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STABILITY ANALYSIS OF HIV-1 DYNAMICS UNDER DISTINCT HAART REGIMES

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Abstract. In this paper, we propose a model for the dynamics of HIV-1 epidemics under distinct regimes and study the emergence of drug resistance. Our main result shows that the stability analysis for HIV-1 infection delay model with HARRT regimes. Finally, an applicability of the results of this paper can be shown by graphically.

Keywords: bifurcation; drug-resistance; HAART regimes; HIV-1; stability switch.

2010 AMS Subject Classification: 92D25, 34C23, 37B25.

1. INTRODUCTION

Progress in the qualitative understanding of the HIV-1 dynamics has been achieved in various infectious diseases using delay differential equation models [1–8]. The general class of models that have been studied [9–15] have a form similar to

$$\begin{aligned} \dot{T} &= s - \mu T - kTV, \\ \dot{T}^* &= kTV - \delta T^*, \\ \dot{V} &= N\delta T^* - cV, \end{aligned} \tag{1}$$

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where the notations are described below in Table I.

The study of the epidemiology of infectious diseases has attracted the attention of scientists from distinct areas of science, suchasbiology, medicine, mathematics, computerscience. Understanding the disease patterns may contribute to the improvement of the quality of patients' life, decrease the economical burden, and help to prevent(or minimize the effects of) future occurrences.

In delay differential equations, if the delays are finite, then the characteristic equations are functions of delays, and hence the roots of these characteristic equations are also functions of delays. As the lengths of delays change, the stability of the trivial solution may also change. Such phenomena are often referred to as stability switches. In this article, we consider the question of stability switches in HIV-1 infection dynamics system of delay differential equations.

Specifically, we shall show that the stability of a given steady state is simply determined by the graphs of certain functions of delays which can be expressed explicitly and thus can be easily depicted by *Waterloo Maple* software. In fact, for most application problems, we need only look at one such function and locate its zeros. This function often has only two zeros, providing thresholds for stability switches. The common scenario is that as time delay increases, stability changes from stable to unstable to stable. We hope this work will show that it is important and possible to systematically study stability aspects of some models with delay dependent parameters.

The focus of this paper is, to develop and analyze a mathematical model for the perturbation of HIV-1 infection delay with HAART. The study analyzes the effectiveness of such therapy under various efficiencies of the anti-HIV response of the immune system [17–19]. An analytic study is carried out to show that the model has a stability switch at its steady state, that is jumping from one another and exchanging their stability at a critical boundary.

2. THE MODEL

2.1. Deterministic dynamic behaviour of the delay system with HAART. Models of this simple form have been adequate to summarize the effects of drug therapy on the virus concentration. The most important of these drugs consists in a combination of distinct drugs-also

known as, Highly Active Antiretroviral Therapy (HAART), such as reverse transcriptase inhibitors (RTIs) and protease inhibitors (PIs). RTIs inhibit the infection of $CD4^+$ T cells and macrophages by virus. On the other hand, PIs prevent the production of infectious virus from already infected cells. Drug-resistance is associated with high virus replication and mutation rates, poor adherence to therapy,or poor absorption and pharmacokinetics. Protease inhibitors (PIs) enzymes are used by the viruses to cleave nascent proteins for final assembly of new virus. The new virus are noninfectious. Virions that were created prior to drug treatment remain infectious.Thus, in the presence of a protease inhibitor, two types of virus particles (i.e., infectious virions and noninfectious virions) should be considered [20]. We need the drug to be highly effective if we use single drug to treat. Hence, combination anti-HIV therapy is now the standard of care for people with HIV. So far as we know, there are few mathematical models about the effects of combination anti-HIV therapy. Monica and Pitchaimani [20, 21] have considered that drug therapy delay model for HIV infection, in host was extended to incorporate logistic growth and an intracellular delay. However, none of these models have incorporated antiretroviral therapy, logistic growth of the $CD4^+$ T cells, and intracellular delay. Here, we build on the basic model of HIV-1 infection, adding the effects of antiretroviral therapy, logistic growth of the $CD4^+$ T cells, and intracellular delay. Hence, we can obtain the following model:

