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Analysis of mathematical model of HIV-1 infection of CD4⁺ T cells with CTL response and antiretroviral treatment

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Abstract. A mathematical model is developed to capture the spread of HIV-1 infection within host cells caused by the contact of cell to cell and CTL response. In this paper, we propose a mathematical model of HIV-1 infection in CD4⁺T cells taking into account viral transmission from cell to cell and CTL response. The HIV transmission from cell to cell is one of the main factor in the spread of HIV infection and CTL response determines viral set point. We analyse the model to investigate the existence and stability of the equilibria. We analyse the local stability of disease free equilibrium by linearization, while the global stability of endemic equilibrium of the system by constructing Lyapunov function. Numerical simulations are presented to find the effectiveness of antiretroviral treatment in different scenarios and to the implication of CTL response in controlling the progression of HIV-1 infection.

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1. Introduction

Human Immunodeficiency Virus (HIV) is a virus that destroy the immune cells leading to death of human in the world. HIV/AIDS become serious problem of health in worldwide. Currently, about 46.9 million people live with HIV [1]. The majority of host cells infected HIV-1 is CD4⁺T cells. The infection via the contact of cell to cells leads to productive infection compared to the infection form free virus [2, 3]. When CD4⁺T cells was activated by virus, these cells stimulate cytotoxic T lymphocyte cells (CTL) as effector cells that inhibit viral replication. CTL have important role in controlling viral load by killing the infected CD4⁺ T cells.

HIV binds immune cells that express CD4⁺ molecule, including CD4⁺T cells. After virus enter into host cell, it releases viral RNA, and converts into viral DNA using reverse transcriptase enzyme. Next stage, the viral DNA integrates to the host's DNA, called HIV infected host cell. Using the host's RNA polymerase enzyme, viral DNA transcribes to messenger RNA (mRNA), then create the HIV proteins in long chains. Using protease enzyme, the long chains of HIV proteins are cut into smaller viral particles, then these particles move out through membrane's host cells become mature, and ready to infect other host cells [3, 4].

CD4⁺T cells have important role in the transmission of virus. The activated cells lead to productive infection, but the resting cells inhibit the process of reverse transcription of virus, thereby the virus fails in completing HIV reverse transcription, viral degradation occur in cytoplasm [6]. The failed infection may be due to inefficient reverse transcription. In addition, reverse transcription and complementary deoxyribonucleic acid (cDNA) processing of viral are very inefficient, and the viral DNA is degraded by enzymes in resting CD4⁺T cells [4, 5].



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Highly active antiretroviral treatment (HAART) involving the RTIs and PIs treatments is one of strategies to control HIV-1 infection. Reverse transcriptase inhibitors (RTIs) treatment function to prevent the infection process infection, while protease inhibitors to inhibit the activity for viral replication of the mature viral particles [7].

Recently, some studies have been done regarding HIV-1 infection in host cells. Srivastava *et al.* [8] established modelling of CD4⁺ T cells in HIV response based on the process of reverse transcription. These cells was separated in two classes. The first class is CD4⁺T cells of incomplete reverse transcription, namely pre-RT class and return to healthy. The second class is CD4⁺T cells of complete reverse transcription and become the infectious, namely post-RT class. Srivastava *et al.* incorporated the effect of RTI drug without PI drug in the model. Moreover they have not considered the HIV-1 transmission due to cell-to-cell contact, and CTL class in the model.

Chirove *et al.* [9] and Sutimin *et al.* [10, 11] established a model to capture the effect of the infection of Langerhans and CD4⁺T cells in early infection. They assumed that host cell infection can be transmitted via the contact from infected host cells to healthy hosts as well as cell-free viral. Instead, they have not accommodated both the process of reverse transcription and CTL response. Next study, Tarfulea *et al.* [12, 13] proposed a simple model involving the interaction of free virus and healthy CD4⁺T cell and CTL response. They incorporated CTL class and antiretroviral in controlling HIV-1 infection.

