Global Analysis of a General HBV Infection Model

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Abstract—Mathematical models have been used to understand the factors that govern infectious disease progression in viral infections. Two basic models of within-host viral infection, proposed by Nowak et. al. and Perelson et. al. respectively, have been widely used in the studies of HBV and HIV infections. However, the loss term of viral particles when it enters the target cells are both ignored by these two models. Leenheer and Smith provided a general virus dynamic model with the loss term of viral particles, which make the above two basic models only be special cases. But the basic reproduction numbers of all above models are proportional to the number of total cells of the host’s organ prior to the infection (when used for HBV infection) or the normal target cell level (when used for HIV infection). On the other hand, the global asymptotically stable condition of the endemic equilibrium about Leenheer and Smith’s model is related to the initial value of the growth function of uninfected cell. In this paper, we formulate an amended Leenheer and Smith’s model with standard incidence, the basic reproduction numbers were no more dependent on the number of total cells of the host’s organ. If the basic reproduction number of virus is less than one, the infection-free equilibrium is globally asymptotically stable and the virus is cleared; if the basic reproduction number is greater than one, then the virus persist in the host, and solutions approach either an endemic equilibrium or a periodic orbit. The periodic orbit can be ruled out in some cases but not in general. The globally asymptotically stable condition of the endemic equilibrium is only determined by the model parameters.

I. INTRODUCTION

The infection with Hepatitis B virus (HBV) is a major health problem in the world. The WHO has reported that more than 2 billion people worldwide has been infected by HBV. There are over 350 millions who are chronically infected with HBV[1], 25-40% of these chronic infection carriers will die from liver cirrhosis or primary hepatocellular carcinoma[2].

Using mathematical models to enhance our understanding of the dynamics of chronic viral infections has been proved fruitful([3], [4], [5]), and using mathematical models to interpret experimental and clinical results has made a significant contribution to the fields of anti- HIV, HBV and or HCV infections([6], [7], [8]). Mathematical analysis of the HBV dynamics not only provide important quantitative insights into the pathogenesis, but also lead to design treatment strategies which would more effectively bring the infection under control[9].

The basic models of within-host viral infection, proposed by Nowak et. al. [2] and Perelson et. al.[10] have been widely used in the studies of HBV and HIV infections. The basic models, describing the dynamics of interaction between uninfected cells \(x(t)\), infected cells \(y(t)\) and free virus \(v(t)\), take the form of

\[
\begin{aligned}
\dot{x} &= f(x) - \beta vx \\
\dot{y} &= \beta vx - ay \\
\dot{v} &= ky - uv
\end{aligned}
\]  

(1)

where the functional form of \(f\) is defined differently by:

1. Nowak and May[2]: \(f(x) = f_1(x) = \lambda - dx\).
2. Perelson and Nelson[10]: \(f(x) = f_2(x) = \lambda - dx + px(1 - \frac{x}{x_{max}})\).

Uninfected cells are assumed to be produced at the constant rate \(\lambda\), die at the rate of \(dx\) and become infected at the rate of \(\beta vx\). Infected cells are thus produced at the rate of \(\beta vx\) and die at the rate of \(ay\). Free virions are generated from infected cells at the rate of \(ky\) and decay at the rate of \(uv\). Parameter \(p\) is the maximum proliferation rate of uninfected cells and \(x_{max}\) is the maximum capacity of host’s organ cells.

Obviously, as pointed by Leenheer and Smith[11], both Perelson et. al. and Nowak et. al. ignored that the loss term \(\beta vx\) should appear in the \(v\) equation, i.e.,

\[
\dot{v} = ky - uv - \beta vx
\]  

(2)

representing the loss of free virus particles when they enter the target. Leenheer and Smith discussed a more general model as follows:

\[
\begin{aligned}
\dot{x} &= f(x) - \beta vx \\
\dot{y} &= \beta vx - ay \\
\dot{v} &= ky - uv - \iota \beta vx
\end{aligned}
\]  