$$
\begin{aligned}
\dot{T} &= s + rT(t)\left(1 - \frac{T(t)}{T_{max}}\right) - \mu_1 T(t) - (1-\varepsilon_r)ke^{-m\tau_1}T(t-\tau_1)V_I(t-\tau_1),\\
\dot{T}^* &= (1-\varepsilon_r)ke^{-m\tau}T(t-\tau)V_I(t-\tau) - \delta T^*(t),\\
\dot{V}_I &= (1-\varepsilon_p)N\delta e^{-\nu\tau_2}T^*(t-\tau_2) - cV_I(t), \qquad (2)\\
\dot{V}_{NI} &= \varepsilon_p N\delta e^{-\nu\tau_2}T^*(t-\tau_2) - cV_{NI}(t),
\end{aligned}
$$

where ε_p is the efficacy of the protease inhibitor scaled such that $\varepsilon_p = 1$ corresponds to a completely effective drug that results only in the production of non-infectious virions V_{NI}, ε_r is the efficacy of the RTI, and τ is the total intracellular delay, τ_1 is the delay corresponding to the loss of target cells by infection [16], and τ_2 is the delay representing the time necessary for a newly infected virus to become mature and then infectious. r is the maximum proliferation rate, T_{max} is the T cell population density at which proliferation shuts off. The term $e^{-m\tau_1}$ accounts for cells that are infected at time t but die before becoming productively infected τ_1 time units

later i.e., the survival probability of infected cell is given by $e^{-m\tau_1}$ [16], where $\frac{1}{m}$ represents the average life time of an infected cell and thus the incorporation of the term $e^{-m\tau}$. The probability of survival of immature virions is given by $e^{-v\tau_2}$ [16], where $\frac{1}{v}$ is the average life time of an immature virus.

Table I: In Vitro Model Parameters

Notation	Description
T	Uninfected target cells
T^*	Infected cells that are producing virus
V	Virus ($V = V_I + V_{NI}$
	V_I - infectious virus and V_{NI} - non-infectious virus)
s	Rate at which new target cells are generated
μ_1	Specific death rate of target cells
k	Constant rate that characterizing target cell infection
δ	Over all death rate of target cells
N	New virus particles
c	Clearance rate of virus cells
r	Growth rate of T cells
T_{max}	Carrying capacity of T cells

3. EXISTENCE OF BIFURCATION PARAMETER

Let us consider the following general form of linear delay differential equation with single delay $\tau(\tau > 0)$:

$$\sum_{k=0}^{n} A_k \frac{d^k}{dt^k} x(t) + \sum_{k=0}^{n} \frac{d^k}{dt^k} x(t-\tau) = 0, \tag{3}$$

where $\frac{d^0}{dt^0} x(t) \equiv x(t)$.

Further, the stability analysis of equation (3) is very much equivalent to the problem of determining conditions under which all roots of its characteristic equation. At steady state, the corresponding characteristic equation of DDE (3), will have the form

$$H(\lambda, \tau) = P(\lambda) + Q(\lambda) e^{-\lambda \tau} = 0, \tag{4}$$

where τ is the length of the discrete delay added, and P and Q are polynomials defined as follows:

$$P(\lambda) = \sum_{j=0}^{N} \alpha_j \lambda^j;\ Q(\lambda) = \sum_{j=0}^{M} \beta_j \lambda^j. \tag{5}$$

where $N, M \in \mathbb{N}_0 = \mathbb{N} \cup \{0\}$. Stabilities of the steady states are investigated by analyzing the corresponding characteristic equation. By choosing the time delay as a bifurcation parameter, a sufficient condition has been established for existence of bifurcation at the steady states. The following demonstrates how to determine whether or not such a τ exists, by reducing (4) to a polynomial problem and seeking particular types of roots, thus determining whether a bifurcation can occur as a result of the introduction of delay.

We begin by looking for a purely imaginary root, $\lambda = i\omega,\ \omega \in \mathbb{R}$ of (4). Equation (4) becomes,

$$P(i\omega) + Q(i\omega)e^{-i\omega\tau} = 0.$$

Since P and Q are polynomials with real coefficients

$$\overline{P(-i\omega)} = P(i\omega),\ \overline{Q(-i\omega)} = Q(i\omega),$$

where $\bar{X}$ denotes complex conjugate of X.

