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GLOBAL DYNAMICS ON A REACTION-DIFFUSION HIV COINFECTION MODEL BETWEEN CD4$^+$ T CELL AND MACROPHAGES WITH HUMORAL IMMUNITY

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Abstract. In this paper, a reaction-diffusion HIV coinfection model between CD4$^+$ T cells and macrophages with humoral immunity and recovery of infected CD4$^+$ T cell is proposed in heterogeneous environment. First, the existence and ultimate boundedness of global solutions are discussed, the basic reproduction number $\Re_0$ is obtained. Second, criteria on the globally asymptotic stability of infection-free steady state is established if $\Re_0 < 1$, the uniform persistence of disease is obtained if $\Re_0 > 1$ in the absence of humoral immune response. Furthermore, the immune response reproduction number R_1 is calculated under the homogeneous environment, by which criteria on the globally asymptotic stability of humoral immune-free equilibrium and chronic-infection equilibrium are obtained, respectively. Finally, the theoretical results are demonstrated by numerical simulations, we find that ignoring the HIV infection with macrophages will underestimate the viral loads of HIV within body, meanwhile, diffusion could cause great impact on HIV spread, it could change the situation of HIV infection at some positions from no infection to infection.

Keywords: HIV Coinfection, Reaction-Diffusion, Humoral Immunity, Global Stability, Persistence.

AMS Subject Classification: 35B35, 35K57, 37N25.

1. Introduction

As well known, Human Immunodeficiency Virus (HIV) infection remains a major global public health threat, which has caused an estimated 42.3 million deaths so far [43], by attacking the immune system of human body, especially the CD4$^+$ T cells [7, 31]. Usually, the productive infection of T lymphocytes by HIV relies on the proliferation of infected cells [5], meanwhile, the nonproliferating resting CD4$^+$ T cells also can be infected by HIV and remain inactive [19]. It was found in [32, 50] that the viral genome cannot complete reverse transcription in a quiescent state. Besides, there is a gradual decay for the unintegrated provirus and some unstable transcribed DNA of HIV to finish integration and reverse transcription in resting cells

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[51], which means that a portion of resting infected cells could return to the uninfected state before the viral genome is integrated into the lymphocyte genome [6].

A HIV virus-to-cell model with resting $CD4^+$ T cells activation and recovery was proposed in [27]. The following HIV infection model, in which a small amount of infected $CD4^+$ T cells could return to the uninfected cells, was further studied in [33].

$$\begin{cases} \dfrac{dT}{dt} = s - dT - kVT + bT^*, \\ \dfrac{dT^*}{dt} = kVT - (b+\delta)T^*, \\ \dfrac{dV}{dt} = N\delta T^* - cV, \end{cases}$$

where T, T^* and V characterize the concentration of susceptible $CD4^+$ T cells, infected $CD4^+$ T cells and viruses; s is the constant productivity of $CD4^+$ T cells; k is the infection rate of T cells; d is the mortality rate; b is the rate that T^* return to T; δ is the mortality rate of T^*; N is the amount of virus produced by an infected cell; c is the death rate of virus. It was found that effective drug treatment is crucial for inhibiting the development of HIV infection.

Although Highly Active Anti-Retroviral Therapy (HAART) is currently the most effective drug to treat HIV patients, there are almost no cases of complete elimination of the virus in human body. One of the most important reasons is that $CD4^+$ T cell is not the unique attack target of HIV [52]. It has been proven that the macrophages infection with HIV are considered as another important reservoirs of HIV [11]. Furthermore, it is found [2, 3, 12, 21, 23, 47, 54] that macrophages are targets of HIV in which remain active even in the absence of T cells. Thereupon, the infection of macrophages cannot be ignored in describing the HIV spread process in body. The following HIV coinfection model between $CD4^+$ T cells and macrophages was studied in [21].

$$\begin{cases} \dfrac{dT}{dt} = s - pT(1 - \dfrac{T}{T_{\max}}) - d_T T - kVT, \\ \dfrac{dT^*}{dt} = kVT - \delta T^*, \\ \dfrac{dM}{dt} = s_M - d_M M - k_M VM, \\ \dfrac{dM^*}{dt} = k_M VM - \mu_M M^*, \\ \dfrac{dV}{dt} = N\delta T^* + p_M M^* - cV, \end{cases}$$

where M and M^* represents the concentration of uninfected macrophages and infected macrophages, respectively. Moreover, a HIV coinfection model between $CD4^+$ T cells and macrophages was considered in [10]. In 2021, a HIV coinfection model with two types of target cells incorporating CTL immune responses was studied [24].

Usually, the antigen-specific responses of human could be activated once pathogens invade the body, which mainly include humoral immunity and cellular immunity. It has been revealed that the former is more crucial in the immune system of patients with AIDS for disease control [26, 37]. Furthermore, it was discovered that B cells could randomly walk within the follicle at a rate of approximately 6 $\mu m \cdot min^{-1}$, which means that the spatial movement of cells cannot be ignored during HIV infection [20].

Meanwhile, it is found that spatial diffussion is one of the crucial factors to characterize the dynamics of viral spread [1, 40, 41, 44, 45]. A HBV infection model with virus diffusion in the body was considered in [38] to explore the influence of spatial spread on virus-immune dynamics. A delayed HBV model with diffusion and saturation incidence was studied in [48]. A delayed

virus-to-cell infection model with diffusion and general incidence was investigated in [16, 18]. It was found that diffusion could greatly affect the profile of virus infection.

Moreover, it has been proven that macrophages have a certain ability of migration in the human body [4, 35, 49], once the CD4$^+$ T lymphocytes mature in the thymus, it would leave for other tissues all over the body [13, 36]. Therefore, the spatial movement of CD4$^+$ T cells within the body cannot be ignored as well.

Based on the above considerations, we propose a reaction-diffusion HIV coinfection model between CD4$^+$ T cells and macrophages incorporating humoral immunity and recovery of infected CD4$^+$ T cell as follows.

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C\Delta H_1 + \lambda_1(x) - d_1(x)H_1 - \beta_1(x)H_1V + \delta(x)I_1,\ t \geq 0, x \in \Omega, \\ \dfrac{\partial I_1(x,t)}{\partial t} = D_C\Delta I_1 + \beta_1(x)H_1V - (\delta(x) + a_1(x))I_1,\ t \geq 0, x \in \Omega, \\ \dfrac{\partial H_2(x,t)}{\partial t} = D_C\Delta H_2 + \lambda_2(x) - d_2(x)H_2 - \beta_2(x)H_2V,\ t \geq 0, x \in \Omega, \\ \dfrac{\partial I_2(x,t)}{\partial t} = D_C\Delta I_2 + \beta_2(x)H_2V - a_2(x)I_2,\ t \geq 0, x \in \Omega, \\ \dfrac{\partial V(x,t)}{\partial t} = D_V\Delta V + k_1(x)I_1 + k_2(x)I_2 - d(x)V - q(x)VB,\ t \geq 0, x \in \Omega, \\ \dfrac{\partial B(x,t)}{\partial t} = D_B\Delta B + c(x)VB - u(x)B,\ t \geq 0, x \in \Omega, \end{cases} \tag{1}$$

with the homogeneous Neumann boundary conditions

$$\frac{\partial H_1}{\partial \vec{n}} = \frac{\partial I_1}{\partial \vec{n}} = \frac{\partial H_2}{\partial \vec{n}} = \frac{\partial I_2}{\partial \vec{n}} = \frac{\partial V}{\partial \vec{n}} = \frac{\partial B}{\partial \vec{n}} = 0, \tag{2}$$

for $(x,t) \in \partial\Omega \times (0,+\infty)$, and $\Omega \subset R^n$ is bounded domain ($n \geq 1$). Here H_1, I_1, H_2, I_2 represent the concentrations of susceptible CD4$^+$ T cells, infected CD4$^+$ T cells, susceptible macrophages and infected macrophages, respectively. $\lambda_1(x)$ and $d_1(x)$ represent the productivity and death rate of H_1 at position x, respectively, $\delta(x)$ is the rate of infected cells I_1 return to H_1, and the mortality rate of I_1 is $a_1(x)$. $\beta_1(x)$ and $\beta_2(x)$ are the infection rates of H_1 and H_2, respectively. $\lambda_2(x)$ and $d_2(x)$ represent the productivity and death rates of H_2 at position x, respectively, the death rate of I_2 is $a_2(x)$. V and B are the concentrations of HIV and B cells produced by antigen stimulation, respectively. HIV is produced by I_1 and I_2 that have been lysed at the rates $k_1(x)$ and $k_2(x)$, then it is cleared by B cells at the rate of $q(x)$, and decayed with the rate $d(x)$. $c(x)$ and $u(x)$ are the immune activation rate and decay rate of B cells, respectively. Δ denotes the Laplace operator, and $\frac{\partial}{\partial \vec{n}}$ is the outward normal derivative on smooth boundary $\partial\Omega$, Ω is connected and bounded in $\mathbb{R}^n$. In addition, we assume that $\lambda_i(x)$, $d_i(x)$, $a_i(x)$, $\beta_i(x)$, $\delta(x)$, $d(x)$, $q(x)$, $c(x)$, $u(x)$, $k_i(x)$, $(i = 1, 2)$ are all positive Hölder continuous functions on $\bar{\Omega}$.

We introduce the following initial conditions of model (1):

$$\begin{aligned} &H_1(x,0) = \varphi_1(x) \geq 0,\ I_1(x,0) = \varphi_2(x) \geq 0,\ H_2(x,0) = \varphi_3(x) \geq 0, \\ &I_2(x,0) = \varphi_4(x) \geq 0,\ V(x,0) = \varphi_5(x) \geq 0,\ B(x,0) = \varphi_6(x) \geq 0,\ x \in \Omega, \end{aligned} \tag{3}$$

where $\varphi_i (i = 1, 2, \cdots, 6)$ are bounded and Hölder continuous functions on $\bar{\Omega}$.

Based on the real biological background, we further make the following assumption.

(A_1) The mortality rate of infected cells is higher than that of the uninfected cells, i.e., $d_j(x) < a_j(x)$, $j = 1, 2$.

The organization of the paper is as follows. In Section 2, we give some preliminaries, including the existence and boundedness of solutions and basic reproduction number of model (1). In Section 3, the globally asymptotically stability of infection-free steady state and uniform persistence of immune-free steady state are discussed. In Section 4, criteria on the locally and globally

asymptotically stability of all feasible equilibria for model (1) under spatial homogeneous is established. Numerical simulations are provided in Section 5 to illustrate the theoretical results. In Section 6, a brief conclusion is given.

2. Preliminaries

2.1. **Existence of solutions.** We define a continuous function space from $\bar{\Omega}$ to $\mathbb{R}^6_+$ as $\mathcal{X} = C(\bar{\Omega}, \mathbb{R}^6)$ with supremum norm $\|\cdot\|$. The non-negative cone $\mathcal{X}_+ = C(\bar{\Omega}, \mathbb{R}^6_+) \subset \mathcal{X}$ generates the standard partial ordering on $\mathcal{X}$.

We set $\mathbf{w}^s = \sup_{x\in\Omega} \mathbf{w}(x)$ and $\mathbf{w}^i = \inf_{x\in\Omega} \mathbf{w}(x)$ for any set $\Omega \subset \mathbb{R}^n$. We first introduce the following result from [15].

Lemma 1. *For the following reaction-diffusion system,*

$$\begin{cases} \dfrac{\partial F(x,t)}{\partial t} = D\Delta F + \lambda(x) - \nu(x)F, x \in \Omega, \\ \dfrac{\partial F(x,t)}{\partial \vec{n}} = 0, x \in \partial\Omega, \end{cases} \tag{4}$$

where $\lambda(x), \nu(x) > 0$, $x \in \bar{\Omega}$ are Hölder continuous functions. $F_0(x)$ is the unique positive steady state of system (4), with

$$D\Delta F_0(x) + \lambda(x) - \nu(x)F_0(x) = 0, x \in \Omega,$$

where $\frac{\partial F(x,t)}{\partial \vec{n}} = 0, x \in \partial\Omega$. Moreover, F_0 is globally asymptotically stable in $C(\bar{\Omega}, \mathbb{R}_+)$. Especially, when $\lambda(\cdot) \equiv \lambda > 0$ and $\nu(\cdot) \equiv \nu > 0$, we have $F_0(x) = \frac{\lambda}{\nu}$.

Let C_0-semigroup $\mathbb{T}_i(t) : C(\bar{\Omega}, \mathbb{R}) \to C(\bar{\Omega}, \mathbb{R}), i = 1, 2, \cdots, 6$, associating with operators $\kappa_i(x)$ separately, where

$$\kappa_1(x) = D_C\Delta - d_1(x),\ \kappa_2(x) = D_C\Delta - (a_1(x) + \delta(x)),\ \kappa_3(x) = D_C\Delta - d_2(x),$$
$$\kappa_4(x) = D_C\Delta - a_2(x),\ \kappa_5(x) = D_V\Delta - d(x),\ \kappa_6(x) = D_B\Delta - a_2(x).$$

According to [25], when $t > 0$, we have

$$(\mathbb{T}_i(t)\varphi)(x) = \int_\Omega \varphi(y)\mathcal{G}_i(x, y, t)dy,\ (i = 1, 2, \cdots, 6),\ \varphi \in C(\bar{\Omega}, \mathbb{R}), \tag{5}$$

where $\mathcal{G}_i(x, y, t)$ are Green functions related to $\kappa_i(x)$, respectively. Then, $\mathbb{T}_i(t)$ $(i = 1, 2, \cdots, 6)$ are strongly positive and compact.

Define α_i the principle eigenvalue of operators $\kappa_i(x)$, $i = 1, 2, \cdots, 6$. From [25], we have $\| \mathbb{T}_i(t) \| \leq A_i e^{\alpha_i t}$, where $A_i > 0$ are constants. Set $\mathrm{F} = (\mathrm{F}_1, \mathrm{F}_2, \cdots, \mathrm{F}_6)^T : \mathcal{X}_+ \to \mathcal{X}$, by:

$$\begin{cases} \mathrm{F}_1(\varphi)(x) = \lambda_1(x) - \beta_1(x)\varphi_1(x)\varphi_5(x) + \delta(x)\varphi_2(x), \\ \mathrm{F}_2(\varphi)(x) = \beta_1(x)\varphi_1(x)\varphi_5(x), \\ \mathrm{F}_3(\varphi)(x) = \lambda_2(x) - \beta_2(x)\varphi_3(x)\varphi_5(x), \\ \mathrm{F}_4(\varphi)(x) = \beta_2(x)\varphi_3(x)\varphi_5(x), \\ \mathrm{F}_5(\varphi)(x) = k_1(x)\varphi_2(x) + k_2(x)\varphi_4(x) - q(x)\varphi_5(x)\varphi_6(x), \\ \mathrm{F}_6(\varphi)(x) = c(x)\varphi_5(x)\varphi_6(x), \end{cases}$$

where $\varphi = (\varphi_1, \varphi_2, \cdots, \varphi_6) \in \mathcal{X}_+$, so that model (1) can be transformed into the integral equations (6) as:

$$K(t, \cdot, \varphi) = \mathbb{T}(t)\varphi + \int_0^t \mathbb{T}(t - s)\mathrm{F}(K(s, \cdot, \varphi))ds, \tag{6}$$

where $K = (H_1, I_1, H_2, I_2, V, B)$ is the solution of model (1) with φ=(φ_1,φ_2,$\cdots$,φ_6)$\in \mathcal{X}_+$, and $\mathbb{T}(t) = (\mathbb{T}_1(t), \mathbb{T}_2(t), \cdots, \mathbb{T}_6(t))$.

