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Stability Analysis of Endemic Equilibrium of an HIV-1 in Vivo Dynamics in the Presence of Chemotherapy

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Abstract: *Mathematical modelling have and continuously provide insight on the dynamics of an infectious diseases such as HIV-1, Human Papilloma Virus, Tuberculosis etc. In this paper we develop an HIV-1 mathematical model having six parameters (H, H^*, I, I^*, U, U^*). Effects of chemotherapy, time delay and immune response on Endemic Equilibrium Point (EEP) is studied both analytically and numerically. The analytic results shows that the EEP is stale whenever delay exceeds ten days, Chemotherapy below 72.3% efficacy and CD8+T-cells above 500. The analytic results were confirmed using Matlab dde23 solver.*

Keywords: *HIV, Reproduction Number, Time Delay, Stability, Endemic Equilibrium point, Chemotherapy, Immune Response, Efficacy*

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I. Introduction

Human immunodeficiency virus (HIV) is an etiological agent of Acquired Immunno Deficiency Syndrome (AIDS). HIV-1 is a type of HIV that is virulent and more widely spread across the world than HIV-2. HIV-1 affects the immune system which would normally fight it.Scientists in medicine and mathematical biology work day and night to find out intervention strategies/cure of HIV-1 infection. Remarkable efforts have been put in place in order to comprehend and categorize the underlying dynamics of the disease. Mathematical modelling of infectious diseases is particularly employed by epidemiologists to study the dynamics of HIV-1 in vivo. HIV-1 causes havoc to a class of lymphocytes or white blood cells referred to as CD4+T-cells.These lymphocytes would in normal circumstances be involved in the body's defense against infection.Thereby leading to vulnerability to all manner of infection. The HIV undergoes seven stages; binding, fusion, reverse transcription, integration, replication, assembling and budding. **Binding** is the initial step**,** also called attachment. At this step the HIV attaches itself onto the receptor on the surface of the CD4+ T cell. Once it has bind **Fusion** takes place**.** After binding to the CD4+ T cell is ample, the cell membrane of the CD4+ T cell and HIV virus then fuses its envelope (which serves as the covering of the virus). Penetration of the virus to the CD4+ T-cell is facilitated. **Reverse transcription** stage is the step that follows after fusion; for HIV to duplicate it must transform from RNA (Ribonucleic Acid) to DNA (Deoxyribonucleic Acid). To enable this transformation to take place HIV uses a protein (enzyme) called Reverse Transcriptase. The HIV RNA changes to HIV DNA under the influence of this catalyst. **Integration** step then follows; integrase enzyme will be used to put together vital HIV DNA into the DNA of the CD4+ T-cell. **Replication** is the next step where positioning of HIV virus right inside the nucleus of the CD4+ T-cell is done. Combination of the HIV DNA with the CD4+ T-cell DNA takes place. This generate extra HIV lengthy chains proteins thus multiplying the HIV protein copies. Once the production of the HIV long chains proteins is done, they relocate to the surface of the CD4+ T-cell membrane to gather into immature non-infectious HIV by a step called assembly. **Budding** is the final step that a HIV virus undergoes**.** during this step a protease enzyme assist to smite the long chains of HIV protein short proteins that can be released as soon as the HIV virus move to the surface by the CD4+ T-cell membrane. When these short chains of HIV proteins come together they form mature HIV virus. This is very infective and it is capable of infecting another new CD4+ T cell. The CD4+ T-cell count in the body is minimized by these cycle of replication and infection and therefore reducing the immunity of the HIV patient.

II. Literature Review

In [5] they showed in their model that the time delay in immunologic response will destabilize the endemic equilibrium and should grounds to Hopf-bifurcations. In their model they thought-about dual parameters: cellular division rate of target CD4+ T- cells and intracellular delay in incidence of contagion. They renowned that intracellular delay will grounds to Hopf-bifurcations only if cellular division rate is positive and amply enormous whereas intracellular delay will cause instability. According to [2]) they steered that, there's an expensive likelihood of prevalence of drug resistant virus before initiation of drug medical care. This happens thanks to mutations, single or combination. They thought-about a model that used five parameters: the speed of

