Dynamical analysis model of HIV-1 infection in CD4+ T cells with antibody response

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Abstract. The spread of HIV infection one of which is affected by cell to cell transmission. A dynamical model of HIV-1 infection in CD4+T cells with considering viral transmission from cell to cell and antibody response is constructed in this paper. Antibody response determines viral load in early HIV-1 infection. The existence and stability of the equilibrium is investigated by the basic reproduction ratio. The local stability of uninfected equilibrium is analyzed using Routh Hurwitz linearization. After investigating the local stability, we construct a Lyapunov function to investigate the global stability of endemic equilibrium. Numerical simulation is given to illustrate the control of HIV-1 infection based on the effect of antibody response and the effectiveness of antiretroviral treatment.

1. Introduction

Human Immunodeficiency Virus (HIV) is a retrovirus type that infects the host cells having CD4+T molecule. In the body, HIV can be transmitted through cell-to-cell among CD4+T cells. In HIV infection of CD4+T cells, the viral transmission via cell-to-cell is more effective compared to the transmission from free virus to host cells [1, 2]. When an antigen has been identified, the adaptive immune cells, called B-lymphocytes, produce antibodies to neutralize the antigen. The B-lymphocytes have antibody molecules on the surface named B-cells receptor that can bind the virus [3]. These antibodies bind to the viral particles and mark them to be killed by macrophage. Antibodies have role in controlling viral load of HIV-1 infection, and in blocking HIV replication. Antibodies is able to reduce the viral load up to very low level [3, 4].

The most of host cells that is infected by HIV-1 type, is CD4+T cells. These cells have fundamental role in the spread of HIV-1 infection in the body. The CD4+T cells infected by HIV-1 stimulate among CD4+T cells. The interaction of the infected CD4+T cell and the activated CD4+T is more effective infection. While resting CD4+T cells are able to inhibit transcription of viral RNA, lead to the abortive infection and these cells turn to healthy [5]. The fail infection in the resting CD4+T cells may be due to inefficient reverse transcription [6, 7].

Mathematical modelling has provided the understanding of dynamics of HIV-1 infection in immune system. Some studies have developed mathematical models of antibody response of HIV-1 infection. They separated CD4+T cells into two sub classes. Srivastava et al. [8] modelled dynamics of CD4+T cells in HIV-1 response. Under infection, CD4+T cells divided into latent and infected class by considering reverse transcription of viral RNA, where the infection is generated from free virus. This study has not considered HIV-1 infection by cell-cell contact.

Mathematical models incorporating Langerhans to capture the implication of HIV-1 infection in early infection stage [9, 10, 11]. These model incorporated cell-cell contact through Langerhans, CD4+T cells and its combination. Instead, in the studies have not considered antibodies response in the
dynamics of immune system. Other modelling, Tarfulea et al. [12, 13] established a mathematical model by considering CTL response in HIV-1 infection of CD4\(^+\)T (host) cells. The model did not incorporate cell-cell contact among CD4\(^+\)T cells in transmitting the virus. Recent studies, dynamical models involving the interaction of infected CD4\(^+\)T cell and healthy CD4\(^+\)T cell for spreading HIV-1 infection were developed by Sutimin et al. [14, 15]. These model were analysed to explore the dynamical behaviour of these models.

In this study, it is developed a model to study the effect of antibody response in controlling the viral load during acute infection. We study the dynamical behaviour of the model, including the existence and stability of equilibrium for the model, and present the evolution of host cells, free virus and antibodies concentration in long terms.

2. Model formulation
The model is developed to capture the effect antibodies response to host cells. The model consists of five nonlinear equations describing populations of healthy (\(T\)), latent (\(L\)), actively infected of CD4\(^+\)T cells (\(i\)), free virus (\(V\)), and antibodies molecule (\(A\)). The mathematical model is presented in the following

\[
\frac{dT}{dt} = \lambda - \beta_1 VT - \beta_2 iT - \mu_1 T \tag{1}
\]

\[
\frac{dL}{dt} = \beta_1 (1-p)VT + \beta_2 (1-q)IT - (\mu_1 + \mu_a + \alpha) L \tag{2}
\]

\[
\frac{dI}{dt} = p\beta_1 VT + q\beta_2 iT - (\mu_1 + \delta) I + \alpha L \tag{3}
\]

\[
\frac{dV}{dt} = N\delta Ti - \mu_3 V - \phi AV \tag{4}
\]

\[
\frac{dA}{dt} = \eta AV - \mu_a A \tag{5}
\]