We obtain the following theorem regarding the existence of classical solution for model (1).

Theorem 1. *Model* (1) *admits a unique non-negative solution* $K(\cdot, t, \varphi)$ *with boundary conditions* (2) *on* $[0, \tau_{\max})$ *for initial condition* φ=(φ_1,φ_2,φ_3,φ_4,φ_5,φ_6)$\in \mathcal{X}_+$, *where* $\tau_{\max} \leq \infty$, *then* $\lim\limits_{t\to\tau_{\max}^-} \|K(\cdot, t)\| = \infty$ *if* $\tau_{\max} < \infty$. *Furthermore,* $K(\cdot, t, \varphi)$ *is classical solution of model* (1) *for* $t \in [0, \tau_{\max})$.

Proof. When $p \geq 0$, we have

$$\varphi(x) + pF(\varphi)(x) = \begin{pmatrix} \varphi_1(x) + p(\lambda_1(x) - \beta_1(x)\varphi_1(x)\varphi_5(x) + \delta(x)\varphi_2(x)) \\ \varphi_2(x) + p\beta_1(x)\varphi_1(x)\varphi_5(x) \\ \varphi_3(x) + p(\lambda_2(x) - \beta_2(x)\varphi_3(x)\varphi_5(x)) \\ \varphi_4(x) + p\beta_2(x)\varphi_3(x)\varphi_5(x) \\ \varphi_5(x) + p(k_1(x)\varphi_2(x) + k_2(x)\varphi_4(x) - q(x)\varphi_5(x)\varphi_6(x)) \\ \varphi_6(x) + pc(x)\varphi_5(x)\varphi_6(x) \end{pmatrix}$$

$$\geq \begin{pmatrix} \varphi_1(x)(1 - p\beta_1(x)\varphi_5(x)) \\ \varphi_2(x) \\ \varphi_3(x)(1 - p\beta_2(x)\varphi_5(x)) \\ \varphi_4(x) \\ \varphi_5(x)(1 - pq(x)\varphi_6(x)) \\ \varphi_6(x) \end{pmatrix},$$

for $\forall\ \varphi \in \mathcal{X}_+$. This indicates that,

$$\lim_{p\to 0^+} \frac{1}{p} dist(\varphi + pF(\varphi), \mathcal{X}_+) = 0.$$

According to the Corollary 4 from [17], there is the unique non-negative solution $K(\cdot, t)$ on $[0, \tau_{\max})$ with initial condition φ=(φ_1,φ_2, $\cdots$,φ_6) if $\tau_{\max} < \infty$, then $\lim\limits_{t\to\tau_{\max}^-} \|K(\cdot, t)\| = \infty$. And $K(\cdot, t)$ is the classical solution of model (1) for $t \in [0, \tau_{\max})$. □

Next, we obtain the following result regarding the existence and boundedness of global solutions for model (1).

Theorem 2. *When* $t \in [0, +\infty)$, *model* (1) *exists a unique non-negative and ultimately bounded solution* K=(H_1, I_1, H_2, I_2, V, B) *for any* $\varphi \in \mathcal{X}_+$, *with initial and boundary conditions* (2) *and* (3).

Proof. From the third equation of model (1), we have

$$\frac{\partial H_2(x,t)}{\partial t} \leq D_C \Delta H_2(x,t) + \lambda_2^s - d_2^i H_2(x,t),\ x \in \Omega,\ t \in [0, \tau_{\max}).$$

It is evident that $H_2(x,t) \leq U_3(x,t)$ from the comparison principle [22], for $x \in \Omega,\ t \in [0, \tau_{\max})$, and U_3 is the solution to the following equation:

$$\frac{\partial U_3(x,t)}{\partial t} = D_C \Delta H_2(x,t) + \lambda_2^s - d_2^i H_2(x,t),\ x \in \Omega,\ t \in [0, \tau_{\max}),$$

then $\lim\limits_{t\to\infty} U_3(x,t) = \frac{\lambda_2^s}{d_2^i}$. Therefore, when $x \in \Omega,\ t \in [0, \tau_{\max})$, we have $H_2(x,t) < M_1$ for constant $M_1 > 0$.

Let

$$P(t) = \int_\Omega \left[(H_1 + I_1)\frac{2k_1^s}{a_1^i} + (H_2 + I_2)\frac{2k_2^s}{a_2^i} + V + \frac{q^i}{c^s} B \right] dx.$$

Derivativing $P(t)$ on both sides, for any $t \in [0, \tau_{\max})$, we have

$$\begin{aligned}\frac{dP(t)}{dt} = \int\limits_{\Omega} \Big\{ &\big[D_C\Delta H_1 + D_C\Delta I_1 + \lambda_1(x) - a_1(x)I_1 - d_1H_1\big]\frac{2k_1^s}{a_1^i} \\ &+ \big[D_C\Delta H_2 + D_C\Delta I_2 + \lambda_2(x) - a_2(x)I_2 - d_2H_2\big]\frac{2k_2^s}{a_2^i} \\ &+ \big[D_V\Delta V + k_1(x)I_1 + k_2(x)I_2 - d(x)V - q(x)VB\big] \\ &+ \big[D_B\Delta B + c(x)VB - u(x)B\big]\frac{q^i}{c^s}\Big\}dx.\end{aligned}$$

Combining Neumann boundary conditions and divergence theorem, then

$$\begin{aligned}\frac{dP(t)}{dt} &\le \int\limits_{\Omega}\left[\lambda_1^s\frac{2k_1^s}{a_1^i} + \lambda_2^s\frac{2k_2^s}{a_2^i} - \frac{2k_1^sd_1^i}{a_1^i}H_1 - \frac{2k_2^sd_2^i}{a_2^i}H_2 - k_1^sI_1 - k_2^sI_2 - \frac{q^iu^i}{c^s}B - d^iV\right]dx \\ &= \int\limits_{\Omega}\left[\lambda_1^s\frac{2k_1^s}{a_1^i} + \lambda_2^s\frac{2k_2^s}{a_2^i}\right]dx - \eta_1P(t) \\ &= \left[\lambda_1^s\frac{2k_1^s}{a_1^i} + \lambda_2^s\frac{2k_2^s}{a_2^i}\right]|\Omega| - \eta_1P(t),\end{aligned}$$

where $|\Omega|$ is volume of Ω, and $\eta_1 = \min\Big\{d_1^i, d_2^i, \frac{2}{a_1^i}, \frac{2}{a_2^i}, u^i, d^i\Big\}$. For $t \in [0, \tau_{\max})$, we have $P(t) \le Q(t)$ from comparison principle, and $Q(t)$ is the solution of Eqn. (7) with initial condition $Q(0) = P(0)$,

$$\frac{dQ(t)}{dt} = \left[\lambda_1^s\frac{2k_1^s}{a_1^i} + \lambda_2^s\frac{2k_2^s}{a_2^i}\right]|\Omega| - \eta_1Q(t). \tag{7}$$

Then, it follows from Eqn. (7) that

$$\lim_{t\to\infty} Q(t) = \frac{\left(\lambda_1^s\frac{2k_1^s}{a_1^i} + \lambda_2^s\frac{2k_2^s}{a_2^i}\right)|\Omega|}{\eta_1},$$

and the solution $Q(t)$ is defined on $t \in [0, \infty)$. Therefore, we have $P(t) \le M_2$ for constant $M_2 > 0$ when $t \in [0, \tau_{\max})$. Then

$$\int\limits_{\Omega}(H_1 + I_1)dx < \frac{a_1^i}{2k_1^s}M_2,\ \int\limits_{\Omega}Vdx < M_2,\ \int\limits_{\Omega}(H_2 + I_2)dx < \frac{a_2^i}{2k_2^s}M_2,\ \int\limits_{\Omega}Bdx < \frac{c^s}{q^i}M_2.$$

By the Green function $\mathcal{G}_V$ and [9], we obtain

$$\mathcal{G}_V(t, x, y) = \sum_{n=1}^{\infty} e^{\tau_n t}\phi_n(x)\phi_n(y),$$

and τ_n is eigenvalue of $D_V\Delta - d(x)$ corresponding to eigenfunction $\phi_n(x)$, with $\tau_1 > \tau_2 > \cdots \tau_n > \cdots$. Evidently, we have $G_V(t, x, y) \le W_2\sum\limits_{n=1}^{\infty} e^{\tau_n t}$ for constant $W_2 > 0$ when $t > 0$.

We will define v_n as the eigenvalue of $D_V\Delta - d^i$, satisfying $v_1 = -d^i > v_2 > v_3 > \cdots > v_n > \cdots$, then we obtain $v_n > \tau_n$ from [39], where $n = 1, 2, \cdots$. When $t > 0$, we have $\mathcal{G}_V(t, x, y) \le W_2\sum\limits_{n=1}^{\infty} e^{v_n t} \le \sigma_5 e^{-d^i t}$ for constant $\sigma_5 > 0$.

From the fifth equation of model (1), we get

$$\frac{\partial V(x,t)}{\partial t} \leq D_V \Delta V - d(x)V + k_1(x)\frac{a_1^i}{k_1^s}M_2 + k_2(x)\frac{a_2^i}{k_2^s}M_2.$$

From Eqns. (5), (6) and the principle of comparison, we get

$$\begin{aligned}
V(x,t) \leq & \mathbb{T}_5 V(x,0) + \int_0^t \mathbb{T}_5(t-s)\left[k_1(x)\frac{a_1^i}{k_1^s} + k_2(x)\frac{a_2^i}{k_2^s}\right]M_2 ds \\
= & \mathbb{T}_5 V(x,0) + \int_0^t \int_\Omega \mathcal{G}_V(t-s,x,y)\left[k_1(y)\frac{a_1^i}{k_1^s} + k_2(y)\frac{a_2^i}{k_2^s}\right]M_2 dy ds \\
\leq & A_5 e^{\alpha_5 t}\|V(x,0)\|_{\mathcal{X}} + \int_0^t \sigma_5 e^{-d^i(t-s)} \int_\Omega \left(a_1^i + a_2^i\right) M_2 dy ds \\
\leq & A_5 e^{\alpha_5 t}\|V(x,0)\|_{\mathcal{X}} + M_2\frac{\sigma_5}{d^i}|\Omega|\left(a_1^i + a_2^i\right) \\
\triangleq & M_5.
\end{aligned}$$

Similarly, it can be obtained that $B \leq M_6$, and $I_2 \leq M_4$ when $x \in \Omega$, $t \in [0, \tau_{\max})$ for constants $M_4, M_6 > 0$. Adding the first and second equations of model (1), we provide

$$\frac{\partial H_1(x,t)}{\partial t} + \frac{\partial I_1(x,t)}{\partial t} \leq D_C \Delta(H_1 + I_1) + \lambda_1^s - \eta_2(H_1 + I_1),$$

where $\eta_2 = \min\{d_1^s, a_1^s\}$. Based on the principle of comparison, we have $\lim\limits_{t\to\infty}(H_1 + I_1) \leq \frac{\lambda_1^s}{\eta_2}$. Thus, we obtain that $H_1 + I_1 \leq M_7$ for constant M_7 when $x \in \Omega$, $t \in [0, \tau_{\max})$. Finally, it can be concluded that the solution of model (1) is bounded for $t \in [0, \tau_{\max})$, $x \in \Omega$. Hence, $\tau_{\max} = \infty$, and the solution is defined for all $t \in [0, \infty)$.

Due to $\lim\limits_{t\to\infty}(H_1 + I_1) \leq \frac{\lambda_1^s}{\eta_2}$, for $x \in \bar{\Omega}$, which indicates that H_1 and I_1 are ultimately bounded. Similarly, H_2 and I_2 are ultimately bounded for $x \in \bar{\Omega}$. Therefore, there must be constants $l_j > 0$ and time $t_j > 0$ $j = 1, 2, 3, 4$, such that

$$H_1 < l_1,\ I_1 < l_2,\ H_2 < l_3,\ I_2 < l_4,$$

for $t > t' = \max\{t_j, j = 1, 2, 3, 4\}$. Based on the above process, we can conclude that

$$\limsup_{t\to\infty} P(t) = \frac{\left(\lambda_1^s \frac{2k_1^s}{a_1^i} + \lambda_2^s \frac{2k_2^s}{a_2^i}\right) \mid \Omega \mid}{\eta_1}.$$

Meanwhile, we have $P(t) \leq l_5$ for constant $l_5 > 0$, and time $t_5 > 0$. Then, $\int\limits_\Omega V dx \leq l_5$, $\int\limits_\Omega B dx \leq \frac{c^s}{q^i} l_5$. For $t > \tilde{t} = \max\{t_j, j = 1, 2, 3, 4, 5\}$, we have that

$$\begin{aligned}
V(x,t) \leq & \mathbb{T}_5 V(x,\tilde{t}) + \int_{\tilde{t}}^t \mathbb{T}_5(t-s)\left[\frac{\lambda_1^s}{\eta_2}k_1(x) + \frac{\lambda_2^s}{\eta_3}k_2(x)\right] ds \\
\leq & \mathbb{T}_5 e^{\alpha_5}(t-\tilde{t}) \parallel V(x,\tilde{t}) \parallel_{\mathcal{X}} + \sigma_5|\Omega|\frac{1}{d^i}\left[\frac{\lambda_1^s}{\eta_2}k_1^s + \frac{\lambda_2^s}{\eta_3}k_2^s\right].
\end{aligned}$$

Since $\alpha_5 < 0$, then we get

$$\limsup_{t\to\infty} V(t) \leq \sigma_5|\Omega|\frac{1}{d^i}\left[\frac{\lambda_1^s}{\eta_2}k_1^s + \frac{\lambda_2^s}{\eta_3}k_2^s\right] \triangleq l_5,$$

for all $x \in \Omega$, $t > \tilde{t}$. It indicates that V is ultimately bounded. In summary, it can be concluded that the solution K=(H_1, I_1, H_2, I_2, V, B) of model (1) is ultimately bounded. □

