Global stability for a delayed HIV-1 infection model with nonlinear incidence of infection

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Keywords: Time delay, Global stability, Lyapunov functional, Nonlinear incidence

Abstract

In this paper, a delayed HIV-1 infection model with nonlinear incidence of infection is reinvestigated. It is shown that if the reproduction number $R_0 > 1$, then the system is permanent, and the infective equilibrium of the system is globally asymptotically stable. Thus, the global dynamics of the system is completely determined by the reproduction number $R_0$. The results obtained enrich and improve the corresponding results given by Wang et al. [X. Wang, Y. Tao, X. Song, A delayed HIV-1 infection model with Beddington–DeAngelis functional response, Nonlinear Dynamics 62 (2010) 67–72]. The conclusions we established also verify the numerical simulation results on the global asymptotic stability of the infective equilibrium in the paper [D. Li, W. Ma, Asymptotic properties of an HIV-1 infection model with time delay, J. Math. Anal. Appl. 335 (2007) 683–691].

1. Introduction

In recent years, dynamic models of HIV-1 infection with or without time delay have received much attention and many excellent results have been obtained (see [1–12]). Dynamics of a basic HIV-1 infection model [10–12] can be described by the following simple differential equations

$$
\begin{align*}
\frac{dT}{dt} &= s - dT - \beta T V,
\frac{dI}{dt} &= \beta T V - pI,
\frac{dV}{dt} &= kl(t) - \mu V,
\end{align*}
$$

where $T(t), I(t),$ and $V(t)$ denote the concentration of uninfected target cells, infected cells that produce virus, and HIV-1 virus particles at time $t$, respectively. Parameter $s$ is the rate at which new target cells are generated, $d$ is the death rate of uninfected target cells, $p$ is the death rate of infected cells. Free virus is produced from the infected cells at the rate $kl(t)$. Parameter $\mu$ is the rate at which HIV-1 virus particles are removed from the immune system. It is assumed that the incidence rate of HIV-1 infection is given by the product of the numbers of uninfected target cells and free virus particles, namely $\beta T(t) V(t)$. All parameters are positive constants. In paper [13,14], it has been shown that the global dynamics of the model is completely determined by the basic reproduction number $R_0 = \frac{s\beta}{d\mu}$. Based on system (1.1), Li and Shu [15] consider an in-host viral model with intracellular delay, and show that the underlying mechanism for sustained oscillation in in-host models...
is the target cell divisions, rather than intracellular delays. They found that ignoring the delay will produce overestimation of
the reproduction number. Recently, some viral infection mathematical models with the nonlinear incidence rate are investi-
gated by some authors [16–20]. We shall mainly refer to the paper [19], where a delayed HIV-1 infection model with non-
linear incidence of infection is analyzed. They consider the nonlinear incidence of infection as Holling type II functional
response or a saturation response in the model. Their results show that intracellular delay and the nonlinear incidence have
no effect on both global asymptotic properties of the virus free equilibrium and local asymptotic properties of the infective
equilibrium. However, the global stability of the infective equilibrium is not rigorously proved. They only pointed out that
the time delay may have no effect on the stability of the infective equilibrium by numerical simulations. Recently, based on
some biological meaning and paper [17], Wang et al. [21] have investigated the following delayed HIV-1 infection model

\[
\begin{align*}
\dot{T}(t) &= s - dT(t) - \frac{d(t)VT(t)}{\alpha + d(t)TV(t)}, \\
\dot{I}(t) &= e^{-\gamma t} - \frac{\beta(t)I(t)V(t)}{\alpha + \beta(t)I(t)V(t)} - pI(t), \\
\dot{V}(t) &= kl(t) - \mu V(t),
\end{align*}
\]  

where the state variables, \(T(t), I(t), V(t)\), and parameters \(s, d, \beta, p, k, \mu\) and \(\gamma\) have the same biological meanings as in the model
(1.1). We refer the readers to paper [21]. Here, \(\gamma\) is assumed a constant death rate for infected but not yet virus-producing
cells. The term \(e^{-\gamma t}\) accounts for the probability of surviving cells that are infected at time \(t\), but that die before becoming
productively infected \(\tau\) time units later [12]. Since in addition to background mortality, productive cells are visible to the
immune system, \(\gamma\) may not be equal to \(p\). The initial conditions for (1.2) are

\[
T(\theta) = \phi_1(\theta), \quad I(\theta) = \phi_2(\theta), \quad V(\theta) = \phi_3(\theta), \quad \theta \in [-\tau, 0], \quad \phi_i(0) > 0, \quad i = 1, 2, 3.
\]  