(3)

which \(f(x)\) is a smooth function satisfying:

\[
\begin{aligned}
f(x) &> 0, 0 \leq x < \bar{x}, \\
f(\bar{x}) = 0, f'(\bar{x}) < 0, \\
f(x) &< 0, x > \bar{x}
\end{aligned}
\]  

(4)

where \(\bar{x}\) represents the number of total cells of the host’s organ prior to the infection when it is used for HBV infection or normal target cell level when it is used for HIV infection. Here \(i = 0\) means ignoring the loss of viral particle, \(i = 1\) otherwise. Thus \(f_1(x) = \lambda - dx\) and \(f_2(x) = \lambda - dx + px(1 - x/x_{max})\) are the special cases. Leenheer and Smith also gave the stable analysis of the model (3) and oscillation behaviors when \(f(x) = f_2(x)\). Obviously the rate of infection in model (3) is bilinear in the virus \(v\) and the uninfected target cells \(x\), the basic reproduction number of models (3) is given by \(R_0 = \bar{x}(\beta k - \iota a)/\iota a\), since \(R_0\) is proportional to \(\bar{x}\), which implies that an individual with a smaller organ or smaller target cell level may be more resistant to virus infection. Hence, it...
may not be reasonable for the basic mathematical models to
describe virus infection in a sense. Paper[12] pointed out that
actual incidence rates are probably not strictly linear, then, they
proposed a HIV model with saturated mass action $\beta xv/(1 +
\alpha v)$ under the assumption that a less than linear response in$v$
could occur due to saturation at high virus concentration.
Paper [13], [14] employed a standard incidence function to
describe the hepatitis B virus infection as follows:

Paper[13], [14] employed a standard incidence function to
which also make the basic reproduction number of Model (5)
asymptotical stability of the endemic equilibrium was given
solutions approach either an endemic equilibrium or a periodic
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may not be reasonable for the basic mathematical models to

\begin{align}
\dot{x} &= \lambda - dx - \frac{\beta xv}{x + y} \\
\dot{y} &= \frac{\beta xv}{x + y} - ay \\
\dot{v} &= ky - uv.
\end{align}

The basic reproduction number of model (5) is $R_0 = \beta k/au$
which is independent of the number of total cells of human
This is proved if if $R_0 < 1$, then the infection-free steady state is globally asymptotically stable[13]. If $R_0 >
1$, then the endemic steady state is globally asymptotically stable[14].

Mover, the other amended mother model based on Perelson
and Nelson's model was discussed by Yu Ji[15] as follows:

\begin{align}
\dot{x} &= \lambda - dx + px(1 - \frac{x}{x_{max}}) - \frac{\beta xv}{x + y} \\
\dot{y} &= \frac{\beta xv}{x + y} - ay \\
\dot{v} &= ky - uv.
\end{align}

The basic reproduction number of model (6) is $R_0 = \beta k/au$
which is also independent of the number of human liver cells.
The result showed that if $R_0 < 1$, then the infection-free equilibrium is globally asymptotically stable and the virus is
cleared; if $R_0 > 1$, then the virus persists in the host, and
solutions approach either an endemic equilibrium or a periodic
orbit. But the local stability which is needed for globally asymptotical stability of the endemic equilibrium was given
with another additional condition $a_1 a_2 > a_3$.

Obviously, both model (5) and model (6) all ignored the loss
term of viral particles. In this paper, we formulate a general
model as follows:

\begin{align}
\dot{x} &= f(x) - \frac{\beta xv}{x + y} \\
\dot{y} &= \frac{\beta xv}{x + y} - ay \\
\dot{v} &= ky - uv - i \frac{\beta xv}{x + y}.
\end{align}

