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Research Article

Global Dynamics of an HIV Infection Model with Two Classes of Target Cells and Distributed Delays

A. M. Elaiw[1,2]

[1] *Department of Mathematics, Faculty of Science, King Abdulaziz University, P.O. Box 80203, Jeddah 21589, Saudi Arabia*
[2] *Department of Mathematics, Faculty of Science, Al-Azhar University, Assiut 71511, Egypt*

Correspondence should be addressed to A. M. Elaiw, a_m_elaiw@yahoo.com

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We investigate the global dynamics of an HIV infection model with two classes of target cells and multiple distributed intracellular delays. The model is a 5-dimensional nonlinear delay ODEs that describes the interaction of the HIV with two classes of target cells, $CD4^+$ T cells and macrophages. The incidence rate of infection is given by saturation functional response. The model has two types of distributed time delays describing time needed for infection of target cell and virus replication. This model can be seen as a generalization of several models given in the literature describing the interaction of the HIV with one class of target cells, $CD4^+$ T cells. Lyapunov functionals are constructed to establish the global asymptotic stability of the uninfected and infected steady states of the model. We have proven that if the basic reproduction number R_0 is less than unity then the uninfected steady state is globally asymptotically stable, and if $R_0 > 1$ then the infected steady state exists and it is globally asymptotically stable.

1. Introduction

In the last decade, several mathematical models have been developed to describe the interaction of the human immunodeficiency virus (HIV) with target cells [1]. HIV is responsible for acquired immunodeficiency syndrome (AIDS). Mathematical modeling and model analysis of the HIV dynamics are important for exploring possible mechanisms and dynamical behaviors of the viral infection process, estimating key parameter values, and guiding development efficient antiviral drug therapies. Some of the existing HIV infection models are given by nonlinear ODEs by assuming that the infection could occur and the viruses are produced from infected target cells instantaneously, once the uninfected target cells are contacted by the virus particles (see e.g., [2–4]). Other accurate models incorporate the delay

between the time, the viral entry into the target cell, and the time the production of new virus particles, modeled with discrete time delay or distributed time delay using functional differential equations (see e.g., [5–9]). The basic virus dynamics model with distributed intracellular time delay has been proposed in [9] and given by

$$\dot{x}(t) = \lambda - dx(t) - (1 - u_{rt})\overline{\beta}x(t)v(t), \tag{1.1}$$

$$\dot{y}(t) = (1 - u_{rt})\overline{\beta}\int_0^\infty f(\tau)e^{-m\tau}x(t-\tau)v(t-\tau)d\tau - ay(t), \tag{1.2}$$

$$\dot{v}(t) = (1 - u_p)\overline{p}\int_0^\infty g(\tau)y(t-\tau)d\tau - cv(t), \tag{1.3}$$

where $x(t)$, $y(t)$ and $v(t)$ represent the populations of uninfected $CD4^+$ T cells, infected cells, and free virus particles at time t, respectively. Here, λ represents the rate of which new $CD4^+$ T cells are generated from sources within the body, d is the death rate constant, and $\overline{\beta}$ is the constant rate at which a target cell becomes infected via contacting with virus. Equation (1.2) describes the population dynamics of the infected cells and shows that they die with rate constant a. The virus particles are produced by the infected cells with rate constant $\overline{p}$ and are removed from the system with rate constant c. The model includes two kinds of antiretroviral drugs, reverse transcriptase inhibitors (RTI) to prevent the virus from infecting cells and protease inhibitors (PI) drugs to prevent already infected host cells from producing infectious virus particles. The parameters $u_{rt} \in [0,1]$ and $u_p \in [0,1]$ are the efficacies of RTI and PI, respectively. To account for the time lag between viral contacting a target cell and the production of new virus particles, two distributed intracellular time delays are introduced. It is assumed that the target cells are contacted by the virus particles at time $t - \tau$ become infected cells at time t, where τ is a random variable with a probability distribution $f(\tau)$. The factor $e^{-m\tau}$ accounts for the loss of target cells during time period $[t-\tau, t]$. On the other hand, it is assumed that a cell infected at time $t - \tau$ starts to yield new infectious virus at time t, where τ is distributed according to a probability distribution $g(\tau)$.

A tremendous effort has been made in developing various mathematical models of HIV infection with discrete or distributed delays and studying their basic and global properties, such as positive invariance properties, boundedness of the model solutions, and stability analysis [5–20]. Most of the existing delayed HIV infection models are based on the assumption that the virus attacks one class of target cells, $CD4^+$ T cells. In 1997, it was observed by Perelson et al. [21] that the HIV attacks two classes of target cells, $CD4^+$ T cells and macrophages. In [3, 4], an HIV model with two target cells has been proposed. Also, in very recent works [22–25], we have proposed several HIV models with two target cells and investigated the global asymptotic stability of their steady states. In [26], we have studied a class of virus infection models assuming that the virus attacks multiple classes of target cells. In very recent works, [27, 28], discrete-time delays have been incorporated into the HIV models.

