J. Math. Anal. Appl. 375 (2011) 75–81

Contents lists available at ScienceDirect

Journal of Mathematical Analysis and Applications

www.elsevier.com/locate/jmaa

Global stability of an HIV-1 infection model with saturation infection and intracellular delay ☆

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ARTICLE INFO

Article history:
Received 6 May 2010
Available online 26 August 2010
Submitted by J. Shi

Keywords:
HIV-1 infection
Intracellular delay
Global stability
LaSalle invariant principle

ABSTRACT

In this paper, an HIV-1 infection model with a saturation infection rate and an intracellular delay accounting for the time between viral entry into a target cell and the production of new virus particles is investigated. By analyzing the characteristic equations, the local stability of an infection-free equilibrium and a chronic-infection equilibrium of the model is established. By using suitable Lyapunov functionals and the LaSalle invariant principle, it is proved that if the basic reproduction ratio is less than unity, the infection-free equilibrium is globally asymptotically stable; if the basic reproduction ratio is greater than unity, the chronic-infection equilibrium is globally asymptotically stable.

1. Introduction

Mathematical modeling combined with experimental measurements has yielded important insights into HIV-1 pathogenesis and has enhanced progress in the understanding of HIV-1 infection (see, for example, [1,7,17–20]). Models used to study HIV-1 infection have involved the concentrations of uninfected target cells, x, infected cells that are producing virus, y, and virus, v. After protease inhibitors are given, virus is classified as either infectious, v_I, i.e., not influenced by the protease inhibitor, or as non-infectious, v_{NI}, due to the action of the protease inhibitor which prevents virion maturation into infectious particles. A basic mathematical model describing HIV-1 infection dynamics that has been studied in [8,16,17,20] is of the form

$$\begin{aligned} \dot{x}(t) &= \lambda - dx(t) - \beta x(t)v(t), \\ \dot{y}(t) &= \beta x(t)v(t) - ay(t), \\ \dot{v}(t) &= ky(t) - uv(t), \end{aligned} \tag{1.1}$$

where uninfected, susceptible cells are produced at a rate, λ, uninfected cells die at rate d, and become infected at rate βxv, where β is the rate constant describing the infection process; infected cells are produced at rate βxv and die at rate ay; free virions are produced from infected cells at rate ky and are removed at rate uv.

It is assumed in model (1.1) that the infection process is governed by the mass-action principle, i.e. that the infection rate per host and per virus is a constant. However, experiments reported in [4] strongly suggested that the infection rate of microparasitic infections is an increasing function of the parasite dose, and is usually sigmoidal in shape (see, for example, [21]). In [21], to place the model on more sound biological grounds, Regoes et al. replaced the mass-action infection

☆ This work was supported by the National Natural Science Foundation of China (Nos. 11071254, 10671209) and the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry.

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0022-247X/$ – see front matter
doi:10.1016/j.jmaa.2010.08.055

rate with a dose-dependent infection rates. In [22], a more general saturated infection rate, $\frac{\beta x v^p}{1+\alpha v^q}$, was suggested, where p, q and α are positive constants.

The binding of a viral particle to a receptor on a target cell initiates a cascade of events that ultimately lead to the target cell becoming productively infected, i.e. producing new virus. We note that in model (1.1) this process was assumed to occur instantaneously: as soon as virus contacts a target cell the cell begins producing virus. This is not biologically sensible. In reality, there is a time delay between initial viral entry into a cell and subsequent viral production. There has been some work on the effect of intracellular delay accounting for the time between viral entry into a target cell and the production of new virus particles (see, for example, [2,3,6,12–15,23,24]). In [6], Herz et al. used a discrete delay to model the intracellular delay in an HIV model and showed that the incorporation of a delay would substantially shorten the estimate for the half-life of free virus.