Here $f(x)$ satisfy the condition (4), and i = 0 means we ignore
the loss of viral particles when it enters target cell, otherwise,
we choose i = 1. Thus model (5) and model (6) are only
two special cases of our model (7) when i = 0. The basic
reproduction number of our model is $R_0 = \beta(k - ia)/au$,
which also make the basic reproduction number of Model (5)
and (6) the special case when i = 0. If $R_0 \geq 1$, our model
has two steady states:

$$E_0 = (\bar{x}, 0, 0), E_\epsilon = (x_\epsilon, y_\epsilon, v_\epsilon).$$

where $f(\bar{x})=0, v_\epsilon = \frac{k - ia}{u} y_\epsilon, y_\epsilon = \frac{f(x_\epsilon)}{a}$, and $x_\epsilon$ satisfy

$$f(x_\epsilon) - a(R_0 - 1)x_\epsilon = 0. \quad (9)$$

Since $f(x)$ satisfy condition (4), we know that there must exist
$x_\epsilon \in (0, \bar{x})$ which satisfy (9). These two steady states represent
the infection-free steady state and the endemic steady state
respectively. Note the biological meaning, $E_\epsilon$ does not exist
if $R_0 < 1$, and it becomes $E_0$ when $R_0 = 1$. It is easy to see
that $x_\epsilon < \bar{x}$ when $R_0 > 1$. This means the infection of
the virus will reduce the total number of uninfected cells in host.

The main purpose of this paper is to discuss the globally
asymptotical stability of $E_0$ and $E_\epsilon$ for both i = 0, i = 1.

For the endemic equilibrium $E_\epsilon$, when i = 0, $f(x) = f_2(x)$, the
local stable condition $a_1 a_2 > a_3$ was proved without any
additional condition. We also consider the oscillation behaviors of
system (7), and give some parameter condition of oscillation
behaviors when $f(x) = f_2(x)$, for both i = 0, i = 1. Simulations
were also given to test the theoretical conclusion.

II. STABILITY ANALYSIS OF THE INFECTION-FREE STEADY
STATE

Before the analysis of the stability of the equilibria, we
will show that the solution of model (7) always positive and
bounded. The proof of positive solution is easy, the bound
proof is similar to lemma 3.1 in [11], we only describe the
result as follows:

**Theorem 2.1:** There is an $M > 0$ such that all solutions satisfy

$$x(t) < M, y(t) < M, v(t) < M \text{ for all large } t.$$ 

Define

$$D = \{(x, y, v) \in R^3_+ : 0 < x(t) \leq \bar{x}, 0 \leq y(t), v(t) \leq M\}.$$ 

If $x(0) \leq \bar{x}$, from the first equation of model (7), we have

$$x(t) \leq \bar{x} \text{ when } t > 0.$$ 

It is easy to see that $D$ is a positively invariant region for model (7).

**Theorem 2.2:** the disease-free state $E_0$ is globally asymptotically stable when $R_0 < 1$, and becomes unstable when

$R_0 > 1$.

**Proof:** First, we will analyze the locally asymptotical stability of $E_0$. The Jacobian matrix of the vector field corresponding to model (7) is

$$J = \begin{pmatrix}
\frac{f'(x) - \beta y v}{(x + y)^2} & \frac{\beta x v}{(x + y)^2} & -\frac{\beta x}{x + y} \\
\frac{\beta y v}{(x + y)^2} & -\frac{\beta x v}{(x + y)^2} & \frac{\beta x}{x + y} \\
-k + i \frac{\beta x v}{(x + y)^2} & -u - i \frac{\beta x v}{x + y}
\end{pmatrix}.$$ 

The above Jacobian matrix evaluated at $E_0$ is

$$J_{E_0} = \begin{pmatrix}
f'(\bar{x}) & -\beta \\
0 & -a & \beta \\
0 & k & -u - i \beta
\end{pmatrix}.$$ 

Here $f'(\bar{x}) < 0$ is an eigenvalue, since the trace of the two-
by-two lower right submatrix is negative and the determinant is $au(1 - R_0)$, if $R_0 < 1$, the remaining two eigenvalues are
also negative, so $E_0$ is locally asymptotically stable. If $R_0 > 1$, there must exist a positive eigenvalue, so $E_0$ is unstable.