The global stability of the infection-free equilibrium and the local stability of the infective equilibrium of system (1.2) have been investigated in [21]. It has been shown that if the reproduction number \(\mathcal{R}\) is less than one, then the infection-free equilibrium is globally asymptotically stable. If \(\mathcal{R}\) is greater than one, then the infective equilibrium is locally asymptotically stable. However, the global stability of the infective equilibrium of system (1.2) is still unresolved. Recently, by constructing

Lyapunov function, Huang et al. [18] have established the global stability of the infective equilibrium of system (1.2) without
time delay.

Although the models incorporation of time delay have more real biological meaning, they are difficult to deal with it
mathematically. However, the Lyapunov functional and the LaSalle-type theorem in [22] can provide a direct and effective
method to establish global dynamical properties for the system of those nonlinear functional differential equations. Recently,
Korobeinikov [23,24], Cai et al. [25], McCluskey [26,27] and Huang et al. [28] have investigated the global dynamical prop-
erties of epidemiological models with and without delay by constructing suitable Lyapunov functional methods.

Inspired by the work in McCluskey [26] and Li and Shu [15], Huang et al. [18], we constructing a global Lyapunov func-
tional, and show that the infective equilibrium of system (1.2) is globally asymptotically stable if \(\mathcal{R} > 1\). Furthermore, we apply Hale and Waltman’s persistence theory (see [29], we also refer to Thieme [30]). For its applications, we refer the reader to Pawelek et al. [31], Lou and Zhao [32], and Qiu et al. [33], and show that if the reproduction number \(\mathcal{R} > 1\), then the system (1.2) is permanent.

This paper is organized as follows: The permanent results of system (1.2) are obtained in Section 2; In Section 3, we gives
our main result, the global stability of the infective equilibrium of system (1.2) for \(\mathcal{R} > 1\). We end the paper with some brief
remarks.

2. Permanence of system (1.2)

In this section, we shall explore under which conditions the populations of system (1.2) will coexist permanently. Before
we deal with this problem, we state some permanent results from [21].

System (1.2) has always an infection-free equilibrium \(E_0(\frac{s}{\mu}, 0, 0)\). The reproduction number of system (1.2) is

\[
\mathcal{R} = \frac{e^{-\gamma t}sk\beta}{as\mu + dp\mu}.
\]

If \(\mathcal{R} \leq 1\), then \(E_0\) is the unique equilibrium. If \(\mathcal{R} > 1\), then system (1.2) has a unique infective equilibrium
\(E = (T^*, I^*, V^*)\), where,

\[
T^* = \frac{p\mu + kbs}{k\beta e^{-\gamma t} + bdk - ap\mu}, \quad I^* = \frac{s\beta k}{p(k\beta e^{-\gamma t} + bdk - ap\mu)} \left(1 - \frac{1}{\mathcal{R}}\right), \quad V^* = \frac{s\beta k^2}{p\mu(k\beta e^{-\gamma t} + bdk - ap\mu)} \left(1 - \frac{1}{\mathcal{R}}\right).
\]  

Proposition 2.1. All solutions \((T(t), I(t), V(t))\) of system (1.2) satisfying conditions (1.3) exist and are always positive and
bounded for all \(t > 0\).
Theorem 2.1. If \( \Re \leq 1 \), then the infection-free equilibrium \( E_0 \) of system (1.2) is globally asymptotically stable for all \( \tau \geq 0 \).

Theorem 2.2. If \( \Re > 1 \), then the infective equilibrium \( E' \) of system (1.2) is locally asymptotically stable for all \( \tau \geq 0 \).