Motivated by the works of Herz et al. [6] and Song and Neumann [22], in the present paper, we are concerned with the effect of saturation infection rate and intracellular delay describing the time between viral entry into a target cell and the production of new virus particles on the global dynamics of HIV-1 infection. To this end, we consider the following delay differential equation model

$$\begin{aligned}
\dot{x}(t) &= \lambda - dx(t) - \frac{\beta x(t) v(t)}{1+\alpha v(t)},\\
\dot{y}(t) &= \frac{\beta e^{-m\tau} x(t-\tau) v(t-\tau)}{1+\alpha v(t-\tau)} - ay(t),\\
\dot{v}(t) &= ky(t) - uv(t),
\end{aligned} \tag{1.2}$$

where the parameter τ accounts for the time between viral entry into a target cell and the production of new virus particles. The recruitment of virus producing cells at time t is given by the number of cells that were newly infected at time $t-\tau$ and are still alive at time t. Here, m is assumed to be a constant death rate for infected but not yet virus-producing cells. Thus, the probability of surviving the time period from $t-\tau$ to t is $e^{-m\tau}$.

The initial conditions for system (1.2) take the form

$$\begin{aligned}
&x(\theta) = \phi_1(\theta), \qquad y(\theta) = \phi_2(\theta), \qquad v(\theta) = \phi_3(\theta),\\
&\phi_i(\theta) \geqslant 0, \qquad \theta \in [-\tau, 0), \qquad \phi_i(0) > 0 \quad (i = 1, 2, 3),
\end{aligned} \tag{1.3}$$

where $(\phi_1(\theta), \phi_2(\theta), \phi_3(\theta)) \in C([-\tau, 0], \mathbb{R}^3_{+0})$, the Banach space of continuous functions mapping the interval $[-\tau, 0]$ into $\mathbb{R}^3_{+0}$, where $\mathbb{R}^3_{+0} = \{(x_1, x_2, x_3)\colon\ x_i \geqslant 0,\ i = 1, 2, 3\}$.

It is well known by the fundamental theory of functional differential equations [5], system (1.2) has a unique solution $(x(t), y(t), v(t))$ satisfying the initial conditions (1.3). It is easy to show that all solutions of system (1.2) with initial conditions (1.3) are defined on $[0, +\infty)$ and remain positive for all $t \geqslant 0$.

In this paper, our primary goal is to carry out a complete mathematical analysis of system (1.2) and establish its global dynamics. The organization of this paper is as follows. In the next section, by analyzing the corresponding characteristic equations, we study the local asymptotic stability of an infection-free equilibrium and a chronic-infection equilibrium of model (1.2). In Section 3, we discuss the global stability of the infection-free equilibrium and the chronic-infection equilibrium by means of suitable Lyapunov functionals and LaSalle's invariant principle, respectively. The global stability of the infection equilibrium rules out any possibility for the existence of Hopf bifurcations and sustained oscillations in system (1.2). A brief remark is given in Section 4 to conclude this work.

2. Equilibria and local stability

In this section, we study the local stability of each of feasible equilibria of system (1.2).

Clearly, system (1.2) always has an infection-free equilibrium $E_1(\lambda/d, 0, 0)$.

Denote

$$\mathscr{R}_0 = \frac{k\lambda\beta e^{-m\tau}}{adu}. \tag{2.1}$$

Here, $\mathscr{R}_0$ is called the basic reproduction ratio of system (1.2).

It is easy to show that if $\mathscr{R}_0 > 1$, system (1.2) admits a unique chronic-infection equilibrium $E^*(x^*, y^*, v^*)$, where

$$x^* = \frac{au}{k\beta e^{-m\tau}}\left(1+\alpha v^*\right), \qquad y^* = \frac{u}{k} v^*, \qquad v^* = \frac{d}{\beta + d\alpha}(\mathscr{R}_0 - 1). \tag{2.2}$$

The characteristic equation of system (1.2) at the infection-free equilibrium E_1 is of the form

$$(s+d)\left[s^2 + (a+u)s + au - k\beta\frac{\lambda}{d} e^{-m\tau} e^{-s\tau}\right] = 0. \tag{2.3}$$

Clearly, Eq. (2.3) always has a negative real root $s_1 = -d$. Other roots of (2.3) are determined by the following equation

$$s^2 + (a+u)s + au - k\beta\frac{\lambda}{d}e^{-m\tau}e^{-s\tau} = 0. \tag{2.4}$$

