



Research article

A new general age-structured HIV model with two routes of infection, ART, and humoral immunity

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Abstract: In this paper, a new general age-structured human immunodeficiency virus (HIV) model with two routes of infection, antiretroviral therapy, and humoral immunity was proposed, different from common age-structured models due to the consideration of dominant activation of latently infected cells into infected cells rather than in the boundary condition. First, the well-posedness of the model solutions was given. Second, considering the dominant activation, we discussed the existence of immune inactivation equilibrium E_1 and immune activation equilibrium E^* in two special cases. Then, the global stability of the disease-free equilibrium E_0 was analyzed by constructing appropriate Lyapunov functions. Finally, the global behavior of the model with a saturated functional response was further investigated through numerical simulations, and the role of antiretroviral therapy in slowing down HIV transmission in the body was analyzed.

Keywords: age-structured HIV model; two routes of infection; ART; humoral immunity

1. Introduction

Human immunodeficiency virus (HIV) continues to pose one of the most serious public health threats worldwide, despite decades of intense research and intervention efforts. According to the Joint United Nations Programme on HIV and acquired immune deficiency syndrome (AIDS), an estimated 40.9 million people were living with HIV in 2025, with 1.2 million new infections and 570,000 AIDS-related deaths recorded in that year alone [1]. This persistent burden is largely attributable to the highly complex transmission mechanisms of HIV within the human body, including both conventional virus-to-cell (VTC) infection and cell-to-cell (CTC) transmission. In VTC infection, the virus replicates within cells and produces viral particles, which are released into the

extracellular environment and subsequently infect nearby healthy CD4⁺ T cells; this is the classic pathway of HIV infection. In contrast, CTC transmission enables the direct transfer of virus particles between cells via the formation of virological synapses, allowing infected cells to directly infect healthy T cells [2]. Several researchers have also investigated the mechanism of intercellular infection from a virological perspective, specifically focusing on the transfer of viral particles from infected to uninfected cells [3–5]. For example, Dimitrov et al. [3] found that the infectivity constant is a key parameter affecting the kinetics of HIV infection, and that HIV is more infectious than cell-free viruses during cell-to-cell transmission. In [5], Signal et al. concluded that cell-to-cell transmission of HIV indeed reduces the efficacy of antiretroviral therapy, because cell-to-cell infection induces multiple infections of target cells, thereby reducing susceptibility to antiretroviral drugs. Therefore, the CTC transmission mechanism plays an important role in HIV infection. Over time, both VTC infection and CTC transmission eventually lead to AIDS. Concurrent with these cellular infection pathways, the host also mounts a humoral immune response against HIV. Specifically, B cells become activated and secrete antibodies that neutralize viral particles and suppress viral replication. A large number of studies have shown that humoral immunity plays an important auxiliary role in controlling the process of HIV infection [6–8]. For instance, Luo et al. [9] incorporated humoral immunity into a viral infection model and systematically analyzed its impact on viral dynamics. These findings underscore that humoral immunity is an integral component of the host's anti-HIV defense and therefore warrants inclusion in mathematical models of HIV infection.

Additionally, as science and technology advance and researchers deepen their understanding of HIV, an increasing variety of antiretroviral drugs are used to treat HIV infection, such as reverse transcriptase inhibitors [10], integrase inhibitors, protease inhibitors, and entry/fusion inhibitors [11, 12]. At the end of December 2023, 30.7 million [27–31.9 million] people were accessing antiretroviral therapy, up from 7.7 million [6.7–8 million] in 2010 [1]. In addition, because age structure can effectively characterize the process of viral particle production, a key factor in the spread of infectious diseases, researchers have incorporated age structure into their models. For example, Nelson et al. [13] and Huang et al. [14] investigated age-structured HIV infection models by treating age as a continuous variable, noting that the mortality rate of infected cells and the rate of viral production depend on the age at which the cells become infected. In [15], an age-structured model of HIV-1 combination antiretroviral therapy was considered, modeled as follows

$$\begin{cases} \frac{dU_T(t)}{dt} = \lambda - dU_T(t) - \kappa(1 - \zeta_E)U_T(t)U_{V1}(t), \\ \frac{\partial r(a, t)}{\partial t} + \frac{\partial r(a, t)}{\partial a} = -\mu_r(a)r(a, t), \\ \frac{dU_{V1}(t)}{dt} = \int_0^\infty (1 - \zeta_P)(1 - \vartheta(a))\theta(a)r(a, t)da - cU_{V1}(t), \\ \frac{dU_{V2}(t)}{dt} = \int_0^\infty \zeta_P(1 - \vartheta(a))\theta(a)r(a, t)da - cU_{V2}(t), \\ r(0, t) = \kappa(1 - \zeta_E)U_T(t)U_{V1}(t), \end{cases} \quad (1.1)$$

where Rong et al. [15] performed a detailed stability analysis of model (1.1), and compared the effects of different antiretroviral drugs combinations on viral dynamics.

In addition to the complex process of HIV infection described above, in recent years, some researchers have found that there is a period of latent infection in T cells [16], during which healthy

cells can be infected [17]. Moreover, during the latent period, there is a dominant activation process whereby latently infected cells convert to productively infected cells [18, 19]. This phenomenon in the complex transmission process has attracted the attention of many researchers. Therefore, to address this issue, researchers have established some models and achieved further results. For example, Kumar and Abbas [19] considered an age-structured HIV model with VTC infection and dominant activation, and discussed the global asymptotic stability of the disease-free equilibrium and the effect of antiretroviral therapy. In [20], Alshorman et al. introduced latently infected cells in an age-structured HIV model and studied the dynamic behavior of the model. Besides, nonlinear incidence functions are often used to describe the viral infection process, explaining biological phenomena by capturing the nonlinear features of the infection process. Therefore, in recent years, researchers have introduced nonlinear incidence into the process of viral infection [21].

Although multiple factors (e.g., humoral immunity, nonlinear incidence, dominant activation of latently infected cells into infected cells, antiretroviral therapy, etc.) have been considered in the above models for the spread of HIV in the host, and good theoretical results have been obtained, there are very few models that consider the combined effects of the above factors at the same time. Therefore, based on the above discussion, in this paper, we propose a new age-structured HIV model that incorporates two routes of infection, antiretroviral therapy, a dominant activation rate α , and humoral immunity. The purpose of this paper is to study the kinetics of the model (2.1), including CTC transmission and the effect of antiretroviral therapy on HIV transmission. The paper is organized as follows. In Section 2, we formulate our model and provide some preliminary results on the well-posedness of its solutions. Section 3 determines the equilibria and defines the basic reproduction number R_0 . Global asymptotic stability of the disease-free equilibrium E_0 is given in Section 4. We give several special cases of the model (2.1) in Section 5. In Section 6, we perform numerical simulations to investigate the effects of CTC transmission and antiretroviral therapy. Section 7 presents the conclusions.

2. Model formulation and preliminary

In this section, taking into account latent infection, CTC transmission, humoral immunity, antiretroviral therapy, and nonlinear incidence functions, we develop an age-structured HIV model. The transfer diagram of the model is shown in Figure 1.

According to Figure 1, we have the following model:

$$\begin{cases} \frac{dU_X}{dt} = \lambda - dU_X(t) - \kappa(1 - \zeta_f)F(U_X(t))G(U_Y(t)) - U_X(t)\mathcal{J}_1(t) - U_X(t)\mathcal{J}_2(t), \\ \frac{\partial j(a, t)}{\partial t} + \frac{\partial j(a, t)}{\partial a} = -\mu_j(a)j(a, t) - \alpha j(a, t), \\ \frac{\partial r(a, t)}{\partial t} + \frac{\partial r(a, t)}{\partial a} = -\mu_r(a)r(a, t) + \alpha j(a, t), \\ \frac{dU_Y}{dt} = \int_0^\infty (1 - \zeta_p)(1 - \vartheta(a))\theta(a)r(a, t)da - uU_Y(t) - qU_Y(t)U_Z(t), \\ \frac{dU_Z}{dt} = kU_Y(t)U_Z(t) - \delta U_Z(t), \end{cases} \quad (2.1)$$

with the initial and boundary conditions

$$U_X(0) = U_{X0}, \quad j(a, 0) = j_0, \quad r(a, 0) = r_0, \quad U_Y(0) = U_{Y0}, \quad U_Z(0) = U_{Z0},$$

$$j(0, t) = \sigma(1 - \zeta_f)\kappa F(U_X(t))G(U_Y(t)),$$

$$r(0, t) = (1 - \sigma)(1 - \zeta_f)\kappa F(U_X(t))G(U_Y(t)) + U_X(t)\mathcal{J}_1(t) + U_X(t)\mathcal{J}_2(t),$$

where $U_X(t)$, $U_Y(t)$, $U_Z(t)$ represent the concentrations of uninfected cells, free viruses, and B cells at time t , respectively; and $j(a, t)$, $r(a, t)$ are the densities of latently infected and infected cells with infection age a at time t . Moreover, the interactions of uninfected cells with latently infected and infected cells are modeled by the terms $U_X(t)\mathcal{J}_1(t)$ and $U_X(t)\mathcal{J}_2(t)$, with $\mathcal{J}_1(t) = \int_0^\infty \omega_1(a)j(a, t)da$, $\mathcal{J}_2(t) = \int_0^\infty \omega_2(a)r(a, t)da$. The meanings of all other parameters are listed in Table 1.

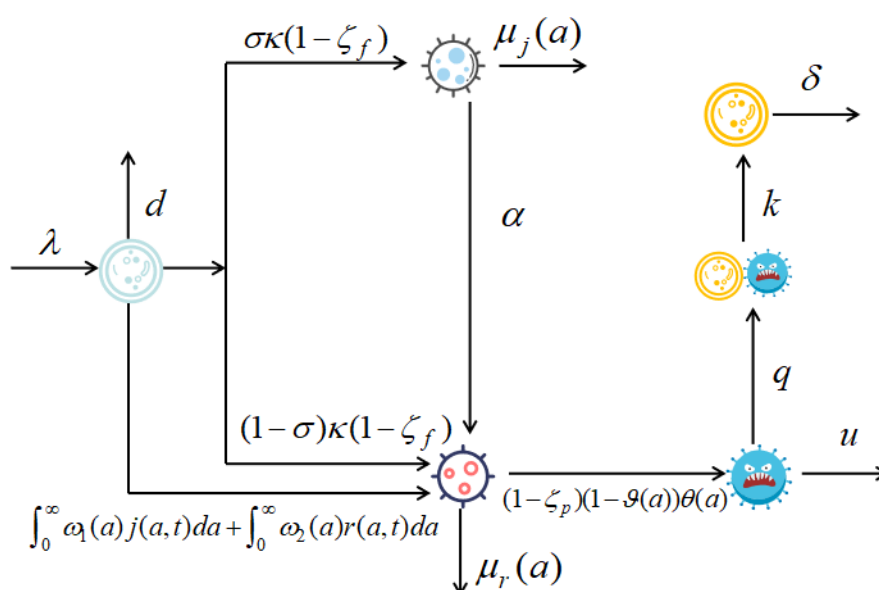


Figure 1. Transfer diagram of the model (2.1).