Now we give a result on the uniform persistence of system (1.2). Here we apply the persistence theory for infinite-dimensional systems from paper [29]. We also refer to Thieme [30]. The methods and techniques have been recently employed in papers [31–34] for a discrete delay system.

To proceed, we introduce the following notation and terminology. Let \( X = C([-\tau, 0], \mathbb{R}^3) \) be the Banach space of continuous functions mapping the interval \([-\tau, 0]\) into \( \mathbb{R}^3 \), which equipped with the sup-norm. \( X^0 = \{(\phi_1, \phi_2, \phi_3) \in X : \phi_2(0) > 0, \phi_3(0) > 0, 0, 0 \in [-\tau, 0]\}, \partial X = X/ X^0 = \{(\phi_1, \phi_2, \phi_3) \in X : \phi_2(0) = 0, \text{ or } \phi_3(0) = 0, 0, 0 \in [-\tau, 0]\} = X_0. \) Denote \( P(t) \), for \( t \geq 0 \) as the family of solution operators corresponding to (1.2). Define the \( \omega \)-limit as \( \omega(x) := \{y \in X \} \) there exists a sequence \( t_n \to \infty \) as \( n \to \infty \) with \( P(t_n)x \to y \) as \( n \to \infty \). The following result is referred to ([29], Theorem 4.2):

**Lemma 2.3.** Suppose that we have the following:

(i) \( X^0 \) is open and dense in \( X \) with \( X^0 \cup X_0 = X \) and \( X^0 \cap X_0 = \emptyset \);

(ii) the solution operators \( P(t) \) satisfy \( P(t) : X^0 \to X^0 \); \( P(t) : X_0 \to X_0 \);

(iii) \( P(t) \) is point dissipative in \( X \);

(iv) \( \gamma(U) \) is bounded in \( X \) if \( U \) is bounded in \( X \);

(v) \( P(t) \) is asymptotically smooth;

(vi) \( \Omega_2 = \bigcup_{\phi} \omega(x) \) is isolated and has acyclic covering \( N \), where \( \Omega_2 \) is the global attractor of \( P(t) \) restricted to \( X_0 \) and \( N = \bigcap_{\phi} N \); 

(vii) for each \( N_i \in N \), \( W^i(N_i) \cap X^0 = \emptyset \), where \( W^i \) refers to the stable set.

Then \( P(t) \) is a uniform repeller with respect to \( X_0 \), i.e., there is an \( \eta > 0 \) such that for any \( x \in X_0 \), \( \liminf_{t \to +\infty} d(P(t), X_0) \geq \eta \).

**Theorem 2.4.** If \( \Re > 1 \), then system (1.2) is uniformly persistent in \( \text{Int}^\tau \), i.e., there exists a constant \( 0 < \eta < 1 \) (independent of initial conditions), such that any solution \( (T(t), I(t), V(t)) \) of (1.2) satisfy \( \liminf_{t \to +\infty} T(t) > \eta \), \( \liminf_{t \to +\infty} I(t) > \eta \), \( \liminf_{t \to +\infty} V(t) > \eta \).

**Proof.** By Proposition 2.1, it is straightforward to see that (i)–(v) of Lemma 2.3 always hold. Thus, we only need to verify the conditions (vi) and (vii). To do this, we set

\( M_\delta = \{\phi \in X : P(t)\phi \text{ satisfies system (1.2) and } P(t)\phi \in \partial X, \forall t \geq 0\} \).

We first claim that \( M_\delta = \{\{0, 0\}\} \). Assuming \( P(t) \in M_\delta \), \( \forall t \geq 0, \) it suffices to show that \( I(t) = V(t) = 0, \forall t \geq 0 \). We proceed to prove this assertion by contradiction. Assume that on the contrary, there exists \( t_0 > 0 \) such that either (a) \( I(t_0) > 0, V(t_0) = 0 \); or (b) \( I(t_0) = 0, V(t_0) > 0 \).