The healthy CD4\(^+\)T cells are generated from thymus at the rate \(\lambda\). Parameter \(\mu_1\) represents the natural mortality rate of susceptible CD4\(^+\)T cells. Parameter \(\beta_1\) is the infection rate of susceptible CD4\(^+\)T cells by free virus, while parameter \(\beta_2\) is infected CD4\(^+\)T cell. A fraction of CD4\(^+\)T cells that remove to fast progression from susceptible CD4\(^+\)T cells to infectious caused by free virus and infectious CD4\(^+\)T cell are denoted by \(p\), \(q\) respectively. While the fraction of \(1-p\) and \(1-q\) of healthy CD4\(^+\)T cells go to latent class. We denote \(\mu_1\) as the rate of latent CD4\(^+\)T cells die due to inflammation. The population of latent CD4\(^+\)T cells remove to infectious class at the rate \(\alpha\). The average of new virions produced by infected CD4\(^+\)T cells is \(N\), and lisis death of CD4\(^+\)T is at the rate \(\delta\). By \(\mu_3\) and \(\phi\) we denote the death rate and viral clearance of the free virus population, respectively. Parameter \(\eta\) and \(\mu_a\) are related to the rate at which the molecule of antibody produced by B-cells and the death rate of antibody, respectively.

3. Model analysis
The model (1-5) is studied to get the basic reproduction ratio and explore the stability of uninfected state, and stability of endemic equilibrium.

3.1 Basic reproduction ratio
To analyse the local stability of uninfected equilibrium, we derive the basic reproduction ratio, \(R_0\), using the next generation matrix. The parameter of this ratio guarantees the existence of endemic
equilibrium [16]. It is straightforward to see that the model (1-5) has an uninfected equilibrium point 
\[ E_0 = \left( \frac{\lambda}{\mu_i}, 0, 0, 0, 0 \right) \]. From Dickmann [17], we can obtain the next generation matrix as follows,

\[
K = \begin{bmatrix}
\Psi_1 & \Psi_2 & \frac{\beta_i (1-p) \lambda_i}{\mu_i \mu_v} \\
\Psi_3 & \Psi_4 & \frac{p \beta_i \lambda_i}{\mu_v} \\
0 & 0 & 0
\end{bmatrix}
\]  

(6)

where,
\[
\Psi_1 = \frac{\beta_i (1-p) \alpha N \delta_i}{\mu_i (\mu_i + \alpha + \mu_v) \mu_v (\delta + \mu_i)} + \frac{\beta_i (1-q) \alpha \lambda_i}{\mu_i (\mu_i + \alpha + \mu_v) (\delta + \mu_i)},
\]
\[
\Psi_2 = \frac{\beta_i (1-p) N \delta_i}{\mu_i \mu_v (\delta + \mu_i)} + \frac{\beta_i (1-q) \lambda_i}{\mu_i (\delta + \mu_i)},
\]
\[
\Psi_3 = \frac{p \beta_i N \delta_i}{\mu_i (\mu_i + \alpha + \mu_v) \mu_v (\delta + \mu_i)} + \frac{q \beta_i \alpha \lambda_i}{\mu_i (\mu_i + \alpha + \mu_v) (\delta + \mu_i)},
\]
\[
\Psi_4 = \frac{p \beta_i N \delta_i}{\mu_i (\delta + \mu_i)} + \frac{q \beta_i \lambda_i}{\mu_i (\delta + \mu_i)}.
\]

The eigenvalues of matrix \( K \) are \( 0, 0, -\frac{\lambda_i N \delta_i (p \mu_i + p \mu_v + \alpha) \beta_i}{\mu_i (\mu_i + \alpha + \mu_v) \mu_v (\delta + \mu_i)} + \frac{\lambda_i (q \mu_i + q \mu_v + \alpha) \beta_i}{\mu_i (\mu_i + \alpha + \mu_v) (\delta + \mu_i)} \).