For the parameters and functions F and G in model (2.1), we make the following basic assumptions.

Assumption 1. (i) For sufficiently large a , $j(a, t) = 0$, $r(a, t) = 0$ holds; (ii) for any $a \geq 0$, there exists $u_2 \in (0, d]$ such that $\mu_j(a)$, $\mu_r(a) \geq \mu_2$; (iii) $\omega_1(\cdot)$, $\omega_2(\cdot)$, $\mu_j(\cdot)$, $\mu_r(\cdot)$, $\vartheta(\cdot)$, $\theta(\cdot) \in L_+^\infty(0, \infty)$. In addition, define $\bar{h} := \text{esssup}_{a \in [0, \infty)} h(a)$, for $h = \omega_1, \omega_2, \mu_j, \mu_r, \vartheta, \theta$.

Assumption 2. The functions F and G : $R_+ \rightarrow R_+$ satisfy: (i) $F(0) = G(0) = 0$, $F'(U_X) > 0$, $G'(U_Y) > 0$ and $G''(U_Y) \leq 0$; (ii) $\frac{F(U_X)}{U_X}$ and $\frac{G(U_Y)}{U_Y}$ are monotonically nonincreasing with respect to $U_X > 0$ and $U_Y > 0$, respectively; (iii) $F(U_X)$ is continuously differentiable and monotonically increasing with respect to U_X , for any constant $x > 0$, $M_x \triangleq \sup_{0 < U_X \leq x} \frac{F(U_X)}{U_X} < \infty$.

To solve the two partial differential equations for $j(a, t)$ and $r(a, t)$ in model (2.1), we use the method

of characteristics. First, we consider the equation for $j(a, t)$, which is given by

$$\begin{cases} \frac{\partial j(a, t)}{\partial a} + \frac{\partial j(a, t)}{\partial t} = -\mu_j(a)j(a, t) - \alpha j(a, t), \\ j(0, t) = \sigma(1 - \zeta_f)\kappa F(U_X(t))G(U_Y(t)). \end{cases}$$

Let $0 \leq a < t$ and assume that $t = s$, $a = 0$, $j = \sigma(1 - \zeta_f)\kappa F(U_X(t))G(U_Y(t))$. Characteristic curves are solutions of

$$\frac{dt(\tau, s)}{d\tau} = 1, \quad \frac{da(\tau, s)}{d\tau} = 1.$$

Therefore, along the characteristic line $t - a = \text{constant}$, the solution is given by

$$j(a, t) = \begin{cases} j(0, t - a)\Upsilon_j(a), & 0 \leq a < t, \\ j_0(a - t)\frac{\Upsilon_j(a)}{\Upsilon_j(a - t)}, & 0 < t \leq a. \end{cases}$$

Similarly, applying the method of characteristics to the differential equation in $r(a, t)$, we get

$$r(a, t) = \begin{cases} r(0, t - a)\Upsilon_r(a) + \int_t^{t+a} \frac{\Upsilon_r(a)}{\Upsilon_r(t - \iota)} \alpha j(t - t, t - a) d\iota, & 0 \leq a < t, \\ r_0(a - t)\frac{\Upsilon_r(a)}{\Upsilon_r(a - t)} + \int_a^{t+a} \frac{\Upsilon_r(a)}{\Upsilon_r(t - \iota)} \alpha j(t - t, t - a) d\iota, & 0 < t \leq a, \end{cases}$$

where $\Upsilon_j(a) = e^{-\int_0^a (\mu_j(\epsilon) + \alpha) d\epsilon}$, $\Upsilon_r(a) = e^{-\int_0^a \mu_r(\epsilon) d\epsilon}$. From assumption 1, $0 \leq \Upsilon_j(a), \Upsilon_r(a) \leq e^{-\mu_2 a}$.

Table 1. Description of model (2.1) parameters.

Symbol	Meanings
λ	recruitment rate of uninfected cells
d	natural death rate of uninfected cells
κ	infection rate of uninfected cell by infected virus
α	conversion of latently infected cells into infected cells with dominant activation rate
$\omega_1(a)$	infectivity of $j(a, t)$ with latent age a
$\omega_2(a)$	infectivity of $r(a, t)$ with infection age a
$\mu_j(a)$	infection age dependent per capita death rate of latently infected T cells
$\mu_r(a)$	infection age dependent per capita death rate of infected T cells
$\theta(a)$	age dependent viral production rate of an infected cell
u	natural death rate of free virus
q	removed rate by immune system
k	production rate of the antibody response
δ	natural death rate of B cells
ζ_f	efficacy of fusion, reverse transcriptase and integrase inhibitors
ζ_p	efficacy of protease inhibitors
$\vartheta(a)$	infection age dependent proportion of infected cells that have not completed reverse transcription
σ	proportion of cells converted to $j(a, t)$,

Theorem 1. For any $t \geq 0$, the solutions $(U_X(t), j(a, t), r(a, t), U_Y(t), U_Z(t))$ of model (2.1) with nonnegative initial and boundary conditions are nonnegative and bounded.

Proof. The nonnegativity of the solutions can be shown easily using a similar argument as in [4]. To gain the boundedness of solution of the model (2.1), we define $W_1(t) = U_X(t) + \int_0^\infty j(a, t)da + \int_0^\infty r(a, t)da$ and $W_2(t) = U_Y(t) + \frac{q}{k}U_Z(t)$, respectively; then taking the derivative of time t on both sides and combining with the principle of comparing differential equations, we have

$$\limsup_{t \rightarrow \infty} (U_X(t) + \int_0^\infty j(a, t)da + \int_0^\infty r(a, t)da) \leq \frac{\lambda}{\mu_0}, \quad \limsup_{t \rightarrow \infty} (U_Y(t) + \frac{q}{k}U_Z(t)) \leq \frac{\bar{\theta}\lambda(1 - \zeta_p)}{\mu_0\mu_1},$$

where $\mu_0 = \min\{d, \mu_2\}$ and $\mu_1 = \min\{u, \frac{q\delta}{k}\}$. $\square$

Therefore, model (2.1) has the following positive invariant set

$$\Omega = \left\{ (U_X, j, r, U_Y, U_Z) \in \Gamma; U_X(t) + \int_0^\infty j(a, t)da + \int_0^\infty r(a, t)da \leq \frac{\lambda}{\mu_0}, U_Y(t) + \frac{q}{k}U_Z(t) \leq \frac{\bar{\theta}\lambda(1 - \zeta_p)}{\mu_0\mu_1} \right\}.$$

By using a similar argument as in Section 3 of [22], we can obtain the existence of a global attractor for model (2.1).

Lemma 1. In $\mathcal{H}$, the solution semi-flow Υ has a global attractor.

3. Existence of equilibria

It is clear that model (2.1) always has a disease-free equilibrium $E_0 = (U_{X0}, 0, 0, 0, 0)$ with $U_{X0} = \frac{\lambda}{d}$. In addition, the presence of dominant activation rate α makes it more difficult to obtain for the immune inactivation equilibrium E_1 and the immune activation equilibrium E^* . Therefore, we will discuss the existence of E_1 and E^* from the following two cases.

For the immune inactivation equilibrium $E_1 = (U_{X1}, j_1(a), r_1(a), U_{Y1}, 0)$, we have

$$j_1(a) = j_1(0)\Upsilon_j(a), \quad r_1(a) = r_1(0)\Upsilon_r(a) + \int_0^a \alpha j_1(z)e^{\int_a^z \mu_r(s)ds} dz. \quad (3.1)$$

Because the expression for $r_1(a)$ is complex and the dominant activation rate α is involved, obtaining E_1 is challenging. In order to establish the existence of this immune inactivation equilibrium E_1 , we discuss the following two cases separately.

Case 1: $\omega_1(a) = 0$, $\omega_2(a) = 0$ (only VTC infection). From (3.1) it follows directly that

$$j_1(a) = j_1(0)\Upsilon_j(a), \quad r_1(a) = \frac{j_1(0)}{\sigma} \left[\int_0^a \alpha \sigma \Upsilon_j(z)e^{\int_a^z \mu_r(s)ds} dz + (1 - \sigma)\Upsilon_r(a) \right].$$

A straightforward calculation yields

$$U_{X1} = \frac{\lambda\sigma - j_1(0)}{d\sigma}, \quad U_{Y1} = \frac{j_1(0)(1 - \zeta_p)}{u\sigma} \int_0^\infty (1 - \vartheta(a))\theta(a) \left[\int_0^a \alpha \sigma \Upsilon_j(z)e^{\int_a^z \mu_r(s)ds} dz + (1 - \sigma)\Upsilon_r(a) \right] da.$$

The above expressions are all expressed in terms of $j_1(0)$; therefore, we only need to discuss the existence of $j_1(0)$. Substituting U_{X1} , $r_1(0)$, U_{Y1} into the expression for $j_1(0)$, we find that $j_1(0) \in [0, \lambda\sigma)$ and that it is a zero of $P_1(x)$ with

$$P_1(x) := x - \sigma(1 - \zeta_f)\kappa F\left(\frac{\lambda\sigma - x}{d\sigma}\right) \times G\left(\frac{x(1 - \zeta_p)}{u\sigma} \int_0^\infty (1 - \vartheta(a))\theta(a)\Phi(a)da\right),$$

where $\Phi(a) = \int_0^a \alpha\sigma\Upsilon_j(z)e^{\int_a^z \mu_r(s)ds}dz + (1 - \sigma)\Upsilon_r(a)$. Clearly, $P_1(0) = 0$ under the assumption that $F(\cdot)G(0) = 0$. Further computation yields $P'_1(0) = 1 - R_{01}$ with

$$R_{01} = \frac{\kappa(1 - \zeta_f)(1 - \zeta_p)}{u} \int_0^\infty (1 - \vartheta(a))\theta(a) \left[\int_0^a \alpha\sigma\Upsilon_j(z)e^{\int_a^z \mu_r(s)ds}dz + (1 - \sigma)\Upsilon_r(a) \right] da F(U_{X0})G'(0).$$

Hence, if $R_{01} > 1$, then $P_1(x)$ is negative for sufficiently small $x > 0$. Therefore, if $P_1(\lambda\sigma) > 0$, then there is a zero in $(0, \lambda\sigma)$ for P_1 which is the value of $j_1(0)$. Thus, when $R_{01} > 1$, there exists an immune inactivation equilibrium $E_1 = (U_{X1}, j_1(a), r_1(a), U_{Y1}, 0)$ for model (2.1).