In case (a), from the third equation of (1.2), we have

\[ V(t) |_{t=t_0} = kl(t_0) > 0. \]

Hence, there is a sufficiently small constant \( \epsilon_0 \) such that \( V(t) > 0, \forall t \in (t_0, t_0 + \epsilon_0) \). On the other hand, from \( I(t_0) > 0 \), we obtain a positive \( \epsilon_1 (0 < \epsilon_1 < \epsilon_0) \). Thus, we obtain \( I(t) > 0, V(t) > 0, \forall t \in (t_0, t_0 + \epsilon_1) \). This is in contradiction with the assumption that \( (T(t), I(t), V(t)) \in M_\delta, \forall t \geq 0 \). Similarly, we can show the case (b) does not hold.

Let \( \Omega_2 = \bigcup_{\phi} \omega(x) \), where \( \Omega_2 \) is the global attractor of \( P(t) \) restricted to \( \partial X \). We now show that \( \Omega_2 = \{E_0\} \). In fact, it follows from \( \Omega_2 \subseteq M_\delta \) and the first equations of (1.2). We have \( \lim_{t \to +\infty} T(t) = \frac{\beta}{d} \). Thus, \( \{E_0\} \) is the isolated invariant set in \( X \).

Now we need to show that \( W^i(E_0) \cap X^0 = \emptyset \). Assume that on the contrary, there exists a positive orbit \( (T(t), I(t), V(t)) \in X^0 \) of (1.2) such that

\[ \lim_{t \to +\infty} T(t) = \frac{\beta}{d} \quad \lim_{t \to +\infty} I(t) = 0 \quad \lim_{t \to +\infty} V(t) = 0. \quad (2.2) \]

Then, for any sufficiently small enough constant \( \epsilon > 0 \), there exists a positive constant \( T_0 = T_0(\epsilon) \), such that

\[ T(t) > \frac{\beta}{d} - \epsilon > 0, \quad V(t) < \epsilon, \quad \forall t \geq T_0. \quad (2.3) \]

Thus, for the chosen constant \( \epsilon \), it follows from system (1.2) that, for \( t \geq T_0 + \tau \),

\[ \dot{I}(t) \geq e^{-\tauT} \frac{\beta(\alpha + \epsilon)}{d + \alpha(\alpha + \epsilon)} - p(t), \]

\[ \dot{V}(t) = kT(t) - \mu V(t). \quad (2.4) \]
System (2.4) has the following significant properties: The right-hand side of the first equation is increasing as a function of the delayed variable \(V(t - \tau)\), and the right-hand side of the second equation increases with respect to \(I(t)\). These properties give the system (2.4) a quasi-monotone structure.

To apply comparison principle, we consider the following differential system:

\[
\begin{align*}
\dot{u}_1(t) &= e^{-\tau \gamma} \beta(s/d - \delta) u_1(t - \tau) u_2(t - \tau) - pu_1(t), \\
\dot{u}_2(t) &= ku_1(t) - \mu u_2(t), \quad t \geq T_0 + \tau,
\end{align*}
\]

with the initial condition \(u_1(t) = h(t), \quad u_2(t) = V(t), \quad \forall t \in [T_0, T_0 + \tau]\). Obviously, all solutions \((u_1(t), u_2(t))\) of system (2.5) are nonnegative.

To verify the conditions of Theorem 5.1.1 on Page 78 of [35], we follow the notations of Theorem 5.1.1 and define \((f_1(t, \phi_1), f_2(t, \phi_2)) = (I(t, \phi_1), V(t, \phi_1), \phi_1(0), \phi_2(0)) = (u_1(t, \phi_2), u_2(t, \phi_2))\).