We break the polynomial up into its real and imaginary parts, we obtain the new polynomials as follows,

$$\begin{aligned} P_R(\omega) &= \sum_{j=0}^{M} (-1)^j \alpha_{2j} \omega^{2j}, \\ P_I(\omega) &= \sum_{j=0}^{M} (-1)^j \alpha_{2j+1} \omega^{2j+1}, \\ Q_R(\omega) &= \sum_{j=0}^{N} (-1)^j \beta_{2j} \omega^{2j}, \\ \text{and} \quad Q_I(\omega) &= \sum_{j=0}^{N} (-1)^j \beta_{2j+1} \omega^{2j+1}. \end{aligned}$$

Note that because $i\omega$ is purely imaginary, P_R and Q_R are even polynomials of ω, while P_I and Q_I are odd polynomials. After some little algebra, we can write $\dfrac{Q_R(\omega^*)}{C} = \cos\alpha$ and

$\frac{Q_I(\omega^*)}{C} = \sin\alpha$, where $C = |Q(\omega)|$ and then

$$\begin{aligned} -P_R(\omega^*) &= C\cos(\omega^*\tau - \alpha), \text{and} \\ P_I(\omega^*) &= Csin(\omega^*\tau - \alpha). \end{aligned}$$

Since the point $(-P_R(\omega^*), P_I(\omega^*))$ lies on the circle of radius C, it is then clear that there is a positive value $\tau = \tau^*$ that satisfies both equations simultaneously. An alternate approach, more geometrical in nature, on finding the roots of the characteristic equation (4) is taken in [22]. In this case, for $\lambda = i\omega$, we rewrite (4) as

$$-\frac{P(i\omega)}{Q(i\omega)} = e^{-i\omega\tau}. \tag{6}$$

As τ varies, plotting the right hand side in the complex plane traces out a unit circle, and the left hand side is a rational curve. The intersections of these curves represent the critical delays in which we are interested.

4. Stability Switch Criterion for HIV-1 Dynamics

Recently the author [23] examined the possible occurrence of stability switch for the characteristic equation (4). Here, we explore the occurrence of stability switch for our model (2), which involves with delay dependent parameters are as follows,

$$H(\lambda, \bar{\tau}) = P(\lambda) + e^{-\lambda\bar{\tau}}Q(\lambda) = 0, \tag{7}$$

where

$$\begin{aligned} P(\lambda) &= \lambda^4 + a_{11}\lambda^3 + a_{22}\lambda^2 + a_{33}\lambda + a_{44} \\ Q(\lambda) &= b_{11}\lambda^2 + b_{22}\lambda + b_{33}e^{-\lambda\bar{\tau}} \end{aligned}$$

Let $\lambda = i\omega(\omega > 0)$ be a purely imaginary root of (7). Substituting it into (7) and separating the real and imaginary parts, it leads to

$$P_R(\omega) = \omega^4 - \omega^2 a_{22} + a_{44}; \quad Q_R(\omega) = -b_{11}\omega^2\cos(\omega\bar{\tau}) + b_{22}\omega\sin(\omega\bar{\tau}) + b_{33}\cos(\omega\bar{\tau}),$$

$$P_I(\omega) = -a_{11}\omega^3 - \omega a_{22} + a_{33}; \quad Q_I(\omega) = b_{11}\omega^2\sin(\omega\bar{\tau}) + b_{22}\omega\cos(\omega\bar{\tau}) - b_{33}\sin(\omega\bar{\tau})$$

Squaring and adding the above equation (8), we obtain the Eighth degree equation for ω as follows:

$$F(\omega) = \omega^8 + \omega^6(a_{11}^2 - 2a_{22}) + \omega^4(a_{22}^2 - b_{11}^2 + 2a_{44} - 2a_{11}a_{33}) + \omega^2(a_{33}^2 - 2a_{22}a_{44} - b_{22}^2 + 2b_{11}b_{33}) + a_{44}^2 - b_{33}^2 = 0. \tag{9}$$

Putting $\omega^2 = \mu$ into (9), we can get the following equation:

$$F(\mu) = \mu^4 + \mu^3\rho_1 + \mu^2\rho_2 + \mu\rho_3 + \rho_4 = 0. \tag{10}$$