Case 2: $\kappa = 0$ (only CTC transmission). From (3.1), a simple calculation yields

$$r_1(a) = r_1(0)\Upsilon_r(a), \quad j_1(a) = 0, \quad U_{X1} = \frac{\lambda - r_1(0)}{d}, \quad U_{Y1} = \frac{(1 - \zeta_p)r_1(0)}{u} \int_0^\infty (1 - \vartheta(a))\theta(a)\Upsilon_r(a)da,$$

where $r_1(0) = \frac{d}{\int_0^\infty \omega_2(a)\Upsilon_r(a)da}(R_{02} - 1)$.

We can define the threshold parameter as $R_{02} = \frac{1}{d} \int_0^\infty \omega_2(a)\Upsilon_r(a)da$. Thus, when $R_{02} > 1$, there exists an immune inactivation equilibrium $E_1 = (U_{X1}, j_1(a), r_1(a), U_{Y1}, 0)$ for model (2.1).

Now, in the presence of both VTC infection and CTC transmission, we define the threshold parameter as

$$R_0 = \max\{R_{01}, R_{02}\},$$

where R_{01} and R_{02} are the basic reproduction numbers for the cases with only VTC infection and only CTC transmission, respectively. Consequently, when $R_0 > 1$, model (2.1) admits at least one immune inactivation equilibrium $E_1 = (U_{X1}, j_1(a), r_1(a), U_{Y1}, 0)$.

Remark 1. We observe that R_0 depends on the viral production kernel $\theta(a)$ and the variance of infectivity $\omega_2(a)$ of infected cells. Hence, if $\omega_2(a)$ dominates $\theta(a)$, the disease-free steady state may remain unstable even when $R_0 < 1$.

For the immune activation equilibrium $E^* = (U_X^*, j^*(a), r^*(a), U_Y^*, U_Z^*)$, we have

$$j^*(a) = j^*(0)\Upsilon_j(a), \quad r^*(a) = r^*(0)\Upsilon_r(a) + \int_0^a \alpha j^*(z)e^{\int_a^z \mu_r(s)ds}dz. \quad (3.2)$$

Similarly, due to the complexity of the expression for $r^*(a)$ and the involvement of the dominant activation rate α , the equilibrium E^* is more difficult to obtain. Hence, we discuss its existence using the same method as for E_1 in the following two cases.

Case 1: $\omega_1(a) = 0$, $\omega_2(a) = 0$ (only VTC infection). From (3.2), a simple calculation yields

$$j^*(a) = j^*(0)\Upsilon_j(a), \quad U_X^* = \frac{\lambda\sigma - j^*(0)}{d\sigma}, \quad U_Y^* = \frac{\delta}{k},$$

$$r^*(a) = \frac{j^*(0)}{\sigma} \left[\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz + (1 - \sigma) \Upsilon_r(a) \right], \quad U_Z^* = \frac{u}{q} (R_a - 1),$$

where $R_a = \frac{j^*(0)k(1-\zeta_p)}{u\delta\sigma} \int_0^\infty (1 - \vartheta(a))\theta(a) \left[\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz + (1 - \sigma) \Upsilon_r(a) \right] da$.

Substituting U_X^* , $r^*(0)$, and U_Y^* into the expression for $j^*(0)$, we obtain that $j^*(0) \in [0, \lambda\sigma)$ is a zero of $P_2(y)$ with

$$P_2(y) := y - \sigma(1 - \zeta_f)\kappa F\left(\frac{\lambda\sigma - y}{d\sigma}\right)G\left(\frac{\delta}{k}\right).$$

Clearly, $P_2(0) < 0$, $P_2(\lambda\sigma) > 0$, and $P_2'(y) > 0$. Thus, there exists a zero of P_2 in $(0, \lambda\sigma)$, and this zero is exactly $j^*(0)$.

Hence, when $R_a > 1$, there exists an immune activation equilibrium $E^* = (U_X^*, j^*(a), r^*(a), U_Y^*, U_Z^*)$ for model (2.1).

Case 2: $\kappa = 0$ (only CTC transmission). From (3.2), by a simple calculation, we obtain

$$r^*(a) = r^*(0)\Upsilon_r(a), \quad j^*(a) = 0, \quad U_X^* = \frac{\lambda - r^*(0)}{d}, \quad U_Y^* = \frac{\delta}{k}, \quad U_Z^* = \frac{u}{q}(R_b - 1),$$

where $r^*(0) = \frac{d}{\int_0^\infty \omega_2(a)\Upsilon_r(a)da}(R_{02} - 1)$, $R_b = \frac{kd(1-\zeta_p) \int_0^\infty (1-\vartheta(a))\theta(a)\Upsilon_r(a)da}{u\delta \int_0^\infty \omega_2(a)\Upsilon_r(a)da}(R_{02} - 1)$. Hence, when $R_b > 1$, there exists an immune activation equilibrium $E^* = (U_X^*, j^*(a), r^*(a), U_Y^*, U_Z^*)$ for model (2.1).

Now, in the presence of both VTC infection and CTC transmission, we define the threshold parameter as

$$R_1 = \max \{R_a, R_b\}.$$

Here, R_a and R_b denote the immune activation reproduction numbers under only VTC infection and only CTC transmission, respectively. They measure the average number of antibody-producing cells generated by virus and infected cell during the entire infection course, respectively. A larger antibody production rate k enhances the humoral response and thus increases both R_a and R_b .

In summary, if $R_1 > 1$, there exists at least one immune activation equilibrium $E^* = (U_X^*, j^*(a), r^*(a), U_Y^*, U_Z^*)$ for model (2.1). Clinically, $R_1 > 1$ indicates that the host can mount a sufficient humoral immune response to establish a persistent antibody-mediated defense.

Remark 2. It can be seen that R_1 depends on the viral production kernel $\theta(a)$, the infectivity variance $\omega_2(a)$ of infected cells, and the antibody production rate k . Hence, if $\omega_2(a)$ dominates $\theta(a)$, the disease-free steady state may still be unstable even for $R_0 < 1$. Additionally, when k is sufficiently small such that $R_b < 1$, the immune activation equilibrium E^* may not exist.

4. Stability analysis

In this section, we assume that κ is arbitrarily small and u is sufficiently large so that $\kappa(1 - \zeta_f)U_{X0}M_{U_{X0}}G'(0) - Mu < 0$.

Theorem 2. If $R_0 < 1$, the disease-free equilibrium E_0 is globally asymptotically stable.

Proof. Define

$$L(t) = (U_X(t) - U_{X0} - U_{X0} \ln \frac{U_X(t)}{U_{X0}}) + M \int_0^\infty \phi(a)j(a, t)da + M \int_0^\infty \varphi(a)r(a, t)da + MU_Y(t) + M\frac{q}{k}U_Z(t),$$

then

$$\begin{aligned}
L'(t) &= (1 - \frac{U_{X0}}{U_X(t)})(\lambda - dU_X(t) - \kappa(1 - \zeta_f)F(U_X(t))G(U_Y(t)) - U_X(t) \int_0^\infty \omega_1(a)j(a, t)da \\
&\quad - U_X(t) \int_0^\infty \omega_2(a)r(a, t)da) + M \int_0^\infty \phi(a) \frac{\partial j(a, t)}{\partial t} da + M \int_0^\infty \varphi(a) \frac{\partial r(a, t)}{\partial t} da \\
&\quad + M(\int_0^\infty (1 - \zeta_p)(1 - \vartheta(a))\theta(a)r(a, t)da - uU_Y(t) - qU_Y(t)U_Z(t)) + M \frac{q}{k}(kU_Y(t)U_Z(t) - \delta U_Z(t)) \\
&\leq -\frac{d}{U_X}(U_X - U_{X0})^2 + (M\varphi(0) - 1)r(0, t) + (M\phi(0) - 1)j(0, t) + (\omega_1(1 - \zeta_f)U_{X0}M_{U_{X0}}G'(0) - Mu)U_Y \\
&\quad - M \frac{q\delta}{k}U_Z + M \int_0^\infty (\phi'(a) - \mu_j(a)\phi(a) - \alpha\phi(a) + \alpha\varphi(a) + \frac{U_{X0}}{M}\omega_1(a))j(a, t)da \\
&\quad + M \int_0^\infty (\varphi'(a) - \mu_r(a)\varphi(a) + (1 - \zeta_p)(1 - \vartheta(a))\theta(a) + \frac{U_{X0}}{M}\omega_2(a))r(a, t)da,
\end{aligned}$$

where

$$\begin{aligned}
\varphi(a) &= \int_a^\infty [\frac{U_{X0}}{M}\omega_2(s) + (1 - \zeta_p)(1 - \vartheta(s))\theta(s)]e^{-\int_a^s \mu_r(\tau)d\tau} ds, \\
\phi(a) &= \int_a^\infty [\frac{U_{X0}}{M}\omega_1(s) + \alpha\varphi(s)]e^{-\int_a^s (\alpha + \mu_j(\tau))d\tau} ds, \\
\phi'(a) - \mu_j(a)\phi(a) - \alpha\phi(a) + \alpha\varphi(a) + \frac{U_{X0}}{M}\omega_1(a) &= 0, \\
\varphi'(a) - \mu_r(a)\varphi(a) + (1 - \zeta_p)(1 - \vartheta(a))\theta(a) + \frac{U_{X0}}{M}\omega_2(a) &= 0, \\
M &= \max \left\{ \frac{(R_0 - R_{01})}{\int_0^\infty (1 - \zeta_p)(1 - \vartheta(s))\theta(s)\Upsilon_r(s)ds}, \frac{R_0}{\int_0^\infty (\mu_j(s)\phi(s) + \alpha\phi(s) - \phi'(s))\Upsilon_j(s)ds} \right\}.
\end{aligned}$$

Hence,

$$\begin{aligned}
L'(t) &\leq -\frac{d}{U_X}(U_X - U_{X0})^2 + (M\varphi(0) - 1)r(0, t) + (M\phi(0) - 1)j(0, t) \\
&\quad + (\kappa(1 - \zeta_f)U_{X0}M_{U_{X0}}G'(0) - Mu)U_Y - M \frac{q\delta}{k}U_Z.
\end{aligned}$$

Under $R_0 < 1$, it is easy to see that $M\varphi(0) < 1$, and $M\phi(0) < 1$. Hence, if $R_0 < 1$, then $L'(t) \leq 0$, and $L'(t) = 0$, if and only if, $U_X(t) = U_{X0}$, $j(a, t) = 0$, $r(a, t) = 0$, $U_Y(t) = 0$, $U_Z(t) = 0$. Therefore, by the Lyapunov-LaSalle invariance principle, the disease-free equilibrium E_0 is globally asymptotically stable when $R_0 < 1$. $\square$

Note that the proof of Theorem 2 relies on the technical assumptions that κ is sufficiently small and μ is sufficiently large, corresponding to low viral infectivity and rapid viral clearance, respectively. These conditions are not essential for stability but facilitate the construction of the Lyapunov function. Numerical simulations (Section 6) will show that E_0 remains stable for moderate values of κ and μ when $R_0 < 1$. Our future work will focus on relaxing these assumptions.