From Proposition 2.1, we know \(I(t), V(t)\) is bounded. Thus, for (2.4) and (2.5), it is obvious that \((f_1(t, \phi_1), f_2(t, \phi_2))\) and \((g_1(t, \phi_2), g_2(t, \phi_2))\) are continuous, Lipschitz on each compact subset of \(X\), and \((f_1(t, \phi_2), f_2(t, \phi_2))\) satisfies the condition \((Q)\): whenever \(\phi \leq \psi\) and \(\phi(0) = \psi(0)\) for some \(i\), then \(f_i(\phi) \leq f_i(\psi)\). Hence, in system (2.4), all the conditions of Theorem 5.1.1 [35] are satisfied. In (2.2), since we have assumed that \(I(t) \to 0\) and \(V(t) \to 0\) as \(t \to \infty\), thus, by a comparison principle (Theorem 5.1.1 on Page 78 [35]), the solutions \((u_1(t), u_2(t))\) of system (2.5) with the above initial conditions converge to \((0, 0)\) as well.

Set

\[
\bar{W}(t) = u_1(t) + \frac{e^{-\tau \gamma} \beta(s/d - \delta)}{\mu(1 + a(s/d - \delta) + b\epsilon)} u_2(t) + \frac{e^{-\tau \gamma} \beta(s/d - \delta)}{1 + a(s/d - \delta) + b\epsilon} \int_{t-\tau}^t u_2(\theta) d\theta.
\]

From the solutions \((u_1(t), u_2(t)) \to (0, 0)\) as \(t \to \infty\), we obtain

\[
\lim_{t \to +\infty} \bar{W}(t) = 0.
\]

On the other hand, by calculating the time derivative of \(\bar{W}(t)\) along the positive solution of system (2.5), we obtain

\[
\frac{d\bar{W}(t)}{dt} \big|_{(2.5)} = \left[ \frac{ke^{-\tau \gamma} \beta(s/d - \delta)}{\mu(1 + a(s/d - \delta) + b\epsilon)} - p \right] u_1(t)
\]

Since \(\Re > 1\), we can choose a sufficiently small constant \(\epsilon\) such that

\[
\frac{ke^{-\tau \gamma} \beta(s/d - \delta)}{\mu(1 + a(s/d - \delta) + b\epsilon)} - p > 0.
\]

Therefore, \(\bar{W}(t)\) goes to either infinity or a positive number as \(t \to \infty\). This is a contradiction to Eq. (2.6). Thus, we have \(W^*(E_0) \cap X^0 = \emptyset\). By applying Lemma 2.3 we obtain that for some constant \(\eta_1 > 0\)

\[
\lim inf_{t \to +\infty} I(t) > \eta_1, \quad \text{and} \quad \lim inf_{t \to +\infty} V(t) > \eta_1.
\]

From the first equation of system (1.2), one can show that

\[
\hat{T}(t) \geq s - dT(t) - \frac{\beta T(t)}{b}, \quad \text{for large } t.
\]

This shows that \(T(t)\) is uniformly bounded away from zero. That is, there exists a constant \(\eta_2 > 0\) such that \(\lim inf_{t \to +\infty} T(t) > \eta_2\).

This completes the proof of Theorem 2.4.

### 3. Global asymptotic stability for \(\Re > 1\)

In this section, we shall analyze the global asymptotic stability of the infective equilibrium \(E'(T^*, I^*, V^*)\) in system (1.2) by using the method of Lyapunov functional. We recall that the infective equilibrium \(E'(T^*, I^*, V^*)\) exists if and only if \(\Re > 1\). We have the following result:

**Theorem 3.1.** If \(\Re > 1\), then the infective equilibrium \(E'(T^*, I^*, V^*)\) system (1.2) is globally asymptotically stable.

**Proof.** In order to simplify the expressions which follow, we first note that the infective equilibrium \(E'\) satisfies the following relation

\[
s - dT' = \frac{\beta T' V'}{1 + aT' + bV'}, \quad \frac{\beta T' V'}{1 + aT' + bV'} = p e^{\tau \gamma} I', \quad k l' = \mu V'.
\]

