Dynamic Behavior in a HIV Infection Model for the Delayed Immune Response*

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Abstract: -Considering full Logistic proliferation of CD4+ T-cells and retarded immune response, we analyze a HIV model in this paper. Global asymptotic stability of the infection-free equilibrium and immune-absent equilibrium is investigated, and some conditions for Hopf bifurcation around infected equilibrium to occur are also obtained by using the time delayed as a bifurcation parameter. Numerical simulating works are presented to illustrate the main results, and we can observe the effects of the proliferation rate of CD4+ T-cells for the dynamics of system. This result can be used to explain the complexity of the immune state of AIDS.

Key-Words: Global stability; Delayed immune response; Logistic proliferation

1 Introduction

Human Immunodeficiency Virus(HIV) has spread in successive waves in various regions around the globe and becoming a serious threat to public health. Over the last several years extensive research has been made in our understanding of the pathogenesis of HIV infection, many mathematical models [1-5] provide quantitative insights. The results of these models help to design treatment strategies which would more effectively bring the infection under control.

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Immune response after viral infection is universal and necessary to eliminate or control HIV. A normal immune response to a viral usually contains antibodies, cytokines, natural killer cells, and T cells. However, cytotoxic T lymphocytes(CTL) play a critical role in antiviral defense by killing the infected cells in vivo. It is reasonable to consider the number of CTLs into mathematical [6-9] model. The turnover of free virus is much faster than that of infected cells [10,11], so we assume that the amount of free virus is simply proportional to the number of infected cells. Thus, we construct a mathematical model describing the basic dynamics of the interaction between susceptible host cells, infected cells, CTLs.

Time delay [6,12,13] has been introduced to describe the period that antigenic stimulations generating CTLs need. Time delay cannot ignored, delay-differential equations exhibit much more complicated dynamics than ordinary differential equations since a time delay could cause a stable equilibrium to become unstable and cause the

populations to fluctuate. The CTL response at the time may depend on the population of antigen and CTLs at a previous time.

In a normal healthy individual's peripheral blood, the level of CD4+ T-cells is between 800 and 1200/m^{*m*³}. The body is believed to produce CD4+ T cells from precursors in the bone marrow and thymus at a constant rate λ , and have natural nature death rate *d*, When stimulated by antigen or mitogen, T cells multiply through mitosis with a rate *r*, some scholars[14,15] incorporate simple Logistic proliferation term rx(1-x/xmax) into healthy CD4+ T cells. However, HIV infection will interrupt the normal CD4+ cells dynamics, a reasonable model for the number of this cells is

$$= \lambda - dx + rx(1 - (x + y) / x_{max}).$$

Therefore, we shall establish a mathematical model as follow:

$$\begin{cases} \frac{dx}{dt} = \lambda - dx + rx(1 - \frac{x+y}{x_{max}}) - kxy, \\ \frac{dy}{dt} = kxy - ay - pyz, \\ \frac{dz}{dt} = ce^{-a\tau}y(t-\tau)z(t-\tau) - bz \end{cases}$$
(1)

where x is the population of susceptible CD4+ Tcells, y is the population of infected CD4+ T-cells, z is the number of virus-specific CTL cells; we supposed that uninfected cells are recruited at a constant rate λ from the source within the body, such as the bone marrow and precursors. r denotes the maximum proliferation rate of CD4+ T-cells, x_{max} is the maximum level of CD4+ T-cells density at which proliferation shuts off. d, a, b denote nature death rates of uninfected CD4+ T-cells and infected CD4+ T-cells and the decay rate of CTL cells, respectively. when x reaches x_{max} , x' must be negative, so we require $\lambda < dTmax$, the Logistic $rx(1-(x+y)/x_{max})$ functions denotes the proliferation of healthy CD4+ T-cells.the terms kxy denotes the incidence of HIV infection of health CD4+ T-cells. p is the efficacy of the immune response in killing infected cells. The immune response, which is activated, depends not only on the population of infected cells but also depends on the population of CTL cells at a previous time, then the term $ce^{-a\tau}y(t-\tau)z(t-\tau)$ accounts for the increasing of immune activity. Furthermore, τ is the time delay of immune response. The initial values of system (1) are

$$x(\varsigma) = \phi_1(\varsigma), y(\varsigma) = \phi_2(\varsigma), z(\varsigma) = \phi_3(\varsigma), -\tau \le \varsigma \le 0$$
(2)

where $(\phi_1(\varsigma), \phi_2(\varsigma), \phi_3(\varsigma)) \in C([-\tau, 0], R^3_+)$, and $C([-\tau, 0], R^3_+)$ is the Banach space of continuous functions mapping the interval $[-\tau, 0]$ into R^3_+ .