The purpose of this paper is to propose a delayed HIV infection model with two target cells and establish the global stability of its steady states. We assume that the infection rate is given by saturation functional response. We incorporate two types of distributed delays into this model to account the time delay between the time the target cells are contacted by the virus particle and the time the emission of infectious (matures) virus particles. The global stability of this model is established using Lyapunov functionals, which are similar in nature to

those used in [29]. We prove that the global dynamics of these models are determined by the basic reproduction number R_0. If $R_0 \leq 1$, then the uninfected steady state is globally asymptotically stable (GAS) and if $R_0 > 1$, then the infected steady state exists and it is GAS.

2. HIV Infection Model with Two Classes of Target Cells and Distributed Delays

In this section, we propose a mathematical model of HIV infection which describes two cocirculation populations of target cells, potentially representing CD4$^+$ T cells and macrophages taking into account the saturation infection rate and multiple distributed intracellular delays. This model can be considered as an extension of HIV infection models given in [3, 4, 22].

Consider the following:

$$\dot{x}_1(t) = \lambda_1 - d_1 x_1(t) - \frac{\beta_1 x_1(t) v(t)}{1 + \alpha_1 v(t)}, \tag{2.1}$$

$$\dot{y}_1(t) = \beta_1 \int_0^\infty f_1(\tau) e^{-m_1 \tau} \frac{x_1(t-\tau) v(t-\tau)}{1 + \alpha_1 v(t-\tau)} d\tau - a_1 y_1(t), \tag{2.2}$$

$$\dot{x}_2(t) = \lambda_2 - d_2 x_2(t) - \frac{\beta_2 x_2(t) v(t)}{1 + \alpha_2 v(t)}, \tag{2.3}$$

$$\dot{y}_2(t) = \beta_2 \int_0^\infty f_2(\tau) e^{-m_2 \tau} \frac{x_2(t-\tau) v(t-\tau)}{1 + \alpha_2 v(t-\tau)} d\tau - a_2 y_2(t), \tag{2.4}$$

$$\dot{v}(t) = p_1 \int_0^\infty g_1(\tau) e^{-n_1 \tau} y_1(t-\tau) d\tau + p_2 \int_0^\infty g_2(\tau) e^{-n_2 \tau} y_2(t-\tau) d\tau - c v(t). \tag{2.5}$$

The state variables describes the plasma concentrations of: x_1, the uninfected CD4$^+$ T cells; y_1, the infected CD4$^+$ T cells; x_2, the uninfected macrophages; y_2, the infected macrophages; v, the free virus particles. Here, α_i, $i = 1, 2$ are positive constants, $\beta_i = (1 - u_{rt})\overline{\beta}_i$, and $p_i = (1 - u_p)\overline{p}_i$, $i = 1, 2$. The factors $e^{-n_i \tau}$, $i = 1, 2$ account for the cells loss during the delay period. All the other parameters of the model have the same meanings as given in (1.1)–(1.3).

The probability distribution functions $f_i(\tau)$ and $g_i(\tau)$ are assumed to satisfy $f_i(\tau) > 0$ and $g_i(\tau) > 0$, $i = 1, 2$ and

$$\begin{gathered} \int_0^\infty f_i(\tau) d\tau = \int_0^\infty g_i(\tau) d\tau = 1, \quad i = 1, 2, \\ \int_0^\infty f_i(r) e^{sr} dr < \infty, \quad \int_0^\infty g_i(r) e^{sr} dr < \infty, \quad i = 1, 2, \end{gathered} \tag{2.6}$$

where s is a positive number. Then

$$0 < \int_0^\infty f_i(\tau)e^{-m_i\tau}d\tau \le 1, \quad \text{for } m_i \ge 0,\ i = 1,2,$$
$$0 < \int_0^\infty g_i(\tau)e^{-n_i\tau}d\tau \le 1, \quad \text{for } n_i \ge 0,\ i = 1,2. \tag{2.7}$$