immigration of prone cells from a pool of precursor cells, the passing away rate of disease-ridden cells, population densities of infected prone cells, and also the restrictive impact of drug medical care on virus replication. They distinguished that beneath a good vary of conditions, treatment failure happens recognitions to pre-existence of drug resistant virus and this destabilizes stability. In [4] they established a mathematical model that studied underlying transmission mechanisms of HIV infections. They used next generation methodology to estimate artificial language. The domestically and globally asymptotically stable wellness free equilibrium conditions for the model were established. They distinguished that once artificial language when $R_0 > 1$ the unwellness free equilibrium state is asymptotically unstable then the unwellness persist. According to [18]they analyzed an external age designed HIV contagion model for the incident of the saturation contagion rate. The fundamental copy variety is shown to be a pointy threshold worth for the worldwide dynamics. That means, infection-free equilibrium is globally steady if copy variety stands at a smaller amount than one. In [17]they studied a mathematical model with each infective agent strains to research HIV dynamics beneath multidrug medical care. They investigated the response of the ARVs drug medical care for each infective agent strains. According to Attarian *et al*. (2017) they developed a best management approach to structure treatment interruptions for HIV patients wherever they found that HIV virus attacks the CD4 T- cells since on its surface they need a macromolecule which will bind to foreign substances like HIV. According to [8] they studied a mathematical model that considered stability analysis at EEP. They found out that stability is attained when $R_0 > 1$. In their study the role of $CD8^+$T-cells were not considered, even though [3] factored in the role of $CD8^+$T-cells in viral replication in their model it only studied stability at DFE. Therefore most of these studies didn't factored in the role of $CD8^+$T-cells with time delay in attaining stability at EEP.

III. Model Assumptions, flow charts, formulation and analysis

3.1 Model Assumptions

Our model will comprise of six state variables namely: healthy $CD4^+$T-cells (H), sick $CD4^+$T- cells (H^*), infectious virus (I), noninfectious virus (I^*) used $CD8^+$T-cells (U) and un-used $CD8^+$T-cells (U^*) .

The following are the assumptions which will be useful in formulation of our model:

1) The Model under study assumes that there are only six compartments namely; healthy $CD4^+$T-cells, sick $CD4^+$T-cells, infectious virus, noninfectious virus, used $CD8^+$T- cells and un-used $CD8^+$T-cells.
2) Chemotherapy effect involves prevention of infections and inhibitions of viral replications through inhibition of the functions of reverse transcriptase and protease enzymes respectively which are virally encoded.
3) There are limited mutations of viral genes which would lead to production of drug resistant strain of the virus.
4) There is no cell-to-cell infections of $CD4^+$T cells, infections are only by free virus.
5) Healthy $CD4^+$T cells are recruited at a constant rate from the thymus gland.
6) Some of the $CD4^+$T cells recover on chemotherapy.
7) $CD8^+$T cells are produced at constant rate from the source (thymus).
8) $CD4^+$T cell populations are reduced by infection and by the action of $CD8^+$T cells.

3.2 Model Flow Chart

T-cell compartments

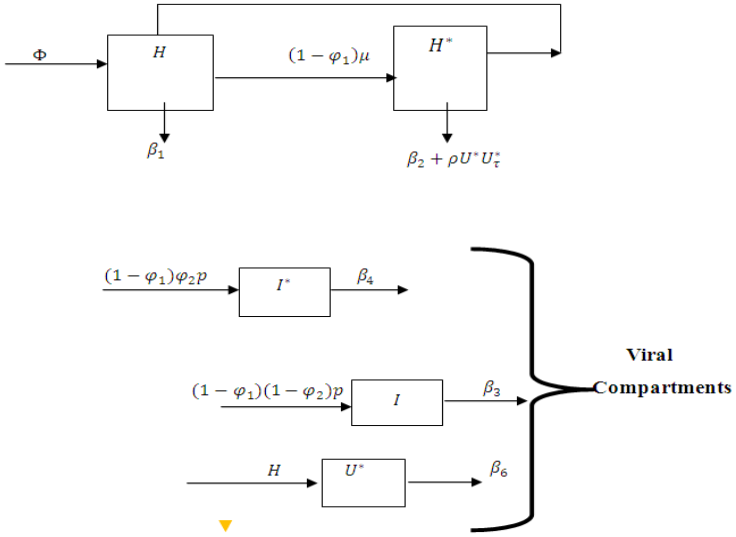

Figure 1 flow chart showing T-cell compartments and viral compartments

3.3 Model Equations

$$\left.\begin{aligned}
\frac{dH}{dt} &= \phi - \beta_1 H - (1-\varphi_1)\mu I_\tau H + \varphi_1 H^* \\
\frac{dH^*}{dt} &= (1-\varphi_1)\mu I_\tau H - \beta_2 H^* - \varphi_1 H^* - \rho H_\tau^* U^* \\
\frac{dI}{dt} &= (1-\varphi_1)(1-\varphi_{2)} p H_\tau^* - \beta_3 I \quad \text{system 1} \\
\frac{dI^*}{dt} &= (1-\varphi_1)\varphi_2 p H_\tau^* - I_\tau^* I^* \\
\frac{dU}{dt} &= \rho H_\tau^* U^* - \beta_4 U \\
\frac{dU^*}{dt} &= \omega - \beta_6 U^*
\end{aligned}\right\}$$

$\tau > 0$ is the time lag required by the host cell to produce infectious virus. It will also represent the time needed for infected cells to be treated by chemotherapy.

3.5 Model Preliminary Analysis

Analysis of results will be done after showing positivity and boundedness of the model. The model compartments represents the cell population of healthy $CD4^+$T cells. Sick $CD4^+$T cells, infectious virus, non-infectious virus, used $CD8^+$T cells and un-used $CD8^+$T cells which are supposed to be positive and bounded for biological reasons.