In this study, we are interested in HIV-1 infection process with reverse transcriptase within CD4⁺T cells. We develop a modelling from Srivastava *et al.* [8] to capture HIV-1 infection in CD4⁺T cells, by taking into account the HIV-1 transmission from infected cell to cells, and incorporating CTL class response. We analyse the model to explore the behaviour of the model and viral clearance effect of virus. In numerical simulations, we present the dynamics of CD4⁺T cells, and free virus populations in the various treatment scenarios

2. Model formulation

In this study, the model is developed from Srivastava *et al.* [8] by considering HIV-1 transmission from infected CD4⁺T cell to CD4⁺T cells, incorporating the effectiveness of PI drug, and CTL response. Under infection, the population of CD4⁺T cells are divided into two classes. Pre-RT class, in which viral reverse transcription is incomplete in CD4⁺T cells and post-RT class, in which viral reverse transcription is complete, namely infectious class. The model of nonlinear differential equation that describe the dynamics of susceptible CD4⁺T cells (T), pre-RT cells (L), post-RT (T_i) cells, CTL cells and free viruses (V) populations can be given as follows.

$$\frac{dT}{dt} = \lambda - \beta_1 VT - \beta_2 T_i T + (\varepsilon_{RTI} \alpha + \rho) L - \mu_1 T \quad (1)$$

$$\frac{dL}{dt} = \beta_1 VT + \beta_2 T_i T - (\mu_1 + \alpha + \rho) L \quad (2)$$

$$\frac{dT_i}{dt} = (1 - \varepsilon_{RTI}) \alpha L - (\mu_1 + \delta) T_i - \omega T_i Z \quad (3)$$

$$\frac{dZ}{dt} = \tau T_i - \mu_2 Z \quad (4)$$

$$\frac{dV}{dt} = N \delta (1 - \varepsilon_{PI}) T_i - (\mu_v + \phi) V \quad (5)$$

The susceptible CD4⁺T cells are produced with the constant rate λ , and die naturally with a constant rate μ_1 . The infection rates of CD4⁺T cells by free virus and infected CD4⁺T cell are β_1 and β_2 , respectively. The CD4⁺T cells increase due to RTI drug and incomplete viral reverse transcription at the constant rates $\varepsilon_{RTI} \alpha$ and ρ , respectively. Parameters ε_{RTI} and ε_{PI} are the efficacy of RTI and PI drugs. Population of pre-RT class die due to inflammation with a constant rate μ_1 .

Upon RTI treatment, a part of $\alpha \varepsilon_{RTI} L$ in pre-RT class moves to the healthy CD4⁺T cells, and $(1 - \varepsilon_{RTI}) \alpha L$ become infectious. The HIV-1 infection rate in pre-RT class reduces from α to $(1 - \varepsilon_{RTI}) \alpha$. Upon PI treatment, the viral production of the infected CD4⁺T cells reduced by $N \delta (1 - \varepsilon_{PI})$. Infected CD4⁺T cells die due to killing by CTL with the constant rate ω . The population of CTL increases at a constant rate τ and dies with the constant rate μ_z . The free virus population diminishes with the death and viral clearance rates μ_v and ϕ , respectively. Next section, we analyse the stability of equilibriums for the model.

8 Model analysis

We use the basic reproduction ratio derived from the next generation matrix to analyse the local stability of uninfected equilibrium. The uninfected equilibrium point is $E_0 = (\frac{\lambda}{\mu_t}, 0, 0, 0)$ and the next generation matrix can be written by (see Dickmann [14])

$$G = \begin{pmatrix} \Psi_1 & \Psi_2 & \frac{\lambda \beta_1}{\mu_t (\phi + \mu_v)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad (6)$$

where,

$$\Psi_1 = -\frac{(1 - \delta_{RTI}) \lambda \beta_2 \alpha}{\mu_t (\mu_t + \alpha + \rho) (\mu_t + \delta)} + \frac{(1 - \delta_{RTI}) \lambda \beta_1 \alpha (1 - \delta_{PI}) N \delta}{\mu_t (\mu_t + \alpha + \rho) (\mu_t + \delta) (\phi + \mu_v)},$$

$$\Psi_2 = \frac{\lambda \beta_2}{\mu_t (\mu_t + \delta)} + \frac{\lambda \beta_1 (1 - \delta_{PI}) N \delta}{\mu_t (\mu_t + \delta) (\phi + \mu_v)}.$$

