Global analysis of a delay virus dynamics model with Beddington-DeAngelis incidence rate and CTL immune response

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***Abstract*—In this paper, an HIV-1 infection model with Beddington-DeAngelis infection rate and CTL immune response is investaged. We derive the basic reproduction number R_0 for the viral infection model. By constructing suitable Lyapunov functionals and using LaSalle invariant principle for the delay differential equations, we find when $R_0 \le 1$, the infection-free equilibrium is globally asymptotically stable. And if the CTL immune reproductive number $R_1 \le 1$, the immune-free equilibrium and the endemic equilibrium are globally asymptotically stable.**

***Keywords*—Beddington-DeAngelis; CTL immune response ; Lyapunov functional; LaSalle invariant principle;Global stabiliy**

I. Introduction

In recent years, the dynamics of HIV-1 infection model have been studied due to such models can be helpful in the control of endemic diseases and provide insights into the dynamics of viral load [1-8]. The analysis of these dynamic behaviors may play a significant role in the development of a better understanding of diseases and various drug therapy strategies against them.

A basic viral infection model [9] has been widely used for investigating the dynamics of virus infections, which has the following forms:

$$\begin{cases} \dot{x} = \lambda - dx - \beta xv \\ \dot{y} = \beta xv - ay \\ \dot{v} = ky - uv \end{cases} \tag{1.1}$$

where susceptible cells $x(t)$ are produced at a constant rate λ, die at a density-dependent rate dx, and become infected with a rate βxv; infected cells $y(t)$ are produced at a rate βxv and die at a rate ay; free virus particles $v(t)$ are released from infected cells at a rate ky and die at a rate uv.

In reality, Cytotoxic T Lymphocytes (CTL) immune response is universal and necessary to eliminate or control the disease after the infection. Indeed, it is believed that CTL cells are the main host immune factor that determines virus load [10]. Therefore, the dynamics of virus infection with CTL response has recently drawn much attention of researchers in the related areas [11-16], paper [22] gave the following immune model

$$\begin{cases} \dot{x} = \lambda - dx - \beta vx \\ \dot{y} = \beta vx - ay - pyz \\ \dot{v} = ky - \mu v \\ \dot{z} = cyz - bz \end{cases} \tag{1.2}$$

where infected cells $y(t)$ are killed at a rate pyz by the CTL immune response and the virus-specific CTL cells proliferated at a rate cyz by contact with infected cells, and die at a rate bz.The variables and other parameters have same biological meanings as in the model (1.1).

Besides the bilinear incidence rate βvx used in model (1.1) and (1.2), the Beddington-DeAngelis functional reasponse $\frac{\beta xv}{1+mx+nv}$ was often used for virus infection model [17,18]. Xia Wang [23] and Youde Tao construct the following model:

$$\begin{cases} \dot{x} = \lambda - dx - \frac{\beta xv}{1+mx+nv} \\ \dot{y} = \frac{\beta xv}{1+mx+nv} - ay - pyz \\ \dot{v} = ky - uv \\ \dot{z} = cyz - bz \end{cases} \tag{1.3}$$

where x, y, v, z, have the same biological meanings as in the model (1.2).

Recently, it has been realized that time delay should be taken into consideration [19-21]. Because there may be a lag between the time for target cells to be contacted by the virus particles and the time for the contacted cells to become actively affected. That is, the contacting virions need time to enter cells. Then G. Huang, W. Ma [23] propose the following model:

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$$\begin{cases} x'(t) = \lambda - dx(t) - \dfrac{\beta x(t)v(t)}{1+ax(t)+bv(t)} \\ y'(t) = e^{-p\tau}\dfrac{\beta x(t-\tau)v(t-\tau)}{1+ax(t-\tau)+bv(t-\tau)} - py(t) \\ v'(t) = ky(t) - uv(t) \end{cases} \quad (1.4)$$

where the state variable and constant have same meaning as model (1.3), and τ represents the time delay.

Based on above discussion, we propose the following model:

$$\begin{cases} \dot{x}(t) = \lambda - dx(t) - \dfrac{\beta x(t)v(t)}{1+mx(t)+nv(t)} \\ \dot{y}(t) = e^{-a\tau}\dfrac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)} - ay(t) - py(t)z(t) \\ \dot{v}(t) = ky(t) - uv(t) \\ \dot{z}(t) = cy(t)z(t) - bz(t) \end{cases} \quad (1.5)$$

where the state variable and constant have same meaning as model (1.4).

