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Hopf bifurcation for a discontinuous HTLV-1 model

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Abstract. Developing accurate mathematical models for host immune response in immunosuppressive diseases such as HIV and HTLV-1 are essential to achieve an optimal drug therapy regime. Since for HTLV-1 specific CTL response typically occurs after a time lag, we consider a discontinuous response function to better describe this lagged response during the early stage of the infectious, thus the system of HTLV-1 model will be a discontinuous system. For analyzing the dynamic of the system we use Filippov theory and find conditions in which the Filippov system undergoes a Hopf bifurcation. The Hopf bifurcation help us to find stable and unstable periodic oscillations and can be used to predict whether the CTL response can return to a steady state condition. Also, Hopf bifurcation in sliding mode is investigated. In this case the solutions will remain in the hyper-surface of discontinuity and as a consequence the disease cannot progress, at least for a long time. Finally we use numerical simulations to demonstrate the results by example.

1. Introduction

Human T lymphotropic virus type 1 (HTLV-1) belongs to the retroviruses family. It mainly infects the CD4⁺ T cells resulting in persistent human infection [1]. It is estimated that HTLV-1 virus infects 15-20 million worldwide. HTLV-1 retrovirus is responsible for significant mortality. Additionally, HTLV-1 related pathological conditions are associated with no effective treatment. HTLV-1 virus usually remains without showing any symptoms during the lifelong host period. In 2-5 percent of cases it develops pathological conditions, ATL or HAM/TSP. ATL is an aggressive, fatal T-cell malignancy, adult T-cell leukemia, while HAM/TSP is a chronic, progressive neurologic disorder termed HTLV-1-associated myelopathy/tropical spastic paraparesis. Cytotoxic T cells (CTLs, CD8⁺ T cells) are another group of T cells which protect the host by controlling the proviral load and it seems that the CD8⁺ cytotoxic T lymphocyte response is an important determinant of the outcome of HTLV-1 infection [2]. It was suggested that in HAM/TSP the HTLV-1 does not infect the neuronal cells directly. Evidences have showed that the pathological condition associated with HAM/TSP were induced by CTLs via secretion of a neurotoxic substance. In the peripheral blood, HTLV-1 preferentially infects CD4⁺ helper T cells [3]. HTLV-1 does not exist as free virions in vivo and infection of healthy CD4⁺ T cells is achieved through cell-to-cell contact with infected CD4⁺ T cells [4]. The immune system reacts to HTLV-1 infection with

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a strong cytotoxic T lymphocyte (CTL) response [5]. Understanding the pathogenesis of the HTLV-1 within the host has important implications for the development of therapeutic measures and for the identification of risk factors for HAM/TSP. Because HAM/TSP occurs only in the human CNS, formal tests of the mechanisms of pathogenesis are impossible and the evidence will therefore remain circumstantial. The evidence indicates that the CTL response to HTLV-1 plays a major role, perhaps the decisive role, in determining the equilibrium provirus load of HTLV-1 [3]. Mathematical models have been developed to capture the interaction in vivo among HTLV-1, its target cells, and the CTL immune response in order to explain the pathogenesis of HTLV-1 associated diseases [4]. One of the mathematical models that introduced for HTLV-1 is [4]

$$\begin{cases} \dot{x} = \lambda - \beta xy - \mu_1 x \\ \dot{y} = \sigma \beta xy - \gamma yz - \mu_2 y \\ \dot{z} = \nu y f(z) - \mu_3 z \end{cases} \quad (1.1)$$

In this model, there are three main types of cells which are critical to the modeling effort: The uninfected CD4⁺ target cells x , infected CD4⁺ target cells y , and HTLV-1 specific CD8⁺ CTLs z , with turnover rates of μ_1 , μ_2 and μ_3 respectively. Let $x(t)$, $y(t)$, $z(t)$ denote the cell concentration of the corresponding compartment at time t . Healthy CD4⁺ T cells are produced at a constant rate λ . The infection of healthy CD4⁺ T cells is through direct cell to cell contact with a proviral CD4⁺ T cell. This interaction is modeled by the mass action term βxy , the infectivity, $\beta > 0$ represents the ability of a proviral cell to transmit HTLV-1 to a susceptible cell. Of course, not every transmission of HTLV-1 results in a new proviral cell; for example, the reverse transcription and integration of HTLV-1 into the host genome can be fatal. In order to represent this reality it is necessary to introduce the $\sigma \in [0, 1]$ which represents the probability of a transmission of HTLV-I resulting in a new proviral cell. The loss of proviral CD4⁺ T cells due to CTL lysis is given by γyz . In other words γ is the rate of CTL-initiated lysis. The term $\nu y f(z)$ represents the production of CTLs in response to HTLV-1, where $f(z)$ is the CTL response function. CTLs replicate in response to the presence of proviral cells. So, it may be expected that the expression for the CTL response function depends on y . Moreover, since replication of CTLs is done by mitosis the CTL response function also depend on z . In the literature, CTL response function has taken a linear form $f(z) = z$ [6] or a density dependent form $f(z) = \frac{z}{z+a}$ with $a > 0$ [1, 7–9]. In [4] a sigmoidal response function of the form $f(z) = \frac{z^n}{z^n+a}$ with $a > 0$ and $n \geq 2$ is considered. Sigmoidal response function shows the time lag during the early stage of the infection when z is small [4].

In this paper we consider the special 3–dimension model (1.1), with discontinuous response function $f(z)$. The reason for discontinuous response function is because, if there exist only a few antigens then antigen presenting cells (APCs) do not induce immune cells, but if there exist relatively many antigens then immune cells are gradually induced and the proliferation of immune cells is saturated for sufficiently many antigens, see Figure 1 (i), [10]. Our HTLV-1 model is discontinuous which according to our knowledge is not considered in other recent similar studies [4, 9, 11–17].

From a biological point of view, [10] introduced a mathematical model for personal immune response function. A reasonable function, $f(z)$, for immune cell inducement has been shown in Figure 1 (i). Figure 1 (ii) and (iii) are two different approximation of Figure 1 (i)

Figure 1 (ii) is corresponding to the function $f_1(z) = kz$ and Figure 1 (iii) is corresponding to $f_2(z) = \frac{mz^2}{h^2+z^2}$ (sigmoid function). The discontinuous CTL response function $f(z)$, seen below, was introduced in place of the linear function $f_1(z)$ and sigmoid function $f_2(z)$.

$$f(z) = \begin{cases} \frac{z^2}{z^2+a^2} & \text{if } z > a \\ c & \text{if } 0 \leq z < a \end{cases} \quad (1.2)$$

Note that $0 \leq f(z) \leq 1$.

The model (1.2) has some advantages. First, it is generally based on sigmoidal function and

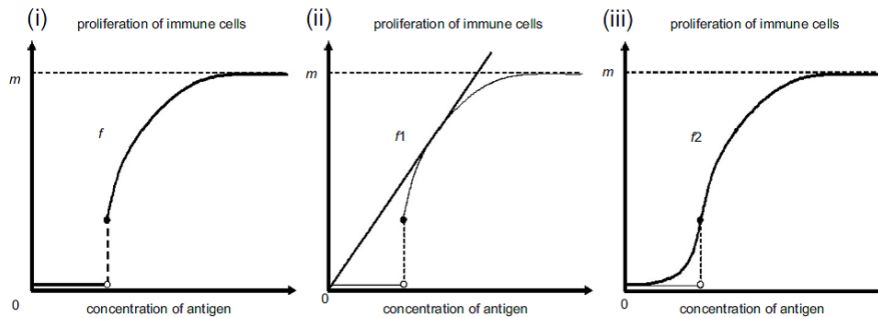


Figure 1: The Figure was taken from [10] .

