Hopf bifurcation of an age-structured HIV infection model with logistic target-cell growth

Zhong-Kai Guo\textsuperscript{a,c}, Hai-Feng Huo\textsuperscript{a,b} and Hong Xiang\textsuperscript{b}

\textsuperscript{a}College of Electrical and Information Engineering, Lanzhou University of Technology, Lanzhou, People’s Republic of China; \textsuperscript{b}Department of Applied Mathematics, Lanzhou University of Technology, Lanzhou, People’s Republic of China; \textsuperscript{c}Department of Science, College of Technology and Engineering, Lanzhou University of Technology, Lanzhou, People’s Republic of China

ABSTRACT
In this paper, we investigate an age-structured HIV infection model with logistic growth for target cell. We rewrite the model as an abstract non-densely defined Cauchy problem and obtain the condition which guarantees the existence of the unique positive steady state. By linearizing the model at steady state and analysing the associated characteristic transcendental equations, we study the local asymptotic stability of the steady state. Furthermore, by using Hopf bifurcation theorem in Liu et al., we show that Hopf bifurcation occurs at the positive steady state when bifurcating parameter crosses some critical values. Finally, we perform some numerical simulations to illustrate our results.

1. Introduction
The HIV (Human Immunodeficiency Virus) that causes AIDS (Acquired Immune Deficiency Syndrome) has attracted the attention of numerous researchers. According to the [28] report, there are more than 36.7 million people infected worldwide and 1.1 million deaths in 2015. The virus main attacks CD4\textsuperscript{+} T cell (target cell), which is very important to the human immune system. The HIV pandemic is one of the greatest challenges in the field of global public health.

Recently, it has been realized that mathematical models are very necessary to understand HIV infection. Ho et al. [7] and Perelson et al. [22] considered two different ordinary differential equations (ODEs) to describe the interaction of susceptible cell, infected cell and free virus. Since then, a lot of mathematical models of HIV infection or other infectious disease have been extensively investigated by incorporating various factors [2,3,5,8–10,13,27,29,30,32,34,35,37]. These models include ODEs, DDEs (delay differential equations) and PDEs (partial differential equations).

The age-structured models have been studied by many authors, such as [4,11,33]. Taking into account the effect of age-structured is thought to be very important for virus
infection models \[20,21,23,24,30\]. Shu et al. \[24\] provided some general results applicable to immune system dynamics and found that the logistic growth of uninfected cells on virus models with distributed delays could induce sustained oscillations. Their results showed that the nonlinear target-cell growth rate was very important in causing oscillatory dynamics. Mohebbi et al. \[20\] studied a new age-structured within-host virus model with logistic growth of target cells and viral absorption by infected cells. They presented that infection free steady state is globally asymptotically stable when the basic reproduction number was less than unity. When the basic reproduction number was greater than unity, the system underwent a Hopf bifurcation through which the infection equilibrium lost the stability and periodic solutions appeared. They also found that the logistic growth of uninfected cells is the key factor which can induce sustained oscillations.

By using centre manifold theory and Hopf bifurcation theorem of non-densely defined Cauchy problems in \[17\] and \[14\], Liu et al. \[15\] showed that age-structured model of consumer-resource mutualism undergoes a Hopf bifurcation at the positive equilibrium under some conditions. Wang and Liu \[31\] considered an age-structured compartmental pest–pathogen model. Their results showed that Hopf bifurcation occurred at a positive steady state as bifurcating parameter passed some values.

Motivated by above, we study an age-structured HIV infection model with logistic target-cell growth and employ Hopf bifurcation theorem in Liu et al. to study that Hopf bifurcation occurs at the positive steady state when bifurcating parameter crosses some critical values in this paper. Our model consists of three variables: susceptible CD4\(^+\) T cell whose concentration at time \(t\) is denoted by \(T(t)\); infected CD4\(^+\) T cell whose concentration at time \(t\) with age \(a\) is denoted by \(i(t,a)\); \(V(t)\) represents the concentration of free virus at \(t\). We make the following assumptions in this paper:

(i) The infected CD4\(^+\) T cell is assumed to be age-structured, whereas the susceptible CD4\(^+\) T cell and the free virus are not age-structured.

(ii) The constant recruitment rate of the susceptible CD4\(^+\) T cell is \(\Lambda\) and the natural death rate is \(d_1\).

(iii) Once stimulated by antigen, susceptible CD4\(^+\) T cell undergoes mitosis immediately, and the mitosis can be described by

\[
rT(t)(1 - \frac{T(t) + \int_0^{+\infty} i(t,a)da}{K}),
\]

where \(K\) is the maximum level of CD4\(^+\) T cells in the body, \(r\) is the intrinsic growth rate.

(iv) Free viral particle can infect susceptible CD4\(^+\) T cell, and the infection rate is \(\beta\). The natural death rate of infected cell is \(d_2\).

(v) \(\alpha(a)\) is new free virus particle production rate of an infected cell with infected age \(a\) and defined by

\[
\alpha(a) = \begin{cases} 
\alpha^*, & a \geq \tau, \\
0, & \text{otherwise,} 
\end{cases}
\]

let \(K_0 := \int_0^{+\infty} \alpha(a)e^{-d_2a}da\), i.e. \(\alpha^* = d_2K_0e^{d_2\tau}\), where \(\tau\) represents the time from initial infection to release of new free virus particle, \(d_3\) is the clearance rate of free
virus. \(K_0\) represents the total number of virus particles produced by an infected cell during its life span. Based on the above discussion and assumptions, we obtain the following HIV infection model with logistic target-cell growth and virus-to-cell infection.

\[
\frac{dT(t)}{dt} = \Lambda + rT(t)(1 - \frac{T(t) + \int_0^{+\infty} i(t, a)da}{K}) - d_1 T(t) - \beta T(t) V(t),
\]

\[
\frac{\partial i(t, a)}{\partial t} + \frac{\partial i(t, a)}{\partial a} = -d_2 i(t, a),
\]

\[
\frac{dV(t)}{dt} = \int_0^{+\infty} \alpha(a)i(t, a)da - d_3 V(t),
\]

\[
i(0, 0) = \beta T(0) V(0),
\]

\[
i(t, a, 0) = i_0(a) \in L_1^+(\{0, +\infty\}, \mathbb{R}), \quad T(0) = x_0 > 0, \quad V(0) = v_0 > 0. \quad (1.2)
\]

The rest of this paper is organized as follows. In the next section, we summarize the main results on Hopf bifurcation theorem obtained in [14]. In Section 3, the stability of the steady state and the existence of Hopf bifurcation are investigated. In Section 4, we perform numerical simulations to verify our analytical results. Finally, in Section 5, a brief conclusion is given.

2. Preliminaries

We recall the Hopf bifurcation theorem in [14] for the following non-densely defined abstract Cauchy problem:

\[
\frac{du(t)}{dt} = Au(t) + F(\mu, u(t)), \quad t \geq 0, \quad u(0) \in D(A), \quad (2.1)
\]

where \(\mu \in \mathbb{R}\) is the bifurcation parameter, \(A : D(A) \subset X \to X\) is a linear operator on a Banach space \(X\) with \(D(A)\) not dense in \(X\) and \(A\) is not necessary to be a Hille–Yosida operator, \(F : \mathbb{R} \times D(A) \to X\) is a \(C^k\) map with \(k \geq 4\). Set

\[X_0 := \overline{D(A)},\]

and \(A_0\) is the part of \(A\) in \(X_0\), which is defined by

\[A_0 x = Ax, \quad \forall x \in D(A_0) = \{x \in D(A) : Ax \in X_0\}.
\]

We denote by \(\{T_A(t)\}_{t \geq 0}\) the \(C_0\) semigroup of bounded linear operators on \(X\) (respectively \(\{S_A(t)\}_{t \geq 0}\) the integrated semigroup) generated by \(A\).