It is well known by the fundamental theory of functional differential equations [16] system (1) has a unique solution $(x(\varsigma), y(\varsigma), z(\varsigma))$ satisfying the initial conditions (2).

The organization of this paper is as follow: the next section deals with some basic results. In Section 3, the dynamic behavior of system of (1) is investigated. Some numerical simulations are performed to illustrate the analytical results in Section 4. The paper ends with conclusions.

2 Main Results

It is important to show positivity and boundedness for the system (1) as they represent the

x'

concentration of CD4+ T-cells. Positivity implies that they survive and boundedness may be interpreted as a natural restriction to growth as a consequence of limited resources. In this section, we present some basic results, such as the positive invariance of system (1), the existence of equilibria, the boundedness of solutions.

2.1 Positive invariance

Theorem 1. For all $t \ge 0$, all solutions of system (1) with the initial conditions (2) are positive.

Proof. Suppose x(t) is not always positive. Then, we let $t_0 > 0$ be the first time such that $x(t_0) = 0$, By the first equation of (1), we have $x'(t_0) = \lambda > 0$, that is x(t) < 0 for $t \in (t_0 - t, t_0)$, where *t* is an arbitrarily small positive constant. This is a contradiction, it follow that x(t) is always positive. By the second and third equation of system (1.1), we can get

$$y(t) = y(0)e^{\int_{t}^{0} (kx(\varsigma) - a - pz(\varsigma))d\varsigma}$$

$$z(t) > z(0)e^{-bt}$$

Then, it is easy to see that y(t) and z(t) are positive on the existence interval.

2.2 Equilibria

It is easy to see that system (1) always has a infected-free equilibria $E_0 = (x_0, 0, 0)$, where

$$x_0 = \frac{x_{max}}{2r} \left[\sqrt{\left(r-d\right)^2 + \frac{4r\lambda}{x_{max}}} + r - d \right],$$

which shows the state that the HIV viruses are absent.

$$R_0 = \frac{x_{max}k}{2ar} \left[\sqrt{(r-d)^2 + \frac{4r\lambda}{x_{max}}} + r - d \right],$$

We denote

$$R_{1} = \frac{x_{max}k}{2ar} \left[\sqrt{\left(r - d - \frac{rbe^{a\tau}}{cx_{max}} - \frac{kbe^{a\tau}}{c}\right)^{2} + \frac{4r\lambda}{x_{max}}} + r - d - \frac{rbe^{a\tau}}{cx_{max}} - \frac{kbe^{a\tau}}{c} \right].$$

If $R_1 < R_0 < 1$, there only exists an infected-free equilibrium E_0 .

If $R_0 > 1$, $R_1 < 1$, the system (1) has an immuneabsent equilibrium $E_1 = (x_1, y_1, 0)$, which corresponding to the survival of free virus and the extinction of CTL, except E_0 where

$$x_1 = \frac{a}{k}, y_1 = \frac{\lambda x_{max} + (r-d)x_1 x_{max} - rx_1^2}{rx_1 + ax_{max}}$$

If $R_0 > R_1 > 1$, the system (1) has an infected equilibrium $E_2 = (x_2, y_2, z_2)$, which corresponding to the survival of free virus and CTL, except E_0 and E_1 . here

$$\begin{aligned} x_2 &= \frac{x_{max}}{2r} \left[\sqrt{\left(r - d - \frac{rbe^{a\tau}}{cx_{max}} - \frac{kbe^{a\tau}}{c}\right)^2 + \frac{4r\lambda}{x_{max}}} \\ &+ r - d - \frac{rbe^{a\tau}}{cx_{max}} - \frac{kbe^{a\tau}}{c} \right], \\ y_2 &= \frac{be^{a\tau}}{c}, z_2 = \frac{kx_2 - a}{p} \end{aligned}$$

2.3 Boundedness of solutions

Theorem 2.There is an M > 0 such that for any solutions (x(t), y(t), z(t)) of system (1) with the initial conditions(2), x(t) < M, y(t) < M, z(t) < M for all t > 0.