Where

$$\begin{aligned}
a_{11} &= \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right) + c\right)(c+\delta) + (c+\delta) \\
a_{22} &= \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right)c\right) \\
&\quad + \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right) + c\right)(c+\delta) + c\delta \\
a_{33} &= \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right)c\right) \\
&\quad + \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right) + c\right)c\delta \\
a_{44} &= \mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right)c^2\delta
\end{aligned}$$

$$\begin{aligned}
b_{11} &= -c\delta \\
b_{22} &= R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}} - \mu_1 T^*\right)\right)c\delta \\
&\quad - \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right) + c\right)c\delta \\
b_{33} &= R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}} - \mu_1 T^*\right)\right)c\delta \\
&\quad - \left(\mu_1 - r + \frac{2rT^*}{T_{max}} + R_0\left(s + rT^*\left(1 - \frac{T^*}{T_{max}}\right)\right)\right)c^2\delta
\end{aligned}$$

and

$$\begin{aligned}\rho_1 &= a_{11}^2 - 2a_{22}\\ \rho_2 &= a_{22}^2 - b_{11}^2 + 2a_{44} - 2a_{11}a_{33}\\ \rho_3 &= a_{33}^2 - 2a_{22}a_{44} - b_{22}^2 + 2b_{11}b_{33}\\ \rho_4 &= a_{44}^2 - b_{33}^2.\end{aligned}$$

Taking derivative with respect to μ of equation (10), we get

$$\dot{F}(\mu) = 4\mu^3 + 3\mu^2\rho_1 + 2\mu\rho_2 + \rho_3 = 0. \tag{11}$$

It is easy to verify that the coefficient in the above equation (11) are all positive and hence $\dot{F}(\mu) > 0$. By Descartes rule of signs, equation (10) has positive root μ and thus equation (9) has a pair of purely imaginary roots $i\omega$.

We assume that $P(\lambda)$ and $Q(\lambda)$ are analytic function in λ and differentiable in $\bar{\tau}$ and

(i) $P_0 + Q_0 \neq 0$, i.e., $\lambda = 0$ is not a characteristic root of (7).

(ii) If $\lambda = i\omega$, then $P(i\omega) + Q(i\omega) \neq 0$,

(iii) $\limsup\left\{\left|\frac{Q(\lambda)}{P(\lambda)}\right| : \lambda \to \infty,\ \Re\lambda \geq 0\right\} < 1$,

(iv) $F(\omega) = |P(\omega)|^2 - |Q(\omega)|^2$ has at most a finite number of real zeros,

(v) Each positive root ω of $F(\omega)$ is continuous in $\bar{\tau}$ whenever exists.

First, it is easy to see that

$$P_0 + Q_0 = a_{44} + b_{33} > 0 \tag{12}$$

which implies that (i) is satisfied. It is easy to see that, if $\lambda = i\omega$, then

$$P(i\omega) + Q(i\omega) \neq 0$$

and then the criterion (ii) is satisfied.

From (7), we know that for each $\bar{\tau}$,

$$\lim_{|\lambda|\to\infty}\left|\frac{Q(\lambda)}{P(\lambda)}\right| = 0$$

and the criterion (iii) holds.

Let $\lambda = i\omega^*(\omega^* > 0)$ be a purely imaginary root of (7), separating the real and imaginary parts, it leads to

$$\omega^{*4} - \omega^{*2}a_{22} + a_{44} = (b_{11}\omega^{*2} - b_{33})\cos(\omega^*\bar{\tau}) - b_{22}\omega^*\sin(\omega^*\bar{\tau}),$$

$$\omega^{*3}a_{11} - \omega^* a_{33} = (b_{11}\omega^{*2} - b_{33})\sin(\omega^*\bar{\tau}) + b_{22}\omega^*\cos(\omega^*\bar{\tau}) \tag{13}$$

Hence ω^* satisfies

$$\sin(\omega^*\bar{\tau}) = \frac{-b_{11}\omega^*(\omega^{*4} - \omega^{*2}a_{22} + a_{44}) + (b_{11}\omega^{*2} - b_{33})(-\omega^* a_{33} + \omega^{*3}a_{11})}{(b_{11}\omega^{*2} - b_{33})^2 + (b_{22}\omega^*)^2}$$

$$\cos(\omega^*\bar{\tau}) = \frac{(b_{11}\omega^{*2} - b_{33})\left(\omega^{*4} - \omega^{*2}a_{22} + a_{44}\right) + b_{22}\omega^*(-\omega^* a_{33} + \omega^{*3}a_{11})}{(b_{11}\omega^{*2} - b_{33})^2 + (b_{22}\omega^*)^2} \tag{14}$$