Remark 3. In the absence of CTC transmission, antiretroviral therapy, and humoral immunization, with $F(U_X(t))G(U_Y(t)) = U_X(t)U_Y(t)$, the model simplifies to that in [19]. Similarly, without humoral

immunity, antiretroviral therapy, and infection of healthy cells by latently infected cells, and with $F(U_X(t))G(U_Y(t)) = U_X(t)U_Y(t)$, the model reduces to that in [18]. Although different Lyapunov functions are chosen here, the same conclusion is reached: the disease-free equilibrium E_0 is globally asymptotically stable when $R_0 < 1$. Thus, our model is more general and comprehensive than those considered in [18, 19].

5. Some special cases

5.1. No CTC transmission and no antiretroviral therapy

In this section, we consider the case without CTC transmission and without antiretroviral therapy, i.e., $\omega_1(a) = \omega_2(a) = 0$, $\zeta_f = \zeta_p = \vartheta(a) = 0$, and $F(U_X(t))G(U_Y(t)) = U_X(t)U_Y(t)$. Then, model (2.1) degenerates to

$$\begin{cases} \frac{dU_X}{dt} = \lambda - dU_X(t) - \kappa U_X(t)U_Y(t), \\ \frac{\partial j(a,t)}{\partial t} + \frac{\partial j(a,t)}{\partial a} = -\mu_j(a)j(a,t) - \alpha j(a,t), \\ \frac{\partial r(a,t)}{\partial t} + \frac{\partial r(a,t)}{\partial a} = -\mu_r(a)r(a,t) + \alpha j(a,t), \\ \frac{dU_Y}{dt} = \int_0^\infty \theta(a)r(a,t)da - uU_Y(t) - qU_Y(t)U_Z(t), \\ \frac{dU_Z}{dt} = kU_Y(t)U_Z(t) - \delta U_Z(t), \end{cases} \quad (5.1)$$

with the initial and boundary conditions given by

$$\begin{aligned} U_X(0) &= U_{X0}, \quad j(a, 0) = j_0, \quad r(a, 0) = r_0, \quad U_Y(0) = U_{Y0}, \quad U_Z(0) = U_{Z0}, \\ j(0, t) &= \sigma \kappa U_X(t)U_Y(t), \quad r(0, t) = (1 - \sigma)\kappa U_X(t)U_Y(t), \end{aligned}$$

and applying the same steps as in Section 4 the model (5.1) possesses the following equilibria.

(i) The disease-free equilibrium $E_0 = (U_{X0}, j_0(a), r_0(a), U_{Y0}, U_{Z0}) = (\frac{\lambda}{d}, 0, 0, 0, 0)$, where the basic reproduction number

$$R_0 = \frac{\lambda \kappa}{du} \int_0^\infty \theta(a) \left[\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz + (1 - \sigma) \Upsilon_r(a) \right] da,$$

can be obtained as a special case of the basic reproduction number of model (2.1).

(ii) The immune inactivated equilibrium $E_1^1 = (U_{X1}^1, j_1^1(a), r_1^1(a), U_{Y1}^1, 0)$, where

$$\begin{aligned} U_{X1}^1 &= \frac{u}{\kappa \int_0^\infty \theta(a) \left[\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz + (1 - \sigma) \Upsilon_r(a) \right] da}, \quad j_1^1(a) = \sigma \kappa U_{X1}^1 U_{Y1}^1 \Upsilon_j(a), \\ r_1^1(a) &= \kappa U_{X1}^1 U_{Y1}^1 \left[\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz + (1 - \sigma) \Upsilon_r(a) \right], \quad U_{Y1}^1 = \frac{d}{\kappa} (R_0 - 1). \end{aligned}$$

(iii) The immune activated equilibrium $E^{1*} = (U_X^{1*}, j^{1*}(a), r^{1*}(a), U_Y^{1*}, U_Z^{1*})$.

Different from [19], model (5.1) also has an immune activation equilibrium E^{1*} , which is satisfies

$$\begin{cases} \lambda - dU_X^{1*} - \kappa U_X^{1*} U_Y^{1*} = 0, \\ \frac{dj^{1*}(a)}{da} = -\alpha j^{1*}(a) - \mu_j(a) j^{1*}(a), \\ \frac{dr^{1*}(a)}{da} = \alpha j^{1*}(a) - \mu_r(a) r^{1*}(a), \\ \int_0^\infty \theta(a) r^{1*}(a) da - u U_Y^{1*} - q U_Y^{1*} U_Z^{1*} = 0, \\ k U_Y^{1*} U_Z^{1*} - \delta U_Z^{1*} = 0, \\ j^{1*}(0) = \sigma \kappa U_X^{1*} U_Y^{1*}, r^{1*}(0) = (1 - \sigma) \kappa U_X^{1*} U_Y^{1*}. \end{cases}$$

By simple calculating, we have

$$\begin{aligned} j^{1*}(a) &= \sigma \kappa U_X^{1*} U_Y^{1*} \Upsilon_j(a), \quad U_X^{1*} = \frac{\lambda k}{dk + \kappa \delta}, \quad U_Y^{1*} = \frac{\delta}{k}, \\ r^{1*}(a) &= \kappa U_X^{1*} U_Y^{1*} \left[\int_0^\infty \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(\tau) d\tau} dz + (1 - \sigma) \Upsilon_r(a) \right], \quad Z^{1*} = \frac{u}{q} (R_1^1 - 1), \end{aligned}$$

where

$$R_1 = \frac{\kappa \lambda k}{(dk + \kappa \delta) u} \int_0^\infty \theta(a) \left[\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(\tau) d\tau} dz + (1 - \sigma) \Upsilon_r(a) \right] da.$$

Clearly, R_1 can similarly be deduced from the immune activation reproduction number in model (2.1). Therefore, an immune activation equilibrium E^{1*} exists when the immune activation reproduction number satisfies $R_1 > 1$.

We choose the Lyapunov function

$$\begin{aligned} L_1(t) &= (U_X(t) - U_{X0} - U_{X0} \ln \frac{U_X(t)}{U_{X0}}) + M \int_0^\infty \phi(a) j(a, t) da + M \int_0^\infty \varphi(a) r(a, t) da \\ &\quad + M U_Y(t) + M \frac{q}{k} U_Z(t), \end{aligned}$$

where

$$\begin{aligned} M &= \max \left\{ \frac{\lambda \kappa}{du} \left[\frac{\int_0^\infty \theta(a) \left(\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz + (1 - \sigma) \Upsilon_j(a) \right) da}{\int_0^\infty \theta(a) \Upsilon_r(a) da} \right], \right. \\ &\quad \left. \frac{\lambda \kappa \left[\int_0^\infty \theta(a) \left(\int_0^a \alpha \sigma \Upsilon_j(z) e^{\int_a^z \mu_r(s) ds} dz \right) da + (1 - \sigma) \int_0^\infty \theta(a) \Upsilon_r(a) da \right]}{du \alpha \int_0^\infty \varphi(s) \Upsilon_j(a) ds} \right\}, \\ \varphi(a) &= \int_a^\infty \theta(s) e^{-\int_a^s \mu_r(\tau) d\tau} ds, \quad \phi(a) = \int_a^\infty \alpha \varphi(s) e^{-\int_a^s (\alpha + \mu_j(\tau)) d\tau} ds, \\ \varphi'(a) &= \mu_r(a) \varphi(a) + \theta(a), \quad \phi'(a) = (\mu_j(a) + \alpha) \phi(a) - \alpha \varphi(a). \end{aligned}$$

Differentiating with respect to t yields

$$L_1' \leq -\frac{d}{U_X} (U_X - U_{X0})^2 + (M \varphi(0) - 1) r(0, t) + (M \phi(0) - 1) j(0, t) - M \phi(a) j(a, t) \big|_{a=\infty}$$

$$-M\varphi(a)r(a,t)|_{a=\infty} + (\kappa U_{X0} - Mu)U_Y - M\frac{q\delta}{k}U_Z.$$

Under the $R_0 < 1$, it's easy to see that

$$M\varphi(0) = M \int_0^\infty \theta(s)\Upsilon_r(s)ds < 1, \quad M\phi(0) = M \int_0^\infty \alpha\varphi(s)\Upsilon_j(s)ds < 1.$$

It can be shown that the uninfected equilibrium is globally asymptotically stable when $R_0 < 1$. Therefore, Theorem 2 holds for model (5.1).

Remark 4. When humoral immunity is neglected, the model simplifies to that in [19]. Despite employing different Lyapunov functions, we arrive at the identical conclusion: the disease-free equilibrium is globally asymptotically stable provided $R_0 < 1$. Hence, our model is more general and comprehensive than that considered in [19].

5.2. No latently infected T cells

If there are no latently infected T cells, i.e., $\alpha = 0$, $\sigma = 0$, and we set $\omega_2(a) = 0$, then model (2.1) reduces to

$$\begin{cases} \frac{dU_X}{dt} = \lambda - dU_X(t) - \kappa(1 - \zeta_f)F(U_X(t))G(U_Y(t)), \\ \frac{\partial r(a,t)}{\partial t} + \frac{\partial r(a,t)}{\partial a} = -\mu_r(a)r(a,t), \\ \frac{dU_Y}{dt} = \int_0^\infty (1 - \zeta_p)(1 - \vartheta(a))\theta(a)r(a,t)da - uU_Y(t) - qU_Y(t)U_Z(t), \\ \frac{dU_Z}{dt} = kU_Y(t)U_Z(t) - \delta U_Z(t), \end{cases} \quad (5.2)$$

with the initial and boundary conditions given by

$$U_X(0) = U_{X0}, U_Y(0) = U_{Y0}, U_Z(0) = U_{Z0}, r(0,t) = \kappa(1 - \zeta_f)F(U_X(t))G(U_Y(t)).$$

By following the same steps as in Section 4, we find that model (5.2) has the following equilibria.

(i) The disease-free equilibrium is $E_0 = (U_{X0}, r_0(a), U_{Y0}, U_{Z0}) = (\frac{\lambda}{d}, 0, 0, 0)$, where the basic reproduction number

$$R_0 = \frac{\kappa(1 - \zeta_f)(1 - \zeta_p)F(U_{X0})}{u} G'(0) \int_0^\infty (1 - \vartheta(a))\theta(a)\Upsilon_r(a)da.$$

can be derived from the basic reproduction number of model (2.1).