Hence, the ratio \( R_0 \) for system (1) – (5) can be written by
\[
R_0 = \frac{\lambda_i N \delta_i (p \mu_i + p \mu_v + \alpha) \beta_i}{\mu_i (\mu_i + \alpha + \mu_v) \mu_v (\delta + \mu_i)} + \frac{\lambda_i (q \mu_i + q \mu_v + \alpha) \beta_i}{\mu_i (\mu_i + \alpha + \mu_v) (\delta + \mu_i)} \]  

(7)

Next, the local stability of equilibrium is presented in the following subsection.

3.2 Local stability of uninfected equilibrium

By linearization using Routh- Hurwitz criterion, we prove the local stability of uninfected equilibrium \( E_0 \). The local stability of the system can be proved by using the following theorem.

**Theorem 1:** If \( R_0 < 1 \), the uninfected equilibrium \( E_0 \) is locally asymptotically stable (LAS).

**Proof**

The system (1) – (5) has Jacobian matrix at \( E_0 \) in the following,

\[
J(E_0) = \begin{bmatrix}
-\mu_i & 0 & -\frac{\beta_i \lambda_i}{\mu_i} & -\frac{\beta_i \lambda_i}{\mu_i} & 0 \\
0 & -(\mu_i + \alpha) & \frac{\beta_i (1-q) \lambda_i}{\mu_i} & \frac{p \beta_i \lambda_i}{\mu_i} & 0 \\
0 & \alpha & \frac{q \beta_i \lambda_i}{\mu_i} + (\mu_i + \delta) & p \beta_i \lambda_i & 0 \\
0 & 0 & N \delta & -\mu_v & 0 \\
0 & 0 & 0 & 0 & -\mu_v
\end{bmatrix}
\]  

(8)
The Jacobian matrix (8) has five eigenvalues, they are $-\mu, -\mu_0$ and other three eigenvalues are the solution of the equation

$$\zeta^3 + A_2\zeta^2 + A_1\zeta + A_0 = 0,$$

where,

$$A_2 = \mu_v + (\mu_i + \mu + \alpha)(\mu_i + \delta)(1 - R_0) + \frac{\lambda, N\delta(p\mu_v + p\mu_i + \alpha)}{\mu_i(\mu_i + \mu + \alpha)} + \frac{\lambda, \alpha(1-q)\beta_2}{\mu_i(\mu_i + \mu + \alpha)},$$

$$A_1 = (\mu_i + \delta)(\mu_i + \mu_i + \alpha)(1 - R_0) + \mu_i(\mu_i + \mu + \alpha) + \mu_i(\mu_i + \delta)(1 - R_0) + \frac{\lambda, N\delta\beta_i}{\mu_i},$$

$$A_0 = (\mu_i + \mu_i + \alpha)(\mu_i + \delta)\mu_i(1 - R_0).$$

By manipulating the computation $A_1A_2 - A_0$, we have

$$A_1A_2 - A_0 = A_1\left[(\mu_i + \alpha + \mu_i)(\delta + \mu_i)(1 - R_0) + \frac{\lambda, N\delta(p\mu_v + p\mu_i + \alpha)}{\mu_i(\mu_i + \alpha + \mu_i)(\mu_i + \alpha + \mu_i)} + \frac{\lambda, \alpha(1-q)\beta_2}{\mu_i(\mu_i + \alpha + \mu_i)}\right]$$

$$+ \mu_i\left[\frac{\lambda, N\delta\beta_i}{\mu_i}\left(\frac{\alpha(1-p)}{\mu_i(\alpha + \mu_i)} + \frac{(p\mu_v + p\mu_i + \alpha)}{\mu_i}\right) + \mu_i(\delta + \mu_i)(1 - R_0)\right]$$

We see that $A_1A_2 - A_0 > 0$, when $R_0 < 1$. Based on Routh-Hurwitz criterion, $E_0$ is LAS when $R_0 < 1$. The proof is completed.