Squaring and adding both equations of (13) gives

$$L(\omega^*, \bar{\tau}) = \omega^{*8} + z_1\omega^{*6} + z_2\omega^{*4} + z_3\omega^{*2} + z_4 = 0. \tag{15}$$

where

$$\begin{aligned} z_1 &= a_{11}^2 - 2a_{22} \\ z_2 &= a_{22}^2 - b_{11}^2 + 2a_{44} - 2a_{11}a_{33} \\ z_3 &= a_{33}^2 - 2a_{22}a_{44} - b_{22}^2 + 2b_{11}b_{33} \\ z_4 &= a_{44}^2 - b_{33}^2. \end{aligned}$$

Obviously, the criterion (iv) holds for function L. From the Implicit Function Theorem, the criterion (v) is also satisfied. Note that

$$L(0, \bar{\tau}) = a_{44}^2 - b_{33}^2 < 0,$$

and

$$\lim_{\lambda \to +\infty} L(\lambda, \bar{\tau}) = +\infty$$

In addition, from (12), we have $a_{44} > 0$ and $b_{33} > 0$. Therefore if it holds that

$$(D1) \quad a_{44} < b_{33},$$

then $L(\omega^*, \bar{\tau}_2) = 0$ has at least one positive solution.

According to [24], we choose $\theta(\bar{\tau}) \in [0, 2\pi)$ such that $\sin\theta(\bar{\tau})$ and $\cos\theta(\bar{\tau})$ are given by the right sides of (14) respectively, and define

$$S_m(\bar{\tau}) = \bar{\tau} - \frac{\theta(\bar{\tau}) + 2m\pi}{\omega^*}, \;\; m \in \mathbb{N}_0 := \{0, 1, 2, 3, ...\},$$

where $\bar{\tau}$ exists for $(D1)$ to be true. Obviously, $i\omega^*$ is a purely imaginary root of (7) if and only if $\bar{\tau}$ is a root of function S_m for some $m \in \mathbb{N}_0$. summarize the above , we conclude the following theorem.

Theorem 4.1. *If $(D1)$ holds, then the characteristic equation (7) admits a pair of simple pure imaginary roots $i\omega^*(\bar{\tau})$ and $-i\omega^*(\bar{\tau})$, $\omega^*(\bar{\tau}) > 0$ at $\bar{\tau} \in (0, \bar{\tau}_{max})$ if $S_m(\bar{\tau}) = 0$ for some $m \in \mathbb{N}_0$, and it crosses the imaginary axis from left to right (from right to left) if $\Delta(\bar{\tau}) > 0 (< 0)$, where*

$$\Delta(\bar{\tau}) = sign\left\{\left(\frac{d(\Re(\lambda))}{d\bar{\tau}}\right)\right\}_{\lambda = i\omega^*} = sign\left\{L'_{\omega^*}(\omega^*, \bar{\tau})\right\} sign\left\{\left(\frac{dS_m(\bar{\tau})}{d\bar{\tau}}\right)\right\}.$$

In addition, if the root of (15) is unique, then

$$\Delta(\bar{\tau}) = sign\left\{\left(\frac{dS_m(\bar{\tau})}{d\bar{\tau}}\right)\right\}.$$

5. Numerical Simulation

Application in HIV-1 dynamics:

Consider the HIV-1 infection dynamical model (2). The system (2) has two steady states, namely, viral free steady state and infected steady state. Bifurcation occurs only at its infected steady state under certain condition. In this section, we analyze the stability switch and non-degeneracy of this model.