(ii) The immune inactivated equilibrium is $E_1^2 = (U_{X1}^2, r_1^2(a), U_{Y1}^2, 0)$, where

$$\begin{aligned} U_{X1}^2 &= \frac{\lambda - r_1^2(0)}{d}, & r_1^2(a) &= r_1^2(0)\Upsilon_r(a), \\ U_{Y1}^2 &= \frac{r_1^2(0)}{u} \int_0^\infty (1 - \zeta_f)(1 - \vartheta(a))\theta(a)\Upsilon_r(a)da, & r_1^2(0) &\in [0, \lambda]. \end{aligned}$$

(iii) The immune activated equilibrium is $E^{2*} = (U_X^{2*}, r_1^{2*}(a), U_Y^{2*}, U_Z^{2*})$, where

$$U_X^{2*} = \frac{\lambda - r^{2*}(0)}{d}, \quad r^{2*}(a) = r^{2*}(0)\Upsilon_r(a), \quad U_Y^{2*} = \frac{\delta}{k}, \quad U_Z^{2*} = \frac{u}{q}(R_1 - 1),$$

with $R_1 = \frac{kr^{2*}(0)}{u\delta} \int_0^\infty (1 - \zeta_p)(1 - \vartheta(a))\theta(a)\Upsilon_r(a)da$, $r^{2*}(0) \in [0, \lambda)$.

Clearly, R_1 can be similarly obtained from the immune activation reproduction number in model (2.1). Hence, an immune activation equilibrium E^{2*} exists when $R_1 > 1$.

Choose the following Lyapunov function

$$L_2(t) = (U_X(t) - U_{X0} - U_{X0} \ln \frac{U_X(t)}{U_{X0}}) + M \int_0^\infty \varphi(a)r(a, t)da + MU_Y(t) + M\frac{q}{k}U_Z(t),$$

where

$$\varphi(a) = \int_a^\infty (1 - \zeta_p)(1 - \vartheta(\varepsilon))\theta(\varepsilon)e^{-\int_a^\varepsilon \mu_r(s)ds}d\varepsilon,$$

$$\varphi'(a) = \mu_r(a)\varphi(a) - (1 - \zeta_p)(1 - \vartheta(a))\theta(a), \quad M = \frac{\kappa(1 - \zeta_f)F(U_{X0})}{u}G'(0).$$

Differentiating with respect to t yields,

$$L_2' \leq -\frac{d}{U_X}(U_X - U_{X0})^2 - M\frac{q\delta}{k}U_Z + (R_0 - 1)r(0, t) + (U_{X0}M_{U_{X0}}\kappa(1 - \zeta_f)G'(0) - Mu)U_Y.$$

Thus, the infection-free steady state is globally asymptotically stable whenever $R_0 < 1$. Consequently, Theorem 2 holds for model (5.2).

Remark 5. If $\zeta_f = \zeta_p = 0$, $\vartheta(a) = 0$, $\kappa = 1$, and humoral immunity is neglected, model (5.2) reduces to that in [23] (see [23] for details). Despite using different Lyapunov functions, we obtain the identical conclusion-the disease-free equilibrium is globally asymptotically stable provided $R_0 < 1$. Thus, our model is more general than that in [23].

5.3. Special case

Setting $\alpha = 0$, $\omega_1(a) = \omega_2(a) = 0$, $\zeta_f = \zeta_p = \vartheta(a) = 0$, and $F(U_X(t))G(U_Y(t)) = U_X(t)U_Y(t)$, model (2.1) reduces to

$$\begin{cases} \frac{dU_X}{dt} = \lambda - dU_X(t) - \kappa U_X(t)U_Y(t), \\ \frac{\partial j(a, t)}{\partial t} + \frac{\partial j(a, t)}{\partial a} = -\mu_j(a)j(a, t), \\ \frac{\partial r(a, t)}{\partial t} + \frac{\partial r(a, t)}{\partial a} = -\mu_r(a)r(a, t), \\ \frac{dU_Y}{dt} = \int_0^\infty \theta(a)r(a, t)da - uU_Y(t) - qU_Y(t)U_Z(t), \\ \frac{dU_Z}{dt} = kU_Y(t)U_Z(t) - \delta U_Z(t), \end{cases} \quad (5.3)$$

with the initial and boundary conditions given by

$$U_X(0) = U_{X0}, \quad j(a, 0) = j_0, \quad r(a, 0) = r_0, \quad U_Y(0) = U_{Y0}, \quad U_Z(0) = U_{Z0},$$

$$j(0, t) = \sigma \kappa U_X(t) U_Y(t), \quad r(0, t) = (1 - \sigma) \kappa U_X(t) U_Y(t) + \int_0^\infty \xi(a) j(a, t) da,$$

and the basic reproduction number and the immune activation reproduction number given by

$$R_0 = \frac{\lambda \kappa}{du} \int_0^\infty \theta(a) \left[\int_0^\infty \sigma \xi(a) e^{-\int_0^a \mu_j(s) ds} e^{-\int_0^a \mu_r(s) ds} da + (1 - \sigma) e^{-\int_0^a \mu_r(s) ds} \right] da$$

$$= \frac{\lambda \kappa \sigma}{du} K J + \frac{\lambda \kappa (1 - \sigma)}{du} J,$$

$$= \frac{U_X^* \kappa \sigma}{u} K J + \frac{U_X^* \kappa (1 - \sigma)}{u} J,$$

where $K = \int_0^\infty \xi(a) e^{-\int_0^a \mu_j(\tau) d\tau} da$, $J = \int_0^\infty \theta(a) e^{-\int_0^a \mu_r(\tau) d\tau} da$.

Clearly, we obtain the following results concerning the existence and stability of the equilibria for model (5.3).

- Lemma 2.** (i) If $R_0 < 1$, the model (5.3) has a disease-free equilibrium E_0 ,
(ii) If $R_1 < 1 < R_0$, the model (5.3) admits an immune inactivated equilibrium E_1^3 ,
(iii) If $R_1 > 1$, the model (5.3) admits an immune activated equilibrium E^{3*} .

Choosing the following Lyapunov function

$$L(t) = (U_X(t) - U_{X0} - U_{X0} \ln \frac{U_X(t)}{U_{X0}}) + M \int_0^\infty \phi(a) j(a, t) da + M \int_0^\infty \varphi(a) r(a, t) da + M U_Y(t) + M \frac{q}{k} U_Z(t),$$

where

$$M = \max \left\{ \frac{\lambda \kappa \sigma}{du} K + \frac{\lambda \kappa (1 - \sigma)}{du}, \frac{\lambda \kappa \sigma}{du} J + \frac{\lambda \kappa (1 - \sigma)}{du K} J \right\},$$

$$\varphi(a) = \int_a^\infty \theta(s) e^{-\int_a^s \mu_r(\tau) d\tau} ds, \quad \phi(a) = \int_a^\infty \xi(s) e^{-\int_a^s \mu_j(\tau) d\tau} ds.$$

Thus,

$$L' = - \frac{d}{U_X} (U_X - U_{X0})^2 - M \varphi(a) r(a, t) |_{a=\infty} - M \phi(a) j(a, t) |_{a=\infty} - M \frac{q\delta}{k} U_Z$$

$$+ (\kappa U_{X0} - M u) U_Y + (M \phi(0) - 1) j(0, t) + (M \varphi(0) - 1) r(0, t).$$

Under the $R_0 < 1$, it is easy to see that $M \varphi(0) < 1$, $M \phi(0) < 1$. Hence, the infection-free steady state is stable if $R_0 < 1$. Therefore, Theorem 2 holds for model (5.3). Our model is more general and comprehensive than that considered in [24].

6. Numerical simulations

In this section, we apply a finite difference scheme to obtain numerical solutions of model (2.1). Our main objective is to examine the effects of age structure, CTC transmission, and antiretroviral

therapy. Without loss of generality, we give the specific infection function $F(U_X(t))G(U_Y(t)) = U_X(t) \frac{U_Y(t)}{1+eU_Y(t)}$. This form is chosen because it captures the saturation effect of viral load on the infection rate, which is a common feature in HIV dynamics (see, e.g., [25, 26]). The parameter $e > 0$ represents the half-saturation constant: a larger e indicates stronger saturation, meaning that the infection rate increases more slowly as U_Y becomes large. Compared with more complex forms such as the Beddington–DeAngelis or Crowley–Martin functions, the chosen function is simpler and sufficient to illustrate the qualitative dynamics under study. This functional form has been widely used in previous age-structured HIV models (e.g., [25, 26]) and is therefore adopted here for consistency and comparability. We set the parameters as follows: $\lambda = 10$, $d = 0.1$, $\kappa = 0.2$, $\sigma = 0.1$, $u = 2.4$, $\alpha = 0.03$, $q = 0.02$, $k = 0.02$, $\delta = 0.1$, $e = 0.1$, $\zeta_f = 0.5$, $\zeta_p = 0.5$, $\mu_j(a) = 0.001 \times (1 + \frac{\sin(a-5)\pi}{10})$, $\mu_r(a) = 0.01 \times (1 + \frac{\sin(a-5)\pi}{10})$, $\vartheta(a) = 0.1 \times (1 + \frac{\sin(a-5)\pi}{10})$. Take the initial values as $U_{X0} = 30$, $U_{Y0} = 0.6$, $U_{Z0} = 10$, $j_0(a) = 0.1$, and $r_0(a) = 10$.

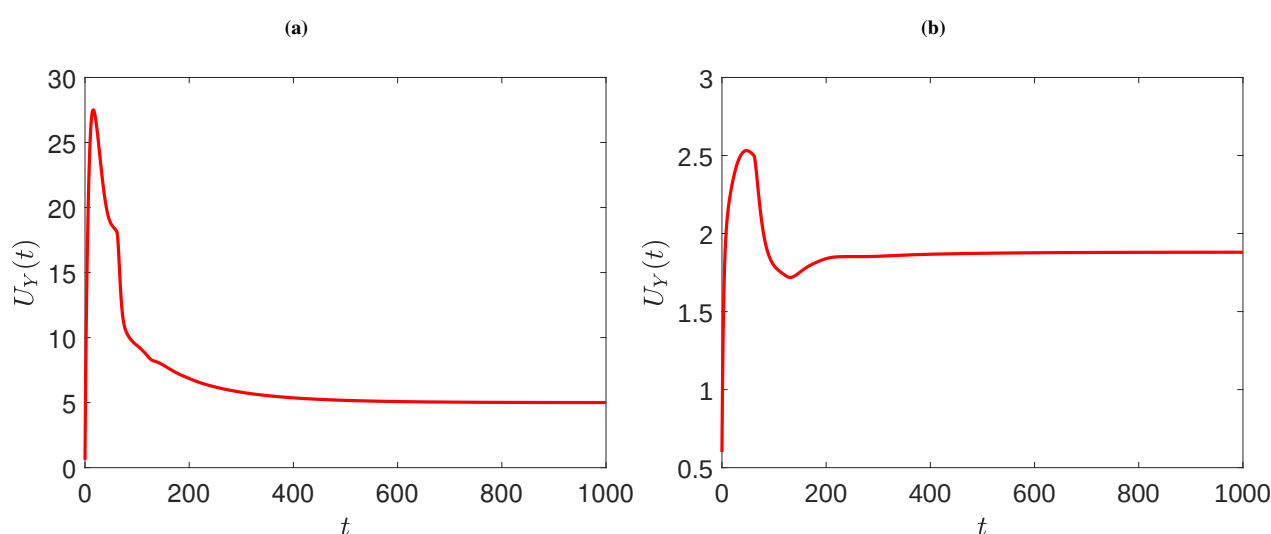


Figure 2. Evolution of viral particles without control. (a) $\omega_1(a) = \omega_2(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 2 \times (1 + \sin \frac{(a-5)\pi}{10})$, (b) $\omega_1(a) = \omega_2(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 0.3 \times (\frac{a}{1+a})$.