Proof. By the first equation of system (1) and $x(t), y(t), z(t) \ge 0$, we get

$$x' \le \lambda - dx + rx(1 - \frac{x}{x_{max}}).$$

Evidently, if $x(0) < x_0$, so $\limsup_{t \to \infty} x(t) \le x_0$ for all $t \ge 0$. Let

$$D(t) = x(t) + y(t) + \frac{e^{a\tau}}{p}z(t+\tau)$$

Calculating the derivate of D(t) along the solutions of system (1), then

$$D'|_{(1)} = \lambda - dx + rx(1 - \frac{x + y}{x_{max}}) - ay - \frac{be^{at}}{p}z(t + \tau)$$

$$\leq \lambda - \mu D + rx(1 - \frac{x}{x_{max}})$$

$$\leq \overline{\omega} - \mu D$$

where $\varpi = \lambda + \frac{rx_{max}}{4}, \mu = \min(d, a, b)$, we can get

$$D(t) \le \frac{\varpi}{\mu} + [D(0) - \frac{\varpi}{\mu}]e^{-\mu t}$$
(3)

Accord to inequality (3), There exists an M > 0that depending only on the parameters of system (1), such that D(t) < M for all $t \ge 0$. Recall that $x(t), y(t), z(t) \ge 0$, then x(t) < M, y(t) < M, z(t) < Mfor all t > 0.

3 Stability of Equilibrium

The purpose of this section is to give a detailed analysis for dynamic behavior of system (1).

Theorem 3. The infected-free equilibrium E_0 is globally asymptotically stable when $R_0 < 1$.

Proof. Let (x(t), y(t), z(t)) be any positive solution of system (1) with initial conditions (2). Define a Lyapunov function as follow:

$$L_{1}(t) = \frac{1}{2}(x(t) - x_{0})^{2} + (1 + \frac{r}{kx_{max}})x_{0}y(t) + \frac{\delta}{c}z(t) + \delta \int_{t}^{t-\tau} y(\zeta)z(\zeta)d\zeta$$

here $\delta = px_0 + \frac{rpx_0}{kx_{max}} > 0$, Calculating the time derivative of $L_1(t)$ along the positive solution of model (1), we have

$$L_{1}'|_{(1)} = (x(t) - x_{0})[-(x(t) - x_{0})(d - r + \frac{r(x_{0} + x(t))}{x_{max}}) - \frac{rx(t)y(t)}{x_{max}} - kx(t)y(t)] + (1 + \frac{r}{x_{max}})x_{0}[kx(t)y(t) - ay(t) - py(t)z(t)] + \frac{\delta}{c}[ce^{-at}y(t - \tau)z(t - \tau) - bz(t)] + \delta[y(t)z(t) - y(t - \tau)z(t - \tau)] \leq -(x(t) - x_{0})^{2}(d - r + \frac{rx_{0}}{x_{max}}) - (x(t) - x_{0})^{2}[\frac{rx(t) + ry(t)}{x_{max}} + ky(t)] - ax_{0}y(t)(1 - R_{0})(1 + \frac{r}{kx_{max}}) - \frac{\delta b}{c}z(t)$$

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From Theorem 1, we can see that x(t), y(t), z(t) are positive, it follows from $R_0 < 1$ that $L_1' \le 0$, and $L_1' = 0$ if and only if $(x, y, z) = (x_0, 0, 0)$. Then from the classical Lyapunov-LaSalle invariance principal [17] E_0 is globally asymptotically stable for any time delay $\tau \ge 0$.

Theorem 4. The immune-absent equilibrium E_1 is globally asymptotically stable when $R_0 > 1$ and $R_1 < 1$.

