A CLASS OF VIRUS DYNAMIC MODEL WITH INHIBITORY EFFECT ON THE GROWTH OF UNINFECTED T CELLS CAUSED BY INFECTED T CELLS AND ITS STABILITY ANALYSIS

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Abstract. A class of virus dynamic model with inhibitory effect on the growth of uninfected T cells caused by infected T cells is proposed. It is shown that the infection-free equilibrium of the model is globally asymptotically stable, if the reproduction number $R_0$ is less than one, and that the infected equilibrium of the model is locally asymptotically stable, if the reproduction number $R_0$ is larger than one. Furthermore, it is also shown that the model is uniformly persistent, and some explicit formulae for the lower bounds of the solutions of the model are obtained.

1. Introduction. The human immunodeficiency virus (HIV) is a lentivirus that causes the acquired immunodeficiency syndrome (AIDS) [5]. Once infected with HIV, T cells are destroyed and the virus particles start to replicate themselves (see, for example, [24, 27] and the references therein).

It is well known that mathematical models have made considerable contributions to our understanding of HIV infection dynamics. A class of classic mathematical model describing HIV infection dynamics has been proposed by Nowak, Perelson and Nelson et al (see, for example, [23, 24, 27, 28] and the references therein),

\[
\begin{align*}
\dot{x}(t) &= s - dx(t) - \beta x(t)v(t), \\
\dot{y}(t) &= \beta x(t)v(t) - py(t), \\
\dot{v}(t) &= ky(t) - uv(t),
\end{align*}
\]

where $x(t)$, $y(t)$, and $v(t)$ denote the concentration of uninfected cells, infected cells, and virus at time $t$, respectively. The constant $s$ ($s > 0$) is the rate at which new uninfected cells are generated. The constants $d$ ($d > 0$) and $\beta$ ($\beta > 0$) are the death rate of uninfected cells and the rate constant characterizing infection of the cells, respectively. The constant $p$ ($p > 0$) is the death rate of the infected cells due either to virus or the immune system. The infected cells produce new virus at the rate $k$ ($k > 0$) during their life which on average has the length $1/p$. The constant $u$ ($u > 0$) is the rate at which the virus is cleared.

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Since cytotoxic T lymphocyte cells, which attack infected cells, and antiviral drugs, which slow down viral activity, are fundamental in antiviral defenses, some researchers have also incorporated the effects of immune responses and antiretroviral treatment (see, for example, [2, 6, 8, 14, 19, 21, 25, 27, 29, 32] and the references therein). Taking into account of the HIV virus from HIV infection to produce new viral particles takes time, therefore, more within-host HIV models including time delay can be found (see, for example, [1, 4, 7, 9, 12, 18, 22, 30, 35, 37, 39] and the references therein). According to the HIV pathogenesis, the contributions of the interaction between uninfected cells and virus to the growth rate of the cells no longer account for by the principle of mass action, and hence the linear infection rate has been replaced with saturation infection rate, Beddington-DeAngelis functional response, sigmoidal function or more general saturated infection rate (see, for example, [3, 13, 16, 17, 20, 28, 34, 38] and the references therein).

In the model (1), the decreasing of uninfected cells is induced by two factors: one is the natural death of uninfected cells (i.e., \( dx(t) \)), the other one is that the uninfected cells become the infected cells (i.e., \( \beta x(t)v(t) \)). On the other hand, with the progress of science and technology and the improvement of research approaches, it has a clearer understanding on the growth of uninfected cells.

HIV gene expression products can produce toxic, which directly or indirectly induces apoptosis in uninfected cells. Productively infected cells were only rarely apoptotic and apoptotic cells were only rarely productively infected (see, [10]). These data suggest that viral proteins interact with uninfected cells and induce an apoptotic signal which induces the death of uninfected cells (see, [31]).

Based on the classic model (1) and biological meanings above, this paper considers the following infection model with inhibitory effect on the growth of uninfected cells by infected cells,

\[
\begin{align*}
\dot{x}(t) &= s - dx(t) - cx(t)y(t) - \beta x(t)v(t), \\
\dot{y}(t) &= \delta x(t-\tau)v(t-\tau) - py(t), \\
\dot{v}(t) &= ky(t) - uv(t).
\end{align*}
\]

In the model (2), \( \delta = \beta e^{-m\tau} \) denotes the surviving rate of infected cells before it becomes productively infected, and \( m (m \geq 0) \) is constant. The constant \( c (c \geq 0) \) is the rate of apoptosis at which infected cells induce uninfected cells. Here, the mass action function \( cx(t)y(t) \) is used. All other parameters in the model (2) completely have the same biological meanings as that in the model (1).