2.2. **Steady state and basic reproduction number.** Assuming $I_1 = 0$, $I_2 = 0$, $V = 0$, $B = 0$, model (1) becomes the following system:

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C \Delta H_1 + \lambda_1(x) - d_1(x) H_1, \ x \in \Omega, \\ \dfrac{\partial H_2(x,t)}{\partial t} = D_C \Delta H_2 + \lambda_2(x) - d_2(x) H_2, \ x \in \Omega, \\ \dfrac{\partial H_1}{\partial \vec{n}} = \dfrac{\partial H_2}{\partial \vec{n}} = 0, \ x \in \partial\Omega. \end{cases} \tag{8}$$

It is known that $E_0(x) = (H_1^0(x),\ 0,\ H_2^0(x),\ 0,\ 0,\ 0)$ is a unique infection-free steady state of model (1) with

$$\begin{cases} D_C \Delta H_1^0(x) + \lambda_1(x) - d_1(x) H_1^0(x) = 0, \ x \in \Omega, \\ D_C \Delta H_2^0(x) + \lambda_2(x) - d_2(x) H_2^0(x) = 0, \ x \in \Omega, \\ \dfrac{\partial H_1^0(x)}{\partial \vec{n}} = \dfrac{\partial H_2^0(x)}{\partial \vec{n}} = 0, \ x \in \partial\Omega. \end{cases}$$

Next, we will calculate the basic reproduction number. Let

$$\mathcal{F} = \begin{pmatrix} 0 & 0 & \beta_1(\cdot) H_1^0(\cdot) \\ 0 & 0 & \beta_2(\cdot) H_2^0(\cdot) \\ 0 & 0 & 0 \end{pmatrix}, \ \mathcal{B} = \begin{pmatrix} a_1(\cdot) + \delta(\cdot) & 0 & 0 \\ 0 & a_2(\cdot) & 0 \\ -k_1(\cdot) & -k_2(\cdot) & d(\cdot) \end{pmatrix}, \ \mathcal{D} = \begin{pmatrix} D_C & 0 & 0 \\ 0 & D_C & 0 \\ 0 & 0 & D_V \end{pmatrix}.$$

Then, linearize the model (1) at $E_0(x)$ to obtain the following linear system:

$$\begin{cases} \dfrac{\partial w_1(x,t)}{\partial t} = D_C \Delta w_1 - d_1(x) w_1 - \beta_1(x) H_1^0(x) w_5 + \delta(x) w_2, \ x \in \Omega, t \geq 0, \\ \dfrac{\partial w_2(x,t)}{\partial t} = D_C \Delta w_2 + \beta_1(x) H_1^0(x) w_5 - (\delta(x) + a_1(x)) w_2, \ x \in \Omega, t \geq 0, \\ \dfrac{\partial w_3(x,t)}{\partial t} = D_C \Delta w_3 - d_2(x) w_3 - \beta_2(x) H_2^0(x) w_5, \ x \in \Omega, t \geq 0, \\ \dfrac{\partial w_4(x,t)}{\partial t} = D_C \Delta w_4 + \beta_2(x) H_2^0(x) w_5 - a_2(x) w_4, \ x \in \Omega, t \geq 0, \\ \dfrac{\partial w_5(x,t)}{\partial t} = D_V \Delta w_5 + k_1(x) w_2 + k_2(x) w_4 - d(x) w_5, \ x \in \Omega, t \geq 0, \\ \dfrac{\partial w_6(x,t)}{\partial t} = D_B \Delta w_6 - u(x) w_6, \ x \in \Omega, t \geq 0, \end{cases}$$

with boundary conditions

$$\frac{\partial w_1}{\partial \vec{n}} = \frac{\partial w_2}{\partial \vec{n}} = \frac{\partial w_3}{\partial \vec{n}} = \frac{\partial w_4}{\partial \vec{n}} = \frac{\partial w_5}{\partial \vec{n}} = \frac{\partial w_6}{\partial \vec{n}} = 0, \ x \in \partial\Omega.$$

Consequently, we only consider the following system,

$$\begin{cases} \dfrac{\partial w(x,t)}{\partial t} = \mathcal{D} \Delta w + (\mathcal{F}(x) - \mathcal{B}(x)) w, \ x \in \Omega, \\ \dfrac{\partial w}{\partial \vec{n}} = 0, \ x \in \partial\Omega, \end{cases} \tag{9}$$

where $w = (w_2, w_4, w_5)^T$. Substituting $w = e^{\lambda t} \phi(x)$ into model (9), it yields

$$\begin{cases} \lambda \phi(x) = \mathcal{D} \Delta \phi(x) + (\mathcal{F}(x) - \mathcal{B}(x)) \phi(x), \ x \in \Omega, \\ \dfrac{\partial \phi(x)}{\partial \vec{n}} = 0, \ x \in \partial\Omega. \end{cases} \tag{10}$$

Based on the Theorem 7.6.1 of [29], we have the following result.

Lemma 2. *$\lambda_0 = \lambda_0(\mathcal{D}, H_1^0, H_2^0)$ is a principle eigenvalue with a strictly positive eigenvector of system* (10).

For the following system (11), we define a semiflow $\mathcal{T}(t) : C(\bar{\Omega}, R^3) \to C(\bar{\Omega}, R^3)$,

$$\begin{cases} \dfrac{\partial \hat{v}(x,t)}{\partial t} = \mathcal{D}\Delta\hat{v} - \mathcal{B}(x)v, \ x \in \Omega, \\ \dfrac{\partial \hat{v}}{\partial \vec{n}} = 0, \ x \in \partial\Omega, \end{cases} \tag{11}$$

where $\hat{v} = (\hat{v}_1, \hat{v}_2, \hat{v}_3)^T$. Assuming the virus is introduced at $t = 0$, and $\phi(x)$=($\phi_2(x)$, $\phi_4(x)$, $\phi_5(x)$)^T represent the infected cells and virus. So, $F(x)\mathcal{T}(t)\phi(x)$ denote the distribution of new infected cells and virus at time t. Furthermore, $\int_0^{+\infty} F(x)\mathcal{T}(t)\phi(x)dt$ can be used to represent the total distribution of them.

Define the following continuous operator $\mathfrak{L}$, which represents the maps $\phi(x)$ to the total quantity of infections generated distribution during the infection period:

$$\mathfrak{L}(\phi)(x) = \int_0^{+\infty} F(x)\mathcal{T}(t)\phi(x)dt = F(x)\int_0^{+\infty} \mathcal{T}(t)\phi(x)dt.$$

According to the derivation in [42], we denote the basic reproduction number of model (1) as $\Re_0 = r(\mathfrak{L})$, where $r(\mathfrak{L})$ is the spectral radius of $\mathfrak{L}$. It is easy to get Lemma 3 based on Theorem 3.1 of [42].

Lemma 3. *(i) The symbols of λ_0 and $\Re_0 - 1$ are consistent;*

(ii) When $\Re_0 < 1$, the infection-free steady state E_0 of model (1) *is locally asymptotically stable, and E_0 is unstable if $\Re_0 > 1$.*

3. Analysis of steady state for model (1)

3.1. **Stability of the infection-free steady state E_0.** First, we will investigate the stability of E_0 when $\Re_0 < 1$, and provide the following result.

Theorem 3. *If $\Re_0 < 1$, then the infection-free steady state E_0 of model* (1) *is globally asymptotically stable.*

Proof. From the third equation of model (1), we obtain that

$$\frac{\partial H_2(x,t)}{\partial t} \le D_C\Delta H_2 + \lambda_2(x) - d_2(x)H_2.$$

Thus, $\limsup_{t\to\infty} H_2 \le H_2^0(x)$ uniformly for $x \in \bar{\Omega}$. Set $S_1 = H_1 + I_1$, and according to (A_1), then

$$\frac{\partial S_1(x,t)}{\partial t} = \frac{\partial H_1(x,t)}{\partial t} + \frac{\partial I_1(x,t)}{\partial t} \le D_C\Delta S_1 + \lambda_1(x) - d_1(x)S_1,$$

define the following comparison equation,

$$\frac{\partial \hat{S}_1(x,t)}{\partial t} = D_C\Delta\hat{S}_1 + \lambda_1(x) - d_1(x)\hat{S}_1. \tag{12}$$

By the principle of comparison, we have $\limsup_{t\to\infty} S_1 \le \hat{S}_1$, meanwhile, the solution of (12) is the same as the solution $H_1^0(x)$ of the first equation of system (8). So, we can further obtain $\limsup_{t\to\infty} S_1 \le H_1^0(x)$, then $\limsup_{t\to\infty} H_1 \le H_1^0(x)$.

Therefore, we have the following inequality:

$$\begin{cases} \dfrac{\partial I_1(x,t)}{\partial t} \le D_C \Delta I_1 + \beta_1(x) H_1^0(x) V - (\delta(x) + a_1(x)) I_1, \\ \dfrac{\partial I_2(x,t)}{\partial t} \le D_C \Delta I_2 + \beta_2(x) H_2^0(x) V - a_2(x) I_2, \\ \dfrac{\partial V(x,t)}{\partial t} \le D_V \Delta V + k_1(x) I_1 + k_2(x) I_2 - d(x) V. \end{cases}$$

Consider the following comparison system:

$$\begin{cases} \dfrac{\partial \breve{I}_1(x,t)}{\partial t} = D_C \Delta \breve{I}_1 + \beta_1(x) H_1^0(x) \breve{V} - (\delta(x) + a_1(x)) \breve{I}_1, \\ \dfrac{\partial \breve{I}_2(x,t)}{\partial t} = D_C \Delta \breve{I}_2 + \beta_2(x) H_2^0(x) \breve{V} - a_2(x) \breve{I}_2, \\ \dfrac{\partial \breve{V}(x,t)}{\partial t} = D_V \Delta \breve{V} + k_1(x) \breve{I}_1 + k_2(x) \breve{I}_2 - d(x) \breve{V}. \end{cases} \tag{13}$$

By the Lemma 3, we have $\lambda_0 < 0$ if $\Re_0 < 1$. Hence, the solution $(\breve{I}_1,\ \breve{I}_2\ \breve{V})$ of system (13) tend to $(0,0,0)$ for $x \in \bar{\Omega}$ as $t \to \infty$. Moreover, $(I_1,\ I_2\ V) \le (\breve{I}_1,\ \breve{I}_2\ \breve{V})$ for $x \in \Omega$ as $t \ge 0$, meanwhile, $(I_1,\ I_2\ V)$ tend to $(0,0,0)$ when $x \in \bar{\Omega}$ as $t \to \infty$.

So, it is easy to have the following limit equations:

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C \Delta H_1 + \lambda_1(x) - d_1(x) H_1, \\ \dfrac{\partial H_2(x,t)}{\partial t} = D_C \Delta H_2 + \lambda_2(x) - d_2(x) H_2, \\ \dfrac{\partial B(x,t)}{\partial t} = D_B \Delta B - u(x) B. \end{cases}$$

We can conclude that H_1, H_2 and B approaches $H_1^0(x)$, $H_2^0(x)$ and 0 for $x \in \bar{\Omega}$ when $t \to \infty$, respectively. Combined with Lemma 3 (ii), we can conclude that E_0 is globally asymptotically stable when $\Re_0 < 1$. This completes the proof of Theorem 3. □

3.2. **Uniform persistence without antibody response.** Next, we will investigate the dynamics of model (1) in the absence of antibody response.

When $B = 0$, model (1) becomes the following form:

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C \Delta H_1 + \lambda_1(x) - d_1(x) H_1 - \beta_1(x) H_1 V + \delta(x) I_1, x \in \Omega, t \ge 0, \\ \dfrac{\partial I_1(x,t)}{\partial t} = D_C \Delta I_1 + \beta_1(x) H_1 V - (\delta(x) + a_1(x)) I_1, x \in \Omega, t \ge 0, \\ \dfrac{\partial H_2(x,t)}{\partial t} = D_C \Delta H_2 + \lambda_2(x) - d_2(x) H_2 - \beta_2(x) H_2 V, x \in \Omega, t \ge 0, \\ \dfrac{\partial I_2(x,t)}{\partial t} = D_C \Delta I_2 + \beta_2(x) H_2 V - a_2(x) I_2, x \in \Omega, t \ge 0, \\ \dfrac{\partial V(x,t)}{\partial t} = D_V \Delta V + k_1(x) I_1 + k_2(x) I_2 - d(x) V, x \in \Omega, t \ge 0, \end{cases} \tag{14}$$

with the following boundary conditions:

$$\frac{\partial H_1}{\partial \vec{n}} = \frac{\partial I_1}{\partial \vec{n}} = \frac{\partial H_2}{\partial \vec{n}} = \frac{\partial I_2}{\partial \vec{n}} = \frac{\partial V}{\partial \vec{n}} = 0, x \in \partial\Omega,$$

satisfying the following initial values:

$$H_1(x,0) = v_1(x), I_1(x,0) = v_2(x), H_2(x,0) = v_3(x), I_2(x,0) = v_4(x), V(x,0) = v_5(x),$$

and $v_j(x) \geq 0$ $(j = 1, 2, \cdots, 5), x \in \Omega$. Obviously, $\widehat{E}_0(x) = (\widehat{H}_1^0(x),\ 0,\ \widehat{H}_2^0(x),\ 0,\ 0)$ is a unique infection-free steady state of system (14).

Next, we will discuss the uniform persistence of model (14), we first present the following result.

Theorem 4. *If $\Re_0 > 1$, for any initial value $v = (v_1, v_2, v_3, v_4, v_5) \in Y_+$, with $v_2 \neq 0$, or $v_4 \neq 0$ and $v_5 \neq 0$, where $Y_+ = C(\bar{\Omega}, \mathbb{R}_+^5)$, there is a constant $\eta_1 > 0$, such that*

$$\limsup_{t\to\infty} \parallel K_1 - \widehat{E}_0 \parallel_{Y_+} \geq \eta_1,$$

for any positive solution $K_1 = (H_1,\ I_1,\ H_2,\ I_2,\ V)$ of model (14).

Proof. According to the parabolic maximum principle in [22], we obtain that $I_1,\ I_2,\ V > 0$ for the initial value $v_2 \neq 0$, $v_4 \neq 0$ and $v_5 \neq 0$. Since $\Re_0 > 1$, then $\lambda_0 > 0$.