Proof. Let (x(t), y(t), z(t)) be any positive solution of system (1) with initial conditions (2). Define a Lyapunov function as follow:

$$L_{2}(t) = \frac{1}{2} (x(t) - x_{1})^{2} + (1 + \frac{r}{kx_{max}}) x_{1} [y(t) - y_{1}$$
$$- y_{1} \ln \frac{y(t)}{y_{1}}] + \frac{\varepsilon e^{a\tau}}{c} z(t) + \varepsilon \int_{t}^{t-\tau} y(\varsigma) z(\varsigma) d\varsigma$$

here $\varepsilon = px_1(1 + r / kx_{max}) > 0$, Calculating the time derivative of $L_2(t)$ along the positive solution of model (1), we get

$$L_{2}'|_{(1)} = (x(t) - x_{1})[-(x(t) - x_{1})(d - r + \frac{r(x_{1} + x(t))}{x_{max}})$$

$$-(\frac{r}{x_{max}} + k)(x(t)y(t) - x_{1}y_{1})]$$

$$+ x_{1}(1 + \frac{r}{kx_{max}})(y(t) - y_{1})[kx(t) - kx_{1} - pz(t)]$$

$$+ \frac{\varepsilon e^{a\tau}}{c}[ce^{-a\tau}y(t - \tau)z(t - \tau) - bz(t)]$$

$$+ \varepsilon[y(t)z(t) - y(t - \tau)z(t - \tau)]$$

$$\leq -(x(t) - x_{1})^{2}(d - r + \frac{rx_{1}}{x_{max}})$$

$$-(x(t) - x_{0})^{2}[\frac{rx(t) + ry(t)}{x_{max}} + ky(t)]$$

$$- px_{1}(1 + \frac{r}{kx_{max}})(\frac{be^{a\tau}}{c} - y_{1})$$

We can easily find that $be^{a\tau} / c - y_1 > 0$ from $R_0 > 1$ and $R_1 < 1$. Thus $L_2 \le 0$, and $L_2 = 0$ if and only if $(x, y, z) = (x_1, y_1, 0)$. Then from the classical Lyapunov-LaSalle invariance principal [17] E_1 is globally asymptotically stable for any time delay $\tau \ge 0$.

From now on, we will analyze the stability of the infected equilibria E_2 of system (1) when $R_1 > 1$. Then the characteristic equation about E_2 is given by

$$\begin{vmatrix} -d + r - \frac{2rx_2}{x_{max}} - \frac{ry_2}{x_{max}} - ky_2 - s & -\frac{rx_2}{x_{max}} - kx_2 & 0 \\ ky_2 & -s & -py_2 \\ 0 & ce^{-at}e^{-st}z_2 & ce^{-at}e^{-st}y_2 - b - s \end{vmatrix}$$

= 0

that is,

$$P(s,\tau) - Q(s,\tau)e^{-s\tau} = 0.$$
(5)

where

$$\begin{split} P(s,\tau) &= s^{3} + A_{1}(\tau)s^{2} + A_{2}(\tau)s + A_{3}(\tau), Q(s,\tau) = B_{1}(\tau)s^{2} + B_{2}(\tau)s + B_{3}(\tau), \\ A_{1}(\tau) &= d - r + \frac{2rx_{2}}{x_{max}} + \frac{ry_{2}}{x_{max}} + ky_{2} + b, \\ A_{2}(\tau) &= bd - br + \frac{2rbx_{2}}{x_{max}} + \frac{rby_{2}}{x_{max}} + bky_{2} + k^{2}x_{2}y_{2} + \frac{rkx_{2}y_{2}}{x_{max}}, \\ A_{3}(\tau) &= bk^{2}x_{2}y_{2} + \frac{rkbx_{2}y_{2}}{x_{max}}, B_{1}(\tau) = ce^{-a\tau}y_{2}, \\ B_{2}(\tau) &= ce^{-a\tau}y_{2}(d - r + \frac{2rx_{2}}{x_{max}} + \frac{ry_{2}}{x_{max}} + ky_{2}) - pce^{-a\tau}y_{2}z_{2}, \\ B_{3}(\tau) &= kce^{-a\tau}y_{2}^{2}(kx_{2} + \frac{rx_{2}}{x_{max}}) - pce^{-a\tau}y_{2}z_{2}(d - r + \frac{2rx_{2}}{x_{max}} + \frac{ry_{2}}{x_{max}} + ky_{2}). \end{split}$$