**Definition 2.1**: Let \(L : D(L) \subset X \to X\) be the infinitesimal generator of a linear \(C_0\) semi-group \(\{T_L(t)\}_{t \geq 0}\) on a Banach space \(X\). Define the growth bound \(\omega_0(L) \in (-\infty, +\infty)\) of \(L\) by
\[ \omega_0(L) := \lim_{t \to +\infty} \frac{\ln(\| T_L(t) \|_{\mathcal{L}(X)})}{t}. \]

The essential growth bound \( \omega_{0,\text{ess}}(L) \in (-\infty, +\infty) \) of \( L \) by

\[ \omega_{0,\text{ess}}(L) := \lim_{t \to +\infty} \frac{\ln(\| T_L(t) \|_{\text{ess}})}{t}, \]

where \( \mathcal{L}(X) \) is the space of bounded linear operators from \( X \) into \( X \), \( \| T_L(t) \|_{\text{ess}} \) is the essential norm of \( T_L(t) \) defined by \( \| T_L(t) \|_{\text{ess}} = \kappa(T_L(t)B_X(0,1)) \), where \( B_X(0,1) = \{ x \in X : \| x \|_{X} \leq 1 \} \), and each bounded set \( B \subset X \) \( \kappa(B) = \inf[\varepsilon > 0 : B \text{ can be covered by a finite number of balls of radius} \leq \varepsilon \) is the Kuratovsky measure of non-compactness.

We make the following assumptions on the linear operator \( A \) and the nonlinear map \( F \).

**Assumption 2.1:** Assume that \( A : D(A) \subset X \to X \) is a linear operator on a Banach space \( (X, \| \cdot \|) \) such that there exist two constants \( \omega_A \in \mathbb{R} \) and \( M_A \geq 1 \), such that \( (\omega_A, +\infty) \subset \rho(A) \) and the following properties are satisfied

(a) \( \lim_{\lambda \to +\infty} (\lambda I - A)^{-1}x = 0, \quad \forall x \in X; \)
(b) \( \| (\lambda I - A)^{-k} \|_{\mathcal{L}(X_0)} \leq M_A/\lambda^k, \quad \forall \lambda > \omega_A, \quad k \geq 1. \)

Assumption 2.1 implies that \( A_0 \) is the infinitesimal generator of a \( C_0 \) semigroup \( \{ T_{A_0}(t) \}_{t \geq 0} \) of bounded linear operator on \( X_0 \) and

\[ \| T_{A_0}(t) \|_{\mathcal{L}(X_0)} \leq M_A e^{\omega_A t}, \quad t \geq 0. \]

By Proposition 2.6 in [17], we know if Assumption 2.1 is satisfied, then \( A \) generates a unique integrated semigroup \( \{ S_A(t) \}_{t \geq 0} \). If we assume in addition that \( A \) is a Hille–Yosida operator, then we have

\[ \| S_A(t) - S_A(s) \|_{\mathcal{L}(X)} \leq M_A \int_s^t e^{\omega_A l}dl, \quad \forall t, s \in [0, +\infty) \quad \text{with} \quad t \geq s \geq 0. \]

Next, we consider the non-homogeneous Cauchy problem

\[ \frac{du(t)}{dt} = Au(t) + f(t), \quad t \geq 0, \quad u(0) \in \overline{D(A)}, \quad (2.2) \]

where \( f \in L^1((0, \tau), X) \).

**Assumption 2.2:** There exists a map \( \delta(t) : [0, +\infty) \to [0, +\infty) \) with

\[ \lim_{t \to 0^+} \delta(t) = 0, \]

such that for each \( \tau > 0 \) and \( f \in C([0, \tau], X) \), \( t \to \int_0^t S_A(t - s)f(s)ds \) is continuously differentiable and

\[ \| \frac{d}{dt} \int_0^t S_A(t - s)f(s)ds \| \leq \delta(t) \sup_{s \in [0, \tau]} \| f(s) \|, \quad \forall t \in [0, \tau]. \]
By Corollary 2.11 in [17], we know if Assumptions 2.1 and 2.2 hold, then for each \( \tau > 0, f \in C([0, \tau], X_0) \), and \( x \in X_0 \), (2.2) has a unique integrated solution \( u(t) \in C([0, \tau], X_0) \). Meanwhile, if \( A \) is a Hille–Yosida operator, then Assumption 2.8 in [18] holds. By Theorem 2.9 in [18], we know Assumption 2.2 holds.

**Assumption 2.3:** Let \( \varepsilon > 0 \) and \( F \in C^k((-\varepsilon, \varepsilon) \times B_{X_0}(0, \varepsilon); X) \) for some \( k \geq 4 \). Assume that the following conditions are satisfied:

(a) \( F(\mu, 0) = 0, \forall \mu \in (-\varepsilon, \varepsilon) \) and \( \partial_x F(0, 0) = 0; \)

(b) (Transversality condition) For each \( \mu \in (-\varepsilon, \varepsilon) \), there exists a pair of conjugated simple eigenvalues of \( (A + \partial_x F(\mu, 0))_0 \), denoted by \( \lambda(\mu) \) and \( \bar{\lambda}(\mu) \), such that

\[
\lambda(\mu) = \alpha(\mu) + i\omega(\mu),
\]

the map \( \mu \to \lambda(\mu) \) is continuously differentiable,

\[
\omega(0) > 0, \quad \alpha(0) = 0, \quad \frac{d\alpha(0)}{d\mu} \neq 0,
\]

and

\[
\sigma(A_0) \cap i\mathbb{R} = \{\lambda(0), \bar{\lambda}(0)\}.
\]

(c) The essential growth rate of \( \{T_{A_0}(t)\}_{t \geq 0} \) is strictly negative, that is

\[
\omega_{0,\text{ess}}(A_0) < 0.
\]

Based on the above discussion and assumptions, now we can state the following Hopf bifurcation theorem in [14].

**Theorem 2.1:** Let assumptions 2.1–2.3 be satisfied. Then there exist \( \varepsilon^* > 0 \), three \( C^{k-1} \) maps, \( \varepsilon \to \mu(\varepsilon) \) from \( (0, \varepsilon^*) \) into \( \mathbb{R} \), \( \varepsilon \to x_\varepsilon \) from \( (0, \varepsilon^*) \) into \( D(A) \), and \( \varepsilon \to \gamma(\varepsilon) \) from \( (0, \varepsilon^*) \) into \( \mathbb{R} \), such that for each \( \varepsilon \in (0, \varepsilon^*) \) there exists a \( \gamma(\varepsilon) \)-periodic function \( u_\varepsilon \in C^k(\mathbb{R}, X_0) \), which is an integrated solution of (2.1) with the parameter value \( \mu(\varepsilon) \) and the initial value \( x_\varepsilon \). So for each \( t \geq 0 \), \( u_\varepsilon \) satisfies

\[
u_\varepsilon(t) = x_\varepsilon + A \int_0^t u_\varepsilon(l)dl + \int_0^t F(\mu(\varepsilon), u_\varepsilon(l))dl.
\]

Moreover, we have the following properties:

(a) There exist a neighbourhood \( N \) of 0 in \( X_0 \) and an open interval \( I \) in \( \mathbb{R} \) containing 0, such that for \( \tilde{\mu} \in I \) and any periodic solution \( \tilde{u} \) in \( N \) with minimal period \( \tilde{\gamma} \) close to \( 2\pi / \omega(0) \) of 2.1 for the parameter value \( \tilde{\mu} \), there exists \( \varepsilon \in (0, \varepsilon^*) \) such that \( \tilde{u}(t) = u_\varepsilon(t + \theta) \) (for some \( \theta \in [0, \gamma(\varepsilon)) \)), \( \mu(\varepsilon) = \tilde{\mu} \) and \( \gamma(\varepsilon) = \tilde{\gamma} \);

(b) The map \( \varepsilon \to \mu(\varepsilon) \) is a \( C^{k-1} \) function and we have the Taylor expansion

\[
\mu(\varepsilon) = \sum_{n=1}^{[\frac{k-1}{2}]} \mu_{2n} \varepsilon^{2n} + O(\varepsilon^{k-1}), \quad \forall \varepsilon \in (0, \varepsilon^*),
\]
where \([k - 2/2]\) is the integer part of \(k - 2/2\).