Consider it yields eigenvalue problem:

$$\begin{cases} \lambda\varsigma_2(x) = D_C\Delta\varsigma_2(x) + \beta_1(x)(H_1^0(x) - \eta_1)\varsigma_5(x) - (\delta(x) + a_1(x))\varsigma_2(x), x \in \Omega, \\ \lambda\varsigma_4(x) = D_C\Delta\varsigma_4(x) + \beta_2(x)(H_2^0(x) - \eta_1)\varsigma_5(x) - a_2(x)\varsigma_4(x), x \in \Omega, \\ \lambda\varsigma_5(x) = D_V\Delta\varsigma_5(x) + k_1(x)\varsigma_2(x) + k_2(x)\varsigma_4(x) - d(x)\varsigma_5(x), x \in \Omega, \\ \dfrac{\partial\varsigma_2(x)}{\partial\vec{n}} = \dfrac{\partial\varsigma_4(x)}{\partial\vec{n}} = \dfrac{\partial\varsigma_5(x)}{\partial\vec{n}} = 0, x \in \partial\Omega. \end{cases} \tag{15}$$

Let the principle eigenvalue of system (15) be $\lambda_0(\eta)$, when the positive constant η_1 is small enough, then for $x \in \bar{\Omega}$, we have $\lambda_0(\eta_1) > 0$, $H_1^0(x) - \eta_1 > 0$ and $H_2^0(x) - \eta_1 > 0$. Moreover, the eigenvector $(\varsigma_2(x), \varsigma_4(x), \varsigma_5(x))$ is strictly positive which corresponds to $\lambda_0(\eta_1) > 0$.

Assuming that

$$\limsup_{t\to\infty} \parallel K_1(x,t) - \widehat{E}_0 \parallel_{Y_+} < \eta_1.$$

So, there is a sufficiently large t_1, for $t > t_1$ $x \in \bar{\Omega}$, we have

$$H_1^0(x) - \eta_1 < H_1 < H_1^0(x) + \eta_1, I_1 < \eta_1, H_2^0(x) - \eta_1 < H_2 < H_2^0(x) + \eta_1, I_2(x,t) < \eta_1, V < \eta_1.$$

Then, we obtain the following inequality:

$$\begin{cases} \dfrac{\partial I_1(x,t)}{\partial t} \geq D_C\Delta I_1 + \beta_1(x)(H_1^0(x) - \eta_1)V - (\delta(x) + a_1(x))I_1, \\ \dfrac{\partial I_2(x,t)}{\partial t} \geq D_C\Delta I_2 + \beta_2(x)(H_2^0(x) - \eta_1)V - a_2(x)I_2, \\ \dfrac{\partial V(x,t)}{\partial t} \geq D_V\Delta V + k_1(x)I_1 + k_2(x)I_2 - d(x)V. \end{cases} \tag{16}$$

Consider the following auxiliary system:

$$\begin{cases} \dfrac{\partial\widehat{I}_1(x,t)}{\partial t} = D_C\Delta\widehat{I}_1 + \beta_1(x)(H_1^0(x) - \eta_1)\widehat{V} - (\delta(x) + a_1(x))\widehat{I}_1, \\ \dfrac{\partial\widehat{I}_2(x,t)}{\partial t} = D_C\Delta\widehat{I}_2 + \beta_2(x)(H_2^0(x) - \eta_1)\widehat{V} - a_2(x)\widehat{I}_2, \\ \dfrac{\partial\widehat{V}(x,t)}{\partial t} = D_V\Delta\widehat{V} + k_1(x)\widehat{I}_1 + k_2(x)\widehat{I}_2 - d(x)\widehat{V}. \end{cases} \tag{17}$$

The system (17) has solution such as $(\widehat{I}_1,\ \widehat{I}_2,\ \widehat{V}) = e^{\lambda_0(\eta_1)(t-t_1)}(\varsigma_2(x),\ \varsigma_4(x),\ \varsigma_5(x))$. From the Theorem 2, we have $(\widehat{I}_1,\ \widehat{I}_2,\ \widehat{V}) > 0$. Therefore, for any $t > t_1$ $x \in \bar{\Omega}$, there is a constant $\eta_2 > 0$ such that $(I_1,\ I_2,\ V) \geq \eta_2(\widehat{I}_1,\ \widehat{I}_2,\ \widehat{V})$. Thereupon, we have $\lim\limits_{t\to\infty} \widehat{I}_1 = \infty$, $\lim\limits_{t\to\infty} \widehat{I}_2 = \infty$, and $\lim\limits_{t\to\infty} \widehat{V} = \infty$. Then, $\lim\limits_{t\to\infty} I_1 = \infty$, $\lim\limits_{t\to\infty} I_2 = \infty$, and $\lim\limits_{t\to\infty} V = \infty$. This is contradictory to the boundedness of $(I_1,\ I_2,\ V)$, and the conclusion is confirmed. □

Corollary 1: (a) Model (14) has a unique, non-negative and ultimately bounded solution $K_1 = (H_1, I_1, H_2, I_2, V)$ on $[0, +\infty) \times \bar{\Omega}$, with the initial value $v(x) = (v_1(x), v_2(x), v_3(x), v_4(x), v_5(x)) \in Y_+$.

(b) Model (14) has a solution semiflow $\varpi(t) : Y_+ \to Y_+$ as $\varpi(t)\varrho = K_1$ for $x \in \bar{\Omega}$ with $v \in Y_+$ when $t \geq 0$. Besides, there is a global compact attractor for $\varpi(t)$ in Y_+.

Next, we define

$$\mathbb{Q}_0 = \{\phi = (\phi_1, \phi_2, \phi_3, \phi_4, \phi_5) \in Y_+ : \phi_1 > 0, \phi_2 \neq 0, \phi_3 > 0, \phi_4 \neq 0 \text{ and } \phi_5 \neq 0\},$$

and $\mathbb{Q}_0$ is the positive invariant set for $\varpi(t)$. Moreover,

$$\partial\mathbb{Q}_0 = \mathbb{C}^+/\mathbb{Q}_0 = \{\phi \in Y_+ : \phi_2 = 0, \text{ or } \phi_4 = 0, \text{ or } \phi_5 = 0\}.$$

Let

$$\mathcal{M}_\alpha := \{\phi \in Y_+ : \Phi(t)\phi \subset \partial\mathbb{Q}_0, t \geq 0\},$$

where $\Phi(t)$ is the solution semiflow of $\Phi(t) = K(H_1, I_1, H_2, I_2, V, B)$ with $\Phi(t)\phi = K(\cdot)$.

Next, we provide the following result about the omega limit set of model (14).

Lemma 4. *Define $\omega(\phi)$ as the omega limit set of $\Phi(t)\phi$ of model (14), and $\mathcal{M}_1 = \{\widehat{E}_0\}$, then we have $\bigcup_{\phi\in\mathcal{M}_\alpha} \omega(\phi) = \mathcal{M}_1$.*

Proof. For $t \geq 0$, we obtain that $\Phi(t)\widehat{E}_0 = \widehat{E}_0$. Therefore, $\mathcal{M}_1 \subset \bigcup_{\phi\in\mathcal{M}_\alpha} \omega(\phi)$. Since $\Phi(t)\phi \in \partial\mathbb{Q}_0$ when $t \geq 0$ for any $\phi \in \mathcal{M}_\alpha$. So, we have $I_1 \equiv 0$ or $I_2 \equiv 0$, or $V \equiv 0$.

If $I_1 \equiv 0$. We can obtain $V = 0$ from the second equation of model (14), and based on the fifth equation, we have $I_2 = 0$. Then, we can obtain the following subsystem of model (14).

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C\Delta H_1 + \lambda_1(x) - d_1(x)H_1, x \in \Omega, \\ \dfrac{\partial H_2(x,t)}{\partial t} = D_C\Delta H_2 + \lambda_2(x) - d_2(x)H_2, x \in \Omega, \\ \dfrac{\partial H_1}{\partial \vec{n}} = \dfrac{\partial H_2}{\partial \vec{n}} = 0, x \in \partial\Omega. \end{cases}$$

It is easy to obtain $\lim\limits_{t\to\infty} H_1 = H_1^0(x)$, $\lim\limits_{t\to\infty} H_2 = H_2^0(x)$. In other words, we have $\omega(\phi) = \widehat{E}_0$.

If $I_2 \equiv 0$. The proof is as similar as the above, so we also obtain the same conclusion.

If $V \equiv 0$. We have $\lim\limits_{t\to\infty} I_1 = 0$ and $\lim\limits_{t\to\infty} I_2 = 0$ from the second and fourth equations of (14). Then, we obtain $\lim\limits_{t\to\infty} H_1 = H_1^0(x)$ and $\lim\limits_{t\to\infty} H_2 = H_2^0(x)$. Then, $\omega(\phi) = \widehat{E}_0$.

Therefore, we have $\bigcup_{\phi\in\mathcal{M}_\alpha} \omega(\phi) \subset \mathcal{M}_1$. This completes the proof of Lemma 4. □

Next, we have the following theorem for the uniform persistence of model (14).

Theorem 5. *When $\Re_0 > 1$, there is a constant $\delta > 0$, such that*

$$\liminf_{t\to\infty} K_1(x, t, \phi) \geq (\delta, \delta, \delta, \delta, \delta),$$

where $K_1 = (H_1, I_1, H_2, I_2, V)$ is any positive solution of model (14), $x \in \bar{\Omega}$ and $\phi \in \mathbb{Q}_0 = \{\phi \in Y_+ : \phi_2(\cdot, 0) \neq 0, \phi_4(\cdot, 0) \neq 0, \text{ and } \phi_5(\cdot, 0) \neq 0\}$.

Proof. According to the Theorem 2, we know that K_1 is non-negative and bounded, and we have $H_1 \leq M_2$, $I_1 \leq M_2$, $H_2 \leq M_2$, $I_2 \leq M_2$, $V \leq M_2$, for a constant $M_2 > 0$ when $x \in \bar{\Omega}$, $t \geq t_0 > 0$.

Thus, for $t \geq t_0$ we have

$$\frac{\partial H_1(x,t)}{\partial t} \geq D_C\Delta H_1 + \lambda_1(x) - d_1(x)H_1 - \beta_1(x)H_1M_2,$$

and

$$\frac{\partial H_2(x,t)}{\partial t} \geq D_C\Delta H_2 + \lambda_2(x) - d_2(x)H_2 - \beta_2(x)H_2M_2.$$

From comparing theory, we obtain that H_1 and H_2 have positive lower bounds, respectively. Therefore, H_1 and H_2 are uniformly persistent in model (14).

Define $\mathcal{P} : Y_+ \to [0, \infty)$ is a continuous function:

$$\mathcal{P}(\phi) := \min\{\min_{x\in\bar{\Omega}} \phi_2(x), \min_{x\in\bar{\Omega}} \phi_4(x), \min_{x\in\bar{\Omega}} \phi_5(x)\},$$

for all $\phi \in Y_+$. Clearly, there are $\min_{x\in\bar{\Omega}} \phi_2(x) > 0$, $\min_{x\in\bar{\Omega}} \phi_4(x) > 0$ and $\min_{x\in\bar{\Omega}} \phi_5(x) > 0$ when $\mathcal{P}(\phi) > 0$, it means that $\mathcal{P}^{-1}(0, \infty) \subset \mathbb{Q}_0$. When $\phi_2(x) \neq 0$, $\phi_4(x) \neq 0$ and $\phi_5(x) \neq 0$, according to the maximum principle of parabolic equation [22], we know that $I_1 > 0$, $I_2 > 0$, $V > 0$ for any $x \in \bar{\Omega}$, $t \geq 0$. Hence, if either $\mathcal{P}(\phi) = 0$ or $\mathcal{P}(\phi) > 0$ with $\phi \in \mathbb{Q}_0$, then $\mathcal{P}(\Phi(t)\phi) > 0$. Thus, $\mathcal{P}$ is a generalized distance function for semiflow $\Phi(t) : Y_+ \to \mathbb{Q}_0$.

Based on the above discussion, for any orbit of $\Phi(t)$ in $\mathcal{M}_\alpha$, when $t \to \infty$, it converges at E_0. Therefore, the subset of M_1 will not form a cycle in $\partial\mathbb{Q}_0$. This means $W^s(M_1) \bigcap \mathbb{Q}_0 = \varnothing$, and M_1 is isolated in Y_+, $W^s(M_1)$ is the stable set of M_1.

According to the boundedness of the solutions, solution semiflow $\Phi(t) : Y_+ \to Y_+$ is point dissipative and compact for $t > 0$, and there is a global compact attractor of $\Phi(t)$ from Theorem 2.2.6 in [46]. Therefore, according to Theorem 3 in [30], there is a constant $\delta > 0$, such that

$$\liminf_{t\to\infty}(H_1, I_1, H_2, I_2, V) \geq (\delta, \delta, \delta, \delta, \delta).$$

for $x \in \bar{\Omega}$, $\phi \in \mathbb{Q}_0$, This indicates the uniform persistence of I_1 I_2 and V. This completes the proof of Theorem 5. □

Therefore, from Theorem 5 and Theorem 1.3.6 in [53], it can be concluded that when $\Re_0 > 1$, model (1) exists the immune-free steady state $E_1(x) = (H_1^{(1)}(x), I_1^{(1)}(x), H_2^{(1)}(x), I_2^{(1)}(x), V^{(1)}(x), 0)$.

Remark 1. From Theorem 5, we know that the disease of model (14) is uniform persistent without antibody response. There is an open question, whether the result is still true for model (1) with antibody response.

4. Stability analysis of model (1) under spatial homogeneity

If all parameters of model (1) are constant, then we have the following homogeneity system:

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C\Delta H_1 + \lambda_1 - d_1H_1 - \beta_1H_1V + \delta I_1, \\ \dfrac{\partial I_1(x,t)}{\partial t} = D_C\Delta I_1 + \beta_1H_1V - (\delta + a_1)I_1, \\ \dfrac{\partial H_2(x,t)}{\partial t} = D_C\Delta H_2 + \lambda_2 - d_2H_2 - \beta_2H_2V, \\ \dfrac{\partial I_2(x,t)}{\partial t} = D_C\Delta I_2 + \beta_2H_2V - a_2I_2, \\ \dfrac{\partial V(x,t)}{\partial t} = D_V\Delta V + k_1I_1 + k_2I_2 - dV - qVB, \\ \dfrac{\partial B(x,t)}{\partial t} = D_B\Delta B + cVB - uB, \end{cases} \tag{18}$$

with boundary conditions,

$$\frac{\partial H_1}{\partial \vec{n}} = \frac{\partial I_1}{\partial \vec{n}} = \frac{\partial H_2}{\partial \vec{n}} = \frac{\partial I_2}{\partial \vec{n}} = \frac{\partial V}{\partial \vec{n}} = \frac{\partial B}{\partial \vec{n}} = 0, x \in \partial\Omega,$$

and the following initial condition,

$$H_1(x, 0) = \psi_1(x, 0) \geq 0, I_1(x, 0) = \psi_2(x, 0) \geq 0, V(x, 0) = \psi_5(x, 0) \geq 0,$$

$$H_2(x,0)=\psi_3(x,0)\geq 0, I_2(x,0)=\psi_4(x,0)\geq 0, B(x,0)=\psi_6(x,0)\geq 0,$$

where $\psi=(\psi_1,\psi_2,\psi_3,\psi_4,\psi_5,\psi_6)\in\mathcal{X}_+$. Define the following bounded set $\mathbb{L}$:

$$\mathbb{L}=\{(H_1,I_1,H_2,I_2,V,B)\,|0\leq H_1,I_1\leq\frac{\lambda_1}{a_1};0\leq H_2,I_2\leq\frac{\lambda_2}{a_2};0\leq V\leq\hat{\eta}_1;0\leq B\leq\eta_2\},$$

where $\hat{\eta}_1=\frac{\frac{\lambda_1 k_1}{a_1}+\frac{\lambda_2 k_2}{a_2}}{\min\{d,u\}}$, $\eta_2=\frac{q(\frac{\lambda_1 k_1}{a_1}+\frac{\lambda_2 k_2}{a_2})}{c\cdot\min\{d,u\}}$.

