 0$, there exists $T_2 > 0$ such that $x_s(x,t) \leq \widehat{x_s}(x) + \varepsilon_0$ for all $t \geq T_2,\ x \in \overline{\Omega}$. Therefore, for all $t \geq T_2$, we obtain the following

$$\begin{cases} \dfrac{\partial u}{\partial t} \leq D_1\Delta u + \Big(\beta(x)(\widehat{x_s}(x)+\varepsilon_0)^q + r(x)\Big)y - \Big(\mu_2+\tau(x)\Big)u, \\ \dfrac{\partial y}{\partial t} \leq D_1\Delta y + \tau(x)u - \mu_3 y, \\ \dfrac{\partial z}{\partial t} \leq D_2\Delta z + v(x)y - \mu_4 z. \end{cases}$$

Then there exists a strongly positive eigenfunction ψ_0 corresponding to $\lambda_0(\widehat{x_s}(x)+\varepsilon_0) < 0$. It then obtains the following linear system

$$\begin{cases} \dfrac{\partial V_1}{\partial t} = D_1\Delta V_1 + \Big(\beta(x)(\widehat{x_s}(x)+\varepsilon_0)^q + r(x)\Big)V_2 - \Big(\mu_2+\tau(x)\Big)V_1, \\ \dfrac{\partial V_2}{\partial t} = D_1\Delta V_2 + \tau(x)V_1 - \mu_3 V_2, \\ \dfrac{\partial V_3}{\partial t} = D_2\Delta V_3 + v(x)V_2 - \mu_4 V_3. \end{cases}$$

$$\frac{\partial V_1}{\partial n} = \frac{\partial V_2}{\partial n} = \frac{\partial V_3}{\partial n} = 0, \qquad x \in \partial\Omega,$$

admits a solution $V(t,x) = e^{\lambda_0(\widehat{x_s}(x)+\varepsilon_0)t}\psi_0(x)$. Since for any given $\phi \in \mathbb{X}_+$, there exists $\acute{\alpha} > 0$ such that

$$\Big(u(T_2,\cdot,\phi), y(T_2,\cdot,\phi), z(T_2,\cdot,\phi)\Big) \leq \acute{\alpha}V(T_2,\cdot,\phi).$$

It then follow from the comparison principle

$$\Big(u(t,x,\phi), y(t,x,\phi), z(t,x,\phi)\Big) \leq \acute{\alpha}e^{\lambda_0(\widehat{x_s}(x)+\varepsilon_0)t}\psi_0(x), \qquad \forall t \geq T_2.$$

We then obtain that $\lim\limits_{t\to+\infty}\Big(u(t,x,\phi), y(t,x,\phi), z(t,x,\phi)\Big) = 0$ uniformly for $x \in \overline{\Omega}$. Therefore, in view of [31], we obtain that

$$\lim_{t\to+\infty} x_s(t,x,\phi) = \widehat{x_s}(x)$$

uniformly for $\forall x \in \overline{\Omega}$. Then we obtain that the infection-free steady state E_0 of the model (1.3) is globally attractive if $R_0 < 1$ in $\mathbb{X}_+$.

Next, we apply method developed in [43] to study the uniform persistence of the model (1.3) when $\mathcal{R}_0 > 1$.

Define

$$\mathbb{X}_0 = \Big\{\phi = (\phi_1,\ \phi_2,\ \phi_3,\ \phi_4) \in \mathbb{X}_+ :\ \phi_2 \not\equiv 0 \text{ and } \phi_3 \not\equiv 0\Big\}.$$

Clearly, we have

$$\partial\mathbb{X}_0 := \mathbb{X}_+ \backslash \mathbb{X}_0 = \Big\{\phi \in \mathbb{X}_+ :\ \phi_2 \equiv 0 \text{ or } \phi_3 \equiv 0\Big\}.$$

In view of (2.4), we obtain that $\mathbb{X}_0$ is positively invariant for the solution semiflow $\Phi(t)$. Define

$$Q_\partial := \Big\{\phi \in \partial\mathbb{X}_0 :\ \Phi(t)\phi \in \partial\mathbb{X}_0,\ \forall\ t \geq 0\Big\}.$$

Let $\omega(\phi)$ be the omega limit set of the orbit of $\Phi(t)$ through $\phi \in \partial\mathbb{X}_0$, and set

$$Q_1 := \Big\{(\widehat{x_s}(x), 0, 0, 0)\Big\}.$$

For any given $\phi \in Q_\partial$, we have $U_t(\phi) \in \partial\mathbb{X}_0$. Due to $U_t(\phi) = U(t, \cdot, \phi)$, we know that for each $t \geq 0$ either $y(t, \cdot, \phi) \equiv 0$ or $u(t, \cdot, \phi) \equiv 0$. For the case where $y(t, \cdot, \phi) \equiv 0,\ \forall\ t \geq 0$, from the second equation of the model (1.3), it can be seen that $\lim\limits_{t\to+\infty} u(t, x) = 0$. From the forth equation of the model (1.3), we obtain $\lim\limits_{t\to+\infty} z(t, x) = 0$. Furthermore, from the first equation of the model (1.3), we know that

$$\lim_{t\to+\infty} x_s(t, x) = \widehat{x_s}(x)$$

uniformly for $x \in \overline{\Omega}$. In the case where $y(t_0, \cdot, \phi) \not\equiv 0$ for some $t_0 > 0$, by parabolic maximum principle, it can be obtained that $y(t, \cdot, \phi) > 0$ for all $t > t_0$ and $x \in \overline{\Omega}$. Thus, we have $u(t, \cdot, \phi) \equiv 0$ for all $t \geq t_0$. From the second equation of the model (1.3), we get $y(t, \cdot, \phi) \equiv 0$, for $t \geq t_0$, which is a contradiction. Thus, we get $\omega(\phi) = Q_1,\ \forall \phi \in Q_\partial$.

Furthermore, we define a continuous function $p :\ \mathbb{X}_+ \to \mathbb{R}^+$ by

$$p(\phi) = \min\Big\{\min_{x\in\overline{\Omega}} \phi_2(x),\ \min_{x\in\overline{\Omega}} \phi_3(x)\Big\},\ \forall\ \phi \in \mathbb{X}_+.$$

It is easy to see that $p^{-1}(0,\ +\infty) \subset \mathbb{X}_0$ and p has the property that if either $p(\phi) = 0$ and $\phi \in \mathbb{X}_0$, or $p(\phi) > 0$, then $p(\Phi(t)(\phi)) > 0$. Consequently, p is a generalized distance function for the semiflow $\Phi(t) :\ \mathbb{X}_+ \to \mathbb{X}_+$. Note that any forward orbit of $\Phi(t)$ in Q_∂ converges to Q_1. From [43, Theorem 3], it can be concluded that Q_1 is isolated invariant set in $\mathbb{X}_+$. Then we know that $W^s(Q_1) \cap \mathbb{X}_0 = \emptyset$. Here $W^s(Q_1)$ represents the stable set of Q_1. Furthermore, we can easily observe that no subset of Q_1 forms a cycle in $\partial\mathbb{X}_0$. In view of [43, Theorem 3], we show that there exists $\zeta > 0$ such that $\min\{p(\psi) :\ \psi \in \omega(\phi)\} > \zeta$ for any $\phi \in \mathbb{X}_0$. We complete the proof. □

According to the [57, Theorem 1.3.6], we easily obtain the following result.