The organization of this paper is as follows. The non-negativity and the boundedness of the solutions of the model (2) are investigated in Section 2. Then, by analyzing the characteristic equations, the local asymptotic stability of the infection-free equilibrium and the infected equilibrium of the model (2) are studied in Section 3. Furthermore, in Section 3, the global asymptotic stability of the infection-free equilibrium is also considered by using Lyapunov-LaSalle invariance principle. The uniform persistence of the model (2) is discussed in Section 4. It should be mentioned here that, in Section 4, some explicit lower bound for any solution \((x(t), y(t), v(t))\) of the model (2) is obtained. Some numerical simulations are given in Section 5. Finally, some remarks are included in Section 6.

2. Non-negativity and boundedness of solutions. Let \( C = C([-\tau, 0]; R^3) \) be the Banach space of continuous functions from \([-\tau, 0]\) to \( R^3 \) equipped with the
sup-norm. The initial condition of the model \((2)\) is given as follows,
\[
x(\theta) = \phi_1(\theta), \quad y(\theta) = \phi_2(\theta), \quad v(\theta) = \phi_3(\theta) \quad (\theta \in [-\tau, 0]),
\]
where \(\phi = (\phi_1, \phi_2, \phi_3) \in C\) such that \(\phi_i(\theta) \geq 0 \ (\theta \in [-\tau, 0], i = 1, 2, 3)\).

The following lemma establishes the non-negativity and boundedness of the solutions of the model \((2)\).

**Lemma 2.1.** The solution \((x(t), y(t), v(t))\) of the model \((2)\) with the initial condition \((3)\) is existent, unique and non-negative on \([0, +\infty)\), and also ultimately bounded.

**Proof.** In fact, by using standard theorems for existence and uniqueness of functional differential equations (see, for example, \([11]\) and \([15]\)), it is easy to show that the solution \((x(t), y(t), v(t))\) of the model \((2)\) with the initial condition \((3)\) is existent, unique and non-negative on \([0, +\infty)\).

Let us consider ultimate boundedness of the model \((2)\). From the first equation of the model \((2)\), it can be shown that \(\lim \sup_{t \to +\infty} x(t) \leq s/d\). Define the function
\[
V(t) = x(t) + \frac{\beta}{\delta} y(t + \tau)
\]
for \(t \geq 0\). It follows from the model \((2)\) that, for \(t \geq 0\),
\[
\dot{V}(t) \leq s - dx(t) - \frac{p\beta}{\delta} y(t + \tau) \leq s - \mu V(t),
\]
where \(\mu = \min\{d, p\}\). Hence, it has \(\lim \sup_{t \to +\infty} V(t) \leq s/\mu\), which further implies that \(\lim \sup_{t \to +\infty} y(t) \leq s\delta/\mu\beta\). Finally, it has from the third equation of the model \((2)\) that \(\lim \sup_{t \to +\infty} v(t) \leq s\delta/\mu\beta\). \(\square\)

### 3. Stability analysis of the equilibria
First, it is easy to have that the basic reproductive ratio of the virus for the model \((2)\) is given as \(R_0 = sk\delta/pdu\) (see, for example, \([23]\)). For the existence of non-negative equilibria of the model \((2)\), the following classifications can be easily obtained.

(i) The model \((2)\) always has the infection-free equilibrium \(E_0 = (x_0, 0, 0)\), where \(x_0 = s/d\).

(ii) If \(R_0 > 1\), the model \((2)\) also has unique infected equilibrium \(E^* = (x^*, y^*, v^*)\), where
\[
x^* = \frac{pu}{\delta k}, \quad y^* = \frac{du(R_0 - 1)}{cu + \beta k}, \quad v^* = \frac{dk(R_0 - 1)}{cu + \beta k}.
\]

The following theorem is main result of the section.

**Theorem 3.1.** (i) If \(R_0 < 1\), \(E_0\) is globally asymptotically stable for any time delay \(\tau \geq 0\). (ii) If \(R_0 = 1\), \(E_0\) is globally attractive for any time delay \(\tau \geq 0\). (iii) If \(R_0 > 1\), \(E_0\) is unstable, and \(E^*\) is locally asymptotically stable for any time delay \(\tau \geq 0\).