Let us consider local stability of E_2 when $\tau = 0$, Eq.(5) reduces to

$$s^{3} + \gamma_{1}s^{2} + \gamma_{2}s + \gamma_{3} = 0$$
 (6)

Where

$$\begin{split} \gamma_1 &= d - r + \frac{2rx_2}{x_{max}} + \frac{ry_2}{x_{max}} + ky_2 = \frac{\lambda}{x_2} + \frac{rx_2}{x_{max}},\\ \gamma_2 &= k^2 x_2 y_2 + \frac{rkx_2 y_2}{x_{max}} + pcy_2 z_2,\\ \gamma_3 &= pcy_2 z_2 (d - r + \frac{2rx_2}{x_{max}} + \frac{ry_2}{x_{max}} + ky_2). \end{split}$$

It is clear that $\gamma_1 > 0$, $\gamma_2 > 0$ and $\gamma_3 > 0$. We also have

$$\gamma_1 \gamma_2 - \gamma_3 = (d - r + \frac{2rx_2}{x_{max}} + \frac{ry_2}{x_{max}} + ky_2)(k^2 x_2 y_2 + \frac{rkx_2 y_2}{x_{max}}) > 0$$

By Routh-Hurwitz Criterion, we have the following theorem.

Theorem 5. If $R_1 > 1$ and $\tau = 0$, the infected equilibrium E_2 is locally asymptotically stable.

In the following, using stability switch criteria, we try to investigate the local stability of infected equilibrium E_2 . we analyze the existence of purely imaginary roots $s = i\omega(\omega > 0)$ to (5). Eq.(5) takes the form of a third-degree exponential polynomial in *s* ,and all the coefficients of *P* and *Q* depend on τ . Beretta and Kuang [18] and Li and Ma [19]

(4)

established a geometrical criterion which gives the existence of purely imaginary of a characteristic equation with delay dependent coefficient. In order to apply this criterion, we need to verify the following properties for all $\tau \in [0, \tau_{max})$, where τ_{max} is the maximum value which E_2 exists.

(i)
$$P(0,\tau) - Q(0,\tau) \neq 0, \forall \tau \in R_{+0};$$

(ii) If $s = i\omega, \omega \in R$, then

 $P(i\omega,\tau) - Q(i\omega,\tau) \neq 0, \tau \in R_{+0};$

(iii) $\limsup\{|Q(s,\tau)/P(s,\tau)|:|s| \to \infty, Res \ge 0\} < 1$ for any τ ;

(iv) $F(\omega, \tau) = |P(i\omega, \tau)|^2 - |Q(i\omega, \tau)|^2$ for each τ has at most a finite number of real zeroes;

(v) Each positive root $\omega(\tau)$ of $F(\omega, \tau) = 0$ is continuous and differentiable in τ whenever it exists.

We can easily find

$$P(0,\tau) - Q(0,\tau) = A_3(\tau) - B_3(\tau) \neq 0$$

which implies that (i) is satisfied.

$$P(i\omega,\tau) - Q(i\omega,\tau) = [A_3(\tau) - B_3(\tau) + B_1(\tau)\omega^2 - A_1(\tau)\omega^2] + i\omega[A_2(\tau) - B_2(\tau) - \omega^2] \neq 0$$

which implies that (ii) is satisfied.

From (5) we can know that $\lim \{ | Q(s,\tau) / P(s,\tau) | : | s | \rightarrow \infty, Res \ge 0 \} = 0$ Therefore (iii) follows.