For the homogeneous model (18), there is a unique infection-free equilibrium $\tilde{E}_0=(\tilde{H}_1^0,\,0,\,\tilde{H}_2^0,\,0,\,0,\,0)=(\frac{\lambda_1}{d_1},0,\frac{\lambda_2}{d_2},0,0,0)$. According to the next generation matrix approach from [34], we have the basic reproduction number of model (18) as follows,

$$R_0=\frac{k_1\beta_1\lambda_1}{dd_1(a_1+\delta)}+\frac{k_2\beta_2\lambda_2}{dd_2a_2},$$

and define $R_{01}=\frac{k_1\beta_1\lambda_1}{dd_1(a_1+\delta)}$ and $R_{02}=\frac{k_2\beta_2\lambda_2}{dd_2a_2}$.

Remark 2. Here, R_{01} represents the basic reproduction number of HIV infection with $CD4^+$ T cells, R_{02} represents the basic reproduction number of HIV infection with macrophages.

Next, we will discuss the existence of the humoral immune-free equilibrium and the chronic-infection equilibrium of model (18).

Let $\tilde{E}_1=(\tilde{H}_1^{(1)},\,\tilde{I}_1^{(1)},\,\tilde{H}_2^{(1)},\,\tilde{I}_2^{(1)},\,\tilde{V}^{(1)},\,0)$ be the humoral immune-free equilibrium of model (18), by calculation, we have

$$\tilde{H}_1^{(1)}=\frac{\lambda_1(a_1+\delta)}{d_1(a_1+\delta)+a_1\beta_1\tilde{V}^{(1)}},\ \tilde{I}_1^{(1)}=\frac{\lambda_1\beta_1\tilde{V}^{(1)}}{d_1(a_1+\delta)+a_1\beta_1\tilde{V}^{(1)}},$$
$$\tilde{H}_2^{(1)}=\frac{\lambda_2}{d_2+\beta_2\tilde{V}^{(1)}},\ \tilde{I}_2^{(1)}=\frac{\lambda_2\beta_2\tilde{V}^{(1)}}{a_2(d_2+\beta_2\tilde{V}^{(1)})},$$

and $\tilde{V}^{(1)}$ is the root of $\mathfrak{h}(V)=1$, and $\mathfrak{h}(V)=\frac{1}{d}\Big[\frac{k_1\lambda_1\beta_1}{d_1(a_1+\delta)+a_1\beta_1V}+\frac{k_2\lambda_2\beta_2}{a_2(d_2+\beta_2V)}\Big]$ monotonically decreases with V. Substitute $V=\frac{1}{d}\Big(\frac{k_1\lambda_1}{a_1}+\frac{k_2\lambda_2}{a_2}\Big)$ into $\mathfrak{h}(V)$, then we have

$$\mathfrak{h}\left[\frac{1}{d}\left(\frac{k_1\lambda_1}{a_1}+\frac{k_2\lambda_2}{a_2}\right)\right]=\frac{1}{1+m}+\frac{1}{1+n},$$

where

$$m=\frac{1}{k_1\lambda_1\beta_1}\left[d_1d(a_1+\delta)+\frac{a_1\beta_1k_2\lambda_2}{a_2}\right],\ n=\frac{1}{k_2\lambda_2\beta_2}\left(a_2d_2d+\frac{a_2\beta_2k_1\lambda_1}{a_1}\right).$$

Obviously, $mn>1$. Besides, we have that $\frac{1}{1+m}+\frac{1}{1+n}<1$ if $mn>1$. Therefore,

$$\mathfrak{h}\left[\frac{1}{d}\left(\frac{k_1\lambda_1}{a_1}+\frac{k_2\lambda_2}{a_2}\right)\right]<1.$$

And $\mathfrak{h}(V)=1$ have a unique positive root $\tilde{V}^{(1)}\in\Big(0,\frac{1}{d}\big(\frac{k_1\lambda_1}{a_1}+\frac{k_2\lambda_2}{a_2}\big)\Big]$ when $\mathfrak{h}(0)=\frac{1}{d}\Big[\frac{k_1\beta_1\lambda_1}{d_1(a_1+\delta)}+\frac{k_2\beta_2\lambda_2}{d_2a_2}\Big]=R_0>1$.

Next, we discuss the existence of immune-activated equilibrium $\tilde{E}^*=(\tilde{H}_1^*,\,\tilde{I}_1^*,\,\tilde{H}_2^*,\,\tilde{I}_2^*,\,\tilde{V}^*,\,\tilde{B}^*)$ of model (18), by calculation, we have

$$\tilde{H}_1^*=\frac{(a_1+\delta)c\lambda_1\beta_1}{cd_1(a_1+\delta)+\beta_1ua_1},\ \tilde{H}_2^*=\frac{a_2c\lambda_2}{d_2a_2c+a_2\beta_2u},\ \tilde{I}_1^*=\frac{\lambda_1\beta_1u}{d_1c(a_1+\delta)+\beta_1ua_1},\ \tilde{V}^*=\frac{u}{c},$$

$$\tilde{I}_2^*=\frac{\lambda_2\beta_2u}{d_2a_2c+a_2\beta_2u},\ \tilde{B}^*=\frac{c}{q}\left[\frac{\lambda_1k_1\beta_1}{d_1c(a_1+\delta)+\beta_1ua_1}+\frac{\lambda_2k_2\beta_2}{d_2ca_2+a_2\beta_2u}-\frac{d}{c}\right]=\frac{d}{q}(R_1-1),$$

where

$$R_1 = \frac{1}{d}\left[\frac{\lambda_1 k_1 \beta_1}{d_1(a_1+\delta)+\beta_1 a_1 \frac{u}{c}} + \frac{\lambda_2 k_2 \beta_2}{d_2 a_2 + a_2 \beta_2 \frac{u}{c}}\right],$$

and R_1 is defined the immune response reproduction number [28]. Therefore, when $R_1 > 1$, we have $\tilde{B}^* > 0$, and model (18) has a immune-activated equilibrium $\tilde{E}^*$. Furthermore, $R_1 < R_0$ holds obviously, we obtain $\tilde{V}^{(1)} < \frac{u}{c}$ if $R_1 < 1 = h(\tilde{V}^{(1)})$ based on the expression of $\mathfrak{h}(V)$ and R_1.

Summarize above discussion into the following results.

Theorem 6. *The following statements are true for model* (18).
(i) If $R_0 < 1$, there is only the infection-free equilibrium $\tilde{E}_0 = (\frac{\lambda_1}{d_1}, 0, \frac{\lambda_2}{d_2}, 0, 0, 0)$, which is globally asymptotically stable;
(ii) If $R_1 < 1 < R_0$, there is a unique humoral immune-free equilibrium $\tilde{E}_1$=($\tilde{H}_1^{(1)}$, $\tilde{I}_1^{(1)}$, $\tilde{H}_2^{(1)}$, $\tilde{I}_2^{(1)}$, $\tilde{V}^{(1)}$, 0);
(iii) If $1 < R_1 < R_0$, there is a chronic-infection equilibrium $\tilde{E}^*$=($\tilde{H}_1^*$, $\tilde{I}_1^*$, $\tilde{H}_2^*$, $\tilde{I}_2^*$, $\tilde{V}^*$, $\tilde{B}^*$).

Since it has been proven in Theorem 3 that the infection-free steady state $E_0(x)$ is globally asymptotically stable for model (1) when $R_0 < 1$ in heterogeneous environment, we will omit the global stability of $\tilde{E}_0$ in homogeneous environment. For the globally asymptotic stability of $\tilde{E}_1$ and $\tilde{E}^*$ of model (18), we have the following theorems.

Theorem 7. *If $R_1 < 1 < R_0$ and $R_{01} < \frac{k_1\lambda_1 a_1 a_2}{\delta(k_1\lambda_1 a_2 + k_2\lambda_2 a_1)}$, the humoral immune-free equilibrium $\tilde{E}_1$ of model* (18) *is globally asymptotically stable in $\overset{\circ}{\mathbb{L}}$, where $\overset{\circ}{\mathbb{L}}$ is the interior of $\mathbb{L}$.*

Proof. For convenience, define the equation

$$G(\zeta) = \zeta - 1 - \ln\zeta,$$

$G(\zeta) \geq 0$ for any $\zeta > 0$, and $G(\zeta) = 0$ if and only if $\zeta = 1$. Define a Lyapunov functional $\hbar_2$ as follow:

$$\begin{aligned}\hbar_2(t) = \int_\Omega \Bigg\{ &\frac{k_1}{a_1+\delta}\left[\tilde{H}_1^{(1)} G\left(\frac{H_1}{\tilde{H}_1^{(1)}}\right) + \tilde{I}_1^{(1)} G\left(\frac{I_1}{\tilde{I}_1^{(1)}}\right)\right] + \frac{k_2}{a_2}\left[\tilde{H}_2^{(1)} G\left(\frac{H_2}{\tilde{H}_2^{(1)}}\right) + \tilde{I}_2^{(1)} G\left(\frac{I_2}{\tilde{I}_2^{(1)}}\right)\right] \\ &+ \frac{q}{c}B + \tilde{V}^{(1)} G\left(\frac{V}{\tilde{V}_1^{(1)}}\right) + \frac{\delta}{2(a_1+d_1)\tilde{H}_1^{(1)}}\left[(H_1 - \tilde{H}_1^{(1)}) + (I_1 - \tilde{I}_1^{(1)})\right]^2 \frac{k_1}{a_1+\delta}\Bigg\} dx.\end{aligned}$$

We take the derivative of $\hbar_2$ on both sides along with any positive solutions of model (18), combining the boundary conditions and Divergence Theorem [8], then

$$\begin{aligned}\frac{d\hbar_2(t)}{dt} \leq \int_\Omega \Bigg\{ &\frac{k_1\tilde{I}_1^{(1)}}{\beta_1\tilde{H}_1^{(1)}\tilde{V}^{(1)}}\Bigg[-\beta_1\tilde{H}_1^{(1)}\tilde{V}^{(1)}\left(\frac{\tilde{H}_1^{(1)}}{\tilde{H}_1^{(1)}} + \frac{I_1\tilde{V}^{(1)}}{\tilde{I}_1^{(1)}V} + \frac{H_1 V\tilde{I}_1^{(1)}}{\tilde{H}_1^{(1)}\tilde{V}^{(1)}I_1} - 3\right) \\ &- \frac{a_1\delta(I_1-\tilde{I}_1^{(1)})^2}{(d_1+a_1)\tilde{H}_1^{(1)}} - \frac{(H_1-\tilde{H}_1^{(1)})^2}{H_1\tilde{H}_1^{(1)}}\Bigg(d_1\tilde{H}_1^{(1)} - \delta\tilde{I}_1^{(1)} + \delta I_1 \\ &+ \frac{d_1\delta}{d_1+a_1}H_1\Bigg)\Bigg] + \frac{k_2\tilde{I}_2^{(1)}}{\beta_2\tilde{H}_2^{(1)}\tilde{V}^{(1)}}\Bigg[\frac{-d_2(H_2-\tilde{H}_2^{(1)})^2}{H_2} \\ &- \beta_2\tilde{H}_2^{(1)}\tilde{V}^{(1)}\left(\frac{\tilde{H}_2^{(1)}}{\tilde{H}_2^{(1)}} + \frac{I_2\tilde{V}^{(1)}}{\tilde{I}_2^{(1)}V} + \frac{H_2 V\tilde{I}_2^{(1)}}{\tilde{H}_2^{(1)}\tilde{V}^{(1)}I_2} - 3\right)\Bigg] + qB\tilde{V}^{(1)} - \frac{qu}{c}B\Bigg\} dx \\ = \int_\Omega \Bigg\{ &\frac{k_1\tilde{I}_1^{(1)}}{\beta_1\tilde{H}_1^{(1)}\tilde{V}^{(1)}}\Bigg[-\beta_1\tilde{H}_1^{(1)}\tilde{V}^{(1)}\left[G\left(\frac{\tilde{H}_1^{(1)}}{H_1}\right) + G\left(\frac{I_1\tilde{V}^{(1)}}{\tilde{I}_1^{(1)}V}\right) + G\left(\frac{H_1 V\tilde{I}_1^{(1)}}{\tilde{H}_1^{(1)}\tilde{V}^{(1)}I_1}\right)\right]\end{aligned}$$

$$
\begin{aligned}
&- \frac{(H_1-\tilde{H}_1^{(1)})^2}{H_1\tilde{H}_1^{(1)}}\Big(d_1\tilde{H}_1^{(1)} - \delta\tilde{I}_1^{(1)} + \delta I_1 + \frac{d_1\delta}{d_1+a_1}H_1\Big) - \frac{a_1\delta(I_1-\tilde{I}_1^{(1)})^2}{(d_1+a_1)\tilde{H}_1^{(1)}}\Big]\\
&- \frac{k_2\tilde{I}_2^{(1)}\beta_2\tilde{H}_2^{(1)}\tilde{V}^{(1)}}{\beta_2\tilde{H}_2^{(1)}\tilde{V}^{(1)}}\Big[G\Big(\frac{\tilde{H}_2^{(1)}}{H_2}\Big) + G\Big(\frac{I_2\tilde{V}^{(1)}}{\tilde{I}_2^{(1)}V}\Big) + G\Big(\frac{H_2V\tilde{I}_2^{(1)}}{\tilde{H}_2^{(1)}\tilde{V}^{(1)}I_2}\Big)\Big]\\
&- \frac{d_2(H_2-\tilde{H}_2^{(1)})^2}{H_2} + qB\Big(\tilde{V}^{(1)} - \frac{u}{c}\Big)\Big\}dx.
\end{aligned}
$$

Based on the previous discussion, we can infer that $\tilde{V}^{(1)} < \frac{u}{c}$ if $R_1 < 1 < R_0$. Further, $d_1\tilde{H}_1^{(1)} - \delta\tilde{I}_1^{(1)} > 0$ is equivalent to $d_1(a_1+\delta) > \delta\beta_1\tilde{V}^{(1)}$, hence we have $d_1(a_1+\delta) > \frac{\delta\beta_1}{d}\big(\frac{k_1\lambda_1}{a_1} + \frac{k_2\lambda_2}{a_2}\big)$ provided that $\tilde{V}^{(1)} \in \Big(0, \frac{1}{d}\big(\frac{k_1\lambda_1}{a_1} + \frac{k_2\lambda_2}{a_2}\big)\Big]$. Furthermore, we can calculate $d_1\tilde{H}_1^{(1)} - \delta\tilde{I}_1^{(1)} > 0$ if $R_{01} < \frac{k_1\lambda_1a_1a_2}{\delta(k_1\lambda_1a_2+k_2\lambda_2a_1)}$.