3.5.1 Positivity and Boundedness

Let $\mathsf{C} = (\mathbf{c}[-\tau, 0], \mathbb{R}^6)$be a Banach space of continuous functions mapping the interval$[-\tau, 0]$into $\mathbb{R}^6$ with the topology of uniform convergence.

By the fundamental theory of differential equations it can be shown that there exists a unique solution $\big(H(t), H^*(t), I(t), I^*(t), U(t), U^*(t)\big)$of the system 1, with initial data $(H(0) > 0, H^*(0) > 0, I(0) > 0, I^*(0) > 0, U(0) > 0, U^*(0) > 0 \in \mathsf{C}$ 3.6

In addition, we assume that the initial data for the system 1 satisfies

$$H_0(\phi) \geq 0, H^*{}_0(\phi) \geq 0, I_0(\phi) \geq 0, I^*{}_0(\phi) \geq 0, U_0(\phi) \geq 0, U^*{}_0(\phi) \geq 0, \phi \in [-\tau, 0] \qquad 3.7$$

The following theorem establishes the positivity and boundedness of solution with initial functions satisfying 3.6 and 3.7

Theorem 3.1 let (H, H^*, I, I^*, U, U^*)be the solution of system 1 satisfying conditions 3.6 and 3.7 then $H, H^*, I, I^*, U,$ and U^* are all positive and bounded for all $t > 0$ at which the solutions exist.

Proof

Note that from system 1 we have

$$H(t) = H(0)e^{-\int_0^t \beta_1 + (1-\varphi_1)\mu(\xi-\tau)d\xi} + \int_0^t [\beta_1 H^*(\eta) + \Phi] e^{-\int_\eta^t \beta_1 + (1-\varphi_1)\mu I(\xi-\tau)d\xi} d\eta \qquad 3.8$$

$$H^*(t) = H^*(0)e^{-\int_0^t \beta_2 + \varphi_1 - \rho H_\tau^* U)d\xi} + \int_0^t [(1-\varphi_1)\mu I(\eta-\tau)H(\eta)] e^{-\int_\eta^t \beta_2 + \varphi_1 - \rho H_\tau^* U))d\xi} d\eta \qquad 3.9$$

$$I(t) = I(0)e^{-\int_0^t \beta_3 d\xi} + \int_0^t [(1-\varphi_1)(1-\varphi_2) p H^*(\eta-\tau)] e^{-\int_\eta^t \beta_3 d\xi} d\eta 3.10$$

$$I^*(t) = I^*(0)e^{-\int_0^t \beta_4 d\xi} + \int_0^t [(1-\varphi_1)\varphi_2 p H^*(\eta-\tau)] e^{-\int_\eta^t \beta_4 d\xi} d\eta 3.11$$

$$U(t) = U(0)e^{-\int_0^t ((\rho H_\tau^* - \beta_5))d\xi} 3.12$$

$$U^*(t) = U^*(0)e^{-\int_0^t (-\beta_6)d\xi} \qquad 3.13$$

Positivity immediately follows from the above integral forms and 3.6 and 3.7

For boundedness we define$\Sigma(t) = H(t) + H^*(t) + I(t) - \frac{1-\varphi_2}{\varphi_2} I^*(t) + U(t) + U^*(t)$ 3.14

Let $\pi = \min(\beta_1 ; \beta_2 ; \beta_3 ; \beta_5 ; \beta_6 ; \beta_4 \left(\frac{1-\varphi_2}{\omega_2}\right))$then

$$\frac{d}{dt}\Sigma(t) = \frac{d}{dt}H(t) + \frac{d}{dt}H^*(t) + \frac{d}{dt}I(t) - \frac{1-\varphi_2}{\varphi_2}\frac{d}{dt}I^*(t) + \frac{d}{dt}U(t) + \frac{d}{dt}U^*(t) \qquad 3.15$$

Thus

$\frac{d}{dt}\Sigma(t) \leq \phi - \gamma$ where $\gamma = \frac{1-\varphi_2}{\varphi_2}$

Implying that $N(t)$ is bounded, and so are $H(t), H^*(t), I(t), I^*(t), U(t), U^*(t)$. This completes the proof of

Theorem 3.1.