### 3.3 Global stability for the endemic equilibrium

Lyapunov function is constructed to evaluate the global stability for the endemic equilibrium. The model (1) – (5) has endemic equilibrium $E^* = (T^*, L_t^*, V^*, A^*)$, where

$$T^* = \frac{\lambda, N\delta\eta}{N\delta\mu_v\beta_i + \mu_v(\mu_v + \phi A)\beta_2 + N\delta\mu_i\eta},$$

$$L_t^* = \frac{\mu_v, \lambda, N\delta\beta_i(1-p) + (1-q)(\mu_v + \phi A)\beta_2}{N\delta\mu_v(\mu_v + \mu_i + \alpha)\beta_2 + \mu_v(\mu_v + \phi A)(\mu_v + \phi A)\beta_2 + N\delta\mu_i(\mu_v + \mu_i + \alpha)},$$

$$T_i^* = \frac{\mu_v(\mu_v + \phi A)}{N\delta\eta},$$

$$V^* = \frac{\mu_v}{\eta}.$$ 

The solution $A^*$ fulfills the equation

$$A_2A_1 + A_1A_0 + A_0 = 0 \tag{9}$$

where,

$$A_2 = \phi^2 \mu_v(\mu_i + \delta)\mu_i + \mu + \alpha)\beta_2,$$

$$A_1 = N\delta\mu_v(\mu_v + \delta)(\mu_v + \mu_i + \alpha) + N\delta\mu_i(\mu_v + \delta)(\mu_v + \mu + \alpha)\beta_1 + [2\phi\mu_v(\delta + \mu_i)\mu_v + \alpha) - N\delta\mu_v(q\mu_v + q\mu_i + \alpha)]\beta_2.$$
\[ A_0 = N\delta\mu_1\mu_i(\mu_i + \delta)(\mu_i + \mu_i + \alpha)(1-\mathcal{R}_0) + N\delta\mu_2\mu_i(\mu_i + \delta)(\mu_i + \mu_i + \alpha)\beta_1 + \mu_j\mu_i^2(\mu_i + \delta)(\mu_i + \mu_i + \alpha)\beta_2. \]

The equation (9) has unique positive solution \( A^* \) if and only if \( \frac{A_0}{A_2} < 0 \) or \( \mathcal{R}_0 > 1 \). Hence, when \( \mathcal{R}_0 > 1 \), the endemic equilibrium exists. Later, we give the global stability theorem for the endemic equilibrium.

**Theorem 2:** If \( \mathcal{R}_0 > 1 \), the endemic equilibrium \( E^* \) of the system (1-5) is globally asymptotically stable (GAS).

**Proof.**

Consider a Lyapunov function, \( F \in C^1 \), as follows,

\[
F = \left( T - T^* - T^* \ln \frac{L'}{L} \right) + c_1 \left( L - L' - L' \ln \frac{L}{L} \right) + c_2 \left( T_i - T_i^* - T_i^* \ln \frac{T_i}{T_i^*} \right) + c_3 \left( V - V^* - V^* \ln \frac{V}{V^*} \right) + c_4 \left( A - A^* - A^* \ln \frac{A}{A^*} \right)
\]

where \( c_1, c_2, c_3, c_4 \) are positive constant. Differentiating this function \( F \) with respect to time \( t \) is given as follows

\[
\frac{dF}{dt} = \left( 1 - \frac{T}{T^*} \right) \frac{dT}{dt} + c_1 \left( 1 - \frac{L'}{L} \right) \frac{dL}{dt} + c_2 \left( 1 - \frac{T_i}{T_i^*} \right) \frac{dT_i}{dt} + c_3 \left( 1 - \frac{V}{V^*} \right) \frac{dV}{dt} + c_4 \left( 1 - \frac{A}{A^*} \right) \frac{dA}{dt}
\]

\[
= \left( \lambda_i + \mu_i T^* + c_1 (\mu_i + \mu_i + \alpha) L^* + c_2 (\mu_i + \delta) T_i^* + c_3 \mu_i V^* + c_4 \mu_i A^* \right) - \mu_i T
\]

\[
+ (-c_1 (\mu_i + \mu_i + \alpha) + c_3 \alpha) L + \beta_i (\mu_i + \delta) T_i^* + c_3 \mu_i A^* - \mu_i T
\]

\[
+ \left( -c_i (\mu_i + \mu_i + \alpha) + c_3 \alpha \right) L + \left( -c_i (\mu_i + \mu_i + \alpha) + c_3 \alpha \right) A + (c_1 (1-p) \beta_i + c_2 p \beta_1 - \beta_i) V T
\]

\[
+ (c_1 (1-q) \beta_i + c_2 q \beta_2 - \beta_2) T_i T + (c_3 \eta c_3 \phi) A V - \left( \lambda_i T^* \right) - \left( c_3 N \delta T_i V^* \right)
\]

\[
- \left( c_1 (1-q) VT L^* \frac{L'}{L} + c_2 (1-q) T_i T L^* \frac{L'}{L} \right) - \left( c_3 p \beta_1 V T_i^* \frac{T_i}{T_i^*} + c_2 q \beta_2 T_i^* T + c_3 \alpha L \frac{T_i}{T_i^*} \right).
\]