Therefore, we have $\frac{d\hbar_2(t)}{dt} \le 0$ when $R_{01} < \frac{k_1\lambda_1a_1a_2}{\delta(k_1\lambda_1a_2+k_2\lambda_2a_1)}$ holds, and $\frac{d\hbar_2(t)}{dt} = 0$ if and only if $H_1 = \tilde{H}_1^{(1)}$, $I_1 = \tilde{I}_1^{(1)}$, $H_2 = \tilde{H}_2^{(1)}$, $I_2 = \tilde{I}_2^{(1)}$, $V = \tilde{V}^{(1)}$ and $B = 0$. Therefore, by LaSalle's invariance principle, we can see that $\tilde{E}_1$ is globally asymptotically stable. □

Theorem 8. *If $R_0 > R_1 > 1$ and $R_{01} < \frac{k_1\beta_1\lambda_1c}{d\delta u}$, the chronic-infection equilibrium $\tilde{E}^*$ of model (18) is globally asymptotically stable in $\overset{\circ}{\mathbb{L}}$, and $\overset{\circ}{\mathbb{L}}$ is the interior of $\mathbb{L}$.*

Proof. Define the following Lyapunov functional

$$
\begin{aligned}
\hbar_3(t) = \int_\Omega \Big\{ &\frac{k_1}{a_1+\delta}\Big[\tilde{H}_1^*G\Big(\frac{H_1}{\tilde{H}_1^*}\Big) + \tilde{I}_1^*G\Big(\frac{I_1}{\tilde{I}_1^*}\Big)\Big] + \frac{k_2}{a_2}\Big[\tilde{H}_2^*G\Big(\frac{H_2}{\tilde{H}_2^*}\Big) + \tilde{I}_2^*G\Big(\frac{I_2}{\tilde{I}_2^*}\Big)\Big]\\
&+ \tilde{V}^*G\Big(\frac{V}{\tilde{V}_1^*}\Big) + \frac{q}{c}\tilde{B}^*G\Big(\frac{B}{\tilde{B}^*}\Big) + \frac{\delta}{2(a_1+d_1)\tilde{H}_1^*}\frac{k_1}{a_1+\delta}\big[(H_1-\tilde{H}_1^*) + (I_1-\tilde{I}_1^*)\big]^2\Big\}dx.
\end{aligned}
$$

By taking derivative of $\hbar_3(t)$ on both sides along with any positive solution of model (18) from Divergence Theorem [8], we have

$$
\begin{aligned}
\frac{d\hbar_3(t)}{dt} \le \int_\Omega \Big\{ &\frac{k_1}{a_1+\delta}\Big(1-\frac{\tilde{H}_1^*}{H_1}\Big)\Big[D_C\Delta H_1 + \beta_1\tilde{H}_1^*\tilde{V}^* - \beta_1H_1V - d_1(H_1-\tilde{H}_1^*) - \delta(I_1-\tilde{I}_1^*)\Big]\\
&+ \frac{k_1}{a_1+\delta}\Big(1-\frac{\tilde{I}_1^*}{I_1}\Big)\Big(D_C\Delta I_1 + \beta_1H_1V - \frac{\beta_1\tilde{H}_1^*\tilde{V}^*I_1}{\tilde{I}_1^*}\Big) + \Big(1-\frac{\tilde{V}^*}{V}\Big)\Big(D_V\Delta V + k_1I_1\\
&+ k_2I_2 + dV + qVB\Big) + \frac{k_2}{a_2}\Big(1-\frac{\tilde{H}_2^*}{H_2}\Big)\Big[D_C\Delta H_2 + \beta_2\tilde{H}_2^*\tilde{V}^* - \beta_1H_2V - d_2(H_2-\tilde{H}_2^*)\Big]\\
&+ \frac{k_2}{a_2}\Big(1-\frac{\tilde{I}_2^*}{I_2}\Big)\Big(D_C\Delta H_2 + \beta_1H_2V - \frac{\beta_1\tilde{H}_2^*\tilde{V}^*}{\tilde{I}_2^*I_2}V\Big) + \frac{q}{c}\Big(1-\frac{\tilde{B}^*}{B}\Big)\Big(D_B\Delta B + cBV - uB\Big)\\
&+ \frac{\delta}{(a_1+d_1)\tilde{H}_1^*}\frac{k_1\tilde{I}_1^*}{\beta_1\tilde{H}_1^*\tilde{V}^*}[(H_1-\tilde{H}_1^*) + (I_1-\tilde{I}_1^*)][-a_1(I_1-\tilde{I}_1^*) - d_1(H_1-\tilde{H}_1^*)]\Big\}dx\\
= \int_\Omega \Big\{ &\frac{k_1\tilde{I}_1^*}{\beta_1\tilde{H}_1^*\tilde{V}^*}\Big[- \frac{(H_1-\tilde{H}_1^*)^2}{H_1\tilde{H}_1^*}\Big(d_1\tilde{H}_1^* - \delta\tilde{I}_1^* + \delta I_1 + \frac{d_1\delta}{d_1+a_1}H_1\Big) - \frac{a_1\delta(I_1-\tilde{I}_1^*)^2}{(d_1+a_1)\tilde{H}_1^*}
\end{aligned}
$$

$$- \beta_1 \tilde{H}_1^* \tilde{V}^* \left[G\left(\frac{\tilde{H}_1^*}{H_1}\right) + G\left(\frac{I_1 \tilde{V}^*}{\tilde{I}_1^* V}\right) + G\left(\frac{H_1 V \tilde{I}_1^*}{\tilde{H}_1^* \tilde{V}^* I_1}\right) \right] + \frac{k_2 \tilde{I}_2^*}{\beta_2 \tilde{H}_2^* \tilde{V}^*} \left[- \frac{d_2 (H_2 - \tilde{H}_2^*)^2}{H_2} \right.$$
$$\left. - \beta_2 \tilde{H}_2^* \tilde{V}^* \left[G\left(\frac{\tilde{H}_2^*}{H_2}\right) + G\left(\frac{I_2 \tilde{V}^*}{\tilde{I}_2^* V}\right) + G\left(\frac{H_2 V \tilde{I}_2^*}{\tilde{H}_2^* \tilde{V}^* I_2}\right) \right] \right] \Bigg\} dx.$$

Therefore, when $d_1 \tilde{H}_1^* - \delta \tilde{I}_1^* > 0$, we have $\frac{d\hbar_3(t)}{dt} \leq 0$, and $\frac{d\hbar_3(t)}{dt} = 0$ if and only if $H_1 = \tilde{H}_1^*$, $I_1 = \tilde{I}_1^*$, $H_2 = \tilde{H}_2^*$, $I_2 = \tilde{I}_2^*$, $V = \tilde{V}^*$. Then, we derive from the sixth equation of model (18) that

$$0 = D_V \Delta V(x,t) + k_1 \tilde{I}_1^* + k_2 \tilde{I}_2^* - d\tilde{V}^* - q\tilde{V}^* B(x,t),$$

which yield $B(x,t) = \tilde{B}^*$. Thus, the maximum invariant set of $\frac{d\hbar_3(t)}{dt} = 0$ is $\tilde{E}^*$.

Further, we can calculate that $d_1 \tilde{H}_1^* - \delta \tilde{I}_1^* > 0$ is equivalent to $R_{01} < \frac{k_1 \beta_1 \lambda_1 c}{d\delta u}$. Therefore, based on the LaSalle's invariance principle [14], when $R_0 > R_1 > 1$ and $R_{01} < \frac{k_1 \beta_1 \lambda_1 c}{d\delta u}$ hold, the chronic-infection equilibrium $\tilde{E}^*$ of model (18) is globally asymptotically stable. This completes the proof of Theorem 8. □

5. Numerical simulations

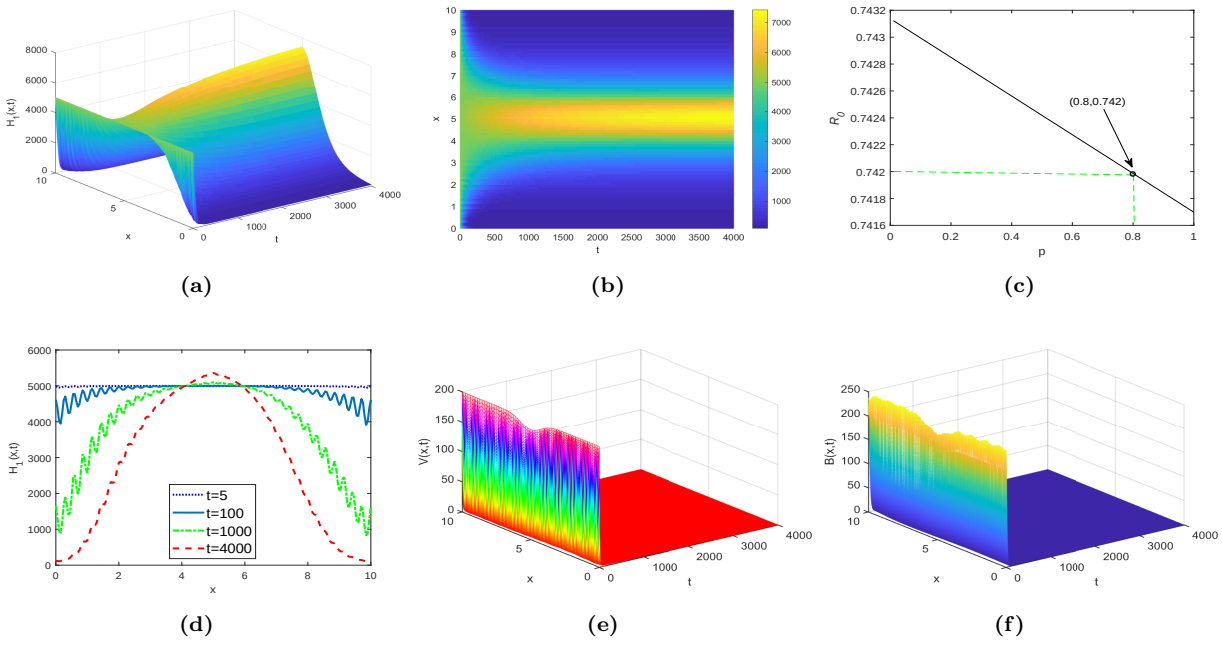


Figure 1. (a) Time variation of H_1 for model (1), (b) the projection on the t-x plane of (a), (c) the relationship between $\Re_0$ and p in $\beta_1(x) = 10^{-4}(1+pz(x))$, (d) the variation of H_1 at different times, (e-f) Time variation of the solution V and B for model (1).

Case 1: Firstly, we illustrate the Theorem 3, and take the following initial value:

$$\begin{aligned} &H_1(x,0) = 5000 - 18\mathbf{e};\ I_1(x,0) = 220 - 18\mathbf{e};\ V(x,0) = 200 - 18\mathbf{e}; \\ &H_2(x,0) = 5000 - 18\mathbf{e};\ I_2(x,0) = 220 - 18\mathbf{e};\ B(x,0) = 200 - 18\mathbf{e}. \end{aligned} \tag{19}$$

When the infection rates of HIV are $\beta_1(x) = \beta_2(x) = 10^{-4}(1 + 0.8z(x))$, and $k_2(x) = 7.11 \times 10^{-6}(1 + e(x) + 0.3z(x))$, we obtain that $\Re_0 = 0.7401 < 1$. From Fig.1 (a-e), it can be seen that the disease ultimately approaches extinction, which means the Theorem 3 is true. Besides, we

choose $\beta_1(x) = 10^{-4}(1 + pz(x))$, $(0 \le p \le 1)$, where p is the extent of spatially heterogeneity of infection rate. We can see that $\Re_0$ decreases with p (as shown in Fig.1 (f)).

TABLE 1. Values of parameters in model (1).

Parameter	Value	Parameter	Value
$\lambda_1(x)$	$3.21 \times \mathbf{z}(x)$	$a_1(x)$	$1.0 \times 10^{-2} \times \mathbf{z}(x)$
$\lambda_2(x)$	$3.21 \times \mathbf{z}(x)$	$a_2(x)$	$7.83 \times 10^{-4} \times \mathbf{z}(x)$
$c(x)$	$10^{-3} \times \mathbf{z}(x)$	$\delta(x)$	$3.11 \times 10^{-7} \times \mathbf{z}(x)$
$k_1(x)$	$10^{-8} \times \mathbf{z}(x)$	$d_1(x)$	$1/(3898exp\{\mid x-5 \mid\}) \times \mathbf{z}(x)$
$q(x)$	$10^{-3} \times \mathbf{z}(x)$	$d_2(x)$	$1/(3898exp\{\mid x-5 \mid\}) \times \mathbf{z}(x)$
$d(x)$	$8.92 \times 10^{-4} \times \mathbf{z}(x)$	$u(x)$	$7.83 \times 10^{-2} \times \mathbf{z}(x)$
D_C	1.25×10^{-4}	D_V	1.25×10^{-3}
D_B	1.25×10^{-2}		

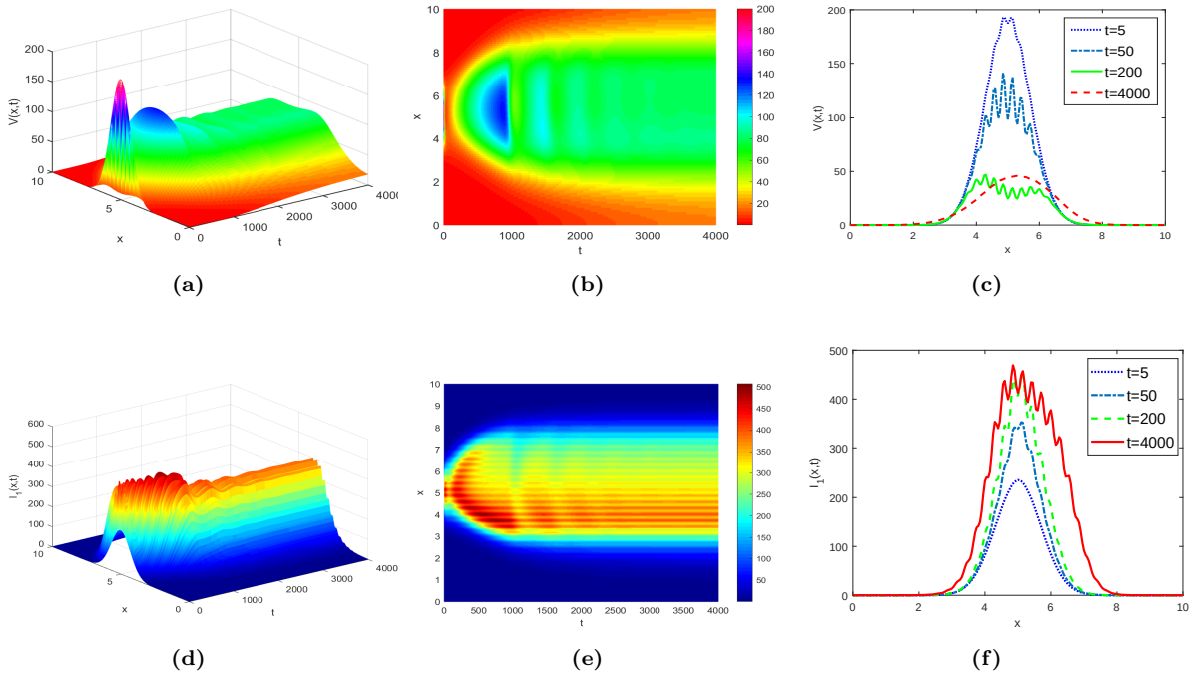


FIGURE 2. (a) Time variation of the solution V of model (14), (b) the projection on the t-x plane of (a), (c) the variation of V at different times, (d) time variation of the solution I_1 of model (14), (e) the projection on the t-x plane of (d), (f) the variation of I_1 at different times.