(c) The period \(\gamma(\varepsilon)\) of \(t \to u_\varepsilon(t)\) is a \(C^{k-1}\) function and

\[
\gamma(\varepsilon) = \frac{2\pi}{\omega(0)} \left[ 1 + \frac{[k - 2]}{2} \right] + O(\varepsilon^{k-1}), \quad \forall \varepsilon \in (0, \varepsilon^*),
\]

where \(\omega(0)\) is the imaginary part of \(\lambda(0)\) defined in Assumption 2.3.

3. Stability of equilibria and existence of Hopf bifurcation

In this section, we will study stability of equilibria and existence of Hopf bifurcation for (1.2)

3.1. The transformation of the Cauchy problem

In system (1.2), by setting

\[
T(t) = \int_0^{+\infty} u(t, a) da, \quad V(t) = \int_0^{+\infty} v(t, a) da,
\]

we can rewrite system (1.2) as the following age-structured model:

\[
\frac{dx(t, a)}{dt} + \frac{dx(t, a)}{da} = -Dx(t, a), \quad x(t, 0) = B(x(t, \cdot)), \quad x(0, a) = x_0 \in L_+^1((0, +\infty), \mathbb{R}^3),
\]

where \(x(t, a) = (u(t, a), i(t, a), v(t, a))^T\), \(D = \text{diag}(d_1, d_2, d_3)\),

\[
B(x(t, \cdot)) = \begin{pmatrix}
    u(t, 0) \\
    i(t, 0) \\
    v(t, 0)
\end{pmatrix} = \begin{pmatrix}
    \Lambda + \Pi - \beta \int_0^{+\infty} u(t, a) da \int_0^{+\infty} v(t, a) da \\
    \beta \int_0^{+\infty} u(t, a) da \int_0^{+\infty} v(t, a) da \\
    \int_0^{+\infty} \alpha(a) i(t, a) da
\end{pmatrix},
\]

where \(\Pi = r \int_0^{+\infty} u(t, a) da (1 - \int_0^{+\infty} u(t, a) da + \int_0^{+\infty} i(t, a) da/K)\).

Consider the Banach space \((X, \| \cdot \|)\)

\[
X = \mathbb{R}^3 \times L^1((0, +\infty), \mathbb{R}^3)
\]
with
\[ \left\| \begin{pmatrix} \alpha \\ \varphi \end{pmatrix} \right\| = \| \alpha \|_{\mathbb{R}^3} + \| \varphi \|_{L^1((0, +\infty), \mathbb{R}^3)} . \]

Define the linear operator \( L : D(L) \to X \) by
\[ L \left( \begin{pmatrix} 0 \\ \varphi \end{pmatrix} \right) = \begin{pmatrix} -\varphi(0) \\ -\varphi' - D\varphi \end{pmatrix} \]
with
\[ D(L) = \{ 0_{\mathbb{R}^3} \} \times W^{1,1}((0, +\infty), \mathbb{R}^3) , \]
we notice \( L \) is non-densely defined since
\[ X_0 := \overline{D(L)} = \{ 0_{\mathbb{R}^3} \} \times L^1((0, +\infty), \mathbb{R}^3) \neq X. \]

Define the nonlinear operator \( F : \overline{D(L)} \to X \) by
\[ F \left( \begin{pmatrix} 0 \\ \varphi \end{pmatrix} \right) = \begin{pmatrix} B(\varphi) \\ 0 \end{pmatrix} . \]

Set
\[ w(t) = \begin{pmatrix} 0 \\ x(t, \cdot) \end{pmatrix} . \]

Now we can rewrite PDEs system 3.1 as the following non-densely defined abstract Cauchy problem
\[ \frac{dw(t)}{dt} = Lw(t) + F(w(t)) , \quad \omega(0) = \begin{pmatrix} 0 \\ x_0 \end{pmatrix} \in \overline{D(L)}. \quad (3.2) \]

The global existence and uniqueness of solutions of system 3.2 follow from the results of [16] and [18].

**3.2. Existence of equilibria**

If \( \overline{w}(a) = (0, \overline{x}(a)) \in X_0 \) is an equilibrium of 3.2, we have
\[ \begin{pmatrix} 0 \\ \overline{x}(a) \end{pmatrix} \in D(L) \text{ and } L \left( \begin{pmatrix} 0 \\ \overline{x}(a) \end{pmatrix} \right) + F \left( \begin{pmatrix} 0 \\ \overline{x}(a) \end{pmatrix} \right) = 0, \]
which is equivalent to
\[ -\dddot{x}(a) - D\ddot{x}(a) = 0, \]
\[ -\dddot{x}(0) + B(\ddot{x}) = 0. \]  \tag{3.3}  

Hence we obtain
\[ \dddot{x}(a) = \left( \begin{array}{c} \dddot{u}(a) \\ \dddot{t}(a) \\ \dddot{v}(a) \end{array} \right) = e^{-Da}\dot{x}(0) \quad \text{and} \quad \dot{x}(0) = \left( \begin{array}{c} \Lambda + rT(1 - \frac{T + I}{K}) - \beta \nabla \bar{T} \\ \beta \nabla T \\ \int_0^{+\infty} \alpha(a)\dddot{t}(a)\,da \end{array} \right), \]  \tag{3.4}  

where \( T = \int_0^{+\infty} u(a)\,da, \ T = \int_0^{+\infty} t(a)\,da, \ V = \int_0^{+\infty} v(a)\,da. \) From 3.4, we can get
\[ d_1 T = \Lambda + rT(1 - \frac{T + I}{K}) - \beta \nabla T, \]
\[ d_2 I = \beta \nabla T, \]
\[ d_3 V = \int_0^{+\infty} \alpha(a)\dddot{t}(a)\,da = \int_0^{+\infty} \alpha(a)\beta \nabla \bar{T} e^{-d_2a}\,da = \beta \nabla \bar{T} K_0. \]

It is easy to see system 3.3 has always the equilibrium \( \bar{x}_1(a) = e^{-Da}(d_1 T_1, 0, 0)^T, \) where
\[ T_1 = \frac{-K(d_1 - r) + \sqrt{K^2(d_1 - r)^2 + 4Kr\Lambda}}{2r}. \]

Furthermore, we define
\[ R_0 = \frac{\beta T_1 K_0}{d_3}, \]

where \( R_0 \) is called the basic reproduction number of model 1.2. Biologically, \( R_0 \) represents the total number of newly infected cells resulted from a single infected cell. When \( R_0 > 1 \) holds, system 3.3 has a unique positive equilibrium
\[ \bar{x}(a) = \left( \begin{array}{c} \bar{u}^*(a) \\ \bar{t}^*(a) \\ \bar{v}^*(a) \end{array} \right) = e^{-Da} \left( \begin{array}{c} d_1 T^* \\ d_2 I^* \\ d_3 V^* \end{array} \right), \]

where
\[ T^* = \frac{d_3}{\beta K_0}, \quad V^* = \frac{\beta K_0 \Lambda + r - d_1 - \frac{rd_3}{K\beta K_0}}{\beta + \frac{rd_3}{Kd_2 K_0}} \quad \text{and} \quad I^* = \frac{\beta T^* V^*}{d_2}. \]
Lemma 3.1: System (1.2) has always the equilibrium $E_1(a) = (T_1, 0, 0)^T$. If $R_0 > 1$ holds, there exists a unique positive equilibrium of system (1.2)

$$E^*(a) = \begin{pmatrix} T^* \\ i^*(a) \\ V^* \end{pmatrix}.$$

3.3. Linearized equation

Let $y(t) := w(t) - \bar{w}(a)$, then system (3.2) is equivalent to the following system:

$$\frac{dy(t)}{dt} = Ly(t) + F(y(t) + \bar{w}(a)) - F(\bar{w}(a)),$$

$$y(0) = \begin{pmatrix} 0 \\ x_0 - \bar{x}(a) \end{pmatrix} \triangleq y_0 \in X_0,$$

(3.5)

and the equilibrium $\bar{w}(a)$ of system (3.3) is transformed into the zero equilibrium of system (3.5).

The linearized system of system (3.5) at the equilibrium 0 is as follows:

$$\frac{dy(t)}{dt} = Ay(t), \quad y_0 \in X_0 \quad t \geq 0,$$

where $A = L + DF(\bar{w})$. Then system (3.5) can be written as

$$\frac{dy(t)}{dt} = Ay(t) + H(y(t)), \quad y_0 \in X_0 \quad t \geq 0,$$

where $H(y(t)) = F(y(t) + \bar{w}(a)) - F(\bar{w}(a)) - DF(\bar{w})y(t)$ satisfying $H(0) = 0$, and $DH(0) = 0$.