Corollary 2.1. *If $\mathcal{R}_0 > 1$, then the model (1.3) has at least one coexistence steady state.*

3. Spatially homogeneous model

In this section, we investigate the global stabilities of the steady states for the spatially homogeneous model in a bounded spatial domain. For convenience, we assume that all the parameters are constants. That is, we consider the following dynamic model

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D_1\Delta x_s + \xi - \mu_1 x_s(x,t) - \beta x_s^q(x,t)y(x,t), \\ \dfrac{\partial u(x,t)}{\partial t} = D_1\Delta u + \beta x_s^q(x,t)y(x,t) + ry(x,t) - (\tau+\mu_2)u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} = D_1\Delta y + \tau u(x,t) - \gamma y(x,t)z(x,t) - \mu_3 y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} = D_2\Delta z + vy(x,t) - \mu_4 z(x,t). \end{cases} \tag{3.1}$$

3.1. The existence of the steady states

The model (3.1) always has an infection-free steady state $E_0(x_H, 0, 0, 0)$, where $x_H = \frac{\xi}{\mu_1}$. Next, we will prove the existence of the unique chronic-infection steady state of the model (3.1),

$$y^* = \frac{\xi - \mu_1 x_s^*}{\beta (x_s^*)^q},\ z^* = \frac{vy^*}{\mu_4},\ u^* = \frac{rv}{\tau\mu_4}(y^*)^2 + \frac{\mu_3}{2}y^*,$$

where x_s^* is the root of the following equation

$$F(x) = \beta x^q + r - (\tau+\mu_2)\Big(\frac{rv}{\tau\mu_4}\frac{\xi - \mu_1 x}{\beta x^q} + \frac{\mu_3}{\tau}\Big) = 0.$$

Obviously, $F(x)$ is a monotonically nondecreasing function of x and $F(0) = -\infty$ on $x \in (0, x_H)$, so x_s^* is unique, if it exists.

Moreover, since

$$F(x_H) = \beta(x_H)^q + r - \frac{\mu_3(\tau+\mu_2)}{\tau} = \frac{(\tau+\mu_2)\mu_3}{\tau}(\mathcal{R}_0^2 - 1),$$

the existence of a unique positive root $x^* \in (0, x_H)$ of $F(x) = 0$ is equivalent to the condition that $\mathcal{R}_0 > 1$. Then we have the following theorem.

Theorem 3.1. *(i) The model (3.1) always has an infection-free steady state $E_0(x_H, 0, 0, 0)$;*

(ii) The model (3.1) has a unique chronic-infection steady state $E^*(x_s^*, u^*, y^*, z^*)$ if and only if $\mathcal{R}_0 > 1$.

3.2. The global stability of the steady states

In general, it seems to be very difficult to establish the global stability of the steady states for reaction-diffusion equation models. In recent years, there are many works to investigate the global stabilities of the steady states by employing the techniques of the upper and lower solutions, monotone iteration and Lyapunov direct method

(see, for example, [51, 56, 58]). Here, by constructing the suitable Lyapunov functions, we discuss the global stabilities of the infection-free steady state E_0 and the chronic-infection steady state E^* of the model (3.1) with the homogeneous Neumann boundary conditions (1.4) and the initial conditions (1.5). The Lyapunov functions are motivated by the works of [20–22, 24–26, 36, 51, 52, 59].

For the global stability of the infection-free steady state E_0 of the model (3.1), we have the following result.

Theorem 3.2. *If $\mathcal{R}_0 < 1$, then the infection-free steady state E_0 of the model (3.1) is globally asymptotically stable.*

Proof. If $q \neq 1$, we construct the following Lyapunov function

$$V_1 = \int_\Omega x_s\Big(1 + \frac{1}{q-1}(\frac{x_H}{x_s})^q\Big)dx + \int_\Omega u(t,x)dx + \frac{\tau+\mu_2}{\tau}\int_\Omega y(x,t)dx + \frac{(\tau+\mu_2)\gamma}{2\tau v}\int_\Omega z^2(x,t)dx.$$

Calculating the time derivative of V_1 along the solution of the model (3.1), we have

$$\begin{aligned}
\frac{\partial V_1}{\partial t} =& - D\int_\Omega \frac{qx_H^q \parallel \nabla x_s \parallel^2}{x_s^{q+1}}dx - \frac{D(\tau+\mu_2)\gamma}{\tau v}\int_\Omega \parallel \nabla z \parallel^2 dx \\
&+ \int_\Omega [\xi - \beta x_s^q y - \mu_1 x_s - (\frac{x_H}{x_s})^q(\xi - \beta x_s^q y - \mu_1 x_s)]dx \\
&+ \int_\Omega [\beta x_s^q y + ry - (\tau+\mu_2)u]dx + \int_\Omega \frac{\tau+\mu_2}{\tau}(\tau u - \gamma yz - \mu_3 y)dx \\
&+ \int_\Omega \frac{(\tau+\mu_2)\gamma}{\tau v}z(vy - \mu_4 z)dx \\
=& - D\int_\Omega \frac{qx_H^q \parallel \nabla x_s \parallel^2}{x_s^{q+1}}dx - \frac{D(\tau+\mu_2)\gamma}{\tau v}\int_\Omega \parallel \nabla z \parallel^2 dx \\
&+ \int_\Omega \mu_1 x_H[1 - \frac{x_s}{x_H} - (\frac{x_H}{x_s})^q + (\frac{x_H}{x_s})^{q-1}]dx \\
&+ \int_\Omega y[\beta x_H^q + r - \frac{\mu_3(\tau+\mu_2)}{\tau}]dx - \int_\Omega \frac{(\tau+\mu_2)\gamma\mu_4}{\tau v}z^2 dx \\
=& - D\int_\Omega \frac{qx_H^q \parallel \nabla x_s \parallel^2}{x_s^{q+1}}dx - \frac{D(\tau+\mu_2)\gamma}{\tau v}\int_\Omega \parallel \nabla z \parallel^2 dx \\
&+ \int_\Omega [1 - \frac{x_s}{x_H}][1 - (\frac{x_H}{x_s})^q]dx + \int_\Omega y[\beta x_H^q + r - \frac{\mu_3(\tau+\mu_2)}{\tau}]dx \\
&- \int_\Omega \frac{(\tau+\mu_2)\gamma\mu_4}{\tau v}z^2 dx \\
=& - D\int_\Omega \frac{qx_H^q \parallel \nabla x_s \parallel^2}{x_s^{q+1}}dx - \frac{D(\tau+\mu_2)\gamma}{\tau v}\int_\Omega \parallel \nabla z \parallel^2 dx \\
&+ \int_\Omega [1 - \frac{x_s}{x_H}][1 - (\frac{x_H}{x_s})^q]dx + \int_\Omega \frac{\mu_3(\tau+\mu_2)}{\tau}(\mathcal{R}_0^2 - 1)ydx \\
&- \int_\Omega \frac{(\tau+\mu_2)\gamma\mu_4}{\tau v}z^2 dx.
\end{aligned}$$

Since

$$[1-\frac{x_s}{x_H}][1-(\frac{x_H}{x_s})^q]\leq 0$$

for all $q,\ x_s>0$.

Hence, $\mathcal{R}_0<1$ ensures $\frac{\partial V_1(x,t)}{\partial t}\leq 0$. For $\frac{\partial V_1(x,t)}{\partial t}=0$, if and only if $x_s=x_H, y=0, z=0$, combined with the model (3.1), we have $u=0$. The largest compact invariant set in $\{(x_s,u,y,z)\in\mathbb{R}^4_+ :\ \frac{\partial V_1(x,t)}{\partial t}=0\}$ is the singleton E_0. By LaSalle invariant principle ([16, Theorem 5.3.1]), the infection-free steady state E_0 of the model (3.1) is globally asymptotically stable.

If $q=1$, a Lyapunov function of the model (3.1) is defined as follows

$$\begin{aligned}V_2=&\int_\Omega\Big(x_s-x_H-x_H\ln\frac{x_s}{x_H}\Big)dx+\int_\Omega u(t,x)dx\\&+\frac{\tau+\mu_2}{\tau}\int_\Omega y(x,t)dx+\frac{(\tau+\mu_2)\gamma}{2\tau v}\int_\Omega z^2(x,t)dx.\end{aligned}$$

Calculating the time derivative of V_2 along the solution of the model (3.1), we have

$$\begin{aligned}\frac{\partial V_2}{\partial t}=&-D\int_\Omega\frac{x_H\parallel\nabla x_s\parallel^2}{x_s^2}dx-\frac{D(\tau+\mu_2)\gamma}{\tau v}\int_\Omega\parallel\nabla z\parallel^2dx\\&-\int_\Omega\frac{\mu_1}{x_s}(x_s-x_H)^2dx+\int_\Omega\frac{\mu_3(\tau+\mu_2)}{\tau}(\mathcal{R}_0^2-1)ydx+\int_\Omega\frac{\gamma\mu_4(\tau+\mu_2)}{\tau v}z^2dx.\end{aligned}$$

Hence, $\mathcal{R}_0<1$ ensures $\frac{\partial V_2(x,t)}{\partial t}\leq 0$. For $\frac{\partial V_2(x,t)}{\partial t}=0$, if and only if $x_s=x_H, y=0, z=0$, combined with the model (3.1), we have $u=0$. The largest compact invariant set in $\{(x_s,u,y,z)\in\mathbb{R}^4_+ :\ \frac{\partial V_2(x,t)}{\partial t}=0\}$ is the singleton E_0. By LaSalle invariant principle ([16, Theorem 5.3.1]), the infection-free steady state E_0 of the model (3.1) is globally asymptotically stable.

