GLOBAL STABILITY OF HIV INFECTION MODELS WITH INTRACELLULAR DELAYS

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ABSTRACT. In this paper, we study the global stability of two mathematical models for human immunodeficiency virus (HIV) infection with intracellular delays. The first 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 taking into account the saturation infection rate. The second model generalizes the first one by assuming that the infection rate is given by Beddington-DeAngelis functional response. Two time delays are used to describe the time periods between viral entry the two classes of target cells and the production of new virus particles. Lyapunov functionals are constructed and LaSalle-type theorem for delay differential equation is used to establish the global asymptotic stability of the uninfected and infected steady states of the HIV infection models. 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 the infected steady state exists, then it is globally asymptotically stable for all time delays.

1. Introduction

Modelling, analysis and control of human immunodeficiency virus (HIV) infection have attracted the interests of mathematicians during the recent years. Several mathematical models exist and adequately explain the interaction of the HIV infection and the immune system up to the stage of clinical latency, as well as viral suppression and immune system recovery after treatment therapy [18]. Some of these models are given by a system of nonlinear ODEs. These models are based on the assumption that, once the virus contacts a target cell, the cell begins producing new virus particles. However in real situation there is a lag between the time of viral entry a target cell and the time of producing new virus particles from the same target cell. Therefore, more accurate models have been proposed which are given by a system of nonlinear delay ODEs to account the intracellular time delay. The first HIV infection model accounting...
the intracellular time delay which represents the time between viral entry into a target cell and the production of new virus particles was proposed in 1996 by Herz et al. [7]. Thereafter, various models using discrete or distributed delays to model the intracellular phase were developed (see e.g. [2], [9], [10], [11], [12], [13], [14], [16], [17], [24], [27]). The basic HIV infection model with intracellular delay can be given in a general form as:

\[ \dot{x}(t) = f(x(t), x_1(t)) - g(x(t), v(t)), \]  
\[ \dot{x}_1(t) = e^{-\nu \tau} g(x(t - \tau), v(t - \tau)) - ax_1(t), \]  
\[ \dot{v}(t) = px_1(t) - rv(t), \]  

where \( x(t), x_1(t) \) and \( v(t) \), represent the concentrations of the uninfected CD4\(^+\) T cells, infected CD4\(^+\) T cells and free virus particles, respectively. The function \( f(x, x_1) \) represents the growth rate of the uninfected CD4\(^+\) T cells and has been used in the literature in delayed HIV infection models in different forms:

- Growth rate without proliferation ([9], [11], [12], [14], [16], [17], [24], [27]):
  \[ f(x, x_1) = \lambda - dx. \]

- Growth rate with simple proliferation ([21], [23], [25]):
  \[ f(x, x_1) = \lambda - dx + \alpha \left( 1 - \frac{x}{x_{\text{max}}} \right). \]

- Growth rate with full proliferation ([2], [8]):
  \[ f(x, x_1) = \lambda - dx + \alpha \left( 1 - \frac{x + x_1}{x_{\text{max}}} \right). \]

The function \( g(x, v) \) represents the incidence rate infection and it has been considered in the delayed HIV infection models by different forms:

- Bilinear incidence rate ([7], [8], [12], [14], [16]):
  \[ g(x, v) = \beta xv. \]

- Saturated incidence rate ([11], [23], [27]):
  \[ g(x, v) = \frac{\beta xv}{1 + b_1 v}. \]

- Beddington-DeAngelis infection rate ([9], [14], [24]):
  \[ g(x, v) = \frac{\beta xv}{1 + a_1 x + b_1 v}. \]

Parameters \( \lambda, d, \alpha, x_{\text{max}}, \beta, a, p, r, a_1 \) and \( b_1 \) are positive constants. Here, \( \lambda \) represents the rate of which new CD4\(^+\) T cells are generated from sources within the body, \( d \) is the death rate constant, \( \alpha \) is the maximum proliferation rate of CD4\(^+\) T cells, \( x_{\text{max}} \) is maximum level of CD4\(^+\) T cells concentration in the body, and \( \beta \) is the rate constant characterizing infection of the cells. Eq.(2) describes the population dynamics of the infected CD4\(^+\) T cells and shows that they die with rate constant \( a \). The virus particles are produced by
the infected CD4\(^+\) T cells with rate constant \(p\), and are cleared from plasma with rate constant \(r\). The parameter \(\tau\) accounts for the time between viral entry into the CD4\(^+\) T cell and the production of new virus particles. The recruitment of virus producing cells at time \(t\) is given by the number of cells that were newly infected CD4\(^+\) T cells at time \(t - \tau\) and are still alive at time \(t\). If we assume a constant death rate \(m\) for infected CD4\(^+\) T cells but not yet virus-producing cells, the probability of surviving the time period from \(t - \tau\) to \(t\) is \(e^{-m\tau}\).

One extension of the basic delayed model (1)-(3) has been introduced by taking into account the Cytotoxic T Lymphocytes (CTL) immune response [15], [21], [22] and [26]. The role of CTL cells is to attack the infected cells. Another extension includes the addition of antiretroviral drug therapies [28] and [25]. A great effort has been devoted to study the basic and global properties of the HIV infection models with delay such as positive invariance properties, boundedness of the model solutions and stability analysis which are important for understanding the associated characteristics of the HIV dynamics (see e.g. [9], [11], [12], [14], [15], [23] and [27]).