3.7 The Endemic Equilibrium Point

Analysis of the endemic equilibrium point is done at the critical point of system 1 which exists when $H > 0, H^* > 0, I > 0, I^* > 0, U > 0, U^* > 0$. The zero solutions of the nonlinear system (1) at EEP is asymptotically stable if and only if the zero solutions of the linear system obtain from (system 1) is asymptotically stable. Therefore asymptotic stability of (system 1) at EEP is established by examining the signs of the Eigen-values of the zero solutions of the linearized system. Endemic equilibrium point of system 1 is the point $E =: H^e > 0, H^{*e} > 0, I^e > 0, I^{*e} > 0, U^e > 0, U^{*e} > 0$, satisfying

$$(1-\varphi_1)\mu I_\tau H - \beta_2\ H^* - \varphi_1 H^* - \rho H_\tau^* U^* = 0$$

$$\left.\begin{array}{l} (1-\varphi_1)\mu I_\tau H - \beta_2\ H^* - \varphi_1 H^* - \rho H_\tau^* U^* = 0 \\ (1-\varphi_1)(1-\varphi_{2)} p H_\tau^*\ - \beta_3 I = 0 \\ \rho H_\tau^* U^* - \beta_4 U\ = 0 \\ (1-\varphi_1)\varphi_2 p H_\tau^*\ - I_\tau^* I^* = 0 \\ \omega -\ \beta_6 U^* = 0 \end{array}\right\} \text{System 2}$$

With simple algebraic calculations we obtain the values of the endemic equilibrium points as;

$$H^e = (\beta_2\ + \varphi_1 - \rho\frac{\omega}{\beta_6})\frac{\beta_3}{(1-\varphi_1)^{U^*}(1-\varphi_2)\mu p} \quad 3.30$$

$$H^{*e} = \frac{\emptyset - \beta_1(\beta_2+\varphi_1+\rho\frac{\omega}{\beta_6})}{\beta_2 + \rho\frac{\omega}{\beta_6}} \quad 3.31$$

$$I^e = \frac{(1-\beta_1)(1-\beta_2)p(\emptyset - \beta_1[\left(\beta_2+\varphi_1-\rho\frac{\omega}{\beta_6}\right)\left(\frac{\beta_3}{(1-\varphi_1)^2(1-\varphi_2)\mu p}\right)]}{(\beta_2+\rho\frac{\omega}{\beta_6})\beta_3} \quad 3.32$$

$$I^{*e} = \frac{(1-\varphi_1)\varphi_2 p(\emptyset - \beta_1[\left(\beta_2+\varphi_1-\rho\frac{\mu}{\beta_6}\right)\left(\frac{\beta_3}{(1-\varphi_1)^2(1-\varphi_2)\mu p}\right)]}{(\beta_2+\rho\frac{\mu}{\beta_6})\beta_4} \quad 3.33$$

$$U^e = \frac{\rho\omega(\emptyset - \beta_1[\left(\beta_2+\varphi_1-\rho\frac{\omega}{\beta_6}\right)\left(\frac{\beta_3}{(1-\varphi_1)^2(1-\varphi_2)\mu p}\right)]}{(\beta_2+\rho\frac{\omega}{\beta_6})\beta_5\beta_6} \quad 3.34$$

$$U^{*e} = \frac{\sigma}{\varepsilon_z} \quad 3.35$$

3.4 Stability of Endemic Equilibrium Point

If all the eigenvalues of the linearization matrix about EEP are negative, then the system 1 is said to be stable. For stability analysis the equilibrium points are made easier by shifting the equilibrium to the origin.

This is done by centering the model equation (1) at endemic equilibrium $E(H^e, H^{*e}, I^e, I^{*e}, U^e, U^{*e},)$ by introducing new variables

$$A_1 = H - H^e, A_2 = H^* - H^{*e}, A_3 = I - I^e, A_4 = I^* - I^{*e}, A_5 = U - U^{e,} A_6 = U^* - U^{*e} \quad 3.36$$

We then rewrite the model equation (1) in terms of the new variables, and because $E(H^e, H^{*e}, I^e, I^{*e}, U^e, U^{*e},)$ is an equilibrium point, the constant term cancel. We also discard the quadratic terms because their partial derivatives at the origin are zero.

The system (1) with the new variables becomes:

$$\left.\begin{array}{l} \dot{A}_1 = \phi - \beta_1(A_1 + H^e) - (1-\varphi_1)\mu(A_{3\tau} + I_\tau^e)(A_1 + H^e) + \varphi_1(A_{2\tau} + H^{*e}) \\ \dot{A}_2 = (1-\varphi_1)(A_{3\tau} + I^e)\mu + \beta_1(A_{2\tau} + H^{*e}) - \varphi_1(A_{2\tau} + H^{*e})\rho(A_{2\tau} + H^{*e})(A_6 + U^{*e}) \\ \dot{A}_3 = (1-\varphi_1)(1-\varphi_2)(A_{2\tau} + H^{*e})p - \beta_3(A_{3\tau} + I^e) \\ \dot{A}_4 = (1-\varphi_1)\varphi_2 p(A_{2\tau} + H^{*e}) -\ \beta_4(A_4 + I^{*e}) \\ \dot{A}_5 = \rho(A_{2\tau} + H^{*e})(A_6 + U^{*e}) - \beta_5(A_5 + U^e) \\ \dot{A}_6 = \omega - \beta_6(A_6 + U^{*e}) \end{array}\right\} \text{System3}$$