consideration of a saturation effect, when z is very large. Moreover, it introduces a time lag for very small values of z . In addition, it has been shown experimentally that there is an estimated threshold of 400 peptides for antigen concentration to stimulate T cells proliferation [18–20]. These results imply that a quantitative threshold exists to commit a T cell to proliferate. In other words, as immune response function changes the states according to the antigen concentration, personal immune response function can be considered as a discontinuous switching function. therefore system (1.1) can be rewritten as follow:

$$sys(I) \begin{cases} \dot{x} = \lambda - \beta xy - \mu_1 x \\ \dot{y} = \sigma \beta xy - \gamma yz - \mu_2 y \\ \dot{z} = \nu cy - \mu_3 z \end{cases} \quad 0 \leq z < a \quad (1.3)$$

And

$$sys(II) \begin{cases} \dot{x} = \lambda - \beta xy - \mu_1 x \\ \dot{y} = \sigma \beta xy - \gamma yz - \mu_2 y \\ \dot{z} = \nu \frac{z^2}{z^2 + a^2} y - \mu_3 z \end{cases} \quad z \geq a \quad (1.4)$$

First it should be clarified what is desirable by the term ‘discontinuous dynamical system’. It is described by differential equations with a discontinuous right-hand side, also called Filippov systems. The paper is organized as follows:

In section 1 a brief explanation is given about Filippov theory. Section 2 is devoted to bifurcation theory of the system concerning discontinuity. Section 3 will give conditions in which the systems (1.3) and (1.4) undergo Hopf and fold bifurcations. Section 4 explains and prove the transversality condition. Section 5 considers the Hopf bifurcation for sliding mode. Section 6 given an example which shows our results.

2. Preliminaries

2.1. Filippov theory

Since this paper is concerned with discontinuous systems, Filippov theory is explained in this section. For more detail of this section one can see [21–25].

A dynamical system is usually expressed as the following set of ordinary differential equations

$$\dot{x} = f(t, x(t)), \quad x(t) \in \mathbb{R}^n \quad (2.1)$$

Where x is the n -dimensional state vector and $f(t, x(t))$ is the vector of right-hand sides describing the time derivative of the state vector. This study is restricted to differential equations with a

right-hand side discontinuity. The state space \mathbb{R}^n is split into two subspaces v_+ and v_- by a hyper-surface Σ such that

$$\mathbb{R}^n = v_- \cup \Sigma \cup v_+ \tag{2.2}$$

The hyper-surface Σ is defined by a scalar indicator function $h(x(t))$. The state $x(t)$ is in Σ when $h(x(t)) = 0$. The normal n perpendicular to the hyper-surface Σ is given by

$$n = n(x(t)) = \text{grad}(h(x(t))) \tag{2.3}$$

An indicator function h to define a certain hyper-surface Σ is not unique. Different indicator functions can define the same Σ .

One can assume that the indicator function $h(x(t))$ is chosen such that it always holds that

$$\text{grad}(h(x(t))) \neq 0 \tag{2.4}$$

The subspaces v_+ and v_- and hyper-surface Σ can be formulated as

$$\begin{cases} v_- = \{x \in \mathbb{R}^n \mid h(x(t)) < 0\} \\ \Sigma = \{x \in \mathbb{R}^n \mid h(x(t)) = 0\} \\ v_+ = \{x \in \mathbb{R}^n \mid h(x(t)) > 0\} \end{cases} \tag{2.5}$$

The function $f(t, x)$ is assumed to be locally continuous, smooth and linearly bounded for all $x \notin \Sigma$. From this assumption it follows that the solution $x(t)$ within each subspace v_+ and v_- exists and is unique (existence and uniqueness of continuous system theorem [26]).

The set-valued extension of $f(t, x(t))$ of (2.1) for $x \in \Sigma$ is given by the closed convex hull of all the limits

$$F(t, x(t)) = \text{c}\bar{\text{o}} \{y \in \mathbb{R}^n \mid y = \lim_{\tilde{x} \rightarrow x} f(t, \tilde{x}), \tilde{x} \in \mathbb{R}^n \setminus \Sigma\} \tag{2.6}$$

Where $\text{c}\bar{\text{o}}(A)$ denotes the smallest closed convex set containing A .

All the limits exist because $f(t, x)$ is assumed to be locally continuous, smooth and linearly bounded for all $x \notin \Sigma$. The following n -dimensional nonlinear system can be considered with the discontinuous right-hand side

$$\dot{x}(t) = f(t, x(t)) = \begin{cases} f_-(t, x(t)) & \text{if } x \in v_- \\ f_+(t, x(t)) & \text{if } x \in v_+ \end{cases} \tag{2.7}$$

With the initial condition $x(0) = x_0$.

The system described by (2.7) does not define $f(t, x(t))$ if $x(t)$ is on Σ . This problem can be overcome through the following set-valued extension $F(t, x)$

$$\dot{x}(t) \in F(t, x(t)) = \begin{cases} f_-(t, x(t)) & \text{if } x \in v_- \\ \text{c}\bar{\text{o}} \{f_-(t, x(t)), f_+(t, x(t))\} & \text{if } x \in \Sigma \\ f_+(t, x(t)) & \text{if } x \in v_+ \end{cases} \tag{2.8}$$

where the convex set with two right-hand sides f_- and f_+ can be cast in

$$\text{c}\bar{\text{o}} \{f_-, f_+\} = \{(1 - q)f_- + qf_+, \forall q \in [0, 1]\} \tag{2.9}$$

where

$$0 \leq q = \frac{(h)_x f_-}{(h)_x (f_- - f_+)} \leq 1 \tag{2.10}$$

The parameter q is a parameter which defines the convex combination and has no physical meaning. The extension (or convexification) of a discontinuous system (2.7) into a convex differential inclusion (2.8) is known as Filippov’s convex method.

Let $x \in \Sigma$ and $n(x)$ be the normal to Σ at x . Moreover $n^T(x)f_-(x)$ and $n^T(x)f_+(x)$ be the projections of $f_-(x)$ and $f_+(x)$ onto the normal to the hyper-surface Σ

(a) Transversal Intersection. If at $x \in \Sigma$

$$[n^T(x)f_-(x)] \cdot [n^T(x)f_+(x)] > 0 \tag{2.11}$$

then any solution of (2.8) with initial condition not in Σ , can reaching Σ at a time t_1 , and having a transversal intersection there, this solution is exists and is unique [23].

(b) Sliding Mode. Let $x \in \Sigma$, one has

$$[n^T(x)f_-(x)] \cdot [n^T(x)f_+(x)] < 0 \tag{2.12}$$

Then one has sliding mode through x . This is further classified as attracting or repulsive.

Definition 1. *Parameters of any system describe the biological considerations for a given model. Eigenvalues that determine the stability of an equilibrium point are functions of these parameters. As the parameters change to reflect changes in biological conditions, the eigenvalues change along with them. Some of eigenvalues may move from the left to right half of the complex plane. The point at which at least one eigenvalue has zero real-part is called the bifurcation point. After the eigenvalues completely cross into the right half plane, the equilibrium point loses its stability and changes to another state. This process is called bifurcation.*

Definition 2. *(Discontinuous bifurcation). A bifurcation point is called a discontinuous bifurcation point if the eigenvalues at the bifurcation point are set-valued and contain a value on the imaginary axis.*

Notice that a necessary condition for the existence of a discontinuous bifurcation of a fixed point of a non-smooth continuous system is a ‘jump’ of an eigenvalue (or pair of them) over the imaginary axis, i.e. the path of the set-valued eigenvalue(s) passes the imaginary axis.