This paper is organized as follows. In Section II, we will give basic reproductive number and two equilibriums. Then we prove that the three equilibriums are globally asymptotically stable in section III. At last, this paper ends with a brief conclusion in Section IV.

II. BASIC REPRODUCTIVE NUMBER AND EQUILIBRIUM

A direct computation shows that the basic reproductive number of model (1.5) is $R_0 = e^{-a\tau}\beta k / au(d+m\lambda)$. It shows there exists an infection-free equilibrium $E_0 = (x_0, 0, 0, 0)$, and $x_0 = \lambda / d$.

If $R_0 > 1$, in the absence of an immune response, there exists an immune-free equilibrium $E_1 = (x_1, y_1, v_1, 0)$,where

$$x_1 = \frac{aue^{a\tau} + n\lambda k}{k\beta + ndk - aume^{a\tau}},$$

$$y_1 = \frac{\lambda k\beta e^{-a\tau}(1-\frac{1}{R_0})}{a(k\beta + ndk - aume^{a\tau})},$$

$$v_1 = \frac{\lambda k^2\beta e^{-a\tau}(1-\frac{1}{R_0})}{au(k\beta + ndk - aume^{a\tau})}.$$

Note that $R_0 > 1$ means $k\beta > aume^{a\tau}$ which can make $x_1 > 0$, so y_1 and v_1 can also be positive with $R_0 > 1$.

As pointed in [24], if we assume that immune responses can potentially develop, the conditions $cy_1 > b$, we introduce an immune response reproduction number

$$R_1 = \frac{cy_1}{b} = \frac{c}{b}\frac{\lambda k\beta e^{-a\tau} - \lambda au(d+m\lambda)}{a(k\beta + ndk - aume^{a\tau})}$$

When $R_1 > 1$, there exists an endemic equilibrium $E_2 = (x_2, y_2, v_2, z_2)$, where

$$x_2 = \frac{\delta + \sqrt{\delta^2 + 4dmuc\lambda kb(n+1)}}{2mduc},$$
$$(\delta = m\lambda uc - \beta kb - duc - dnkb)$$

$$y_2 = \frac{b}{c}, \qquad v_2 = \frac{kb}{uc}, \qquad z_2 = \frac{e^{-a\tau}c(\lambda - dx_2) - ab}{pb}.$$

$z_2 = \dfrac{e^{-a\tau}c(\lambda - dx_2) - ab}{pb} > 0$ is equivalent to $e^{-a\tau}c(\lambda - dx_2) - ab$ >0 which can be proved by $c(\lambda k\beta e^{-a\tau} - \lambda au(d+m\lambda))$ > $b(a(k\beta + ndk - aume^{a\tau}))$ that is $R_1 > 1$.

III. STABILITY OF EQUILIBRIUMS

Theorem 3.1. If $R_0 \le 1$, the infection-free equilibrium point E_0 is global asymptotically stable for any delay $\tau \ge 0$.

Proof. Choosing Lyapunov function $W_0(t)$ as follows

$$W_0(t) = \frac{1}{1+mx_0}[x(t) - x_0 - x_0\ln\frac{x(t)}{x_0}] + e^{a\tau}y(t) + e^{a\tau}\frac{a}{k}v(t)$$
$$+ e^{a\tau}\frac{p}{c}z(t) + \int_0^\tau \frac{\beta x(t-\theta)v(t-\theta)}{1+mx(t-\theta)+nv(t-\theta)}d\theta$$

where $x_0 = \lambda / d$. We calculating the derivative of $W_0(t)$ along the positive solutions of the system (1.5) , and note that $\lambda = dx_0$, we obtain

$$\begin{aligned}\dot{W}_0(t) &= \frac{1}{1+mx_0}[1-\frac{x_0}{x(t)}]\dot{x}(t) + e^{a\tau}\dot{y}(t) + e^{a\tau}\frac{a}{k}\dot{v}(t) + e^{a\tau}\frac{p}{c}\dot{z}(t) \\ &\quad + \frac{\beta x(t)v(t)}{1+mx(t)+nv(t)} - \frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)} \\ &= \frac{1}{1+mx_0}[1-\frac{x_0}{x(t)}](\lambda - dx(t) - \frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}] \\ &\quad + e^{a\tau}(e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)} - ay(t) - py(t)z(t)) \\ &\quad + e^{a\tau}\frac{a}{k}[ky(t) - uv(t)] + e^{a\tau}\frac{p}{c}[cy(t)z(t) - bz(t)] \\ &\quad + \frac{\beta x(t)v(t)}{1+mx(t)+nv(t)} - \frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\end{aligned}$$