Denote

$$\xi := \min\{d_1, d_2, d_3\} \quad \text{and} \quad \Omega := \{\lambda \in \mathbb{C} : \Re(\lambda) > -\xi\}.$$

By applying the results of Liu, Magal and Ruan [14], we obtain the following result.

Lemma 3.2: For $\lambda \in \Omega, \lambda \in \rho(L)$ and

$$(\lambda I - L)^{-1} \begin{pmatrix} \alpha \\ \psi \end{pmatrix} = \begin{pmatrix} 0 \\ \varphi \end{pmatrix} \iff \varphi(a) = e^{-(\lambda I+D)a} \alpha + \int_0^a e^{-(\lambda I+D)(a-s)} \psi(s) ds$$

with $\begin{pmatrix} \alpha \\ \psi \end{pmatrix} \in X$ and $\begin{pmatrix} 0 \\ \varphi \end{pmatrix} \in D(L)$. 

It is readily checked that
\[
\| (\lambda I - L)^{-1} \| \leq \frac{1}{(\text{Re}(\lambda) + \xi)}, \quad \forall \text{Re}(\lambda) > -\xi,
\]
so \( L \) is a Hille–Yosida operator and
\[
\| (\lambda I - L)^{-n} \| \leq \frac{1}{(\text{Re}(\lambda) + \xi)^n}, \quad \forall \text{Re}(\lambda) > -\xi, \quad n \geq 1. \tag{3.6}
\]
Define the part of \( L \) in \( \overline{D(L)} \) by \( L_0 \),
\[
L_0 : D(L_0) \subset X \rightarrow X
\]
with
\[
L_0x = Lx \quad \text{for} \quad x \in D(L_0) = \{ x \in D(L) : Lx \in \overline{D(L)} \},
\]
and we know
\[
D(L_0) = \left\{ \begin{pmatrix} 0 \\ \varphi \end{pmatrix} \in \{0_{\mathbb{R}^3}\} \times W^{1,1}((0, +\infty) \times \mathbb{R}^3) : \varphi(0) = 0 \right\}.
\]
Then, we can claim that \( L_0 \) is the infinitesimal generator of a \( C_0 \) semigroup \( \{T_{L_0}(t)\}_{t \geq 0} \) on \( \overline{D(L)} \) and for each \( t \geq 0 \) the linear operator \( T_{L_0}(t) \) is defined by
\[
T_{L_0}(t) \begin{pmatrix} 0 \\ \varphi \end{pmatrix} = \begin{pmatrix} 0 \\ \hat{T}_{L_0}(t)\varphi \end{pmatrix},
\]
where
\[
\hat{T}_{L_0}(t)(\varphi)(a) = \begin{cases} 
\text{e}^{-Dt}\varphi(a-t), & \text{if} \quad a \geq t, \\
0, & \text{otherwise}. 
\end{cases} \tag{3.7}
\]
Now we estimate the essential growth bound of the \( C_0 \) semigroup generated by \( A_0 \) which is the part of \( A \) in \( \overline{D(A)} \). We observe that for any \( \begin{pmatrix} 0 \\ \varphi \end{pmatrix} \in D(L) \),
\[
DF(\overline{w}) \begin{pmatrix} 0 \\ \varphi \end{pmatrix} = \begin{pmatrix} DB(\overline{x})(\varphi) \\ 0 \end{pmatrix},
\]
where
\[
DB(\overline{x})(\varphi) = \left( \begin{array}{ccc} 
\text{r}(1 - \frac{T + I}{\kappa}) - \beta \overline{V} & -\frac{\text{r}}{\kappa} \overline{T} & -\frac{\beta}{\kappa} \overline{T} \\
\beta \overline{V} & 0 & \beta \overline{T} \\
0 & 0 & 0 
\end{array} \right) \int_0^{+\infty} \varphi(a) da
\]
\[
+ \left( \begin{array}{ccc} 
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & 1 & 0 
\end{array} \right) \int_0^{+\infty} \alpha(a) \varphi(a) da.
\]
Then $DF(\overline{w}) : D(L) \subset X \to X$ is a compact bounded linear operator. From (3.6), we obtain
\[ \| T_{L_0}(t) \| \leq e^{-\xi t}. \]

Then we have
\[ \omega_{0,\text{ess}}(L_0) \leq \omega_0(L_0) \leq -\xi < 0. \]

By applying the perturbation results in [6], we obtain
\[ \omega_{0,\text{ess}}(A_0) \leq -\xi < 0. \]

Thus, by the above discussion and Theorem 3.5.5 in [1], we obtain the following proposition.

**Proposition 3.1:** The linear operator $A$ is a Hille–Yosida operator, and the essential growth rate of the strongly continuous semigroup generated by $A_0$ is strictly negative, that is,
\[ \omega_{0,\text{ess}}(A_0) < 0. \]

In order to apply Theorem 2.1, we remain to precise the spectral properties of $A_0$. Setting $C := DF(\overline{w})$, and let $\lambda \in \Omega$. Since $(\lambda I - L)$ is invertible, it follows that $\lambda I - (L + C)$ is invertible if and only if $I - C(\lambda I - L)^{-1}$ is invertible. If $I - C(\lambda I - L)^{-1}$ is invertible, we obtain
\[ (\lambda I - (L + C))^{-1} = (\lambda I - L)^{-1}(I - C(\lambda I - L)^{-1})^{-1}. \]

Consider the equation
\[ (I - C(\lambda I - L)^{-1}) \begin{pmatrix} \alpha \\ \varphi \end{pmatrix} = \begin{pmatrix} \hat{\alpha} \\ \hat{\varphi} \end{pmatrix}, \]
that is
\[ \begin{pmatrix} \alpha \\ \varphi \end{pmatrix} - C \left( e^{-(\lambda I + D)a} \alpha + \int_0^a e^{-(\lambda I + D)(a-s)} \varphi(s) ds \right) = \begin{pmatrix} \hat{\alpha} \\ \hat{\varphi} \end{pmatrix}. \]

Then, we obtain the system
\[ \alpha - DB(\overline{\alpha})(e^{-(\lambda I + D)a} \alpha + \int_0^a e^{-(\lambda I + D)(a-s)} \varphi(s) ds) = \hat{\alpha}, \]
\[ \varphi(a) = \hat{\varphi}(a), \]
this system can be written as
\[ \alpha - DB(\overline{\alpha})(e^{-(\lambda I + D)a} \alpha) = \hat{\alpha} + DB(\overline{\alpha}) \left( \int_0^a e^{-(\lambda I + D)(a-s)} \varphi(s) ds \right), \]
\[ \varphi = \hat{\varphi}. \]

From the formula of $DB(\overline{\alpha})$, we know
\[ \alpha - DB(\bar{x})(e^{-(\lambda I + D)a}\alpha) = M(\lambda)\alpha, \]

where

\[
M(\lambda) = I - \begin{pmatrix}
 r(1 - \frac{T + I}{K}) - \beta V - \frac{r}{K} - \frac{T T_1}{K} & -\frac{r}{K} T_1 & -\beta T_1 \\
 \beta V & 0 & 0 \\
 0 & 0 & 0
\end{pmatrix} \int_0^{+\infty} e^{-(\lambda I + D)a} da
- \begin{pmatrix}
 0 & 0 & 0 \\
 0 & 0 & 0 \\
 0 & 1 & 0
\end{pmatrix} \int_0^{+\infty} \alpha(a)e^{-(\lambda I + D)a} da.
\]

Denote

\[
S(\lambda, \bar{\varphi}) = DB(\bar{x})(\int_0^a e^{-(\lambda I + D)(a-s)} \bar{\varphi}(s) ds).
\]

Then \(M(\lambda)\alpha = \hat{\alpha} + S(\lambda, \bar{\varphi}).\) When \(M(\lambda)\) is invertible, we have

\[
\alpha = M(\lambda)^{-1}(\hat{\alpha} + S(\lambda, \bar{\varphi})).
\]

From the above discussion and by using the proof of Lemma 3.5 in [31], we obtain the following lemma.