Definition 3. *(Generalized Jacobian) Let x be a fixed point of (2.8). At some value for μ if x is not on Σ , then we can find a single-valued Jacobian matrix $J(x, \mu)$. If x is on Σ , then there are two Jacobian matrices $J_-(x, \mu)$ and $J_+(x, \mu)$ on either side of Σ associated with the vector field in v_- and v_+ .*

Assume that μ varies such that the fixed point x moves from v_- to v_+ via Σ . Let x_Σ denote the unique fixed point on Σ for $\mu = \mu_\Sigma$. The generalized Jacobian is the closed convex hull of $J_-(x, \mu)$ and $J_+(x, \mu)$ at (x_Σ, μ_Σ)

$$J(x_\Sigma, \mu_\Sigma) = \bar{co} \{ (1 - q)J_-(x_\Sigma, \mu_\Sigma) + qJ_+(x_\Sigma, \mu_\Sigma), \forall q \mid q \in [0, 1] \} \tag{2.13}$$

In fact, (2.13) defines how the Jacobian ‘jumps’ at Σ . The generalized Jacobian is, for a system with a single switching boundary, a convex combination of two matrices $J_-(x, \mu)$ and $J_+(x, \mu)$ if $x \in \Sigma$. To be more precise, (2.13) gives the set of values which the generalized Jacobian can attain on Σ . From the set-valued generalised Jacobian the set-valued eigenvalues can be obtained. The $\text{eig}(J(x_\Sigma, \mu_\Sigma))$ together with (2.13) give a unique path of eigenvalues “during” the jump as q is varied from 0 to 1 [25].

Let $S_\lambda = \text{eig}(J(x_\Sigma, \mu_\Sigma))$ denote the subspace in the complex plane of the set-valued eigenvalues and let Im^+ be the subspace of purely imaginary numbers with positive imaginary part containing the origin.

Definition 4. (Single crossing bifurcation). If $S_\lambda \cap Im^+$ comprises only one element, then the bifurcation is a single crossing bifurcation.

2.2. Equilibrium bifurcation in Filippov PWS Systems with Sliding

For more information of this subsection, one can see [27].

Definition 5. One can denote a point $X \in D$ as a regular equilibrium of (2.8) if X is such that either $f_-(X, \mu) = 0$ and $h(X, \mu) > 0$ or $f_+(X, \mu) = 0$ and $h(X, \mu) < 0$. Alternatively, one can say that a point $Y \in D$ is a virtual equilibrium of (2.8) if either $f_-(Y, \mu) = 0$ but $h(Y, \mu) < 0$ or $f_+(Y, \mu) = 0$ but $h(Y, \mu) > 0$.

Definition 6. One can say a point $X \in \mathbb{R}^3$ is a boundary equilibrium of (2.8) if

$$f_-(X) = f_+(X) = 0, \quad \bar{c} \bar{o}\{f_-, f_+\}(X) = 0. \tag{2.14}$$

Definition 7. A boundary equilibrium bifurcation occurs at μ if

- (i) $f_-(X, \mu) = 0$
 - (ii) $h(X, \mu) = 0$
 - (iii) $f_{ix}(X, \mu)$ is invertible for $i = -, +$.
- Where $h(X, \mu) = \bar{c} \bar{o}\{f_-, f_+\}(X, \mu)$.

While the first two conditions state that X is a boundary equilibrium as μ varies, the third condition ensures non-degeneracy.

Definition 8. I).Persistence: At the bifurcation point, a regular equilibrium lying in region v_- is turned into a regular equilibrium lying in region v_+ (or vice versa).

We state that (2.8) exhibits a border-crossing bifurcation (persistence) if, when μ (the bifurcation parameter) is varied in a neighborhood of the origin, one branch of regular equilibria and a branch of virtual equilibria cross at the boundary equilibrium point $X = 0$ when $\mu = 0$, exchanging their properties. Namely, it may be assumed that there exists, smooth branches $X^+(\mu)$ and $X^-(\mu)$ such that $X^+(0) = X^-(0)$ and, without loss of generality (reversing the sign of μ if necessary),

1. $f_-(X^+, \mu) = 0, h(X^+, \mu) > 0$ and $f_+(X^-, \mu) = 0, h(X^-, \mu) > 0$ for $\mu < 0$,
2. $f_-(X^+, \mu) = 0, h(X^+, \mu) < 0$ and $f_+(X^-, \mu) = 0, h(X^-, \mu) < 0$ for $\mu > 0$.

In terms of collision of equilibria with the boundary, this scenario describes how the only regular equilibrium point X^+ for $\mu < 0$ hits the boundary when $\mu = 0$ and turns continuously into the regular equilibrium X^- for $\mu > 0$.

II) Nonsmooth fold: At the bifurcation point, the collision of a stable and unstable equilibrium is observed on the boundary followed by their disappearance.

In the following, we refer to the theorem of equilibrium points branching from a boundary equilibrium,[27, Theorem2.7].

Theorem 1. (equilibrium points branching from a boundary equilibrium). For the systems of interest, assuming that

$$\begin{aligned} \det(A) &\neq 0 \\ D - CA^{-1}B &\neq 0 \\ CA^{-1}E &\neq 0 \end{aligned} \tag{2.15}$$

persistence is observed at the boundary equilibrium bifurcation point if

$$CA^{-1}E < 0 \tag{2.16}$$

if

$$CA^{-1}E > 0 \tag{2.17}$$

then a nonsmooth fold is observed. Where $A = f_{-x}$, $B = f_{-\mu}$, $C = h_x$, $D = h_\mu$ and $E = f_+ - f_-$.

Proof. For the proof see [27] \square

Theorem 2. (Routh-Hurwitz criteria) The Routh-Hurwitz stability criterion is a mathematical method that is a necessary and sufficient condition for determining whether a linear system is stable or not. That is, for an n -order polynomial $P(\Lambda) = \Lambda^n + a_1\Lambda^{n-1} + \dots + a_{n-2}\Lambda^2 + a_{n-1}\Lambda + a_n = 0$, all the following Hurwitz arrangements Δ_i ($i = 1, 2, \dots, n$) should be positive (for proof see [28]).

$$\begin{cases} \Delta_1 = a_1 \\ \Delta_2 = \det \begin{bmatrix} a_1 & 1 \\ a_2 & a_3 \end{bmatrix} \\ \Delta_3 = \det \begin{bmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{bmatrix} \\ \vdots \\ \Delta_n = a_n \cdot \Delta_{n-1} \end{cases} \tag{2.18}$$

3. Bifurcation analysis

3.1. Equilibrium points of system (3.1).

According to the system (2.8), the systems v_- ((1.3)) and v_+ ((1.4)) can be rewritten as

$$\begin{cases} \dot{x} = \lambda - \beta xy - \mu_1 x, \\ \dot{y} = \sigma \beta xy - \gamma yz - \mu_2 y, \\ \dot{z} = (1 - \alpha)vcy + \alpha v y \frac{z^2}{z^2 + a^2} - \mu_3 z, \end{cases} \tag{3.1}$$

where $0 \leq \alpha \leq 1$ is the Filippov parameter.

Notice that the case $\alpha = 0$ gives the system (1.3), $\alpha = 1$ shows the system (1.4), whenever $0 < \alpha < 1$, the system (3.1) will be on the hyper surface Σ .

For each case we try to find the equilibria.

(I) Let in system (3.1), $\alpha = 0$.

Thus the solution interval for z is $0 \leq z \leq a$. For $z = 0$

$$P_0 = \left(\frac{\lambda}{\mu_1}, 0, 0 \right). \tag{3.2}$$

P_0 is called the free disease equilibrium.

