GLOBAL STABILITY OF HIV/HTLV CO-INFECTION MODEL WITH CTL-MEDIATED IMMUNITY

A. M. ELAIW∗
Department of Mathematics, Faculty of Science, King Abdulaziz University
P.O. Box 80203, Jeddah 21589, Saudi Arabia
and
Department of Mathematics, Faculty of Science
Al-Azhar University, Assiut Branch, Assiut, Egypt

N. H. ALSHAMRANI
Department of Mathematics, Faculty of Science, King Abdulaziz University
P.O. Box 80203, Jeddah 21589, Saudi Arabia
and
Department of Mathematics, Faculty of Science, University of Jeddah
P. O. Box 80327, Jeddah 21589, Saudi Arabia

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ABSTRACT. Mathematical modeling of human immunodeficiency virus (HIV) and human T-lymphotropic virus type I (HTLV-I) mono-infections has received considerable attention during the last decades. These two viruses share the same way of transmission between individuals; through direct contact with certain contaminated body fluids. Therefore, a person can be co-infected with both viruses. In the present paper, we construct and analyze a new HIV/HTLV-I co-infection model under the effect of Cytotoxic T lymphocytes (CTLs) immune response. The model describes the interaction between susceptible CD4+ T cells, silent HIV-infected cells, active HIV-infected cells, silent HTLV-infected cells, Tax-expressing (active) HTLV-infected cells, free HIV particles, HIV-specific CTLs and HTLV-specific CTLs. The HIV can spread by two routes of transmission, virus-to-cell (VTC) and cell-to-cell (CTC). Both active and silent HIV-infected cells can infect the susceptible CD4+ T cells by CTC mechanism. On the other side, HTLV-I has only one mode of transmission via direct cell-to-cell contact. The well-posedness of the model is established by showing that the solutions of the model are nonnegative and bounded. We calculate all possible equilibria and define the key threshold parameters which govern the existence and stability of all equilibria of the model. We explore the global asymptotic stability of all equilibria by utilizing Lyapunov function and LaSalle’s invariance principle. We have discussed the influence of CTL immune response on the co-infection dynamics. We have presented numerical simulations to justify the applicability and effectiveness of the theoretical results. In addition, we evaluate the effect of HTLV-I infection on the HIV dynamics and vice versa.

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∗ Corresponding author: A. M. Elaiw.
1. Introduction. From a long time viral infections (such as human immunodeficiency virus (HIV) and human T-lymphotropic virus type I (HTLV-I)) have threatened the human’s life and health. HIV and HTLV-I are two retroviruses which can be transmitted between individuals through direct contact with certain body fluids from infected individuals. Therefore, a person can be co-infected with both viruses. Susceptible CD4\(^+\)T cells which are the major driver of the human immune response are the main target of both HIV and HTLV-I. HIV causes acquired immunodeficiency syndrome (AIDS), while HTLV-I is the causative agent for adult T-cell leukemia and HTLV-I-associated myelopathy/tropical spastic paraparesis. Mathematical models which describe the within-host virus dynamics can improve our understandings about the viral’s progression and even how human body can control it through the long-lasting immunity [38]. In case of HIV infection, Cytotoxic T lymphocytes (CTLs) play an important role in controlling the viral infection. HIV-specific CTLs kill the CD4\(^+\)T cells which are infected by HIV. Nowak and Bangham [39] have introduced the initial HIV infection model which describes the interaction between susceptible CD4\(^+\)T cells, active HIV-infected cells, free HIV particles and HIV-specific CTLs as:

\[
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_1 SV, \\
\dot{I} &= \eta_1 SV - a I - \mu_1 C^I I, \\
\dot{V} &= b I - \varepsilon V, \\
\dot{C}^I &= \sigma_1 C^I I - \pi_1 C^I,
\end{align*}
\]

(1)

where \(S = S(t), I = I(t), V = V(t)\) and \(C^I = C^I(t)\) are the concentrations of susceptible CD4\(^+\)T cells, active HIV-infected cells, free HIV particles and HIV-specific CTLs at time \(t\), respectively. The susceptible CD4\(^+\)T cells are produced at specific constant rate \(\rho\). The term \(\eta_1 SV\) refers to the rate at which new infectious appears by virus-to-cell (VTC) contact between free HIV particles and susceptible CD4\(^+\)T cells. The free HIV particles are generated at rate \(bI\). The proliferation rate of effective HIV-specific CTLs is given by \(\sigma_1 C^I I\). The term \(\mu_1 C^I I\) is the killing rate of active HIV-infected cells due to their specific immunity. The natural death rates of the susceptible CD4\(^+\)T cells, active HIV-infected cells, free HIV particles and HIV-specific CTLs are given by \(\alpha S, aI, \varepsilon V\) and \(\pi_1 C^I\), respectively. Since then several extensions of model (1) have been proposed and analyzed (see e.g. [32,35,43,44]).

In model (1), it has been assumed that the HIV can only spread via VTC mode of transmission. However, several works have reported that HIV can be transmitted directly from an infected cell to a susceptible CD4\(^+\)T cell through the formation of virological synapses and this is known as cell-to-cell (CTC) transmission (see e.g. [24, 25, 42]). It has been shown in [23, 45, 47] that CTC transmission plays an efficient role in the HIV replication. Mathematical model of a within-host HIV dynamics with both VTC and CTC transmissions has been formulated by Iwami et al. [23]. The model presented in [23] has been extended to take into account the CTL-mediated immune response as [8,20,51,58]:

\[
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_1 SV - \eta_3 SI, \\
\dot{I} &= \eta_1 SV + \eta_3 SI - a I - \mu_1 C^I I, \\
\dot{V} &= b I - \varepsilon V, \\
\dot{C}^I &= \sigma_1 C^I I - \pi_1 C^I.
\end{align*}
\]

(2)
The term $\eta_3 S I$ refers to the rate at which new infectious appears by CTC contact between active HIV-infected cells and susceptible CD4$^+$ T cells. It is known that highly active anti-retroviral therapy can repress HIV replication to a low level but it cannot enucleate the virions from the body. One of the main reasons that causing this fact is the presence of silent (latent) infected cells where the HIV provirus can reside [9, 57]. Silent CD4$^+$ T cells live long, but it can be activated to produce new HIV particles. In a very recent work [1], it has been shown that both silent and active infected cells can infect the susceptible CD4$^+$ T cells through CTC mechanism. We note that the mathematical models of HIV dynamics with CTC transmission presented in the literature assumed that the CTC transmission is only due to the active infected CD4$^+$ T cells. In (2020), Wang et al. [54], have formulated a viral infection model by assuming that both silent and active infected cells can share in CTC infection. However, in [54], the role of the immune response has been neglected. Elaiw and Alshamrani [12] have investigated an HIV mon-infection model with silent and active CTC transmissions and CTL immune response.

Human T-lymphotropic virus type I (HTLV-I) can be transmitted to susceptible CD4$^+$ T cells through CTC mechanism [59]. Many researchers have been concerned to study mathematical modeling and analysis of HTLV-I infection in several works [18, 29, 46, 50, 52]. It has been reported in [2] that the CTLs play an effective role in controlling the HTLV-I infection for a long time. CTLs can recognize and kill the Tax-expressing (active) HTLV-infected cells. The within-host HTLV-I dynamics model with CTL-mediated immune response is given by [38]:

$$
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_4 SY, \\
\dot{Y} &= \varphi \eta_4 SY - \delta Y - \mu_2 C^Y Y, \\
\dot{C}^Y &= \sigma_2 C^Y Y - \pi_2 C^Y,
\end{align*}
$$

(3)

where $S = S(t)$, $Y = Y(t)$ and $C^Y = C^Y(t)$ are the concentrations of susceptible CD4$^+$ T cells, Tax-expressing (active) HTLV-infected cells and HTLV-specific CTLs at time $t$, respectively. In contrast of HIV, the transmission of HTLV-I can be only from CTC that is the HTLV virions can survive only inside the host CD4$^+$ T cells and cannot be detectable in the plasma. The rate at which new infectious appears by CTC contact between Tax-expressing HTLV-infected cells and susceptible CD4$^+$ T cells is assumed to be $\eta_4 SY$. A fraction $\varphi \in (0, 1)$ of the newly HTLV-infected cells can survive the antibody response. The proliferation rates for HTLV-specific CTLs is given by $\sigma_2 C^Y Y$. The term $\mu_2 C^Y Y$ is the killing rate of Tax-expressing HTLV-infected cells due to their specific immunity. The natural death rate of the Tax-expressing HTLV-infected cells and HTLV-specific CTLs are represented by $\delta Y$ and $\pi_2 C^Y$, respectively. In the literature, several mathematical models have been proposed to describe the within-host dynamics of HTLV-I under the effect of CTL immune response (see e.g. [19, 30, 37, 38, 40, 53, 55, 56]). These papers have only considered one type of HTLV-infected cells, Tax-expressing HTLV-infected cells. However, there is another type of HTLV-infected cells known as silent HTLV-infected cells which contain provirus and do not make new virions until they are activated. In [28, 31, 33], CTL-mediated immunity HTLV-I dynamics models have been presented by incorporating both silent HTLV-infected cells and Tax-expressing HTLV-infected cells.

During the last 10 years HIV and HTLV-I co-infection has been extensively reported. It has been discovered that the simultaneous infection by the two viruses affects the pathogenic development and influences the outcomes for associated
chronic diseases [7]. In fact, concurrent infections with HTLV-I and HIV have occurred frequently in areas where individuals living at high risk activities such as needle injection sharing and unprotected sexual relationships. In addition, HIV/HTLV-I co-infection have documented in specific geographic regions where both retroviruses become endemic and among those who belonged to a specific ethnic as well [48]. For instance, the co-infection rates in individuals living in some parts of Brazil have reached 16% of HIV-infected patients [5]. In a recent work, it has been estimated that the HIV-infected patients are more exposure to be co-infected with HTLV-I at a higher rate initiating from 100 to 500 times in comparison to the general population [22]. Moreover, some seroepidemiologic studies have reported that HTLV-I-infected patients are at risk to have a concurrent infection with HIV, and vice versa compared to those who are infection-free from the general population [48]. HIV and HTLV-I are mainly attack the CD4+ T cells; as mentioned above; lead to immune dysfunctional as well, however, they also conflict no doubt with respect to the etiology of their pathogenic and clinical outcomes [4]. HIV and HTLV-I dual infection appears to have an overlap on the course of associated clinical outcomes with both viruses [48]. Many researchers have reported that HIV infected individuals who are possibly co-infected with HTLV-I can potentially associated with clinical progression to AIDS. In contrast, HIV can adjust HTLV-I expression in co-infected individuals which leads them to a higher risk of developing HTLV-I related diseases such as ATL and TSP/HAM [17,22,48].

As we mentioned above, there exist many mathematical models which describe the within-host dynamics of HIV and HTLV-I mono-infections. However, to the best of our knowledge, modeling of HIV/HTLV-I co-infection dynamics has not been studied previously. Modeling and analysis of a within-host HIV/HTLV-I co-infection are helpful for clinicians in the regards of estimating an appropriate time to initiate treatment in co-infected patients. Therefore, the aim of the present paper is to construct a new within-host HIV/HTLV-I co-infection model. The HIV is assumed to be spread by VTC, silent HIV-infected CTC and active HIV-infected CTC transmissions. The HTLV-I is only transmitted via CTC mode. We show that the model is well-posed by establishing that the solutions of the model are nonnegative and bounded. We derive a set of threshold parameters which govern the existence and stability of the equilibria of the model. We construct appropriate Lyapunov functions to investigate the global dynamical properties of the model. We perform some numerical simulations to illustrate the strength of our theoretical results.