**Proof.** By using a similar method as in \([15]\), it is not difficult to show that, for any time delay \(\tau \geq 0\), \(E_0\) is locally asymptotically stable when \(R_0 < 1\), and linearly stable when \(R_0 = 1\). Let us consider the local asymptotic stability of \(E^*\) when \(R_0 > 1\). The associated transcendental characteristic equation of the model \((2)\) at \(E^*\) becomes
\[
\lambda^3 + p_2 \lambda^2 + p_1 \lambda + p_0 + (q_1 \lambda + q_0) e^{-\lambda \tau} = 0,
\]
where
\[
p_0 = \frac{du}{cu + \beta k}, \quad p_1 = \frac{du}{cu + \beta k}, \quad p_2 = \frac{du}{cu + \beta k},
\]
and
\[
q_0 = \frac{sk\delta}{\mu\beta}, \quad q_1 = \frac{sk\delta}{\mu\beta}.
\]
where
\[ p_2 = p + u + d + cy^* + \beta v^*, \]
\[ p_1 = (p + u)(d + cy^* + \beta v^*) + pu, \]
\[ p_0 = pu(d + cy^* + \beta v^*), \]
\[ q_1 = p(cy^* - u), \]
\[ q_0 = -pu. \]

For \( \tau = 0 \), from (4), it has that
\[ \lambda^3 + p_2 \lambda^2 + (p_1 + q_1)\lambda + p_0 + q_0 = 0, \] (5)
where
\[ p_2 = p + u + d + cy^* + \beta v^* > 0, \]
\[ p_1 + q_1 = (p + u)(d + cy^* + \beta v^*) + pcy^* > 0, \]
\[ p_0 + q_0 = pu(cy^* + \beta v^*) > 0, \]
\[ p_2(p_1 + q_1) - (p_0 + q_0) = [(p + u)(d + cy^* + \beta v^*) + (p^2 + u^2)(d + cy^* + \beta v^*) + cpy^* + (p + u)(d + cy^* + \beta v^*) + pu(2d + cy^*) + puw^* \beta] > 0. \]

Hence, it follows that any root of (5) has negative real part owing to the Routh-Hurwitz criterion.

Furthermore, from (4), it has \( \lambda = 0 \) is not root of (4). If (4) has pure imaginary root \( \lambda = i\omega (\omega > 0) \) for some \( \tau > 0 \), substituting it into (4) and separating the real and imaginary parts, it has
\[ \omega^3 - p_1\omega = q_1\omega \cos \omega \tau - q_0 \sin \omega \tau, \]
\[ p_2\omega^2 - p_0 = q_1\omega \sin \omega \tau + q_0 \cos \omega \tau. \]
Therefore, it has
\[ g(\varpi) = \varpi^3 + (p_2^2 - 2p_1)\varpi^2 + (p_1^2 - 2p_0p_2 - q_1^2)\varpi + p_0^2 - q_0^2 = 0, \] (6)
where \( \varpi = \omega^2 \). Since
\[ p_2^2 - 2p_1 = p^2 + u^2 + (d + cy^* + \beta v^*)^2 > 0, \]
\[ p_1^2 - 2p_0p_2 - q_1^2 = (d + cy^* + \beta v^*)^2(p^2 + u^2) - (pcy^*)^2 > 0, \]
\[ p_0^2 - q_0^2 = p^2u^2(d + cy^* + \beta v^* + d)(cy^* + \beta v^*) > 0, \]
it arrives at \( g(\varpi) > 0 \), which contradicts \( g(\varpi) = 0 \). This shows that all the roots of (4) have negative real parts for any time delay \( \tau \geq 0 \).

Next, let us show that, if \( R_0 \leq 1 \), \( E_0 \) is globally attractive for any time delay \( \tau \geq 0 \).

Define
\[ G = \{ \phi = (\phi_1, \phi_2, \phi_3) \in C \mid x_0 \geq \phi_1 \geq 0, \phi_2 \geq 0, \phi_3 \geq 0 \}. \]
It is easy to show that \( G \) attracts all solutions of the model (2), and is also positively invariant with respect to the model (2).