The eigenvalues of matrix G are $-\frac{(1 - \delta_{RTI}) \lambda \beta_2 \alpha}{\mu_t (\mu_t + \alpha + \rho) (\mu_t + \delta)} + \frac{(1 - \delta_{RTI}) \lambda \beta_1 \alpha (1 - \delta_{PI}) N \delta}{\mu_t (\mu_t + \alpha + \rho) (\mu_t + \delta) (\phi + \mu_v)}, 0, 0$. The

basic reproduction ratio \mathfrak{R}_0 can be written by,

$$\mathfrak{R}_0 = \frac{(1 - \delta_{RTI}) \lambda \beta_2 \alpha}{\mu_t (\mu_t + \alpha + \rho) (\mu_t + \delta)} + \frac{(1 - \delta_{RTI}) \lambda \beta_1 \alpha (1 - \delta_{PI}) N \delta}{\mu_t (\mu_t + \alpha + \rho) (\mu_t + \delta) (\phi + \mu_v)}. \quad (7)$$

The basic reproduction ratio is defined as the secondary infection generated from one infected CD4⁺T cell during in period infection, when it introduces in all susceptible CD4⁺T cells population.

1. Stability of uninfected state

The stability of uninfected equilibrium of the system is given in the following.

Theorem 1: The uninfected equilibrium E_0 is locally asymptotically stable when $\mathfrak{R}_0 < 1$.

Proof

The Jacobian matrix of the system at E_0 can be written as,

$$J(E_0) = \begin{pmatrix} -\mu_i & \alpha \dot{\delta}_{RTI} + \rho & \frac{-\beta_2 \lambda}{\mu_i} & 0 & \frac{-\beta_1 \lambda}{\mu_i} \\ 0 & -\mu_i - \alpha - \rho & \frac{\beta_2 \lambda}{\mu_i} & 0 & \frac{\beta_1 \lambda}{\mu_i} \\ 0 & (1 - \varepsilon_{RTI}) \alpha & -\mu_i - \delta & 0 & 0 \\ 0 & 0 & \tau & -\mu_z & 0 \\ 0 & 0 & N\delta(1 - \varepsilon_{PI}) & 0 & -\mu_v - \phi \end{pmatrix} \quad (7)$$

The eigenvalues of the Jacobian matrix (7) are $-\mu_i, -\mu_z$ and other three eigenvalues are the solution of the equation

$$\chi^3 + a_2 \chi^2 + a_1 \chi + a_0 = 0,$$

where,

$$a_2 = \mu_i + \mu_i + \mu_v + \alpha + \delta + \phi + \rho > 0,$$

$$a_1 = (\mu_i + \delta)(\mu_i + \alpha + \rho)(1 - \mathfrak{R}_0) + \frac{N\delta(1 - \dot{\delta}_{PI})(1 - \dot{\delta}_{RTI})\beta_1 \lambda \alpha}{\mu_i(\phi + \mu_v)} + (\phi + \mu_v)(\alpha + \delta + \mu_i + \mu_i + \rho)$$

$$a_0 = (\mu_i + \alpha + \rho)(\mu_i + \delta)(\phi + \mu_v)(1 - \mathfrak{R}_0).$$

By manipulating the computation $a_1 a_2 - a_0$, we have

$$a_1 a_2 - a_0 = (\mu_i + \alpha + \rho)(\mu_i + \delta)(1 - \mathfrak{R}_0) \Phi + \frac{(1 - \dot{\delta}_{PI})N\lambda(1 - \dot{\delta}_{RTI})a_2 \beta_1 \alpha \delta}{\mu_i(\phi + \mu_v)} + a_2(\phi + \mu_v) \Phi$$

$$(\phi + \mu_v)(\alpha + \delta + 2\mu_i + \rho)a_2, \text{ where } \Phi = \alpha + \delta + \mu_i + \mu_i + \rho$$

It can be seen that $a_1 a_2 - a_0 > 0$, when $\mathfrak{R}_0 < 1$. All eigenvalues of $J(E_0)$ are negative, when $\mathfrak{R}_0 < 1$. Thus, E_0 is locally asymptotically stable if $\mathfrak{R}_0 < 1$. It completes the proof.