By considering

\[
\lambda_i = \beta_i V T^* + \beta_i T^* T_i^* + \mu_i T
\]

\[
(\mu_i + \mu_i + \alpha) L^* = \beta_i (1-p) V T^* + \beta_i (1-q) T_i T
\]

\[
(\mu_i + \delta) T_i^* = p \beta_i V T^* + q \beta_2 T T_i^* + \alpha L^*
\]

\[
\mu_i V^* = N \delta T_i V^* - \phi A^* V^*
\]

\[
\mu_i A^* = \eta A^* V^*
\]

The equation (10) becomes

\[
\frac{dF}{dt} = \mu_i T^* \left( 2 - \frac{T}{T^*} - \frac{T^*}{T} \right) + \beta_i V T^* \left( 1 - \frac{T}{T^*} \right) + \beta_i T_i T_i^* \left( 1 - \frac{T_i}{T_i^*} \right) + c_1 (1-p) V T^* \left( 1 - \frac{V}{V^*} \right) \frac{T}{T^*} \frac{L}{L^*}
\]

\[
+ \beta_i \left( 1-q \right) V T_i T_i^* \left( 1 - \frac{T_i}{T_i^*} \right) + \beta_i \left( 1-q \right) V T_i T_i^* \left( 1 - \frac{V}{V^*} \right) \frac{T_i}{T_i^*} + c_2 \left( 1-q \right) V T_i T_i^* \left( 1 - \frac{T_i}{T_i^*} \right)
\]
\[ +c_1\alpha L^* \left[ 1 - \frac{L}{T_i^*} \right] + c_3 \eta A^* \left[ 1 - \frac{T_i^*}{V^*} \right] - c_4 \phi A^* V^* + c_4 \eta A^* V^* + (c_4 \eta - c_3 \phi) A V \]
\[ +(c_1 (1-p) \beta_1 + c_2 \beta_1 \beta_1 - \beta_1) V T + (c_1 (1-q) \beta_2 + c_2 q \beta_2 - \beta_2) T T_i + (c_3 \phi V^* - c_3 \mu_v) A \]
\[ +(-c_1 (\mu + \mu_v + \alpha) + c_3 \alpha) L + (\beta_1 T^* - c_2 (\mu + \delta) + c_3 N \delta) T_i + (\beta_2 T^* - c_2 \mu_v - c_4 \eta A^*) V \]  
(16)

We denote \( x = \frac{T}{T_i^*}, y = \frac{L}{L_i^*}, w = \frac{V}{V_i^*}, z = \frac{A}{A_i^*} \). The equation (16) can be written as
\[
\frac{dF}{dt} = \mu T^* \left( 2 - x - \frac{1}{x} \right) + \beta V^* \left( 1 - \frac{1}{x} \right) + \beta_2 T^* T_i^* \left( 1 - \frac{1}{x} \right) + c_1 \beta_1 (1-p) T V^* \left( 1 - \frac{x}{y} \right) \\
+ c_2 \beta_2 (1-q) T^* T_i^* \left( 1 - \frac{x w}{y} \right) + c_3 \beta_2 V V^* \left( 1 - \frac{x w}{y} \right) + c_4 q \beta_2 T^* T_i^* (1-x) + c_2 \alpha L^* \left( 1 - \frac{y}{w} \right) \\
+ c_3 \delta T T_i^* \left( 1 - \frac{w}{v} \right) - c_4 \phi A V^* + c_4 \eta A^* V^* + (c_4 \eta - c_3 \phi) A V + \beta_1 (1-p) + c_2 p - 1) V T \\
+ \beta_2 (1-q) + c_2 q - 1) T T_i + (-c_1 (\mu + \mu_v + \alpha) + c_3 \alpha) L + (\beta_2 T^* - c_2 (\mu + \delta) + c_3 N \delta) T_i \\
+ (\beta_2 T^* - c_2 \mu_v - c_4 \eta A^*) V + (c_3 \phi V^* - c_3 \mu_v) A 
\]  
(17)