If \( R_0 < 1 \), let us define a functional \( W(\phi) \) on \( G \) as follows,
\[ W(\phi) = \frac{k}{p} \phi_2(0) + \phi_3(0) + \gamma \int_{-\tau}^{0} \phi_3(\theta) \, d\theta. \] (7)
Here $\gamma > 0$ is a constant to be chosen later. It can be found that $W(\phi)$ is continuous on the subset $\mathcal{C}$ in $C$. From the invariance of $G$, for any $\phi \in G$, the solution $(x(t), y(t), v(t))$ of the model (2) satisfies $x(t) \leq s/d$ for any $t \geq 0$. It follows from (2) and (7) that

$$W(\phi) = \phi_2(0)(\gamma - u) + \phi_3(-\tau)(\frac{k\delta}{p}\phi_1(-\tau) - \gamma)$$

$$\leq \frac{\phi_3(0)}{d}(d\gamma - du) + \frac{\phi_3(-\tau)}{d}(sk\delta - d\gamma).$$

Since $R_0 < 1$, it is possible to choose $\gamma > 0$ such that $sk\delta/p < d\gamma < du$. Then, it has that, for any $\phi \in G$,

$$\dot{W}(\phi) \leq \frac{\phi_3(0)}{d}(d\gamma - du) \leq 0. \quad (8)$$

This shows that $W(\phi)$ is a Lyapunov function on the subset $G$.

Define $E = \{\phi \in G \mid W(\phi) = 0\}$. $E \subset \{\phi \in G \mid \phi_3(0) = 0\}$ holds due to (8). Let $M$ be the largest set in $E$ which is invariant with respect to the model (2). Clearly, $M$ is not empty since $(x_0, 0, 0) \in M$. For any $\phi \in M$, let $(x(t), y(t), v(t))$ be the solution of the model (2) with the initial function $\phi$. Owing to the invariance of $M$, it is true that $(x_t, y_t, v_t) \in M \subset E$ for any $t \in R$. Thus $y(t) \equiv 0$ for any $t \in R$. According to the second equation of the model (2), we further have that $y(t) \to 0$ as $t \to +\infty$. From the first equation of the model (2) and the above conclusions, it also has that $x(t) \to x_0$ as $t \to +\infty$. Hence, the invariance of $M$ implies that $x(t) \equiv x_0$, $y(t) \equiv 0$ for any $t \in R$. Therefore, $M = \{(x_0, 0, 0)\}$. It has from Lyapunov-LaSalle invariance principle that $E_0$ is globally attractive.

If $R_0 = 1$, let us consider the following functional on $G$,

$$W(\phi) = \phi_2(0) + \frac{p}{k}\phi_3(0) + \delta x_0 \int_{-\tau}^{0} \phi_3(\xi)d\xi. \quad (9)$$

It is clear that $W(\phi)$ is also continuous on subset $\mathcal{C}$ in $C$. From the invariance of $G$, for any $\phi \in G$, the solution $(x(t), y(t), v(t))$ of the model (2) with the initial function $\phi$ satisfies $x(t) \leq x_0$ for all $t > 0$. From (2) and (9), it has that

$$\dot{W}(\phi) = \delta \phi_3(-\tau)(\phi_1(-\tau) - x_0) + (\delta x_0 - \frac{pu}{k})\phi_3(0)$$

$$= \delta \phi_3(-\tau)(\phi_1(-\tau) - x_0) \leq 0.$$

Hence, $W(\phi)$ is also a Lyapunov function on the subset $G$ in $C$. Define $E = \{\varphi \in G \mid W(\varphi) = 0\}$, it has that $E \subset \{\varphi \in G \mid \phi_3(-\tau) = 0 \text{ or } \phi_1(-\tau) = x_0\}$. Let $M$ be the largest set in $E$ which is invariant with respect to the model (2). $M$ is not empty. For any $\phi \in M$, let $(x(t), y(t), v(t))$ be the solution of the model (2) with the initial function $\phi$. According to the invariance of $M$, it has $(x_t, y_t, v_t) \in M \subset E$ for any $t \in R$. Thus, for each $t \in R$, it holds that $x(t - \tau) = x_0$ or $v(t - \tau) = 0$. If $x(t - \tau) = x_0$ for some $t$, $x(t - \tau) = 0$ must hold owing to $x(t) \leq x_0$ and the differentiability of $x(t)$.

The first equation of the model (2) implies that

$$0 = s - dx(t - \tau) - cx(t - \tau)y(t - \tau) - \beta x(t - \tau)v(t - \tau)$$

$$= -c x_0 y(t - \tau) - \beta x_0 v(t - \tau).$$

For the non-negativity of the solutions, it has $v(t - \tau) = y(t - \tau) = 0$. Therefore, $v(t - \tau) \equiv 0$ for any $t \in R$. From the invariance of $M$ and the first and second equations of the model (2), it also has that $x(t) \equiv x_0$ and $y(t) \equiv 0$ for any $t \in R$. 
Therefore, $M = \{(x_0, 0, 0)\}$. It also has from Lyapunov-LaSalle invariance principal that $E_0$ is globally attractive.