3.2. Stability of endemic equilibrium

We study the global stability of endemic equilibrium using Lyapunov function. The endemic equilibrium for the model is $E^* = (T^*, L^*, T_i^*, Z^*, V^*)$, where

$$T^* = \frac{(\phi + \mu_v)(\mu_i + \alpha + \rho)(Z^* \omega + \delta + \mu_i)}{\alpha(1 - \dot{\delta}_{RTI})(N\delta\beta_1(1 - \dot{\delta}_{PI}) + \phi\beta_2 + \beta_2\mu_v)}, \quad L^* = \frac{Z^* \mu_z (Z^* \omega + \delta + \mu_i)}{\alpha\tau(1 - \dot{\delta}_{RTI})},$$

$$T_i^* = \frac{Z^* \mu_z}{\tau}, \quad V^* = \frac{NZ^* \delta \mu_z (1 - \dot{\delta}_{PI})}{\tau(\phi + \mu_v)}.$$

The solution Z^* fulfills the equation

$$A_2 Z^2 + A_1 Z + A_0 = 0, \quad (10)$$

where,

$$A_2 = \omega \mu_z (\alpha(1 - \dot{\delta}_{RTI}) + \mu_i)(N\delta\beta_1(1 - \dot{\delta}_{PI}) + \phi\beta_2 + \beta_2\mu_v) > 0, ,$$

$$A_1 = N\delta(1 - \dot{\delta}_{PI})\mu_z(\mu_i + \delta)(\alpha(1 - \dot{\delta}_{RTI}) + \mu_i)\beta_1 + \mu_z(\phi + \mu_v)(\mu_i + \delta)(\alpha(1 - \dot{\delta}_{RTI}) + \mu_i)\beta_2 + \omega\tau\mu_i(\phi + \mu_v)(\mu_i + \alpha + \rho).$$

$$A_0 = \tau \mu_i (\mu_1 + \alpha + \rho) (\mu_i + \delta) (\phi + \mu_v) (1 - \mathfrak{R}_0).$$

The equation (10) has exactly one positive solution Z^* if only if $\frac{A_0}{A_2} < 0$. It is fulfilled if

$\mathfrak{R}_0 > 1$. Thus the endemic equilibrium exists when $\mathfrak{R}_0 > 1$. It is not difficult to see that set $\Omega = \{(T, L, T_i, Z, V) \in \mathbb{R}_+^5 \mid T + L + T_i + Z + V \leq M\}$, with $M = \max\left\{\frac{\lambda}{\mu_i}, \frac{\tau \lambda}{\mu_2 \mu_i}, \frac{N \delta \lambda (1 - \varepsilon_{pi})}{\mu_i \mu_v}\right\}$ is a

positively invariant for $T(0), L(0), T_i(0), Z(0), V(0) > 0$. Next, we present a theorem of the global stability of endemic equilibrium as follows.

Theorem 2: The endemic equilibrium E^* is globally asymptotically stable when $\mathfrak{R}_0 > 1$.

Proof.

We define a Lyapunov function as follows,

$$F(T, L, T_i, Z, V) = \left(T - T^* - T^* \ln \frac{T}{T^*}\right) + c_1 \left(L - L^* - L^* \ln \frac{L}{L^*}\right) + c_2 \left(T_i - T_i^* - T_i^* \ln \frac{T_i}{T_i^*}\right) + c_3 \left(Z - Z^* - Z^* \ln \frac{Z}{Z^*}\right) + c_4 \left(V - V^* - V^* \ln \frac{V}{V^*}\right),$$

where $c_1, c_2, c_3, c_4 > 0$ are determined. It is clear that $F \in C^1$, $F(E^*) = 0$. The derivative of F with respect to t along solutions of the system (1) – (5) is given by

$$\begin{aligned} \frac{dF}{dt} &= \left(1 - \frac{T^*}{T}\right) \frac{dT}{dt} + c_1 \left(1 - \frac{L^*}{L}\right) \frac{dL}{dt} + c_2 \left(1 - \frac{T_i^*}{T_i}\right) \frac{dT_i}{dt} + c_3 \left(1 - \frac{Z^*}{Z}\right) \frac{dZ}{dt} + c_4 \left(1 - \frac{V^*}{V}\right) \frac{dV}{dt} \\ &= A - \mu_i T - \beta_1 (1 - a_1) VT - \beta_2 (1 - a_1) TT_i - (a_2 (\mu_i + \delta) - \beta_2 T^* - a_3 N \delta (1 - \varepsilon_{pi})) T_i \\ &\quad - (a_1 (\mu_1 + \alpha + \rho) - (\alpha \varepsilon_{RTI} + \rho) - a_2 \alpha (1 - \varepsilon_{RTI})) L - (a_3 (\mu_v + \phi) - \beta_1 T^*) V - \lambda \frac{T^*}{T} - a_1 \beta_2 L^* \frac{TT_i}{L} \\ &\quad - (\alpha \varepsilon_{RTI} + \rho) T^* \frac{L}{T} - a_1 \beta_1 L^* \frac{VT}{L} - a_2 (1 - \varepsilon_{RTI}) \alpha T_i^* \frac{L}{T_i} - a_3 N \delta (1 - \varepsilon_{pi}) V^* \frac{T_i}{V}, \end{aligned} \tag{9}$$