The Jacobian matrix J_2 of system 3 at equilibrium point is given as;

$$J_2 = \begin{bmatrix} -\beta_1 + a_1 & \varphi_1\mu e^{-\lambda\tau} & a_6 & 0 & 0 & 0 \\ 0 & -\beta_2 - a_2 & a_7 & 0 & 0 & a_8 \\ 0 & a_3 & \beta_3 e^{-\lambda\tau} & 0 & 0 & 0 \\ 0 & a_4 & 0 & -\beta_4 & 0 & 0 \\ 0 & a_5 & 0 & 0 & -\beta_6 & a_8 \\ 0 & 0 & 0 & 0 & 0 & -\beta_6 \end{bmatrix} \quad 3.37$$

Where,

$$a_1 = A_{3\tau}\mu + w^* - \varphi_1 A_{3\tau}\mu - \varphi I^e\mu$$
$$a_2 = (\varphi_1 - \rho A_6 - \rho U^{*e})e^{-\lambda\tau}$$
$$a_3 = (p - p\varphi_2 - p\varphi_1 - p\varphi_1\varphi_2)e^{-\lambda\tau}, \quad 3.38$$
$$a_4 = (p\varphi_2 - p\varphi_1\varphi_2)e^{-\lambda\tau},$$
$$a_5 = (\rho A_6 + \rho U^{*e})e^{-\lambda\tau}$$
$$a_6 = (A_1\mu + H^e - \alpha_1 A_1 - \varphi_1 H^e\mu)e^{-\lambda\tau},$$
$$a_7 = (\mu - \varphi_1\mu)e^{-\lambda\tau},$$
$$a_8 = \rho(A_{2\tau} + H^{*e})e^{-\lambda\tau}$$

Clearly, the eigenvalues are;

$$\lambda_1 = -\beta_6, \lambda_2 = -\beta_5, \lambda_3 = -\beta_4, \lambda_4 = -\beta_1 + a_1, \quad 3.39$$
$$\lambda_{5,6} = -(\beta_3 + \beta_2 + a) \pm \sqrt{(\beta_3 + \beta_2 + a_2)^2 - 4(\beta_3\beta_6 - a_3 a_7)}$$

Therefore, Reproduction number at EEP is given by;

$$R_1 = \frac{(1-\varphi_1)^2(1-\varphi_2)pe^{-\lambda\tau}}{(\beta_2 + \varphi_1 - \frac{\omega}{\beta_6})\frac{\omega}{\beta_6}\beta_3}) > 1 \quad 3.40$$

IV. Main Results

Analytic solutions can be demonstrated using analytic results with specific numerical examples. The model equation (1) is considered. Numerical simulations of the model is calculated using list of parameters and their estimated values given in the table 1 & 2. The values have been obtained from [1, 8, 11]. In simulation of the model system (1), the following initial values in each compartment at the onset of infection is assumed to apply; $H(0), H^*(0), I(0), I^*(0), U(0), U^*(0) = (1000, 0, 0.01, 0.01, 500, 30)$ on the interval $[-\tau, 0]$.

Table 1.*Table of Variable, Variable description and Value.*

Variables	Variable description	Value
H	Healthy CD4+ T- cells	1000
H^*	Sick CD4+ T- cells	0
I	Infectious virus	0.001
I^*	Non-infectious virus	0.001
U	CD8+ T-cells used	500
U^*	CD8+ T-cells un-used	30

Table 2.*Table of Parameters, Parameter description and Value.*

Parameters	Parameter description	Value
ϕ	Production rate of healthy $CD4^+$T cells	15 cells/mm^3/day
β_1	Death rate of healthy $CD4^+$T cells	0.06/day
φ_1	Efficacy of RTI	$0 \le \varphi_1 \le 1$
φ_2	Efficacy of PI	$0 \le \varphi_2 \le 1$
μ	Force of infection	0.53
p	Budding size of free virus from sick $CD4^+$T cells	13
β_2	Death rate of sick $CD4^+$T cells	0.26
β_3	Natural death rate of infectious virus from the body	2.4
β_4	Natural death rate of non-infectious virus from the body	2.4
β_5	Natural death rate of used CD8+ T-cells	0.06/day
β_6	Natural death rate of un-used CD8+ T-cells	0.06/day
ω	Production rate of CD8+ T-cells	0.004/day
τ	Time delay	To be determined
ρ	Rate at which CD8+ T-cells are used	20cell/mm^3/day

Figure 1: A figure showing the dynamics population of CD4+T-cells with 10% drug efficacy and immune response. It is evident that sick CD4+ T-cells count is at $3200/\text{mm}^3$