Suppose that $z \neq 0$, it means, the immune cells are present, or in other words there is infection in the body, so also we should consider $y \neq 0$, hence

$$\lambda - \beta xy - \mu_1 x = 0 \Rightarrow y = \frac{\lambda - \mu_1 x}{\beta x}, \quad (3.3)$$

and

$$\sigma \beta xy - \gamma yz - \mu_2 y = 0 \Rightarrow x = \frac{\mu_2 + \gamma z}{\sigma \beta}. \quad (3.4)$$

By substituting (3.4) in (3.3):

$$y = \frac{\lambda \sigma \beta - \mu_1 \mu_2 - \mu_1 \gamma z}{\beta \mu_2 + \beta \gamma z} \quad (3.5)$$

therefore

$$vc \times \frac{\lambda \sigma \beta - \mu_1 \mu_2 - \mu_1 \gamma z}{\beta \mu_2 + \beta \gamma z} - \mu_3 z = 0 \quad (3.6)$$

hence

$$\begin{aligned} v c \lambda \sigma \beta - v c \mu_1 \mu_2 - v c \mu_1 \gamma z - \beta \mu_2 \mu_3 z - \beta \gamma \mu_3 z^2 = \\ z^2 + \frac{v c \mu_1 \gamma + \beta \mu_2 \mu_3}{\beta \gamma \mu_3} z + \frac{c v}{\beta \gamma \mu_3} (\mu_1 \mu_2 - \lambda \sigma \beta) = 0 \end{aligned} \quad (3.7)$$

If (3.7) satisfies in the following condition

$$\mu_1 \mu_2 < \lambda \sigma \beta, \quad (3.8)$$

then exactly one root exist in the interval $0 < z \leq a$. The equilibrium point which z satisfies in (3.7) and condition (3.8) is

$$P_1 = (x_1, y_1, z_1) \quad (3.9)$$

This is called the carrier equilibrium. Thus in v_- , there are two equilibria P_0 and P_1 .

(II) Whenever $\alpha = 1$.

In this case by substituting (3.5) in the third terms of (1.4), we obtain

$$v \lambda \sigma \beta z^2 - v \mu_1 \mu_2 z^2 - v \mu_1 \gamma z^3 - \beta \mu_2 \mu_3 z^3 - \beta \gamma \mu_3 z^4 - \mu_2 \mu_3 \beta a^2 z - \mu_3 \beta \gamma a^2 z^2 = 0 \quad (3.10)$$

$z = 0$ is not in interval of region v_+ . (3.10) can be rewritten as follows:

$$g(z) = \beta \gamma \mu_3 z^3 + (v \mu_1 \gamma + \beta \mu_2 \mu_3) z^2 - v (\lambda \sigma \beta - \mu_1 \mu_2) z + \mu_3 \beta \gamma a^2 z + \mu_2 \mu_3 \beta a^2 = 0 \quad (3.11)$$

In this region $z \geq a$, from a biological point of view, $y > 0$ should be true. From (3.5) it can be concluded that

$$\lambda \sigma \beta - \mu_1 \mu_2 - \mu_1 \gamma z > 0 \Rightarrow \lambda \sigma \beta - \mu_1 \mu_2 > \mu_1 \gamma z \Rightarrow \frac{\lambda \sigma \beta - \mu_1 \mu_2}{\mu_1 \gamma} > z \geq a \quad (3.12)$$

Let

$$R_0 = \frac{\lambda\sigma\beta}{\mu_1\mu_2} \tag{3.13}$$

consequently

$$a \leq z < \frac{\mu_2}{\gamma}(R_0 - 1) \tag{3.14}$$

hence acceptable roots of $g(z)$ are in interval

$$I = \left[a, \frac{\mu_2}{\gamma}(R_0 - 1) \right) \tag{3.15}$$

Note that since $a > 0$ one should have $R_0 > 1$, to have a meaningful interval and it will be true, when (3.8) is satisfied. We prove that there is exactly one root of $g(z)$ in interval (3.15). Denote the equilibrium point in the region v_+ by:

$$P^{**} = (x^{**}, y^{**}, z^{**}) \tag{3.16}$$

where z^{**} satisfies in $g(z)$.

(III) When $0 < \alpha < 1$.

On Σ , $z = a$, thus the equilibria satisfy in system

$$\begin{cases} \lambda - \beta xy - \mu_1 x = 0 \\ \sigma\beta xy - \gamma ya - \mu_2 y = 0 \\ (1 - \alpha)vcy + \frac{1}{2}\alpha v y - \mu_3 a = 0. \end{cases} \tag{3.17}$$

$(1 - \alpha)vcy + \frac{1}{2}\alpha v y - \mu_3 a = 0$, leads to

$$y = \frac{\mu_3 a}{v((1 - \alpha)c + \frac{1}{2}\alpha)}, \tag{3.18}$$

also from (3.17)

$$\begin{cases} \lambda - \beta xy - \mu_1 x = 0 \\ y(\sigma\beta x - \gamma a - \mu_2) = 0. \end{cases} \tag{3.19}$$

In second equation of (3.19), $y = 0$ is not acceptable, because it means there are specific immune cells against HTLV-1, while there is no infection, so

$$\sigma\beta x - \gamma a - \mu_2 = 0 \Rightarrow x = \frac{\gamma a + \mu_2}{\sigma\beta}, \tag{3.20}$$

hence by (3.19)

$$y = \frac{\lambda\sigma\beta - \gamma a\mu_1 - \mu_2\mu_1}{\gamma a\beta + \beta\mu_2} \tag{3.21}$$

Setting equal (3.18) and(3.21) one obtains:

$$\begin{aligned} \frac{\lambda\sigma\beta - \gamma a\mu_1 - \mu_2\mu_1}{\gamma a\beta + \beta\mu_2} &= \frac{\mu_3 a}{v((1 - \alpha)c + \frac{1}{2}\alpha)} \\ \Rightarrow \mu_3 &= \frac{(\lambda\sigma\beta - \gamma a\mu_1 - \mu_2\mu_1)(v((1 - \alpha)c + \frac{1}{2}\alpha))}{\beta a(\gamma a + \mu_2)} \end{aligned} \quad (3.22)$$

Thus by (3.18), (3.20) and $z = a$, one can write the equilibrium point on Σ as:

$$P^* = (x^*, y^*, z^*) = \left(\frac{\gamma a + \mu_2}{\sigma\beta}, \frac{\lambda\sigma\beta - \gamma a\mu_1 - \mu_2\mu_1}{\gamma a\beta + \beta\mu_2}, a \right) \quad (3.23)$$

μ_3 can be rewritten as follow:

$$\mu_3 = \frac{y v (c - \alpha c + \frac{1}{2}\alpha)}{a} \quad (3.24)$$

3.2. Jacobian matrix of system (3.1) at the equilibrium point P^* on Σ

Jacobian of the model (3.1) is

$$A(\alpha) = \begin{bmatrix} -\beta y - \mu_1 & -\beta x & 0 \\ \beta \sigma y & \beta \sigma x - \gamma z - \mu_2 & -\gamma y \\ 0 & Q & N \end{bmatrix}, \quad (3.25)$$

where

$$Q = -\frac{v (\alpha ca^2 + \alpha cz^2 - \alpha z^2 - ca^2 - cz^2)}{a^2 + z^2}, \quad (3.26)$$

$$N = \frac{2 \alpha a^2 v y z - a^4 \mu_3 - 2 a^2 z^2 \mu_3 - z^4 \mu_3}{(a^2 + z^2)^2}. \quad (3.27)$$

Now, by substituting the equilibrium point (3.23) in (3.25), the Jacobian matrix can be obtained as follows:

$$A(\alpha) |_{(P^*)} = \begin{bmatrix} -\frac{N}{l} & -\frac{l}{\sigma} & 0 \\ -\frac{\sigma(l\mu_1 - N)}{l} & 0 & \frac{\gamma(l\mu_1 - N)}{\beta l} \\ 0 & -1/2 v (2 \alpha c - \alpha - 2 c) & -\frac{v c (\alpha l\mu_1 - N\alpha - l\mu_1 + N)}{\beta la} \end{bmatrix}, \quad (3.28)$$

where

$$N = \lambda\sigma\beta, \quad (3.29)$$

$$l = a\gamma + \mu_2. \quad (3.30)$$

The characteristic polynomial of (3.28), by considering condition (3.22), is

$$P = \Lambda^3 + A\Lambda^2 + B\Lambda + C, \tag{3.31}$$

where

$$A = \frac{vc(\alpha - 1)(l\mu_1 - N)}{\beta la} + \frac{N}{l} \tag{3.32}$$

$$B = -\frac{\gamma v(l\mu_1 - N)(2c(\alpha - 1) - \alpha)}{2\beta l} + \frac{vcN(l\mu_1 - N)(\alpha - 1)}{\beta l^2 a} - (l\mu_1 - N) \tag{3.33}$$

and

$$C = -\frac{\gamma vN(l\mu_1 - N)(2c(\alpha - 1) - \alpha)}{2\beta l^2} - \frac{vc(l\mu_1 - N)^2(\alpha - 1)}{\beta la} \tag{3.34}$$