All of the above mentioned delayed HIV infection models are mainly modelled the interaction of the HIV with one target cells, CD4\(^+\) T cells. Perelson et al., observed that after the rapid first phase of decay during the initial 1-2 weeks of antiretroviral treatment, plasma virus levels declined at a considerably slower rate [19]. This second phase of viral decay was attributed to the turnover of a longer-lived virus reservoir of infected cells. These cells are called macrophages and considered as the second target cell for the HIV. Therefore, the two target cells model is more accurate than the one target cells model (see [1] and [20]). Some HIV infection models exist to describe the interaction process of the HIV not only with the CD4\(^+\) T cells but also with the macrophages which are the crucial immune responses and play important roles in phagocytosis (see e.g. [1] and [20]). In very recent works ([3], [4] and [5]), we have proposed several HIV infection models with two target cells and investigated the global asymptotic stability of their steady states. However the intracellular time delay is neglected in these papers.

The purpose of the present paper is to study the global stability of two HIV infection models with two classes of target cells and delays. The first model is a 5-dimensional nonlinear delayed ODEs that describes the interaction of the HIV with two target cells, CD4\(^+\) T cells and macrophages taking into account the saturation infection rate. In the second model, the incidence rate is given by Beddington-DeAngelis functional response. The global stability of these models is established using Lyapunov functionals, which are similar in nature to those used in [10] and [27]. By constructing explicit Lyapunov functionals, 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). If the infected steady state exists, then it is GAS for all time delays.
1.1. HIV infection model with saturation infection rate

We shall use the mathematical model of HIV infection proposed by ([1] and [20]), incorporating to take into account the intracellular delays and saturation infection rate. This model describes two co-circulation populations of target cells, potentially representing CD4$^+$ T cells and macrophages and given by:

\begin{align}
\dot{x}(t) &= \lambda_1 - d_1 x(t) - \frac{\beta_1 x(t)v(t)}{1 + v(t)}, \\
\dot{x}_1(t) &= e^{-m_1 \tau_1} \frac{\beta_1 x(t-\tau_1)v(t-\tau_1)}{1 + v(t-\tau_1)} - ax_1(t), \\
\dot{y}(t) &= \lambda_2 - d_2 y(t) - \frac{\beta_2 y(t)v(t)}{1 + v(t)}, \\
\dot{y}_1(t) &= e^{-m_2 \tau_2} \frac{\beta_2 y(t-\tau_2)v(t-\tau_2)}{1 + v(t-\tau_2)} - \delta y_1(t), \\
\dot{v}(t) &= p_1 x_1(t) + p_2 y_1(t) - rv(t),
\end{align}

where $y$ and $y_1$ are the concentrations of the uninfected and infected macrophages, respectively. The populations of the macrophages are described by Eq.(6), where $\lambda_2$ represents the rate of which new macrophages cells are generated from sources within the body; $d_2$ is the death rate constant, and $\beta_2$ is the infection rate constant. In Eq.(7), $\delta$ is the death rate constant of the infected macrophages. The virus particles are produced by the infected CD4$^+$ T cells and infected macrophages with rate constants $p_1$ and $p_2$, respectively. Here parameters $\tau_1$ and $\tau_2$ account for the times between viral entry into CD4$^+$ T and macrophages cells, respectively, and the production of new virus particles. Also, $m_1$ and $m_2$ are assumed to be the constant death rates for infected CD4$^+$ T and macrophages cells, respectively, but not yet virus-producing cells. Thus, the probability of surviving the time period from $t - \tau_i$ to $t$ is $e^{-m_i \tau_i}$, $i = 1, 2$.

The other variables and parameters have the same biological meaning as given in model (1)-(3). All the parameters of the model are supposed to be positive.

1.2. Initial conditions

The initial conditions for system (4)-(8) take the form

\begin{align}
&x(\theta) = \varphi_1(\theta), \quad x_1(\theta) = \varphi_2(\theta), \quad y(\theta) = \varphi_3(\theta), \quad y_1(\theta) = \varphi_4(\theta), \quad v(\theta) = \varphi_5(\theta), \\
&\varphi_i(\theta) \geq 0, \quad \theta \in [-\max{\{\tau_1, \tau_2\}}, 0), \quad \varphi_i(0) > 0, \quad i = 1, \ldots, 5,
\end{align}

where $(\varphi_1(\theta), \ldots, \varphi_5(\theta)) \in C([-\max{\{\tau_1, \tau_2\}}, 0], \mathbb{R}_+^5)$, $C$ is the Banach space of continuous functions mapping the interval $[-\max{\{\tau_1, \tau_2\}}, 0]$ into $\mathbb{R}_+^5$.

By the fundamental theory of functional differential equations [6], system (4)-(8) has a unique solution $(x(t), x_1(t), y(t), y_1(t), v(t))$ satisfying the initial conditions (9).
1.3. Positivity and boundedness

It is easy to show that all solutions of system (4)-(8) with initial conditions (9) are defined on \([0, \infty)\) and remain positive for all \(t \geq 0\) (see [9] and [12]).