2. Model formulation. We set up an ordinary differential equation model that describes the change of concentrations of eight compartments with respect to time $t$: susceptible CD4+ T cells $S(t)$, silent HIV-infected cells $L(t)$, active HIV-infected cells $I(t)$, silent HTLV-infected cells $E(t)$, Tax-expressing HTLV-infected cells $Y(t)$, free HIV particles $V(t)$, HIV-specific CTLs $C^I(t)$ and HTLV-specific CTLs $C^Y(t)$. We assume that a susceptible CD4+ T cell can be infected with HIV when it is contacted by one of the following: (i) free HIV particle, (ii) silent HIV-infected cell, and (iii) active HIV-infected cell. On the other hand, a susceptible CD4+ T cell can be infected with HTLV when it is contacted with a Tax-expressing HTLV-infected cell. The dynamics of HIV/HTLV-I co-infection is schematically shown in the transfer diagram given in Figure 1. Our proposed model is given by the
following form:

\[
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY, \\
\dot{L} &= \eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma) L, \\
\dot{I} &= \lambda L - \alpha I - \mu_1 C^I, \\
\dot{E} &= \varphi \eta_4 SY - (\psi + \omega) E, \\
\dot{Y} &= \psi E - \delta Y - \mu_2 C^Y, \\
\dot{V} &= bI - \varepsilon V, \\
\dot{C}^I &= \sigma_1 C^I - \pi_1 C^I, \\
\dot{C}^Y &= \sigma_2 C^Y Y - \pi_2 C^Y,
\end{align*}
\]

where \((S, L, I, E, Y, V, C^I, C^Y) = (S(t), L(t), I(t), E(t), Y(t), V(t), C^I(t), C^Y(t))\). The susceptible CD4\(^{+}\) T cells are contacted with silent HIV-infected cells and become infected due to CTC transmission at rate \(\eta_2 SL\). The term \(\lambda L\) is the rate of silent HIV-infected cells that become active HIV-infected cells. The term \(\psi E\) accounts for the rate of silent HTLV-infected cells that become Tax-expressing HTLV-infected cells. Silent HIV-infected cells and silent HTLV-infected cells die at rates \(\gamma L\) and \(\omega E\), respectively. The remaining variables and parameters have the same interpretations given in Section 1. All parameters and their definitions are summarized in Table 1.
### Table 1. Parameter description.

| Parameter | Description |
|-----------|-------------|
| $\rho$    | Recruitment rate for the susceptible CD4$^+$ T cells |
| $\alpha$  | Natural mortality rate constant for the susceptible CD4$^+$ T cells |
| $\eta_1$  | Virus-cell incidence rate constant between free HIV particles and susceptible CD4$^+$ T cells |
| $\eta_2$  | Cell-cell incidence rate constant between silent HIV-infected cells and susceptible CD4$^+$ T cells |
| $\eta_3$  | Cell-cell incidence rate constant between active HIV-infected cells and susceptible CD4$^+$ T cells |
| $\eta_4$  | Cell-cell incidence rate constant between Tax-expressing HTLV-infected cells and susceptible CD4$^+$ T cells |
| $\beta \in (0, 1)$ | Fraction coefficient accounts for the probability of new HIV-infected cells could be active, and the remaining part $1 - \beta$ will be latent |
| $\gamma$  | Death rate constant of silent HIV-infected cells |
| $\delta_1$ | Killing rate constant of active HIV-infected cells due to HIV-specific CTLs |
| $\delta_2$ | Killing rate constant of Tax-expressing HTLV-infected cells due to HTLV-specific CTLs |
| $\varphi \in (0, 1)$ | Probability of new HTLV infections could be enter a silent period |
| $\lambda$ | Transmission rate constant of silent HIV-infected cells that become active HIV-infected cells |
| $\psi$    | Transmission rate constant of silent HTLV-infected cells that become Tax-expressing HTLV-infected cells |
| $\omega$  | Death rate constant of silent HTLV-infected cells |
| $\varepsilon$ | Death rate constant of Tax-expressing HTLV-infected cells |
| $b$       | Generation rate constant of new HIV particles |
| $\varepsilon$ | Death rate constant of free HIV particles |
| $\sigma_1$ | Proliferation rate constant of HIV-specific CTLs |
| $\sigma_2$ | Proliferation rate constant of HTLV-specific CTLs |
| $\pi_1$   | Decay rate constant of HIV-specific CTLs |
| $\pi_2$   | Decay rate constant of HTLV-specific CTLs |
3. Well-posedness of solutions. Let $\Omega_j > 0$, $j = 1, \ldots, 5$ and define
$$\Theta = \{(S, L, I, E, Y, V, C^l, C^Y) \in \mathbb{R}^8_{\geq 0} : 0 \leq S(t), L(t), I(t) \leq \Omega_1,$$
$$0 \leq E(t), Y(t) \leq \Omega_2, 0 \leq V(t) \leq \Omega_3, 0 \leq C^l(t) \leq \Omega_4, 0 \leq C^Y(t) \leq \Omega_5 \} .$$

Proposition 1. The compact set $\Theta$ is positively invariant for system (4).

Proof. We have
$$\dot{S}_{|S=0} = \rho > 0, \quad \dot{L}_{|L=0} = \eta_1 SV + \eta_2 SI \geq 0 \text{ for all } S, V, I \geq 0,$$
$$\dot{I}_{|I=0} = \lambda L \geq 0 \text{ for all } L \geq 0, \quad \dot{E}_{|E=0} = \varphi \eta_4 SY \text{ for all } S, Y \geq 0,$$
$$\dot{Y}_{|Y=0} = \psi E \geq 0 \text{ for all } E \geq 0, \quad \dot{V}_{|V=0} = bI \geq 0 \text{ for all } I \geq 0,$$
$$\dot{C}^l_{|C^l=0} = 0, \quad \dot{C}^Y_{|C^Y=0} = 0.$$

This ensures that, $(S(t), L(t), I(t), E(t), Y(t), V(t), C^l(t), C^Y(t)) \in \mathbb{R}^8_{\geq 0}$ for all $t \geq 0$
when $(S(0), L(0), I(0), E(0), Y(0), V(0), C^l(0), C^Y(0)) \in \mathbb{R}^8_{\geq 0}$. We define a function
$\Psi(t)$ as:
$$\Psi = S + L + I + \frac{1}{\varphi} (E + Y) + \frac{a}{2b} V + \frac{\mu_1}{\sigma_1} C^l + \frac{\mu_2}{\varphi \sigma_2} C^Y .$$

Then
$$\dot{\Psi} = \rho - \alpha S - \gamma L - \frac{a}{2} I - \frac{\omega}{\varphi} E - \frac{\delta}{\varphi} Y - \frac{a \varepsilon}{2b} V - \frac{\mu_1 \pi_1}{\sigma_1} C^l - \frac{\mu_2 \pi_2}{\varphi \sigma_2} C^Y \leq \rho - \phi \Psi,$$

where $\phi = \min\{\alpha, \gamma, \frac{a}{2}, \omega, \delta, \varepsilon, \pi_1, \pi_2\}$. Hence, $0 \leq \Psi(t) \leq \Omega_1$ if $\Psi(0) \leq \Omega_1$ for
$t \geq 0$, where $\Omega_1 = \frac{\rho}{\phi}$. Since $S, L, I, E, Y, V, C^l$, and $C^Y$ are all nonnegative then
$0 \leq S(t), L(t), I(t) \leq \Omega_1$, $0 \leq E(t), Y(t) \leq \Omega_2$, $0 \leq V(t) \leq \Omega_3$, $0 \leq C^l(t) \leq \Omega_4$, $0 \leq C^Y(t) \leq \Omega_5$ if $S(0) + L(0) + I(0) + \frac{1}{\varphi} (E(0) + Y(0)) + \frac{a}{2b} V(0) + \frac{\mu_1 \pi_1}{\sigma_1} C^l(0) + \frac{\mu_2 \pi_2}{\varphi \sigma_2} C^Y(0) \leq \Omega_1$, where $\Omega_2 = \varphi \Omega_1, \Omega_3 = \frac{2b \Omega_1}{a}, \Omega_4 = \frac{\sigma_1 \Omega_1}{\mu_1}$ and $\Omega_5 = \frac{\varphi \sigma_2 \Omega_1}{\mu_2}$.

4. Equilibria. In this section, we derive eight threshold parameters which
guarantee the existence of the equilibria of the model. Let $(S, L, I, E, Y, V, C^l, C^Y)$
be any equilibrium of system (4) satisfying the following equations:

$$0 = \rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY, \quad (5)$$
$$0 = \eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma) L, \quad (6)$$
$$0 = \lambda L - aI - \mu_1 C^l I, \quad (7)$$
$$0 = \varphi \eta_4 SY - (\psi + \omega) E, \quad (8)$$
$$0 = \psi E - \delta Y - \mu_2 C^Y Y, \quad (9)$$
$$0 = bI - \varepsilon V, \quad (10)$$
$$0 = (\sigma_1 I - \pi_1) C^l, \quad (11)$$
$$0 = (\sigma_2 Y - \pi_2) C^Y . \quad (12)$$

The straightforward calculation finds that system (4) admits eight equilibria.

(1) Infection-free equilibrium, $S_0 = (S_0, 0, 0, 0, 0, 0, 0, 0)$, where $S_0 = \rho/\alpha$. This case describes the situation of healthy state where both HIV and HTLV are absent.
(2) Chronic HIV mono-infection equilibrium with inactive immune response, $\mathcal{D}_1 = (S_1, L_1, I_1, 0, 0, V_1, 0, 0)$, where

$$S_1 = \frac{S_0}{\Re_1}, \quad L_1 = \frac{aa\epsilon}{a\epsilon\eta_2 + \lambda(b\eta_1 + \epsilon\eta_3)} (\Re_1 - 1),$$

$$I_1 = \frac{a\epsilon\lambda}{a\epsilon\eta_2 + \lambda(b\eta_1 + \epsilon\eta_3)} (\Re_1 - 1), \quad V_1 = \frac{ab\lambda}{a\epsilon\eta_2 + \lambda(b\eta_1 + \epsilon\eta_3)} (\Re_1 - 1),$$

and $\Re_1$ represents the basic HIV mono-infection reproductive ratio and is defined as:

$$\Re_1 = \frac{S_0}{\Re_1} \left[ \frac{a\epsilon\eta_2 + \lambda(b\eta_1 + \epsilon\eta_3)}{a\epsilon(\gamma + \lambda)} \right] = \Re_{11} + \Re_{12} + \Re_{13},$$

where

$$\Re_{11} = \frac{S_0\lambda b\eta_1}{a\epsilon(\gamma + \lambda)}, \quad \Re_{12} = \frac{S_0\eta_2}{\gamma + \lambda}, \quad \Re_{13} = \frac{S_0\lambda \eta_3}{a(\gamma + \lambda)}.$$

The parameter $\Re_1$ determines whether or not a chronic HIV infection can be established. In fact, $\Re_{11}$ measures the average number of secondary HIV infected generation caused by an existing free HIV particle due to VTC transmission, while $\Re_{12}$ and $\Re_{13}$ measure the average numbers of secondary HIV infected generation caused by living silent and active HIV-infected cells, respectively, due to CTC transmission.

At the equilibrium $\mathcal{D}_1$ the chronic HIV mono-infection persists while the immune response is unstimulated.

(3) Chronic HTLV mono-infection equilibrium with inactive immune response, $\mathcal{D}_2 = (S_2, 0, 0, E_2, Y_2, 0, 0, 0)$, where

$$S_2 = \frac{S_0}{\Re_2}, \quad E_2 = \frac{\alpha\delta}{\eta_4\psi} (\Re_2 - 1), \quad Y_2 = \frac{\alpha}{\eta_4} (\Re_2 - 1),$$

and the parameter $\Re_2$ is the basic HTLV mono-infection reproductive ratio for system (4) and is given by:

$$\Re_2 = \frac{\varphi\eta_4\psi S_0}{\delta (\psi + \omega)}.$$

The parameter $\Re_2$ decides whether or not a chronic HTLV infection can be established. At the equilibrium $\mathcal{D}_2$ the chronic HTLV mono-infection persists while the immune response is unstimulated.

(4) Chronic HIV mono-infection equilibrium with only active HIV-specific CTL, $\mathcal{D}_3 = (S_3, L_3, I_3, 0, 0, V_3, C_{I3}, 0)$, where

$$S_3 = \frac{\rho \epsilon \sigma_1}{b\sigma_1 \eta_1 + \epsilon (\pi_1 \eta_3 + \alpha \sigma_1 + \sigma_1 \eta_2 L_3)}, \quad I_3 = \frac{\pi_1}{\sigma_1}, \quad V_3 = \frac{b}{\epsilon} I_3 = \frac{b\pi_1}{\epsilon \sigma_1}, \quad C_{I3} = \frac{a}{\mu_1} (\Re_3 - 1).$$

The parameter $\Re_3$,

$$\Re_3 = \frac{\lambda \sigma_1 L_3}{a \sigma_1},$$

is the HIV-specific CTL-mediated immunity reproductive ratio in case of HIV mono-infection and determines whether or not the HIV-specific CTL-mediated immune response is stimulated in the absence of HTLV infection. Here, $L_3$ satisfies the quadratic equation

$$\tilde{A}L_3^2 + \tilde{B}L_3 + \tilde{C} = 0,$$  \hspace{0.5cm} (13)
where
\[
\begin{align*}
    \hat{A} &= \varepsilon \eta_2 \sigma_1 (\gamma + \lambda), \\
    \hat{B} &= \pi_1 (b \eta_1 + \varepsilon \eta_3) (\gamma + \lambda) + \varepsilon \sigma_1 [\alpha (\gamma + \lambda) - \eta_2 \rho], \\
    \hat{C} &= -\pi_1 \rho (b \eta_1 + \varepsilon \eta_3).
\end{align*}
\]

Since \( \hat{A} > 0 \) and \( \hat{C} < 0 \), then \( \hat{B}^2 - 4 \hat{A} \hat{C} > 0 \) and there are two distinct real roots of Eq. (13). The positive root is given by
\[
L_3 = \frac{-\hat{B} + \sqrt{\hat{B}^2 - 4 \hat{A} \hat{C}}}{2 \hat{A}}.
\]

(5) Chronic HTLV mono-infection equilibrium with only active HTLV-specific CTL, \( D_4 = (S_4, 0, 0, E_4, Y_4, 0, 0, C^Y_4) \), where
\[
\begin{align*}
    S_4 &= \frac{\sigma_2 \rho}{\pi_2 \eta_4 + \alpha \sigma_2}, \\
    E_4 &= \frac{\pi_2 \eta_4 \rho \phi}{(\psi + \omega)(\pi_2 \eta_4 + \alpha \sigma_2)}, \\
    Y_4 &= \frac{\pi_2}{\sigma_2}, \\
    C^Y &= \frac{\delta}{\mu_2} (R_4 - 1), \\
    R_4 &= \frac{\sigma_2 \rho \eta_4 \psi}{\delta (\psi + \omega)(\pi_2 \eta_4 + \alpha \sigma_2)}.
\end{align*}
\]

Here, \( R_4 \) represents the HTLV-specific CTL-mediated immunity reproductive ratio in case of HTLV mono-infection and determines whether or not the HTLV-specific CTL-mediated immune response is stimulated in the absence of HIV infection.