Let

$$f(s) = s^2 + (a+u)s + au - k\beta\frac{\lambda}{d}e^{-m\tau}e^{-s\tau}.$$

If $\mathscr{R}_0 > 1$, it is easy to show that, for s real,

$$f(0) = au(1-\mathscr{R}_0) < 0, \qquad \lim_{s\to+\infty} f(s) = +\infty.$$

Hence, $f(s) = 0$ has at least one positive real root. Therefore, if $\mathscr{R}_0 > 1$, the infection-free equilibrium E_1 is unstable.

If $\mathscr{R}_0 < 1$, we prove that the infection-free equilibrium E_1 is locally asymptotically stable.

When $\tau = 0$, Eq. (2.4) becomes

$$s^2 + (a+u)s + au - k\beta\frac{\lambda}{d} = 0. \tag{2.5}$$

If $\mathscr{R}_0 < 1$, we have $au > k\beta\lambda/d$. Hence, the equilibrium E_1 is locally asymptotically stable when $\tau = 0$.

If $i\omega$ $(\omega > 0)$ is a solution of Eq. (2.4), separating real and imaginary parts, it follows that

$$\begin{aligned}(a+u)\omega &= -k\beta\frac{\lambda}{d}e^{-m\tau}\sin\omega\tau,\\ au - \omega^2 &= k\beta\frac{\lambda}{d}e^{-m\tau}\cos\omega\tau.\end{aligned} \tag{2.6}$$

Squaring and adding the two equations of (2.6), we derive that

$$\omega^4 + \big(a^2+u^2\big)\omega^2 + (au)^2\big(1-\mathscr{R}_0^2\big) = 0. \tag{2.7}$$

Hence, if $\mathscr{R}_0 < 1$, Eq. (2.7) has no positive roots. Noting that the equilibrium E_1 is locally asymptotically stable when $\tau = 0$, by the general theory on characteristic equations of delay differential equations from Kuang [9, Theorem 3.4.1], we see that if $\mathscr{R}_0 < 1$, E_1 is always locally asymptotically stable.

The characteristic equation of system (1.2) at the chronic-infection equilibrium E^* takes the form

$$s^3 + p_2(\tau)s^2 + p_1(\tau)s + p_0(\tau) + \big(q_1(\tau)s + q_0(\tau)\big)e^{-s\tau} = 0, \tag{2.8}$$

where

$$\begin{aligned}p_0(\tau) &= au\left(d + \frac{\beta v^*}{1+\alpha v^*}\right),\\ p_1(\tau) &= (a+u)\left(d + \frac{\beta v^*}{1+\alpha v^*}\right) + au,\\ p_2(\tau) &= a + u + d + \frac{\beta v^*}{1+\alpha v^*},\\ q_0(\tau) &= -\frac{adu}{1+\alpha v^*},\\ q_1(\tau) &= -\frac{au}{1+\alpha v^*}.\end{aligned} \tag{2.9}$$

When $\tau = 0$, Eq. (2.8) becomes

$$s^3 + p_2(0)s^2 + \big(p_1(0)+q_1(0)\big)s + p_0(0) + q_0(0) = 0. \tag{2.10}$$

It is easy to see that

$$\begin{aligned}p_0(0) + q_0(0) &= \left\{au\left(d + \frac{\beta v^*}{1+\alpha v^*}\right) - \frac{adu}{1+\alpha v^*}\right\}_{\tau=0} > 0,\\ p_1(0) + q_1(0) &= \left\{(a+u)\left(d + \frac{\beta v^*}{1+\alpha v^*}\right) + au - \frac{au}{1+\alpha v^*}\right\}_{\tau=0} > 0,\\ p_2(0)\big(p_1(0)+q_1(0)\big) &- \big(p_0(0)+q_0(0)\big)\\ &= \left\{(a+u)\left(d + \frac{\beta v^*}{1+\alpha v^*}\right)\left(a+u+d+\frac{\beta v^*}{1+\alpha v^*}\right) - \frac{au\beta v^*}{(1+\alpha v^*)^2} + (a+u)\left(au - \frac{au}{1+\alpha v^*}\right)\right\}_{\tau=0} > 0.\end{aligned}$$

Hence, if $\mathscr{R}_0 > 1$, the equilibrium E^* of system (1.2) exists and is locally asymptotically stable when $\tau = 0$.