**Lemma 3.3:** The following results hold:

(i) \(\sigma(L + C) \cap \Omega = \sigma_p(L + C) \cap \Omega = \\{\lambda \in \Omega : \det(M(\lambda)) = 0\};\)

(ii) If \(\lambda \in \rho(L + C) \cap \Omega,\) we have the following formula for the resolvent \((\lambda I - (L + C))^{-1} = \begin{pmatrix} \alpha \\ \varphi \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix},\)

where

\[
\bar{\varphi}(a) = e^{-(\lambda I + D)a}M(\lambda)^{-1}(\alpha + S(\lambda, \varphi)) + \int_0^a e^{-(\lambda I + D)(a-s)} \varphi(s) ds,
\]

and \(M(\lambda), S(\lambda, \varphi)\) defined as above.

From the above discussion, we know that the linear operator \(A\) satisfies Assumptions 2.1, 2.2 and 2.3.

### 3.4. Stability of the boundary equilibrium

Now, we consider the stability of the boundary equilibrium \(E_1(T_1, 0, 0),\) we obtain

\[
M(\lambda) = I - \begin{pmatrix}
 r(1 - \frac{T + I}{K}) - \frac{r}{K} T_1 & -\frac{r}{K} T_1 & -\beta T_1 \\
 \frac{r}{K} T_1 & 0 & 0 \\
 0 & 0 & 0
\end{pmatrix} \int_0^{+\infty} e^{-(\lambda I + D)a} da
- \begin{pmatrix}
 0 & 0 & 0 \\
 0 & 0 & 0 \\
 0 & 1 & 0
\end{pmatrix} \int_0^{+\infty} \alpha(a)e^{-(\lambda I + D)a} da.
\]

Thus we obtain the characteristic equation
\[
\det(M(\lambda)) = \frac{(\lambda + d_1 - r(1 - \frac{T_1}{K}) - \frac{r}{K}T_1)(\lambda^2 + a_1\lambda + a_2 + a_3e^{-\lambda\tau})}{(\lambda + d_1)(\lambda + d_2)(\lambda + d_3)} = f_0(\lambda) = 0,
\]
where \(a_1 = (d_2 + d_3), a_2 = d_2d_3 > 0, a_3 = -\beta d_2 K_0 T_1 < 0.\)
We know that the coefficients \(a_3\) not depend on \(\tau\) by our assumption.
It is easy to see that
\[
\{\lambda \in \Omega : \det(M(\lambda)) = 0\} = \{\lambda \in \Omega : f_0(\lambda) = 0\},
\]
we know that \(E_1\) satisfies system (1.2), so \(r(1 - \frac{T_1}{K}) = d_1 - \frac{\Lambda}{T_1}\), then
\[
\lambda + d_1 - \left( r \left( 1 - \frac{T_1}{K} \right) - \frac{r}{K}T_1 \right) = 0,
\]
we have
\[
\lambda = -d_1 + \left( r \left( 1 - \frac{T_1}{K} \right) - \frac{r}{K}T_1 \right) = - \left( \frac{\Lambda}{T_1} + \frac{r}{K}T_1 \right) < 0,
\]
which have a negative eigenvalue, and the other eigenvalues are given by
\[
\lambda^2 + a_1\lambda + a_2 + a_3e^{-\lambda\tau} = 0. \tag{3.8}
\]
When \(\tau = 0\), Equation (3.8) becomes
\[
\lambda^2 + a_1\lambda + a_2 + a_3 = 0
\]
with \(a_1 > 0\). If \(R_0 < 1\), it is readily obtain that \(a_2 + a_3 > 0\). Hence, equilibrium \(E_1\) is locally asymptotically stable when \(\tau = 0\).

When \(\tau \neq 0\), let \(\lambda = i\omega (\omega > 0)\) is the solution of Equation (3.8), then separating in real and imaginary parts, we obtain
\[
-\omega^2 + a_2 = -a_3\cos(\omega\tau),
\]
\[
a_1\omega = a_3\sin(\omega\tau).
\]
Thus we have
\[
\omega^4 + (a_1^2 - 2a_2)\omega^2 + (a_2^2 - a_3^2) = 0, \tag{3.9}
\]
where \(a_1^2 - 2a_2 > 0\). If \(R_0 < 1\), then \(a_2^2 - a_3^2 = (a_2 + a_3)(a_2 - a_3) > 0\). Equation (3.9) has no positive roots, which is a contradiction with \(\omega > 0\). Thus we have the following theorem.

**Theorem 3.4:** If \(R_0 < 1\), then \(E_1\) is locally asymptotically stable for all \(\tau \geq 0\).
3.5. Stability of the positive equilibrium and Hopf bifurcation

When $R_0 > 1$, the characteristic equation of system (1.2) about the positive equilibrium $E^*(a)$ can be rewritten as

$$\det(M(\lambda)) = \frac{\lambda^3 + a\lambda^2 + b\lambda + c + (d + e\lambda)e^{-\lambda\tau}}{(\lambda + d_1)(\lambda + d_2)(\lambda + d_3)} = \frac{f(\lambda)}{s(\lambda)} = 0,$$

where

$$a = \frac{\Lambda}{T^*} + \frac{rT^*}{K} + d_2 + d_3,$$

$$b = d_2d_3 + (d_2 + d_3)(\frac{\Lambda}{T^*} + \frac{rT^*}{K}) + \frac{rT^*\beta V^*}{K},$$

$$c = d_3(d_2(\frac{\Lambda}{T^*} + \frac{rT^*}{K}) + \frac{rT^*\beta V^*}{K}),$$

$$d = d_2d_3(\beta V^* - \frac{\Lambda}{T^*} - \frac{rT^*}{K}),$$

$$e = -\beta T^* d_2 K_0.$$ 

Since $K_0$ is a constant, we know that the coefficients $a, b, c, d$ and $e$ have nothing to do with $\tau$.

It is easy to see that

$$\{\lambda \in \Omega : \det(M(\lambda)) = 0\} = \{\lambda \in \Omega : f(\lambda) = 0\}.$$ 

If $\tau = 0$, then

$$f(\lambda) = \lambda^3 + a\lambda^2 + (b + e)\lambda + (c + d) = 0.$$ 

Since $a > 0$, by the Routh–Hurwitz criterion, when $\tau = 0$ all the roots of $f(\lambda) = 0$ have negative real parts if and only if

$$(H1) \, a(b + e) > (c + d) > 0$$

holds.

If $\tau \neq 0$, let $\lambda = i\omega$ ($\omega > 0$) be a purely imaginary roots of $f(\lambda) = 0$. Then, we have

$$-i\omega^3 - a\omega^2 + ib\omega + c + de^{-i\omega\tau} + i\omega e^{-i\omega\tau} = 0.$$ 

Separating the real part and the imaginary part in the above equation, we can obtain

$$-\omega^3 + bw = d \sin(\omega\tau) - e\omega\cos(\omega\tau),$$

$$a\omega^2 - c = e\omega\sin(\omega\tau) + d\cos(\omega\tau).$$

Thus we have

$$(-\omega^3 + bw)^2 + (-a\omega^2 + c)^2 = d^2 + (e\omega)^2,$$

i.e.

$$\omega^6 + (a^2 - 2b)\omega^4 + (b^2 - e^2 - 2ac)\omega^2 + (c^2 - d^2) = 0.$$ 

Denote $z = \omega^2$, (3.13) becomes

$$z^3 + (a^2 - 2b)z^2 + (b^2 - e^2 - 2ac)z + (c^2 - d^2) = 0.$$ 

Let $z_1, z_2$ and $z_3$ be three roots of Equation (3.14), if

$$(H2) \, a^2 - 2b > 0, \quad c^2 - d^2 < 0$$

holds, then

$$z_1 + z_2 + z_3 = -(a^2 - 2b) < 0 \text{ and } z_1z_2z_3 = -(c^2 - d^2) > 0.$$
it is easy to know that (3.14) has only one positive real root. We denote this positive real root by $z^*$. Then (3.13) has only one positive real root $\omega_0 = \sqrt{z^*}$.