(3.1)
Let \( g(x) = x - 1 - \ln x \), \( x \in \mathbb{R}_+ \). Then, \( g : \mathbb{R}_+ \rightarrow \mathbb{R}_+ \) has the strict global minimum at \( x = 1 \) and \( g(1) = 0 \). With \( g(x) = x - 1 - \ln x \), we define the following Lyapunov functional

\[
W(t) = W_1(t) + W_2(t) + W_3(t) + W_4(t),
\]

where

\[
W_1(t) = \left( \frac{1 + bV^*}{1 + aT^* + bV^*} \right) T(t), \quad W_2(t) = e^{\gamma T} \left( \frac{I(t)}{T} \right),
\]

\[
W_3(t) = \frac{p}{k} e^{\gamma V} g \left( \frac{V(t)}{V} \right), \quad W_4(t) = p e^{\gamma T} \int_{-\tau}^0 g \left( \frac{(I(t) + V(t))}{pe^{\gamma \tau}} \right) dt.
\]

(3.2)

Here, \( T_1(t) = T(t + \theta), V_1(t) = V(t + \theta) \) for \( \theta \in [0, \tau] \). Thus, we have \( T_1(t) = T(t), V_1(t) = V(t) \) in this notation, and \( g(x) \geq 0 \), for \( x > 0 \). Thus, \( W(t) \geq 0 \) with equality if and only if \( \frac{T}{T(t)} = \frac{I}{t} = 1, \frac{V}{V(t)} = 1 \) for all \( \theta \in [0, \tau] \).

Because of the complexity of the above expressions, we calculate derivative of each component of the Lyapunov functional, separately.

Calculating the time derivative of \( W_i(t) \) for \( i = 1, \ldots, 4 \), along the positive solution of system (1.2), respectively, we obtain

\[
W_1(t)_{|_{i=1,2}} = \frac{1 + bV^*}{1 + aT^* + bV^*} \left( 1 - \frac{T}{T(t)} \right) \frac{\dot{T}(t)}{T(t)} = \frac{T(t) - T - aT(t)T + bT(t)V - bT'V^*}{T(t)(1 + aT + bV^*)} \frac{T(t)}{T(t)}
\]

\[
= \left( 1 - \frac{T}{T(t)} \right) \left( \frac{1 + aT + bV^*}{T(t)(1 + aT + bV^*)} \right) \left( s - \frac{\beta(t) V(t)}{1 + aT(t) + bV(t)} \right)
\]

\[
= \left( 1 - \frac{T}{T(t)} \right) \left( \frac{1 + aT + bV^*}{T(t)(1 + aT + bV^*)} \right) \left( d(T - T(t)) + pe^{\gamma T} \frac{\beta(t) V(t)}{1 + aT(t) + bV(t)} \right)
\]

\[
= d(T - T(t)) \left( 1 - \frac{T}{T(t)} \right) \left( \frac{1 + aT + bV^*}{T(t)(1 + aT + bV^*)} \right) + pe^{\gamma T} \frac{\beta(t) V(t)}{1 + aT(t) + bV(t)} - \frac{\beta(t) V(t)}{T(t)(1 + aT(t) + bV(t))} - \frac{pe^{\gamma T}}{T(t)(1 + aT(t) + bV(t))}
\]

(3.3)

\[
W_2(t)_{|_{i=1,2}} = \gamma e^{\gamma T} \left( 1 - \frac{I}{I(t)} \right) \frac{\dot{I}(t)}{I(t)} = e^{\gamma T} \left( 1 - \frac{I}{I(t)} \right) \left( e^{\gamma T} \frac{\beta(t - \tau) V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)} - p\dot{I}(t) \right)
\]

\[
= \beta(t - \tau) V(t - \tau) \frac{\dot{I}(t)}{I(t)(1 + aT(t - \tau) + bV(t - \tau))} + pe^{\gamma T} \frac{\beta(t - \tau) V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)} + pe^{\gamma T} \frac{\dot{I}(t) V(t)}{V(t)}
\]

(3.4)

\[
W_3(t)_{|_{i=1,2}} = \frac{p}{k} e^{\gamma V} \left( 1 - \frac{V}{V(t)} \right) \frac{\dot{V}(t)}{V(t)} = \frac{p}{k} e^{\gamma V} \left( 1 - \frac{V}{V(t)} \right) \left( k(t) - \mu V(t) \right)
\]

\[
= pe^{\gamma T} \left( 1 - \frac{V}{V(t)} \right) \frac{\dot{V}(t)}{V(t)} = \frac{p}{k} e^{\gamma V} \mu V(t) - pe^{\gamma T} \frac{\dot{V}(t)}{V(t)}
\]