$$|P(i\omega,\tau)|^{2} = \omega^{6} + [-2A_{2}(\tau) + A_{1}^{2}(\tau)]\omega^{4} + [A_{2}^{2}(\tau) - 2A_{1}(\tau)A_{3}(\tau)]\omega^{2} + A_{3}^{2}(\tau)$$

$$|Q(i\omega,\tau)|^{2} = B_{1}^{2}(\tau)\omega^{4} + [B_{2}^{2}(\tau) - 2B_{1}(\tau)B_{3}(\tau)]\omega^{2} + B_{3}^{2}(\tau)$$

we get $F(\omega, \tau) = \omega^6 + \Omega_1 \omega^4 + \Omega_2 \omega^2 + \Omega_3$, here

$$\Omega_{1} = A_{1}^{2}(\tau) - 2A_{2}(\tau) - B_{1}^{2}(\tau), \\ \Omega_{2} = A_{2}^{2}(\tau) + 2B_{1}(\tau)B_{3}(\tau) - 2A_{1}(\tau)A_{3}(\tau) - B_{2}^{2}(\tau),$$

It is obvious that (iv) and (v) is satisfied.

Now, let $s = i\omega(\omega > 0)$ be a root of (5), separating the real and imaginary parts, we have the following

$$\begin{cases} A_3(\tau) - A_1(\tau)\omega^2 = B_2(\tau)\omega\sin(\omega\tau) + [B_3(\tau) - B_1(\tau)\omega^2]\cos(\omega\tau), \\ A_2(\tau)\omega - \omega^3 = -[B_3(\tau) - B_1(\tau)\omega^2]\sin(\omega\tau) + B_2(\tau)\omega\cos(\omega\tau) \end{cases}$$
(7)

Thus

$$\sin(\omega\tau) = \frac{[A_3(\tau) - A_1(\tau)\omega^2]B_2(\tau)\omega - [A_2(\tau)\omega - \omega^3][B_3(\tau) - B_1(\tau)\omega^2]}{[B_3(\tau) - B_1(\tau)\omega^2]^2 + B_2^2(\tau)\omega^2}$$
(8a)

$$\cos(\omega\tau) = \frac{[A_3(\tau) - A_1(\tau)\omega^2][B_3(\tau) - B_1(\tau)\omega^2] + B_2(\tau)\omega[A_2(\tau)\omega - \omega^3]}{[B_3(\tau) - B_1(\tau)\omega^2]^2 + B_2^2(\tau)\omega^2}$$

From (5), and applying the property (i), we have

$$\sin(\omega\tau) = -Im\frac{P(i\omega,\tau)}{Q(i\omega,\tau)}, \cos(\omega\tau) = Re\frac{P(i\omega,\tau)}{Q(i\omega,\tau)}.$$

which yields $P(i\omega,\tau)|^2 = |Q(i\omega,\tau)|^2$ i.e. $\omega(\tau)$ must be a positive root of:

$$F(\omega,\tau) := |P(i\omega,\tau)|^2 - |Q(i\omega,\tau)|^2$$
(9)

Assume that $U \subseteq R_{+0}$ is the set where $\omega(\tau)$ is a positive root of (9) and for τ not in U, $\omega(\tau)$ is not definite. Then for all $\tau \in U, \omega(\tau)$ satisfies that

$$F(\omega,\tau) = 0 \tag{10}$$

And we define the angle $\theta \in [0, 2\pi]$, as the solution of (8),

$$\sin \theta(\tau) = -Im \frac{P(i\omega,\tau)}{Q(i\omega,\tau)}, \cos \theta(\tau) = Re \frac{P(i\omega,\tau)}{Q(i\omega,\tau)}.$$

(11)

We can know that $\omega \tau = \theta(\tau) + 2n\pi, n \in N_0$ Hence we can define the maps : $\tau_n : U \to R_{+0}$ given by

$$\tau_n \coloneqq \frac{\theta(\tau) + 2n\pi}{\omega(\tau)}, n \in N_0, \tau \in U$$

where $\omega(\tau)$ is a positive root of (10). Let us introduce the functions $U \rightarrow R$ given by

$$S_n(\tau) \coloneqq \tau - \tau_n, n \in N_0, \tau \in U$$

that are continuous and differentiable in τ . Thus we give the following theorem following the line of literature [18] and [19].