Thus, for any q, the infection-free steady state E_0 of the model (3.1) is globally asymptotically stable if $\mathcal{R}_0<1$. The proof is completed. □

For the global stability of the chronic-infection steady state E^* of the model (3.1), we have the following result.

Theorem 3.3. *If $\mathcal{R}_0>1$, then the chronic-infection steady state E^* of the model (3.1) is globally asymptotically stable.*

Proof. If $q\neq 1$, we define a Lyapunov function of the model (3.1) as follows

$$\begin{aligned}V_3=&\int_\Omega x_s\Big(1+\frac{1}{q-1}(\frac{x_s^*}{x_s})^q\Big)dx+\int_\Omega(u-u^*-u^*\ln\frac{u}{u^*})dx\\&+\frac{\tau+\mu_2}{\tau}\int_\Omega(y-y^*-y^*\ln\frac{y}{y^*})dx+\frac{\gamma z^*(\tau+\mu_2)}{\tau v}\int_\Omega(z-z^*-z^*\ln\frac{z}{z^*})dx.\end{aligned}$$

Calculating the time derivative of V_3 along the solution of the model (3.1), we have

$$\begin{aligned}\frac{\partial V_3}{\partial t}=&-D\int_\Omega\frac{q(x_s^*)^q\parallel\nabla x_s\parallel^2}{x_s^{q+1}}dx-D\int_\Omega\frac{u^*\parallel\nabla u\parallel^2}{u^2}dx\\&-\frac{D(\tau+\mu_2)}{\tau}\int_\Omega\frac{y^*\parallel\nabla y\parallel^2}{y^2}dx-\frac{\gamma z^*(\tau+\mu_2)}{\tau v}\int_\Omega\frac{z^*\parallel\nabla z\parallel^2}{z^2}dx\\&+\int_\Omega[\xi-\beta x_s^qy-\mu_1x_s-(\frac{x_s^*}{x_s})^q(\xi-\beta x_s^qy-\mu_1x_s)]dx\end{aligned}$$

$$+\int_\Omega \{(1-\frac{u^*}{u})[\beta x_s^q y + ry - (\tau+\mu_2)u]\}dx$$
$$+\int_\Omega [\frac{\tau+\mu_2}{\tau}(1-\frac{y^*}{y})(\tau u - \gamma yz - \mu_3 y) + \frac{\gamma z^*(\tau+\mu_2)}{\tau v}(1-\frac{z^*}{z})(vy-\mu_4 z)]dx.$$

Noting that

$$\begin{cases} \xi = \beta(x_s^*)^q y^* + \mu_1 x_s^*, \\ \beta(x_s^*)^q y^* + ry^* = (\tau+\mu_2)u^*, \\ \tau u^* = \gamma y^* z^* + \mu_3 y^*, \\ vy^* = \mu_4 z^*. \end{cases} \tag{3.2}$$

It follows from (3.2) that

$$\begin{aligned}
\frac{\partial V_3}{\partial t} =& -D\int_\Omega \frac{q(x_s^*)^q \parallel \nabla x_s \parallel^2}{x_s^{q+1}}dx - D\int_\Omega \frac{u^* \parallel \nabla u \parallel^2}{u^2}dx \\
&- \frac{D(\tau+\mu_2)}{\tau}\int_\Omega \frac{y^* \parallel \nabla y \parallel^2}{y^2}dx - \frac{\gamma z^*(\tau+\mu_2)}{\tau v}\int_\Omega \frac{z^* \parallel \nabla z \parallel^2}{z^2}dx \\
&+ \int_\Omega [\mu_1 x_s^* + \beta(x_s^*)^q y^* - \beta x_s^q y - \mu_1 x_s]dx \\
&+ \int_\Omega [-(\mu_1 x_s^* + \beta(x_s^*)^q y^*)(\frac{x_s^*}{x_s})^q + \beta(x_s^*)^q y + \mu_1 x_s(\frac{x_s^*}{x_s})^q + \beta(x_s^*)^q y]dx \\
&+ \int_\Omega [\beta(x_s)^q y + ry - (\tau+\mu_2)u - \frac{u^*}{u}\beta(x_s)^q y - \frac{u^*}{u}ry + (\tau+\mu_2)u^*]dx \\
&+ \int_\Omega \frac{\beta(x_s^*)^q y^* + ry^*}{\tau u^*}(\tau u - \tau u^*\frac{y}{y^*} - \frac{y^*}{y}\tau u + \tau u^*)dx \\
&+ \int_\Omega \frac{\tau+\mu_2}{\tau}(\gamma yz^* - \gamma yz - \gamma y^* z^* + \gamma y^* z)dx \\
&+ \int_\Omega \frac{rz^*(\tau+\mu_2)}{\tau v}(vy - vy^*\frac{z}{z^*} - \frac{z^*}{z}vy + vy^*)dx \\
=& -D\int_\Omega \frac{q(x_s^*)^q \parallel \nabla x_s \parallel^2}{x_s^{q+1}}dx - D\int_\Omega \frac{u^* \parallel \nabla u \parallel^2}{u^2}dx \\
&- \frac{D(\tau+\mu_2)}{\tau}\int_\Omega \frac{y^* \parallel \nabla y \parallel^2}{y^2}dx - \frac{\gamma z^*(\tau+\mu_2)}{\tau v}\int_\Omega \frac{z^* \parallel \nabla z \parallel^2}{z^2}dx \\
&+ \int_\Omega \mu_1 x_s^*(1-\frac{x_s}{x_s^*})[1-(\frac{x_s^*}{x_s})^q]dx + \int_\Omega ry^*(2 - \frac{u^* y}{uy^*} - \frac{uy^*}{u^* y})dx \\
&+ \int_\Omega \frac{\gamma yz^*(\tau+\mu_2)}{\tau}(2 - \frac{z}{z^*} - \frac{z^*}{z})dx \\
&+ \int_\Omega \beta(x_s^*)^q y^*(3 - \frac{(x_s^*)^q}{x_s^q} - \frac{u^* x_s^q y}{u(x_s^*)^q y^*} - \frac{y^* u}{yu^*})dx.
\end{aligned}$$

Hence, $\mathcal{R}_0 > 1$ ensures $\frac{\partial V_3(x,t)}{\partial t} \le 0$. For $\frac{\partial V_3(x,t)}{\partial t} = 0$, if and only if $x_s = x_s^*, u = u^*, y = y^*, z = z^*$. The largest compact invariant set in $\{(x_s, u, y, z) \in \mathbb{R}_+^4 : \frac{\partial V_3(x,t)}{\partial t} = 0\}$ is the singleton E^*. By LaSalle invariant principle ([16, Theorem

5.3.1]), the chronic-infection steady state E^* of the model (3.1) is globally asymptotically stable.