Case 2: Next, we will verify the Theorem 5. We take the following initial values:

$$\begin{aligned} &H_1(x,0) = 1000 - 80\mathbf{e};\ I_1(x,0) = 2200\mathbf{e};\ H_2(x,0) = 2999 - 80\mathbf{e};\\ &I_2(x,0) = 2500\mathbf{e};\ V(x,0) = 200\mathbf{e}. \end{aligned} \tag{20}$$

When we choose parameters $\beta_1(x) = \beta_2(x) = 1 \times 10^{-3}(1 + 0.8z(x))$, $k_2(x)$ =$7.11 \times 10^{-3}(1 + e(x) + 0.8z(x))$, and other parameters are shown in Table 1. It can be calculated that the basic reproduction number $\Re_0 = 3.042 > 1$, and the disease model as in (14) is uniformly persistent, (as shown in Fig.2 (a) and Fig.2 (d)), which confirms the Theorem 5. Besides, we choose parameter $\beta_1(x) = 1 \times 10^{-3}(1 + pz(x))$, $(0 \le p \le 1)$, similarly, p is the extent of spatial heterogenicity, and $\Re_0$ increases with p (as shown in Fig.3 (a)). Furthermore, we select parameter $k_2(x)$ =$7.11 \times 10^{-3}(1 + e(x) + p_1 z(x))$, $(0 \le p_1 \le 1)$, and $\Re_0$ decreases with p_1 (as shown in

Fig.3 (b)). In addition, we also perform the numerical simulation of model (14) under different diffusion rates (as shown in Fig.3(c-d)). It can be seen that in the case of spatial heterogeneity, the diffusion rates of I_1 and V are inversely proportional to the fluctuations of their spatial distribution.

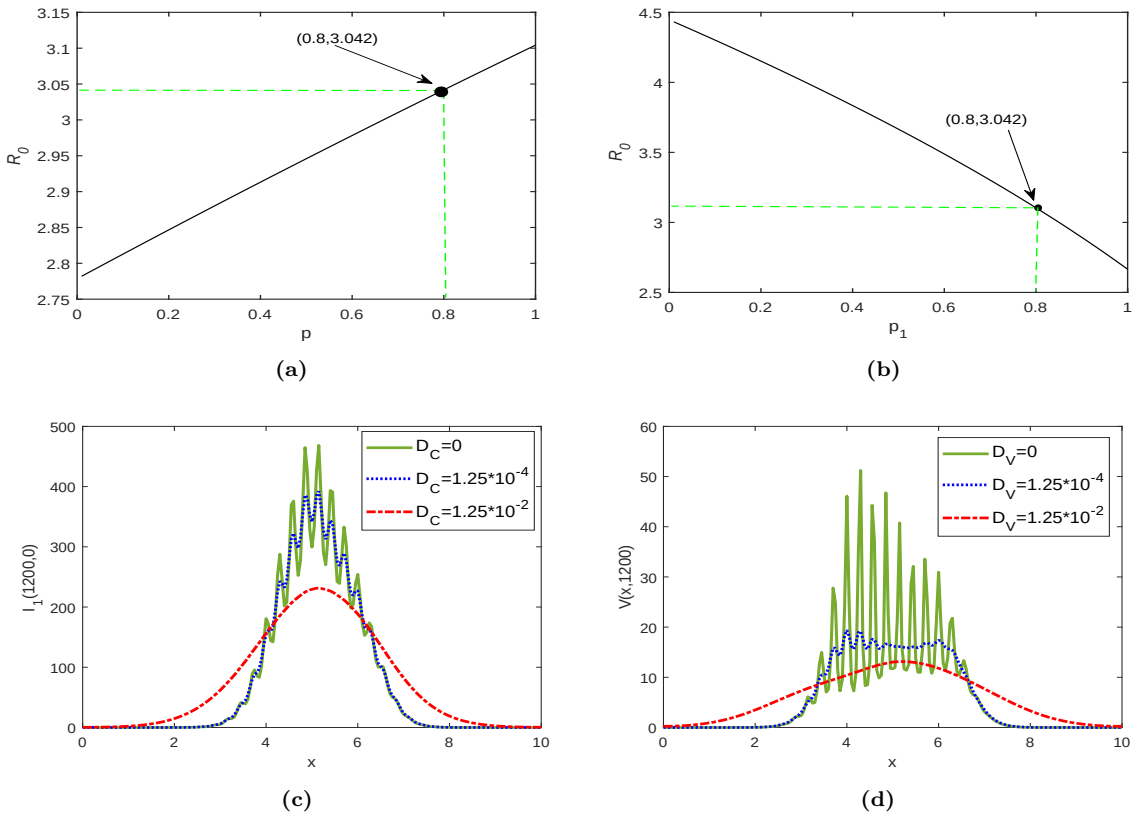
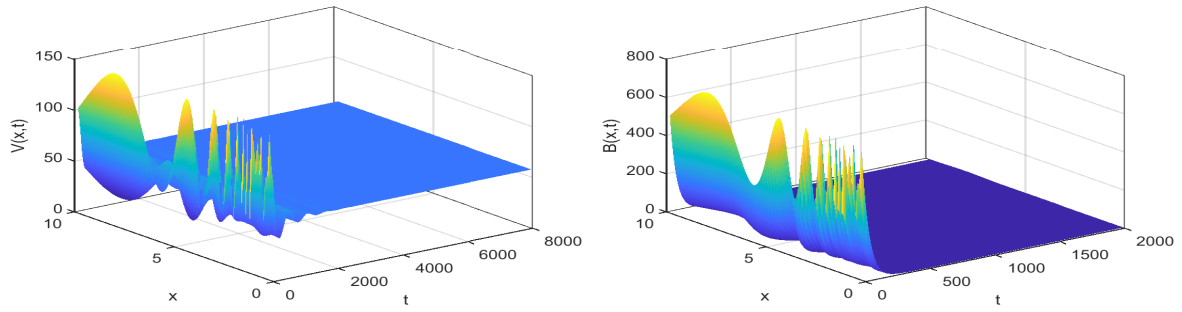


FIGURE 3. (a-b) The basic reproduction number $\Re_0$ of model (14) for $0 \leq p \leq 1$ with $\beta_1(x) = 1 \times 10^{-3}(1 + pz(x))$ and $k_2(x) = 7.11 \times 10^{-3}(1 + e(x) + p_1 z(x))$, respectively, (c) distribution of I_1 at $t = 1200$ for different D_C, (d) distribution of V at $t = 1250$ for different D_V.

For model (18), we choose parameters as:

$$\lambda_1 = \lambda_2 = 10;\ \beta_1 = 4 \times 10^{-4};\ \delta = 0.2;\ a_1 = a_2 = 0.1; k_2 = 0.005;\ u_2 = 0.06;\ d = 0.035;\ c = 3.5.$$

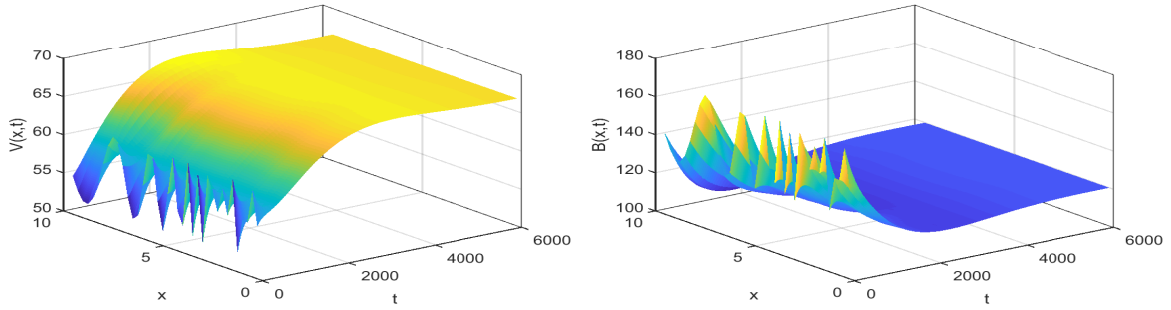
When $d_1 = d_2 = 0.05$; $\beta_2 = 3.51 \times 10^{-4}$; $k_1 = 0.01$; $q = 6 \times 10^{-6}$; $u = 0.02$, by calculation, we have $R_0 = 4.3162$, $R_1 = 0.8785$, the humoral immune-free equilibrium $\tilde{E}_1$ =(135.1351, 32.4324, 135.44, 32.28, 73.2, 0), $R_{01} = 0.0762 < \frac{k_1\lambda_1 a_1 a_2}{\delta(k_1\lambda_1 a_2 + k_2\lambda_2 a_1)} = 0.333$, it satisfies the condition in the Theorem 7. From Fig.4, we know that $\tilde{E}_1$ is globally asymptotically stable, which means the Theorem 7 is true.



(a) **(b)**

FIGURE 4. When $R_1 < 1 < R_0$ and $R_{01} < \frac{k_1\lambda_1 a_1 a_2}{\delta(k_1\lambda_1 a_2 + k_2\lambda_2 a_1)}$, the humoral immune-free equilibrium $\tilde{E}_1$ of model (18) is globally asymptotically stable, (a-b) represent the concentrations of V and B, respectively.

When $d_1 = d_2 = 0.01$; $\beta_2 = 6.51 \times 10^{-4}$; $k_1 = 0.005$; $q = 0.0006$; $u = 0.032$, by calculation, we have $R_0 = 2.83$, $R_1 = 1.12$, the chronic-infection equilibrium $\tilde{E}^* = (568.1, 9.391, 56.346, 620.9, 17.23, 67.9, 117.31)$, $R_{01} = 0.19 < \frac{k_1\beta_1\lambda_1 c}{d\delta u} = 0.313$. From Fig.5, we know that $\tilde{E}^*$ is globally asymptotically stable, which means the Theorem 8 is true.



(a) **(b)**

FIGURE 5. When $R_1 = 3.011 > 1$, and $R_{01} < \frac{k_1\beta_1\lambda_1 c}{d\delta u}$, the chronic-infection equilibrium $\tilde{E}^*$ is globally asymptotically stable, (a-b) represent the concentrations of V and B, respectively.

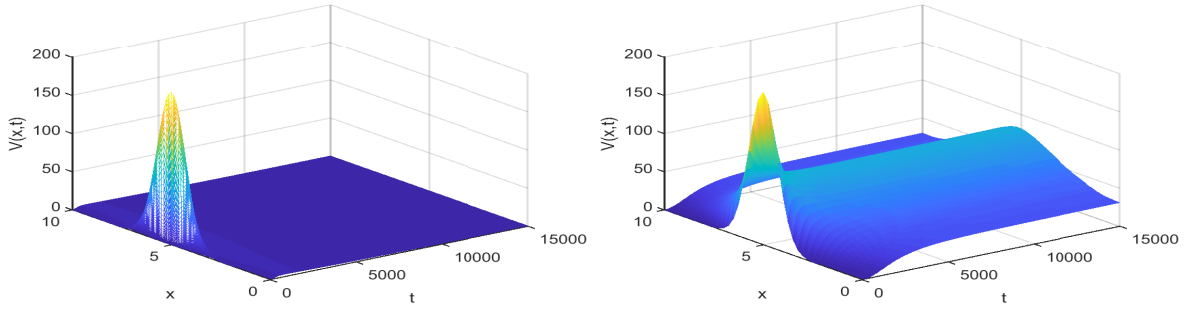
When model (1) degenerates into the model (14) with $B = 0$, and we take the values of parameters as follows:

$$\beta_1(x) = 8.94 \times 10^{-6} \times (1 + 0.8z(x));\ \beta_2(x) = 7.56 \times 10^{-6} \times (1 + 0.8z(x));\ c(x) = 10^{-2} \times \mathbf{z}(x);$$
$$a_1(x) = a_2(x) = 3 \times 10^{-3} \times \mathbf{z}(x);\ k_1(x) = 1.8 \times 10^{-4} \times \mathbf{z}(x);\ k_2(x) = 7.11 \times 10^{-4} \times \mathbf{z}(x);$$
$$d(x) = 5 \times 10^{-4} \times \mathbf{z}(x);\ q(x) = 8 \times 10^{-4} \times \mathbf{z}(x);\ \delta(x) = 3.5 \times 10^{-3} \times \mathbf{z}(x),$$

other parameters are the same as those in Table 1, we further take the initial values as:

$$\begin{aligned} H_1(x,0) &= 500 - 18\mathbf{e};\ I_1(x,0) = 220\mathbf{e};\ V(x,0) = 200\mathbf{e}; \\ H_2(x,0) &= 1000 - 18\mathbf{e};\ I_2(x,0) = 250\mathbf{e};\ B(x,0) = 200\mathbf{e}. \end{aligned} \tag{21}$$

We can see that the disease of model (1) is extinct (as shown in Fig.6(a)), however, the disease of model (14) is uniformly persistent (as shown in Fig.6(b)).



(a) **(b)**

FIGURE 6. (a-b) Time variation of the solution V of model (1) and model (14), respectively.