(6) Chronic HIV/HTLV co-infection equilibrium with only active HIV-specific CTL, \( D_5 = (S_5, L_5, I_5, E_5, Y_5, V_5, C^I_5, 0) \), where
\[
\begin{align*}
    S_5 &= \frac{\delta (\psi + \omega)}{\varphi \eta_4 \psi} = S_2, \\
    L_5 &= \frac{\pi_1 (b \eta_1 + \varepsilon \eta_3)}{\varepsilon \sigma_1 \eta_2 (R_5^* - 1)} = I_5, \\
    I_5 &= \frac{\pi_1}{\sigma_1} = I_3, \\
    E_5 &= \frac{\pi_1 \varphi \eta_4 (b \eta_1 + \varepsilon \eta_3)(\gamma + \lambda) + \alpha \delta e \sigma_1 \eta_2 (\psi + \omega)(R_5^* - 1)}{\eta_4 \psi \varepsilon \sigma_1 \eta_2 (\psi + \omega)(R_5^* - 1)} (R_5 - 1), \\
    Y_5 &= \frac{\varphi \psi \pi_1 \eta_4 (b \eta_1 + \varepsilon \eta_3)(\gamma + \lambda) + \alpha \delta e \sigma_1 \eta_2 (\psi + \omega)(R_5^* - 1)}{\varepsilon \sigma_1 \delta \eta_2 \eta_4 (\psi + \omega)(R_5^* - 1)} (R_5 - 1), \\
    V_5 &= \frac{b \pi_1}{\varepsilon \sigma_1} = V_3, \\
    C^I &= \frac{\alpha \eta_4 \varphi \psi (\gamma + \lambda)}{\mu_1 \delta \eta_2 (\psi + \omega)(R_5^* - 1)} (R_1 / R_2 - 1),
\end{align*}
\]

and \( R_5 \) represents the HTLV infection reproductive ratio in the presence of HIV infection and is stated as:
\[
\begin{align*}
    R_5 &= \frac{\rho \varphi \eta_4 \psi \varepsilon \sigma_1 \eta_2 (R^*_5 - 1)}{\pi_1 \varphi \eta_4 \psi (b \eta_1 + \varepsilon \eta_3)(\gamma + \lambda) + \alpha \delta e \sigma_1 \eta_2 (\psi + \omega)(R^*_5 - 1)}, \\
    R^*_5 &= \frac{\eta_4 \varphi \psi (\gamma + \lambda)}{\delta \eta_2 (\psi + \omega)}.
\end{align*}
\]

The parameter \( R_5 \) determines whether or not HIV-infected patients could be co-infected with HTLV.

(7) Chronic HIV/HTLV co-infection equilibrium with only active HTLV-specific CTL, \( D_6 = (S_6, L_6, I_6, E_6, Y_6, V_6, 0, C^Y_6) \), where
The parameter $S_6 = \frac{ae(\gamma + \lambda)}{a\eta_2 + \lambda(b\eta_1 + \varepsilon_3)} = S_1$, $L_6 = \frac{ae(\pi_2\eta_4 + \alpha\sigma_2)}{\sigma_2 [ae\eta_2 + \lambda(b\eta_1 + \varepsilon_3)]} (R_6 - 1)$,

$I_6 = \frac{\lambda e(\pi_2\eta_4 + \alpha\sigma_2)}{\sigma_2 [ae\eta_2 + \lambda(b\eta_1 + \varepsilon_3)]} (R_6 - 1)$, $E_6 = \frac{ae\pi_2\eta_4(\gamma + \lambda)}{\sigma_2(\psi + \omega)[ae\eta_2 + \lambda(b\eta_1 + \varepsilon_3)]}$,

$Y_6 = \frac{\pi_2}{\sigma_2} = Y_4$, $V_6 = \frac{b\lambda(\pi_2\eta_4 + \alpha\sigma_2)}{\sigma_2 [ae\eta_2 + \lambda(b\eta_1 + \varepsilon_3)]} (R_6 - 1)$, $C_6^\gamma = \delta \mu_2 (R_2/R_1 - 1)$,

and $R_6$ is the HIV infection reproductive ratio in the presence of HTLV infection and is stated as:

$$R_6 = \frac{\rho\sigma_2(\gamma + \lambda)}{ae(\gamma + \lambda)(\pi_2\eta_4 + \alpha\sigma_2)},$$

which determines whether or not HTLV-infected patients could be co-infected with HIV.

(8) Chronic HIV/HTLV co-infection equilibrium with active HIV-specific CTL and HTLV-specific CTL, $D_7 = (S_7, L_7, I_7, E_7, Y_7, V_7, C_7^I, C_7^\gamma)$, where

$$S_7 = \frac{\varepsilon_1\sigma\rho^2}{\pi_1\sigma_2(b\eta_1 + \varepsilon_3) + \varepsilon_1(\pi_2\eta_4 + \alpha\sigma_2 + \eta_2\sigma_2 L_7)},$$

$$E_7 = \frac{\pi_2\varepsilon_1\rho_1\varphi}{(\psi + \omega)\pi_2\varepsilon_4\sigma_1 + \sigma_2 \{\pi_1(b\eta_1 + \varepsilon_3) + \alpha\varepsilon_1 + \varepsilon_2\sigma_1 L_7\}},$$

$I_7 = \frac{\pi_2}{\sigma_2} = I_5$, $Y_7 = \frac{\pi_2}{\sigma_2} = Y_4 = Y_6$, $V_7 = \frac{b\pi_1}{\varepsilon_1} = V_3 = V_5$,

$$C_7^I = \frac{a}{\mu_1} (R_7 - 1), \ C_7^\gamma = \frac{\delta}{\mu_2} (R_8 - 1),$$

with

$$R_7 = \frac{\lambda\sigma_1 L_7}{\alpha\pi_1}, \ R_8 = \frac{\varepsilon_4\rho_1\varphi\psi\sigma_2}{\delta(\psi + \omega) \{\pi_2\varepsilon_1\sigma_1 + \sigma_2 \{\pi_1(b\eta_1 + \varepsilon_3) + \alpha\varepsilon_1 + \varepsilon_2\sigma_1 L_7\}\}},$$

and $L_7$ satisfies the quadratic equation

$$AL_7^2 + BL_7 + C = 0,$$

(15)

where

$$A = \varepsilon_2\sigma_1\sigma_2(\gamma + \lambda),$$

$$B = \varepsilon_2\sigma_4\sigma_1(\gamma + \lambda) + \pi_1\sigma_2(b\eta_1 + \varepsilon_3)(\gamma + \lambda) + \alpha\varepsilon_1\sigma_2(\gamma + \lambda) - \varepsilon_2\rho_1\sigma_1\sigma_2,$$

$$C = -\pi_1\rho_2(b\eta_1 + \varepsilon_3).$$

(16)

Since $A > 0$ and $C < 0$, then $B^2 - 4AC > 0$ and there are two distinct real roots of Eq. (15). The positive root is given by

$$L_7 = \frac{-B + \sqrt{B^2 - 4AC}}{2A}.$$

The parameter $R_7$ refers to the competed HIV-specific CTL-mediated immunity reproductive ratio in case of HIV/HTLV co-infection. On the other hand, the parameter $R_8$ refers to the competed HTLV-specific CTL-mediated immunity reproductive ratio case of HIV/HTLV co-infection.

According to the above discussion, we sum up the existence conditions for all equilibria in Table 2.
Table 2. Model (4) equilibria and their existence conditions.

| Equilibrium point | Definition                                                                 | Existence conditions |
|-------------------|---------------------------------------------------------------------------|----------------------|
| $D_0 = (S_0, 0, 0, 0, 0, 0, 0)$ | Infection-free equilibrium                                                 | None                 |
| $D_1 = (S_1, L_1, I_1, 0, 0, V_1, 0, 0)$ | Chronic HIV mono-infection equilibrium with inactive immune response        | $R_1 > 1$            |
| $D_2 = (S_2, 0, 0, E_2, Y_2, 0, 0, 0)$ | Chronic HTLV mono-infection equilibrium with inactive immune response       | $R_2 > 1$            |
| $D_3 = (S_3, L_3, I_3, 0, 0, V_3, C_I^I_3, 0)$ | Chronic HIV mono-infection equilibrium with only active HIV-specific CTL    | $R_3 > 1$            |
| $D_4 = (S_4, 0, 0, E_4, Y_4, 0, 0, C_Y^I_4)$ | Chronic HTLV mono-infection equilibrium with only active HTLV-specific CTL  | $R_4 > 1$            |
| $D_5 = (S_5, L_5, I_5, E_5, Y_5, V_5, C_I^I_5, 0)$ | Chronic HIV/HTLV co-infection equilibrium with only active HIV-specific CTL | $R_5^*, R_5 > 1$ and $R_1/R_2 > 1$ |
| $D_6 = (S_6, L_6, I_6, E_6, Y_6, V_6, 0, C_Y^I_6)$ | Chronic HIV/HTLV co-infection equilibrium with only active HTLV-specific CTL | $R_6 > 1$ and $R_2/R_1 > 1$ |
| $D_7 = (S_7, L_7, I_7, E_7, Y_7, V_7, C_I^I_7, C_Y^I_7)$ | Chronic HIV/HTLV co-infection equilibrium with active HIV-specific CTL and HTLV-specific CTL | $R_7 > 1$ and $R_8 > 1$ |
5. Global stability analysis. In this section we prove the global asymptotic stability of all equilibria by constructing Lyapunov functional following the method presented in [10, 26]. We will use the arithmetic-geometric mean inequality

\[
\frac{1}{n} \sum_{i=1}^{n} \chi_i \geq \sqrt[n]{\prod_{i=1}^{n} \chi_i}, \quad \chi_i \geq 0, \ i = 1, 2, \ldots
\]

which yields

\[
\begin{align*}
\frac{S_j}{S} - \frac{S IL_j}{S_j I L} - \frac{L I_j}{L_j I} & \geq 3, \quad j = 1, 3, 5, 6, 7, \quad (17) \\
\frac{S_j}{S} + \frac{S V L_j}{S_j V L} + \frac{L I_j}{L_j I} + \frac{IV_j}{I_j V} & \geq 4, \quad j = 1, 3, 5, 6, 7, \quad (18) \\
\frac{S_j}{S} + \frac{S Y E_j}{S_j Y E} + \frac{E Y_j}{E_j Y} & \geq 3, \quad j = 2, 4, 5, 6, 7. \quad (19)
\end{align*}
\]

Let a function \( \Phi_j(S, L, I, E, Y, V, C^I, C^Y) \) and \( \mathcal{Y}_j \) be the largest invariant subset of

\[
\mathcal{Y}_j = \left\{ (S, L, I, E, Y, V, C^I, C^Y) : \frac{d \Phi_j}{dt} = 0 \right\}, \quad j = 0, 1, 2, \ldots, 7.
\]

We define a function

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

**Theorem 5.1.** (a) If \( R_1 \leq 1 \) and \( R_2 \leq 1 \), then \( D_0 \) is globally asymptotically stable (G.A.S); (b) If \( R_1 > 1 \) or \( R_2 > 1 \), then \( D_0 \) is unstable.