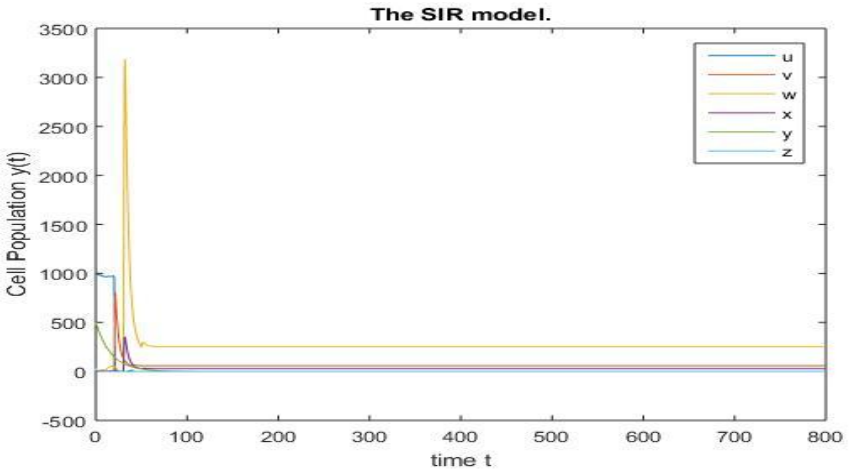

Figure 1*Dynamics cell population of CD4+T-cells and contagious cells with* 10% *drug efficacy and immune response with respect to time.*

Figure 2: A figure showing the dynamics population of CD4+T-cells with 30% drug efficacy and immune response. It is evident that sick CD4+ T-cells count is at $1700/\text{mm}^3$

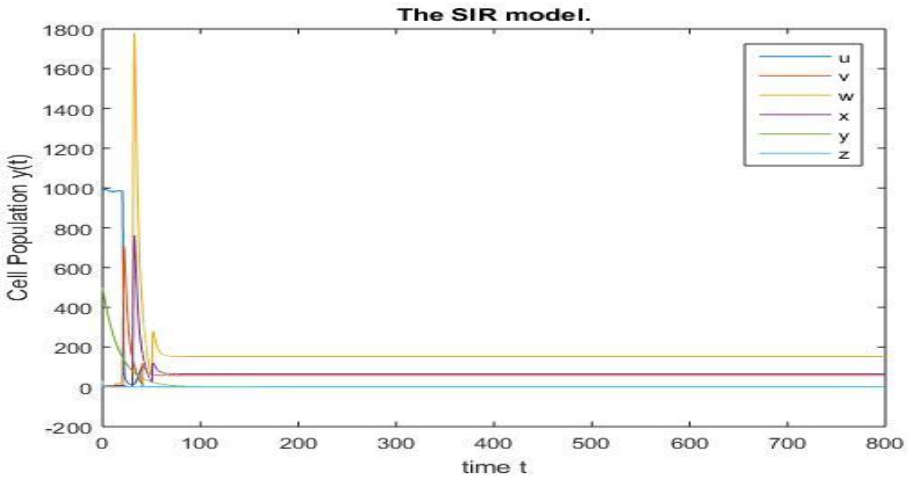

Figure 2 *Dynamics population of CD4+T-cells and contagious cells with* 30% *drug efficacy and immune response with respect to time*

Figure 3: A figure showing the dynamics population of CD4+T-cells with 50% drug efficacy and immune response. It is evident that sick CD4+ T-cells count is at $1700/\text{mm}^3$

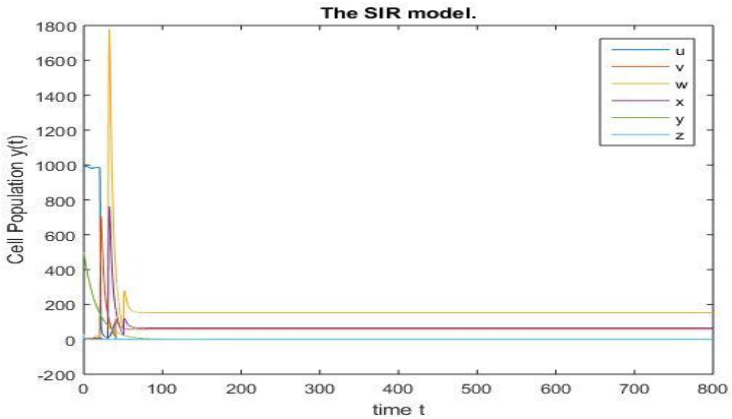

Figure 3.*Dynamics population of CD4+T-cells and contagious cells with* 50% *drug efficacy and immune response with respect to time.*

Figure 4: A figure showing the dynamics population of CD4+T-cells with 72.3% drug efficacy and immune response. It is evident that sick CD4+ T-cells count is below$500/\text{mm}^3$