Next, we’ll discuss the globally asymptotical stability. Consider the Lyapunov function

$$V_2 = y(t) + \frac{a}{k}v(t).$$

Calculating the derivative of $V_2$ along the solutions of the model (7) gives

$$V_2'(t) = \frac{\beta x v}{x + y} - \frac{a u}{k} v - \frac{ia \beta x v}{k} x + y$$

$$\leq \beta v(1 - \frac{ia}{k} - \frac{a u}{k} v)$$

$$= (1 - \frac{1}{R_0}) \beta (k - ia) v \leq 0.$$

Let $E = \{(x, y, v) \in D| V_2(t) = 0\}$, it is clear that $E \subset \{(x, y, v) \in D| v = 0\}$. Let $M$ be the largest positively invariant subset of the set $E$, in the set $M$, $y'(t) = -ay$, so that $y(t) \to 0$ when $t \to \infty$. By the Lyapunov - Lasalle Theorem[16], $\lim_{t \to \infty} y(t) = 0$, $\lim_{t \to \infty} v(t) = 0$. Thus, the first equation of model (7) is asymptotically equivalent to $\dot{x} = f(x)$, because $f(x) > 0$, $x \leq x$ and $f(x) < 0$, $x > x$, we can know that $x(t) \to x$. By the theorem on limiting systems[17], we can know the infection-free equilibrium $E_0$ is globally attractive, combine with the the locally asymptotical stability, $E_0$ is globally asymptotically stable.

III. STABILITY ANALYSIS OF THE ENDIMENT STEADY STATE

A. Local stability of the endemic steady state

We first consider the local stability of the endemic steady state $E_e$.

**Theorem 3.1:** If $R_0 > 1$ and $f'(x_e) \leq 0$, then the endemic steady state $E_e$ is locally asymptotically stable for $i = 0, 1$.

**Proof:** Note that

$$\frac{x_e}{x_e + y_e} = \frac{1}{R_0},$$

$$\frac{\beta x_e v_e}{(x_e + y_e)^2} = \frac{a(R_0 - 1)}{R_0},$$

$$\frac{\beta y_e v_e}{(x_e + y_e)^2} = \frac{a(R_0 - 1)^2}{R_0},$$

the Jacobian matrix of the vector field corresponding to model (7) evaluated at $E_e$ is

$$J_{E_e} = \begin{pmatrix}
\frac{1}{R_0} & a(R_0 - 1) & -\frac{\beta}{R_0} \\
-\frac{a(R_0 - 1)^2}{R_0} & -a & 0 \\
\frac{a(R_0 - 1)}{R_0} & 0 & \frac{\beta}{R_0} \\
\end{pmatrix},$$

which $J_{E_1} = f'(x_e) - a(R_0 - 1)y/R_0$ The characteristic equation associated with $J_{E_e}$ is given by

$$|E - J_{E_e}| = t^3 + a_1 t^2 + a_2 t + a_3 = 0,$$

where

$$a_1 = aR_0 + u - f'(x_e) + \frac{\beta}{R_0} > 0,$$

$$a_2 = -f'(x_e)(a + u + \frac{a(R_0 - 1)}{R_0} + i\frac{\beta}{R_0})$$

$$+ au(R_0 - 1) + \frac{a^2(R_0 - 1)^2}{R_0} > 0,$$

$$a_3 = \frac{a^2 u(R_0 - 1)^2}{R_0} - f'(x_e)au(R_0 - 1) > 0.$$

Let

$$a_1 = u + C, a_2 = -f'(x_e)\frac{a(R_0 - 1)}{R_0} + \frac{a^2(R_0 - 1)^2}{R_0} + D,$$

which

$$C = aR_0 - f'(x_e) + i\frac{\beta}{R_0} > 0,$$

$$D = -f'(x_e)(a + u + i\frac{\beta}{R_0}) + au(R_0 - 1) > 0.$$

By Routh-Hurwitz criterion, $E_e$ is locally asymptotically stable.