If $q = 1$, a Lyapunov function of the model (3.1) is defined as follows

$$V_4 = \int_\Omega \Big(x_s - x_s^* - x_s^* \ln \frac{x_s}{x_s^*}\Big)dx + \int_\Omega \Big(u - u^* - u^* \ln \frac{u}{u^*}\Big)dx + \frac{\tau+\mu_2}{\tau}\int_\Omega \Big(y - y^* - y^* \ln \frac{y}{y^*}\Big)dx + \frac{\gamma z^*(\tau+\mu_2)}{\tau v}\int_\Omega \Big(z - z^* - z^* \ln \frac{z}{z^*}\Big)dx.$$

Calculating the time derivative of V_4 along the solution of the model (3.1), we have

$$\begin{aligned}\frac{\partial V_4}{\partial t} =& \int_\Omega (1 - \frac{x_s^*}{x_s})(D\Delta x_s + \xi - \beta x_s y - \mu_1 x_s)dx \\ &+ \int_\Omega (1 - \frac{u^*}{u})[D\Delta u + \beta x_s y + ry - (\tau+\mu_2)u]dx \\ &+ \frac{\tau+\mu_2}{\tau}\int_\Omega (1 - \frac{y^*}{y})(D\Delta y + \tau u - \gamma y z - \mu_3 y)dx \\ &+ \frac{\gamma(\tau+\mu_2)z^*}{\tau\nu}\int_\Omega (1 - \frac{z^*}{z})(D\Delta z + \upsilon y - \mu_4 z)dx \\ =& - D\int_\Omega \frac{x_s^* \parallel \nabla x_s \parallel^2}{x_s^2}dx - D\int_\Omega \frac{u^* \parallel \nabla u \parallel^2}{u^2}dx - \frac{D(\tau+\mu_2)}{\tau}\int_\Omega \frac{y^* \parallel \nabla y \parallel^2}{y^2}dx \\ &- \frac{\gamma z^*(\tau+\mu_2)}{\tau v}\int_\Omega \frac{z^* \parallel \nabla z \parallel^2}{z^2}dx - \int_\Omega \frac{\mu_1}{x_s}(x_s - x_s^*)^2 dx \\ &+ \int_\Omega \beta x_s^* y^*(3 - \frac{x_s^*}{x_s} - \frac{x_s u^* y}{x_s^* u y^*} - \frac{u y^*}{u^* y})dx \\ &+ \int_\Omega r y^*(2 - \frac{u^* y}{u y^*} - \frac{u y^*}{u^* y})dx - \int_\Omega \frac{\gamma y(\tau+\mu_2)}{\tau}\frac{(z-z^*)^2}{z}dx.\end{aligned}$$

Hence, $\mathcal{R}_0 > 1$ ensures $\frac{\partial V_4(x,t)}{\partial t} \le 0$. For $\frac{\partial V_4(x,t)}{\partial t} = 0$, if and only if $x_s = x_s^*, u = u^*, y = y^*, z = z^*$. The largest compact invariant set in $\{(x_s, u, y, z) \in \mathbb{R}^4_+ : \frac{\partial V_4(x,t)}{\partial t} = 0\}$ is the singleton E^*. By LaSalle invariant principle ([16, Theorem 5.3.1]), the chronic-infection steady state E^* of the model (3.1) is globally asymptotically stable.

Therefore, for any $q > 0$, the chronic-infection steady state E^* of the model (3.1) is globally asymptotically stable if $\mathcal{R}_0 > 1$. The proof is completed. □

4. Non-existence of travelling wave solutions

We are very interested in the existence of travelling wave solutions connecting the infection free steady state E_0 and the chronic-infection steady state E^*. However, for the high dimentional system, it is very difficult to construct the suitable upper-lower solutions. Here, we only discuss the non-existence of travelling wave solutions which connect the infection-free steady state E_0 with itself. For the existence of travelling wave solutions, we only give a numerical example. For mathematical considerations, we assume $q = 1$ and $D_0 = D_1 = D$ in the model (3.1). Then we

only consider the following model

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D\Delta x_s + \xi - \mu_1 x_s(x,t) - \beta x_s(x,t)y(x,t), \\ \dfrac{\partial u(x,t)}{\partial t} = D\Delta u + \beta x_s(x,t)y(x,t) + ry(x,t) - (\tau+\mu_2)u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} = D\Delta y + \tau u(x,t) - \gamma y(x,t)z(x,t) - \mu_3 y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} = D\Delta z + vy(x,t) - \mu_4 z(x,t). \end{cases} \tag{4.1}$$

Without loss of generality, let $\widehat{x}_s = \frac{\xi}{\mu_1} - x_s$. Thus, the model (4.1) is transformed into (omitting the hats on x_s for simplicity)

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D\Delta x_s - \mu_1 x_s(x,t) + \beta\Big(\dfrac{\xi}{\mu_1} - x_s(x,t)\Big)y(x,t), \\ \dfrac{\partial u(x,t)}{\partial t} = D\Delta u + \beta\Big(\dfrac{\xi}{\mu_1} - x_s(x,t)\Big)y(x,t) + ry(x,t) - (\tau+\mu_2)u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} = D\Delta y + \tau u(x,t) - \gamma y(x,t)z(x,t) - \mu_3 y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} = D\Delta z + vy(x,t) - \mu_4 z(x,t). \end{cases} \tag{4.2}$$

Obviously, the model (4.2) has two steady states $E_0(0,0,0,0)$ and $E^*(k_1,k_2,k_3,k_4)$, where $k_1 = \frac{\xi}{\mu_1} - x_s^*,\ k_2 = u^*,\ k_3 = y^*,\ k_4 = z^*$.

A travelling wave solution of the model (4.2) is a solution $(\phi,\varphi,\psi,\gamma)$ of the special form $x_s(x,t) = \phi(x+ct)$, $u(x,t) = \varphi(x+ct)$, $y(x,t) = \psi(x+ct)$, $z(x,t) = \gamma(x+ct)$, where $\phi,\ \varphi,\ \psi,\ \gamma \in C^2(\mathbb{R},\mathbb{R}^4)$ and $c>0$ is a constant accounting for the wave speed. Substituting $x_s(x,t) = \phi(x+ct)$, $u(x,t) = \varphi(x+ct)$, $y(x,t) = \psi(x+ct)$, $z(x,t) = \gamma(x+ct)$ and denoting the travelling wave coordinate $x+ct$ still by t, we derive from the model (4.2) that

$$\begin{cases} D\ddot{\phi} - c\dot{\phi} + f_{c_1}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) = 0, \\ D\ddot{\varphi} - c\dot{\varphi} + f_{c_2}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) = 0, \\ D\ddot{\psi} - c\dot{\psi} + f_{c_3}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) = 0, \\ D\ddot{\gamma} - c\dot{\gamma} + f_{c_4}(\phi_t,\ \varphi_t,\psi_t,\ \gamma_t) = 0, \end{cases} \tag{4.3}$$

where

$$\begin{aligned} f_{c_1}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) &= -\mu_1\phi(t) + \beta(\frac{\xi}{\mu_1} - \phi(t))\psi(t), \\ f_{c_2}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) &= \beta(\frac{\xi}{\mu_1} - \phi(t))\psi(t) + r\psi(t) - (\tau+\mu_2)\varphi(t), \\ f_{c_3}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) &= \tau\varphi(t) - \gamma\psi(t)\gamma(t) - \mu_3\psi(t), \\ f_{c_4}(\phi_t,\ \varphi_t,\ \psi_t,\ \gamma_t) &= v\psi(t) - \mu_4\gamma(t). \end{aligned}$$

Theorem 4.1. *Let $\mathcal{R}_0 < 1$. For any $c \geq 0$, the model (4.2) does not have a travelling wave solution, which connects the infection-free steady state E_0 with itself.*

Proof. Assume that there exists a non-trivial travelling wave solution $(\phi(t), \varphi(t), \psi(t), \gamma(t))$ which connects the infection-free steady state E_0 with itself. Then $(\phi(t), \varphi(t), \psi(t), \gamma(t))$ satisfies the boundary condition

$$\lim_{t\to-\infty}(\phi(t),\ \varphi(t),\ \psi(t),\ \gamma(t)) = (0,\ 0,\ 0,\ 0),$$

and

$$\lim_{t\to\infty}(\phi(t),\ \varphi(t),\ \psi(t),\ \gamma(t)) = (0,\ 0,\ 0,\ 0).$$