**Proposition 1.** The solution of (4)-(8) with the initial conditions (9) is ultimately bounded.

*Proof.* Let \(X(t) = e^{-m_1 \tau_1} x(t - \tau_1) + x_1(t)\) and \(Y(t) = e^{-m_2 \tau_2} y(t - \tau_2) + y_1(t)\). Then

\[
\dot{X}(t) \leq \lambda_1 e^{-m_1 \tau_1} - \sigma_1 X(t),
\]

\[
\dot{Y}(t) \leq \lambda_2 e^{-m_2 \tau_2} - \sigma_2 Y(t),
\]

where \(\sigma_1 = \min\{d_1, \alpha\}\) and \(\sigma_2 = \min\{d_2, \delta\}\). Hence \(\limsup_{t \to \infty} X(t) \leq L_1\), and \(\limsup_{t \to \infty} Y(t) \leq L_2\), where \(L_1 = \frac{\lambda_1 e^{-m_1 \tau_1}}{\sigma_1}\) and \(L_2 = \frac{\lambda_2 e^{-m_2 \tau_2}}{\sigma_2}\). On the other hand,

\[
\dot{v}(t) \leq p_1 L_1 + p_2 L_2 - rv,
\]

then \(\limsup_{t \to \infty} v(t) \leq L_3\), where \(L_3 = \frac{\alpha L_1 + p_2 L_2}{r}\). It follows that the solution of (4)-(8) is ultimately bounded. \(\Box\)

1.4. Steady states

The dynamics of system (4)-(8) crucially depends on the basic reproduction number \(R_0\) given by

\[
R_0 = \frac{e^{-m_1 \tau_1} p_1 \beta_1 \delta x_0 + e^{-m_2 \tau_2} p_2 \beta_2 \gamma y_0}{a \delta r},
\]

where \(x_0 = \frac{\lambda_1}{\delta_1}\), \(y_0 = \frac{\lambda_2}{\delta_2}\). We note that \(R_0\) can be written as:

\[
R_0 = R_1 + R_2,
\]

where

\[
R_1 = \frac{e^{-m_1 \tau_1} p_1 \beta_1 x_0}{a r}, \quad R_2 = \frac{e^{-m_2 \tau_2} p_2 \beta_2 y_0}{\delta r},
\]

are the basic reproduction numbers of each T-cell and macrophages dynamics separately (see [3], [5]).

It is clear that, system (4)-(8) has an uninfected steady state \(E_0 = (x_0, 0, y_0, 0, 0)\). The system can also has a positive infected steady state \(E_1(x^*, x_1^*, y^*, y_1^*, v^*)\). The coordinates of the infected steady state, if they exist, satisfy the equalities:

\[
\lambda_1 = d_1 x^* + \frac{\beta_1 x^* v^*}{1 + v^*}, \quad \lambda_2 = d_2 y^* + \frac{\beta_2 y^* v^*}{1 + v^*},
\]

\[
ax_1^* e^{m_1 \tau_1} = \frac{\beta_1 x^* v^*}{1 + v^*}, \quad \delta y_1^* e^{m_2 \tau_2} = \frac{\beta_2 y^* v^*}{1 + v^*}, \quad rv^* = p_1 x_1^* + p_2 y_1^*.
\]

(10)
1.5. Global stability analysis

In this section, we shall consider the global stability of the uninfected and infected steady states of (4)-(8) by the Lyapunov direct method. To simplify the presentation we shall use the following notation: \( z = z(t), z_i = z(t - \tau_i), i = 1, 2 \), for any \( z \in \{x, x_1, y, y_1, v\} \). We also define a function \( F : \mathbb{R}_+ \to \mathbb{R}_+ \) as

\[
F(z) = z - 1 - \ln z.
\]

We note that \( F(z) \geq 0 \) for any \( z > 0 \) and has the global minimum \( F(1) = 0 \).

**Theorem 1.** (i) If \( R_0 \leq 1 \), then \( E_0 \) is GAS for any \( \tau_1, \tau_2 \geq 0 \).

(ii) If \( E_1 \) exists, then it is GAS for any \( \tau_1, \tau_2 \geq 0 \).

**Proof.** (i) We consider a Lyapunov functional

\[
W_i = x_iF\left(\frac{x_i}{x_0}\right) + e^{m_1}x_1 + \gamma \left[y_0F\left(\frac{y_0}{y}\right) + e^{m_2}y_1\right] + \frac{a}{p_i}e^{m_1}\tau_1,
\]

where \( \gamma = \frac{\rho_{gs}e^{m_1}}{p_i e^{-m_2}} \). We note that \( W_i \) is defined, continuous and positive definite for all \( (x, x_1, y, y_1, v) > 0 \) and \( \theta \in [0, \max\{\tau_1, \tau_2\}] \). Also, the global minimum \( W_1 = 0 \) occurs at the uninfected steady state \( E_0 \). Further, function \( W_1 \) along the trajectories of (4)-(8) satisfies

\[
\frac{dW_1}{dt} = \left(1 - \frac{x_0}{x}\right) \left(\lambda_1 - d_1 x - \frac{\beta_1 x v}{1 + v}\right) + e^{m_1}x_1 \left(e^{-m_1} - \frac{\beta_1 x_1 v \tau_1}{1 + v \tau_1} - ax_1\right)
\]

\[
+ \gamma \left[1 - \frac{y_0}{y}\right] \left(\lambda_2 - d_2 y - \frac{\beta_2 y v}{1 + v}\right) + e^{m_2}y_1 \left(e^{-m_2} - \frac{\beta_2 y_1 v \tau_2}{1 + v \tau_2} - ay_1\right)
\]

\[
+ \frac{a}{p_i}e^{m_1}x_1 + \frac{p_1y_1 - rv}{1 + v} - \frac{\beta_1 x_1 v \tau_1}{1 + v \tau_1} + \frac{\beta_1 x_1 v \tau_1}{1 + v \tau_1} + \gamma \frac{\beta_2 y_1 v \tau_2}{1 + v \tau_2} - \frac{\beta_2 y_1 v \tau_2}{1 + v \tau_2},
\]

\[
= \lambda_1 - d_1 x - \frac{x_0}{x} \left(\lambda_1 - d_1 x - \frac{\beta_1 x v}{1 + v}\right)
\]