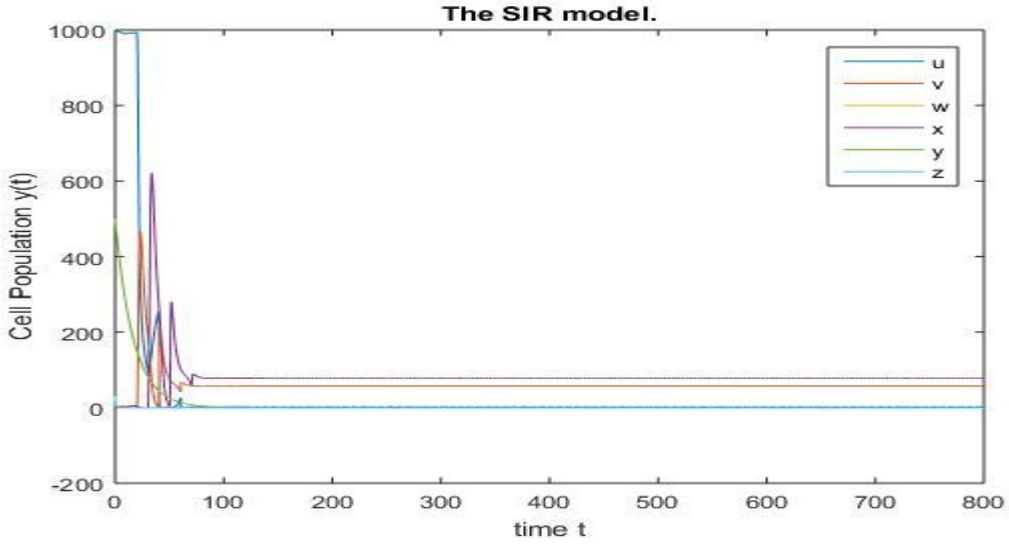

Figure 4.*Dynamics population of CD4+T-cells and contagious cells with* 72.3% *drug efficacy and immune response with respect to time*

Figure 5: A figure showing the dynamics population of CD4+T-cells with 80% drug efficacy and immune response. It is evident that sick CD4+ T-cells count is below$200/\text{mm}^3$

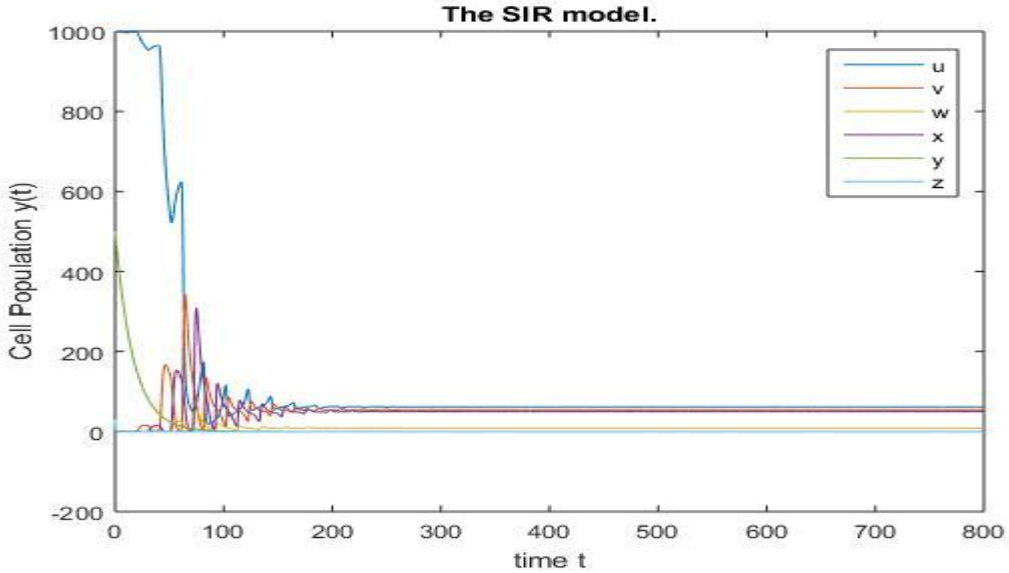

Figure 5.*Dynamics population of CD4+T-cells and contagious cells with* 80% *drug efficacy and immune response with respect to time.*

In figure 6 it is evident that Reproduction number at EEP is directly proportional to drug efficacy.

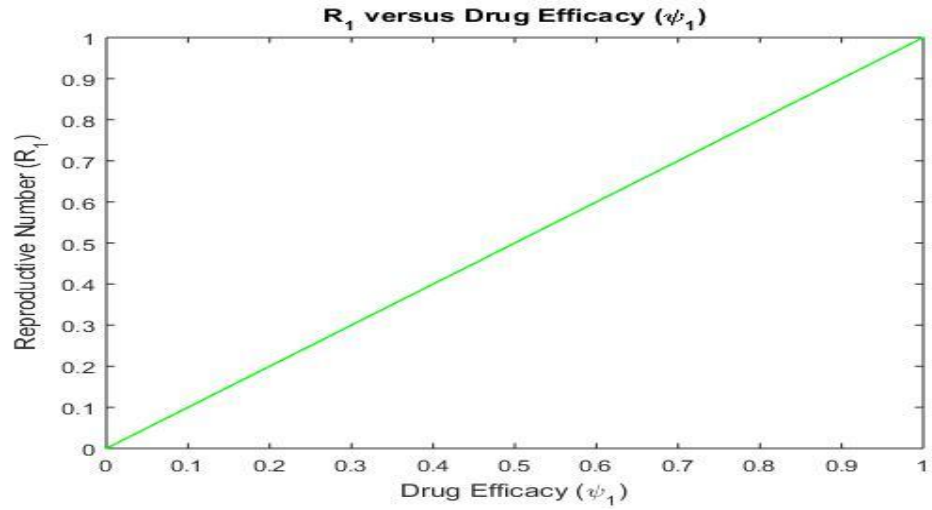

Figure 6.Graph showing Reproduction number at EEP versus Drug Efficacy

In figure 7 it is evident that Reproduction number at EEP is directly proportional to bursting size.