To investigate the effects of the CTC transmission rates $\omega_1(a)$, $\omega_2(a)$ and age-dependent virus production rate $\theta(a)$ of infected cells on the final viral load when the basic reproduction number $R_0 > 1$, we present Figures 2 and 3, respectively. Figure 2 shows that different values of $\theta(a)$ lead to different peak viral loads as well as different steady-state levels, indicating that $\theta(a)$ directly affects the viral load. Figure 3 demonstrates that in the presence of CTC transmission, viral spread is enhanced by cell-to-cell propagation, and the time to reach the steady state is shortened. Both figures show a sharp initial increase in viral particles, followed by a prolonged steady period. After substantial immune system damage, viral particles rise again, marking the onset of AIDS. Thus, controlling $\omega_1(a)$, $\omega_2(a)$, $\theta(a)$, can reduce both the peak value and the steady-state viral load. Biologically, cell-to-cell transmission accelerates viral spread in the body, leading to a faster establishment of infection. Hence, CTC transmission directly influences the viral load. Moreover, Figures 4 and 5 illustrate the dynamics of infected T cells with respect to age and time. It is clear that CTC transmission arises from interactions among latently infected T cells, actively infected T cells, and

healthy T cells, thereby affecting the viral load. Thus, CTC transmission has a direct impact on the number of viral particles. Furthermore, Figures 2–5 clearly show that the infection-free equilibrium is unstable when $R_0 > 1$ because the number of viral particles and infected T cells is not zero over time.

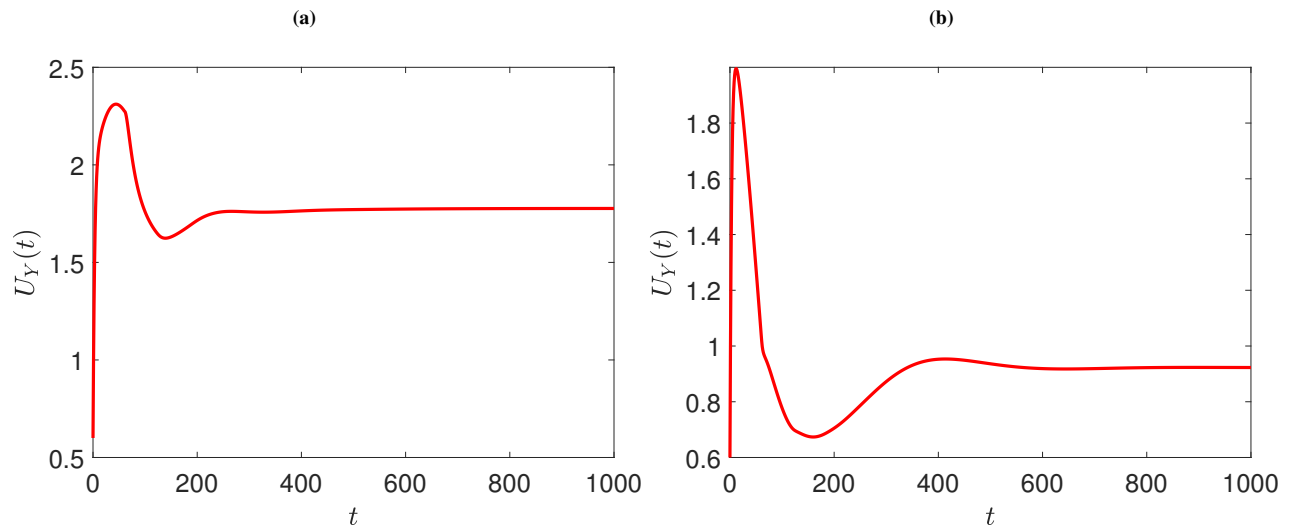


Figure 3. Evolution of viral particles without control. (a) $\omega_1(a) = \omega_2(a) = 0.01 \times (\frac{a}{1+a})$, $\theta(a) = 0.3 \times (\frac{a}{1+a})$; (b) $\omega_1(a) = \omega_2(a) = 0$, $\theta(a) = 0.3 \times (\frac{a}{1+a})$.

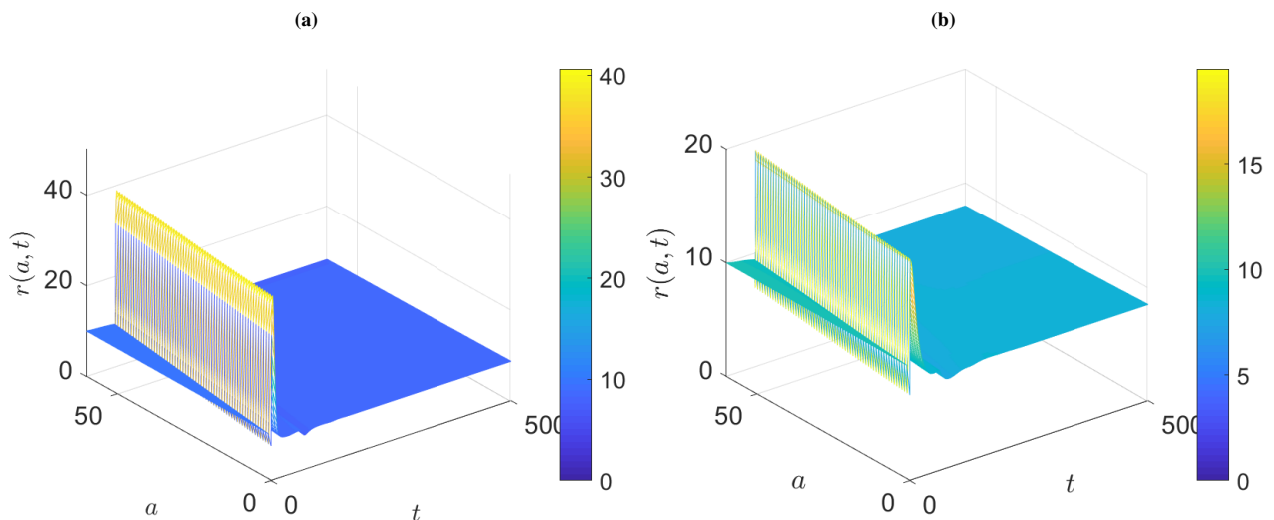


Figure 4. Dynamics of infected T cells without control. (Where (a): $\omega_1(a) = \omega_2(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 2 \times (1 + \sin \frac{(a-5)\pi}{10})$, (b): $\omega_1(a) = \omega_2(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 0.3 \times (\frac{a}{1+a})$.)

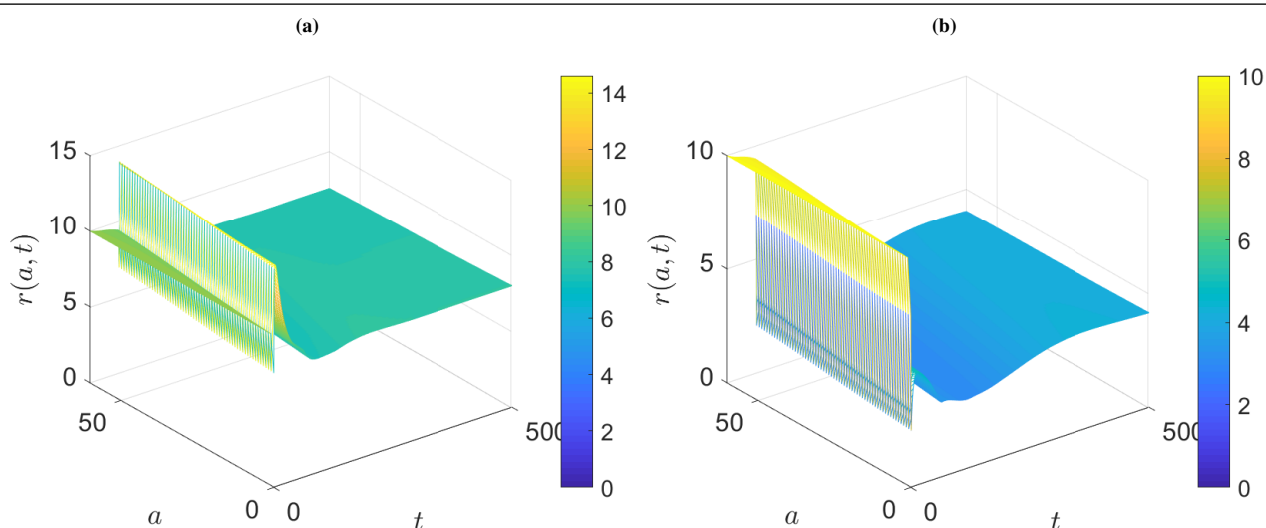


Figure 5. Dynamics of infected T cells without control. (a): $\omega_1(a) = \omega_2(a) = 0.01 \times (\frac{a}{1+a})$, $\theta(a) = 0.3 \times (\frac{a}{1+a})$; (b): $\omega_1(a) = \omega_2(a) = 0$, $\theta(a) = 0.3 \times (\frac{a}{1+a})$.

Second, Figures 6–9 are also validating the results obtained in Theorem 2, i.e., if $R_0 < 1$, the infection-free steady state E_0 is stable, which means the number of healthy T cells will converge to $\frac{\lambda}{d} = 100$. In addition, we choose parameters as $\omega_1(a) = \omega_2(a) = 0.001 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\zeta_f = \zeta_p = 0.8$, $\vartheta(a) = 0.8 \times (1 + \sin \frac{(a-5)\pi}{10})$ to obtain Figure 7, which again yields that the uninfected steady state E_0 is globally asymptotically stable for $R_0 < 1$, confirming the theoretical result of Theorem 2.

Furthermore, when CTC transmission or antiretroviral therapy is not considered, model (2.1) can degenerate into model (5.1) (see Figure 8), model (5.2) (see Figure 9). As can be seen from Figures 8 and 9, the disease-free equilibrium E_0 is globally asymptotically stable when the basic reproduction number $R_0 < 1$, which is consistent with the theoretical result of Theorem 2. By comparing Figures 8 and 9, it can be seen that increasing antiretroviral therapy speeds up the rate at which viral particles reach stabilization and reduces the damage caused by the virus in the body.