4. Uniform persistence. In this section, let us consider the uniform persistence of the model (2).

The model (2) is said to be uniformly persistent (see, for example, [15]), if there are positive constants $m_i$ and $M_i$ ($i = 1, 2, 3$) such that

$$m_1 \leq \liminf_{t \to +\infty} x(t) \leq \limsup_{t \to +\infty} x(t) \leq M_1,$$

$$m_2 \leq \liminf_{t \to +\infty} y(t) \leq \limsup_{t \to +\infty} y(t) \leq M_2,$$

$$m_3 \leq \liminf_{t \to +\infty} v(t) \leq \limsup_{t \to +\infty} v(t) \leq M_3$$

hold for any solution of the model (2). Here $m_i$ and $M_i$ ($i = 1, 2, 3$) are independent of the initial function $\phi$.

Uniform persistence of the model (2) has important significance in biology, and implies that infected T cells ($y(t)$) and virus particles ($v(t)$) can not be completely removed and will ultimately exist.

First, by using the similar method as in [26] and the result in [33], we can prove the following result which will be used in the proof of the main result Theorem 4.2 below.

Lemma 4.1. If $R_0 > 1$, there exists $\eta_0 > 0$ such that the solution $(x(t), y(t), v(t))$ of the model (2) with the initial condition (3) satisfies

$$\liminf_{t \to +\infty} y(t) \geq \eta_0, \quad \liminf_{t \to +\infty} v(t) \geq \eta_0.$$

Now, let us state and prove the main result in this section. We refer to the idea in [36].

Theorem 4.2. If $R_0 > 1$, the model (2) is uniformly persistent for any time delay $\tau \geq 0$, and there exist positive constants $v_1$, $v_2$ and $v_3$ such that, for any solution $(x(t), y(t), v(t))$ of the model (2) with the initial condition (3) the following inequalities

$$\liminf_{t \to +\infty} x(t) \geq \frac{s \mu \beta}{d \mu \beta + cs \delta + \beta \delta k} \equiv v_1,$$

$$\liminf_{t \to +\infty} y(t) \geq \frac{y^*}{2} e^{-p(T_0 + T_1 + \tau + \alpha)} \equiv v_2,$$

$$\liminf_{t \to +\infty} v(t) \geq \frac{k y^*}{2 a} e^{-p(T_0 + T_1 + \tau + \alpha)} \equiv v_3$$

hold, where $T_0, T_1$ and $a$ satisfy

$$\frac{sd\delta}{d\beta} e^{-uT_0} = \frac{y^*}{2}, \quad x^* < \frac{s}{d}(1 - e^{-bT_1}) = z^0, \quad a = \frac{g}{u(1 - q)},$$

$$q = \frac{x^*}{z^0}, \quad b = d + y^* \left(\frac{c}{2} + \frac{\beta k}{u}\right).$$

Proof. In the proof of Lemma 2.1, it has proved that $\limsup_{t \to +\infty} y(t) \leq s \delta / \mu \beta$ and $\limsup_{t \to +\infty} v(t) \leq s k \delta / \mu \beta$. Hence, for any sufficiently small constant $\varepsilon > 0$, there is some sufficiently large $t_1 > 0$ such that, for $t > t_1$, $y(t) \leq s \delta / \mu \beta + \varepsilon$, and
\( v(t) < sk\delta/\mu u \beta + \varepsilon \). From the first equation of the model (2), it has that, for \( t \geq t_1 + \tau \),

\[
\dot{x}(t) \geq s - \left[ d + \left( \frac{cs\delta}{\mu \beta} + \varepsilon \right) + \beta \left( \frac{sk\delta}{\mu u \beta} + \varepsilon \right) \right] x(t),
\]

from which it easily has that

\[
\liminf_{t \to +\infty} x(t) \geq \frac{s\mu \beta}{d\mu \beta + csu\delta + \beta sk + (\beta + 1)\beta \mu \varepsilon}.
\]

Let \( \varepsilon \to 0^+ \), it has \( \liminf_{t \to +\infty} x(t) \geq v_1 \).

Next, let us prove that \( \liminf_{t \to +\infty} y(t) \geq v_2 \).