Now, for the second and third equations of the model (4.3), by using the fundamental theory of second-order ordinary differential equations, we get

$$\begin{aligned}
\varphi(t) &= \frac{1}{\Lambda_1'}\Big(\int_{-\infty}^{t} e^{\lambda_-'(t-s)} f(s)ds + \int_{t}^{\infty} e^{\lambda_+'(t-s)} f(s)ds\Big),\\
\psi(t) &= \frac{1}{\Lambda_2'}\Big(\int_{-\infty}^{t} e^{\gamma_-'(t-s)} g(s)ds + \int_{t}^{\infty} e^{\gamma_+'(t-s)} g(s)ds\Big),
\end{aligned}$$

where

$$\begin{aligned}
&\gamma_-' = \frac{c-\sqrt{c^2+4\mu_3 D}}{2D},\quad \gamma_+' = \frac{c+\sqrt{c^2+4\mu_3 D}}{2D},\\
&\lambda_-' = \frac{c-\sqrt{c^2+4D(\tau+\mu_2)}}{2D},\quad \lambda_+' = \frac{c+\sqrt{c^2+4D(\tau+\mu_2)}}{2D},\\
&\Lambda_1' = D(\lambda_+'-\lambda_-'),\quad \Lambda_2' = D(\gamma_+'-\gamma_-'),\\
&f(s) = \beta(\frac{\xi}{\mu_1}-\phi(s))\psi(s) + r\psi(s),\quad g(s) = \tau\varphi(s) - \gamma\psi(s)\gamma(s).
\end{aligned}$$

By integrating, we have

$$\begin{aligned}
\int_{-\infty}^{+\infty}\varphi(t)dt =& \frac{1}{\Lambda_1'}\Big(\int_{-\infty}^{+\infty}\int_{-\infty}^{t} e^{\lambda_-'(t-s)} f(s)ds + \int_{-\infty}^{+\infty}\int_{-\infty}^{t} e^{\lambda_+'(t-s)} f(s)ds\Big)\\
=& \frac{1}{\Lambda_1'}\Big(\int_{-\infty}^{+\infty}\int_{0}^{+\infty} e^{\lambda_-' s} f(t-s)ds + \int_{-\infty}^{+\infty}\int_{-\infty}^{0} e^{\lambda_+'(s)} f(t-s)ds\Big)\\
=& \frac{1}{\Lambda_1'}\Big(\int_{0}^{+\infty} e^{\lambda_-' s}ds\int_{-\infty}^{+\infty} f(t-s)dt + \int_{-\infty}^{0} e^{\lambda_+' s}ds\int_{-\infty}^{+\infty} f(t-s)dt\Big)\\
=& \frac{1}{\Lambda_1'}\Big(\int_{0}^{+\infty} e^{\lambda_-' s}ds + \int_{-\infty}^{0} e^{\lambda_+' s}ds\Big)\int_{-\infty}^{+\infty} f(t-s)dt\\
=& \frac{1}{\Lambda_1'}\Big(\int_{0}^{+\infty} e^{\lambda_-' s}ds + \int_{-\infty}^{0} e^{\lambda_+' s}ds\Big)\int_{-\infty}^{+\infty} f(s)ds\\
\le& \frac{1}{\tau+\mu_2}\int_{-\infty}^{+\infty}\Big(\frac{\beta\xi}{\mu_1}+r\Big)\psi(t)dt\\
=& \frac{\beta\xi+r\mu_1}{\mu_1(\tau+\mu_2)}\int_{-\infty}^{+\infty}\psi(t)dt.
\end{aligned}$$

Thanks for $\mathcal{R}_0 < 1$, we have

$$\begin{aligned}
\int_{-\infty}^{+\infty}\psi(t)dt =&\frac{1}{\Lambda_2'}\Big(\int_{-\infty}^{+\infty}\int_{-\infty}^{t}e^{\gamma_-'(t-s)}g(s)ds+\int_{-\infty}^{+\infty}\int_{-\infty}^{t}e^{\gamma_+'(t-s)}g(s)ds\Big)\\
\le&\frac{\tau}{\Lambda_2'}\Big(\int_{-\infty}^{+\infty}\int_{0}^{+\infty}e^{\gamma_-'s}\varphi(t-s)ds+\int_{-\infty}^{+\infty}\int_{-\infty}^{0}e^{\gamma_+'(s)}\varphi(t-s)ds\Big)\\
=&\frac{\tau}{\Lambda_2'}\Big(\int_{0}^{+\infty}e^{\gamma_-'s}ds\int_{-\infty}^{+\infty}\varphi(t-s)dt+\int_{-\infty}^{0}e^{\gamma_+'s}ds\int_{-\infty}^{+\infty}\varphi(t-s)dt\Big)\\
=&\frac{\tau}{\Lambda_2'}\Big(\int_{0}^{+\infty}e^{\gamma_-'s}ds+\int_{-\infty}^{0}e^{\gamma_+'s}ds\Big)\int_{-\infty}^{+\infty}\varphi(t-s)dt\\
=&\frac{\tau}{\Lambda_2'}\Big(\int_{0}^{+\infty}e^{\gamma_-'s}ds+\int_{-\infty}^{0}e^{\gamma_+'s}ds\Big)\int_{-\infty}^{+\infty}\varphi(s)ds\\
=&\frac{\tau}{\mu_3}\int_{-\infty}^{+\infty}\varphi(t)dt\\
\le&\frac{\tau(\beta\xi+r\mu_1)}{\mu_1\mu_3(\tau+\mu_2)}\int_{-\infty}^{+\infty}\psi(t)dt\\
<&\int_{-\infty}^{+\infty}\psi(t)dt.
\end{aligned}$$

That is a contradiction. Hence, the proof is completed. □

5. Numerical simulations and conclusions

5.1. Numerical simulations

In this subsection, we simulate the results obtained in Sections 2, 3 and 4. Firstly, we illustrate the threshold dynamics obtained in Theorem 2.3 from the numerical simulations. For this purpose, we truncate the spatial domain Ω by $[0,1]$. We consider the model (1.3) under the Neumann boundary conditions

$$\frac{\partial x_s(x,t)}{\partial n}=\frac{\partial u(x,t)}{\partial n}=\frac{\partial y(x,t)}{\partial n}=\frac{\partial z(x,t)}{\partial n}=0,\ t>0,\ x=0,1, \tag{5.1}$$

and the initial functions as follows

$$x_{s0}(x)=\begin{cases}0.0001 & \text{if } x=0,\\ 0 & \text{if } 0<x\le 1,\end{cases}\quad u_0(x)=\begin{cases}0.0001 & \text{if } x=0,\\ 0 & \text{if } 0<x\le 1,\end{cases}$$

$$y_0(x)=\begin{cases}0.0001 & \text{if } x=0,\\ 0 & \text{if } 0<x\le 1,\end{cases}\quad z_0(x)=\begin{cases}0.0001 & \text{if } x=0,\\ 0 & \text{if } 0<x\le 1.\end{cases} \tag{5.2}$$

We choose the parameters as follows

$$\begin{aligned}
&D_1=D_2=0.0001,\xi=0.3,\mu_1=0.5,\mu_2=3,\ \mu_3=0.2,\\
&\mu_4=0.2,\ r=0.1,\ \gamma=0.2,\overline{\beta}=0.8,\tau=0.2,v=0.2,q=1.
\end{aligned} \tag{5.3}$$

We fix the parameters as (5.3) and vary $\beta(x)$ with the following form

$$\beta(x)=3\overline{\beta}(1+\sin 8\pi x),$$

where $\overline{\beta}$ is a positive constant. From the numerical simulations, we find that the infection free steady state of the model (1.3) is globally attractive. Numerical simulation illustrates the result obtained in Theorem 2.3 (see, Figure 2). Figure 3 is the contour of Figure 2.