Since the aim is to have a pair of purely imaginary eigenvalues, one can assume the eigenvalues of (3.31) as follows:

$$\lambda_1 = G \text{ and } \lambda_{2,3} = \pm i\omega \tag{3.35}$$

Therefore (3.35), the characteristic polynomial is

$$(\Lambda - G)(\Lambda - i\omega)(\Lambda + i\omega) = 0 \Rightarrow \Lambda^3 - G\Lambda^2 + \omega^2\Lambda - \omega^2G = 0 \tag{3.36}$$

Now that is enough to find G and ω . Note that by (3.29), $A = G$, $B = \omega^2$ and $C = \omega^2G$, these relations imply that $\omega^2 = \frac{C}{A} = B$ which leads to following conditions

$$C = AB \tag{3.37}$$

Thus

$$\begin{aligned} & \frac{\gamma vN(2c(\alpha - 1) - \alpha)}{2\beta l^2} - \frac{vc(l\mu_1 - N)(\alpha - 1)}{\beta la} = \\ & \left(\frac{vc(\alpha - 1)(l\mu_1 - N)}{\beta la} + \frac{N}{l} \right) \left(-\frac{\gamma v(2c(\alpha - 1) - \alpha)}{2\beta l} + \frac{vcN(\alpha - 1)}{\beta l^2 a} - 1 \right) \end{aligned} \tag{3.38}$$

Hence one obtains the following condition between the parameters

$$\left(\frac{vc(\alpha - 1)(l\mu_1 - N)}{\beta la} \right) \left(\frac{\gamma v(2c(\alpha - 1) - \alpha)}{2\beta l} \right) + \left(\frac{vc(\alpha - 1)(l\mu_1 - N)}{\beta la} + \frac{N}{l} \right) \frac{N}{l} \frac{vc(\alpha - 1)}{\beta la} - \frac{N}{l} = 0 \tag{3.39}$$

By definition 1, from (3.39) one should calculate the set-valued $0 < \alpha < 1$, which is obtained from

$$(s_0 + s_1)\alpha^2 + (-2s_0 - s_1 + s_2)\alpha + s_0 - s_2 - \frac{N}{l} = 0 \tag{3.40}$$

where

$$s_0 = \frac{v^2 c^2 (l\mu_1 - N)}{\beta^2 l^2 a} \left(\gamma + \frac{N}{l} \right), \quad (3.41)$$

$$s_1 = \frac{\gamma v^2 c (l\mu_1 - N)}{2\beta^2 l^2 a}, \quad (3.42)$$

$$s_2 = \frac{N^2 v c}{\beta l^3 a}. \quad (3.43)$$

The phase portrait and numerical analysis of these parameters values will be shown in simulation section.

4. Transversality

In this section the transversality condition will be checked for the system (3.1)

4.1. Transversal intersection on hyper-surface Σ

Since the Hopf bifurcation is investigated in the transversal case, here one obtains, conditions in which the solutions cross Σ transversally.

By (2.5) we can define Σ

$$\Sigma = \{(x, y, z) \mid z = a\} \quad (4.1)$$

The hyper-surface Σ is defined by a scalar indicator function $h(X(t))$. The state $X(t) = (x(t), y(t), z(t))$ is in Σ when $h(X(t)) = 0$, therefore $h(X) = z - a$ and $\nabla h(X) = (0, 0, 1)$. One can apply the transversality condition (2.11) for the system (3.1):

$$vcy - \mu_3 z > 0 \quad \text{and} \quad vy \frac{z^2}{z^2 + a^2} - \mu_3 z > 0 \quad (4.2)$$

or

$$vcy - \mu_3 z < 0 \quad \text{and} \quad vy \frac{z^2}{z^2 + a^2} - \mu_3 z < 0 \quad (4.3)$$

assume

$$vcy - \mu_3 z < 0 \Rightarrow vcy < \mu_3 z \quad (4.4)$$

Then (3.24) implies,

$$z > \frac{ac}{c - ac + \frac{1}{2}\alpha} \quad (4.5)$$

Also with (4.3), one should have $vy \frac{z^2}{z^2 + a^2} - \mu_3 z < 0$, again with (3.24) one obtains:

$$(c - ac + \frac{1}{2}\alpha) \frac{z^2}{a} - z + (c - ac + \frac{1}{2}\alpha)a > 0 \Rightarrow 4 \frac{(c - ac + \frac{1}{2}\alpha)^2}{a} > 1 \quad (4.6)$$

4.2. Transversal intersection on imaginary axis

In this section first we state the following lemma

Lemma 1. Suppose that $A(\alpha) = D_x f_{\mu_0}(x_0)$ has a simple pair of pure imaginary eigenvalues $(\lambda_{1,2}(\alpha) = \mu(\alpha) \pm i\omega(\alpha), \mu(0) = 0, \omega(0) > 0)$, where α is a set-valued, with $0 < \alpha < 1$, and no other eigenvalues with zero real parts. Let $q \in \mathbb{C}^n$ be a complex eigenvector corresponding to λ_1 :

$$A(\alpha)q = i\omega_0q, A(\alpha)\bar{q} = -i\omega_0\bar{q}. \tag{4.7}$$

Introduce also the adjoint eigenvector $p \in \mathbb{C}^n$ having the properties

$$A(\alpha)^T p = -i\omega_0p, A(\alpha)^T \bar{p} = i\omega_0\bar{p} \tag{4.8}$$

and satisfying the normalization, $\langle p, q \rangle = 1$, where $\langle p, q \rangle = \sum_{i=1}^n \bar{p}_i q_i$. According to Theorem 3.3 in [29],

$$\mu'(0) = \text{Re} \langle p, A'(0)q \rangle \neq 0 \tag{4.9}$$

guarantees the transversality.

Proof. For the proof see [29] \square

4.3. Hopf-like Bifurcation

Now in the following we check the transversality condition and Hopf bifurcation for system (3.1)

Theorem 3. (Hopf-like Bifurcation). Suppose (3.39) is satisfied and α is obtained from (3.40), such that $0 < \alpha < 1$. Also let we have (4.7), (4.8) and (4.9), then the Filippov system (3.1) will undergo a Hopf bifurcation.

Proof. It is shown that if (3.39) is satisfied, then the characteristic polynomial of the system (3.1) can have a set-valued pair of pure imaginary eigenvalues. Therefore for the proof, one must investigate the transversality. First one should find eigenvectors q, p corresponding to (4.7) and (4.8), such that (4.9) is satisfied.