For \( t \geq 0 \), define the differentiable function \( V(t) \) as follows,

\[
V(t) = y(t) + \frac{p}{k} v(t) + \delta x^* \int_{t-\tau}^t v(\theta) d\theta.
\]

(10)

The derivative of \( V(t) \) along the solution of the model (2) satisfies

\[
\dot{V}(t) = \dot{y}(t) + \frac{p}{k} \dot{v}(t) + \delta x^* (v(t) - v(t - \tau)) = \delta (x(t - \tau) - x^*) v(t - \tau).
\]

There exists some sufficiently large \( T > 0 \) such that, for \( t \geq T \),

\[
v(t) \leq \frac{sk\delta}{\mu \beta} + \frac{ky^*}{2u}.
\]

Since \( x^* = s/[d + y^* (c + \beta k/u)] \), it has \( x^* < s/b \), where \( b = d + y^* (c/2 + \beta k/u) \).

Hence, it is possible to choose \( T_0 \) and \( T_1 \) such that \( (s\delta/\mu \beta) e^{-u T_0} = y^*/2 \) and \( x^* < (s/b)(1 - e^{-b T_1}) = x^0 \).

Let us first show that \( y(t) \leq y^*/2 \) (\( \forall t \geq T \)) does not hold.

Suppose the contrary, there exists some \( t_0 \geq T \) such that \( y(t) \leq y^*/2 \) for all \( t \geq t_0 \). It follows from the third equation of the model (2) that, for \( t \geq t_0 \),

\[
\dot{v}(t) = ky(t) - uv(t) \leq \frac{1}{2} ky^* - uv(t),
\]

from which it has

\[
v(t) \leq \frac{ky^*}{2u} + (v(t_0) - \frac{ky^*}{2u}) e^{-u(t-t_0)} \leq \frac{ky^*}{2u} + \frac{sk\delta}{\mu \beta} e^{-u(t-t_0)}.
\]

Hence, it has \( v(t) \leq ky^*/u \) for \( t \geq t_0 + T_0 \). From the first equation of the model (2), it has

\[
\dot{x}(t) \geq s - dx(t) - \frac{cy^*}{2} x(t) - \frac{\beta ky^*}{u} x(t) = s - bx(t).
\]

Furthermore, for \( t \geq t_0 + T_0 \), it has

\[
x(t) \geq e^{-b(t-t_0-T_0)} [x(t_0 + T_0) + s \int_{t_0+T_0}^t e^{b(\theta-t_0-T_0)} d\theta] > \frac{s}{b} (1 - e^{-b(t-t_0-T_0)}).
\]

Hence, for \( t \geq t_0 + T_0 + T_1 \), it has

\[
x(t) > \frac{s}{b} (1 - e^{-b(t-t_0-T_0)}) = \frac{s}{b} (1 - e^{-b T_1}) = x^0 > x^*.
\]

(11)

It follows from (11) that, for \( t \geq t_0 + T_0 + T_1 + \tau \),

\[
\dot{V}(t) = \delta (x(t - \tau) - x^*) v(t - \tau) > \delta (x^0 - x^*) v(t - \tau).
\]

(12)
According to Lemma 4.1, for $\varepsilon = \eta_0/2 > 0$, there exists $T_2 \geq t_0 + T_0 + T_1 + 2\tau$ such that $v(t) > \eta_0/2$ for $t \geq T_2$. Thus, it has that, for all $t \geq t_0 + T_0 + T_1 + 2\tau$,

$$V(t) > \delta \eta_0 (x^0 - x^*)/2 > 0,$$

which clearly implies that $V(t) \to +\infty$ as $t \to +\infty$. Since any solution $(x(t), y(t), v(t))$ of the model (2) with the initial conditions (3) is bounded for all $t \geq 0$, it has that the function $V(t)$ is also bounded for all $t \geq 0$. This is a contradiction to $V(t) \to +\infty (t \to +\infty)$. The claim is proved.

In the rest, there are two cases to be discussed.

(i) $y(t) \geq y^*/2$ for all large $t$.

(ii) $y(t)$ oscillates about $y^*/2$ for all large $t$.