**Proof.** (a) Constructing a Lyapunov functional candidate \( \Phi_0(S, L, I, E, Y, V, C^I, C^Y) \):

\[
\begin{align*}
\Phi_0 = S_0 F \left( \frac{S}{S_0} \right) + L + \frac{S_0 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} I + \frac{1}{\varphi} E + \frac{\psi + \omega}{\varphi \psi} Y \\
+ \frac{\eta S_0}{\varepsilon} V + \frac{\mu_1 S_0 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon \sigma_1} C^I + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} C^Y.
\end{align*}
\]

Clearly, \( \Phi_0(S, L, I, E, Y, V, C^I, C^Y) > 0 \) for all \( S, L, I, E, Y, V, C^I, C^Y > 0 \), and \( \Phi_0(S_0, 0, 0, 0, 0, 0, 0, 0) = 0 \). We calculate \( \frac{d \Phi_0}{dt} \) along the solutions of model (4) as:

\[
\begin{align*}
\frac{d \Phi_0}{dt} = & \left( 1 - \frac{S_0}{S} \right) \left( \rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY \right) + \eta_1 SV + \eta_2 SL + \eta_3 SI \\
& - (\lambda + \gamma) L + \frac{S_0 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} \left( \lambda L - \mu_1 C^I I \right) + \frac{1}{\varphi} (\varphi \eta_4 SY - (\psi + \omega) E) \\
& + \frac{\psi + \omega}{\varphi \psi} \left( \psi E - \delta Y - \mu_2 C^Y Y \right) + \frac{\eta S_0}{\varepsilon} (b I - \varepsilon V) \\
& + \frac{\mu_1 S_0 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon \sigma_1} (\sigma_1 C^I I - \pi_1 C^I) + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} (\sigma_2 C^Y Y - \pi_2 C^Y) \\
= & \left( 1 - \frac{S_0}{S} \right) \left( \rho - \alpha S \right) + \eta_2 S_0 L + \eta_4 S_0 Y - (\lambda + \gamma) L + \frac{\lambda S_0 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} L \\
& - \frac{\delta (\psi + \omega)}{\varphi \psi} Y - \frac{\mu_1 \pi_1 S_0 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon \sigma_1} C^I - \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi \psi \sigma_2} C^Y.
\end{align*}
\]
calculated as follows: which yields that $E(t) = 0$ for all $t > 0$. From the third and sixth equations of system (4), we have
\[
\dot{I} = -\alpha I, \quad \dot{V} = bI - \varepsilon V. \tag{20}
\]

Let us define a Lyapunov function as follows:
\[
\Phi_0 = I + \frac{a}{2b} V. \tag{21}
\]

Therefore, the time derivative of $\Phi_0$ along the solutions of system (20)-(21) can be calculated as follows:
\[
\frac{d\Phi_0}{dt} = -\frac{a}{2} \left( I + \frac{\varepsilon}{b} V \right) \leq 0.
\]

Clearly $\frac{d\Phi_0}{dt} = 0$ when $I = E = V = 0$ for all $t$. Let
\[
\mathcal{T}_0 = \left\{ (S, L, I, E, Y, V, C_I, C_Y) \in \mathcal{T}_0 : \frac{d\Phi_0}{dt} = 0 \right\}.
\]

Thus
\[
\mathcal{T}_0 = \left\{ (S, L, I, E, Y, V, C_I, C_Y) \in \mathcal{T}_0 : S = S_0, L = I = E = Y = V = C_I = C_Y = 0 \right\}
\quad = \{\mathcal{D}_0\}.
\]

Hence, all solution trajectories approach $\mathcal{D}_0$ and this means that $\mathcal{D}_0$ is G.A.S by using Lyapunov-LaSalle asymptotic stability theorem [3, 27, 36].

To prove (b), we need to find the characteristic equation about the equilibrium point. We calculate the Jacobian matrix $J = J(S, L, I, E, Y, V, C_I, C_Y)$ of system (4) as in the following form:
\[
J = \begin{pmatrix}
\eta_1 V + \eta_2 L + \eta_3 I & -\eta_2 S & -\eta_3 S & 0 & -\eta_4 S & -\eta_1 S & 0 & 0 \\
J_{12} & \eta_2 S & \eta_3 S & 0 & 0 & 0 & -\eta_1 S & 0 \\
\eta_4 & 0 & 0 & 0 & 0 & 0 & \mu_1 I & 0 \\
J_{14} & 0 & 0 & \psi & J_{55} & 0 & 0 & -\mu_2 Y \\
J_{15} & 0 & \psi J_{55} & 0 & 0 & 0 & 0 & 0 \\
J_{16} & 0 & 0 & 0 & 0 & 0 & J_{77} & 0 \\
J_{17} & 0 & 0 & 0 & 0 & 0 & \sigma_1 C_I & 0 \\
J_{18} & 0 & 0 & 0 & 0 & 0 & \sigma_2 C_Y & 0
\end{pmatrix}, \tag{22}
\]

where $J_{11} = - (\alpha + \eta_1 V + \eta_2 L + \eta_3 I + \eta_4 Y)$, $J_{12} = \eta_2 S - (\gamma + \lambda)$, $J_{33} = - (\alpha + \mu_1 C_I)$, $J_{14} = - (\psi + \omega)$, $J_{55} = - (\delta + \mu_2 C_Y)$, $J_{66} = - \varepsilon$, $J_{77} = \sigma_1 I - \pi_1$, $J_{88} = \sigma_2 Y - \pi_2$. Then, the characteristic equation at the equilibrium $\mathcal{D}_0$ is given by
\[
\det(J - \Delta I) = (\Delta + \alpha)(\Delta + \pi_1)(\Delta + \pi_2)
\quad \times \left[ \alpha(\Delta + \alpha)(\Delta + \varepsilon)(\Delta + \gamma + \lambda) - \rho \left( \{\Delta + \varepsilon\} (\eta_2 (\Delta + a) + \eta_3 \lambda) + b \eta_1 \lambda \} \right) F_0(\Delta) = 0,
\]

where $\Delta$ is the eigenvalue and
\[
F_0(\Delta) = \alpha \Delta^2 + \alpha (\delta + \psi + \omega) \Delta + \alpha \delta (\psi + \omega) (1 - \Re_2) = 0. \tag{23}
\]

Clearly if $\Re_2 > 1$, then Eq. (23) has a positive root and hence $\mathcal{D}_0$ is unstable. \hfill \Box

**Lemma 5.2.** If $\Re_3 \leq 1$, then $I_1 \leq I_3$. 

Proof. Let \( \Re_3 \leq 1 \), then \( \frac{\lambda \sigma_1 L_3}{a \sigma_1} \leq 1 \) and hence
\[
L_3 \leq \frac{a \sigma_1}{\lambda \sigma_1} \Rightarrow \frac{-\dot{B} + \sqrt{B^2 - 4AC}}{2A} \leq \frac{a \sigma_1}{\lambda \sigma_1} \\
\Rightarrow \sqrt{B^2 - 4AC} \leq \frac{2Aa \sigma_1 + \lambda \sigma_1 \dot{B}}{\lambda \sigma_1} \\
\Rightarrow \left( \frac{2Aa \sigma_1 + \lambda \sigma_1 \dot{B}}{\lambda \sigma_1} \right)^2 + 4AC - \dot{B}^2 \geq 0,
\]
Using Eq. (14), we obtain
\[
\frac{4a \sigma_1 \varepsilon \eta_2 \sigma_1 (\gamma + \lambda)^2 [a \varepsilon \eta_2 + \lambda (b \eta_1 + \varepsilon \eta_3)]}{\lambda^2} (I_3 - I_1) \geq 0.
\]
Hence, \( I_1 \leq I_3 \). \( \square \)

**Theorem 5.3.** Suppose that \( \Re_1 > 1 \), (a) if \( \Re_3/\Re_1 \leq 1 \) and \( \Re_3 \leq 1 \), then \( \mathcal{D}_1 \) is G.A.S. (b) if \( \Re_3/\Re_1 > 1 \) or \( \Re_3 > 1 \), then \( \mathcal{D}_1 \) is unstable.

Proof. (a) Define \( \Phi_1(S, L, I, E, Y, V, C', C') \) as:
\[
\Phi_1 = S_1 F \left( \frac{S}{S_1} \right) + L_1 F \left( \frac{L}{L_1} \right) + \frac{S_1 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} I_1 f \left( \frac{I}{I_1} \right) + \frac{1}{\varphi} E \\
+ \frac{\psi + \omega}{\varphi \psi} Y + \frac{b \eta_1 + \varepsilon \eta_3}{\varepsilon} \left( V_1 \right) + \frac{1}{\varphi} \left( \frac{\psi + \omega}{\varphi \psi} \right) C'.
\]
Calculating \( \frac{d \Phi_1}{dt} \) as:
\[
\frac{d \Phi_1}{dt} = \left( 1 - \frac{S_1}{S} \right) (\rho - aS - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY) \\
+ \left( 1 - \frac{L_1}{L} \right) (\eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma) L) \\
+ \frac{S_1 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} \left( 1 - \frac{I_1}{I} \right) (\lambda L - aI - \mu_1 C' I) + \frac{1}{\varphi} (\varphi \eta_4 SY - (\psi + \omega) E) \\
+ \frac{\psi + \omega}{\varphi \psi} (\psi E - \delta Y - \mu_2 C'Y) + \frac{b \eta_1 + \varepsilon \eta_3}{\varepsilon} \left( 1 - \frac{V_1}{V} \right) (bI - \varepsilon V) \\
+ \frac{\mu_1 S_1 (b \eta_1 + \varepsilon \eta_3)}{a \sigma_1} (\sigma_1 C' I - \pi_1 C') + \frac{\mu_2 (\psi + \omega)}{\varphi \psi} (\sigma_2 C' Y - \pi_2 C') \\
= \left( 1 - \frac{S_1}{S} \right) (\rho - aS) + \eta_2 S_1 L + \eta_4 S_1 Y - (\lambda + \gamma) L - \eta_1 SV \frac{L_1}{L} - \eta_2 SL \frac{L_1}{L} \\
- \eta_3 SI \frac{L_1}{L} + (\lambda + \gamma) L + \lambda S_1 (b \eta_1 + \varepsilon \eta_3) L \frac{a \varepsilon}{a \varepsilon} \frac{L_1}{L} I_1 \\
+ \frac{S_1 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} I_1 + \frac{\mu_1 S_1 (b \eta_1 + \varepsilon \eta_3)}{a \sigma_1} C' I_1 - \frac{\delta (\psi + \omega)}{\varphi \psi} Y \\
- \frac{b \eta_1 + \varepsilon \eta_3}{\varepsilon} V_1 + \eta_1 S_1 V_1 - \frac{\mu_1 \pi_2 S_1 (b \eta_1 + \varepsilon \eta_3)}{a \sigma_1} C' - \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi \psi} C'.
\]
The equilibrium conditions for $\mathcal{D}_1$ are given by

$$
\rho = \alpha S_1 + \eta_1 S_1 V_1 + \eta_2 S_1 L_1 + \eta_3 S_1 I_1,
\eta_1 S_1 V_1 + \eta_2 S_1 L_1 + \eta_3 S_1 I_1 = (\lambda + \gamma) L_1,
$$

$$
\frac{\lambda L_1}{\alpha} = I_1, \quad V_1 = \frac{b I_1}{\epsilon}.
$$

Then, we get

$$
\eta_1 S_1 V_1 + \eta_3 S_1 I_1 = \frac{S_1 (b \eta_1 + \varepsilon \eta_3)}{\varepsilon} I_1 = \frac{\lambda S_1 (b \eta_1 + \varepsilon \eta_3)}{\alpha \varepsilon} L_1,
$$

and

$$
\frac{d\Phi}{dt} = - (\alpha + \eta_2 L_1) \frac{(S - S_1)^2}{S} + \eta_1 S_1 V_1 \left(4 - \frac{S_1}{S} - \frac{SV L_1}{S_1 V_1 L} - \frac{IV_1}{I_1 V} - \frac{L I_1}{L_1 I}\right) + \eta_3 S_1 I_1 \left(3 - \frac{S_1}{S} - \frac{S L_1}{S_1 I_1 L} - \frac{L I_1}{L_1 I}\right) + \frac{\delta (\psi + \omega)}{\varphi \psi} (R_2 / R_1 - 1) Y
$$

$$
+ \frac{\mu_1 S_1 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} (I_1 - I_3) C^I - \frac{\mu_2 \pi_1 (\psi + \omega)}{\varphi \psi \sigma_2} C^Y.
$$

Using Lemma 5.2 we get that $I_1 \leq I_3$ whenever $R_3 \leq 1$. Since $R_2 / R_1 \leq 1$, then using inequalities (17)-(18) we get $\frac{d\Phi}{dt} \leq 0$ for all $S, L, I, Y, V, C^I, C^Y > 0$ and $\frac{d\Phi}{dt} = 0 \text{ when } S = S_1, L = L_1, I = I_1, V = V_1$ and $Y = C^I = C^Y = 0$. The solutions of system (4) converge to $\mathcal{Y}_1$ which includes elements with $S = S_1, L = L_1, I = I_1, V = V_1$ and $Y = C^I = C^Y = 0$ and then $\dot{Y} = 0$. The fifth equation of system (4) implies $0 = \dot{Y} = \psi E$, which yields $E(t) = 0$ for all $t$. Hence, $\mathcal{Y}_1 = \{\mathcal{D}_1\}$ and $\mathcal{D}_1$ is G.A.S using Lyapunov-LaSalle asymptotic stability theorem.