The two non-negative steady states as follows: viral free steady state:

$S_v = (\hat{T}, \hat{T}^*, \hat{V}_I, \hat{V}_{NI}) = \left(\frac{T_{max}}{2r}\left(r - \mu_1 + \sqrt{(r-\mu_1)^2 + \frac{4rs}{T_{max}}}\right), 0, 0, 0\right)$

and infected steady state:

$S_i = (\bar{T}, \bar{T}^*, \bar{V}_I, \bar{V}_{NI})$

$$= \left\{\frac{\hat{T}}{R_0}, \frac{c\bar{V}_I}{(1-\varepsilon_p)Ne^{-\nu\tau_2}}, \frac{R_0}{(1-\varepsilon_r)ke^{-m\tau_1}\left(s + r\bar{T}\left(1 - \frac{\bar{T}}{T_{max}}\right) - \mu_1\bar{T}\right)}, \frac{\varepsilon_p N\delta e^{-\nu\tau_2}\bar{T}^*}{c}\right\}$$

Here,

$$R_0 = \frac{kN(1-\varepsilon_p)\hat{T}e^{-m\tau}e^{-\nu\tau_2}}{c}, \tag{16}$$

is the basic reproductive ratio which denotes the expected number of infected cells produced by one infected cell in the expected life time in the initial infection.

In order to illustrate some of the effects of distributed delay, we numerically solve the system of delay differential equation using *Maple*. In this section, we perform some numeric simulations to demonstrate the theoretical results obtained in previous sections. We present the numerical simulations to observe the dynamics of the system with a set of parameter values in Table - II.

Table II: List of Variables and Parameters and their values which are taken from [15] and [25].

Variable and Parameter	Value	Units
$T(0)$	180	cells/mm^3
$T^*(0)$	3.6	cells/mm^3
$V_I(0)$	134	virions/mm^3
$V_{NI}(0)$	0	
s	$1-10$	(cells/mm^3)/day
μ	$0.01-0.03$	/day
δ	$0.26-0.68$	/ days
N	$326-503$	virions /cells
c	$2.06-3.81$	/ days

We integrated the system (2) numerically for the parametric values as in Table II. By extracting the values from [15, 25], we choose a set of parameters as follows: $s = 1-10, d_T = 0.03, \delta = 0.26-0.68, N = 326-503, c = 2.06-3.81$. The drug efficacy ε_p varies and we simulated for different values of ε_p $(\varepsilon_p = 0.45, 0.75, 0.95)$ keeping $N = 480$ and $s = 10$, and with initial condition $T(0) = 180, T^*(0) = 3.6, V_I(0) = 134, V_{NI} = 0$. It may be pointed out that for $\varepsilon_p = 1$ corresponds to a completely effective drug that results only in the production of non-infectious virions V_{NI}. The numerical simulation shows that system approaches to the infected steady state for $\varepsilon_p = 0.45$ and to the viral free steady state for other values of ε_p considered. As ε_p increases from 0.45 to 0.75 the viral level decreases and in the case when $\varepsilon_p = 0.95$ it approaches to zero.

The results are plotted from Fig. 3(a) - 3(c) It can be easily seen that the level of CD4$^+$ T cells increases with increase in ε_p.

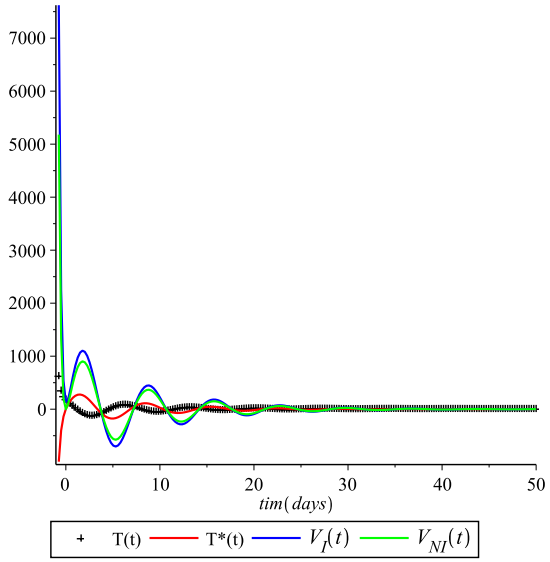

Figure - 3(a)