For the case (i), it clearly has that

$$\liminf_{t \to +\infty} y(t) \geq (y^*/2)e^{-p(T_0 + T_1 + a + \tau)} = v_2.$$

Let us consider the case (ii). Let $t_1$ and $t_2$ be sufficiently large such that

$$y(t_1) = y(t_2) = \frac{1}{2}y^*,$$

$$y(t) < \frac{1}{2}y^* (t_1 < t < t_2). \quad (13)$$

If $t_2 - t_1 \leq T_0 + T_1 + a + \tau$, from the second equation of the model (2), it has

$$\dot{y}(t) > -py(t).$$

Hence, for $t_1 \leq t \leq t_2$, it has

$$y(t) \geq y(t_1)e^{-p(t-t_1)} \geq (y^*/2)e^{-p(T_0 + T_1 + a + \tau)} = v_2.$$

If $t_2 - t_1 > T_0 + T_1 + a + \tau$, it is easily obtained that $y(t) \geq v_2$ for $t \in [t_1, t_1 + T_0 + T_1 + a + \tau]$. Then, proceeding exactly as the proof above, it can be shown that $y(t) \geq v_2$ for $t \in [t_1 + T_0 + T_1 + a + \tau, t_2]$.

In fact, if not, there exists a $T_3 > 0$ such that $y(t) \geq v_2$ for $t_1 \leq t \leq t_1 + T_0 + T_1 + a + \tau + T_3$, $y(t_1 + T_0 + T_1 + a + \tau + T_3) = v_2$ and $\dot{y}(t_1 + T_0 + T_1 + a + \tau + T_3) \leq 0$. On the other hand, if $t_1 \leq t \leq t_1 + T_0 + T_1 + a + \tau + T_3$, it has from the third equation of the model (2) that

$$\dot{v}(t) = ky(t) - uv(t) \geq kv_2 - uv(t),$$

where $q = x^*/x^0 < 1$. There the following two subcases to be discussed.

(ii) $v(t_1) \geq kv_2/u$. It has that, for $t_1 \leq t \leq t_1 + T_0 + T_1 + a + \tau + T_3$,

$$v(t) \geq \left(v(t_1) - \frac{kv_2}{u}\right)e^{-u(t-t_1)} + \frac{kv_2}{u} \geq \frac{kv_2}{u}.$$

Furthermore, for $t = t_1 + T_0 + T_1 + a + \tau + T_3$, it has from the second equation of the model (2) that

$$\dot{y}(t) = \delta x(t - \tau)v(t - \tau) - py(t) \geq \frac{qk\delta v_2}{u}x(t - \tau) - pv_2 \geq \frac{qk\delta v_2}{pu}x^0 - 1 \geq pv_2 \left(\frac{qk\delta v_2}{pu}x^0 - 1\right) = 0. \quad (14)$$

This is a contradiction to $\dot{y}(t_1 + T_0 + T_1 + a + \tau + T_3) \leq 0$.

(ii) $v(t_1) < kv_2/u$. Define

$$\bar{t} = \sup\{t \in (t_1, t_1 + T_0 + T_1 + a + T_3) \mid v(s) < \frac{kv_2}{u}, s \in (t_1, t)\}.$$
Then, it has \( v(\bar{t}) \leq qkv_2/u \) holds for \( \bar{t} \in (t_1, t_1 + T_0 + T_1 + a + T_3) \). From the third equation of the model (2), it has

\[
\dot{v}(t) = ky(t) - uv(t) \geq k v_2 (1 - q).
\]

Integrating from \( t_1 \) to \( \bar{t} \) leads

\[
k v_2 (1 - q) (\bar{t} - t_1) \leq v(\bar{t}) - v(t_1) < \frac{qkv_2}{u}.
\]

Therefore, it has \( \bar{t} - t_1 < q/(u(1-q)) = a \). Consequently, \( \bar{t} \in (t_1, t_1 + T_0 + T_1 + a + T_3) \), it has \( v(\bar{t}) = qkv_2/u \). Since

\[
\dot{v}(t) \geq qkv_2 - uv(t),
\]

it has that, for \( t \in [\bar{t}, t_1 + T_0 + T_1 + a + \tau + T_3] \),

\[
v(t) \geq \left( v(\bar{t}) - \frac{qkv_2}{u} \right) e^{-u(t-\bar{t})} + \frac{qkv_2}{u} = \frac{qkv_2}{u}.
\]

Therefore, (14) is satisfied, that means that \( \dot{y}(t_1 + T_0 + T_1 + a + \tau + T_3) > 0 \), which is a contradiction to \( \dot{y}(t_1 + T_0 + T_1 + a + \tau + T_3) \leq 0 \).