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$$= -\frac{d(x_0 - x(t))^2}{x(t)(1+mx_0)} + [-\frac{\beta x(t)v(t)}{(1+mx_0)(1+mx(t)+nv(t))}$$
$$+\frac{1}{1+mx_0}\frac{\beta x_0 v(t)}{1+mx(t)+nv(t)} + \frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}]$$
$$-e^{a\tau}\frac{au}{k}v(t) - e^{a\tau}\frac{pb}{c}z(t)$$
$$= -\frac{d(x_0 - x(t))^2}{x(t)(1+mx_0)} + \frac{1+mx(t)}{1+mx_0}\frac{\beta x_0 v(t)}{1+mx(t)+nv(t)}.$$
$$-e^{a\tau}\frac{au}{k}v(t) - e^{a\tau}\frac{pb}{c}z(t)$$
$$\le -\frac{d(x_0 - x(t))^2}{x(t)(1+mx_0)} + \frac{\beta x_0 v(t)}{1+mx_0} - e^{a\tau}\frac{au}{k}v(t) - e^{a\tau}\frac{pb}{c}z(t)$$
$$= -\frac{d(x_0 - x(t))^2}{x(t)(1+mx_0)} + e^{a\tau}\frac{au}{k}(R_0 - 1)v(t) - e^{a\tau}\frac{pb}{c}z(t)$$

Obviously, when $R_0 < 1$, we have $\dot{W}_0(x,y,z,v) \le 0$ for all $x,y,z,v > 0$. Therefore, the infection-free equilibrium E_0 is stable. $\dot{W}_0(x,y,z,v) = 0$ if and only if $x = x_0, z = 0\ v = 0$. Let M be the largest invariant set of $\{(x,y,z,v) \in R_+^4 : \dot{W}_0 = 0\}$, then from the second equation of (1.5), we obtain $y = 0$, which shows $M = \{E_0\}$, so we get the global asymptotical stability of E_0 by LaSalle invariance principle. If $R_0 = 1$, we obtain $\dot{W}_0(x,y,z,v) = 0$ if and only if $x = x_0, z = 0$, Let M be the largest invariant set of $\{(x,y,z,v) \in R_+^4 : \dot{W}_0 = 0\}$, then from the second and third equations, we obtain $y = v = 0$, so by LaSelle invariance principle, we can know $R_0 = 1$ can also ensure the globally asymptotical stability of E_0.

Theorem 3.2. If $R_1 \le 1$, the immune-free equilibrium point E_1 is global asymptotically stable.

Proof. Define a Lyapunov function W_1 as follows

$$W_1(t) = e^{-a\tau}[x(t) - x_1 - \int_{x_1}^{x(t)} \frac{1+m\theta+nv_1}{1+mx_1+nv_1}\frac{x_1}{\theta}d\theta] + [y(t) - y_1 - y_1\ln\frac{y(t)}{y_1}]$$
$$+\frac{a}{k}[v(t) - v_1 - v_1\ln\frac{v(t)}{v_1}] + \frac{p}{c}z(t)$$
$$+ay_1\int_0^{\tau} g(\frac{e^{-a\tau}\beta x(t-\theta)v(t-\theta)}{ay_1(1+mx(t-\theta)+nv(t-\theta))})d\theta$$

where $g(x) = x - 1 - \ln x$. We calculating the derivative of W_1 along the positive solutions of the system (1.5) .