The initial conditions for system (2.1)–(2.5) take the form

$$\begin{aligned} x_1(\theta) &= \varphi_1(\theta), \qquad y_1(\theta) = \varphi_2(\theta), \\ x_2(\theta) &= \varphi_3(\theta), \qquad y_2(\theta) = \varphi_4(\theta), \\ v(\theta) &= \varphi_5(\theta), \\ \varphi_j(\theta) &\ge 0, \quad \theta \in (-\infty, 0),\ j = 1,\dots,5, \\ \varphi_j(0) &> 0, \quad j = 1,\dots,5, \end{aligned} \tag{2.8}$$

where $(\varphi_1(\theta), \varphi_2(\theta), \dots, \varphi_5(\theta)) \in UC((-\infty, 0], \mathbb{R}_+^5)$, and UC is the Banach space of fading memory type defined as [30]

$$\begin{aligned} &UC\left((-\infty,0],\mathbb{R}_+^5\right) \\ &= \left\{\varphi \in C\left((-\infty,0],\mathbb{R}_+^5\right) : \varphi(r)e^{sr} \text{ is uniformly continuous on } (-\infty,0], \|\varphi\| = \sup_{r\le 0}\varphi(r)e^{sr} < \infty\right\}, \end{aligned} \tag{2.9}$$

where $C((-\infty, 0], \mathbb{R}_+^5)$ is the Banach space of continuous functions mapping the interval $(-\infty, 0]$ into $\mathbb{R}_+^5$. By the fundamental theory of functional differential equations [31], system (2.1)–(2.5) has a unique solution satisfying the initial conditions (2.8).

2.1. Nonnegativity and Boundedness of Solutions

In the following, we establish the nonnegativity and boundedness of solutions of (2.1)–(2.5) with initial conditions (2.8).

Proposition 2.1. *Let $(x_1(t), y_1(t), x_2(t), y_2(t), v(t))$ be any solution of (2.1)–(2.5) satisfying the initial conditions (2.8), then $x_1(t)$, $y_1(t)$, $x_2(t)$, $y_2(t)$ and $v(t)$ are all nonnegative for $t \ge 0$ and ultimately bounded.*

Proof. From (2.1) and (2.3) we have

$$x_i(t) = x_i(0)e^{-\int_0^t [d_i + \beta_i v(\xi)/(1+\alpha_i v(\xi))]d\xi} + \lambda_i \int_0^t e^{-\int_\eta^t [d_i + \beta_i v(\xi)/(1+\alpha_i v(\xi))]d\xi} d\eta, \quad i = 1,2, \tag{2.10}$$

which indicates that $x_i(t) \geq 0$, for all $t \geq 0$. Now from (2.2), (2.4), and (2.5) we have

$$\begin{aligned} y_i(t) &= y_i(0)e^{-a_i t} + \beta_i \int_0^t e^{-a_i(t-\eta)} \int_0^\infty f_i(\tau) e^{-m_i\tau} \frac{x_i(\eta-\tau)v(\eta-\tau)}{1+\alpha_i v(\eta-\tau)} d\tau\, d\eta, \quad i = 1,2, \\ v(t) &= v(0)e^{-ct} + p_1 \int_0^t e^{-c(t-\eta)} \int_0^\infty g_1(\tau) e^{-n_1\tau} y_1(\eta-\tau) d\tau\, d\eta \\ &\quad + p_2 \int_0^t e^{-c(t-\eta)} \int_0^\infty g_2(\tau) e^{-n_2\tau} y_2(\eta-\tau) d\tau\, d\eta, \end{aligned} \tag{2.11}$$

confirming that $y_1(t)$, $y_2(t) \geq 0$, and $v(t) \geq 0$ for all $t \geq 0$.

Next we show the boundedness of the solutions. From (2.1) and (2.3) we have $\dot{x}_i(t) \leq \lambda_i - d_i x_i(t)$, $i = 1,2$. This implies $\limsup_{t\to\infty} x_i(t) \leq \lambda_i/d_i$, $i = 1,2$.

Let $X_i(t) = \int_0^\infty f_i(\tau)e^{-m_i\tau}x_i(t-\tau)d\tau + y_i(t)$, $i = 1,2$, then

$$\begin{aligned} \dot{X}_i(t) &= \int_0^\infty f_i(\tau)e^{-m_i\tau}\left(\lambda_i - d_i x_i(t-\tau) - \frac{\beta_i x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)}\right)d\tau \\ &\quad + \int_0^\infty f_i(\tau)e^{-m_i\tau}\frac{\beta_i x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)}d\tau - a_i y_i(t) \\ &= \lambda_i \int_0^\infty f_i(\tau)e^{-m_i\tau}d\tau - d_i \int_0^\infty f_i(\tau)e^{-m_i\tau}x_i(t-\tau)d\tau - a_i y_i(t) \\ &\leq \lambda_i \int_0^\infty f_i(\tau)e^{-m_i\tau}d\tau - \sigma_i\left[\int_0^\infty f_i(\tau)e^{-m_i\tau}x_i(t-\tau)d\tau + y_i(t)\right] \\ &= \lambda_i \int_0^\infty f_i(\tau)e^{-m_i\tau}d\tau - \sigma_i X_i(t) \\ &\leq \lambda_i - \sigma_i X_i(t), \end{aligned} \tag{2.12}$$