Making the coefficients of \( VT, TT_i, AV, L, T_i, V, A \) are equal to 0, so we have the relationship
\[ c_1 (1-p) + c_2 p = 1 \]  
(18)
\[ c_1 (1-q) + c_2 q = 1 \]  
(19)
\[ c_1 (\mu + \mu_v + \alpha) = c_2 \alpha \]  
(20)
\[ c_1 (\mu + \mu_v + \alpha) = c_2 \alpha \]  
(21)
\[ c_2 (\mu + \delta) = \beta_2 T^* + c_3 N \delta \]  
(22)
\[ c_3 \mu_v = \beta_2 T^* - c_3 \eta A^* \]  
(23)
\[ c_4 \mu_v = c_3 \phi V^* \]  
(24)

Replacing \( c_1 (1-p) + c_2 p = 1 \) and \( c_1 (1-q) + c_2 q = 1 \), also using the fact that \( c_4 \eta = c_3 \phi \), equation (17) becomes
\[
\frac{dF}{dt} = \mu T^* \left( 2 - x - \frac{1}{x} \right) + c_1 \beta_1 (1-p) T V^* \left( 2 - \frac{1}{x} - \frac{x v}{y} \right) + c_2 p \beta_2 V V^* \left( 2 - \frac{1}{x} - \frac{x w}{y} \right) + c_2 \alpha L^* \left( 1 - \frac{y}{w} \right) \\
+ c_2 \beta_2 (1-q) T^* T_i^* \left( 2 - \frac{1}{x} - \frac{x w}{y} \right) + c_2 q \beta_2 V V^* \left( 2 - \frac{1}{x} - \frac{x w}{v} \right) + c_3 N \bar{\delta} T T_i^* \left( 1 - \frac{w}{v} \right) 
\]  
(25)

Multiplying equation (12) by \( c_1 \) and equation (21) by \( L^* \) gives
\[
\begin{aligned}
\left( c_1 (\mu + \mu_v + \alpha) \right) L^* &= c_1 \beta_1 (1-p) V^* T^* + c_i \beta_2 (1-q) T^* T_i^* \\
\left( c_1 (\mu + \mu_v + \alpha) \right) L^* &= c_2 \alpha L^*
\end{aligned}
\]

Hence, it clearly appears that
\[ c_1 \beta_1 (1-p) V^* T^* + c_2 \beta_2 (1-q) T^* T_i^* - c_2 \alpha L^* = 0 \]  
(26)

Now multiplying equation (26) by \( F_i(u) \), where \( u = (x, y, w, v, z) \) gives
\[c_1(1-p)V'T'F_i(u) + c_2(1-q)T'T_i^*F_i(u) - c_3\alpha L'F_i(u) = 0 \quad (27)\]

Then, multiplying equation (13) by \(c_2\) and equation (22) by \(T_i^*\) gives

\[
\begin{align*}
\left[c_2(\mu + \delta)T_i^* = c_2p\beta V'T' + c_2q\beta T'T_i^* + c_3\alpha L' \right.
\left.\left[c_2(\mu + \delta)T_i^* = \beta xT_i^* + c_4N\delta T_i^* \right.
\]
\end{align*}
\]

Hence, it clearly appears that

\[c_2p\beta V'T' + c_2q\beta T'T_i^* + c_3\alpha L' - \beta xT_i^* - c_4N\delta T_i^* = 0 \quad (28)\]

Now, multiplying equation (28) by \(F_2(u)\), where \(u = (x, y, w, v, z)^T\), and using equation (19) gives

\[c_2p\beta V'T'F_2(u) + c_2q\beta T'T_i^*F_2(u) - c_1(1-p)\beta xT_i^*F_2(u) - c_3\alpha L'F_2(u) = 0 \quad (29)\]

Then, multiplying equation (14) by \(c_3\) and equation (23) by \(V^*\) gives

\[
\begin{align*}
\left[c_3\mu V^* = c_3N\delta T_i^* - c_\phi A'V^* \right.
\left.\left[c_3\mu V^* = \beta xT^* - c_\eta A'V^* \right.
\]
\end{align*}
\]

Hence, it clearly appears that

\[c_3N\delta T_i^* - c_\phi A'V^* - \beta xT^* + c_\eta A'V^* = 0 \quad (30)\]