If $i\omega$ ($\omega > 0$) is a solution of Eq. (2.8), separating real and imaginary parts, it follows that

$$\begin{aligned}&\omega^3 - p_1(\tau)\omega = q_1(\tau)\omega\cos\omega\tau - q_0(\tau)\sin\omega\tau,\\ &p_2(\tau)\omega^2 - p_0(\tau) = q_1(\tau)\omega\sin\omega\tau + q_0(\tau)\cos\omega\tau.\end{aligned} \tag{2.11}$$

Squaring and adding the two equations of (2.11), we derive that

$$\omega^6 + \big(p_2^2(\tau) - 2p_1(\tau)\big)\omega^4 + \big(p_1^2(\tau) - 2p_0(\tau)p_2(\tau) - q_1^2(\tau)\big)\omega^2 + p_0^2(\tau) - q_0^2(\tau) = 0. \tag{2.12}$$

Direct calculations show that

$$\begin{aligned}&p_2^2(\tau) - 2p_1(\tau) = a^2 + u^2 + \left(d + \frac{\beta v^*}{1+\alpha v^*}\right)^2 > 0,\\ &p_0(\tau) + q_0(\tau) = au\left(d + \frac{\beta v^*}{1+\alpha v^*}\right) - \frac{adu}{1+\alpha v^*} > 0,\\ &p_1^2(\tau) - 2p_0(\tau)p_2(\tau) - q_1^2(\tau) = \big(a^2+u^2\big)\left(d + \frac{\beta v^*}{1+\alpha v^*}\right)^2 + a^2u^2 - \frac{a^2u^2}{(1+\alpha v^*)^2} > 0.\end{aligned}$$

Hence, if $\mathscr{R}_0 > 1$, Eq. (2.12) has no positive roots. Noting that the equilibrium E^* is locally asymptotically stable when $\tau = 0$, by the general theory on characteristic equations of delay differential equations from Kuang [9, Theorem 3.4.1], we see that if $\mathscr{R}_0 > 1$, the equilibrium E^* is locally asymptotically stable.

From what has been discussed above, we have the following result.

Theorem 2.1. *For system* (1.2)*, if* $\mathscr{R}_0 < 1$*, the infection-free equilibrium* $E_1(\lambda/d, 0, 0)$ *is locally asymptotically stable*; *if* $\mathscr{R}_0 > 1$*,* E_1 *is unstable and the chronic-infection equilibrium* $E^*(x^*, y^*, v^*)$ *exists and is locally asymptotically stable.*

3. Global stability

In this section, we study the global stability of each of feasible equilibria of system (1.2). The strategy of proofs is to use suitable Lyapunov functionals and LaSalle's invariant principle. The Lyapunov functionals used here are similar in nature to those used in [10,11] in which the global dynamics are resolved for SEIR and SIR models with time delay, respectively.

We first state and prove our result on the global stability of the infection-free equilibrium $E_1(\lambda/d, 0, 0)$.

Theorem 3.1. *The disease-free equilibrium* $E_1(\lambda/d, 0, 0)$ *of system* (1.2) *is globally asymptotically stable if* $\mathscr{R}_0 < 1$.

Proof. Let $(x(t), y(t), v(t))$ be any positive solution of system (1.2) with initial conditions (1.3). Denote $x_0 = \lambda/d$.