where $A = \lambda + \mu_i T^* + a_1 (\mu_1 + \alpha + \rho) L^* + a_2 (\mu_i + \delta) T_i^* + a_3 \mu_2 Z^* + a_4 (\mu_v + \phi) V^*$. We denote

$x = \frac{T}{T^*}, y = \frac{L}{L^*}, w = \frac{T_i}{T_i^*}, z = \frac{Z}{Z^*}, v = \frac{V}{V^*}$. The equation (9) becomes

$$\begin{aligned} \frac{dF}{dt} &= A - \mu_i T^* x + \beta_1 (a_1 - 1) V^* T^* x v + \beta_2 (a_1 - 1) T^* T_i^* x w + (a_2 \omega T_i^* - a_3 \mu_2) Z^* z \\ &\quad + (\beta_2 T^* - a_2 (\mu_i + \delta) + a_4 N \delta (1 - \varepsilon_{pi}) + a_3 \tau) T_i^* w + (\beta_1 T^* - a_4 (\mu_v + \phi)) V^* v \\ &\quad + (\alpha \varepsilon_{RTI} + \rho) - (a_1 (\mu_1 + \alpha + \rho) + a_2 (1 - \varepsilon_{RTI}) \alpha) L^* y - \lambda \frac{1}{x} - a_2 \omega T_i^* Z^* w z - (\varepsilon_{RTI} \alpha + \rho) L^* \frac{y}{x} \\ &\quad - a_2 (1 - \varepsilon_{RTI}) \alpha L^* \frac{y}{w} - a_3 \tau T_i^* \frac{w}{z} - a_4 N \delta (1 - \varepsilon_{pi}) T_i^* \frac{w}{v} - a_1 \beta_1 T^* V^* \frac{xv}{y} - a_1 \beta_2 T^* T_i^* \frac{xw}{y} \end{aligned} \tag{10}$$

If we make the coefficients of y, w, z, v, xv, xw are equal to 0, so we have the relationship

$$\begin{aligned}
a_1 &= 1, \\
a_1(\mu_1 + \alpha + \rho) &= (\alpha\varepsilon_{RTI} + \rho) + a_2\alpha(1 - \varepsilon_{RTI}), \\
a_2(\mu_t + \delta) &= \beta_2 T^* + a_4 N\delta(1 - \varepsilon_{PI}) + a_3\tau, \\
a_3\mu_z &= a_2\omega T_i^*, \\
a_4(\mu_v + \phi) &= \beta_1 T^*.
\end{aligned} \tag{11}$$

The right hand side in (10) becomes

$$\begin{aligned}
& b_1\left(2 - x - \frac{1}{x}\right) + b_2\left(3 - \frac{1}{x} - \frac{y}{w} - \frac{xw}{y}\right) + b_3\left(4 - \frac{1}{x} - \frac{y}{w} - \frac{w}{v} - \frac{xv}{y}\right) - (\alpha\varepsilon_{RTI} + \rho)L^* \frac{y}{x} \\
& - a_2\omega T_i^* Z^* xw - a_3\tau T_i^* \frac{w}{z}
\end{aligned} \tag{12}$$

The constants $b_1, b_2, b_3, a_1, a_2, a_3$ can be determined by considering the following relations,

$$\begin{aligned}
\lambda &= \beta_1 V^* T^* + \beta_2 T^* T_i^* + \mu_t T^* - (\varepsilon_{RTI}\alpha + \rho)L^*, \\
\beta_1 V^* T^* + \beta_2 T^* T_i^* &= (\mu_1 + \alpha + \rho)L^*, \\
(\mu_t + \delta)T_i^* &= (1 - \varepsilon_{RTI})\alpha L^*, \\
(\mu_v + \phi)V^* &= N\delta(1 - \varepsilon_{PI})T_i^*.
\end{aligned} \tag{12}$$