Now, multiplying equation (30) by \(F_3(u)\), where \(u = (x, y, w, v, z)^T\), and using equation (18) gives

\[c_3N\delta T_i^*F_3(u) - c_\phi A'V^*F_3(u) - c_1(1-p)\beta xT_i^*F_3(u) - c_3\alpha L'\beta xT_i^*F_3(u) = 0 \quad (31)\]

Also, multiplying equation (15) by \(c_4\) and equation (24) by \(A^*\) gives

\[
\begin{align*}
\left[c_4\mu A^* = c_4\eta A'V^* \right.
\left.\left[c_4\mu A^* = \beta xT^* - c_\phi A'V^* \right.
\]
\end{align*}
\]

Hence, it clearly appears that

\[c_4\eta A'V^* - c_\phi A'V^* = 0 \quad (32)\]

Now, multiplying equation (32) by \(F_4(u)\), where \(u = (x, y, w, v, z)^T\), gives

\[c_4\eta A'V^*F_4(u) - c_\phi A'V^*F_4(u) = 0 \quad (33)\]

Thus, after adding equation (27), (29), (31), (33) into equation (25), one obtains

\[
\frac{dF}{dt} = \mu xT^* \left(2 - x - \frac{1}{x}\right) + c_2q\beta xT'T_i^* \left(2 - x - \frac{1}{x}\right) + c_1(1-p)V'T^* \left(2 - \frac{1}{x} - \frac{xy}{y} + F_i(u) - F_3(u) \right) \\
+ c_2p\beta xT'^* \left(2 - \frac{1}{x} - \frac{xy}{w} + F_2(u) - F_3(u) \right) + c_2q\beta xT'T_i^* \left(2 - \frac{1}{x} - \frac{xy}{y} + F_i(u) - F_3(u) \right) \\
+ c_3\alpha L' \left(2 - \frac{y}{w} + F_3(u) - F_3(u) \right) + c_3N\delta T_i^* \left(2 - \frac{y}{w} - F_3(u) + F_3(u) \right) - c_\phi A'V^*F_3(u) \\
+ c_\eta A'V^*F_4(u) + c_\eta A'V^*F_4(u) - c_\phi A'V^*F_4(u)
\]

because \(c_4\eta = c_\phi \) then

\[
\frac{dF}{dt} = \mu xT^* \left(2 - x - \frac{1}{x}\right) + c_2q\beta xT'T_i^* \left(2 - x - \frac{1}{x}\right) + c_1(1-p)V'T^* \left(2 - \frac{1}{x} - \frac{xy}{y} + F_i(u) - F_3(u) \right) \\
+ c_2p\beta xT'^* \left(2 - \frac{1}{x} - \frac{xy}{w} + F_2(u) - F_3(u) \right) + c_2q\beta xT'T_i^* \left(2 - \frac{1}{x} - \frac{xy}{y} + F_i(u) - F_3(u) \right)
\]
\[ +c_{2}\alpha L\left(1-\frac{y}{w}+F_{2}(u)-F_{1}(u)\right) +c_{3}N\delta T_{i}^{*}\left(1-\frac{w}{v}-F_{2}(u)+F_{3}(u)\right) \]

Functions \( F_{1}(u) \), \( F_{2}(u) \) and \( F_{3}(u) \) are chosen such that the coefficients of \( L^{*} \) and \( T_{i}^{*} \) are equal to zero. In this case, \( F_{1}(u)-F_{2}(u) = 1-\frac{y}{w}, F_{2}(u)-F_{3}(u) = 1-\frac{w}{v}, \) and \( F_{1}(u)-F_{3}(u) = 2-\frac{y}{w}-\frac{w}{v}. \)

Then, one finally has
\[
\frac{dF}{dt} = \mu T^{*}\left(2-x-\frac{1}{x}\right) + c_{i}\beta_{1}(1-p)V^{*}T^{*}\left(4-\frac{1}{x}+\frac{y}{w}-\frac{w}{v}+\frac{xv}{y}\right) + c_{2}\beta_{2}(1-q)T^{*}T_{i}^{*}\left(3-\frac{1}{x}+\frac{y}{w}-\frac{w}{v}\right) + c_{3}\beta_{3}\alpha \beta_{3}(1-q)T^{*}T_{i}^{*}\left(3-\frac{1}{x}+\frac{y}{w}-\frac{w}{v}\right) + c_{4}\beta_{4}(1-q)T^{*}T_{i}^{*}\left(2-x-\frac{1}{x}\right) \leq 0. \tag{34} \]

One can see that \( \frac{dF}{dt} = 0 \) for \( T = T^{*}, L = L^{*}, T_{i} = T_{i}^{*}, V = V^{*}, A = A^{*} \), hence the maximum invariant set of \( \left\{ (T,L,T,V,A) | \frac{dF}{dt} = 0 \right\} \) is set of point \( \{ E^{*} \} \). We deduce that \( E^{*} \) is GAS.