$$\dot{W}_1(t) = e^{-a\tau}[\dot{x}(t) - \frac{1+mx(t)+nv_1}{1+mx_1+nv_1}\frac{x_1}{x(t)}\dot{x}(t)] + [\dot{y}(t) - \frac{y_1}{y}\dot{y}(t)]$$
$$+\frac{a}{k}[\dot{v}(t) - \frac{v_1}{v}\dot{v}(t)] + \frac{p}{c}\dot{z}(t) + e^{-a\tau}\frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}$$
$$-e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)} + ay_1\ln\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx(t)+v(t)}{x(t)v(t)}$$
$$= e^{-a\tau}[1 - \frac{1+mx(t)+nv_1}{1+mx_1+nv_1}\frac{x_1}{x(t)}][\lambda - dx(t) - \frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}]$$
$$+(1-\frac{y_1}{y})[e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)} - ay(t) - py(t)z(t)]$$
$$+\frac{a}{k}(1-\frac{v_1}{v})[ky(t) - uv(t)] + \frac{p}{c}[cy(t)z(t) - bz(t)]$$
$$+e^{-a\tau}\frac{\beta x(t)v(t)}{1+mx(t)+nv(t)} - e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}$$
$$+ay_1\ln\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx(t)+nv(t)}{x(t)v(t)}$$

Note that

$$\lambda = dx_1 + e^{a\tau}ay_1$$
$$\frac{\beta x_1 v_1}{1+mx_1+nv_1} = e^{a\tau}ay_1$$
$$\frac{u}{k} = \frac{y_1}{v_1}$$

$$\dot{W}_1(t) = -\frac{de^{-a\tau}(x(t)-x_1)^2(1+nv_1)}{x(t)(1+mx_1+nv_1)}$$
$$+ay_1\ln\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx(t)+nv(t)}{x(t)v(t)}$$
$$+ay_1[3 - \frac{x_1}{x(t)}\frac{1+mx(t)+nv_1}{1+mx_1+nv_1} - \frac{y_1}{y(t)}\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}$$
$$\frac{1+mx_1+nv_1}{x_1v_1} - \frac{v_1}{v(t)}\frac{y(t)}{y_1}] + ay_1[-\frac{v(t)}{v_1} + \frac{v(t)}{v_1}\frac{1+mx(t)+nv_1}{1+mx(t)+nv(t)}]$$
$$+pz(t)(y_1 - \frac{b}{c})$$
$$= -\frac{de^{-a\tau}(x(t)-x_1)^2(1+nv_1)}{x(t)(1+mx_1+nv_1)} - ay_1[\frac{x_1}{x(t)}\frac{1+mx(t)+nv_1}{1+mx_1+nv_1} - 1$$
$$-\ln\frac{x_1}{x(t)}\frac{1+mx(t)+nv_1}{1+mx_1+nv_1}] - ay_1(\frac{y_1}{y(t)}\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx_1+nv_1}{x_1v_1}$$
$$-1 - \ln\frac{y_1}{y(t)}\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx_1+nv_1}{x_1v_1}] - ay_1[\frac{v_1}{v(t)}\frac{y(t)}{y_1} - 1$$
$$-\ln\frac{v_1}{v(t)}\frac{y(t)}{y_1}] - ay_1[\frac{1+mx(t)+nv(t)}{1+mx(t)+nv_1} - 1 - \ln\frac{1+mx(t)+nv(t)}{1+mx(t)+nv_1}]$$
$$+ay_1[-1 - \frac{v(t)}{v_1} + \frac{v(t)}{v_1}\frac{1+mx(t)+nv_1}{1+mx(t)+nv(t)} + \frac{1+mx(t)+nv(t)}{1+mx(t)+nv_1}]$$
$$+pz(t)(y_1 - \frac{b}{c})$$

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$$= -\frac{de^{-a\tau}(x(t)-x_1)^2(1+nv_1)}{x(t)(1+mx_1+nv_1)} - ay_1 g\left(\frac{x_1}{x(t)}\frac{1+mx(t)+nv_1}{1+mx_1+nv_1}\right)$$
$$-ay_1 g\left(\frac{y_1}{y(t)}\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx_1+nv_1}{x_1v_1}\right)$$
$$-ay_1 g\left(\frac{v_1}{v(t)}\frac{y(t)}{y_1}\right) - ay_1 g\left(\frac{1+mx(t)+nv(t)}{1+mx(t)+nv_1}\right)$$
$$-\frac{n(1+mx(t))(v(t)-v_1)^2}{v_1(1+mx(t)+nv_1)(1+mx(t)+nv(t))} + pz(t)\frac{b}{c}(R_1-1)$$