In order to have the eigenvector $q \neq (0, 0, 0)$ corresponding to eigenvalue $\lambda_1 = i\omega_0$, one should have (by the computation):

$$\begin{cases} (i\omega + \frac{N}{l})V_1 + \frac{1}{\sigma}V_2 = 0 \\ \sigma(\frac{l\mu_1 - N}{l})V_1 + (i\omega)V_2 - (\gamma\frac{l\mu_1 - N}{\beta l})V_3 = 0 \\ (\frac{1}{2}\nu(2\alpha c - 2c - \alpha))V_2 + (i\omega + \frac{\nu c(\alpha - 1)(l\mu_1 - N)}{\beta la})V_3 = 0 \end{cases} \tag{4.10}$$

Where V_1, V_2 and V_3 are the elements of eigenvector q . From first term of (4.10)

$$V_1 = -\frac{l^2}{\sigma(i\omega l + N)}V_2 \tag{4.11}$$

By substituting (4.11) in the second term of (4.10), one obtains

$$-\frac{1}{2} \frac{\gamma\nu(l\mu_1 - N)(2\alpha c - 2c - \alpha)}{\beta l} + (i\omega + \frac{\nu c(\alpha - 1)(l\mu_1 - N)}{\beta la})(i\omega - \frac{l(l\mu_1 - N)}{i\omega l + N})V_3 = 0 \tag{4.12}$$

In (4.12) one requires that $V_3 \neq 0$, so suppose that the real and imaginary parts of its coefficients are equal to zero, thus

$$\frac{1}{2} \frac{\gamma v(l\mu_1 - N)(2\alpha c - 2c - \alpha)}{\beta l} = \frac{\omega^2 l^2(l\mu_1 - N)}{-\omega^2 l^2 - N^2} - \omega^2 + \frac{N(l\mu_1 - N)^2 v c(\alpha - 1)}{\beta a(-\omega^2 l^2 - N^2)} \tag{4.13}$$

$$\frac{Nl}{-\omega^2 l^2 - N^2} + \frac{vc(\alpha - 1)}{\beta la} + \frac{l(l\mu_1 - N)vc(1 - \alpha)}{\beta a(-\omega^2 l^2 - N^2)} = 0 \tag{4.14}$$

With (4.13) and (4.14), the eigenvector corresponding to $\lambda = i\omega$ is

$$q = \left[1, \quad -\sigma \frac{i\omega l + N}{l^2}, \quad \frac{\beta \sigma l(l\mu_1 - N + \omega^2 l) - i\omega \beta \sigma N}{\gamma l(l\mu_1 - N)} \right] \tag{4.15}$$

Similarly the adjoint eigenvector $p \neq (0, 0, 0)$ corresponding to $\lambda_2 = -i\omega_0$, is:

$$\begin{cases} (-i\omega + \frac{N}{l})W_1 + \frac{\sigma(l\mu_1 - N)}{l}W_2 = 0 \\ \frac{1}{\sigma}W_1 - (i\omega)W_2 + (\frac{1}{2}v(2\alpha c - 2c - \alpha))W_3 = 0 \\ -(\gamma \frac{l(l\mu_1 - N)}{\beta l})W_2 + (-i\omega + \frac{vc(\alpha - 1)(l\mu_1 - N)}{\beta la})W_3 = 0 \end{cases} \tag{4.16}$$

Thus

$$p = \left[1, \quad \frac{i\omega l - N}{\sigma(l\mu_1 - N)}, \quad \frac{\gamma(i\omega l - N)(vc(\alpha - 1)(l\mu_1 - N) + i\omega \beta la)}{v^2 c^2 (\alpha - 1)^2 (l\mu_1 - N)^2 + \omega^2 \beta la} \right] \tag{4.17}$$

If, one has the following relation.

$$\begin{aligned} &(-i\omega + (\frac{vc(\alpha - 1)(l\mu_1 - N)}{\beta la}))(\frac{l(l\mu_1 - N) + \omega^2 l + i\omega N}{\sigma(l\mu_1 - N)}) = \\ &(\frac{1}{2}v(2\alpha c - 2c - \alpha))(\frac{\gamma(i\omega l - N)}{\sigma \beta l}) \end{aligned} \tag{4.18}$$

Taking the inner product of p with the derivative of

$$A(\alpha)q = \lambda(\alpha)q, \tag{4.19}$$

one has

$$\left\langle p, \frac{dA}{d\alpha} q \right\rangle = \mu'(\alpha) \pm i\omega'(\alpha). \tag{4.20}$$

Thus, the transversality condition is given by

$$\mu'(\alpha) = \text{Re} \left\langle p, \frac{dA}{d\alpha} q \right\rangle, \tag{4.21}$$

because

$$\frac{dA}{d\alpha} q = (0, 0, \frac{1}{2} \frac{v(2c - 1)\sigma(i\omega l + N)}{l^2} + \frac{lvc\sigma(l\mu_1 - N + \omega^2 l) - i\omega \beta \sigma N}{\gamma al}). \tag{4.22}$$

A simple calculation implies then the transversality condition (4.9). Therefore by condition (3.39) and (4.9), the Hopf bifurcation can be occurred. \square

5. Sliding mode Bifurcation.

In sliding mode condition, by (2.12), one of the following relation should be satisfied,

$$vcy - \mu_3z < 0 \quad \text{and} \quad vy \frac{z^2}{z^2 + a^2} - \mu_3z > 0 \tag{5.1}$$

or

$$vcy - \mu_3z > 0 \quad \text{and} \quad vy \frac{z^2}{z^2 + a^2} - \mu_3z < 0 \tag{5.2}$$

(5.2) is satisfied.

By definition 5, (2.14), and (1.2), P^* is a boundary equilibrium if and only if

$$c = \frac{1}{2} \tag{5.3}$$

Next step is to investigate the conditions of the definition 6 for the system (3.1). The condition (i) and (ii) comes from (5.3). The third condition of definition 6, is satisfied if $(\det(f_{ix}) \neq 0)$ for $i = \pm$ by (5.3) one has:

$$\det(f_{ix}) = \det \begin{pmatrix} -\frac{\beta(-a\gamma\mu_1 + \beta\lambda\sigma - \mu_1\mu_2)}{a\beta\gamma + \beta\mu_2} - \mu_1 & -\frac{a\gamma + \mu_2}{\sigma} & 0 \\ \frac{\beta\sigma(-a\gamma\mu_1 + \beta\lambda\sigma - \mu_1\mu_2)}{a\beta\gamma + \beta\mu_2} & 0 & -\frac{\gamma(-a\gamma\mu_1 + \beta\lambda\sigma - \mu_1\mu_2)}{a\beta\gamma + \beta\mu_2} \\ 0 & 1/2v & -\mu_3 \end{pmatrix} = \tag{5.4}$$

$$1/2 \frac{(a\gamma\mu_1 - \beta\lambda\sigma + \mu_1\mu_2)(2a^2\gamma^2\mu_3 + 4a\gamma\mu_2\mu_3 + \gamma\lambda v\sigma + 2\mu_2^2\mu_3)}{(a\gamma + \mu_2)^2}$$

(5.4) can not be equal to zero, because

$$\frac{1}{2} \frac{(a\gamma\mu_1 - \beta\lambda\sigma + \mu_1\mu_2)(2a^2\gamma^2\mu_3 + 4a\gamma\mu_2\mu_3 + \gamma\lambda v\sigma + 2\mu_2^2\mu_3)}{(a\gamma + \mu_2)^2} = \tag{5.5}$$

$$\frac{1}{2} \frac{(a\gamma\mu_1 - \beta\lambda\sigma + \mu_1\mu_2)}{a\gamma + \mu_2} \frac{(2a^2\gamma^2\mu_3 + 4a\gamma\mu_2\mu_3 + \gamma\lambda v\sigma + 2\mu_2^2\mu_3)}{a\gamma + \mu_2} =$$

$$-\frac{1}{2}y^* \frac{(2a^2\gamma^2\mu_3 + 4a\gamma\mu_2\mu_3 + \gamma\lambda v\sigma + 2\mu_2^2\mu_3)}{a\gamma + \mu_2} \neq 0$$

Since $y^* \neq 0$ and all the parameters are positive. The possible birth of a family of stable limit cycles bifurcating from a boundary equilibrium bifurcation can be sought with the following steps.

1. First, the origin should be the asymptotically stable equilibrium of the piecewise linear system formed by linearizing f_- and f_+ about their values at the origin.
2. Second, the boundary equilibrium bifurcation at $\mu = 0$ must represent a persistence scenario with a regular stable focus equilibrium becoming unstable.

To investigate the first step of this aim, the fixed point P^* is transformed which is defined in (3.23) to the origin.