From Figures 2–9, we can see that as the age-dependent variance of infectiousness of latently infected cells $\omega_1(a)$, the age-dependent variance of infectiousness of infected cells $\omega_2(a)$, and the age-dependent viral production rate of infected cells $\theta(a)$ change, so do infected T cells and viral particles. In summary, CTC transmission plays a crucial role in HIV dynamics.

Finally, we took three different values of ζ_f , ζ_p respectively (see Figure 10) to investigate how antiretroviral therapy plays a role in HIV transmission. As can be seen in Figure 10, the peak value reached by the viral particles in the initial phase gradually decreases and stabilizes with increasing antiretroviral therapy, and the stabilized value gradually decreases. Thus antiretroviral therapy plays a crucial role in slowing down the spread of viral particles. Therefore, long-term sustained use of antiretroviral drugs is biologically important in helping to control HIV transmission.

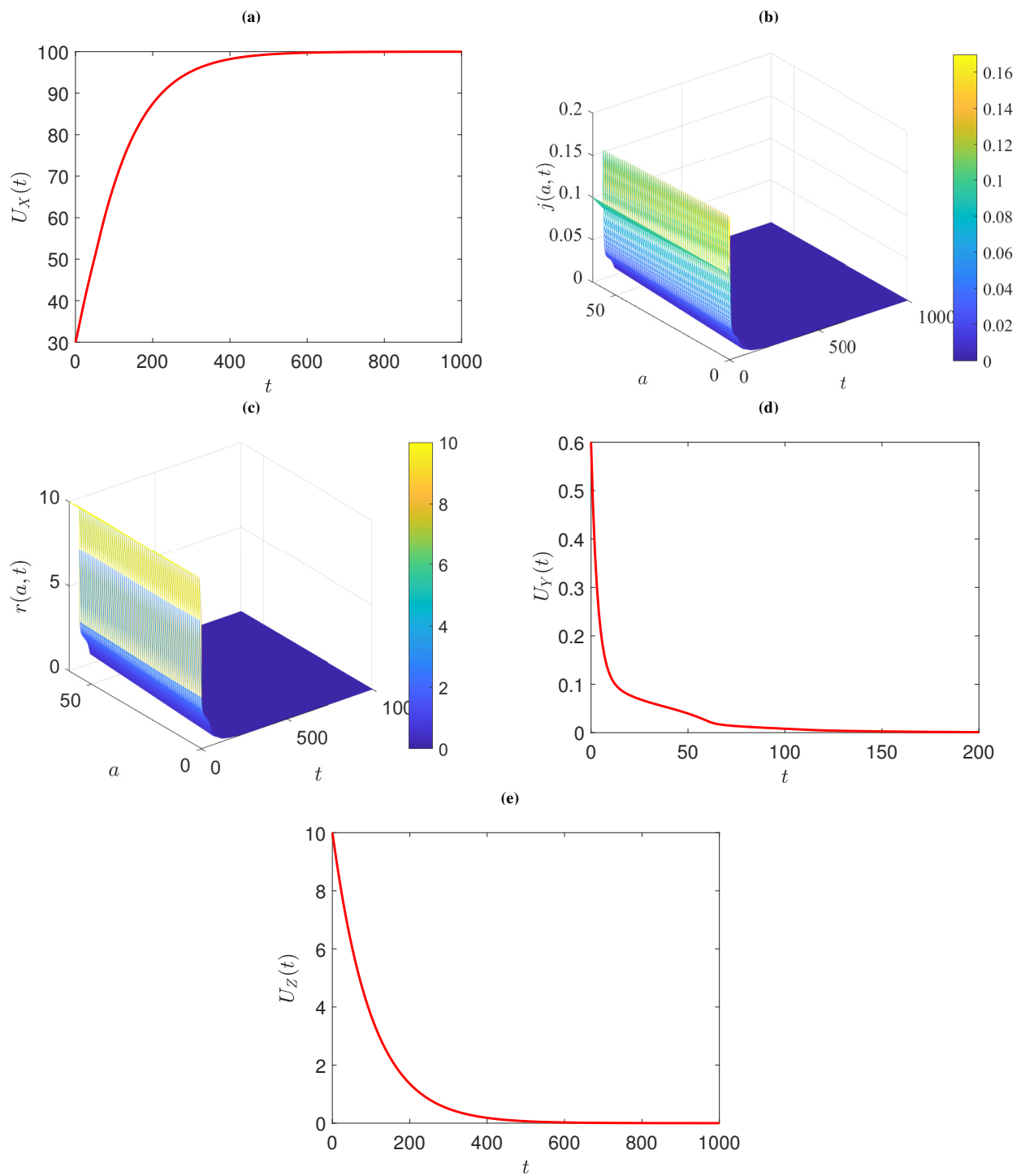


Figure 6. Stability of infection-free steady state for $R_0 < 1$. $\omega_1(a) = \omega_2(a) = 0.001 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\zeta_f = \zeta_p = 0.5$, $\vartheta(a) = 0.1 \times (1 + \sin \frac{(a-5)\pi}{10})$.

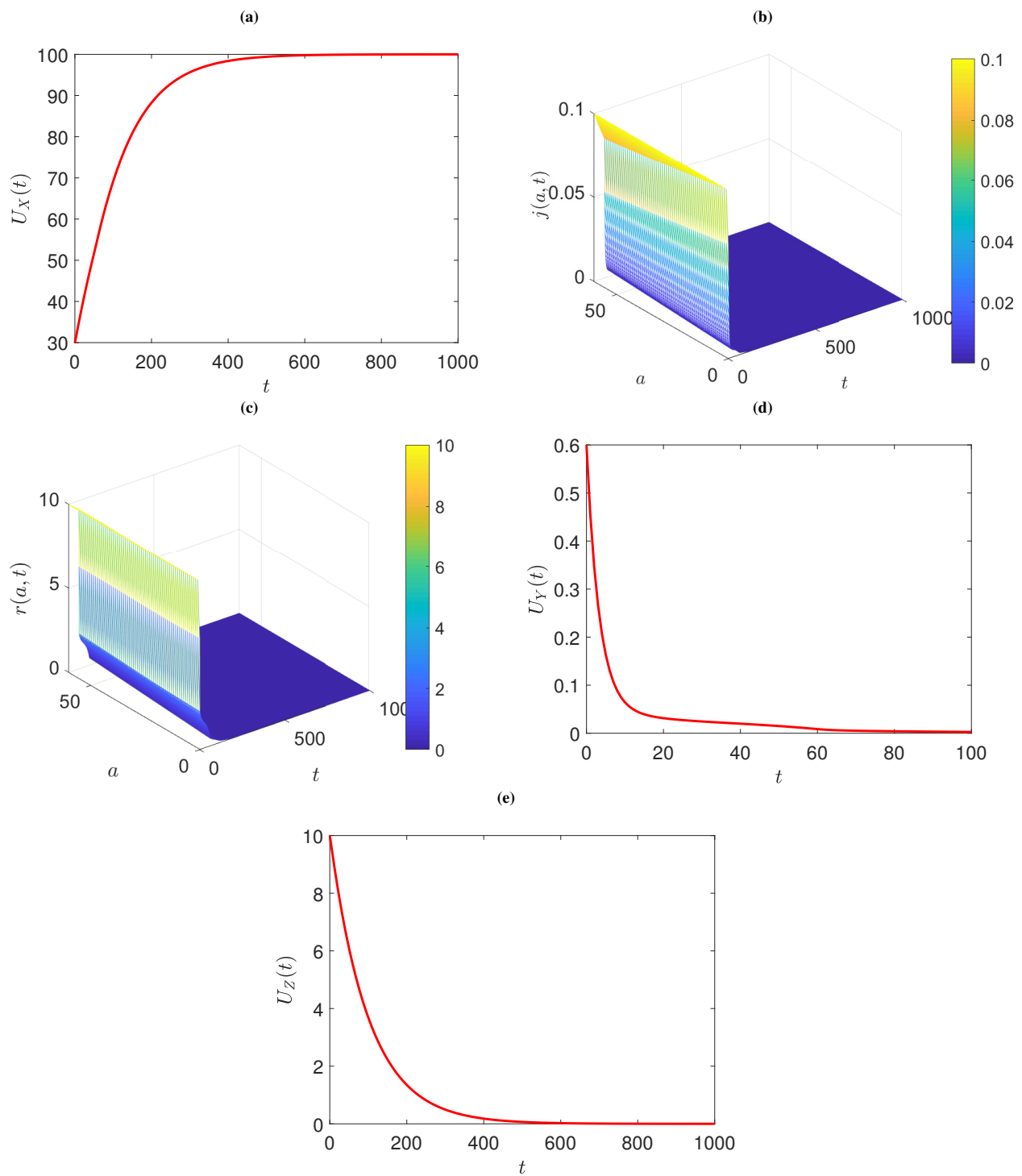


Figure 7. Stability of infection-free steady state for $R_0 < 1$ with $\omega_1(a) = \omega_2(a) = 0.001 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\theta(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\zeta_f = \zeta_p = 0.8$, and $\vartheta(a) = 0.1 \times (1 + \sin \frac{(a-5)\pi}{10})$.