\[
+ \gamma \left[\lambda_2 - d_2 y - \frac{y_0}{y}\left(\lambda_2 - d_2 y - \frac{\beta_2 y v}{1 + v}\right)\right] - \frac{ar}{p_i}e^{m_1}\tau_1 v
\]

\[
= \lambda_1 \left[2 - \frac{x_0}{x} - \frac{x}{x_0}\right] + \gamma \lambda_2 \left[2 - \frac{y_0}{y} - \frac{y}{y_0}\right] + \frac{\beta_1 x_0 v}{1 + v} - \frac{\beta_2 y_0 v}{1 + v} + \gamma \frac{\beta_2 y_0 v}{1 + v}
\]

\[
= \lambda_1 \left[2 - \frac{x_0}{x} - \frac{x}{x_0}\right] + \gamma \lambda_2 \left[2 - \frac{y_0}{y} - \frac{y}{y_0}\right] + \frac{ar e^{m_1} \tau_1 v}{p_i (1 + v)} + \frac{e^{m_1} \tau_1 p_1 \beta_1 x_0}{ar} + \frac{e^{-m_2} p_2 \beta_2 y_0}{\delta r} - 1 - \frac{ar e^{m_1} \tau_1 v^2}{p_i (1 + v)}
\]
\[ e^{\lambda_1 \left[ 2 - \frac{x_0}{x} - \frac{x}{x_0} \right]} + \gamma e^{\lambda_2 \left[ 2 - \frac{y_0}{y} - \frac{y}{y_0} \right]} + \frac{ae^{m_1 \tau_1} v}{p_1(1 + v)}(R_0 - 1) - \frac{ae^{m_1 \tau_1} v^2}{p_1(1 + v)} \]

Since the arithmetical mean is greater than or equal to the geometrical mean, then the first two terms of (11) are less than or equal to zero. Therefore, if \( R_0 \leq 1 \), then \( \frac{dW_2}{dt} \leq 0 \) for all \( x, x_1, y, y_1, v > 0 \). By Theorem 5.3.1 in [6], the solutions of system (4)-(8) limit to \( M \), the largest invariant subset of \( \{ \frac{dW_2}{dt} = 0 \} \). Clearly, it follows from (11) that \( \frac{dW_2}{dt} = 0 \) if and only if \( x = x_0, y = y_0, v = 0 \). Each element of \( M \) satisfies \( x = x_0, y = y_0, v = 0 \) for all \( t \), then \( \dot{v} = 0 \). From Eq.(8) we drive that

\[ 0 = \dot{v} = p_1 x_1 + p_2 y_1. \]

Since \( x_1, y_1 \geq 0 \), then \( p_1 x_1 + p_2 y_1 = 0 \) if and only if \( x_1 = y_1 = 0 \). Hence \( \frac{dW_2}{dt} = 0 \) if and only if \( x = x_0, y = y_0, x_1 = y_1 = v = 0 \). From LaSalle’s Invariance Principle, \( E_0 \) is GAS for any \( \tau_1, \tau_2 \geq 0 \).

(ii) Define a Lyapunov functional

\[ W_2 = x^* F \left( \frac{x}{x^*} \right) + e^{m_1 \tau_1} x_1^* F \left( \frac{x_1}{x_1^*} \right) + \gamma \left[ y^* F \left( \frac{y}{y^*} \right) + e^{m_2 \tau_2} y_1^* F \left( \frac{y_1}{y_1^*} \right) \right] + \frac{a}{p_1} e^{m_1 \tau_1} v^* F \left( \frac{v}{v^*} \right) + \frac{\beta_1 x^* v^*}{1 + v^*} \int_0^{\tau_2} F \left( \frac{x(t - \theta)v(t - \theta)(1 + v^*)}{x^* v^*(1 + v(t - \theta))} \right) d\theta + \frac{\beta_2 y^* v^*}{1 + v^*} \int_0^{\tau_2} F \left( \frac{y(t - \theta)v(t - \theta)(1 + v^*)}{y^* v^*(1 + v(t - \theta))} \right) d\theta. \]

It is easy to see that \( W_2 \geq 0 \) and \( W_2 = 0 \) if and only if \( (x, x_1, y, y_1, v) \) take the steady state value \( (x^*, x_1^*, y^*, y_1^*, v^*) \) and \( x(t - \theta) = x^*, y(t - \theta) = y^*, v(t - \theta) = v^* \) for all \( \theta \in [0, \max\{\tau_1, \tau_2\}] \).

Differentiating with respect to time yields

\[ \frac{dW_2}{dt} = \left( 1 - \frac{x^*}{x} \right) (e^{m_1 \tau_1} (1 - \frac{x_1}{x_1^*}) (e^{-m_1 \tau_1} \frac{\beta_1 x_1 \tau_1}{1 + v_1} - ax) + \gamma \left( (1 - \frac{y^*}{y}) (e^{m_2 \tau_2} (1 - \frac{y_1}{y_1^*}) (e^{-m_2 \tau_2} \frac{\beta_2 y_1 \tau_2}{1 + v_2} - \delta y) + \frac{a}{p_1} e^{m_1 \tau_1} (1 - \frac{v^*}{v}) (p_1 x_1 + p_2 y_1 - rv) + \frac{\beta_1 x \tau_1}{1 + v} + \frac{\beta_1 x \tau_1}{1 + v} + \frac{\beta_1 x \tau_1}{v} + \frac{\beta_1 x \tau_1}{v} + \frac{x \tau_1}{v} (1 + v) \right) \]