B. Globally asymptotic stability of the disease steady state

In order to prove the global stability, we need to show the uniform persistence of system (7) when $R_0 > 1$. By Theorem 4.3 in paper [20], we choose $X = R^3$ and $E = D$. The maximal invariant set $N$ on the boundary $\partial D$ is the singleton $E_0$ and is isolated, so the uniform persistence is equivalent to the unstability of $E_0$. Hence, by theorem 2.2, we know if $R_0 > 1$, the system (7) is uniform persistence. Consequently, there exists a compact absorbing set $K \subset D$[21].

**Theorem 3.2:** Suppose that $R_0 > 1$, $f'(x_e) < 0$ for $x \in [0, \bar{x}]$, and denote $0 < \alpha < \max_{x \in [0, \bar{x}]} f'(x)$. If $i = 0$ or if $i = 1$ and $\beta < \min(\alpha, \alpha)$, then $E_0$ is globally asymptotically stable with initial conditions in $D$ but not on the $x$ axis.

**Proof:** By the first statement of theorem 3.3, if the omega limit set does contain $E_e$, because $x_e < \bar{x}$, we must have $f'(x_e) < 0$ , combine with the first statement of theorem 3.1, we establish the claim. If system (7) possesses a nontrival periodic solution, similar to the arguments in Muldowney’paper[19], we will show the periodic solution must be asymptotically orbitaly stable. Denote the periodic solution by $p(t) \equiv (p_1, p_2, p_3)^T$ and suppose its minimal period is $\omega > 0$, by the positive invariance of $D$, we know

$$0 \leq p_1 \leq \bar{x}, \forall t \in [0, \omega].$$

Next, we only need to prove the system

$$\dot{z} = (DF(z(t)))z(t).$$

2011 IEEE International Conference on Systems Biology (ISB) 315 Zhuhai, China, September 2–4, 2011
is asymptotically stable, where $DF^{[2]}$ is the second additive compound matrix of Jacobian (11).

$$
    DF^{[2]} = \left( \begin{array}{ccc}
        D_{11} & \frac{\beta x}{x+y} & \frac{\beta x}{x+y} \\
        \frac{k + i \beta x v}{(x+y)^2} & D_{22} & \frac{i \beta x v}{(x+y)^2} \\
        i \frac{\beta y v}{(x+y)^2} & \frac{\beta y v}{(x+y)^2} & D_{33}
    \end{array} \right).
$$

which

$$
    D_{11} = f'(x) - a - \frac{\beta v}{x+y},
    D_{22} = f'(x) - \frac{\beta y v}{(x+y)^2} - u - i \frac{\beta x}{x+y},
    D_{33} = -a - u - \frac{\beta x v}{(x+y)^2} - i \frac{\beta x}{x+y}
$$

We will show that the function

$$
    V(z_1, z_2, z_3; p(t)) = \sup \left\{ |z_1|, \frac{p_2}{p_3} (|z_2| + |z_3|) \right\}
$$

is a Lyapunov function for system (25). We have

$$
    D_+ (|z_1(t)|) \leq - (f'(p_1) + a + \frac{\beta p_3}{p_1 + p_2}) |z_1| + \frac{\beta p_3}{p_1 + p_2} \frac{p_2}{p_3} (|z_2| + |z_3|)
$$

$$
    \leq \frac{p_2}{p_3} \left( k + i \frac{\beta p_3}{p_1 + p_2} \right) |z_1| - \frac{p_2}{p_3} (f'(p_1) |z_2| + a |z_3|) + \frac{p_2}{p_3} \frac{p_3}{p_1 + p_2} |z_3|
$$