Define

$$V_{11}(t) = x - x_0 - x_0\ln\frac{x}{x_0} + e^{m\tau}y + \frac{a}{k}e^{m\tau}v. \tag{3.1}$$

Calculating the derivative of $V_{11}(t)$ along positive solutions of system (1.2), it follows that

$$\begin{aligned}\frac{d}{dt}V_{11}(t) &= \left(1 - \frac{x_0}{x}\right)\left[\lambda - dx - \frac{\beta x(t)v(t)}{1+\alpha v(t)}\right]\\ &\quad + e^{m\tau}\left[\frac{\beta e^{-m\tau}x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)} - ay(t)\right]\\ &\quad + \frac{a}{k}e^{m\tau}\big[ky(t) - uv(t)\big]\\ &= \left(1 - \frac{x_0}{x}\right)\left[-d(x - x_0) - \frac{\beta x(t)v(t)}{1+\alpha v(t)}\right]\\ &\quad + e^{m\tau}\left[\frac{\beta e^{-m\tau}x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)} - ay(t)\right]\\ &\quad + \frac{a}{k}e^{m\tau}\big[ky(t) - uv(t)\big]\\ &= \left(1 - \frac{x_0}{x}\right)\big[-d(x - x_0)\big]\\ &\quad - \frac{\beta x(t)v(t)}{1+\alpha v(t)} + \frac{\beta x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}\end{aligned}$$

$$+\left[\frac{\beta x_0}{1+\alpha v(t)}-\frac{au}{k}e^{m\tau}\right]v(t). \tag{3.2}$$

Define

$$V_1(t)=V_{11}(t)+\beta\int_{t-\tau}^{t}\frac{x(s)v(s)}{1+\alpha v(s)}\,ds. \tag{3.3}$$

We therefore derive from (3.2) and (3.3) that

$$\frac{d}{dt}V_1(t)=-d\frac{(x-x_0)^2}{x}+\left[\frac{\beta x_0}{1+\alpha v(t)}-\frac{au}{k}e^{m\tau}\right]v(t). \tag{3.4}$$

Noting that

$$\frac{\beta x_0}{1+\alpha v(t)}-\frac{au}{k}e^{m\tau}\leqslant\beta x_0-\frac{au}{k}e^{m\tau}=\frac{au}{k}e^{m\tau}(\mathscr{R}_0-1)<0,$$

it follows from (3.4) that $V_1'(t)\leqslant 0$. By Theorem 5.3.1 in [5], solutions limit to $\mathcal{M}$, the largest invariant subset of $\{V_1'(t)=0\}$. Clearly, it follows from (3.4) that $V_1'(t)=0$ if and only if $x=x_0$, $v=0$. Noting that $\mathcal{M}$ is invariant, for each element in $\mathcal{M}$, we have $v=0$, $v'(t)=0$. We therefore derive from the third equation of system (1.2) that

$$0=v'(t)=ky(t),$$

which yields $y=0$. Hence, $V_1'(t)=0$ if and only if $(x,y,v)=(x_0,0,0)$. Accordingly, the global asymptotic stability of E_1 follows from LaSalle's invariance principle. This completes the proof. □

We are now in a position to establish the global stability of the chronic-infection equilibrium E^* of system (1.2).

Theorem 3.2. *If $\mathscr{R}_0>1$, then the chronic-infection equilibrium $E^*(x^*,y^*,v^*)$ of system (1.2) is globally asymptotically stable.*

Proof. Let $(x(t),y(t),v(t))$ be any positive solution of system (1.2) with initial conditions (1.3).

Define

$$V_{21}(t)=x-x^*-x^*\ln\frac{x}{x^*}+e^{m\tau}\left(y-y^*-y^*\ln\frac{y}{y^*}\right)+\frac{a}{k}e^{m\tau}\left(v-v^*-v^*\ln\frac{v}{v^*}\right).$$

Calculating the derivative of $V_{21}(t)$ along positive solutions of system (1.2) it follows that

$$\begin{aligned}\frac{d}{dt}V_{21}(t)&=\left(1-\frac{x^*}{x}\right)\left[\lambda-dx(t)-\frac{\beta x(t)v(t)}{1+\alpha v(t)}\right]\\&\quad+e^{m\tau}\left(1-\frac{y^*}{y}\right)\left[\frac{\beta e^{-m\tau}x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}-ay(t)\right]\\&\quad+\frac{a}{k}e^{m\tau}\left(1-\frac{v^*}{v}\right)\left[ky(t)-uv(t)\right].\end{aligned} \tag{3.5}$$