Since $g(x)\ge 0$ for all $x\ge 0$, if $R_1<1$, then $\dot{W}_1(x,y,v,z)\le 0$. And $\dot{W}_1(x,y,v,z)=0$ if and only if $x=x_1, y=y_1, v=v_1, z=0$, so E_1 is globally asymptotically stable. When $R_1=1$, we have $\dot{W}_1(x,y,v,z)=0$ if and only if $x=x_1, y=y_1, v=v_1$, from the second equation of (1.5), it is easy to know the largest invariant set of $\{(x,y,z,v)\in R_+^4 : \dot{W}_1=0\}$ is E_1, so by LaSelle invariance principle, we can know $R_1=1$ can also ensure the globally asymptotical stability of E_1.

Theorem 3.3. The endemic equilibrium point E_2 is global asymptotically stable.

Proof. We construct a Lyapunov function as follows

$$W_2(t)=e^{-a\tau}[x(t)-x_2-\int_{x_2}^{x(t)}\frac{1+m\theta+nv_2}{1+mx_2+nv_2}\frac{x_2}{\theta}d\theta]+[y(t)-y_2-y_2\ln\frac{y(t)}{y_2}]$$
$$+\frac{a+pz_2}{k}[v(t)-v_2-v_2\ln\frac{v(t)}{v_2}]+\frac{p}{c}[z(t)-z_2-z_2\ln\frac{z(t)}{z_2}]$$
$$+(ay_2+py_2z_2)\int_0^{\tau} g\left(\frac{e^{-a\tau}\beta x(t-\theta)v(t-\theta)}{(ay_2+py_2z_2)(1+mx(t-\theta)+nv(t-\theta)}\right)d\theta$$

where $g(x)=x-1-\ln x, x>0$. By calculating the derivative of $W_2(x,y,v,z)$ along the positive solutions of the system (1.5)

$$\dot{W}_2(t)=e^{-a\tau}[\dot{x}(t)-\frac{1+mx(t)+nv_2}{1+mx_2+nv_2}\frac{x_2}{x(t)}\dot{x}(t)]+[\dot{y}(t)-\frac{y_2}{y}\dot{y}(t)]$$
$$+\frac{a+pz_2}{k}[\dot{v}(t)-\frac{v_2}{v}\dot{v}(t)]+\frac{p}{c}[\dot{z}(t)-\frac{z_2}{z(t)}\dot{z}(t)]$$
$$+e^{-a\tau}\frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}-e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}$$
$$+(ay_2+py_2z_2)\ln\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx(t)+nv(t)}{x(t)v(t)}$$
$$=e^{-a\tau}[1-\frac{1+mx(t)+nv_2}{1+mx_2+nv_2}\frac{x_2}{x(t)}][\lambda-dx(t)-\frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}]$$
$$+(1-\frac{y_2}{y(t)})[e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}-ay-py(t)z(t)]$$
$$+\frac{a+pz_2}{k}(1-\frac{v_2}{v(t)})[ky(t)-uv(t)]$$
$$+\frac{p}{c}(1-\frac{z_2}{z(t)})[cy(t)z(t)-bz(t)]$$
$$+e^{-a\tau}\frac{\beta x(t)v(t)}{1+mx(t)+nv(t)}-e^{-a\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}$$
$$+(ay_2+py_2z_2)\ln\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx(t)+nv(t)}{x(t)v(t)}$$

Note that,

$$\lambda=dx_2+e^{a\tau}(ay_2+py_2z_2)$$
$$\frac{\beta x_2v_2}{1+mx_2+nv_2}=e^{a\tau}(ay_2+py_2z_2)$$
$$\frac{u}{k}=\frac{y_2}{v_2}$$
$$y_2=\frac{b}{c}$$