(3.5)

Following the method given in [26], we obtain the time derivative of \( W_4(t) \)

\[
\dot{W}_4(t)_{|_{i=1,2}} = pe^{\gamma T} \int_{-\tau}^0 \frac{d}{dt} g \left( \frac{(I(t) + V(t))}{pe^{\gamma \tau}} \right) \frac{d\theta}{dt} = pe^{\gamma T} \int_{-\tau}^0 \frac{d}{d\theta} g \left( \frac{(I(t) + V(t))}{pe^{\gamma \tau}} \right) d\theta
\]

\[
= \beta(t) V(t) \left( 1 + aT(t) + bV(t) \right) - pe^{\gamma T} \frac{\beta(t) V(t)}{1 + aT(t) + bV(t)} + \frac{\beta(t - \tau) V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)} + pe^{\gamma T} \frac{\dot{I}(t) V(t)}{V(t)}
\]

\[
\times \ln \frac{\beta(t)}{1 + aT(t) + bV(t)} - \frac{\beta(t - \tau) V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)}.
\]

(3.6)

Adding all the four components of the Lyapunov functional, we obtain

\[
\dot{W}(t)_{|_{i=1,2}} = d(T - T(t)) \left( 1 - \frac{T}{T(t)} \right) \left( 1 + aT(t) + bV(t) \right)
\]

\[
+ pe^{\gamma T} \frac{T(t)}{T(t)(1 + aT(t) + bV(t))} - \frac{\beta(t) V(t)}{1 + aT(t) + bV(t)} - \frac{\beta(t - \tau) V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)} + pe^{\gamma T} \frac{\dot{I}(t) V(t)}{V(t)}
\]

\[
+ pe^{\gamma T} \ln \frac{\beta(t)}{1 + aT(t) + bV(t)} + pe^{\gamma T} \ln \frac{\beta(t - \tau) V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)}.
\]

(3.7)
Eq. (3.7) can be rewritten in the following manner
\[
W(t)_{|12} = d(T' - T(t))\left(1 - \frac{T'(1 + aT(t) + bV(t))}{T(t)(1 + aT + bV)}\right) + p\epsilon^t I\left(1 - \frac{T'(1 + aT + bV)}{T(t)(1 + aT + bV)}\right) + V(t)(1 + aT(t) + bV) + V(t)(1 + aT + bV)
\]
\[
- p\epsilon^t F\left[\Gamma \beta(t - \tau) V(t - \tau) + 1 - \ln \frac{p\epsilon^t I(t)(1 + aT(t) + bV(t - \tau))}{1 + aT(t - \tau) + bV(t - \tau)}\right]
\]
\[
- \frac{p\epsilon^t e^{\gamma t}}{V(t)T} - 1 - \ln \frac{p\epsilon^t e^{\gamma t}(1 + aT(t) + bV(t - \tau))}{1 + aT(t - \tau) + bV(t - \tau)} + V(t)
\]
\[
+ \ln \frac{\beta(t)(t - \tau)V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)} - \ln \frac{\beta(t)(t - \tau)V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)}.
\] (3.8)

Notice that
\[
\ln \frac{\beta(t)(t - \tau)V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)} = \ln \frac{V(t)}{V(t)T} + \ln \frac{\beta(t)V(t)}{1 + aT(t) + bV(t)} - \ln \frac{\beta(t)(t - \tau)V(t - \tau)}{1 + aT(t - \tau) + bV(t - \tau)}
\] (3.9)