Let 
\[
g(z) = z^3 + (a^2 - 2b)z^2 + (b^2 - e^2 - 2ac)z + (c^2 - d^2),
\]
it is easy to know that $g'(z)|_{z=z^*} > 0$, then we have 
\[
(3z^2 + (2a^2 - 4b)z + (b^2 - e^2 - 2ac))|_{z=z^*} > 0,
\]
i.e.
\[
(3\omega^4 + (2a^2 - 4b)\omega^2 + (b^2 - e^2 - 2ac))|_{\omega=\omega_0} > 0. \tag{3.15}
\]

From (3.11), we know that $f(\lambda) = 0$ with $\tau = \tau_k$ has a pair of purely imaginary roots $\pm i\omega_0$, where 
\[
\tau_k = \begin{cases} 
\frac{1}{i\omega_0} \left( \arccos \frac{\omega_0^4 + (ad - be)\omega_0^2 - cd}{d^2 + e^2\omega_0^2} + 2k\pi \right), & \eta \geq 0, \\
\frac{1}{i\omega_0} \left( - \arccos \frac{\omega_0^4 + (ad - be)\omega_0^2 - cd}{d^2 + e^2\omega_0^2} + 2(k + 1)\pi \right), & \text{otherwise},
\end{cases} \tag{3.16}
\]
for $k = 0, 1, 2, \ldots$ and with $\eta = (ae - d)\omega^3 + (be - ce)\omega$.

**Lemma 3.5:** Assume that $R_0 > 1$ and (H2) be satisfied, then $\frac{df(\lambda)}{d\lambda} |_{\lambda=i\omega_0} \neq 0$. Therefore $\lambda = i\omega_0$ is a simple root of $f(\lambda) = 0$.

**Proof:** Differentiating the equation $f(\lambda) = 0$ with respect to $\lambda$ and taking the derivative of $\lambda$ with respect to $\tau$ in $f(\lambda) = 0$, we have 
\[
\frac{f(\lambda)}{d\lambda} |_{\lambda=i\omega_0} = (3\lambda^2 + 2a\lambda + b + ee^{-\tau}\lambda - \tau (e\lambda + d)e^{-\tau}\lambda) |_{\lambda=i\omega_0}.
\]
Thus if 
\[
\frac{df(\lambda)}{d\lambda} |_{\lambda=i\omega_0} = 0,
\]
separating the real part and the imaginary part in the above equation, we can obtain 
\[
-3\omega_0^2 + b = -e \cos(\omega_0\tau_k) + \tau_k(d \cos(\omega_0\tau_k) + e\omega_0 \sin(\omega_0\tau_k)),
\]
\[
2a\omega_0 = e \sin(\omega_0\tau_k) + \tau_k(e\omega_0 \cos(\omega_0\tau_k) - d \sin(\omega_0\tau_k)). \tag{3.17}
\]
Now defining 
\[
G(\omega) = g(\omega^2) = (-\omega^3 + b\omega^2 - d^2 + (a\omega^2 - c)^2 - (e\omega)^2),
\]
then $G(\omega_0) = 0$.
\[
G'(\omega) = 2(-\omega^3 + b\omega)(-3\omega^2 + b) + 2(a\omega^2 - c)(2a\omega) - 2e^2\omega.
\]
According to Equation (3.11), we know 
\[
-\omega_0^3 + b\omega_0 = d \sin(\omega_0\tau_k) - e\omega_0 \cos(\omega_0\tau_k), \tag{3.18}
\]
\[
a\omega_0^2 - c = d \cos(\omega_0\tau_k) + e\omega_0 \sin(\omega_0\tau_k).
\]
With the help of Equations (3.17) and (3.18), we deduce that $G'(\omega_0) = 0$. 

Figure 1. The trajectory of susceptible CD4$^+$ T cells $T(t)$, infected CD4$^+$ T cells $\int_0^{+\infty} i(t, a) da$, free virus $V(t)$ versus time with the initial condition $(1, 10^{e^{-0.5a}}, 10)$. When $\tau = 1, \tau = 5$ the equilibrium point $E_1$ is local asymptotically stable.

Figure 2. The trajectory of susceptible CD4$^+$ T cells, infected CD4$^+$ T cells and free virus concentration versus time with the initial condition $(1, 10^{e^{-0.5a}}, 10)$, when $\tau = 1.4 < \tau_0$.

However, $G'(\omega_0) = 2\omega_0 g'(\omega_0^2) = 2\omega_0 g'(z^*) > 0$, thus

$$\frac{df(\lambda)}{d\lambda} \bigg|_{\lambda=i\omega_0} \neq 0.$$

This completes the proof.
Figure 3. The phase portrait of free virus $V(t)$ versus susceptible CD4$^+$ T cells $T(t)$ and infected CD4$^+$ T cells $\int_0^{+\infty} i(t,a) da$ with the initial condition $(1, 10e^{-0.5a}, 10)$, when $\tau = 1.4 < \tau_0$.

Figure 4. The trajectory of susceptible CD4$^+$ T cells and free virus concentration versus time with the initial condition $(1, 10e^{-0.5a}, 10)$, when $\tau = 1.7 > \tau_0$.

Lemma 3.6: Assume that $R_0 > 1$ and (H2) be satisfied, denote the root $\lambda(\tau) = \alpha(\tau) + i\omega(\tau)$ of $f(\lambda) = 0$, satisfying $\alpha(\tau_k) = 0$, $\omega(\tau_k) = \omega_0$, where $\tau_k$ is defined in (3.16). Then

$$\alpha'(\tau_k) = \text{Re}\left(\frac{d\lambda}{d\tau}\right)|_{\tau=\tau_k} > 0.$$
Figure 5. The surface of infected CD4$^+$ T cells concentration $i(t, a)$ versus time $t$ and age $a$ with the initial condition $(1, 10e^{-0.5a}, 10)$, when $\tau = 1.7 > \tau_0$.

Proof: Taking the derivative of $\lambda$ with respect to $\tau$ in $f(\lambda) = 0$, it is easy to have

$$(3\lambda^2 + 2a\lambda + b)\frac{d\lambda}{d\tau} + ee^{-\lambda\tau}\frac{d\lambda}{d\tau} - (e\lambda + d)e^{-\lambda\tau}(\tau\frac{d\lambda}{d\tau} + \lambda) = 0,$$

$$(\frac{d\lambda}{d\tau})^{-1} |_{\tau=\tau_k} = (-\frac{(3\lambda^2 + 2a\lambda + b)}{\lambda(\lambda^3 + a\lambda^2 + b\lambda + c)} + \frac{e}{(e\lambda + d)\lambda} - \frac{\tau}{\lambda}) |_{\tau=\tau_k}.$$

By using (3.12), we obtain

$$Re\left(\frac{d\lambda}{d\tau}\right)^{-1} |_{\tau=\tau_k} = \frac{3\omega_0^4 + (2a^2 - 4b)\omega_0^2 + (b^2 - e^2 - 2ac)}{(f\omega_0^2 + (g - e\omega_0^2)^2}.$$

By using (3.15), it is easy know that

$$Re\left(\frac{d\lambda}{d\tau}\right)^{-1} |_{\tau=\tau_k} > 0.$$

Noting that

$$\text{sign}\left(Re\left(\frac{d\lambda}{d\tau}\right) |_{\tau=\tau_k}\right) = \text{sign}\left(Re\left(\frac{d\lambda}{d\tau}\right)^{-1} |_{\tau=\tau_k}\right),$$

thus

$$Re\left(\frac{d\lambda}{d\tau}\right) |_{\tau=\tau_k} > 0.$$

This completes the proof. 

Theorem 3.7: If $R_0 > 1$, (H1) and (H2) hold, then the following results hold:
Figure 6. The phase portrait of free virus $V(t)$ versus susceptible CD4$^+$ T cells $T(t)$ and infected CD4$^+$ T cells $\int_0^{\infty} i(t,a) da$ with the initial condition $(1, 10e^{-0.5a}, 10)$, when $\tau = 1.7 > \tau_0$.

(i) If $\tau \in [0, \tau_0)$, then the positive equilibrium $E^*(a)$ of system (1.2) is asymptotically stable.