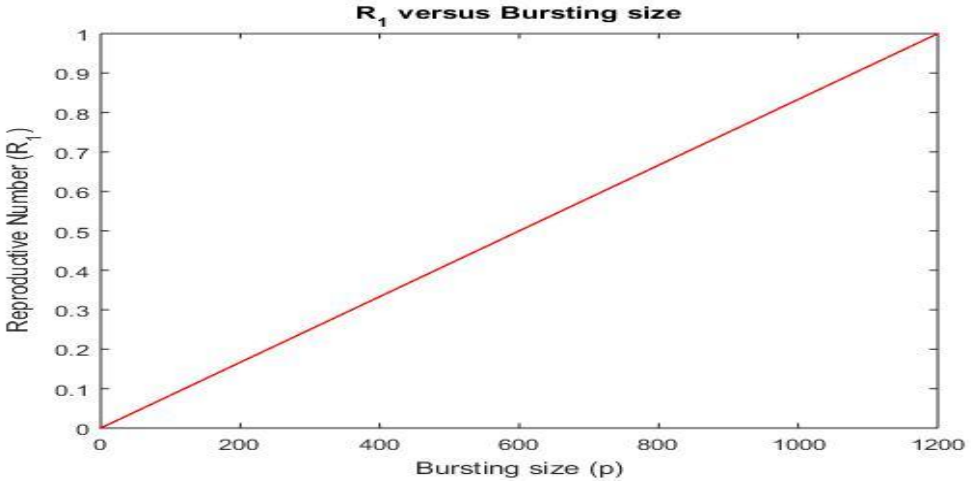

Figure 7.Graph showing Reproduction number at EEP versus Bursting size.

In figure 8 it is evident that Reproduction number at EEP is directly proportional to time delay.

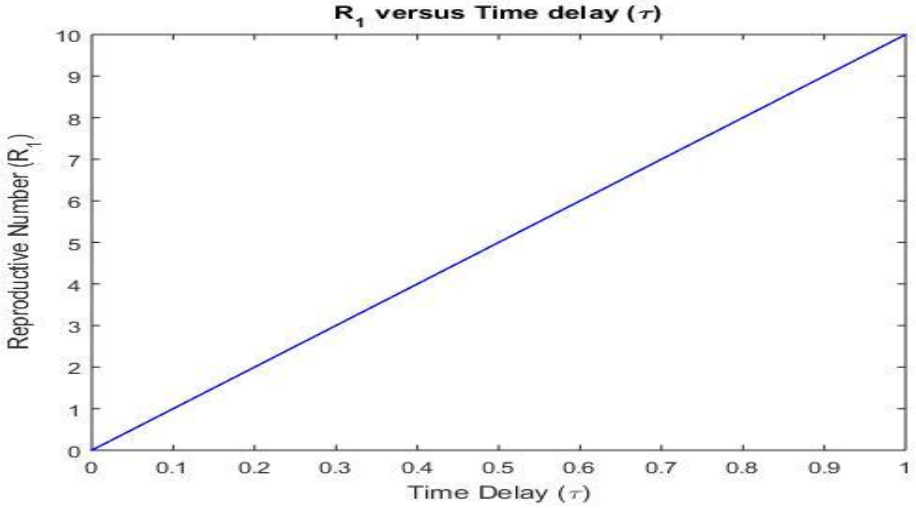

Figure 8.Graph showing Reproduction number at EEP versus Time delay

V. Conclusion

The study was mainly to formulate an HIV-1 in vivo dynamical model using delay differential equations and then study stability analysis at EEP both analytically and numerically using MATLAB dde23 solver. The effects of time delay, chemotherapy and immune response on HIV-1 dynamics were also studied. The parameter values were obtained from the literature. This study found out that time delay, chemotherapy and immune response plays a major role in attaining stability at EEP. Stability at EEP is attained when $\boldsymbol{R_1} > 1$. It also found out that if time delay is reduced to below 7 days the stability would be achieved faster than when the delay is more than 7 days and Chemotherapy at 72.3% drug efficacy is the best for attaining stability at EEP.

VI. Suggestions for Further Research

This study has not explored all about HIV-1 In vivo dynamics. Sensitivity analysis and Hopf bifurcation is not captured in the study. Also, Studies on chemotherapy using Structured Treatment Interference (STI) regime by narrowing to the delay for stabilities at EEP is not captured.

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