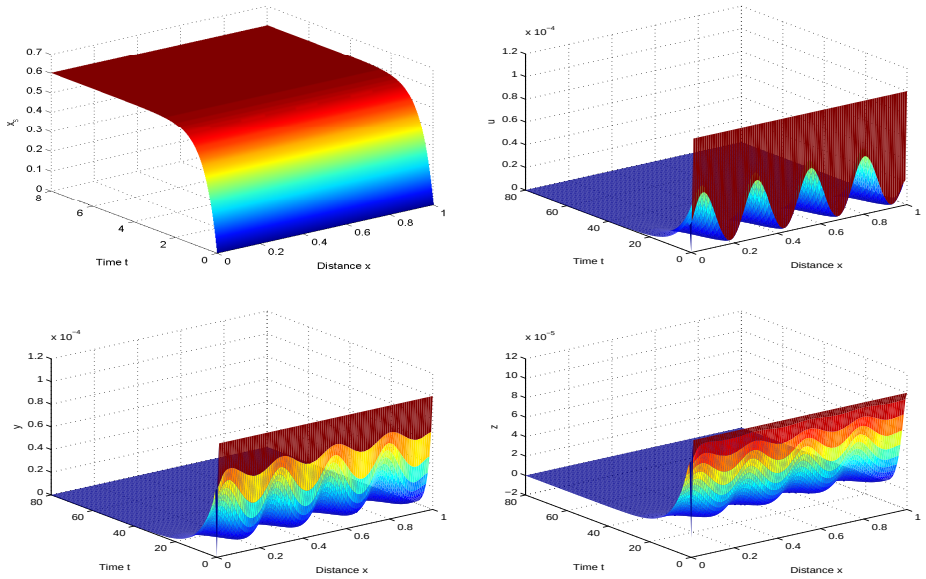

Figure 2. The infection free steady state E_0 of the model (1.3) is globally attractive under the Neumann boundary conditions (5.1) and initial conditions (5.2) with parameters (5.3).

If $\xi = 6,\ r = 0.2$ and the other parameters are the same as (5.3), from the numerical simulations, we observe that the model exists a unique positive nonconstant steady state, which is also globally attractive. Numerical simulation illustrates the results obtained in Theorem 2.3 (see, Figure 4). Figure 5 is the contour of Figure 4.

Secondly, we illustrate the global dynamics of the model (3.1) obtained in Theorems 3.2 and 3.3 from the numerical simulations. We choose the parameters as follows

$$\begin{aligned} &D_1 = D_2 = 0.01, \xi = 1.3, \mu_1 = 0.5, \mu_2 = 3, \mu_3 = 0.2, \mu_4 = 0.2, \\ &r = 0.1, \gamma = 0.2, \beta = 0.8, \tau = 0.2, v = 0.2, q = 1. \end{aligned} \tag{5.4}$$

By a simple computation, we find that $\mathcal{R}_0 < 1$. From Theorem 3.2, we obtain that the infection free steady state E_0 of the model (3.1) is globally asymptotically stable. Numerical simulation illustrates the results (see, Figure 6). However, if $\xi = 6,\ r = 0.2$ and the other parameters are the same as (5.4), we find that the model (3.1) exists a unique chronic-infection steady state E^* which is globally asymptotically stable. Numerical simulation illustrates the result of Theorem 3.3 (see, Figure 7).

We are very interested in the existence of travelling wave solutions connecting the infection-free steady state E_0 and the chronic-infection steady state E^*. From the biological considerations, the existence and non-existence of travelling wave

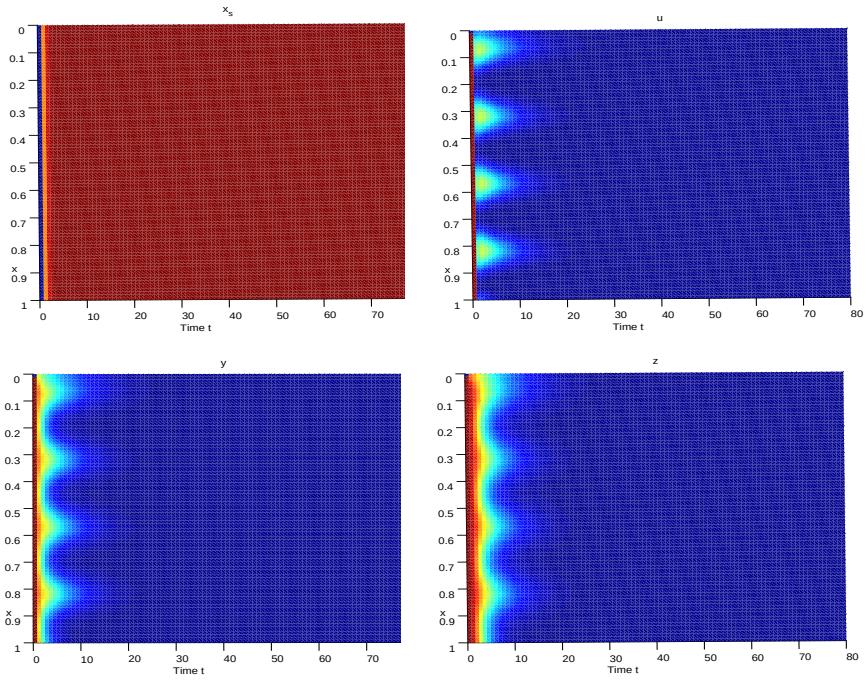

Figure 3. The contour of Figure 2.

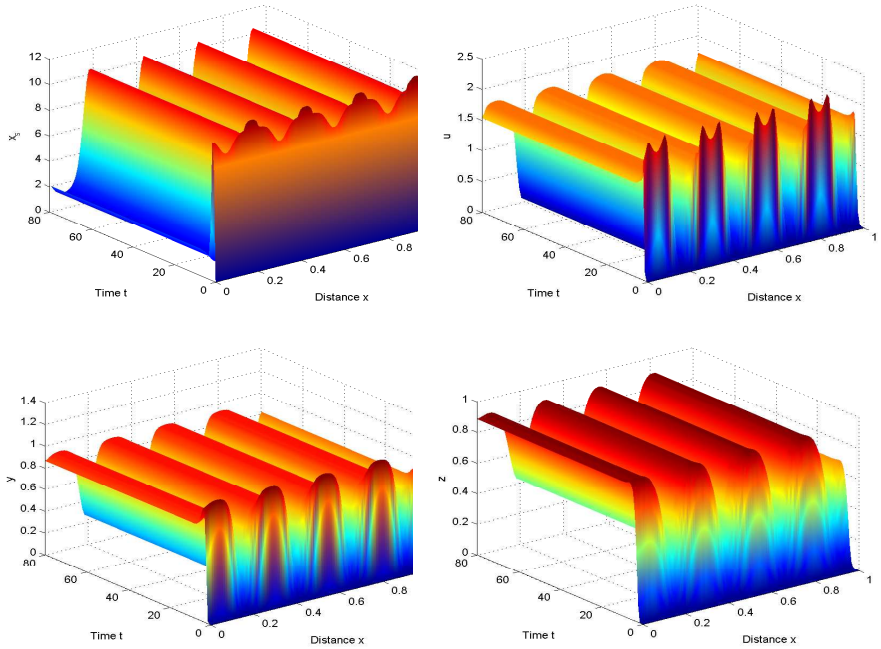

Figure 4. The infection steady state E_0 of the model converges to a positive nonconstant distribution under the Neumann boundary conditions (5.1) and initial conditions (5.2) with $\xi = 6,\ r = 0.2$ and the other parameters are the same as (5.3).