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\[ + \gamma \left[ \frac{\beta_2 y v}{1 + v} - \frac{\beta_2 y_{r_2} v_{r_2}}{1 + v_{r_2}} + \frac{\beta_2 y^* v^*}{1 + v^*} \ln \left( \frac{y_{r_2} v_{r_2}(1 + v)}{y v(1 + v_{r_2})} \right) \right] . \]

Using the infected steady state conditions (10) and the following equality
\[
\frac{ar}{p_1} e^{m_{1r_1} v} = \frac{ar}{p_1} e^{m_{1r_1} v^*} = \frac{a}{p_1} e^{m_{1r_1} (p_1 x_1^* + p_2 y_1^*) v^*} = a x_1^* e^{m_{1r_1} v^*} + \gamma \delta y_1^* e^{m_{2r_2} v^*},
\]
we obtain
\[
\frac{dW_2}{dt} = d_1 x^* - d_1 x - \frac{x^*}{x} (d_1 x^* + a x_1^* e^{m_{1r_1}} - d_1 x) + \frac{\beta_1 x^* v}{1 + v} - \frac{x_1^* \beta_1 x_1 v_{r_1}}{1 + v_{r_1}}
\]
\[+ 3 a x_1^* e^{m_{1r_1}} - a x_1^* e^{m_{1r_1}} \frac{v}{v^*} - a x_1^* e^{m_{1r_1}} \frac{v x_1}{v x_1} \]
\[+ \gamma \left[ d_2 y^* - d_2 y - \frac{y^*}{y} (d_2 y^* + \delta y_1^* e^{m_{2r_2}} - d_2 y) \right] \]
\[+ \gamma \left[ \frac{\beta_2 y v}{1 + v} - \frac{y_1^* \beta_2 y_{r_2} v_{r_2}}{1 + v_{r_2}} + 3 \delta y_1^* e^{m_{2r_2}} - \delta y_1^* e^{m_{2r_2}} \frac{v}{v^*} - \delta y_1^* e^{m_{2r_2}} \frac{v y_1^*}{y_1^*} \right] \]
\[+ a x_1^* e^{m_{1r_1}} \ln \left( \frac{x_{r_2} v_{r_2}(1 + v)}{x v(1 + v_{r_1})} \right) + \gamma \delta y_1^* e^{m_{2r_2}} \ln \left( \frac{y_{r_2} v_{r_2}(1 + v)}{y v(1 + v_{r_2})} \right) \]
\[= d_1 x^* \left( 2 - \frac{x^*}{x} - x^* \right) - a x_1^* e^{m_{1r_1}} \frac{x^*}{x} + a x_1^* e^{m_{1r_1}} \frac{v}{v^*} (1 + v^*)
\]
\[- a x_1^* e^{m_{1r_1}} x_1^* v_{r_1}(1 + v^*) \frac{x_1^* v_{r_1}}{x_1^* v_{r_1} v(1 + v_{r_1})} + 3 a x_1^* e^{m_{1r_1}} - a x_1^* e^{m_{1r_1}} \frac{v}{v^*}
\]
\[- a x_1^* e^{m_{1r_1}} \frac{v x_1}{v x_1} + a x_1^* e^{m_{1r_1}} \ln \left( \frac{x_{r_2} v_{r_2}(1 + v)}{x v(1 + v_{r_1})} \right) \]
\[+ \gamma \left[ d_2 y^* \left( 2 - \frac{y^*}{y} - \frac{y^*}{y} \right) - \delta y_1^* e^{m_{2r_2}} \frac{y^*}{y} + \delta y_1^* e^{m_{2r_2}} \frac{v}{v^*} (1 + v^*)
\]
\[= - \delta y_1^* e^{m_{2r_2}} \frac{v y_1^*}{y_1^*} + \delta y_1^* e^{m_{2r_2}} \ln \left( \frac{y_{r_2} v_{r_2}(1 + v)}{y v(1 + v_{r_2})} \right) \right] ,
\]
and using also the following equalities
\[
\ln \left( \frac{x_{r_2} v_{r_2}(1 + v)}{x v(1 + v_{r_1})} \right) = \ln \left( \frac{x^*}{x} \right) + \ln \left( \frac{x_1^* v^*}{x_1^* v} \right) + \ln \left( \frac{x_1^* x_{r_2} v_{r_2}(1 + v^*)}{x_1^* v_{r_1} v(1 + v_{r_1})} \right)
\]
\[+ \ln \left( \frac{1 + v}{1 + v^*} \right) ,
\]
\[
\ln \left( \frac{y_{r_2} v_{r_2}(1 + v)}{y v(1 + v_{r_2})} \right) = \ln \left( \frac{y^*}{y} \right) + \ln \left( \frac{y y_1^*}{y_1^*} \right) + \ln \left( \frac{y y_{r_2} v_{r_2}(1 + v^*)}{y_1 y y_{r_2} v_{r_2}(1 + v_{r_2})} \right) .
\]
we get

\[
\begin{aligned}
-1 - \frac{v}{v^*} + \frac{v}{v^*(1 + v)} + \frac{1 + v}{1 + v^*} = -\frac{(v - v^*)^2}{v^*(1 + v)(1 + v^*)}.
\end{aligned}
\]

Since the arithmetical mean is greater than or equal to the geometrical mean, then the first two terms of (12) are less than or equal to zero. It is easy to see that if \(x^*, x^*_1, y^*, y^*_1, v^* > 0\), then \(\frac{dW_2}{dt} \leq 0\). By Theorem 5.3.1 in [6], the solutions of system (4)-(8) limit to \(M\), the largest invariant subset of \(\{\frac{dW_2}{dt} = 0\}\).