where $\sigma_i = \min\{d_i, a_i\}$. Hence $\limsup_{t\to\infty} X_i(t) \leq L_i$, where $L_i = \lambda_i/\sigma_i$, $i = 1,2$. On the other hand,

$$\begin{aligned} \dot{v}(t) &\leq p_1 L_1 \int_0^\infty g_1(\tau)e^{-n_1\tau}d\tau + p_2 L_2 \int_0^\infty g_2(\tau)e^{-n_2\tau}d\tau - cv \\ &\leq p_1 L_1 + p_2 L_2 - cv, \end{aligned} \tag{2.13}$$

then $\limsup_{t\to\infty} v(t) \leq (p_1L_1 + p_2L_2)/c$. Therefore, $x_1(t)$, $y_1(t)$, $x_2(t)$, $y_2(t)$, and $v(t)$ are ultimately bounded. □

2.2. Steady States

It is clear that system (2.1)–(2.5) has an uninfected steady state $E_0 = (x_1^0, 0, x_2^0, 0, 0)$, where $x_i^0 = \lambda_i/d_i$, $i = 1,2$. In addition to E_0, the system can also have a positive infected steady

state $E_1(x_1^*, y_1^*, x_2^*, y_2^*, v^*)$. The coordinates of the infected steady state, if they exist, satisfy the following equalities:

$$\lambda_i = d_i x_i^* + \frac{\beta_i x_i^* v^*}{1 + \alpha_i v^*}, \quad i = 1, 2, \tag{2.14}$$

$$a_i y_i^* = F_i \frac{\beta_i x_i^* v^*}{1 + \alpha_i v^*}, \quad i = 1, 2, \tag{2.15}$$

$$c v^* = G_1 p_1 y_1^* + G_2 p_2 y_2^*, \tag{2.16}$$

where

$$F_i = \int_0^\infty f_i(\tau) e^{-m_i \tau} d\tau, \quad G_i = \int_0^\infty g_i(\tau) e^{-n_i \tau} d\tau, \quad i = 1, 2. \tag{2.17}$$

Following van den Driessche and Watmough [32], we define the basic reproduction number for system (2.1)–(2.5) as

$$R_0 = \sum_{i=1}^{2} R_i = \sum_{i=1}^{2} \frac{F_i G_i \beta_i p_i \lambda_i}{a_i d_i c}, \tag{2.18}$$

where R_1 and R_2 are the basic reproduction numbers of the HIV dynamics with $CD4^+$ T cells (in the absence of macrophages) and the HIV dynamics with macrophages (in the absence of $CD4^+$ T cells), respectively.

Lemma 2.2. *If $R_0 > 1$, then there exists a positive steady state E_1.*

Proof. From (2.14) and (2.15) we have

$$x_i^* = \frac{x_i^0 (1 + \alpha_i v^*)}{(1 + \delta_i v^*)}, \quad i = 1, 2, \tag{2.19}$$

$$y_i^* = \frac{F_i \beta_i x_i^0 v^*}{a_i (1 + \delta_i v^*)}, \quad i = 1, 2, \tag{2.20}$$

where $\delta_i = \alpha_i + \beta_i / d_i$. From (2.20) into (2.16) we get

$$1 = \frac{F_1 G_1 p_1 \beta_1 x_1^0}{a_1 c (1 + \delta_1 v^*)} + \frac{F_2 G_2 p_2 \beta_2 x_2^0}{a_2 c (1 + \delta_2 v^*)} = \frac{R_1}{1 + \delta_1 v^*} + \frac{R_2}{1 + \delta_2 v^*}. \tag{2.21}$$

Equation (2.21) can be written as

$$\delta_1 \delta_2 v^{*2} + (\delta_1 R_1 + \delta_2 R_2 + (1 - R_0)(\delta_1 + \delta_2)) v^* + 1 - R_0 = 0. \tag{2.22}$$

If $R_0 > 1$, then the positive solution of (2.21) is given by:

$$v^* = \frac{-(\delta_1 R_1 + \delta_2 R_2 + (1-R_0)(\delta_1+\delta_2)) + \sqrt{(\delta_1 R_1 + \delta_2 R_2 + (1-R_0)(\delta_1+\delta_2))^2 - 4\delta_1\delta_2(1-R_0)}}{2\delta_1\delta_2}. \tag{2.23}$$

It follows that, if $R_0 > 1$ then x_1^*, y_1^*, x_2^*, y_2^* and v^* are all positive. □

2.3. Global Stability

In this section, we prove the global stability of the uninfected and infected steady states of system (2.1)–(2.3) employing the method of Lyapunov functional which is used in [29] for SIR epidemic model with distributed delay. Next we shall use the following notation: $z = z(t)$, for any $z \in \{x_1, y_1, x_2, y_2, v\}$. We also define a function $H : (0,\infty) \to [0,\infty)$ as

$$H(z) = z - 1 - \ln z. \tag{2.24}$$

It is clear that $H(z) \geq 0$ for any $z > 0$ and H has the global minimum $H(1) = 0$.