$$\dot{W}_2(t)=-\frac{de^{-a\tau}(1+nv_2)(x_2-x(t))^2}{x(t)(1+mx_2+nv_2)}+(ay_2+py_2z_2)[-\frac{v(t)}{v_2}+$$
$$\frac{v(t)}{v_2}\frac{1+mx(t)+nv_2}{1+mx(t)+nv(t)}]+(ay_2+py_2z_2)[3-\frac{1+mx(t)+nv_2}{1+mx_2+nv_2}\frac{x_2}{x(t)}$$
$$-\frac{v_2}{v(t)}\frac{y(t)}{y_2}-\frac{y_2}{y(t)}\frac{x(t-\tau)v(t-\tau)}{x_2v_2}\frac{1+mx_2+nv_2}{1+mx(t-\tau)+nv(t-\tau)}]+$$
$$(ay_2+py_2z_2)\ln\frac{x(t-\tau)v(t-\tau)}{1+mx(t-\tau)+nv(t-\tau)}\frac{1+mx(t)+nv(t)}{x(t)v(t)}$$
$$=-\frac{de^{-a\tau}(1+nv_2)(x_2-x(t))^2}{x(t)(1+mx_2+nv_2)}-(ay_2+py_2z_2)[\frac{1+mx(t)+nv_2}{1+mx_2+nv_2}\frac{x_2}{x(t)}-1$$
$$-\ln\frac{1+mx(t)+nv_2}{1+mx_2+nv_2}\frac{x_2}{x(t)}]-(ay_2+py_2z_2)[\frac{y_2}{y(t)}\frac{x(t-\tau)v(t-\tau)}{x_2v_2}$$
$$\frac{1+mx_2+nv_2}{1+mx(t)+n(t)}-1-\ln\frac{y_2}{y(t)}\frac{x(t-\tau)v(t-\tau)}{x_2v_2}\frac{1+mx_2+nv_2}{1+mx(t-\tau)+nv(t-\tau)}]$$
$$-(ay_2+py_2z_2)[\frac{1+mx(t)+nv(t)}{1+mx(t)+nv_2}-1-\ln\frac{1+mx(t)+nv(t)}{1+mx(t)+nv_2}]$$
$$-(ay_2+py_2z_2)g[\frac{v_2}{v(t)}\frac{y(t)}{y_2}]$$
$$-\frac{n(1+mx(t))(v(t)-v_2)^2}{v_2(1+mx(t)+nv(t))(1+mx(t)+nv_2)}$$
$$=-\frac{de^{-a\tau}(1+nv_2)(x_2-x(t))^2}{x(t)(1+mx_2+nv_2)}-[ay_2+py_2z_2)g[\frac{1+mx(t)+nv_2}{1+mx_2+nv_2}\frac{x_2}{x(t)}]$$
$$-(ay_2+py_2z_2)g[\frac{y_2}{y(t)}\frac{x(t-\tau)v(t-\tau)}{x_2v_2}\frac{1+mx_2+nv_2}{1+mx(t)+n(t)}]$$
$$-(ay_2+py_2z_2)g[\frac{1+mx(t)+nv(t)}{1+mx(t)+nv_2}]$$
$$-(ay_2+py_2z_2)g[\frac{v_2}{v(t)}\frac{y(t)}{y_2}]$$
$$-\frac{n(1+mx(t))(v(t)-v_2)^2}{v_2(1+mx(t)+nv(t))(1+mx(t)+nv_2)}$$

Since $g(x)\ge 0$ for all $x>0$, we have that $\dot{W}_2(x,y,z,v)\le 0$ for all $x,y,z,v>0$. Therefore, the endemic equilibrium E_2 is stable. $\dot{W}_2(x,y,v,z)=0$ if and only if

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$x = x_2, y = y_2, v = v_2$. Let M be the largest invariant set of $\{(x, y, z, v) \in R_+^4 : \dot{W}_2 = 0\}$, then from the forth equation of (1.5), we obtain $z = z_2$, by LaSelle invariance principle, the endemic equilibrium E_2 is also globally asymptotically stable.

IV CONCLUSIONS

In this paper, based on Beddington-DeAngelis infection rate and CTL immune response, we have discussed a virus infection model with time delay. The stable analysis of the given model is carried out. While $R_0 \le 1$, the infection-free equilibrium E_0 is globally asymptotically stable for any $\tau \ge 0$. By constructing suitable Lyapunov function and using LaSalle invariance principle, we have that when $R_1 \le 1$, the immune-free equilibrium E_1 is also globally asymptotically stable, when $R_1 > 1$, we also prove the global stability of the endemic equilibrium E_2 .

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