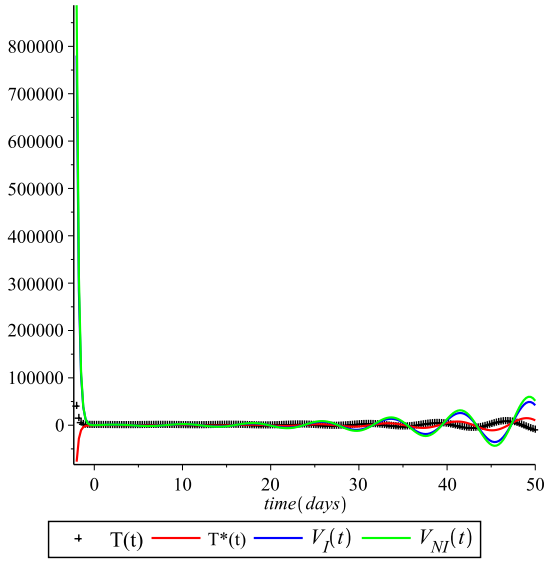

Figure - 3(b)

Figure 3(a)-3(b): Solution trajectories of system (2) for different values keeping $\varepsilon_r = (0.45, 0.75)$ and $\varepsilon_p = (0.45, 0.75)$. All other remaining parameters are same as in Table II.

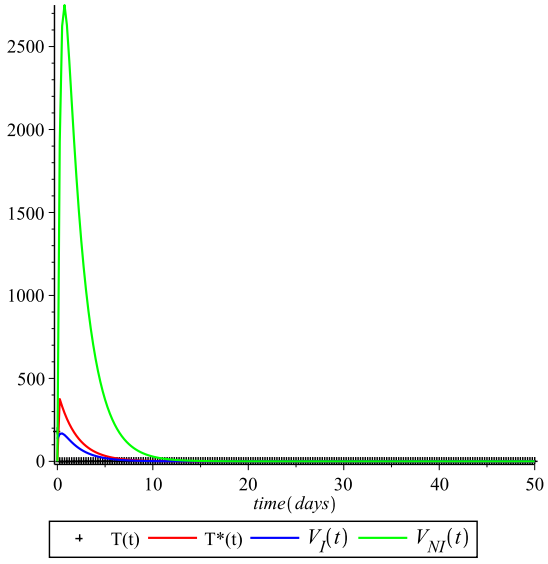

Figure - 3(c)

Figure 3(c): Solution trajectories of system (2) for different values keeping $\varepsilon_r = 0.95$ and $\varepsilon_p = 0.95$. All other remaining parameters are same as in Table II.

The interpretation of this figure strongly suggests that ε_r and ε_p have the strongest influence over the solution in our model compartment. Therefore, for the use of equation (2) (as a model to simulate HIV pathogenesis), both the viral production rate and the death rate for acutely infected cells should be given top priority when choosing which parameters to determine with a high degree of accuracy when the consumption of drug therapy.

We obtained that the numerical solution of equation of (2) of infected equilibrium. S_i is locally stable when $R_0 > 1, \bar{\tau} \in [0, \bar{\tau}), \bar{\tau} = 1.85$. It was shown using numerical simulations that for the given set of parameters, when the drug efficacy was 45%, the infected steady state is stable, and when we assume the drug efficacy to be 75% and 95%, the level of uninfected cell increases but infection still persists. When the efficacy was increased to 95% the infection was cleared. Thus, our numerical results are reasonable representatives of our model. Moreover, small perturbations of parameters will give small perturbation of the matrix entries used in finding eigenvalues for determining the stability of two steady state points. The stability results in our numerical calculation are biologically reasonable and represent a qualitative outcome that is possible for the parameter values.

From the numerical calculation as well as the graphical results in Figures we reveals that how the reproduction ratio plays an important role in the stability of the steady states and the increment of drug efficacy will help to clear the virus. Hence we observe that shortening the drug period will reduce the infection. This results can be obtained from the application of general algorithm for determining stability to HIV-1 infection dynamical model with HAART.

6. CONCLUSION

We study the emergence of drug-resistance in a model for HIV epidemics, under distinct HAART regimes. We numerically simulate the model for different therapy regimes,namely equal RTI and PI efficacies. The results of applying equal drug efficacy therapies point to an optimal treatment, able to reduce drug-sensitive virus and prolonging the emergence of resistance. In this sense, RTI-based and PI-based regimes were simulated. The RTI-based drugs identify higher efficacy RTI drugs, and the later define higher efficacy PI drugs. We observe that PI-based treatments seem to produce better results in terms of disease progression,than RTI-based ones.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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