Consider

$$\begin{cases} \bar{x} = x - \frac{\gamma a + \mu_2}{\sigma \beta} \\ \bar{y} = y - \frac{\lambda \sigma \beta - \gamma a \mu_1 - \mu_2 \mu_1}{\gamma a \beta + \beta \mu_2} \\ \bar{z} = z - a \end{cases} \tag{5.6}$$

By the variable $(\bar{x}, \bar{y}, \bar{z})$, the system (3.1) is:

$$\begin{cases} \dot{\bar{x}} = -\beta\bar{x}\bar{y} - \frac{\lambda\sigma\beta}{\gamma a + \mu_2}\bar{x} - \frac{\gamma a + \mu_2}{\sigma\beta}\bar{y} \\ \dot{\bar{y}} = \sigma\beta\bar{x}\bar{y} + \frac{\sigma(\lambda\sigma\beta - \mu_1(\gamma a + \mu_2))}{\gamma a + \mu_2}\bar{x} - \gamma\bar{y}\bar{z} - \frac{\gamma(\lambda\sigma\beta - \mu_1(\gamma a + \mu_2))}{\beta(\gamma a + \mu_2)}\bar{z} \\ \dot{\bar{z}} = (1 - \alpha)v c \bar{y} + ((1 - \alpha)vc \frac{\lambda\sigma\beta - \mu_1(\gamma a + \mu_2)}{\beta(\gamma a + \mu_2)} - \mu_3 a) + \alpha v \bar{y} \frac{(\bar{z} + a)^2}{(\bar{z} + a)^2 + a^2} + \alpha v \frac{\lambda\sigma\beta - \mu_1(\gamma a + \mu_2)}{\beta(\gamma a + \mu_2)} \frac{(\bar{z} + a)^2}{(\bar{z} + a)^2 + a^2} - \mu_3 \bar{z} \end{cases} \quad (5.7)$$

Note that at $\bar{z} = 0$ in the third terms of (5.7), one has $(\frac{\lambda\sigma\beta - \mu_1(\gamma a + \mu_2)}{\beta(\gamma a + \mu_2)}((1 - \alpha)vc + \frac{1}{2}\alpha v) - \mu_3 a)$ and this is equal to zero with the condition (3.24). Thus $(0, 0, 0)$ is the equilibrium of (5.7). Now the asymptotically stability for the origin with respect to two cases $\alpha = 0, 1$ will be investigated.

(I) If $\alpha = 0$ in (5.7), with (5.3) the matrix is

$$A^- = \begin{bmatrix} -\frac{N}{l} & \frac{l}{\sigma\beta} & 0 \\ \frac{\sigma(-l\mu_1 + N)}{l} & 0 & -\frac{\gamma(-l\mu_1 + N)}{\beta l} \\ 0 & 1/2 v & -\mu_3 \end{bmatrix}. \quad (5.8)$$

The characteristic polynomial of (5.8) is

$$a_3 \Lambda^3 + a_2 \Lambda^2 + a_1 \Lambda + a_0, \quad (5.9)$$

where

$$\begin{aligned} a_3 &= 1, \\ a_2 &= \frac{l\mu_3 + N}{l}, \\ a_1 &= 1/2 \frac{(-\gamma l v \mu_1 + 2 N \beta \mu_3 + N \gamma v + 2 l^2 \mu_1 - 2 N l)}{\beta l}, \\ a_0 &= 1/2 \frac{(-l\mu_1 + N)(N \gamma v - 2 l^2 \mu_3)}{l^2 \beta}. \end{aligned} \quad (5.10)$$

By the Routh-Hurwitz stability criterion of third order polynomials, Theorem 2, (5.9) is asymptotically stable if all the coefficients of (5.10) are positive and $a_2 a_1 > a_3 a_0$, where a_3, a_2, a_1 and a_0 are the coefficient of $\Lambda^i, i = 0, 1, 2, 3$. It can be noticed that $a_3 = 1, a_2 > 0$ (since all the elements are positive parameters). One can choose the suitable parameters in order to have a_1 and a_0 positive and it will happen if

$$-\gamma l v \mu_1 + 2 N \beta \mu_3 + N \gamma v + 2 l^2 \mu_1 - 2 N l > 0 \Rightarrow N \beta \mu_3 + l^2 \mu_1 - N l > \frac{1}{2}(\gamma v(\mu_1 l - N)), \quad (5.11)$$

$$(-l\mu_1 + N)(N \gamma v - 2 l^2 \mu_3) > 0 \quad (5.12)$$

$a_2 a_1 > a_3 a_0$ implies from the following condition

$$(l\mu_3 + N)(-\gamma l v \mu_1 + 2 N \beta \mu_3 + l^2 \mu_1 - N l) > (-l\mu_1 + N)(N \gamma v - 2 l^2 \mu_3) \quad (5.13)$$

(II) In case $\alpha = 1$ in (5.7) with (5.3), (5.6) the matrix is

$$A^+ = \begin{bmatrix} -\frac{N}{l} & \frac{l}{\sigma\beta} & 0 \\ \frac{\sigma(-l\mu_1 + N)}{l} & 0 & -\frac{\gamma(-l\mu_1 + N)}{\beta l} \\ 0 & 0 & -\mu_3 \end{bmatrix} \quad (5.14)$$

The characteristic polynomial of (5.14):

$$\Lambda^3 + \frac{(l\mu_3 + N)\Lambda^2}{l} + \frac{(N\beta\mu_3 + l^2\mu_1 - Nl)\Lambda}{\beta l} - \frac{\mu_3(-l\mu_1 + N)}{\beta} \tag{5.15}$$

Again by Routh-Hurwitz, likewise case $\alpha = 0$, one must have

$$\begin{aligned} (N\beta\mu_3 + l^2\mu_1 - Nl) > 0 &\Rightarrow N\beta\mu_3 > l(-l\mu_1 + N) \\ -l\mu_1 + N < 0 & \end{aligned} \tag{5.16}$$

Note that because of (5.16) in (5.12), one obtains

$$N\gamma v < 2l^2\mu_3 \tag{5.17}$$

For asymptotically stability of (5.15) in addition to (5.16) and (5.17), the following relation should be satisfied

$$(l\mu_3 + N)(N\beta\mu_3 + l^2\mu_1 - Nl) > \mu_3(l\mu_1 - N). \tag{5.18}$$

Further, the second step of occurring Hopf bifurcation in sliding mode is investigated.

By the definition of A , E and C in Theorem 1, one has

$$A^{-1} = \begin{bmatrix} -\frac{\gamma lv}{N\gamma v - 2\mu_3 l^2} & -2\frac{l^3\mu_3}{\sigma(-l\mu_1 + N)(N\gamma v - 2\mu_3 l^2)} & 2\frac{\gamma l^2}{\sigma\beta(N\gamma v - 2\mu_3 l^2)} \\ -2\frac{\sigma l\mu_3\beta}{N\gamma v - 2\mu_3 l^2} & -2\frac{Nl\mu_3\beta}{(-l\mu_1 + N)(N\gamma v - 2\mu_3 l^2)} & 2\frac{N\gamma}{N\gamma v - 2\mu_3 l^2} \\ -\frac{\sigma lv\beta}{N\gamma v - 2\mu_3 l^2} & -\frac{Nlv\beta}{(-l\mu_1 + N)(N\gamma v - 2\mu_3 l^2)} & 2\frac{l^2}{N\gamma v - 2\mu_3 l^2} \end{bmatrix} \tag{5.19}$$

and

$$E = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1/2 v & 0 \end{bmatrix} \tag{5.20}$$

also

$$h(X) = h(x, y, z) = [0 \quad 0 \quad z] \Rightarrow C = h_X = [0 \quad 0 \quad 1] \tag{5.21}$$

therefore

$$CA^{-1}E = \left[0 \quad v\left(\frac{l^2}{N\gamma v - 2l^2\mu_3}\right) \quad 0 \right] \tag{5.22}$$

By (5.22), by (5.17) and (5.12) one gives

$$v\left(\frac{l^2}{N\gamma v - 2l^2\mu_3}\right) < 0 \tag{5.23}$$

At present by using Theorem 1, one can conclude that the boundary equilibrium point P^* is a bifurcation point. In the numerical section the periodic solutions on the hyper-surface Σ will be shown. This is a new result for the disease, with which one can preserve the solutions in a steady state, for a long time in a surface.