(b) Using the Jacobian matrix $J$ given by Eq. (22), we carry out the characteristic equation at the equilibrium $\mathcal{D}_1$ as follows:

$$
\det(J - \Delta I) = (\Delta + \pi_2) \left[\Delta + \pi_1 + \frac{\alpha \lambda \sigma_1 \varepsilon}{a \eta_2 \varepsilon + \lambda (b \eta_1 + \varepsilon \eta_3)} (1 - R_1)\right] F_1(\Delta) = 0, \quad (25)
$$

where

$$
F_1(\Delta) = \Delta^6 + a_5 \Delta^5 + a_4 \Delta^4 + a_3 \Delta^3 + a_2 \Delta^2 + a_1 \Delta + a_0,
$$

and

$$
a_0 = \alpha \alpha \delta \varepsilon (\gamma + \lambda) (\psi + \omega) [a \varepsilon \eta_2 + \lambda (b \eta_1 + \varepsilon \eta_3)] (R_1 - 1) \left(1 - \frac{R_2}{R_1}\right).
$$

Since $R_1 > 1$ and $\frac{R_2}{R_1} > 1$, then $F_1(0) = a_0 < 0$. Moreover, we have $\lim_{{\Delta \to \infty}} F_1(\Delta) = \infty$. Therefore, there exists a positive root for Eq. (25) and hence the equilibrium $\mathcal{D}_1$ is unstable.

\[\square\]

**Theorem 5.4.** Let $R_2 > 1$ and, (a) if $R_1 / R_2 \leq 1$ and $R_4 \leq 1$, then $\mathcal{D}_2$ is G.A.S, (b) if $R_1 / R_2 > 1$ or $R_4 > 1$, then $\mathcal{D}_2$ is unstable.

**Proof.** (a) Define $\Phi_2(S, L, I, E, Y, V, C^I, C^Y)$

$$
\Phi_2 = S_2 F \left(\frac{S}{S_2}\right) + L + \frac{S_2 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon} I + \frac{1}{\varphi} E_2 F \left(\frac{E}{E_2}\right) + \frac{\psi + \omega}{\varphi \psi} Y_2 F \left(\frac{Y}{Y_2}\right) + \frac{\eta_2 S_2 (b \eta_1 + \varepsilon \eta_3)}{a \varepsilon \sigma_1} C^I + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} C^Y.
$$
Hence, Theorem 5.5.

If $R_4 > 1$ and $R_5 \leq 1$, then $D_3$ is G.A.S.
Proof. Define \( \Phi_3(S, L, I, E, Y, V, C^I, C^Y) \) as:

\[
\Phi_3 = S_3F \left( \frac{S}{S_3} \right) + L_3F \left( \frac{L}{L_3} \right) + \frac{S_3(b_1 + \varepsilon \eta_3)}{\varepsilon (a + \mu_1 C^I_3)} I_3 F \left( \frac{I}{I_3} \right) + \frac{1}{\varphi} E + \frac{\psi + \omega + Y}{\varphi \psi}.
\]

We calculate \( \frac{d\Phi_3}{dt} \) as:

\[
\frac{d\Phi_3}{dt} = \left( 1 - \frac{S}{S_3} \right) (\rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY) + \left( 1 - \frac{L}{L_3} \right) (\eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma)L) + \frac{S_3(b_1 + \varepsilon \eta_3)}{\varepsilon (a + \mu_1 C^I_3)} \left( 1 - \frac{I}{I_3} \right) (\lambda L - a I - \mu_1 C^I I) + \frac{1}{\varphi} (\varphi \eta_4 SY - (\psi + \omega) E) + \frac{\psi + \omega + Y}{\varphi \psi} \left( \psi E - \delta Y - \mu_2 C^Y Y \right) + \frac{\mu_3 S_3(b_1 + \varepsilon \eta_3)}{\varepsilon \sigma_1 (a + \mu_1 C^I_3)} \left( 1 - \frac{C^I}{C^I_3} \right) (\sigma_1 C^I I - \pi_1 C^I) + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} \left( \sigma_2 C^Y Y - \pi_2 C^Y \right).
\]

Using the equilibrium conditions for \( D_3 \):

\[
\rho = \alpha S_3 + \eta_1 S_3 V_3 + \eta_2 S_3 L_3 + \eta_3 S_3 I_3, \\
\eta_1 S_3 V_3 + \eta_2 S_3 L_3 + \eta_3 S_3 I_3 = (\gamma + \lambda) L_3, \\
\lambda L_3 = (a + \mu_1 C^I_3) I_3, \quad I_3 = \frac{\pi_1}{\sigma_1}, \quad V_3 = \frac{\delta}{\varepsilon} I_3,
\]

we get,

\[
\eta_1 S_3 V_3 + \eta_3 S_3 I_3 = \frac{S_3(b_1 + \varepsilon \eta_3)}{\varepsilon} = \frac{\lambda S_3(b_1 + \varepsilon \eta_3)}{\varepsilon (a + \mu_1 C^I_3)} L_3.
\]

Further, we obtain

\[
\frac{d\Phi_3}{dt} = -(\alpha + \eta_2 L_3) \left( \frac{S - S_3}{S} \right)^2 + \eta_1 S_3 V_3 \left( 4 - \frac{S_3}{S} - \frac{S V_3}{S_3 L_3} - \frac{L I_3}{L_3 I} - \frac{I V_3}{I_3 V} \right)
\]

\[
+ \eta_3 S_3 I_3 \left( 3 - \frac{S_3}{S} - \frac{S I_3}{S_3 L_3} - \frac{L I_3}{L_3 I} \right) + \eta_4 (S_3 - S_5) Y - \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi \psi \sigma_2} C^Y.
\]

Hence, if \( \mathbb{R}_5 \leq 1 \), then \( D_5 \) does not exist since \( E_3 \leq 0 \) and \( Y_5 \leq 0 \). In this case

\[
\dot{E} = \varphi \eta_4 SY - (\psi + \omega) E \leq 0, \\
\dot{Y} = \psi E - \delta Y - \mu_2 C^Y Y \leq 0.
\]

It follows that,

\[
\dot{E} + \frac{\psi + \omega}{\psi} \dot{Y} = \varphi \eta_4 SY - \frac{\delta (\psi + \omega)}{\psi} Y - \frac{\mu_2 (\psi + \omega)}{\psi} C^Y Y
\]

\[
= \varphi \eta_4 \left[ S - \frac{\delta (\psi + \omega)}{\eta_4 \psi} \right] Y - \frac{\mu_2 (\psi + \omega)}{\psi} C^Y Y \leq 0 \text{ for all } C^Y, Y > 0.
\]

This happens when \( S_3 \leq \frac{\delta (\psi + \omega)}{\eta_4 \varphi \psi} = S_5 \). Then using inequalities (17)-(18) we get \( \frac{d\Phi_3}{dt} \leq 0 \) for all \( S, L, I, E, Y, V, C^I, C^Y > 0 \) with equality holding when \( S = S_3, L = L_3, I = I_3, V = V_3 \text{ and } Y = C^Y = 0 \). The solutions of system (4) converge to
which includes elements with \( S = S_3, L = L_3, I = I_3, V = V_3, \) and then \( \dot{I} = \dot{Y} = 0. \) The third and fifth equations of system (4) imply

\[
0 = \dot{I} = \lambda L_3 - a I_3 - \mu_3 C_I I_3, \\
0 = \dot{Y} = \psi E,
\]

which yield \( C_I(t) = C_I^4 \) and \( E(t) = 0 \) for all \( t \) and hence \( \mathcal{Y}_3' = \{ \mathcal{D}_3 \}. \) By applying Lyapunov-LaSalle asymptotic stability theorem we get that \( \mathcal{D}_3 \) is G.A.S. \( \square \)

**Theorem 5.6.** Let \( \Re_4 > 1 \) and, (a) if \( \Re_6 \leq 1, \) then \( \mathcal{D}_4 \) is G.A.S, (b) if \( \Re_6 > 1, \) then \( \mathcal{D}_4 \) is unstable.

**Proof.** (a) Define \( \Phi_4(S, L, I, E, Y, V, C_I', C_Y') \) as:

\[
\Phi_4 = S_4 F \left( \frac{S}{S_4} \right) + L + S_4(a \eta_3 + \varepsilon \eta_3) I + \frac{1}{\varphi} E_4 \left( \frac{E}{E_4} \right) + \frac{\psi + \omega}{\varphi \psi} Y_4 \left( \frac{Y}{Y_4} \right) + \frac{\eta_3 S_4}{\varepsilon} V + \frac{\mu_1 S_4(b \eta_1 + \varepsilon \eta_1)}{a \varphi \sigma_1} C_I' + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} C_Y' \left( \frac{C_Y'}{C_Y^4} \right).
\]

Calculating \( \frac{d\Phi_4}{dt} \) as:

\[
\frac{d\Phi_4}{dt} = \left( 1 - \frac{S_4}{S} \right) \left( \rho - \alpha S - \eta_3 SV - \eta_3 S_L - \eta_3 SI - \eta_3 SY \right) + \eta_1 SV + \eta_2 SL + \eta_3 SI \\
- (\lambda + \gamma) \left( \frac{1}{\alpha} \right) \left( \lambda L - a I - \mu_1 C_I I \right) + \frac{1}{\varphi} \left( 1 - \frac{E_4}{E} \right) \left( \varphi \eta_4 SY \right) \\
- (\psi + \omega) E \left( \frac{1}{\varphi \psi} \right) \left( 1 - \frac{Y_4}{Y} \right) \left( \psi E - \delta Y - \mu_2 C_Y Y \right) + \frac{\eta_1 S_4}{\varepsilon} (b I - \varepsilon V) \\
+ \frac{\mu_1 S_4 (b \eta_1 + \varepsilon \eta_1)}{a \varphi \sigma_1} \left( \sigma_1 C_I I - \pi_1 C_I \right) + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} \left( 1 - \frac{C_Y'}{C_Y^4} \right) \left( \sigma_2 C_Y Y - \pi_2 C_Y \right).
\]

Using the equilibrium conditions for \( \mathcal{D}_4: \)

\[
\rho = \alpha S_4 + \eta_4 S_4 Y_4, \quad Y_4 = \frac{\pi_2}{\sigma_2}, \\
\eta_4 S_4 Y_4 = \frac{\psi + \omega}{\varphi} E_4 = \delta \left( \frac{\psi + \omega}{\varphi \psi} \right) Y_4 + \frac{\mu_2 (\psi + \omega)}{\varphi \psi} C_Y Y_4, \\
\]

we obtain

\[
\frac{d\Phi_4}{dt} = -\alpha \left( \frac{S - S_4}{S} \right)^2 + \eta_4 S_4 Y_4 \left( \frac{3 - S_4}{S} - \frac{S Y E_4 - E Y_4}{S_4 Y_4 E - E_4 Y} \right) \\
+ (\gamma + \lambda) (\Re_6 - 1) L - \frac{\mu_1 \pi_1 S_4 (b \eta_1 + \varepsilon \eta_3)}{a \varphi \sigma_1} C_I.
\]

Hence, if \( \Re_6 \leq 1, \) then using inequality (19) we get \( \frac{d\Phi_4}{dt} \leq 0 \) for all \( S, L, I, E, Y, V, C_I', \) \( C_Y > 0 \) where \( \frac{d\Phi_4}{dt} = 0 \) when \( S = S_4, E = E_4, Y = Y_4 \) and \( L = C_I = 0. \) The solutions of system (4) converge to \( \mathcal{Y}_4' \) which contains elements with \( S = S_4, \) \( E = E_4, \) \( Y = Y_4 \) and \( L = C_I = 0, \) then \( \dot{Y} = 0. \) The fifth equation of system (4) implies

\[
0 = \dot{Y} = \psi E_4 - \delta Y_4 - \mu_2 C_Y Y_4,
\]

which gives \( C_Y'(t) = C_Y'^4 \) for all \( t. \) Similar to the proof of Theorem 1 one can show that \( \mathcal{D}_4 \) is G.A.S.
(b) Using the Jacobian matrix $J$ given by Eq. (22), we carry out the characteristic equation at the equilibrium $p_4$ as follows:

$$
det(J - \Delta I) = (\Delta + \pi_1) F_3(\Delta) F_4(\Delta) = 0,$$

where

$$F_3(\Delta) = -\eta_4 \rho \sigma_2^2 \varphi \psi (\psi + \omega)(\Delta + \alpha) \Delta + \pi_2(\Delta + \psi + \omega)[\sigma_2(\Delta + \alpha) + \eta_4 \pi_2] \eta_4 \rho \sigma_2 \varphi \psi - \delta(\alpha \sigma_2 + \eta_4 \pi_2)(\psi + \omega) + (\Delta + \psi + \omega)[\sigma_2(\Delta + \alpha) + \eta_4 \pi_2] \eta_4 \rho \sigma_2 \varphi \psi + (\alpha \sigma_2 + \eta_4 \pi_2)(\psi + \omega) \Delta.$$

$$F_4(\Delta) = \Delta^3 + a_2 \Delta^2 + a_1 \Delta + a \varepsilon (\gamma + \lambda)(1 - \mathcal{R}_0) = 0.$$

It is obvious that whenever $\mathcal{R}_0 > 1$, then $F_4(0) < 0$ and $\lim_{\Delta \to \infty} F_4(\Delta) = \infty$. Hence, exist a positive root for Eq. (29) and hence the equilibrium $\mathcal{D}_4$ is unstable. \hfill \square

**Theorem 5.7.** If $\mathcal{R}_3 > 1$, $\mathcal{R}_5^* > 1$, $\mathcal{R}_8 \leq 1$ and $\mathcal{R}_1/\mathcal{R}_2 > 1$, then $\mathcal{D}_5$ is G.A.S.