Equating coefficients in equation (10) and (12), we get the relationship

$$\begin{aligned}
2b_1 + 3b_2 + 4b_3 &= C, \quad 1 - a_1 = 0, \quad b_1 = \mu_t T^*, \quad b_1 + b_2 + b_3 = \lambda, \\
a_1(\mu_1 + \alpha + \rho) &= (\alpha\varepsilon_{RTI} + \rho) + a_2\alpha(1 - \varepsilon_{RTI}), \quad a_2(\mu_t + \delta) = \beta_2 T^* + a_4 N\delta(1 - \varepsilon_{PI}) + a_3\tau, \\
a_3\mu_z &= a_2\omega T_i^*, \quad a_3 N\delta(1 - \varepsilon_{PI}) = a_2(\mu_t + \delta) - \beta_2 T^*, \\
b_2 + b_3 &= a_2(1 - \varepsilon_{RTI})\alpha L^*, \quad b_2 = a_1\beta_2 T^* T_i^*, \quad b_3 = a_3 N\delta(1 - \varepsilon_{PI})T_i^* = a_1\beta_1 V^* T^*, \quad a_4(\mu_v + \phi) = \beta_1 T^*.
\end{aligned}$$

So we can fix $a_i, i=1,2,3$ where $a_1 = 1, a_2 = \frac{\mu_t + (1 - \varepsilon_{RTI})\alpha}{(1 - \varepsilon_{RTI})\alpha}, a_3 = \frac{(\alpha(1 - \varepsilon_{RTI}) + \mu_t)\omega T_i^*}{\alpha(1 - \varepsilon_{RTI})\mu_z},$

$a_4 = \frac{\beta_1 T^*}{\mu_v + \phi}$. From the inequality of arithmetic and geometric mean, we can see that

$$\begin{aligned}
\frac{dF}{dt} &= \mu_t T^* \left(2 - x - \frac{1}{x}\right) + \beta_2 T^* T_i^* \left(3 - \frac{1}{x} - \frac{y}{w} - \frac{xw}{y}\right) + \beta_1 V^* T^* \left(4 - \frac{1}{x} - \frac{y}{w} - \frac{w}{z} - \frac{xz}{y}\right) \\
& - (\alpha\varepsilon_{RTI} + \rho)L^* \frac{y}{x} - a_2\omega T_i^* Z^* wz - a_3\tau T_i^* \frac{w}{z} \leq 0.
\end{aligned}$$

It is clear that $\frac{dF}{dt} = 0$ for $T = T^*, L = L^*, T_i = T_i^*, Z = Z^*, V = V^*$, thus the largest invariant set of

$\left\{(T, L, T_i, Z, V) \mid \frac{dF}{dt} = 0\right\}$ is the singleton $\{E^*\}$. We conclude that E^* is globally asymptotically stable.

4. Numerical simulations ¹⁷

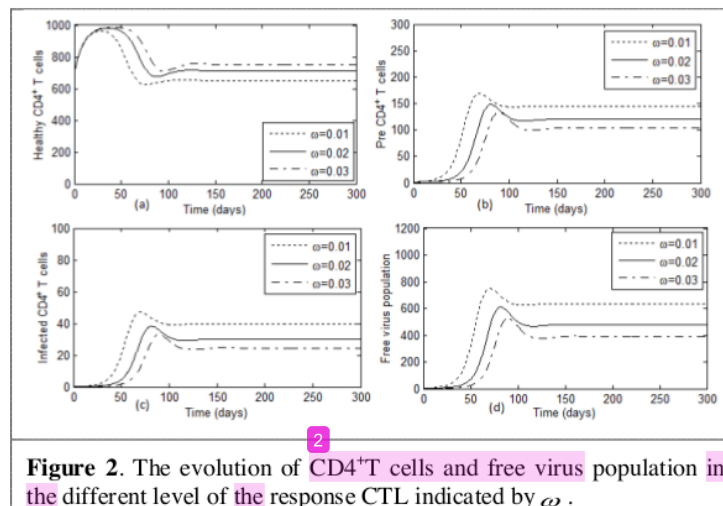
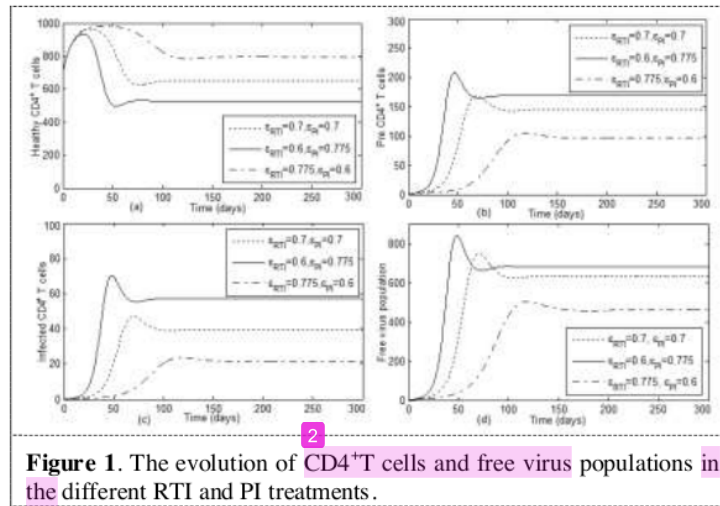
We present the simulations of the dynamics of CD4⁺ T cells and free virus populations and the impact of RTI and PI treatments. For the simulations, we take $T(0) = 700$ cells/mm³, $L(0) = 0$ cell/mm³, $T_i(0) = 0$ cell/mm³, $Z(0) = 0$ cell/mm³, and $V(0) = 0.001$ virions/mm³ [15]. The value of parameter are presented in Table 1.