Theorem 2.3. *If $R_0 \leq 1$, then E_0 is GAS.*

Proof. Define a Lyapunov functional W_1 as follows:

$$\begin{aligned} W_1 = \sum_{i=1}^{2} \gamma_i \Bigg[& x_i^0 H\left(\frac{x_i}{x_i^0}\right) + \frac{1}{F_i} y_i + \frac{\beta_i}{F_i} \int_0^\infty f_i(\tau) e^{-m_i\tau} \int_0^\tau \frac{x_i(t-\theta)v(t-\theta)}{1+\alpha_i v(t-\theta)} d\theta\, d\tau \\ & + \frac{a_i}{F_i G_i} \int_0^\infty g_i(\tau) e^{-n_i\tau} \int_0^\tau y_i(t-\theta) d\theta d\tau \Bigg] + v, \end{aligned} \tag{2.25}$$

where $\gamma_i = p_i F_i G_i / a_i$, $i = 1, 2$.

The time derivative of W_1 along the trajectories of (2.1)–(2.5) satisfies

$$\begin{aligned} \frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \Bigg[& \left(1 - \frac{x_i^0}{x_i}\right)\left(\lambda_i - d_i x_i - \frac{\beta_i x_i v}{1+\alpha_i v}\right) + \frac{\beta_i}{F_i} \int_0^\infty f_i(\tau) e^{-m_i\tau} \frac{x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)} d\tau \\ & - \frac{a_i}{F_i} y_i + \frac{\beta_i}{F_i} \int_0^\infty f_i(\tau) e^{-m_i\tau} \left(\frac{x_i v}{1+\alpha_i v} - \frac{x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)}\right) d\tau \\ & + \frac{a_i}{F_i G_i} \int_0^\infty g_i(\tau) e^{-n_i\tau} \left(y_i - y_i(t-\tau)\right) d\tau \Bigg] \\ & + \sum_{i=1}^{2} p_i \int_0^\infty g_i(\tau) e^{-n_i\tau} y_i(t-\tau) d\tau - cv. \end{aligned} \tag{2.26}$$

Collecting terms of (2.26) we get

$$\begin{aligned}\frac{dW_1}{dt} &= \sum_{i=1}^{2}\gamma_i\left(\lambda_i - d_i x_i - \lambda_i\frac{x_i^0}{x_i} + d_i x_i^0 + \frac{\beta_i x_i^0 v}{1+\alpha_i v}\right) - cv \\ &= \sum_{i=1}^{2}\gamma_i\lambda_i\left(2 - \frac{x_i}{x_i^0} - \frac{x_i^0}{x_i}\right) - cv + cv\sum_{i=1}^{2}\frac{F_i G_i p_i \beta_i x_i^0}{a_i c(1+\alpha_i v)} \\ &= -\sum_{i=1}^{2}\gamma_i d_i\frac{\left(x_i - x_i^0\right)^2}{x_i} - cv + cv\sum_{i=1}^{2}\frac{R_i}{1+\alpha_i v} \\ &= -\sum_{i=1}^{2}\gamma_i d_i\frac{\left(x_i - x_i^0\right)^2}{x_i} - \sum_{i=1}^{2}\frac{R_i\alpha_i c v^2}{1+\alpha_i v} + (R_0 - 1)cv.\end{aligned} \tag{2.27}$$

If $R_0 \le 1$ then $dW_1/dt \le 0$ for all $x_1, x_2, v > 0$. By Theorem 5.3.1 in [31], the solutions of system (2.1)–(2.5) limit to M, the largest invariant subset of $\{dW_1/dt = 0\}$. Clearly, it follows from (2.27) that $dW_1/dt = 0$ if and only if $x_i = x_i^0$, $i = 1, 2$, and $v = 0$. Noting that M is invariant, for each element of M we have $v = 0$, then $\dot{v} = 0$. From (2.5) we drive that

$$0 = \dot{v} = p_1\int_0^\infty g_1(\tau)e^{-n_1\tau}y_1(t-\tau)d\tau + p_2\int_0^\infty g_2(\tau)e^{-n_2\tau}y_2(t-\tau)d\tau. \tag{2.28}$$

This yields $y_1 = y_2 = 0$. Hence $dW_1/dt = 0$ if and only if $x_i = x_i^0$, $y_i = 0$, $i = 1, 2$, and $v = 0$. From La Salle's Invariance Principle, E_0 is GAS. □