It can be seen that \(\frac{dW_2}{dt} = 0\) if and only if \(x = x^*, y = y^*, v = v^*,\) and \(F = 0\) i.e.,

\[
\begin{aligned}
\frac{x_1v^*}{x_1^*v} = \frac{y_1v^*}{y_1^*v} = \frac{x_1^*x_1, v_1(1 + v^*)}{x_1x^*v^*(1 + v_1)} = \frac{y_1^*y_2v_2(1 + v^*)}{y_1y^*v^*(1 + v_2)} = 1.
\end{aligned}
\]

If \(v = v^*\), then from (13) we have \(x_1 = x_1^*\) and \(y_1 = y_1^*\). LaSalle’s Invariance Principle implies global stability of \(E_1\). \(\-boxed{}\)

2. HIV infection model with Beddington-DeAngelis functional response

In this section we study the global stability of HIV infection model with two target cells and delays by assuming that the infection rate is given by the Beddington-DeAngelis functional response:

\[
\begin{aligned}
\dot{x}(t) &= \lambda_1 - d_1x(t) - \frac{\beta_1x(t)v(t)}{1 + a_1x(t) + b_1v(t)}, \\
\dot{x}_1(t) &= e^{-m_1\tau_1} \frac{\beta_1x(t - \tau_1)v(t - \tau_1)}{1 + a_1x(t - \tau_1) + b_1v(t - \tau_1)} - ax_1(t), \\
\dot{y}(t) &= \lambda_2 - d_2y(t) - \frac{\beta_2y(t)v(t)}{1 + a_2y(t) + b_2v(t)}, \\
\dot{y}_1(t) &= e^{-m_2\tau_2} \frac{\beta_2y(t - \tau_2)v(t - \tau_2)}{1 + a_2y(t - \tau_2) + b_2v(t - \tau_2)} - dy_1(t),
\end{aligned}
\]
\[ \dot{v}(t) = p_1 x_1(t) + p_2 y_1(t) - rv(t). \]

Here \( \frac{\beta_1 x_1}{1 + a_1 x_1 b_1} \) and \( \frac{\beta_2 y_1}{1 + a_2 y_1 b_2} \) represent the Beddington-DeAngelis functional response of the CD4\(^+\) T cells and macrophages, respectively, where \( a_1, b_1, a_2, b_2 \) are positive constants. All the variables and parameters of the model have the same definitions as given in the previous section. This model can be considered as an extension of the model given in [9], [14] which describes the interaction of the HIV with one target cells, CD4\(^+\) T cells.

### 2.1. Steady states

It is clear that, system (14)-(18) has an uninfected steady state \( E_0 = (x_0, 0, y_0, 0, 0) \), where \( x_0 = \frac{\lambda_0}{a_1} \), \( y_0 = \frac{\lambda_2}{a_2} \). The system can also has a positive infected steady state \( E_1(x^*, x_1^*, y^*, y_1^*, v^*) \). The coordinates of the infected steady state, if they exist, satisfy the equalities:

\[ \lambda_1 = d_1 x^* + \frac{\beta_1 x^* v^*}{1 + a_1 x^* + b_1 v^*}, \]
\[ \lambda_2 = d_2 y^* + \frac{\beta_2 y^* v^*}{1 + a_2 y^* + b_2 v^*}, \]
\[ a x_1^* e^{-\tau_1} = \frac{\beta_1 x^* v^*}{1 + a_1 x^* + b_1 v^*}, \]
\[ \delta y_1^* e^{-\tau_2} = \frac{\beta_2 y^* v^*}{1 + a_2 y^* + b_2 v^*}, \]
\[ rv^* = p_1 x_1^* + p_2 y_1^*. \]

The basic reproduction number \( R_0 \) for system (14)-(18) is given by:

\[ R_0 = e^{-\tau_1} p_1 \beta_1 x_0 \delta (1 + a_2 y_0) + e^{-\tau_2} p_2 \beta_2 y_0 a (1 + a_1 x_0) a \delta r (1 + a_1 x_0) (1 + a_2 y_0). \]

We note that \( R_0 \) can be written as:

\[ R_0 = R_1 + R_2, \]

where

\[ R_1 = \frac{e^{-\tau_1} p_1 \beta_1 x_0}{a \delta r (1 + a_1 x_0)}, \quad R_2 = \frac{e^{-\tau_2} p_2 \beta_2 y_0}{\delta r (1 + a_2 y_0)}. \]

### 2.2. Global stability analysis

In this section, we prove the global stability of the uninfected and infected steady states of system (14)-(18).

**Theorem 2.** (i) If \( R_0 \leq 1 \), then \( E_0 \) is GAS for any \( \tau_1, \tau_2 \geq 0 \).

(ii) If \( E_1 \) exists, then it is GAS for any \( \tau_1, \tau_2 \geq 0 \).