### 4. Numerical simulation

We give a numerical simulation to illustrate the evolution of susceptible, latent and infected CD4+T cells, free virus populations and antibodies concentration. For the simulation, we choose the initial concentration \( T(0) = 950 \mu/L, \) \( L(0) = 0 \mu/L, T_{i}(0) = 0 \mu/L, A(0) = 0 \mu/L, \) and \( V(0) = 0.001 \mu/L. \) The values of various parameters are shown in the Table 1. Numerical result is given in Figure 1.

| Parameters | Values | Units | References |
|------------|--------|-------|------------|
| \( \lambda \) | 100 | \( \mu \) day\(^{-1} \) | [16] |
| \( \alpha \) | 0.4 | day\(^{-1} \) | [7] |
| \( \beta_{1} \) | 0.00002 | L day\(^{-1} \) | [14] |
| \( \beta_{2} \) | 0.001 | L day\(^{-1} \) | [8] |
| \( \mu_{i} \) | 0.1 | day\(^{-1} \) | [15] |
| \( \mu_{i} \) | 0.12 | day\(^{-1} \) | [7] |
| \( \mu_{i} \) | 2.4 | day\(^{-1} \) | [13] |
| \( \delta \) | 0.216 | day\(^{-1} \) | [16] |
| \( \phi \) | 9 | day\(^{-1} \) | [17, 18] |
| \( N \) | 500 | \( \mu \) day\(^{-1} \) | [19] |
| \( \mu_{i} \) | 0.25 | day\(^{-1} \) | [20] |
| \( \eta \) | 0.0091 | day\(^{-1} \) | [20] |
| \( p \) | 0.1 | | |
| \( q \) | 0.1 | | |
We can see Figure 1, it shows that free virus increases sharply after day 40 and then decrease drastically after day 50. The antibody begin to respond HIV-1 after 50 days, quantities of antibody molecule increases slowly and approach to constant number about 30 \( \mu / L \). The concentration of healthy CD4\(^+\)T cells, in the initially increases slowly, after 50 days start decreasing drastically tend constant number in HIV-1 set point of acute infection period. It shows that in the period of acute infection, the viral load reaches stable. In the time, the immune cells start to respond and fight the virus.

![Figure 1](image)

**Figure 1.** The evolution of CD4\(^+\)T cells, free virus populations and antibodies concentrations with the parameter values, \( \lambda = 100, \beta_1 = 0.00002, \beta_2 = 0.001, \mu_i = 0.1, \mu_e = 0.12, \mu_v = 2.4, \alpha = 0.4, \delta = 0.216, \phi = 9, N = 500, \mu_a = 0.25, \eta = 0.0091, p = q = 0.1 \)

### 5. Conclusion

In the study, we developed a mathematical model to describe the implication of antibodies response to dynamics of CD4\(^+\)T cells during acute HIV-1 infection stage. The model was proposed by taking into account viral from cell to cell of CD4\(^+\)T cells. We proved the local stability of uninfected equilibrium and the global stability of endemic equilibrium. The next generation matrix plays a crucial role to obtain the basic reproduction ratio. The basic reproduction ratio is less than one means that the uninfected equilibrium is LAS. By constructing Lyapunov function, we proved that the endemic equilibrium is GAS. The global stability of endemic equilibrium is achieved when the ratio exceeds one. Antibodies response start to fight HIV-1 infection when the viral load reaches set point, it is occurred in acute (early) infection stage. In the acute infection period, the immune system start to fight HIV-1. We can conclude that there will be a decrease in the number of free virus when the antibodies concentration increases. In this infection stage, the immune system are still able to control HIV-1 infection with healthy CD4\(^+\)T cells about 600 \( \mu / L \).

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