On substituting $\lambda=dx^*+\frac{\beta x^*v^*}{1+\alpha v^*}$ into (3.5), we derive that

$$\begin{aligned}\frac{d}{dt}V_{21}(t)&=\left(1-\frac{x^*}{x}\right)\left[-d\big(x(t)-x^*\big)-\frac{\beta x(t)v(t)}{1+\alpha v(t)}+\frac{\beta x^*v^*}{1+\alpha v^*}\right]\\&\quad+e^{m\tau}\left(1-\frac{y^*}{y}\right)\left[\frac{\beta e^{-m\tau}x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}-ay(t)\right]\\&\quad+\frac{a}{k}e^{m\tau}\left(1-\frac{v^*}{v}\right)\left[ky(t)-uv(t)\right]\\&=\left(1-\frac{x^*}{x}\right)\left[-d\big(x(t)-x^*\big)\right]\\&\quad-\frac{\beta x(t)v(t)}{1+\alpha v(t)}+\frac{\beta x^*v(t)}{1+\alpha v(t)}+\frac{\beta x^*v^*}{1+\alpha v^*}\left(1-\frac{x^*}{x}\right)\\&\quad+\frac{\beta x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}-\frac{\beta y^*x(t-\tau)v(t-\tau)}{y(t)(1+\alpha v(t-\tau))}+ae^{m\tau}y^*\\&\quad+\frac{a}{k}e^{m\tau}\left[-uv(t)-kv^*\frac{y(t)}{v(t)}+uv^*\right].\end{aligned} \tag{3.6}$$

Noting that $\frac{\beta e^{-m\tau}x^*v^*}{1+\alpha v^*} = ay^*$, $ky^* = uv^*$, it follows from (3.6) that

$$\begin{aligned}\frac{d}{dt}V_{21}(t) &= \left(1-\frac{x^*}{x}\right)\left[-d\big(x(t)-x^*\big)\right]\\ &\quad -\frac{\beta x(t)v(t)}{1+\alpha v(t)}+\frac{\beta x^*v(t)}{1+\alpha v(t)}+\frac{\beta x^*v^*}{1+\alpha v^*}\left(1-\frac{x^*}{x}\right)\\ &\quad +\frac{\beta x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}-\frac{\beta x^*v^*}{1+\alpha v^*}\frac{y^*(1+\alpha v^*)}{x^*v^*}\frac{x(t-\tau)v(t-\tau)}{y(t)(1+\alpha v(t-\tau))}\\ &\quad -\frac{\beta x^*v^*}{1+\alpha v^*}\frac{v(t)}{v^*}-\frac{\beta x^*v^*}{1+\alpha v^*}\frac{v^*}{y^*}\frac{y(t)}{v(t)}+\frac{2\beta x^*v^*}{1+\alpha v^*}.\end{aligned} \tag{3.7}$$

Define

$$V_2(t) = V_{21}(t)+\beta\int_{t-\tau}^{t}\left[\frac{x(s)v(s)}{1+\alpha v(s)}-\frac{x^*v^*}{1+\alpha v^*}-\frac{x^*v^*}{1+\alpha v^*}\ln\frac{(1+\alpha v^*)x(s)v(s)}{x^*v^*(1+\alpha v(s))}\right]ds. \tag{3.8}$$