**Proof.** Define $\Phi_5(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\Phi_5 = S_5 F \left( \frac{S}{S_5} \right) + L_5 F \left( \frac{L}{L_5} \right) + S_5(\eta_1 + \varepsilon \eta_3) I_5 F \left( \frac{I}{I_5} \right) + \frac{1}{\varphi} E_5 F \left( \frac{E}{E_5} \right) \frac{\psi + \omega}{\varphi \psi} Y_5 F \left( \frac{Y}{Y_5} \right) + \frac{1}{\varphi} \psi \varphi Y_5 F \left( \frac{Y}{Y_5} \right) + \mu_2 \frac{\psi + \omega}{\varphi \psi} C^Y. \frac{\psi + \omega}{\varphi \psi} C^Y.$$

Calculating $\frac{d\Phi_5}{dt}$ as:

$$\frac{d\Phi_5}{dt} = \left(1 - \frac{S_5}{S}\right) (\rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY) + \left(1 - \frac{L_5}{L}\right) (\eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma)L) + \frac{S_5(\eta_1 + \varepsilon \eta_3)}{\varepsilon (\alpha + \mu_1 C^I_5)} \frac{1}{I_5} \frac{I}{I_5} (\lambda L - \rho C^I_5 I) + \frac{1}{\varphi} \frac{1}{I_5} \frac{E_5}{E_5} \frac{\psi + \omega}{\varphi \psi} \left(1 - \frac{Y_5}{Y}\right) (\psi E - \delta Y - \mu_2 C^Y Y) + \frac{1}{\varphi} \psi \varphi \left(1 - \frac{Y_5}{Y}\right) (\frac{bI}{\varepsilon V} + \mu_1 S_5(\eta_1 + \varepsilon \eta_3)) \frac{\psi + \omega}{\varphi \psi} \left(1 - \frac{C^I_5}{C^I}\right) \left(\sigma_5 C^I\right) \frac{\psi + \omega}{\varphi \psi} \left(1 - \frac{C^Y}{C^Y}\right) \left(\sigma_5 C^Y\right).$$

Using the equilibrium conditions for $\mathcal{D}_5$:

$$\rho = \alpha S_5 + \eta_1 S_5 V_5 + \eta_2 S_5 L_5 + \eta_3 S_5 I_5 + \eta_4 S_5 Y_5,$$

$$\eta_1 S_5 V_5 + \eta_2 S_5 L_5 + \eta_3 S_5 I_5 = (\gamma + \lambda)L_5,$$

$$\lambda L_5 = (\alpha + \mu_1 C^I_5) I_5, \quad I_5 = \frac{\pi_1}{\sigma_1}, \quad V_5 = \frac{b}{\varepsilon} I_5,$$

$$\eta_4 S_5 Y_5 = \frac{\psi + \omega}{\varphi} E_5 = \frac{\delta (\psi + \omega)}{\varphi \psi} Y_5,$$
we get,
\[ \eta_3 S_5 V_5 + \eta_3 S_5 I_5 = \frac{S_5 (b\eta_1 + \varepsilon \eta_3)}{\varepsilon} I_5 = \frac{\lambda S_5 (b\eta_1 + \varepsilon \eta_3)}{\varepsilon (a + \mu_1 C_1^t)} L_5. \]

Further, we obtain
\[
\frac{d\Phi_5}{dt} = -\left(\alpha + \eta_2 L_5\right) \frac{(S - S_5)^2}{S} + \eta_2 S_5 V_5 \left(4 - \frac{S_5}{S} - \frac{SVL_5}{S_5 V_5} \right) + \eta_3 S_5 I_5 \left(3 - \frac{S_5}{S} - \frac{S I L_5}{S_5 I_5} - \frac{L I_5}{I_5} - \frac{L I_5}{I_5} \right) + \eta_4 S_5 Y_5 \left(3 - \frac{S_5}{S} - \frac{S Y E_5}{S_5 Y_5 E} - \frac{E Y_5}{E_5 Y} \right) + \frac{\mu_2 (\psi + \omega)}{\varphi\psi} (Y_5 - Y_7) C^Y.
\]

Hence, if \( R_8 \leq 1 \), then \( D_7 \) does not exist since \( C_7^Y = \frac{\delta}{\mu_2} (R_8 - 1) \leq 0 \). This implies that, \( \dot{C}^Y = \sigma_2 \left( Y - \frac{\mu_2}{\sigma_2} \right) C^Y \leq 0 \) for all \( C^Y > 0 \). Thus, \( Y_5 \leq \frac{\mu_2}{\sigma_2} = Y_7 \). Hence, using inequalities (17)-(19) we get \( \frac{d\Phi_6}{dt} \leq 0 \) for all \( S, L, I, E, Y, V, C^I, C^Y \geq 0 \), where \( \frac{d\Phi_6}{dt} = 0 \) at \( S = S_5, L = L_5, I = I_5, E = E_5, Y = Y_5, V = V_5 \) and \( C^Y = 0 \). The solutions of system (4) converge to \( \Upsilon_5 \) which contains elements with \( L = L_5, I = I_5, \) and then \( I = 0 \). The third equation of system (4) implies
\[ 0 = \dot{I} = \lambda L_5 - a I_5 - \mu_1 C^I I_5, \]
which yields \( C^I(t) = C_5^I \) for all \( t \) and then \( \Upsilon_5 = \{ D_5 \} \). By applying Lyapunov-LaSalle asymptotic stability theorem we get \( D_5 \) is G.A.S. \( \square \)

**Theorem 5.8.** If \( R_6 > 1, R_7 \leq 1 \) and \( R_2/R_1 > 1 \), then \( D_6 \) is G.A.S.

**Proof.** Define \( \Phi_6(S, L, I, E, Y, V, C^I, C^Y) \) as:
\[
\Phi_6 = S_6 F \left( \frac{S}{S_6} \right) + L_6 F \left( \frac{L}{L_6} \right) + \frac{S_6 (b\eta_1 + \varepsilon \eta_3)}{\varepsilon} I_6 F \left( \frac{I}{I_6} \right) + \frac{1}{\varphi} \frac{E_6 F}{E_6} + \frac{\psi + \omega}{Y_6} \frac{Y_6 F}{Y_6} + \frac{\eta_3 S_6 V_6 F}{\varepsilon} \frac{V_6}{V_6} + \frac{\mu_1 S_6 (b\eta_1 + \varepsilon \eta_3)}{a \varepsilon \sigma_1} C^I + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} C^Y F \left( \frac{C^Y}{C^Y} \right).
\]
Calculating \( \frac{d\Phi_6}{dt} \) as:
\[
\frac{d\Phi_6}{dt} = \left(1 - \frac{S_6}{S} \right) \left( \rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY \right) \frac{1}{L} (s - L_6) (\eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma) L) + \frac{S_6 (b\eta_1 + \varepsilon \eta_3)}{a \varepsilon} \left(1 - \frac{I_6}{I} \right) (\lambda L - a I - \mu_1 C^I I) + \frac{1}{\varphi} \left(1 - \frac{E_6}{E} \right) \times (\varphi \eta_4 SY - (\psi + \omega) E) + \frac{\psi + \omega}{\varphi \psi} \left(1 - \frac{Y_6}{Y} \right) (\psi E - \delta Y - \mu_2 C^Y Y) + \frac{\eta_3 S_6}{\varepsilon} \left(1 - \frac{V_6}{V} \right) (b I - \varepsilon V) + \frac{\mu_1 S_6 (b\eta_1 + \varepsilon \eta_3)}{a \varepsilon \sigma_1} (\sigma_1 C^I I - \pi_1 C^I) + \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} \left(1 - \frac{C^Y}{C^Y} \right) (\sigma_2 C^Y Y - \pi_2 C^Y).
Using the equilibrium conditions for $\mathbb{D}_6$:

$$
\begin{align*}
\rho &= \alpha S_6 + \eta_1 S_6 V_6 + \eta_2 S_6 L_6 + \eta_3 S_6 I_6 + \eta_4 S_6 Y_6, \\
\eta_1 S_6 V_6 + \eta_2 S_6 L_6 + \eta_3 S_6 I_6 &= (\gamma + \lambda) L_6, \\
Y_6 &= \frac{\pi_2}{\sigma_2} V_6 = \frac{bI_6}{\varepsilon} - \frac{\lambda}{\alpha} L_6 = I_6, \\
\eta_4 S_6 Y_6 &= \frac{\psi + \omega}{\varphi} E_6 = \frac{\delta (\psi + \omega)}{\varphi \psi} Y_6 + \frac{\mu_2 (\psi + \omega)}{\varphi \psi} C_6 Y_6.
\end{align*}
$$

It follows that

$$
\eta_3 S_6 V_6 + \eta_3 S_6 I_6 = \frac{S_6 (b\eta_1 + \varepsilon \eta_3)}{\varepsilon} I_6 = \frac{\lambda S_6 (b\eta_1 + \varepsilon \eta_3) L_6}{\alpha \varepsilon}.
$$

Then, we obtain

$$
\begin{align*}
\frac{d\Phi_6}{dt} &= - (\alpha + \eta_2 L_6) \frac{(S - S_6)^2}{S} + \eta_1 S_6 V_6 \left( 4 - \frac{S_6}{S} \frac{SVL_6}{S_6 V_6 L} - \frac{LI_6}{S_6 V_6 L} - \frac{IV_6}{S_6 V_6 L} \right) \\
+ \eta_3 S_6 I_6 \left( 3 - \frac{S_6}{S} \frac{SIL_6}{S_6 I_6 L} - \frac{LI_6}{S_6 I_6 L} \right) + \eta_4 S_6 Y_6 \left( 3 - \frac{S_6}{S} \frac{SVE_6}{S_6 Y_6 E} - \frac{YE_6}{S_6 Y_6 E} \right) \\
+ \frac{\mu_1 S_6 (b\eta_1 + \varepsilon \eta_3)}{\alpha \varepsilon} (I_6 - I_7) C_7.
\end{align*}
$$

Hence, if $\Re_7 \leq 1$, then $\mathbb{D}_7$ does not exists since $C_7^I = \frac{a}{\mu_1} (\Re_7 - 1)$. This implies that, $\dot{C}_7^I = \sigma_1 \left( I - \frac{\eta_4}{\mu_1} \right) C_7^I \leq 0$ for all $C_7^I > 0$. Thus, $I_6 \leq \frac{\eta_4}{\mu_1} = I_7$. Then using inequalities (17)-(19) we get $\frac{d\Phi_6}{dt} \leq 0$ for all $S, L, I, E, Y, V, C^I, C^Y > 0$. Moreover $\frac{d\Phi_6}{dt} = 0$ when $S = S_6, L = L_6, I = I_6, E = E_6, Y = Y_6, V = V_6$ and $C^I = 0$. The solutions of system (4) converge to $\mathcal{Y}_6$ which has elements with $E = E_6, Y = Y_6$, and then $Y = 0$. The fifth equation of system (4) implies

$$
0 = \dot{Y} = \psi E_6 - \delta Y_6 - \mu_2 C^Y Y_6,
$$

which yields $C^Y(t) = C_6^Y$ for all $t$ and then $\mathcal{Y}_6 = \{D_6\}$. We apply Lyapunov-LaSalle asymptotic stability theorem to get that $\mathbb{D}_6$ is G.A.S.