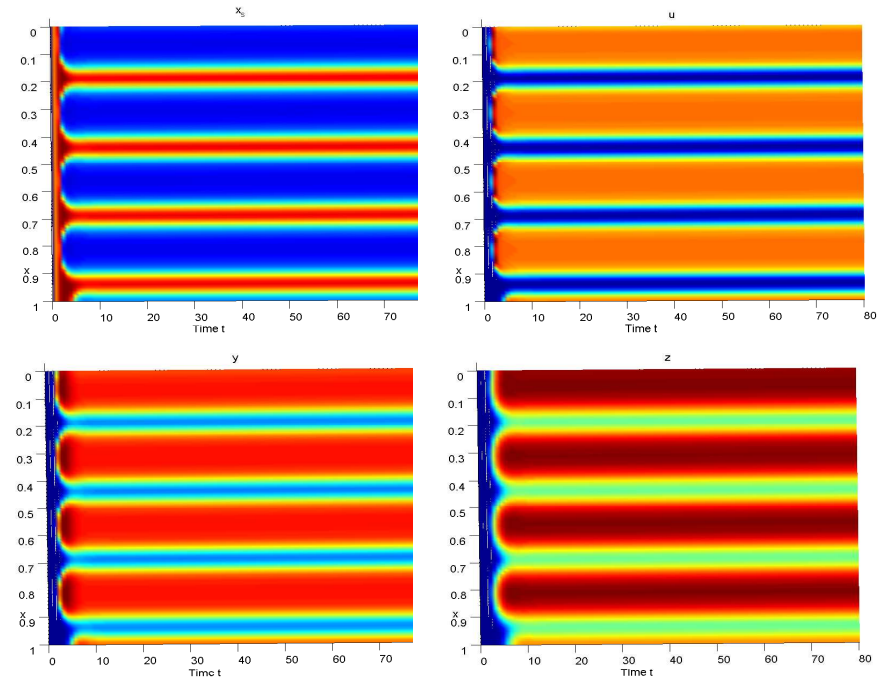

Figure 5. The contour of Figure 4.

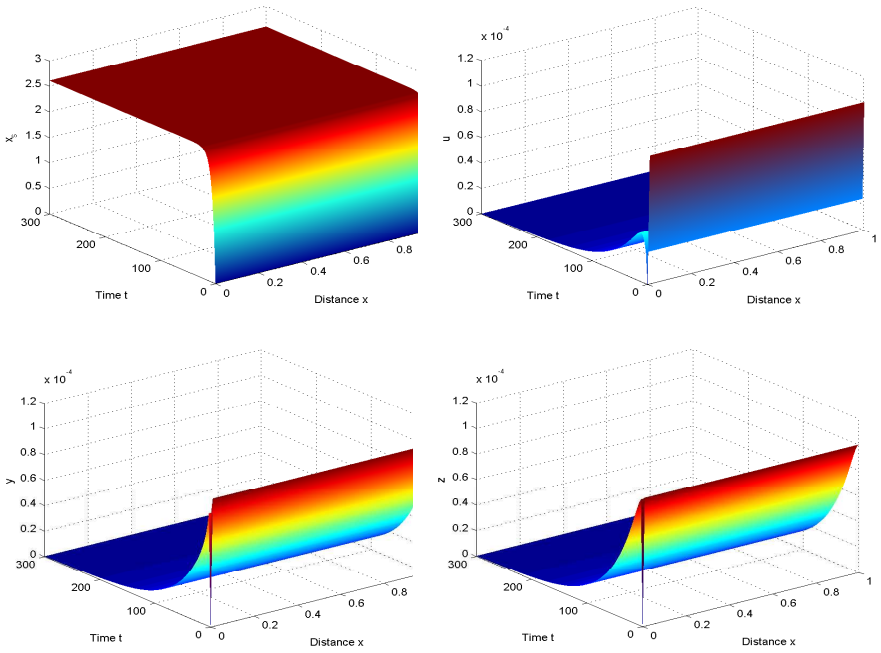

Figure 6. The infection free steady state E_0 is globally asymptotically stable under the Neumann boundary conditions (5.1) and initial conditions (5.2) with parameters (5.4).

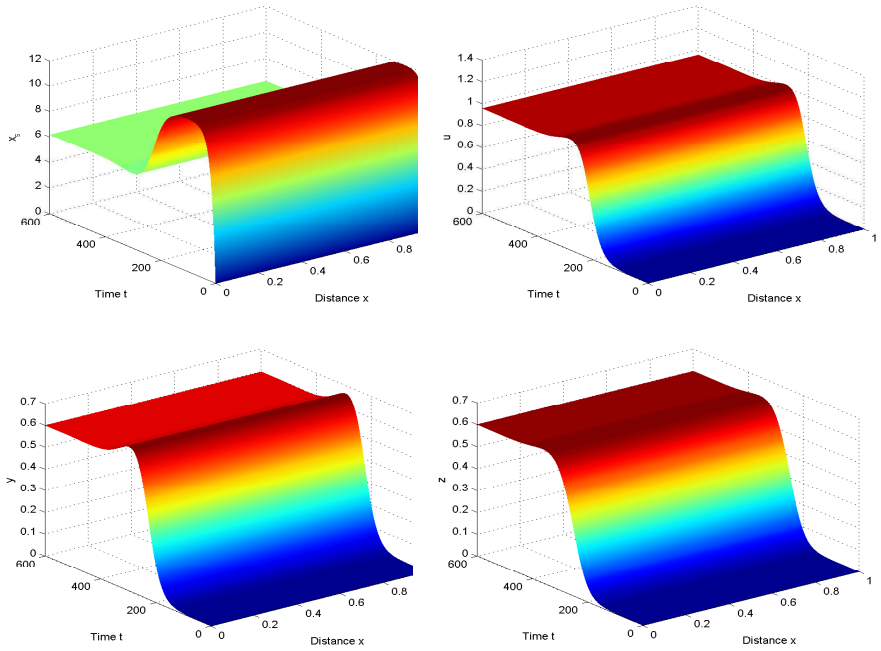

Figure 7. The chronic-infection steady state E^* is globally asymptotically stable under the Neumann boundary conditions (5.1) and initial conditions (5.2) with $\xi = 6$, $r = 0.1$ and the other parameters are the same as (5.4).

solutions reveal whether the disease can spread or not. This can give us some disease control strategies of HTLV-I. However, it is very difficult to construct the suitable upper-lower solutions for the reaction-diffusion equations governed by four variables. Here, we simulate the existence of travelling wave solution numerically.

If the parameters are chosen as,

$$\begin{aligned} &D = 0.01, \xi = 100, \mu_1 = 0.5, \mu_2 = 0.4, \mu_3 = 0.2, \mu_4 = 0.2, \\ &r = 0.000001, \gamma = 0.6, \beta = 0.008, \tau = 0.2, v = 0.8, q = 1, c = 8, \end{aligned} \tag{5.5}$$

the travelling wave solutions are illustrated from the numerical simulations (see Figure 8).

We find that diffusion coefficient D can influence the wave speed c of the travelling wave solution connecting the infection-free steady state E_0 and the chronic-infection steady state E^*. If diffusion coefficient $D = 0.001$ is reduced, the wave speed of the travelling wave solution is decreasing from the numerical simulations (see Figure 9).

5.2. Conclusions

From the biological considerations, it can be obtained that $CD4^+$ (both healthy cells and infected cells) and $CD8^+$ CTLs can move ([6, 7, 23, 28, 46]) and go from regions of high concentration to regions of low concentration. It is widely known that diffusion process may cause different cell movements because of the different concentration levels of cells. In order to seek this interesting phenomenon, in the

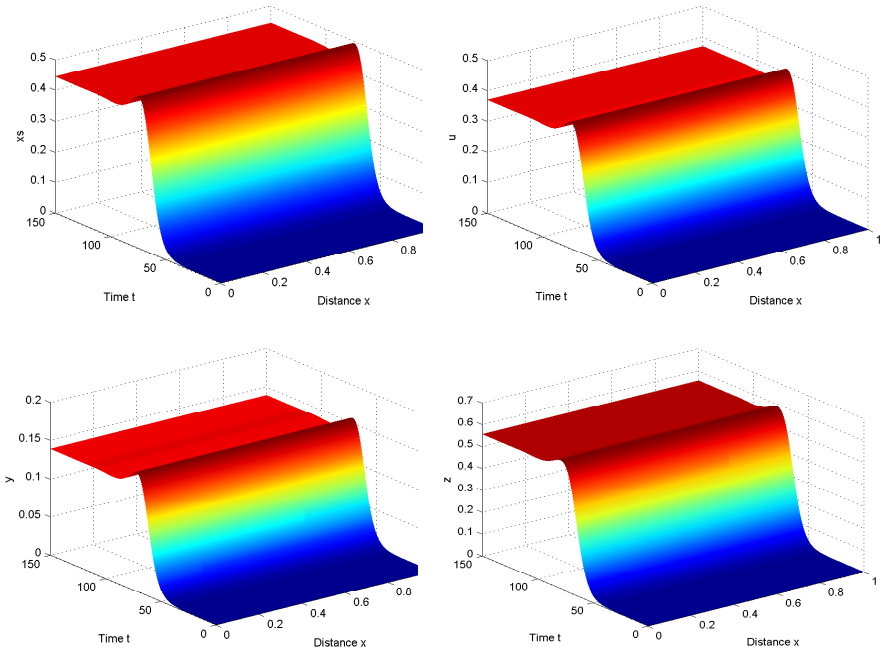

Figure 8. The travelling wave solutions are observed in the model (4.2) under the Neumann boundary conditions (5.1) and initial conditions (5.2) with the parameters (5.5).