Finally, it has \( y(t) \geq v_2 \) for \( t \in [t_1, t_2] \). Since this kind of interval \([t_1, t_2]\) is chosen in an arbitrary way, it has \( y(t) \geq v_2 \) holds for any sufficiently large \( t \). Hence, \( \liminf_{t \to +\infty} y(t) \geq v_2 \). Moreover, according to the third equation of the model (2), it easily has that

\[
\liminf_{t \to +\infty} v(t) \geq k v_2/u = v_3.
\]

Remark 1. From Lemma 4.1 and the third equation of the model (2), it has \( \liminf_{t \to +\infty} v(t) \geq k\eta_0/u \). Therefore, from a point of view in mathematics, both Lemma 4.1 and Theorem 4.2 give completely the same conclusion for the uniform persistence of the model (2). On the other hand, comparing Theorem 4.2 with Lemma 4.1, the explicit lower bounds \( v_1, v_2 \) and \( v_3 \) of \( \liminf_{t \to +\infty} x(t) \), \( \liminf_{t \to +\infty} y(t) \) and \( \liminf_{t \to +\infty} v(t) \) are given in Theorem 4.2 by using some analytic techniques. Hence, both in mathematics and biology, Theorem 4.2 gives more practical meaning.

5. Numerical simulations. In Sections 3-4, the analysis of the global asymptotic properties of the infection-free equilibria \( E_0 = (x_0, 0, 0) \) and the infected equilibria \( E^* = (x^*, y^*, v^*) \) are given. In this section, let us give some numerical simulations to summarize the applications of the results.

Figure 1 shows that the solutions of the model (2) converge to the infection-free equilibrium \( E_0 = (x_0, 0, 0) \) as \( t \to +\infty \). Figure 2 shows that the solutions of the model (2) converge to the infected equilibrium \( E_1 = (x^*, y^*, v^*) \) as \( t \to +\infty \). Furthermore, it should be mentioned here that Figure 2 strongly suggest that the infected equilibrium \( E^* = (x^*, y^*, v^*) \) should be globally asymptotically stable for any time delay \( \tau > 0 \). However, it seems that it is not easy work to give a proof by constructing suitable Lyapunov functionals or using other methods!
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Figure 1. The orbits of the model (2) with $E_0 = (x_0, 0, 0) = (10300, 0, 0)$ and $R_0 \approx 0.99 < 1$. $c = \beta/100$, and all the other parameters $s$, $d$, $\beta$, $\delta$, $p$ and $u$ are chosen from [26].

Figure 2. The orbits of the model (2) with $E^* = (x^*, y^*, v^*) \approx (1107, 340, 127713)$ and $R_0 \approx 9.31 > 1$. $c = \beta/100$, and all the other parameters $s$, $d$, $\beta$, $\delta$, $p$ and $u$ are chosen from [26].

6. Conclusions. In this section, let us give a summary on the main results of the paper. First, motivated by the classic model (1) and some biological meanings, the model (2) is proposed. In the model (2), inhibitory effect on the growth of uninfected cells by infected cells is considered by introducing the mass action function $cx(t)y(t)$. Then, the existence of the infection-free equilibrium $E_0 = (x_0, 0, 0)$ and the infected equilibrium $E^* = (x^*, y^*, v^*)$ are discussed by using the basic reproductive ratio $R_0 = sk\delta/pdu$. It is found that the the basic reproductive ratio $R_0$ for the model (2) is completely the same as that for the model (1) and is independent of the constant $c$ which reflects inhibitory effect on the growth of uninfected cells by infected cells. Furthermore, the value of $x^*$ is also independent on the constant $c$, and the values of $y^*$ and $v^*$ are the decreasing functions with respect to the variable $c$. In biology, these phenomenon can be explained as follows. From the first equation of the model (2), it has that, infected cells have inhibitory effect on the growth of uninfected cells. Hence, the number of infected cells will decrease, which further results in the decrease of the number of virus particles. The decrease of virus particles results in the decrease of the amount of uninfected cells which are becoming infected cells.

In Theorem 3.1, completed theoretical analysis of global asymptotic property of the infection-free equilibrium $E_0 = (x_0, 0, 0)$ (see Figure 1) and local asymptotic property of the infected equilibrium $E^* = (x^*, y^*, v^*)$ are given. In Theorem 4.2, uniform persistence of the model (2) is considered. Notice the definition of uniform
persistence, it has from Theorems 3.1 and 4.2 that, the basic reproductive ratio \( R_0 = \frac{sk\delta}{pdv} \) completely determines whether virus particles can be removed. Finally, numerical simulations suggest that the time delay also has no effect on global asymptotic properties of the infected equilibrium \( E_1 \) of the HIV infection model.

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