(ii) If $\tau > \tau_0$, the positive equilibrium $E^*(a)$ of system (1.2) is unstable.

By Theorem 2.1, the above results can be summarized as the following Hopf bifurcation theorem for system (1.2).

**Theorem 3.8:** If $R_0 > 1$ and (H2) holds. Then there exist $\tau_k > 0, k = 0, 1, 2, \ldots$, where $\tau_k$ is defined in (3.16), such that age-structured HIV infection model (1.2) undergoes a Hopf bifurcation at the positive equilibrium $E^*(a)$. In particular, when $\tau = \tau_k$, a non-trivial periodic solution bifurcates from the equilibrium $E^*(a)$.

**4. Numerical simulations**

In this section, we present some numerical simulations to verify the main results by using MATLAB programs. On the one hand, we simulate the system (1.2) by choosing the parameters $\Lambda = 1$, $r = 2$, $K = 25$, $\beta = 0.01$, $d_1 = 0.4$, $d_2 = 0.4$, $d_3 = 0.6$, $K_0 = 1$, we can calculate $\alpha^* = 0.4e^{0.4\tau}$, $R_0 = 0.3434 < 1$, by Theorem 3.4 we can expect that the virus-free equilibrium $E_0(20.6066, 0, 0)$ is local asymptotically stable for all $\tau \geq 0$, see Figure 1. On the other hand, we take the parameters $\Lambda = 2$, $r = 2$, $K = 150$, $\beta = 0.05$, $d_1 = 0.2$, $d_2 = 0.4$, $d_3 = 0.6$, $K_0 = 3$, we can calculate $\alpha^* = 1.2e^{0.4\tau}$, $R_0 = 34.03 > 1$, then (1.2) has only one positive equilibrium $E^*(a) = (4, 7.9294e^{0.4a}, 39.6471)$. By algorithms in the previous sections, we obtain $\omega_0 = 0.4831$, $\tau_0 = 1.5889$, and readily check that (H1) and (H2) hold. Thus, by Figures 2 and 3, $E^*(a)$ is stable when $\tau \in [0, \tau_0)$. From the numerical simulations, we can see the solution of system (1.2) with the initial condition $(1, 10e^{-0.5a}, 10)$ and parameter $\tau = 1.4$ tends to the positive equilibrium $E^*(a)$. By Figures
4–6, when τ through the critical value τ₀, E*(a) loses its stability and Hopf bifurcation occurs at τ = τ₀ = 1.5889.

5. Conclusion and discussion

As in Mohebbi et al. [20], we can derive an equivalent discrete delay system as opposed to our age-structured model when t > τ. For the system (1.2), we let I = ∫₀⁺∞ i(t, a) da, and note that i(t, a) = e⁻ⁿτθi(t⁻τ, a⁻τ), then the system (1.2) can be reformulated as the following DDEs when t > τ:

\[
\frac{dT(t)}{dt} = \Lambda + rT(t) \left( 1 - \frac{T(t) + I(t)}{K} \right) - d₁T(t) - βT(t)V(t),
\]

\[
\frac{dI}{dt} = βTV - d₂I,
\]

\[
\frac{dV(t)}{dt} = α^*e^{-d₂τI(t-τ)} - d₃V(t).
\]

(5.1)

We can study the Hopf bifurcation of the system (5.1) using similar methods of [12,19,25,26,36].

In this paper, we use a different method, that is, by using the centre manifold theory and Hopf bifurcation theorem of non-densely defined Cauchy problems in [17] and [14], to study the Hopf bifurcation of an age-structured HIV infection model with logistic target-cell growth and virus-to-cell infection. By choosing τ as the bifurcation parameter and analysing the corresponding characteristic equation, we can conclude that the local asymptotically stability of infection-free equilibrium E₁ is completely determined by the basic reproduction number R₀. If R₀ < 1, then the infection-free equilibrium E₁ is local asymptotically stable for τ ≥ 0. If R₀ > 1, the sufficient conditions for the local stability of the positive equilibrium and the existence of Hopf bifurcation are obtained. Finally, numerical simulations are given to verify the theoretical analysis. From these waveforms and the phase trajectories above, it is shown that these results are in accord with the theoretical analysis.

Our analytical results indicate that introduction of parameter τ can affect the dynamic behaviour of the system (1.2) and that there is a threshold τ₀, when τ = τ₀, the model exhibits Hopf bifurcation. Through these results, it can be concluded that delay τ plays an important role in the HIV spread and induces Hopf bifurcation with Logistic growth in our model.

For studying that the logistic growth of target cells is necessary for oscillation with or without intracellular delay. We let r = 0, that means, there is no logistic growth rate in system (1.2), we know that the system (1.2) has only a boundary equilibrium E₁ = (Λ/d₁, 0, 0), when basic reproduction number R₀ = βΛK₀/d₁d₃ < 1, if R₀ > 1, besides E₁, the system (1.2) has a unique positive equilibrium E*(a) = (T*, i* (a), V*), where T* = d₃/βK₀, V* = (R₀ - 1)d₁/β, i* (a) = 1/β(Λ - d₁d₃/βK₀)e⁻ⁿτ. Then the characteristic equation of system (1.2) about the positive equilibrium E*(a) is

\[
\text{det}(M(λ)) = \frac{λ^3 + aλ^2 + bλ + c + (d + eλ)e^{-λτ}}{(λ + d₁)(λ + d₂)(λ + d₃)} = \frac{f(λ)}{s(λ)} = 0,
\]

(5.2)
where \( a = \Lambda/\bar{T^*} + d_2 + d_3, \quad b = d_2d_3 + (d_2 + d_3)\Lambda/\bar{T^*}, \quad c = d_2d_3\Lambda/\bar{T^*}, \quad d = d_2d_3 (\beta\bar{V}^* - \Lambda/\bar{T^*}), \quad e = -d_2d_3, \) respectively.

If \( \tau = 0, \) then
\[
f(\lambda) = \lambda^3 + a\lambda^2 + (b + e)\lambda + (c + d) = 0.
\]

Since \( a > 0 \) and \( \Lambda/\bar{T^*} - \beta\bar{V}^* = d_1 > 0, \) it is easy to deduce that
\[
a(b + e) > (c + d) > 0,
\]
by the Routh–Hurwitz criterion, we know that all the roots of \( f(\lambda) = 0 \) have negative real parts when \( \tau = 0. \) Hence, the equilibrium \( E^*(a) \) is locally asymptotically stable when \( \tau = 0. \)

If \( \tau \neq 0, \) let \( \lambda = i\omega (\omega > 0) \) be a purely imaginary roots of \( f(\lambda) = 0. \) Then, we have
\[
-i\omega^3 - a\omega^2 + ib\omega + c + de^{-i\omega\tau} + ie\omega e^{-i\omega\tau} = 0.
\]

Separating the real part and the imaginary part in the above equation, we can obtain
\[
\begin{align*}
-\omega^3 + b\omega &= d\sin(\omega\tau) - e\omega\cos(\omega\tau), \\
\omega^2 - c &= e\omega\sin(\omega\tau) + d\cos(\omega\tau).
\end{align*}
\]

Thus we have
\[
(-\omega^3 + b\omega)^2 + (-\omega^2 + c)^2 = d^2 + (e\omega)^2,
\]
i.e.
\[
\omega^6 + (a^2 - 2b)\omega^4 + (b^2 - e^2 - 2ac)\omega^2 + (c^2 - d^2) = 0. \quad (5.5)
\]

Denote \( z = \omega^2, \) (5.5) becomes
\[
z^3 + (a^2 - 2b)z^2 + (b^2 - e^2 - 2ac)z + (c^2 - d^2) = 0. \quad (5.6)
\]

By simple calculation, we deduce that
\[
a^2 - 2b > 0, (a^2 - 2b)(b^2 - e^2 - 2ac) > (c^2 - d^2) > 0,
\]
by the Routh–Hurwitz criterion, we know that Equation (5.6) has no positive roots, which is a contradiction with \( \omega > 0. \) Thus we have the following conclusion. If \( R_0 > 1, \) then \( E^*(a) \) is locally asymptotically stable for all \( \tau \geq 0. \)

Then the system (1.2) does not undergo Hopf bifurcation at the positive equilibrium \( E^*(a). \) This conclusion is consistent with that of [20,24], the logistic growth of target cells is necessary for the observed oscillatory dynamics in the system (1.2). Furthermore, we have done some simulations (not shown). We did not find other critical parameters for Hopf bifurcation. Above results suggest that delay and the logistic growth of uninfected cells are both the factor which can induce sustained oscillations.