**Proof.** We consider a Lyapunov functional

\[ W_1 = \frac{x_0}{1 + a_1 x_0} F \left( \frac{x}{x_0} \right) + e^{m_1 \tau_1} x_1 + \frac{y_0}{1 + a_2 y_0} F \left( \frac{y}{y_0} \right) + e^{m_2 \tau_2} y_1, \]
We note that $W_1$ is defined, continuous and positive definite for all $(x, x_1, y, y_1, v) > 0$. Also, the global minimum $W_1 = 0$ occurs at the uninfected steady state $E_0$. The time derivative of $W_1$ along the solution of (14)-(18) is given by

\[
\frac{dW_1}{dt} = \frac{1}{1 + a_1 x_0} \left( 1 - \frac{x_0}{x} \right) \left( \lambda_1 - d_1 x - \frac{\beta_1 x v}{1 + a_1 x + b_1 v} \right) + \frac{\beta_1 x v}{1 + a_1 x + b_1 v} - \frac{\beta_1 x v}{1 + a_1 x + b_1 v}
\]

\[
- a e^{m_1 r_1} x_1 + \gamma \left[ \frac{1}{1 + a_2 y_0} \left( 1 - \frac{y_0}{y} \right) \left( \lambda_2 - d_2 y - \frac{\beta_2 y v}{1 + a_2 y + b_2 v} \right) \right] + \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \beta_1 x v - \frac{\beta_1 x v}{1 + a_1 x + b_1 v} - \frac{\beta_1 x v}{1 + a_1 x + b_1 v} + \gamma \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
- \gamma \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
\frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
- \frac{\beta_1 x v}{1 + a_1 x + b_1 v} + \frac{\beta_1 x v}{1 + a_1 x + b_1 v} + \frac{\beta_1 x v}{1 + a_1 x + b_1 v} - \frac{\beta_1 x v}{1 + a_1 x + b_1 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
= \frac{\lambda_1}{1 + a_1 x_0} \left[ 2 - \frac{x}{x_0} - \frac{x_0}{x} \right] + \gamma \frac{\lambda_2}{1 + a_2 y_0} \left[ 2 - \frac{y}{y_0} - \frac{y_0}{y} \right]
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} + \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]

\[
+ \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \frac{\beta_2 y v}{1 + a_2 y + b_2 v}
\]
Since the arithmetical mean is greater than or equal to the geometrical mean, then the first two terms of (24) are less than or equal to zero. Therefore, if \( R_0 \leq 1 \), then \( R_1, R_2 \leq 1 \) and \( \frac{dW}{dt} \leq 0 \) for all \( x, x_1, y, y_1, v > 0 \). The global stability of \( E_0 \) follows from LaSalle’s Invariance Principle.

(ii) Define a Lyapunov functional

\[
W_2 = x - x^* - \int_{x_1}^{x} \left( 1 + a_1 x + b_1 v^* \right) \frac{dy}{\eta} + e^{m_1 \tau_1} x_1^* F \left( \frac{x_1}{x_1^*} \right) \\
+ \gamma \left( y - y^* - \int_{y_1}^{y} \left( 1 + a_2 y + b_2 v^* \right) \frac{dy}{\eta} + e^{m_2 \tau_2} y_1^* F \left( \frac{y_1}{y_1^*} \right) \right) \\
+ \frac{a}{p_1} e^{m_1 \tau_1} v^* F \left( \frac{v}{v^*} \right) \\
+ \frac{\beta_1 x^* v^*}{1 + a_1 x + b_1 v^*} \int_{\theta_1}^{\theta} \frac{F \left( \frac{x(t - \theta)}{x^*} \left( 1 + a_1 x(t - \theta) + b_1 v(t - \theta) \right) \right)}{F \left( \frac{y(t - \theta)}{y^*} \left( 1 + a_2 y(t - \theta) + b_2 v(t - \theta) \right) \right)} d\theta \\
+ \frac{\beta_2 y^* v^*}{1 + a_2 y + b_2 v^*} \int_{\theta_1}^{\theta} \left[ \int_{y_1}^{y} \frac{dy}{\eta} + e^{m_2 \tau_2} y_1^* F \left( \frac{y_1}{y_1^*} \right) \right] d\theta.
\]

Differentiating with respect to time yields

\[
\frac{dW_2}{dt} = \left( 1 - \frac{x^*}{x} \right) \frac{1 + a_1 x + b_1 v^*}{1 + a_1 x + b_1 v} \left( \lambda_1 - d_1 x - \frac{\beta_1 x v}{1 + a_1 x + b_1 v} \right) \\
+ e^{m_1 \tau_1} \left( 1 - \frac{x_1^*}{x_1} \right) \left( \frac{e^{m_1 \tau_1} \beta_1 x_1 v_1}{1 + a_1 x_1 + b_1 v} - ax_1 \right) \\
+ \gamma \left( \left( 1 - \frac{y^*}{y} \right) \frac{1 + a_2 y + b_2 v^*}{1 + a_2 y + b_2 v} \left( \lambda_2 - d_2 y - \frac{\beta_2 y v}{1 + a_2 y + b_2 v} \right) \\
+ e^{m_2 \tau_2} \left( 1 - \frac{y_1^*}{y_1} \right) \left( \frac{e^{m_2 \tau_2} \beta_2 y_2 v_2}{1 + a_2 y_2 + b_2 v_2} - ay_1 \right) \right) \\
+ \frac{a}{p_1} e^{m_1 \tau_1} \left( 1 - \frac{v^*}{v} \right) \left( p_1 x_1 + p_2 y_1 - rv \right) + \frac{\beta_1 x v}{1 + a_1 x + b_1 v} \\
- \frac{\beta_1 x_1 v_1}{1 + a_1 x_1 + b_1 v_1} + \frac{\beta_1 x^* v^*}{1 + a_1 x^* + b_1 v^*} \ln \left( \frac{x_1 v_1}{x^*} \right) \left( 1 + a_1 x + b_1 v \right) \\
+ \gamma \frac{\beta_2 y v}{1 + a_2 y + b_2 v} - \gamma \frac{\beta_2 y_2 v_2}{1 + a_2 y_2 + b_2 v_2} \\
+ \gamma \frac{\beta_2 y^* v^*}{1 + a_2 y^* + b_2 v^*} \ln \left( \frac{y_2 v_2}{y^*} \right) \left( 1 + a_2 y + b_2 v \right).
\]
Using the infected steady state $E_1$ conditions (19)-(23) we obtain