**Theorem 5.9.** If $\Re_7 > 1$ and $\Re_8 > 1$, then $\mathbb{D}_7$ is G.A.S.

**Proof.** Define $\Phi_7(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$
\begin{align*}
\Phi_7 &= \frac{S}{S_7} F \left( \frac{S}{S_7} \right) + \frac{L}{L_7} F \left( \frac{L}{L_7} \right) + \frac{S_7 (b\eta_1 + \varepsilon \eta_3)}{\varepsilon (a + \mu_1 C_7^I)} I_7 F \left( \frac{I}{I_7} \right) + \frac{1}{\varphi} E_7 F \left( \frac{E}{E_7} \right) \\
+ \frac{\psi + \omega}{\varphi \psi} Y_7 F \left( \frac{Y}{Y_7} \right) + \frac{\eta_1 S_7}{\varepsilon} V_7 F \left( \frac{V}{V_7} \right) + \mu_1 S_7 (b\eta_1 + \varepsilon \eta_3) C_7^I \left( \frac{C_7^I}{C_7^I} \right) \\
+ \frac{\mu_2 (\psi + \omega)}{\varphi \psi \sigma_2} C_7^Y F \left( \frac{C_7^Y}{C_7^Y} \right).
\end{align*}
$$

Calculating $\frac{d\Phi_7}{dt}$ as:

$$
\begin{align*}
\frac{d\Phi_7}{dt} &= \left( 1 - \frac{S_7}{S} \right) (\rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY) \\
+ \left( 1 - \frac{L_7}{L} \right) (\eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma) L)
\end{align*}
$$




by killing infected cells. Model (4) in the absence of CTL immune response leads to equations of system (4) imply that solutions of system (4) converge to \( \Upsilon \). Hence, using inequalities (17)-(19) we get
\[
\begin{align*}
\frac{d\Phi}{dt} &= -(\alpha + \eta_2 L_7) \left( \frac{S - S^*}{S} \right)^2 + \eta_3 S_7 V_7 \left( 4 \frac{S_7}{S} - \frac{S V L_7}{S_7 V_7 L} - \frac{L I_7}{L_7 I} - \frac{I V_7}{I_7 V} \right) \\
&\quad + \eta_3 S_7 I_7 \left( 3 - \frac{S}{S} - \frac{S I L_7}{S I L_7} - \frac{L I_7}{L_7 I} \right) + \eta_3 S_7 V_7 \left( 3 - \frac{S}{S} - \frac{S Y E_2}{S Y E_2} - \frac{E Y_7}{E Y_7} \right).
\end{align*}
\]
Hence, using inequalities (17)-(19) we get \( \frac{d\Phi}{dt} \leq 0 \) for all \( S, L, I, E, Y, V, C^I, C^Y > 0 \). Further \( \frac{d\Phi}{dt} = 0 \) when \( S = S_7, L = L_7, I = I_7, E = E_7, Y = Y_7 \) and \( V = V_7 \). The solutions of system (4) converge to \( \Upsilon^* \), which has elements with \( S = S_7, L = L_7, I = I_7, E = E_7, Y = Y_7 \) and \( V = V_7 \), and then \( \dot{I} = \dot{Y} = 0 \). The third and fifth equations of system (4) imply that
\[
\begin{align*}
0 &= \dot{I} = \lambda L_7 - a I_7 - \mu_1 C^I I_7, \\
0 &= \dot{Y} = \psi E_7 - \delta Y_7 - \mu_2 C^Y Y_7,
\end{align*}
\]
which yield \( C^I(t) = C^I_0 \) and \( C^Y(t) = C^Y_0 \) for all \( t \) and hence \( \Upsilon^* = \{ D_7 \} \). Applying Lyapunov-LaSalle asymptotic stability theorem we get \( D_7 \) is G.A.S.

In Table 3, we summarize the global stability results given in Theorems 5.1-5.9.

6. Model without CTL immune response. As we discussed in Section 1 that CTLs have significant important in controlling HIV and HTLV-I mono-infections by killing infected cells. Model (4) in the absence of CTL immune response leads
Numerical simulations.

7. This extension for future works. Therefore, our model can be extended to mono-infection models with two classes of target cells have been studied in several HIV and HTLV-I can be occurred even when the immune system is inactive. HIV cells and macrophages. In this case, HIV has two resources and then coexistence of viral progression, the competition between HIV and HTLV-I is also suppressed and maximum basic reproductive ratio can survive. However, in our proposed model (4) to a model with competition between HIV and HTLV-I on CD4+ T cells:

\[
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI - \eta_4 SY, \\
\dot{L} &= \eta_1 SV + \eta_2 SL + \eta_3 SI - (\lambda + \gamma) L, \\
\dot{I} &= \lambda L - aI, \\
\dot{E} &= \varphi \eta_4 SY - (\psi + \omega) E, \\
\dot{Y} &= \psi E - \delta Y, \\
\dot{V} &= bI - \varepsilon V.
\end{align*}
\]

This system has only three equilibria, infection-free equilibrium, \( \mathcal{D}_0 = (S_0, 0, 0, 0, 0, 0) \), chronic HIV mono-infection equilibrium, \( \mathcal{D}_1 = (S_1, L_1, I_1, 0, 0, V_1) \) and chronic HTLV mono-infection equilibrium, \( \mathcal{D}_2 = (S_2, 0, 0, E_2, Y_2, 0) \), where \( S_0, S_1, L_1, I_1, V_1, S_2, E_2 \) and \( Y_2 \) are given in Section 4. The existence of these three equilibria is determined by two threshold parameters \( R_1 \) and \( R_2 \) which are also defined in Section 4.

**Corollary 1.** For system (30), the following statements hold true.

(i) If \( R_1 \leq 1 \) and \( R_2 \leq 1 \), then \( \mathcal{D}_0 \) is G.A.S.

(ii) If \( R_1 > 1 \) and \( R_2/R_1 \leq 1 \), then \( \mathcal{D}_1 \) is G.A.S.

(iii) If \( R_2 > 1 \) and \( R_1/R_2 \leq 1 \), then \( \mathcal{D}_2 \) is G.A.S.

Therefore, the system will tend to one of the three equilibria \( \mathcal{D}_0, \mathcal{D}_1 \) and \( \mathcal{D}_2 \). The above result says that in the absence of immune response, the competition between HIV and HTLV-I consuming common resources, only one type of viruses with maximum basic reproductive ratio can survive. However, in our proposed model (4) involving HIV- and HTLV-specific CTLs, HIV and HTLV-I coexist at equilibrium. We can consider this situation as follows. Since CTL immune responses suppress viral progression, the competition between HIV and HTLV-I is also suppressed and the coexistence of HIV and HTLV-I is occurred [21].

It has been reported in [41] that, HIV has two classes of target cells, CD4+ T cells and macrophages. In this case, HIV has two resources and then coexistence of HIV and HTLV-I can be occurred even when the immune system is inactive. HIV mono-infection models with two classes of target cells have been studied in several works. (see e.g., [10] and [6, 11, 13–16, 34]). Therefore, our model can be extended to take into account the second class of target cells for HIV, macrophages. We leave this extension for future works.

7. **Numerical simulations.** In this section, we illustrate the results of Theorems 5.1-5.9 by performing numerical simulations. Moreover, we study the effect of
HTLV-I infection on the HIV mono-infected individuals by making a comparison between the dynamics of HIV mono-infection and HIV/HTLV-I co-infection. Otherwise, we investigate the influence of HIV infection on the HTLV-I mono-infected individuals by conducting a comparison between the dynamics of HTLV-I mono-infection and HIV/HTLV-I co-infection.

To solve system (4) numerically we fix the values of some parameters (see Table 4) and the others will be varied.

### Table 4. The data of model (4).

| Parameter | Value | Parameter | Value | Parameter | Value |
|-----------|-------|-----------|-------|-----------|-------|
| $\rho$    | 10    | $\varphi$ | 0.2   | $\varepsilon$ | 2     |
| $\alpha$  | 0.01  | $\delta$  | 0.5   | $\gamma$  | 0.02  |
| $\eta_1$  | Varied | $\beta$  | 1    | $\sigma_1$ | Varied |
| $\eta_2$  | Varied | $\pi_1$  | 0.1  | $\sigma_2$ | Varied |
| $\eta_3$  | Varied | $\pi_2$  | 1    | $\Lambda$  | 0.2   |
| $\eta_4$  | Varied | $\mu_1$  | 0.2  | $\omega$  | 0.01  |
| $\alpha$  | 0.5   | $\mu_2$  | 0.2  | $\psi$    | 0.003 |

#### 7.1. Stability of the equilibria.** In this subsection, we choose the following three different initial conditions for system (4):

- **Initial-1**: $(S, L, I, E, Y, V, C^I, C^V)(0) = (550, 5, 1, 30, 0.18, 3, 1, 1)$,
- **Initial-2**: $(S, L, I, E, Y, V, C^I, C^V)(0) = (500, 10, 2, 40, 0.2, 6, 2, 2)$,
- **Initial-3**: $(S, L, I, E, Y, V, C^I, C^V)(0) = (450, 15, 3, 50, 0.22, 9, 3, 3)$.

Choosing selected values of $\eta_1$, $\eta_2$, $\eta_3$, $\eta_4$, $\sigma_1$ and $\sigma_2$ under the above initial conditions leads to the following scenarios:

**Scenario 1 (Stability of $D_0$):** $\eta_1 = 0.00006$, $\eta_2 = 0.00005$, $\eta_3 = 0.00007$, $\eta_4 = 0.001$, $\sigma_1 = 0.3$ and $\sigma_2 = 0.5$. For this set of parameters, we have $R_1 = 0.63 < 1$ and $R_2 = 0.23 < 1$. Figure 2 displays that the trajectories initiating with Initial-1, Initial-2 and Initial-3 reach the equilibrium $D_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$. This shows that $D_0$ is G.A.S according to Theorem 5.1. In this situation both HIV and HTLV will be died out.

**Scenario 2 (Stability of $D_1$):** $\eta_1 = 0.0001$, $\eta_2 = 0.0002$, $\eta_3 = 0.0003$, $\eta_4 = 0.0005$, $\sigma_1 = 0.003$ and $\sigma_2 = 0.2$. With such choice we get $R_2 = 0.12 < 1 < 1.91 = R_1$, $R_3 = 0.23 < 1$ and hence $R_2/R_1 = 0.06 < 1$. Therefore, the conditions in Table 2 is verified. In fact, the equilibrium point $D_1 = (523.81, 21.645, 8.658, 0, 0, 21.645, 0, 0)$.

**Scenario 3 (Stability of $D_2$):** $\eta_1 = 0.0001$, $\eta_2 = 0.00005$, $\eta_3 = 0.00007$, $\eta_4 = 0.006$, $\sigma_1 = 0.001$ and $\sigma_2 = 0.05$. Then, we calculate $R_1 = 0.81 < 1 < 1.38 = R_2$, $R_4 = 0.63 < 1$ and then $R_1/R_2 = 0.58 < 1$. Hence, the conditions in Table 2 is satisfied. The numerical results show that $D_2 = (722.222, 0, 0, 42.735, 0.641, 0, 0, 0)$ exists. Figure 4 displays that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to $D_2$. Thus, the numerical results consistent with Theorem 5.4. This situation leads to a persistent HTLV mono-infection with unstimulated CTL-mediated immune response.

**Scenario 4 (Stability of $D_3$):** $\eta_1 = 0.001$, $\eta_2 = 0.0001$, $\eta_3 = 0.0003$, $\eta_4 = 0.001$, $\sigma_1 = 0.05$ and $\sigma_2 = 0.005$. Then, we calculate $R_3 = 3.91 > 1$ and $R_5 = \ldots$
0.22 < 1. Table 2 and Figure 5 show that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to $D_3 = (569.593, 19.564, 2, 0, 0, 5, 7.282, 0)$. Therefore, $D_3$ is G.A.S and this agrees with Theorem 5.5. Hence, a chronic HIV mono-infection with HIV-specific CTL-mediated immune response is attained.

**Scenario 5 (Stability of $D_4$):** $\eta_1 = \eta_2 = 0.0001, \eta_3 = 0.0002, \eta_4 = 0.035, \sigma_1 = 0.05$ and $\sigma_2 = 0.4$. Then, we calculate $\Re_4 = 4.31 > 1$ and $\Re_5 = 0.68 < 1$. According to Table 2, $D_4$ exists with $D_4 = (533.333, 0, 0, 71.795, 0.25, 0, 0, 3.308)$. In Figure 6, we show that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to $D_4$ and then it is G.A.S which agrees with Theorem 5.6. Hence, a chronic HTLV mono-infection with HTLV-specific CTL-mediated immune response is active and the HTLV-specific CTL-mediated immune response is unstimulated.

**Scenario 6 (Stability of $D_5$):** $\eta_1 = 0.0001, \eta_2 = 0.0001, \eta_3 = 0.0002, \eta_4 = 0.011, \sigma_1 = 0.1$ and $\sigma_2 = 0.01$. Then, we calculate $\Re_6 = 5.58 > 1$, $\Re_5 = 1.91 > 1$, $\Re_8 = 0.2 < 1$ and $\Re_1/\Re_2 = 2.11 > 1$. Table 2 and the numerical results demonstrated in Figure 7 show that $D_5 = (393.939, 5.889, 1, 73.307, 1.1, 2.5, 3.389, 0)$ exists and it is G.A.S and this agrees with Theorem 5.7. As a result, a chronic co-infection with HIV and HTLV is attained where the HIV-specific CTL-mediated immune response is active and the HTLV-specific CTL-mediated immune response is unstimulated.