Thus, by direct calculation, we have
\[
1 - \frac{T'(1 + aT(t) + bV(t))}{V(t)} = \frac{V(t)(1 + aT(t) + bV)}{V(t)(1 + aT(t) + bV)} - \ln \frac{T(t)(1 + aT(t) + bV(t))}{T(t)(1 + aT(t) + bV(t))}
\]
\[
= \frac{V(t)(1 + aT(t) + bV)}{V(t)(1 + aT(t) + bV)} - 1 - \frac{1 + aT(t) + bV(t)}{1 + aT(t) + bV(t)} - g\left(\frac{T'(1 + aT(t) + bV)}{T(t)(1 + aT(t) + bV(t))}\right) - g\left(\frac{1 + aT(t) + bV(t)}{1 + aT(t) + bV(t)}\right)
\] (3.10)

and,
\[
d(T' - T(t))\left(1 - \frac{T'(1 + aT(t) + bV(t))}{T(t)(1 + aT + bV)}\right) = -d(T' - T(t))^2 T'(1 + bV(t))
\] (3.11)

By (3.10) and (3.11), Eq. (3.8) can be reduced to the following equation
\[
W(t)_{|12} = -d(T' - T(t))^2 T'(1 + bV(t)) - \frac{b\epsilon^t e^{\gamma t}(1 + aT(t))(V(t) - V')}{1 + aT(t) + bV(t)} - \frac{p\epsilon^t e^{\gamma t}(1 + aT(t) + bV(t)(1 + aT(t) + bV))V'}{1 + aT(t) + bV(t)}
\]
\[
- p\epsilon^t g\left(\frac{T'(1 + aT(t) + bV(t)}{T(t)(1 + aT(t) + bV(t))}\right) - p\epsilon^t g\left(\frac{1 + aT(t) + bV(t)}{1 + aT(t) + bV(t)}\right)
\] (3.12)

By (3.12), and that \(g(t) \geq 0\) with equality only if the argument is 1, we see that \(W(t)_{|12} \leq 0\) holds for all \(T(t), I(t), V(t) > 0\).

And if \(W(t)_{|12} = 0\), we can obtain \(T(t) = T', I(t) = I', V(t) = V'\) for all \(t > 0\). The largest compact invariant set in \(\Gamma = \{(T(t), I(t), V(t)): W(T(t), I(t), V(t) = 0)\}\) is the singleton \(E\). By Theorem 2.2 and LaSalle invariance principle [36], we can conclude that the infective equilibrium \(E\) of system (1.2) is globally asymptotically stable.

This completes the proof of Theorem 3.1.

4. Concluding remarks

In the present paper, we reinvestigate a class of delayed HIV-1 infection model with nonlinear incidence of infection. By applying the persistence theory of Hale and Waltmann [29] for infinite dimensional systems, we obtain that the populations of system (1.2) can coexist permanently if \(R(t) > 1\). By constructing Lyapunov functionals, we prove that if the infective equilibrium \(E\) of system (1.2) exists, then it is globally asymptotically stable. The results obtained here are consistent with the results in the literature [15,17], which state that the basic reproduction \(R(t)\) determines the dynamics of the model, and the underlying mechanism for sustained oscillation in host viral models is the target cell divisions, rather than intracellular delays. Considering \(R(t) = R(t)/\tau(t)\) as a function of \(\tau(t)\), we see that it is decreasing in \(\tau(t)\) with \(R(t) = 0\). Thus, intracellular delay \(\tau(t)\) can reduce the basic reproduction number \(R(t)\) if cells die during the delay period. As a consequence, ignoring the delay will produce overestimation of the reproduction number \(R(t)\). We notice that if \(a > 0\) and \(b > 0\), model (1.2) is reduced to the delayed virus infection model with nonlinear incidence of infection in paper [19], and Theorem 3.1 holds only depending on the value of the reproduction number \(R(t)\). Thus, our results show that the infective equilibrium for the delayed HIV virus model with nonlinear incidence of infection is also globally asymptotically stable if it exists. Therefore, we rigorously verify the numerical simulation results for the global stability of the infective equilibrium in paper [19].
We are very grateful to the anonymous referee for his/her careful reading, constructive comments, and suggestions, in particular, for improving Theorem 2.4 and Theorem 3.1. It is worth mentioning that according to the referee unique insights and suggestions, the terminology "nonlinear incidence of infection" in the present paper has replaced "Beddington-DeAngelis functional response" in the origin version. We also thank Omar Saucedo for his help and discussion in improving the manuscript.

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