Theorem 2.4. *If $R_0 > 1$, then E_1 is GAS.*

Proof. We construct the following Lyapunov functional:

$$\begin{aligned}W_2 = \sum_{i=1}^{2}\gamma_i\Bigg[&x_i^* H\left(\frac{x_i}{x_i^*}\right) + \frac{1}{F_i}y_i^* H\left(\frac{y_i}{y_i^*}\right) \\ &+ \frac{1}{F_i}\frac{\beta_i x_i^* v^*}{1+\alpha_i v^*}\int_0^\infty f_i(\tau)e^{-m_i\tau}\int_0^\tau H\left(\frac{x_i(t-\theta)v(t-\theta)(1+\alpha_i v^*)}{x_i^* v^*(1+\alpha_i v(t-\theta))}\right)d\theta\,d\tau \\ &+ \frac{a_i y_i^*}{F_i G_i}\int_0^\infty g_i(\tau)e^{-n_i\tau}\int_0^\tau H\left(\frac{y_i(t-\theta)}{y_i^*}\right)d\theta\,d\tau\Bigg] + v^* H\left(\frac{v}{v^*}\right).\end{aligned} \tag{2.29}$$

Differentiating with respect to time yields

$$\begin{aligned}\frac{dW_2}{dt} = \sum_{i=1}^{2}\gamma_i\Bigg[&\left(1 - \frac{x_i^*}{x_i}\right)\left(\lambda_i - d_i x_i - \frac{\beta_i x_i v}{1+\alpha_i v}\right) \\ &+ \frac{1}{F_i}\left(1 - \frac{y_i^*}{y_i}\right)\left(\beta_i\int_0^\infty f_i(\tau)e^{-m_i\tau}\frac{x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)}d\tau - a_i y_i\right)\end{aligned}$$

$$+\frac{\beta_i}{F_i}\int_0^\infty f_i(\tau)e^{-m_i\tau}$$
$$\times\left(\frac{x_i v}{1+\alpha_i v}-\frac{x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)}+\frac{x_i^* v^*}{1+\alpha_i v^*}\ln\left(\frac{x_i(t-\tau)v(t-\tau)(1+\alpha_i v)}{x_i v(1+\alpha_i v(t-\tau))}\right)\right)d\tau$$
$$+\frac{a_i}{F_i G_i}\int_0^\infty g_i(\tau)e^{-n_i\tau}\left(y_i-y_i(t-\tau)+y_i^*\ln\left(\frac{y_i(t-\tau)}{y_i}\right)\right)d\tau\Bigg]$$
$$+\left(1-\frac{v^*}{v}\right)\left(\sum_{i=1}^{2}p_i\int_0^\infty g_i(\tau)e^{-n_i\tau}y_i(t-\tau)d\tau-cv\right). \tag{2.30}$$

Collecting terms we obtain

$$\frac{dW_2}{dt}=\sum_{i=1}^{2}\gamma_i\Bigg[\lambda_i-d_i x_i-\frac{\lambda_i x_i^*}{x_i}+d_i x_i^*+\frac{\beta_i x_i^* v}{1+\alpha_i v}-\frac{\beta_i y_i^*}{F_i y_i}\int_0^\infty f_i(\tau)e^{-m_i\tau}\frac{x_i(t-\tau)v(t-\tau)}{1+\alpha_i v(t-\tau)}d\tau$$
$$+\frac{a_i}{F_i}y_i^*+\frac{1}{F_i}\frac{\beta_i x_i^* v^*}{1+\alpha_i v^*}\int_0^\infty f_i(\tau)e^{-m_i\tau}\ln\left(\frac{x_i(t-\tau)v(t-\tau)(1+\alpha_i v)}{x_i v(1+\alpha_i v(t-\tau))}\right)d\tau$$
$$+\frac{a_i y_i^*}{F_i G_i}\int_0^\infty g_i(\tau)e^{-n_i\tau}\ln\left(\frac{y_i(t-\tau)}{y_i}\right)d\tau\Bigg]-cv$$
$$-\frac{v^*}{v}\sum_{i=1}^{2}p_i\int_0^\infty g_i(\tau)e^{-n_i\tau}y_i(t-\tau)d\tau+cv^*. \tag{2.31}$$