**Scenario 7 (Stability of $D_6$):** $\eta_1 = 0.0006, \eta_2 = 0.0001, \eta_3 = 0.0002, \eta_4 = 0.04, \sigma_1 = 0.001$ and $\sigma_2 = 0.7$. We compute $\Re_6 = 2.26 > 1$, $\Re_7 = 0.17 < 1$ and $\Re_2/\Re_1 = 2.6 > 1$. Based on the conditions in Table 2, the equilibrium $D_6 = (282.051, 25.308, 10.123, 24.796, 0.143, 25.308, 0, 1.604)$ exists. Moreover, the numerical results plotted in Figure 8 show that $D_6$ is G.A.S and this illustrates Theorem 5.8. As a result, a chronic co-infection with HIV and HTLV is attained where the HIV-specific CTL-mediated immune response is active and the HTLV-specific CTL-mediated immune response is unstimulated.

**Scenario 8 (Stability of $D_7$):** $\eta_1 = 0.0006, \eta_2 = 0.0001, \eta_3 = 0.0002, \eta_4 = 0.03, \sigma_1 = 0.04$ and $\sigma_2 = 0.5$. These data give $\Re_7 = 1.83 > 1$ and $\Re_8 = 3.24 > 1$. According to Table 2, the equilibrium $D_7$ exists. Figure 9 illustrates that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to $D_7 = (467.368, 11.464, 2.5, 43.142, 0.2, 6.25, 2.086, 2.236)$. The numerical results displayed in Figure 9 show that $D_7$ is G.A.S based on Theorem 5.9. In this case, a chronic co-infection with HIV and HTLV is attained where both HIV-specific CTL-mediated and HTLV-specific CTL-mediated immune responses are working.

To further confirmation, we calculate the eigenvalues $\lambda_i, i = 1, 2, ..., 8$ of the matrix $J$ given by Eq. (22) at each equilibrium. The examined steady will be locally stable if all its eigenvalues satisfy the following condition:

$$\Re(\lambda_i) < 0, \ i = 1, 2, ..., 8.$$

We use the parameters $\eta_1, \eta_2, \eta_3, \eta_4, \sigma_1$ and $\sigma_2$ the same as given above to compute all positive equilibria and the corresponding eigenvalues. From the scenarios 1-8, we present in Table 5 the positive equilibria, the real parts of the eigenvalues and whether the equilibrium is locally stable or unstable.
| Scenario | The equilibrium | \((\text{Re}(\lambda), i = 1, 2, 3, 0))\) | Stability |
|----------|----------------|--------------------------------------|-----------|
| 1 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0)\) | \((-1.98, -0.63, -0.2, -0.1, -0.1, -0.07, -0.01, -0.01)\) | stable |
| 2 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (523.81, 21.65, 8.66, 0, 0, 21.65, 0, 0)\) | \((-1.96, -0.7, -0.2, 0.15, -0.1, -0.1, -0.01, -0.01)\), \((-1.98, -0.64, -0.2, -0.1, -0.07, -0.01, -0.01, -0.01)\) | unstable, unstable |
| 3 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (722.22, 0.0, 42.74, 0.64, 0, 0, 0)\) | \((-1.96, -0.68, -0.22, -0.1, -0.1, -0.03, -0.01, 0.004)\), \((-1.97, -0.64, -0.21, -0.1, -0.07, -0.07, -0.01, -0.01)\) | unstable, stable |
| 4 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (180.33, 37.26, 14.9, 0, 0, 37.26, 0, 0)\), \(\mathcal{D}_2 = (569.59, 19.56, 2, 0, 0, 5.7, 28, 0)\) | \((-1.51, -1.51, 0.41, -0.2, -0.1, -0.1, -0.01, -0.01)\), \((-1.92, -0.79, 0.05, -0.2, -0.1, -0.02, -0.02, -0.01)\), \((-2.03, -2.03, -0.2, -0.03, -0.03, -0.1, -0.02, -0.01)\) | unstable, unstable, stable |
| 5 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (785.71, 9.74, 3.9, 0, 0, 9.74, 0, 0)\), \(\mathcal{D}_2 = (123.81, 0, 0, 134.8, 2.02, 0, 0, 0)\) | \((-1.96, -0.7, -0.28, -0.1, -0.1, 0.07, 0.04, -0.01)\), \((-1.97, -0.67, -0.27, -0.1, 0.09, 0.05, -0.01, -0.01)\), \((-2.07, -0.54, -0.22, -0.17, -0.1, -0.06, -0.01)\) | unstable, unstable, unstable |
| 6 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (393.94, 0, 0, 93.24, 1.4, 0, 0, 0)\), \(\mathcal{D}_2 = (714.37, 12.98, 1, 0, 2.5, 10.48, 0)\) | \((-1.82, -1, -0.21, 0.13, -0.1, -0.09, -0.01, -0.01)\), \((-2.34, -2.34, -0.22, -0.03, -0.03, -0.1, -0.01, 0.01)\), \((-1.66, 1.66, -0.21, -0.02, 0.02, -0.09, -0.01, -0.01)\) | unstable, unstable, unstable |
| 7 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (108.33, 0, 0, 137.18, 2.06, 0, 0, 0)\), \(\mathcal{D}_2 = (636.36, 0, 0, 55.94, 0.14, 0, 0, 0)\) | \((-1.65, -1.24, -0.29, 0.27, -0.1, -0.1, 0.07, -0.01)\), \((-1.93, -0.77, -0.23, -0.1, -0.09, -0.01, -0.01, -0.02)\), \((-1.83, -1.1, -0.98, 0.15, -0.1, -0.07, -0.02, -0.01)\) | unstable, unstable, unstable |
| 8 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (282.05, 32.63, 13.05, 0, 0, 32.63, 0, 0)\), \(\mathcal{D}_2 = (144.44, 0, 0, 131.62, 1.97, 0, 0, 0)\) | \((-1.93, -0.77, 0.42, -0.22, -0.1, -0.01, -0.01, 0.01)\), \((-1.97, 0.89, -0.66, -0.22, -0.1, -0.08, -0.05, -0.01)\), \((-1.73, -1.73, -0.25, -0.1, -0.02, -0.02, 0.04, -0.02)\) | unstable, unstable, unstable |
| 9 | \(\mathcal{D}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)\), \(\mathcal{D}_1 = (282.05, 32.63, 13.05, 0, 0, 32.63, 0, 0)\) | \((-1.93, -0.77, 0.42, -0.22, -0.1, -0.01, -0.01, 0.01)\) | unstable |
7.2. Comparison results. In this subsection, we study the influence of HTLV-I infection on HIV mono-infection dynamics, and how affect the HIV infection on the dynamics of HTLV-I mono-infection as well.

**Impact of HTLV-I infection on HIV mono-infection dynamics**

To investigate the effect of HTLV-I infection on HIV mono-infection dynamics, we make a comparison between model (4) and the following HIV mono-infection model:

\[
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_1 SV - \eta_2 SL - \eta_3 SI, \\
\dot{L} &= \lambda L - aL - \mu_1 C_I I, \\
\dot{I} &= \lambda L - \alpha I - \mu_1 C_I I, \\
\dot{V} &= bI - \varepsilon V, \\
\dot{C}_Y &= \sigma_1 C_I I - \pi_1 C_I.
\end{align*}
\]

(31)

We fix parameters \(\eta_1 = 0.0008, \eta_2 = 0.0003, \eta_3 = 0.0004, \sigma_1 = 0.07, \) and \(\sigma_2 = 0.5\) and consider the following initial condition:

**Initial-4:** \((S, L, I, E, Y, V, C_I, C_Y)(0) = (430, 16, 1.4, 66, 0.2, 3.5, 8, 3.9).\)

We choose two values of the parameter \(\eta_4\) as \(\eta_4 = 0.06\) (HIV/HTLV-I co-infection), and \(\eta_4 = 0.0\) (HIV mono-infection). It can be seen from Figure 10 that when the HIV mono-infected individual is co-infected with HTLV-I then the concentrations of susceptible CD4\(^+\) T cells, silent HIV-infected cells and HIV-specific CTLs are decreased. Although, the concentration of free HIV particles tend to the same value in both HIV mono-infection and HIV/HTLV-I co-infection. Indeed, such observation are compatible with the study that has been performed by Vandormael et al. in 2017 [49]. The researchers have not found any worthy differences in the concentration of HIV virus particles in comparison between HIV mono-infected and HIV/HTLV-I co-infected patients.

**Impact of HIV infection on HTLV-I mono-infection dynamics**

To investigate the effect of HIV infection on HTLV-I mono-infection dynamics, we make a comparison between model (4) and the following HTLV-I mono-infection model:

\[
\begin{align*}
\dot{S} &= \rho - \alpha S - \eta_4 SY, \\
\dot{E} &= \varphi \eta_4 SY - (\psi + \omega) E, \\
\dot{Y} &= \psi E - \delta Y - \mu_2 C^Y, \\
\dot{C}^Y &= \sigma_2 C^Y - \pi_2 C^Y.
\end{align*}
\]

(32)

We fix parameters \(\eta_4 = 0.02; \sigma_1 = 0.05, \) and \(\sigma_2 = 0.5\) and consider the following initial condition:

**Initial-5:** \((S, L, I, E, Y, V, C^I, C^Y)(0) = (500, 15, 2, 25, 0.19, 5, 8, 1).\)

We choose two values of the parameters \(\eta_1, \eta_2, \eta_3\) as \(\eta_1 = 0.001, \eta_2 = 0.0005, \eta_3 = 0.0007\) (HIV/HTLV-I co-infection), and \(\eta_1 = \eta_2 = \eta_3 = 0.0\) (HTLV-I mono-infection). It can be seen from Figure 11 that when the HTLV-I mono-infected individual is co-infected with HIV then the concentrations of susceptible CD4\(^+\) T cells, silent HTLV-infected cells and HTLV-specific CTLs are decreased. Although, the concentration of Tax-expressing HTLV-infected cells tend to the same value in both HTLV-I mono-infection and HIV/HTLV-I co-infection.
Figure 2. The behavior of solution trajectories of system (4) when $\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$. 

(a) Susceptible CD4$^+$ T cells 
(b) Silent HIV-infected cells
(c) Active HIV-infected cells 
(d) Silent HTLV-infected cells
(e) Tax-expressing HTLV-infected cells 
(f) Free HIV particles 
(g) HIV-specific CTLs 
(h) HTLV-specific CTLs
Figure 3. The behavior of solution trajectories of system (4) when $R_1 > 1$, $R_2/R_1 \leq 1$ and $R_3 \leq 1$. 
Figure 4. The behavior of solution trajectories of system (4) when $\mathcal{R}_2 > 1$, $\mathcal{R}_1/\mathcal{R}_2 \leq 1$ and $\mathcal{R}_4 \leq 1$.
Figure 5. The behavior of solution trajectories of system (4) when $\mathcal{R}_3 > 1$ and $\mathcal{R}_5 \leq 1$. 
Figure 6. The behavior of solution trajectories of system (4) when $\mathcal{R}_4 > 1$ and $\mathcal{R}_6 \leq 1$. 
Figure 7. The behavior of solution trajectories of system (4) when $R_5^* > 1$, $R_5 > 1$, $R_8 \leq 1$ and $R_1/R_2 > 1$. 
Figure 8. The behavior of solution trajectories of system (4) when $R_6 > 1$, $R_7 \leq 1$ and $R_2/R_1 > 1$. 

(A) Susceptible CD4$^+$ T cells

(b) Silent HIV-infected cells

(c) Active HIV-infected cells

(d) Silent HTLV-infected cells

(e) Tax-expressing HTLV-infected cells

(f) Free HIV particles

(g) HIV-specific CTLs

(h) HTLV-specific CTLs
Figure 9. The behavior of solution trajectories of system (4) when $\mathcal{R}_7 > 1$ and $\mathcal{R}_8 > 1$. 
Figure 10. The influence of HTLV-I infection rate ($\eta_4 \neq 0$) on HIV mono-infection dynamics (31) will cause a chronic HIV/HTLV-I co-infection.
Figure 11. The influence of HIV infection rates ($\eta_1, \eta_2, \eta_3 \neq 0$) on HTLV mono-infection dynamics (32) will cause a chronic HIV/HTLV-I co-infection.
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40 A. M. ELAIW AND N. H. ALSHAMRANI

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E-mail address: a_m.elaiw@yahoo.com
E-mail address: nhalshamrani@uoj.edu.sa