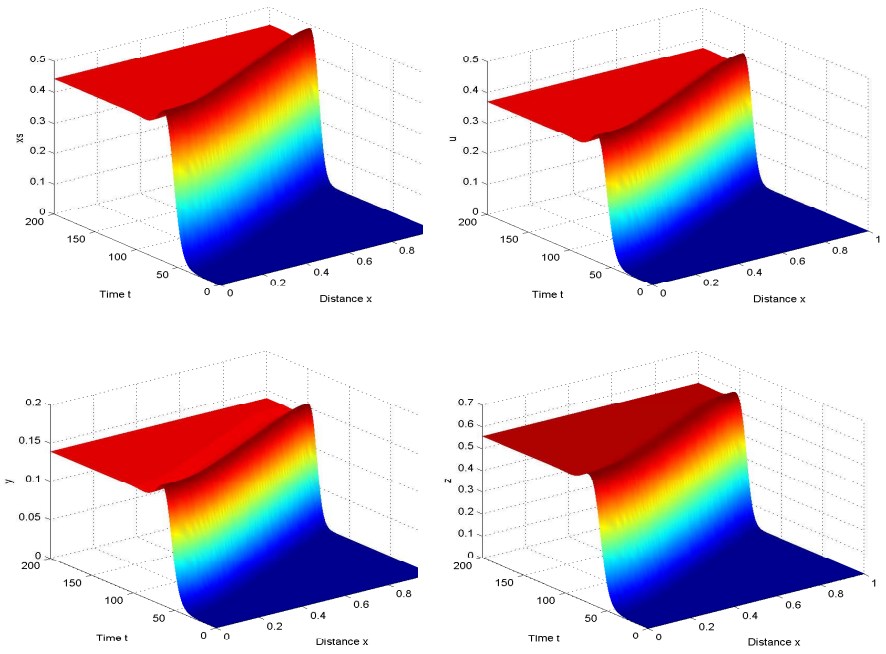

Figure 9. The travelling wave solutions are observed in the model (4.2) under the Neumann boundary conditions (5.1) and initial conditions (5.2) with $D = 0.001$ and the other parameters are the same as (5.5).

current paper, a reaction-diffusion HTLV-I infection model with mitotic division of actively infected cells, CTL immune response and nonlinear incidence is proposed.

The well posedness of the model (1.3) is investigated. The basic reproduction number $\mathcal{R}_0$ is established by defining the the spectral radius of the next infection operator. However, the explicit formula of $\mathcal{R}_0$ cannot be given if at least one of the parameters are spatially dependent. If all the parameters are spatially independent, we actually derive the explicit formula of $\mathcal{R}_0$. In this paper, we give the explicit formula of $\mathcal{R}_0$ for the spatially homogeneous model. It is worth noting that the diffusion coefficients have no effects on the basic reproduction number $\mathcal{R}_0$ for the case of spatially homogeneous model. However, from the numerical simulations, we find that the basic reproduction number $\mathcal{R}_0$ is a decreasing function of D_1 for the spatially heterogeneous model. Therefore, the larger the diffusion coefficients, the smaller the basic reproduction number will be. Biologically, we obtain that the random movements of cells result in less infection risk.

In the case of a bounded spatial domain, we establish the threshold dynamics in terms of the basic reproduction number $\mathcal{R}_0$ for the spatially heterogeneous model. Further, for the spatially homogeneous model, we obtain the global dynamics in terms of the basic reproduction number $\mathcal{R}_0$. If $\mathcal{R}_0 < 1$, the infection-free steady state E_0 is globally asymptotically stable. If $\mathcal{R}_0 > 1$, there exists a unique chronic-infection steady state E^* whose global asymptotical stability is established by means of Lyapunov functions. The global stability results show that $\mathcal{R}_0$ may be used to control the disease transmission and to estimate the infection level.

From the expression of the basic reproduction number $\mathcal{R}_0$ of the homogeneous model, it can be obtained that the disease can be eradicated if one of the following two cases occurs: (a) either the production rate of latently infected cells or the rate of the latently infected cells translating to the actively infected cells and the production rate of actively infected cells by mitosis is reduced; (b) either the death rate of latently infected cells or actively infected cells is increased. The global stability results show that $\mathcal{R}_0$ may be used to control the disease transmission and to estimate the infection level. Noticing that $\mathcal{R}_0$ has no relation to the diffusion coefficient D_1 for the homogeneous model, the free diffusion of the cells has no effect on the global stabilities of such HTLV-I infection problem with Neumann homogeneous boundary conditions.

In recent years, great attentions have been paid to the existence and non-existence of travelling wave solutions in virus dynamical models with spatial diffusion. The virus dynamical models governed by reaction diffusion models can give rise to a moving zone of transition free from an infection steady state to the other infection steady state. From the biological considerations, the existence and non-existence of travelling wave solutions reveal whether the disease can spread or not. This can give us some disease control strategies of HTLV-I. Our numerical simulations confirm the existence of travelling wave solutions connecting E_0 and E^*. In our numerical simulations, we set $c = 8$. We find that there exists travelling wave solutions connecting the infection-free steady state E_0 and the chronic-infection steady state E^* with the parameters (5.5). It is very difficult to construct the suitable upper-lower solutions by employing Schauder's fixed point theorem to prove the existence of travelling wave solutions connecting the infection free steady state E_0 and the chronic-infection steady state E^*, especially for virus infection dynamical models. It is widely known that the virus infection dynamical models are neither a cooperative system nor a competitive system. In fact, the

target cells and free virus have a relationship similar to a prey-predator system, while infected cells and free virus are cooperative. However, it is very interesting to investigate the minimal wave speed of travelling wave solutions. We will leave it for further investigation.

The purpose of the paper is to investigate the dynamics of a reaction and diffusion model for an HTLV-I infection with mitotic division of actively infected cells and CTL immune response. In the model (1.3), we assume that the proliferation of CTL cells occurs instantly. However, it is well-known that the existence of time delays is inevitable in biology. In fact, antigenic stimulation generating CTLs may need a period of time θ, i.e., the CTL response at time t may depend on the population of antigen at a previous time $t-\theta$. In view of the above biological considerations, we further propose an HTLV-I infection dynamic model with time as follows

$$\begin{cases} \dfrac{\partial x_s(x,t)}{\partial t} = D_1\Delta x_s + \xi(x) - \mu_1 x_s(x,t) - \beta(x)x_s^q(x,t)y^p(x,t), \\ \dfrac{\partial u(x,t)}{\partial t} = D_1\Delta u + \beta(x)x_s^q(x,t)y^p(x,t) + r(x)y(x,t) - (\tau(x)+\mu_2)u(x,t), \\ \dfrac{\partial y(x,t)}{\partial t} = D_1\Delta y + \tau(x)u(x,t) - \gamma(x)y(x,t)z(x,t) - \mu_3 y(x,t), \\ \dfrac{\partial z(x,t)}{\partial t} = D_2\Delta z + v(x)y(x,t-\theta) - \mu_4 z(x,t). \end{cases} \tag{5.6}$$

Threshold dynamics and the existence of travelling wave solutions for the model (5.6) will be given in other paper. A more challenging problem is to investigate the relationship between spreading speeds and the minimal wave speed. We leave these interesting problems for future investigation.

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