Using the infected steady state conditions (2.14)–(2.16), and the following equality:

$$cv=cv^*\frac{v}{v^*}=\frac{v}{v^*}\sum_{i=1}^{2}G_i p_i y_i^*=\frac{v}{v^*}\sum_{i=1}^{2}\frac{\gamma_i a_i}{F_i}y_i^*, \tag{2.32}$$

we obtain

$$\frac{dW_2}{dt}=\sum_{i=1}^{2}\gamma_i\Bigg[d_i x_i^*+\frac{a_i}{F_i}y_i^*-d_i x_i-\frac{x_i^*}{x_i}\left(d_i x_i^*+\frac{a_i}{F_i}y_i^*\right)+d_i x_i^*+\frac{a_i}{F_i}y_i^*\frac{v(1+\alpha_i v^*)}{v^*(1+\alpha_i v)}$$
$$-\frac{a_i}{F_i^2}y_i^*\int_0^\infty f_i(\tau)e^{-m_i\tau}\frac{y_i^* x_i(t-\tau)v(t-\tau)(1+\alpha_i v^*)}{y_i x_i^* v^*(1+\alpha_i v(t-\tau))}d\tau+\frac{a_i}{F_i}y_i^*$$
$$+\frac{a_i}{F_i^2}y_i^*\int_0^\infty f_i(\tau)e^{-m_i\tau}\ln\left(\frac{x_i(t-\tau)v(t-\tau)(1+\alpha_i v)}{x_i v(1+\alpha_i v(t-\tau))}\right)d\tau$$

$$+\frac{a_i}{F_iG_i}y_i^*\int_0^\infty g_i(\tau)e^{-n_i\tau}\ln\left(\frac{y_i(t-\tau)}{y_i}\right)d\tau$$
$$-\frac{a_i}{F_i}y_i^*\frac{v}{v^*}-\frac{a_i}{F_iG_i}y_i^*\int_0^\infty g_i(\tau)e^{-n_i\tau}\frac{v^*y_i(t-\tau)}{vy_i^*}d\tau+\frac{a_i}{F_i}y_i^*\Bigg]. \tag{2.33}$$

Then collecting terms of (2.33) and using the following equalities:

$$\begin{aligned}\ln\left(\frac{x_i(t-\tau)v(t-\tau)(1+\alpha_iv)}{x_iv(1+\alpha_iv(t-\tau))}\right) &= \ln\left(\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_iv^*)}{y_ix_i^*v^*(1+\alpha_iv(t-\tau))}\right)+\ln\left(\frac{x_i^*}{x_i}\right)\\ &\quad+\ln\left(\frac{v^*y_i}{vy_i^*}\right)+\ln\left(\frac{1+\alpha_iv}{1+\alpha_iv^*}\right),\quad i=1,2,\\ \ln\left(\frac{y_i(t-\tau)}{y_i}\right)&=\ln\left(\frac{vy_i^*}{v^*y_i}\right)+\ln\left(\frac{v^*y_i(t-\tau)}{vy_i^*}\right),\quad i=1,2\\ \ln\left(\frac{v^*y_i}{vy_i^*}\right)&+\ln\left(\frac{vy_i^*}{v^*y_i}\right)=\ln(1)=0,\quad i=1,2\end{aligned} \tag{2.34}$$

we obtain

$$\begin{aligned}\frac{dW_2}{dt}=\sum_{i=1}^{2}\gamma_i\Bigg[&d_ix_i^*\left(2-\frac{x_i^*}{x_i}-\frac{x_i}{x_i^*}\right)+\frac{a_i}{F_i}y_i^*\left(1-\frac{x_i^*}{x_i}\right)+\frac{2a_i}{F_i}y_i^*\\ &+\frac{a_i}{F_i}y_i^*\left(\frac{v(1+\alpha_iv^*)}{v^*(1+\alpha_iv)}-\frac{v}{v^*}\right)-\frac{a_i}{F_i^2}y_i^*\int_0^\infty f_i(\tau)e^{-m_i\tau}\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_iv^*)}{y_ix_i^*v^*(1+\alpha_iv(t-\tau))}d\tau\\ &+\frac{a_i}{F_i^2}y_i^*\int_0^\infty f_i(\tau)e^{-m_i\tau}\\ &\times\left(\ln\left(\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_iv^*)}{y_ix_i^*v^*(1+\alpha_iv(t-\tau))}\right)+\ln\left(\frac{x_i^*}{x_i}\right)+\ln\left(\frac{v^*y_i}{vy_i^*}\right)+\ln\left(\frac{1+\alpha_iv}{1+\alpha_iv^*}\right)\right)d\tau\\ &+\frac{a_i}{F_iG_i}y_i^*\int_0^\infty g_i(\tau)e^{-n_i\tau}\left(\ln\left(\frac{vy_i^*}{v^*y_i}\right)+\ln\left(\frac{v^*y_i(t-\tau)}{vy_i^*}\right)\right)d\tau\\ &-\frac{a_i}{F_iG_i}y_i^*\int_0^\infty g_i(\tau)e^{-n_i\tau}\frac{v^*y_i(t-\tau)}{vy_i^*}d\tau\Bigg].\end{aligned} \tag{2.35}$$