Table 1. Table of parameter values, units and references.

Parameters	Values	Units	References
λ	100	Cells/day	[19]
α	0.1	1/day	[8]
β_1	(0.00002,0.001)	mm ³ /day	[17]
β_2	(0.00001,0.01)	mm ³ /day ⁶	[9]
μ_t	0.02, 0.1	1/day	[18]
μ_1	0.015	1/day	[8]
μ_v	2.4	1/day	[16]
\mathcal{D}	0.24	1/day	[19]
ϕ	(2,9)	1/day	[20, 21]
N	(100, 1000)	cells/day	[22]
μ_z	0.05	1/day	[23]
τ	0.01	1/day	[23]
ω	0.01	1/day	[23]

In Figure 1, it presents the evolutions of CD4⁺T cells and free virus populations in different scenarios for endemic state. We consider the overall efficacy (ε) when RTI and PI drugs are administered simultaneously [13] that is defined as $\varepsilon = 1 - (1 - \varepsilon_{RTI})(1 - \varepsilon_{PI})$. We determine the value $\varepsilon = 0.91$ and use the different values of $\varepsilon_{RTI}, \varepsilon_{PI}$ in the simulation. We can see in Figure 1, first in long term the population of CD4⁺T cells and free virus approach to endemic equilibrium, it describes *theorem 2*. Second it shows that the increasing in efficacy value RTI drug is faster in the increasing of the healthy CD4⁺T cells compared to the efficacy value PI drug. It is related to effectiveness of RTI drug in preventing the progression of infection.

Figure 2 shows CTL clearance level ⁷ of infected CD4⁺T cells leads to the increase of the healthy CD4⁺T cells. It is related to the reducing of the infected CD4⁺T cells and free virus populations. It may suggest that when CTL cells can respond fairly ⁹ to HIV-1, the number of free virus can be prevented in individuals with HIV in early infection. Thus the progression of HIV-1 infection in individual can be pressed.



5. Conclusion

In the study, we modified a modelling of HIV-1 infection in host. The model was developed by considering viral transmission from the infected CD4⁺T cell to healthy CD4⁺T cell and the effect of CTL response. We analyse the model to address the stability of equilibriums. The basic reproduction ratio was obtained through the next generation matrix, and used it to analyse the local stability of uninfected equilibrium and the existence of endemic equilibrium. We construct Lyapunov function to analyse the global stability of endemic equilibrium. The basic reproduction ratio can be express in the sum of two sub reproduction ratios. The locally asymptotically stable of uninfected equilibrium is achieved if the ratio less than unity. The globally stable of endemic equilibrium is achieved if the ratio larger than unity.

We study the simulations to illustrate the evolution of CD4⁺T cells and virus populations in long term under the various treatment scenarios. Based on the efficacy value, we can conclude that treatment of RTI drug is more effective that of PI drug in preventing HIV-1 infection. In the immune

response of CTL, when fair level in responding HIV-1, these cytotoxic cells is still able to press the progression of HIV-1 infection.

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