Theorem 6. Assume that $\omega(\tau)$ is a positive root of (10) defined for $\tau \in U, U \subseteq R_{+0}$, and at some $\hat{\tau} \in U, S_n(\tau)$ for some $n \in N_0$, then a pair of simple conjugate pure imaginary roots $s = \pm i\omega$ exists at $\tau = \hat{\tau}$ which crosses the imaginary axis from left to right if $\delta(\hat{\tau}) > 0$ and crosses the imaginary axis from right to left if $\delta(\hat{\tau}) < 0$, here

$$\delta(\hat{\tau}) = sign\{\frac{dRes}{d\tau}|_{s=i\omega(\hat{\tau})}\} = sign\{F'_{\omega}(\tau),\tau\}\{\frac{dS_n(\tau)}{d\tau}|_{\tau=\tau}\}.$$

Applying Theorem 6 and the Hopf bifurcation theorem [20] for functional differential equation, we can conclude the following theorem.

Theorem 7. For system (1), then there is a value $\hat{\tau} \in U$, the infected equilibrium E_2 is locally asymptotically stable when $\tau \in [0, \hat{\tau})$, and unstable when τ staying in some right neighborhood of $\hat{\tau}$, Furthermore, when $\tau = \hat{\tau}$, system (1) undergoes a Hopf bifurcation to periodic solutions at E_2 .

4 Numerical Simulation

In this section, we will give numerical simulations of system (1). To investigate the dynamical behaviors of the system, we choose the parameters as those in papers [6, 12, 14, 15]. We obtain the following numerical results by using the software Mathematica 7.0.

First, considering $\lambda = 269, d = 0.05, a = 0.5, b = 0.3$, $r = 0.0001, x_{max} = 1000, k = 0.0001, p = 0.005, c = 0.08$, we can draw the graph of S_0 versus τ on U in Fig 1 which show two critical values τ , denote by τ_1 and τ_2 , and $\tau_1 \approx 0.21$. By using Theorem 6 and Theorem 7, we can know that, system (1) undergoes a Hopf bifurcation to periodic solutions at E_2 when $\tau = \tau_1^{\square}$. Fig 2 and Fig 3 confirm our results of Theorem 7. Fig 2 shows that the phase trajectories of system (1) with $\tau = 0.05$ converges to the positive equilibrium $E_2 = (529379, 3.84493, 58758)$ and Fig 3 shows that with $\tau = 0.3$ stability of system switch occurs.

To study the effects of the proliferation rate of CD4+ T-cells r, we choose a set of parameters as follow: $\lambda = 1000$, d = 0.1, a = 5, b = 0.1, xmax = 2000, k = 0.002, p = 0.1, c = 0.2, $\tau = 0.75$. When r = 1, the phase trajectories of system (1) converges to the immune-absent equilibrium $E_1 = (2500, 20, 0)$ as shown in Fig 4. When r = 0.7, the phase trajectories of system converges to the infected $E_2 = (264979, 21.2605, 299578)$ equilibrium shown in Fig 5. When r = 0.08 the system becomes unstable as shown in Fig 6. These results infer that the change of r infects stability of system, and it is necessary to consider the full Logistic proliferation of CD4+ T-cells into HIV infection model.

5 Conclusions

In this paper, we proposed and analyzed, both analytically and numerically, a HIV infection model. The results obtained shown that if $R_0 < 1$, the uninfected equilibrium E_0 of the system is globally asymptotically stable for any $\tau \ge 0$. Biologically, HIV/AIDS will be eradicated. We also presented that if $R_0 > 1$ and $R_1 < 1$, the immune-absent equilibrium E_2 is globally asymptotically stable. In addition, some conditions for Hopf bifurcation around infected equilibrium to occur are obtained by using the time delayed as a bifurcation parameter. Numerical simulations confirm our previous analysis and show that it is necessary to consider the full Logistic proliferation of CD4+ T-cells into HIV infection model. These results also prove the complexity of the immune state of AIDS.









Fig. 2. The figure depicts the infected equilibrium E_2 locally asymptotically stable.





Fig. 3. The figure depicts the infected equilibrium E_2 unstable.



Fig.4. The figure depicts the trajectories converges to the immune-absent equilibrium $E_1 = (2500, 20, 0)$ with r = 1.



Fig.5. The figure depicts the trajectories converges to the equilibrium $E_2 = (264979, 21.2605, 299578)$ with r = 0.7.



Fig.6. The figure depicts periodic oscillations of the trajectories emerge with r = 0.08.

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