**Disclosure statement**

No potential conflict of interest was reported by the authors.
Funding

This work is supported by the NNSF of China (11861044 and 11661050), the NSF of Gansu Province (148RJZA024) and the Development Program of HongLiu first-class disciplines in Lanzhou University of Technology.

References

[1] W. Arendt, C. Batty, M. Hieber and F. Neubrander, Vector-Valued Laplace Transforms and Cauchy Problems, Birkhäuser Verlag, Basel, 2001.

[2] B. Buonomo and C. Vargas-De-León, Global stability for an HIV-1 infection model including an eclipse stage of infected cells, J. Math. Anal. Appl. 385(2) (2012), pp. 709–720.

[3] Y. Cai, J. Jiao, Z. Güi, Environmental variability in a stochastic epidemic model. Appl. Math. Comput. 329 (2018), pp. 210–236.

[4] J. Cushing, An Introduction to Structured Population Dynamics, Society for Industrial and Applied Mathematics, Philadelphia, PA, 1998.

[5] Z. Du and Z. Feng, Existence and asymptotic behaviors of traveling waves of a modified vector-disease model, Commun. Pur. Appl. Anal. 17 (2018), pp. 1899–1920.

[6] A. Ducrot, Z. Liu and P. Magal, Essential growth rate for bounded linear perturbation of non densely defined Cauchy problems, J. Math. Anal. Appl. 341(1) (2008), pp. 501–518.

[7] D.D. Ho, A.U. Neumann, A.S. Perelson, W. Chen, J.M. Leonard and M. Markowitz, Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection, Nature 373(6510) (1995), pp. 123–126.

[8] H.F. Huo, R. Chen and X.Y. Wang, Modelling and stability of HIV/AIDS epidemic model with treatment, Appl. Math. Model 40(13–14) (2016), pp. 6550–6559.

[9] H.F. Huo, F.F. Cui and H. Xiang, Dynamics of an SAITS alcoholism model on unweighted and weighted networks, Physica A 496 (2018), pp. 249–262.

[10] H.F. Huo and M.X. Zou, Modelling effects of treatment at home on tuberculosis transmission dynamics, Appl. Math. Model 40 (2016), pp. 9474–9484.

[11] M. Iannelli, Mathematical Theory of Age-Structured Population Dynamics, Giadini Editori Stampatori, Pisa, 1994.

[12] Z. Jiang, W. Ma and J. Wei, Global Hopf bifurcation and permanence of a delayed SEIRS epidemic model, Math. Comput. Simulat. 122 (2016), pp. 35–54.

[13] F. Li and J. Wang, Analysis of an HIV infection model with logistic target-cell growth and cell-to-cell transmission, Chaos Soliton. Fract. 81 (2015), pp. 136–145.

[14] Z. Liu, P. Magal and S. Ruan, Hopf bifurcation for non-densely defined Cauchy problems, Z. Angew. Math. Phys. 62(2) (2011), pp. 191–222.

[15] Z. Liu, P. Magal and S. Ruan, Oscillations in age-structured models of consumer-resource mutualisms, Discrete Cont. Dyn-B 21(2) (2016), pp. 537–555.

[16] P. Magal, Compact attractors for time-periodic age structured population models, Electron J. Differ. Eq. 2001(65) (2001), pp. 1–35.

[17] P. Magal and S. Ruan, Center manifolds for semilinear equations with non-dense domain and applications on Hopf bifurcation in age structured models, Mem. Am. Math. Soc. 202 (2009), pp. 951.

[18] P. Magal and S. Ruan, On semilinear Cauchy problems with non-dense domain, Adv. Differ. Equ.14(11–12) (2009), pp. 1041–1084.

[19] Y.Y. Meng and Y.Q. Wu, Bifurcation and control in a singular phytoplankton–zooplankton–fish model with nonlinear fish harvesting and taxation, Int. J. Bifurcat. Chaos 28(3) (2018), pp. 1850042. (24 pages).

[20] H. Mohebbi, A. Aminataei, C. Browne and M.R. Razvan, Hopf bifurcation of an age-structured virus infection model, Discrete Cont. Dyn-B 23 (2018), pp. 861–885.

[21] P.W. Nelson, M.A. Gilchrist, D. Coombs, J.M. Hyman and A.S. Perelson, An age-structured model of HIV infection that allows for variations in the production rate of viral particles and the death rate of productively infected cells, Math. Biosci. Eng. 1(2) (2004), pp. 267–288.
[22] A.S. Perelson, A.U. Neumann, M. Markowitz, J.M. Leonard and D.D. Ho, *HIV-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time*, Science 271(5255) (1996), pp. 1582–1586.

[23] L. Rong, Z. Feng and A.S. Perelson, *Mathematical analysis of age-structured HIV-1 dynamics with combination antiretroviral therapy*, SIAM J. Appl. Math. 67(3) (2007), pp. 731–756.

[24] H. Shu, L. Wang and J. Watmough, *Global stability of a nonlinear viral infection model with infinitely distributed intracellular delays and CTL immune responses*, SIAM J. Appl. Math. 73(3) (2013), pp. 1280–1302.

[25] H. Shu, L. Wang and J. Wu, *Bounded global Hopf branches for stage-structured differential equations with unimodal feedback*, Nonlinearity 30(3) (2017), pp. 943–964.

[26] Y. Song, T. Yin and H. Shu, *Dynamics of a ratio-dependent stage-structured predator-prey model with delay*, Math. Method Appl. Sci. 40, pp. 6451–6467.

[27] X. Tian and R. Xu, *Global stability and Hopf bifurcation of an HIV-1 infection model with saturation incidence and delayed CTL immune response*, Appl. Math. Comput. 237(7) (2014), pp. 146–154.

[28] Unaids, *Unaids announces 18.2 million people on antiretroviral therapy, but warns that 15–24 years of age is a highly dangerous time for young women*, accessed 1 Dec 2016 (2016).

[29] W. Wang, Y. Cai, Z. Ding and Z. Gui, *A stochastic differential equation SIS epidemic model incorporating Ornstein–Uhlenbeck process*, Physica A 509 (2018), pp. 921–936.

[30] J. Wang, J. Lang and X. Zou, *Analysis of an age structured HIV infection model with virus-to-cell infection and cell-to-cell transmission*, Nonlinear Anal. Real 34 (2017), pp. 75–96.

[31] Z. Wang and Z. Liu, *Hopf bifurcation of an age-structured compartmental pest-pathogen model*, J. Math. Anal. Appl. 385(2) (2012), pp. 1134–1150.

[32] X. Wang, X. Liu, W.C. Xie, W. Xu and Y. Xu, *Global stability and persistence of HIV models with switching parameters and pulse control*, Math. Comput. Simulat. 123(C) (2016), pp. 53–67.

[33] G. Webb, *Theory of Nonlinear Age-Dependent Population Dynamics*, Marcel Dekker, New York, NY, 1985.

[34] H. Xiang, Y.L. Tang and H.F. Huo, *A viral model with intracellular delay and humoral immunity*, B. Malays. Math. Sci. Soc. 40 (2017), pp. 1011–1023.

[35] H. Xiang, Y.Y. Wang and H.F. Huo, *Analysis of the binge drinking models with demographics and nonlinear infectivity on networks*, J. Appl. Anal. Comput. 8(5) (2018), pp. 1535–1554.

[36] J. Yang, X. Wang and F. Zhang, *A differential equation model of HIV infection of CD4 T-cells with delay*, Discrete Dyn. Nat. Soc. 2008 (2008).

[37] X.B. Zhang, Q.H. Shi, S.H. Ma, H.F. Huo and D.G. Li, *Dynamic behavior of a stochastic SIQS epidemic model with Lévy jumps*, Nonlinear Dyn. 93 (2018), pp. 1481–1493.