Furthermore, we also simulate the solutions of model (1) when the HIV only infects T cells. We take the same parameters and initial value as those in the case 2, where $H_2 = I_2 = 0$ in model (1). So, model (1) can be transformed into the following subsystem:

$$\begin{cases} \dfrac{\partial H_1(x,t)}{\partial t} = D_C \Delta H_1 + \lambda_1(x) - d_1(x) H_1 - \beta_1(x) H_1 V + \delta(x) I_1, \\ \dfrac{\partial I_1(x,t)}{\partial t} = D_C \Delta I_1 + \beta_1(x) H_1 V - (\delta(x) + a_1(x)) I_1, \ x \in \Omega, \\ \dfrac{\partial V(x,t)}{\partial t} = D_V \Delta V + k_1(x) I_1 - d(x) V - q(x) V B, \\ \dfrac{\partial B(x,t)}{\partial t} = D_B \Delta B + c(x) V B - u(x) B, \end{cases} \tag{22}$$

with the homogeneous Neumann boundary conditions

$$\frac{\partial H_1}{\partial \vec{n}} = \frac{\partial I_1}{\partial \vec{n}} = \frac{\partial V}{\partial \vec{n}} = \frac{\partial B}{\partial \vec{n}} = 0, \ x \in \partial\Omega.$$

By calculation, the basic reproduction number $R_0 = 0.7493$, meanwhile, from Fig.7 (a) we can see that the virus in model (22) ultimately tends to extinction. We choose parameter $\beta_1(x) = 1 \times 10^{-3}(1 + pz(x))$ where $0 \le p \le 1$. Similarly, we can see from Fig.7 (b) that R_0 increases with the extent of spatially heterogeneity of infection rate $\beta_1(x)$. This means that if we only consider the infection of T cells by HIV and ignore the infection of macrophages, it will underestimate the degree of infection.

In addition, we also explore the impact of diffusion on the dynamics of model (1) with the following parameters values:

$$\begin{aligned} &\lambda_1(x) = \lambda_2(x) = 3.25 \times \mathbf{z}(x); \ \delta(x) = 3.11 \times 10^{-6} \times \mathbf{z}(x); \ a_1(x) = 4 \times 10^{-2} \times \mathbf{z}(x); \\ &\beta_1(x) = 10^{-4} \times (1 + 0.8z(x)); \ \beta_2(x) = 2 \times 10^{-5} \times (1 + 0.8z(x)); \ a_2(x) = 10^{-2} \times \mathbf{z}(x); \\ &k_1(x) = 10^{-6} \times \mathbf{z}(x); \ k_2(x) = 10^{-4} \times \mathbf{z}(x); \ d(x) = 8.92 \times 10^{-3} \times \mathbf{z}(x); \\ &q(x) = 10^{-4} \times \mathbf{z}(x); \ c(x) = 3 \times 10^{-2} \times \mathbf{z}(x); \ u(x) = 7.83 \times 10^{-2} \times \mathbf{z}(x). \end{aligned}$$

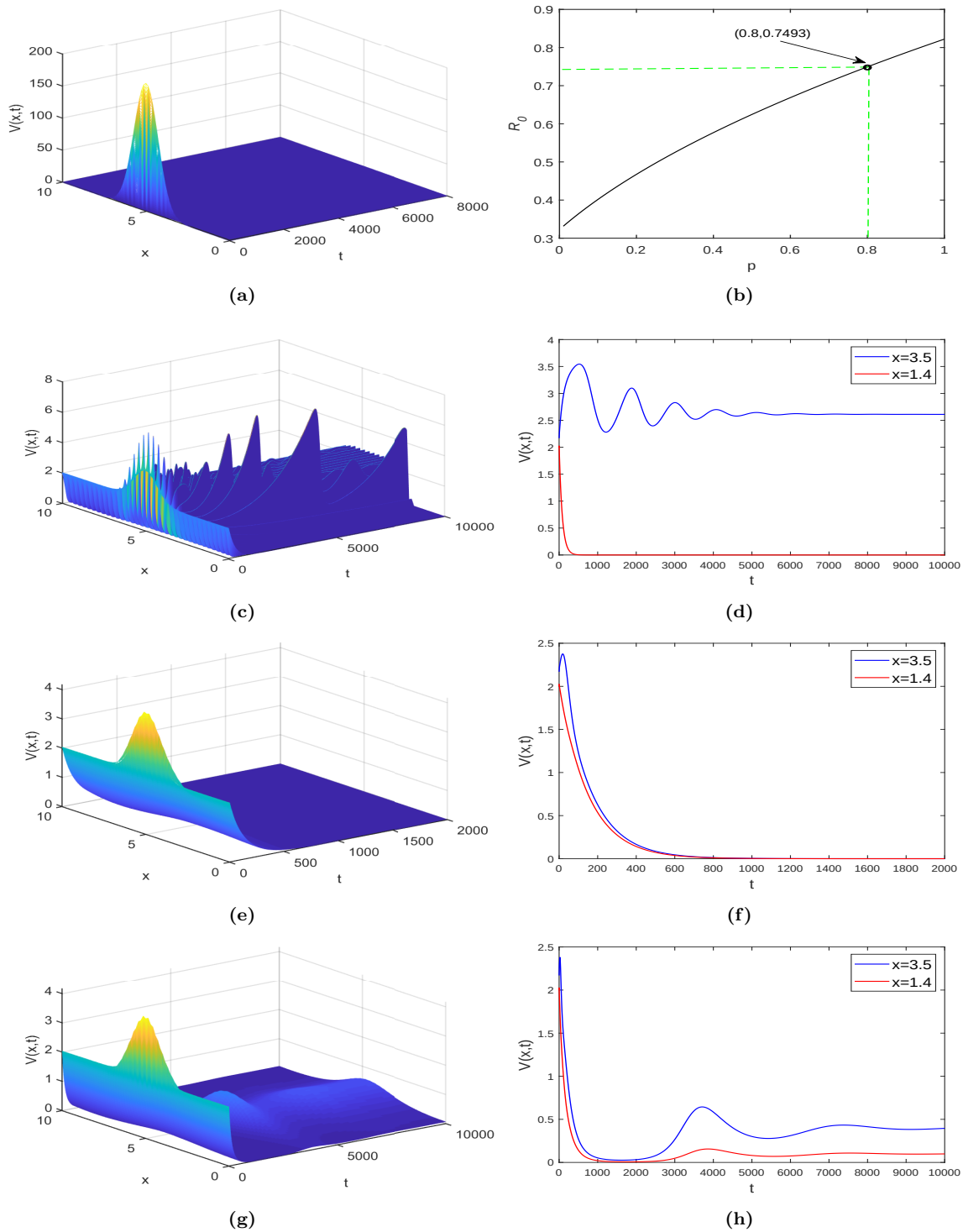


FIGURE 7. (a) Time variation of the solution V of model (22), (b) the basic reproduction number $\Re_0$ of model (22) for $0 \leq p \leq 1$ with $\beta_1(x) = 1 \times 10^{-3}(1 + pz(x))$, (c-h) are the time variation of V for model (1) at different diffusion rates, (c) $D_C = D_V = D_B = 0$; (e) $D_C = D_B = D_V = 1.25 \times 10^{-2}$; (g) $D_C = 1.25 \times 10^{-8}$, $D_V = 1.25 \times 10^{-2}$, $D_B = 1.25 \times 10^{-6}$; (d), (f) and (h) are the variation of of (c), (e) and (g) at different locations, respectively.

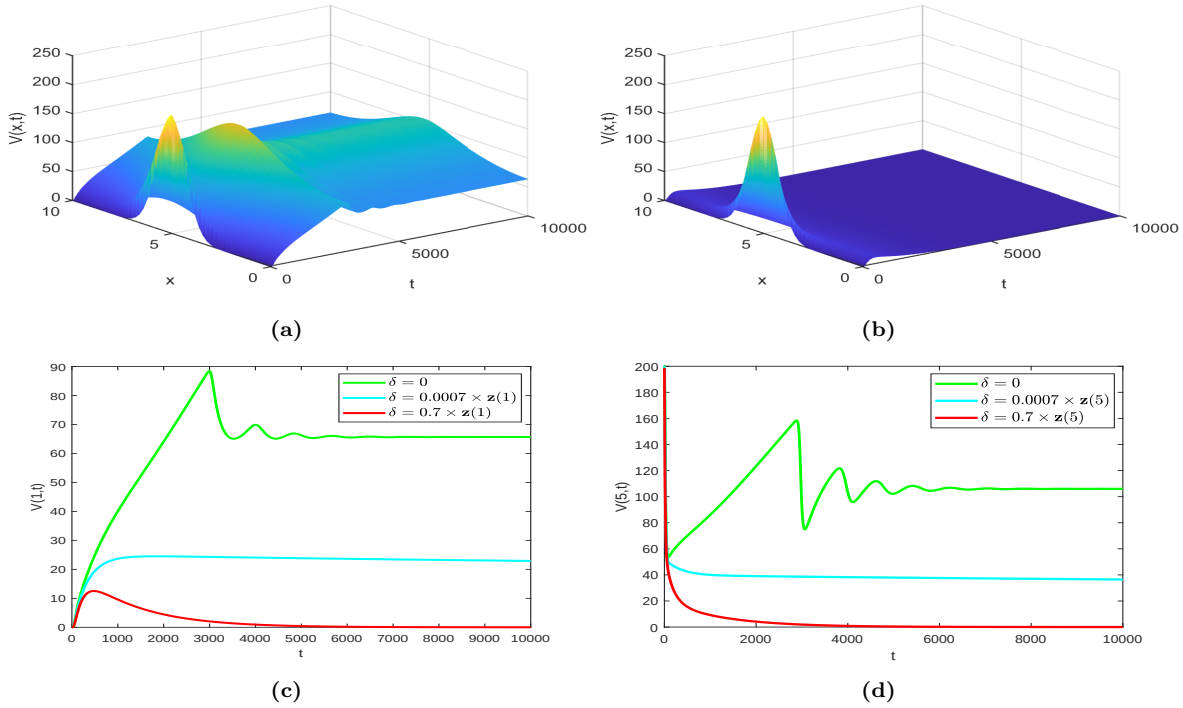


FIGURE 8. (a-b) Time variation of the solution V of model (3) when $\delta = 0$ and $\delta = 0.7 \times \mathbf{z}(x)$, respectively. (c) The variation of $V(1,t)$ when $\delta = 0$, $\delta = 0.0007 \times \mathbf{z}(1)$ and $\delta = 0.7 \times \mathbf{z}(1)$. (d) The variation of $V(5,t)$ when $\delta = 0$, $\delta = 0.0007 \times \mathbf{z}(5)$ and $\delta = 0.7 \times \mathbf{z}(5)$.

When $D_C = D_V = D_B = 0$, we find that the disease is persistent and extinct respectively when $x = 3.5$ and $x = 1.4$ from the Fig.7 (c) and (d). When $D_C = D_B = D_V = 1.25 \times 10^{-2}$, the disease is extinct at all positions (as shown in Fig.7 (e)). When $D_C = 1.25 \times 10^{-8}$, $D_V = 1.25 \times 10^{-2}$, $D_B = 1.25 \times 10^{-6}$, the disease is persistent at all positions (as shown in Fig.7 (g)). Therefore, it can be inferred that the disease could be extinct in some positions of space, but persist in some other positions if there is no diffusion. However, when the diffussion rate of virus is much higher than that of cells, the states of disease at some position could change from extinction to persistence, vice versa.

Next, we will investigate the impact of recovery rate δ on disease, and take the values of parameters as follows:

$$\beta_1(x) = 9 \times 10^{-9} \times (1 + 0.8z(x)); \ \beta_2(x) = 2 \times 10^{-5} \times (1 + 0.8z(x));$$
$$c(x) = 3 \times 10^{-2} \times \mathbf{z}(x); \ q(x) = 10^{-4} \times \mathbf{z}(x); \ k_1(x) = 10^{-6} \times \mathbf{z}(x); \ k_2(x) = 10^{-4} \times \mathbf{z}(x),$$

other parameters are the same as those in Table 1, with the initial values as (21). When recovery rate $\delta = 0$, we can see that the disease is persistent in all positions (as shown in Fig.8(a)). When $\delta = 0.7 \times \mathbf{z}(x)$, we can see that the disease is extinct in all positions (as shown in Fig.8(b)). In order to more clearly illustrate the changes in viral load in the body under different recovery rates, we take the time series graphs of Fig.8 (a-b) at $x = 1$ and $x = 5$ when $\delta = 0$, $\delta = 0.0007 \times \mathbf{z}(x)$, $\delta = 0.7 \times \mathbf{z}(x)$ (as shown in Fig.8 (c-d)). If resting infected $CD4^+$ T cells could revert to susceptible cells, the viral load in the patient's body would decrease compared to the case of recovery rate $\delta = 0$. Furthermore, the virus in the patient's body can be ultimately eliminated, when the recovery rate of $CD4^+$ T cells increases to a certain extent. It indicates that improving the recovery rate of $CD4^+$ T cells in clinical practice may be a breakthrough for disease treatment and patient rehabilitation.

6. Discussion

In this paper, a reaction-diffusion HIV coinfection model between $CD4^+$ T cells and macrophages incorporating humoral immunity and recovery of infected $CD4^+$ T cell is proposed under the heterogenous environment, the basic reproduction number $\Re_0$ is obtained in the form of operators. When $\Re_0 < 1$, the globally asymptotic stability of infection-free steady state E_0 is proved. We also obtain that the uniform persistence of disease in the absence of immunity when $\Re_0 > 1$. Specifically, criteria on the existence and globally asymptotic stability of immune-free infection equilibrium are obtained when $1 < R_0$ in the case of homogenous model. Furthermore, the immune response reproduction number R_1 is defined by which criteria on the existence and globally asymptotic stability of chronic-infection equilibrium are established when $1 < R_1 < R_0$. Finally, the theoretical results are demonstrated through numerical simulations.

We find that the basic reproduction number $\Re_0$ is not only dependent on the diffusion rates of $CD4^+$ T cells and macrophages, as well as virus and B cell, but also depends on the degree of heterogeneity of environments.

Moreover, diffusion rate of cells is inversely proportional to the oscillation amplitude of the spatial distribution of viruses in human body, i.e., the increase in the transmission rate of virus in some certain location within the body would promote rapid infection of cells by the virus, ultimately lends to the extensive persistence of disease. In addition, we can also see that the diffusion rates could change the dynamic behavior of model (1) at different positions of spatial distribution, which means that the diffusion of virus and cells is significant in disease spread.

In a word, it would greatly underestimate the scale of virus load within human body if we only consider the HIV infection of $CD4^+$ T cells, HIV coinfection of $CD4^+$ T cells and macrophages are both important to fully understand the HIV spread dynamics.

Acknowledgments

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