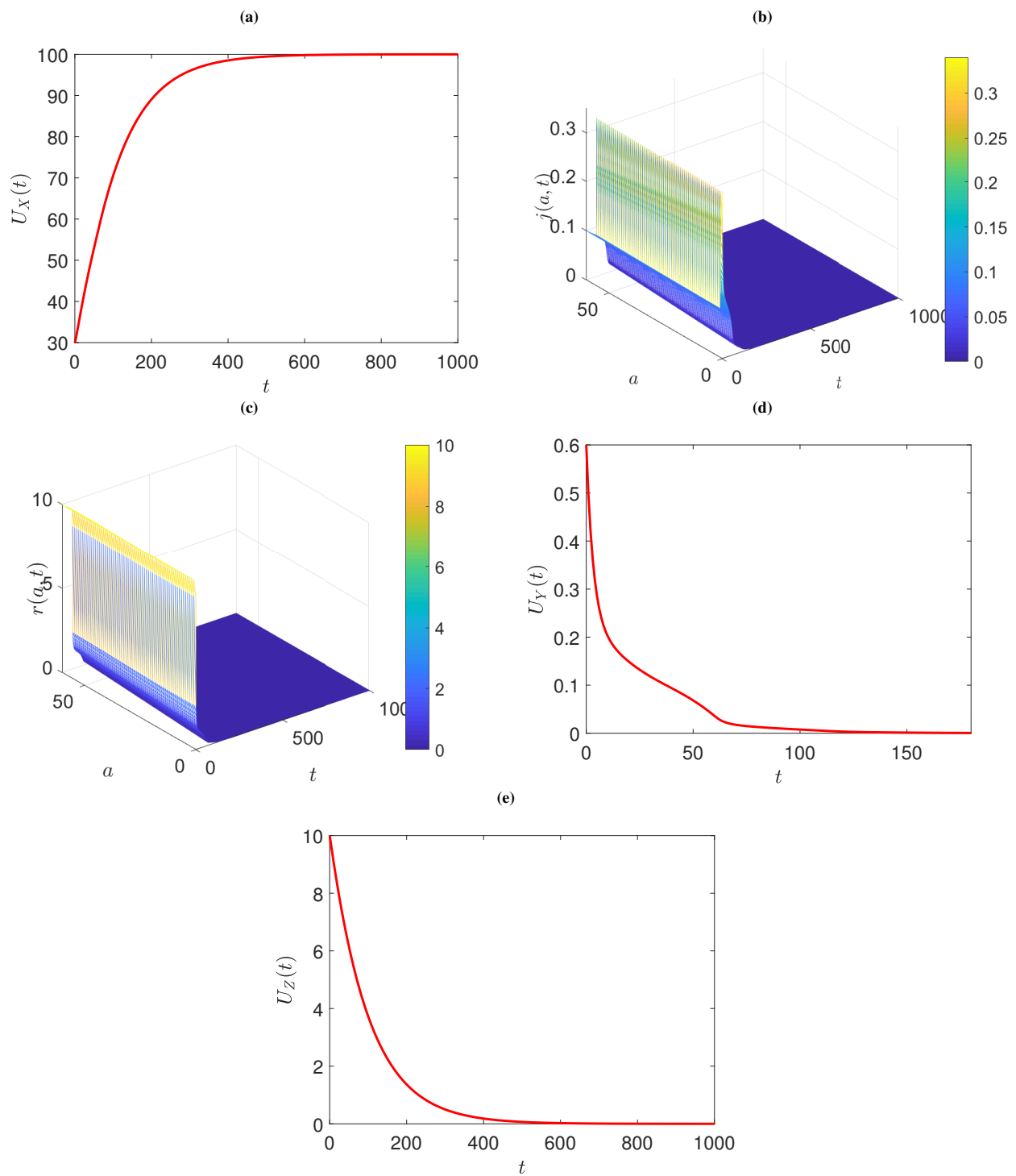


Figure 8. Stability of infection-free steady state for $R_0 < 1$. ($\omega_1(a) = \omega_2(a) = 0$, $\theta(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\zeta_f = \zeta_p = \vartheta(a) = 0$).

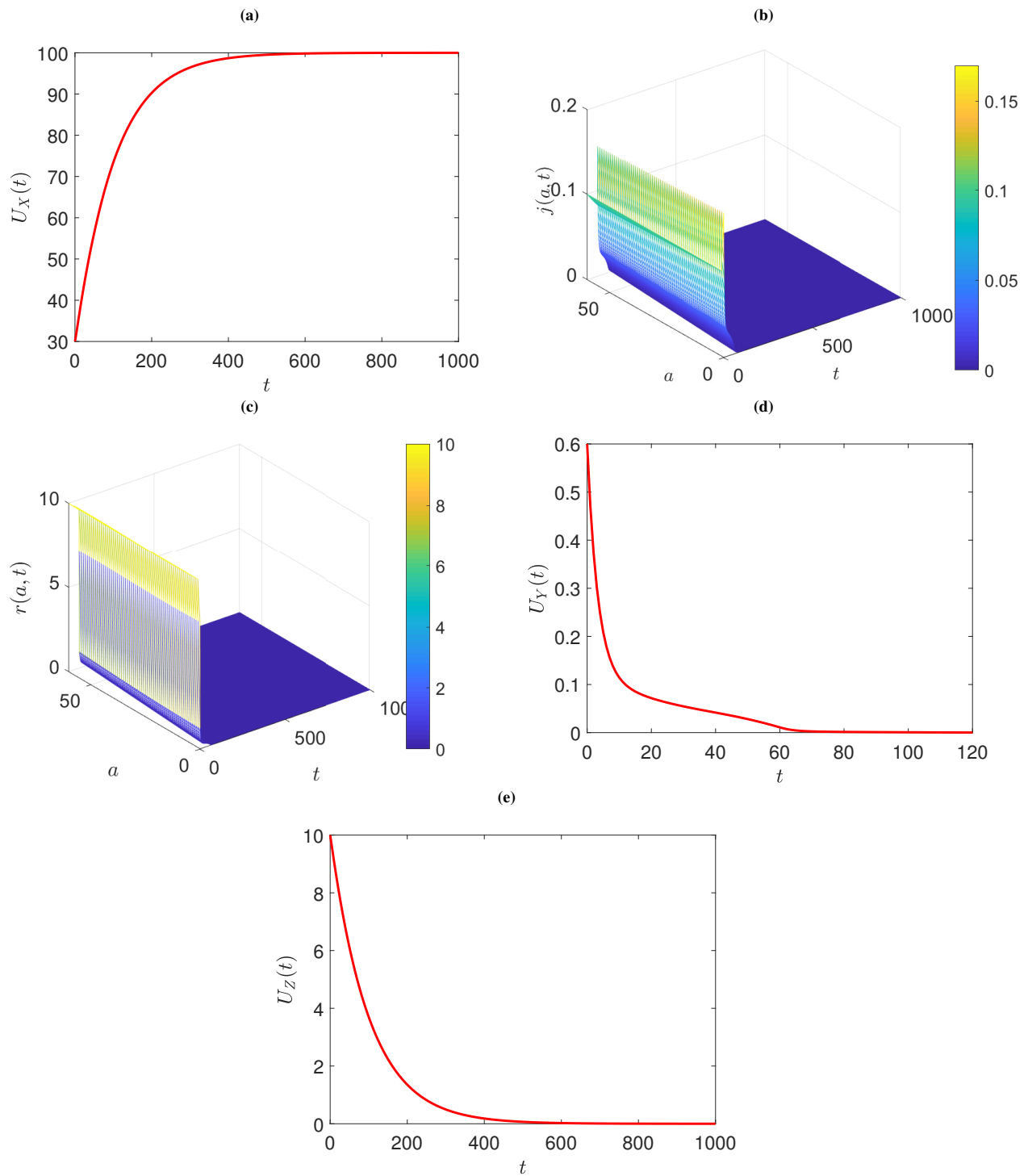


Figure 9. Stability of infection-free steady state for $R_0 < 1$ with $\omega_1(a) = \omega_2(a) = 0$, $\theta(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\zeta_f = \zeta_p = 0.5$, $\vartheta(a) = 0.1 \times (1 + \sin \frac{(a-5)\pi}{10})$.

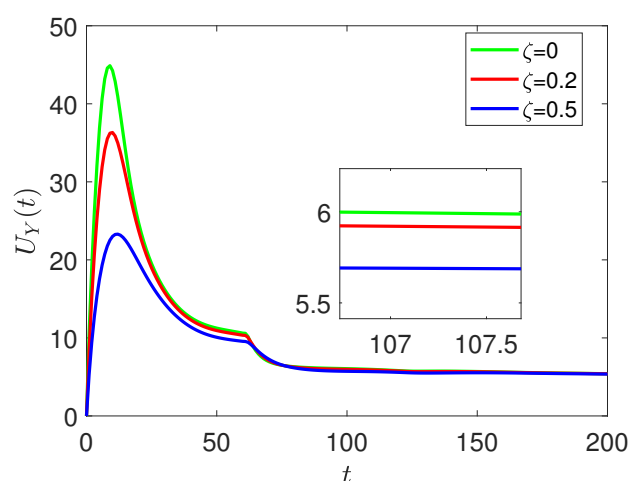


Figure 10. The graph trajectories of Y versus time t are shown. The effect of antiretroviral therapy at different levels. ($\zeta_f = \zeta_p = \zeta$, $u = 0.4$, $\theta(a) = 2 \times (1 + \sin \frac{(a-5)\pi}{10})$, $\omega_1(a) = \omega_2(a) = 0.01 \times (1 + \sin \frac{(a-5)\pi}{10})$).

7. Conclusions

In this paper, we present a new general age-structured HIV model with two routes of infection, antiretroviral therapy, and humoral immunity to discuss and analyze the influence of factors such as dominant activation of latently infected cells into infected cells and humoral immunity on HIV transmission. To start, the consideration of the dominant activation rate α poses a great difficulty in the analysis of the model, and the existence of E_1 and E^* is analyzed in two cases. Then, the global stability of the disease-free equilibrium E_0 is given by constructing an appropriate Lyapunov function. Finally, through numerical simulations, it is obtained that CTC transmission and antiretroviral therapy play a crucial role in HIV dynamics.

Theoretically, the global stability of E_0 is thus resolved. However, the presence of the dominant activation rate α also complicates the derivation of asymptotic smoothness, which in turn makes it difficult to obtain uniform persistence and, consequently, the global stability of E_1 and E^* remains an open problem. This question can be approached in future studies by employing uniform persistence theory combined with Lyapunov-LaSalle techniques to establish global asymptotic stability under suitable parameter conditions, or by performing numerical bifurcation analysis to detect possible Hopf bifurcations and periodic orbits. Resolving these stability issues would provide a complete picture of the global dynamics, clarifying whether the system can sustain chronic infection or exhibit oscillatory behavior, which is clinically meaningful for predicting long-term viral load patterns and evaluating treatment outcomes. These directions will be the focus of our subsequent research.

Turning to the numerical results, we provide several simulations that verify the global stability of the disease-free equilibrium E_0 (see Figures 6 and 7). Moreover, we find that the inclusion of antiretroviral therapy accelerates the convergence of latently infected T cells, productively infected cells, and viral particles to their steady states, thereby reducing the overall damage to the host. Importantly, the simulations also reveal phenomena that are not yet accessible analytically. For instance, when $R_0 > 1$, the disease-free equilibrium E_0 is unstable as can be clearly seen from

Figures 2–5, where viral particles and infected T cells persist over time. In addition, when CTC transmission or antiretroviral therapy is not considered, model (2.1) can degenerate into model (5.1) (see Figure 8), model (5.2) (see Figure 9), or we selected a different antiretroviral treatment (see Figure 10). Thus, from Figures 8–10, it can be obtained that increasing antiretroviral therapy helps to reduce the damage caused by the virus in the human body.

In summary, we present a new general age-structured HIV model with two routes of infection, antiretroviral therapy, and humoral immunity, and found through numerical simulations that CTC transmission and antiretroviral therapy play a crucial role in HIV dynamics. Therefore, taking antiretroviral drugs and taking measures to cut off CTC transmission, etc., can help control HIV transmission. From a biological point of view, this study is very important because the introduction of latently infected T cells, age of infection, antiretroviral therapy, and so on make the model more realistic.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare there is no conflict of interest.

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