Thus, we obtain that

$$
    D_+ V(t) \leq \sup (g_1(t), g_2(t)) V(t).
$$

where

$$
    g_1(t) = - (f'(p_1) + a + \frac{\beta p_3}{p_1 + p_2}) + \frac{\beta p_3}{p_1 + p_2} p_3
    = -(f'(p_1) + \frac{\beta p_3}{p_1 + p_2}) + \frac{p_2(t)}{p_2}
    \leq -\alpha + \frac{p_2(t)}{p_2}.
$$

$$
    g_2(t) = k \frac{p_2}{p_3} + i \frac{\beta p_2}{p_1 + p_2} + \frac{\dot{p}_2(t)}{p_2} - \frac{\dot{p}_3(t)}{p_3} - u
    - i \frac{\beta p_1}{p_1 + p_2} - \min (\alpha, a)
    = i \frac{\beta p_2}{p_1 + p_2} + \frac{\dot{p}_2(t)}{p_2} - \min (\alpha, a).
$$

Hence $g_1(t) < g_2(t)$, so we have

$$
    D_+ V(t) \leq g_2(t) V(t).
$$

If the following holds:

$$
    \int_0^\omega g_2(t) dt < 0,
$$

it follows that $V$ must be a Lyapunov function for system (13). When $i = 0$,,

$$
    \int_0^\omega g_2(t) dt = \int_0^\omega \left( \frac{\dot{p}_2(t)}{p_2} - \min (\alpha, a) \right) dt
    = - \min (\alpha, a) \omega < 0.
$$

When $i = 1$,

$$
    \int_0^\omega g_2(t) dt = \int_0^\omega \left( \frac{\beta p_2}{p_1 + p_2} + \frac{\dot{p}_2(t)}{p_2} - \min (\alpha, a) \right) dt
    \leq \int_0^\omega \beta dt + \int_0^\omega \left( \frac{\dot{p}_2(t)}{p_2} - \min (\alpha, a) \right) dt
    = (\beta - \min (\alpha, a)) \omega < 0.
$$

Combine with (15) we know that $\lim V(t) = 0$, which means $z_1(t), z_2(t), z_3(t) \to 0$, so the system (13) is asymptotically stable, this completes the proof.

IV. OSCILLATIONS

When $f(x) = f_2(x)$, if the condition $f'(x_c) \leq 0$ in theorem 3.1 couldn’t be satisfied, there would exist an orbitally asymptotically stable periodic solution, and we have the following theorem.

**Theorem 4.1:** If $R_0 > 1$ and $a_1 a_2 < a_3$, then model (6) exists an orbitally asymptotically stable periodic solution.

**Proof:** When $f = f_2$,

$$
    E_c = (x_c, (R_0 - 1)x_c, \frac{(k - ia)(R_0 - 1)}{u} v_c).
$$

which

$$
    x_c = \frac{x_{max}}{2p} [p - d - a(R_0 - 1) + \sqrt{\Delta}]
$$

where

$$
    \Delta = (p - d - a(R_0 - 1))^2 + \frac{4p\lambda}{x_{max}} > a^2(R_0 - 1)^2.
$$

The Jacobian matrix of the vector field corresponding to model (7) evaluated at $E_c$ when $f = f_2$ is

$$
    J = \left( \begin{array}{ccc}
        -B & a(R_0 - 1) & \frac{\beta}{R_0} \\
        a(R_0 - 1)^2 & -a(R_0 - 1) - a & \frac{\beta}{R_0} \\
        -\frac{a(R_0 - 1)^2}{R_0} & k + i \frac{a(R_0 - 1)}{R_0} & -u - i \frac{\beta}{R_0}
    \end{array} \right).
$$

which \( B = \sqrt{\Delta} - \frac{a(R_0 - 1)}{R_0} \). The parameters of equation (11) become as follows:

\[
\begin{align*}
a_1 &= \sqrt{\Delta} + a + u + i \frac{\beta}{R_0} > 0, \\
a_2 &= \sqrt{\Delta}(a + u + \frac{a(R_0 - 1)}{R_0}) + i \frac{\beta}{R_0} \\
&\quad - (R_0 - 1)(a^2 + i \frac{\beta a}{R_0}), \\
a_3 &= \sqrt{\Delta}a(R_0 - 1) > 0
\end{align*}
\]

When \( R_0 > 1 \), the second part of \( a_2 \) is positive, so we can choose a proper parameters \( p \) and a large enough \( x_{\max} \) such that \( \sqrt{\Delta} \) be very small, so \( a_2 \) may be negative and \( a_1a_2 < a_3 \) holds, which means \( E_c \) is unstable.