Equation (2.35) can be rewritten as

$$\begin{aligned}\frac{dW_2}{dt} = \sum_{i=1}^{2}\gamma_i\Bigg[&d_i x_i^*\left(2-\frac{x_i^*}{x_i}-\frac{x_i}{x_i^*}\right)-\frac{a_i}{F_i}y_i^*\left(\frac{x_i^*}{x_i}-1-\ln\left(\frac{x_i^*}{x_i}\right)\right)\\&+\frac{a_i}{F_i}y_i^*\left(-1+\frac{v(1+\alpha_i v^*)}{v^*(1+\alpha_i v)}-\frac{v}{v^*}+\frac{1+\alpha_i v}{1+\alpha_i v^*}\right)\\&-\frac{a_i}{F_i}y_i^*\left(\frac{1+\alpha_i v}{1+\alpha_i v^*}-1-\ln\left(\frac{1+\alpha_i v}{1+\alpha_i v^*}\right)\right)\\&-\frac{a_i}{F_i^2}y_i^*\int_0^\infty f_i(\tau)e^{-m_i\tau}\\&\times\left(\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_i v^*)}{y_i x_i^* v^*(1+\alpha_i v(t-\tau))}-1-\ln\left(\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_i v^*)}{y_i x_i^* v^*(1+\alpha_i v(t-\tau))}\right)\right)d\tau\\&-\frac{a_i}{F_iG_i}y_i^*\int_0^\infty g_i(\tau)e^{-n_i\tau}\left(\frac{v^*y_i(t-\tau)}{vy_i^*}-1-\ln\left(\frac{v^*y_i(t-\tau)}{vy_i^*}\right)\right)d\tau\Bigg].\end{aligned} \tag{2.36}$$

Using the following equality:

$$-1+\frac{v(1+\alpha_i v^*)}{v^*(1+\alpha_i v)}-\frac{v}{v^*}+\frac{1+\alpha_i v}{1+\alpha_i v^*}=\frac{-\alpha_i(v-v^*)^2}{v^*(1+\alpha_i v^*)(1+\alpha_i v)},\quad i=1,2, \tag{2.37}$$

we can rewrite dW_2/dt as

$$\begin{aligned}\frac{dW_2}{dt} = -\sum_{i=1}^{2}\gamma_i\Bigg[&d_i\frac{(x_i-x_i^*)^2}{x_i}+\frac{a_i}{F_i}y_i^*\frac{\alpha_i(v-v^*)^2}{v^*(1+\alpha_i v^*)(1+\alpha_i v)}\\&+\frac{a_i}{F_i}y_i^*H\left(\frac{x_i^*}{x_i}\right)+\frac{a_i}{F_i}y_i^*H\left(\frac{1+\alpha_i v}{1+\alpha_i v^*}\right)\\&+\frac{a_iy_i^*}{F_i^2}\int_0^\infty f_i(\tau)e^{-m_i\tau}H\left(\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_i v^*)}{y_i x_i^* v^*(1+\alpha_i v(t-\tau))}\right)d\tau\\&+\frac{a_iy_i^*}{F_iG_i}\int_0^\infty g_i(\tau)e^{-n_i\tau}H\left(\frac{v^*y_i(t-\tau)}{vy_i^*}\right)d\tau\Bigg].\end{aligned} \tag{2.38}$$

It is easy to see that if $x_i^*, y_i^*, v^* > 0$, $i = 1, 2$, then $dW_2/dt \le 0$. By Theorem 5.3.1 in [31], the solutions of system (2.1)–(2.5) limit to M, the largest invariant subset of $\{dW_2/dt = 0\}$. It can be seen that $dW_2/dt = 0$ if and only if $x_i = x_i^*$, $v = v^*$, and $H = 0$, that is,

$$\frac{y_i^*x_i(t-\tau)v(t-\tau)(1+\alpha_i v^*)}{y_i x_i^* v^*(1+\alpha_i v(t-\tau))}=\frac{v^*y_i(t-\tau)}{vy_i^*}=1\quad\text{for almost all } \tau\in(0,\infty). \tag{2.39}$$

If $v = v^*$ then from (2.39) we have $y_i = y_i^*$, and hence dW_2/dt equal to zero at E_1. LaSalle's Invariance Principle implies global stability of E_1. □

3. Conclusion

In this paper, we have proposed an HIV infection model describing the interaction of the HIV with two classes of target cells, $CD4^+$ T cells and macrophages taking into account the saturation infection rate. Two types of distributed time delays describing time needed for infection of target cell and virus replication have been incorporated into the model. The global stability of the uninfected and infected steady states of the model has been established by using suitable Lyapunov functionals and LaSalle invariant principle. We have proven that, if the basic reproduction number R_0 is less than unity, then the uninfected steady state is GAS and if $R_0 > 1$, then the infected steady state exists and it is GAS.

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