$$\frac{dW_2}{dt} = \left( 1 - \frac{x^*}{x} + \frac{a_1 x + b_1 v^*}{x + a_1 x^* + b_1 v^*} \right) (d_1 x^* - d_1 x)$$

$$- ax_1^* e^{m_1 r_1} \frac{x^*}{x} + a_1 x + b_1 v^*$$

$$+ 3 ax_1^* e^{m_1 r_1} x_1 \frac{v^*}{v} - a_1 x + b_1 v^*$$

$$- ax_1^* e^{m_1 r_1} x_1^* x_1 v (1 + a_1 x + b_1 v)$$

$$+ ax_1^* e^{m_1 r_1} v^* - ax_1^* e^{m_1 r_1} v^* x_1$$

$$+ ax_1^* e^{m_1 r_1} \ln \left( \frac{x_1 v_r (1 + a_1 x + b_1 v)}{x v (1 + a_1 x_1 + b_1 v)} \right)$$

$$+ \gamma \left[ (1 - \frac{y^*}{y} + \frac{a_2 y + b_2 v^*}{y + a_2 y^* + b_2 v^*}) (d_2 y^* - d_2 y) \right]$$

$$- \delta y_1^* e^{m_2 r_2} \frac{y^*}{y} + a_2 y + b_2 v^*$$

$$- \delta y_1^* e^{m_2 r_2} y_1^* v y_2 v (1 + a_2 y + b_2 v^*)$$

$$- \delta y_1^* e^{m_2 r_2} v^* - \delta y_1^* e^{m_2 r_2} v^* y_1$$

$$+ \gamma y_1^* e^{m_2 r_2} \ln \left( \frac{y_2 v_r (1 + a_2 y + b_2 v)}{y r (1 + a_2 y_2 + b_2 v_2)} \right).$$

By a straightforward calculations we get for $x$:

$$\left( 1 - \frac{x^*}{x} + \frac{a_1 x + b_1 v^*}{x + a_1 x^* + b_1 v^*} \right) (d_1 x^* - d_1 x) = - \frac{d_1 (x - x^*)^2 (1 + b_1 v^*)}{x (1 + a_1 x^* + b_1 v^*)},$$

$$- 1 + \frac{v}{v^*} \frac{1 + a_1 x + b_1 v}{1 + a_1 x + b_1 v} - \frac{v}{v^*} \frac{1 + a_1 x + b_1 v}{1 + a_1 x + b_1 v^*}$$

$$= - \frac{v^* (1 + a_1 x + b_1 v) (1 + a_1 x + b_1 v^*)}{b_1 (1 + a_1 x) (v - v^*)^2} \cdot$$

$$\ln \left( \frac{x_r v_r (1 + a_1 x + b_1 v)}{x v (1 + a_1 x_1 + b_1 v)} \right)$$

$$= \ln \left( \frac{x^*}{x} + \frac{a_1 x + b_1 v^*}{x + a_1 x^* + b_1 v^*} \right) + \ln \left( \frac{x_1 v^*}{x^*_1 v} \right).$$
Similar equalities can be deduced for \( y \). Then, \( \frac{dW_y}{dt} \) can be written as:

\[
\frac{dW_y}{dt} = -\frac{d_1 (x - x^*)^2 (1 + b_1 v^*)}{x(1 + a_1 x + b_1 v^*)} - ax_1 e^{\mu_1 t} \frac{b_1 (1 + a_1 x)(v - v^*)^2}{v^* (1 + a_1 x + b_1 v^*) (1 + a_1 x + b_1 v^*)} - \gamma d_2 (y - y^*)^2 \frac{(1 + b_2 v^*)}{y (1 + a_2 y^* + b_2 v^*)} - \delta y_1 e^{\mu_2 t} \frac{\gamma b_2 (1 + a_2 y)(v - v^*)^2}{v^* (1 + a_2 y + b_2 v^*)(1 + a_2 y + b_2 v^*)} - ax_1 e^{\mu_1 t} \left[ F \left( \frac{x^* + 1 + a_1 x + b_1 v^*}{x^* + 1 + a_1 x^* + b_1 v^*} \right) + F \left( \frac{x_1 v^*}{x_1^* v^*} \right) \right] + F \left( \frac{1 + a_1 x + b_1 v^*}{1 + a_1 x + b_1 v^*} \right) + F \left( \frac{x_1 v^*}{x_1^* v^*} \right) + F \left( \frac{y_1 v^*}{y_1^* v^*} \right) + F \left( \frac{y_1 y_2 v^*}{y_1 y_2^* v^*} \right)
\]

It is easy to see that if \( x^*, x_1^*, y^*, y_1^*, v^* > 0 \), then \( \frac{dW_y}{dt} \leq 0 \) for all \( (x, x_1, y, y_1, v) > 0 \) where the equality holds if and only if \( (x, x_1, y, y_1, v) \) take the steady state value \( (x^*, x_1^*, y^*, y_1^*, v^*) \). LaSalle’s Invariance Principle implies global stability of \( E_1 \).

\[\square\]

3. Conclusion

In this paper, we have studied the global stability of two HIV infection models with intracellular delays accounting for the times between viral entry into the target cells, the CD4\(^+\) T and macrophages, and the production of new virus particles. The first model takes into account the saturation infection rate. In the second model the infection rate is given by Beddington-DeAngelis functional response. The global stability of the uninfected and infected steady states have 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 the infected steady state exists then it is GAS for all time delays.

References

GLOBAL STABILITY OF HIV INFECTION MODELS


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