The conclusion follows from Theorem 1.2 [22] and the fact that nonlinearities in model (7) are analytic in \( D \). In order to apply that result, we take the domain for (7) to be the interior of the positive orthant, in which the only steady state is \( Q_2 \). If \( R_0 > 1 \) and \( a_1a_2 < a_3 \), then \( Q_2 \) is unstable. The dissipativity hypothesis of Theorem 1.2 [22] follows from Theorem 2.1 and the persistence of model (7). By looking at the Jacobian matrix \( J \) and choosing the matrix \( H = \text{diag}(1, -1, 1) \), then \( HJH \) is a matrix with non-positive off-diagonal elements. Hence, the model (7) is competitive in \( D \). Taking \( l = 0 \) in the characteristic equation (11), we have \( |J_{Q_2}| = -a_3 < 0 \). Hence, all conditions of Theorem 1.2 [22] are satisfied. This completes the proof.

V. NUMERICAL SIMULATIONS

In this section, we will give some numerical simulations of system (7) when \( f(x) = f_2(x) \). When we simulate the orbitally asymptotically stable of stable periodic solution, by the theorem 4.1, we only need to choose parameters satisfying \( R_0 > 1 \) and \( a_1a_2 - a_3 < 0 \). When \( i = 0 \), we choose parameters as follows: \( \lambda = 2.5267e + 005, \ d = 0.00379, \ u = 0.16, \ p = 3, \ a = 0.0533, \beta = 1.6891e + 003, \ k = 2.4500e - 004, \ X_{\max} = 6.6667e + 007, \ R_0 = 48.52 > 1, \) thus we have \( a_1a_2 - a_3 = -2.5024e + 003 < 0 \), which satisfy the theorem 4.1, we choose the initial condition \( X_0 = [3.3333 \times 10^7, 3.3333 \times 10^7, 10^3] \), the system (7) has an orbitally asymptotically stable periodic solution( see fig.1) which is consistent with the statement of theorem 4.1.

When \( i = 1 \), we choose \( \lambda = 2.5267e + 005, \ d = 0.00379, \ u = 0.650, \ p = 0.0311, \ a = 0.00379, \beta = 2.8957e - 004, \ k = 70, \ X_{\max} = 6.6667e + 12, \ R_0 = 8.2276 > 1, \ a_1a_2 - a_3 = -2.2537e - 005 < 0 \), which satisfy the note of the theorem 4.1, we choose \( X_0 = [6 \times 10^7, 6.6667e + 006, 10^3] \), the system 7 has an orbitally asymptotically stable periodic solution( see fig.2).

VI. CONCLUDING REMARKS

In this paper, based on Leenheer and Smith’s model[11], we consider an amended viral infection model with standard incidence. By stability analysis we give sufficient conditions for the global stability of infection-free steady-state and the the endemic steady state. That is when \( R_0 = \beta(k - ia)/au < 1 \), the infection-free equilibrium \( E_0 \) is globally asymptotically stable and becomes unstable when \( R_0 > 1 \). If \( R_0 > 1 \), the globally asymptotically stability of endemic equilibrium \( E_c \) is related to \( f(x) \) which determine the dynamic behavior of uninfected cell in system (7) both for \( i = 0 \) and \( i = 1 \). But when \( i = 1 \), another condition of parameters must hold , that is \( \beta < \min(\alpha, \kappa) \). We also show that periodic oscillations of system (7) are possible. When \( f(x) = f_2(x) \), we give the sufficient condition of the parameters to obtain the periodic oscillations. The numerical simulation results confirm our analytic results.

ACKNOWLEDGMENTS

We would like to thank the anonymous referees which have improved the quality of our study.
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