We derive from (3.7) and (3.8) that

$$\begin{aligned}\frac{d}{dt}V_2(t) &= \left(1-\frac{x^*}{x}\right)\left[-d\big(x(t)-x^*\big)\right]\\ &\quad -\frac{\beta x(t)v(t)}{1+\alpha v(t)}+\frac{\beta x^*v(t)}{1+\alpha v(t)}+\frac{\beta x^*v^*}{1+\alpha v^*}\left(1-\frac{x^*}{x}\right)\\ &\quad +\frac{\beta x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}-\frac{\beta x^*v^*}{1+\alpha v^*}\frac{y^*(1+\alpha v^*)}{x^*v^*}\frac{x(t-\tau)v(t-\tau)}{y(t)(1+\alpha v(t-\tau))}\\ &\quad -\frac{\beta x^*v^*}{1+\alpha v^*}\frac{v(t)}{v^*}-\frac{\beta x^*v^*}{1+\alpha v^*}\frac{v^*}{y^*}\frac{y(t)}{v(t)}+\frac{2\beta x^*v^*}{1+\alpha v^*}\\ &\quad +\beta\left[\frac{x(t)v(t)}{1+\alpha v(t)}-\frac{x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)}+\frac{x^*v^*}{1+\alpha v^*}\ln\frac{(1+\alpha v(t))x(t-\tau)v(t-\tau)}{x(t)v(t)(1+\alpha v(t-\tau))}\right]\\ &= -d\frac{(x(t)-x^*)^2}{x}\\ &\quad -\frac{\beta x^*v^*}{1+\alpha v^*}\left[\frac{x^*}{x(t)}-1-\ln\frac{x^*}{x(t)}\right]\\ &\quad -\frac{\beta x^*v^*}{1+\alpha v^*}\left[\frac{y^*(1+\alpha v^*)x(t-\tau)v(t-\tau)}{x^*v^*y(t)(1+\alpha v(t-\tau))}-1-\ln\frac{y^*(1+\alpha v^*)x(t-\tau)v(t-\tau)}{x^*v^*y(t)(1+\alpha v(t-\tau))}\right]\\ &\quad -\frac{\alpha\beta x^*v^*(v(t)-v^*)^2}{v^*(1+\alpha v^*)^2(1+\alpha v(t))}\\ &\quad -\frac{\beta x^*v^*}{1+\alpha v^*}\left[\frac{1+\alpha v(t)}{1+\alpha v^*}-1-\ln\frac{1+\alpha v(t)}{1+\alpha v^*}\right]\\ &\quad -\frac{\beta x^*v^*}{1+\alpha v^*}\left[\frac{v^*y(t)}{y^*v(t)}-1-\ln\frac{v^*y(t)}{y^*v(t)}\right].\end{aligned} \tag{3.9}$$

Noting that $x^*, y^*, v^* > 0$, we have that $V_2'(t) \leqslant 0$. By Theorem 5.3.1 in [5], solutions limit to $\mathcal{M}$, the largest invariant subset of $\{V_2'(t) = 0\}$. It is readily seen from (3.9) that $V_2'(t) = 0$ if and only if $x = x^*$, $v = v^*$, $\frac{y^*(1+\alpha v^*)x(t-\tau)v(t-\tau)}{x^*v^*y(t)(1+\alpha v(t-\tau))} = \frac{1+\alpha v(t)}{1+\alpha v^*} = \frac{v^*y(t)}{y^*v(t)} = 1$. Using a similar argument as that in the proof of Theorem 3.1 and by the LaSalle's invariant principle, the global asymptotic stability of E^* follows. This completes the proof. □

4. Conclusion

In this paper, we have studied the global dynamics of an HIV-1 infection model with a saturation infection rate and an intracellular delay accounting for the time between viral entry into a target cell and the production of new virus particles. The global stability of the infection-free equilibrium and the chronic-infection equilibrium of system (1.2) has been completely established by using the Lyapunov–LaSalle type theorem. By Theorem 3.1 we see that if the basic reproduction ratio $\mathscr{R}_0$ is less than unity, the infection-free equilibrium is globally asymptotically stable. In this case, the virus is cleared up. By Theorem 3.2 we see that if the basic reproduction ratio $\mathscr{R}_0$ is greater than unity, the chronic-infection equilibrium is

globally asymptotically stable. From Theorems 3.1 and 3.2, we see that the intracellular delay describing the time between viral entry into a target cell and the production of new virus particles does not affect the stability of the feasible equilibria and therefore does not induce periodic oscillations and the possibility of Hopf bifurcations is therefore ruled out.

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