Results

The four equilibria, P_0, P_1, P^* and P^{**} are related to different stages of the disease. In other words, we have v_- region for free disease equilibrium (P_0) and also for the early stage of the infection where immune cells z are too small (carrier equilibrium P_1). In Σ , the symptoms of the disease progress as immune cells (CTL response) develop (P^*). By increasing in intensity of the disease and saturation of immune cells, the trajectories will go to region v_+ , where we have the equilibrium (P^{**}). We investigated the conditions for the parameters in which the system undergoes Hopf bifurcation. Hopf bifurcation help us to find the periodic solutions in order to entrap the disease in a cycle and prevent it from progressing. In fact two cases were considered; first the case that the equilibrium point starts from P^* on Σ , entering to region v_- , then intersects the hyper-surface Σ transversally again and after going to region v_+ again will back to the first point, and secondly the case that is the sliding mode case, in which solutions intersect Σ tangentially or may leave Σ tangentially, or even has a section of sliding motion in hyper-surface Σ . The second case is a situation that is unique to non-smooth systems, specifically, when the system dynamics do something degenerate with respect to a discontinuity boundary. For example, this might involve an invariant set gaining a first contact with a certain Σ , or the onset of sliding along the orbits of that invariant set. These events are refereed to as discontinuity-induced bifurcations (DIBs) because, as we shall see, depending on the circumstances this may or may not lead to a bifurcation in either of the classical senses as a parameter is varied. Our main interest is about DIBs of equilibria which for more details we refer to [27].

6. Simulation (An example)

Now we give an example to show our results by numerical techniques. In Figure 2 one obtains regions of $(\omega, \nu, \gamma), (\omega, \nu, \lambda), (\omega, \lambda, \gamma)$, in which one has a pair of pure imaginary eigenvalues for system (3.1) in transversal case. In Figure 3 for the specific values, which is in consistent with (3.39), one can observe the occurrence of Hopf bifurcation in transversal case. In Figure 4.(i) one considers parameters such that they satisfy in sliding mode conditions, i.e, $\lambda = 1, a = 0, \beta = 1, \mu_2 = 2, \mu_1 = 0.01, \mu_3 = 0.1, \sigma = 0.25, \nu = 1.5, \gamma = 2, \beta = 1$. The Figure 4.(ii) is shown that the solutions of Figure 4.(i) in the hyper-surface Σ and after 100 days one sees the asymptotically stable.

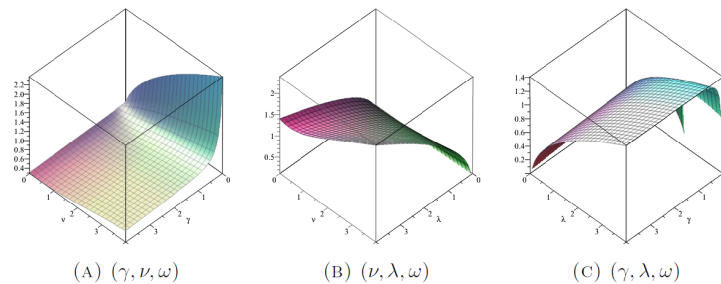


Figure 2: Parameter regions, where in (A) are considers $\mu_1 = 0.01, \mu_2 = 0.1, \mu_3 = 0.1, \beta = 1, \alpha = 0.5, \lambda = 0.25, \sigma = 0.5, a = 0.7, c = \frac{2}{3}$, in (B), $\mu_1 = 0.01, \mu_2 = 0.1, \mu_3 = 0.1, \beta = 1, \alpha = 0.5, \gamma = 4, \sigma = 0.5, a = 0.7, c = \frac{2}{3}$ and in (C), $\mu_1 = 0.01, \mu_2 = 0.1, \mu_3 = 0.1, \beta = 1, \alpha = 0.05, \nu = 1.25, \sigma = 0.5, a = 0.7, c = \frac{2}{3}$.

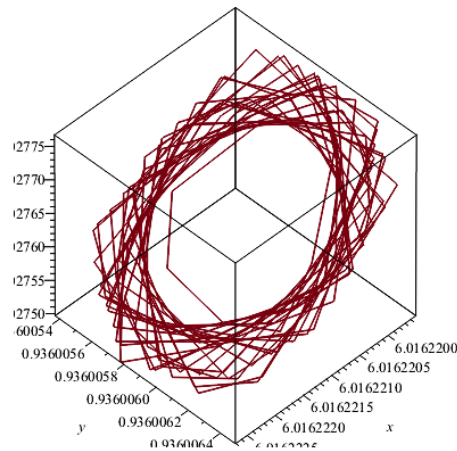


Figure 3: Limit cycle, After 150 days. one considers $\mu_1 = 0.1, \mu_2 = 1, \mu_3 = 0.9054734682, \beta = 1, \alpha = 0.6, \lambda = 6.23284081, \sigma = 0.5, a = \frac{3}{4}, c = \frac{3}{4}$ and $\gamma = 4$.

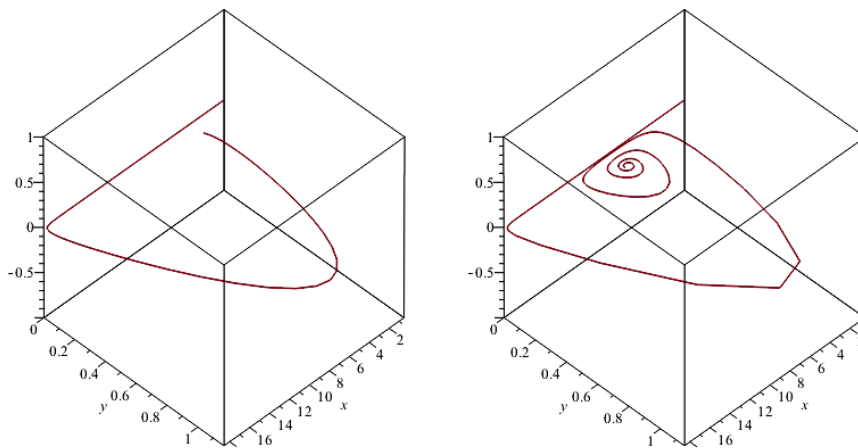


Figure 4: The solution is established on the hyper-surface Σ and one has sliding mode solutions.

7. Conclusion

A discontinuous response function for an HTLV-1 immuno-suppressive model was considered that was previously unobserved. This response function divided the system (1.1) into two systems (1.3) and (1.4). To analyze systems (1.3) and (1.4) Filippov theory was used and three solution regions ν_-, Σ and ν_+ were found. In the next step, equilibria, P_0, P_1, P^* and P^{**} , corresponding to each region were calculated. To define the parameter conditions in which the trajectories of the system move from basin of P^{**} in ν_+ (HAM/TSP region) to basin of P_1 in ν_- (carrier equilibrium) a stable periodic solution was needed. Thus, the general conditions under which the system undergoes Hopf bifurcation was investigated. Hopf bifurcation helps ensure a steady state in the carrier equilibrium region of the disease. For this purpose regions of different parameters were found. Furthermore, bifurcation for sliding mode, which is a new approach in the field of infections, were considered. Moreover, by numerical simulation the results were applied as examples. According to figures a stable periodic oscillation that system trajectories attracted to the basin of P_1 is present. Continuous models which were proposed by previous works could trap the disease in a progressed state. Our study based on sliding mode condition will give the opportunity for trapping the situation of the disease in a mild condition that was achieved by

considering the discontinuous model.

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