Bifurcation analysis of an age structured HIV infection model with both virus-to-cell and cell-to-cell transmissions

Xiangming Zhang\textsuperscript{a,*} and Zhihua Liu\textsuperscript{a,*,†}

\textsuperscript{a}School of Mathematical Sciences, Beijing Normal University, Beijing, 100875, People’s Republic of China

Abstract

We make a mathematical analysis of an age structured HIV infection model with both virus-to-cell and cell-to-cell transmissions to understand the dynamical behavior of HIV infection in vivo. In the model, we consider the proliferation of uninfected CD4\textsuperscript{+} T cells by a logistic function and the infected CD4\textsuperscript{+} T cells are assumed to have an infection-age structure. Our main results concern the Hopf bifurcation of the model by using the theory of integrated semigroup and the Hopf bifurcation theory for semilinear equations with non-dense domain. Bifurcation analysis indicates that there exist some parameter values such that this HIV infection model has a non-trivial periodic solution which bifurcates from the positive equilibrium. The numerical simulations are also carried out.

Key words: HIV infection model; Logistic growth; Virus-to-cell; Cell-to-cell; Age structure; Non-densely defined Cauchy problem; Hopf bifurcation

Mathematics Subject Classification: 34C20; 34K15; 37L10

1 Introduction

The human immunodeficiency virus, HIV, gives rise to acquired immune deficiency syndrome, AIDS. Nowadays AIDS still severely threatens the people’s health all over the world. The main target of HIV infection is a class of lymphocytes, or white blood cells, known as CD4\textsuperscript{+}
T cells. In general, there are two fundamental modes of viral infection and transmission, one is the classical virus-to-cell infection and the other is direct cell-to-cell transmission. In the classical mode, viral particles that released from infected cells arbitrarily move around any distance to discover a new target cell to infect. For the direct cell-to-cell transmission, HIV infection can occur by the movement of viruses by means of direct contact between infected cells and uninfected cells via some structures, such as membrane nanotubes [1]. In recent years, HIV infection model which involves different infection modes, such as the classical virus-to-cell infection [2–6], the direct cell-to-cell transmission [7–9], and both virus-to-cell infection and cell-to-cell transmission [10–12], has been extensively studied by many scholars.

In population dynamics, age structure, in many situations, can affect population size and growth in a major way because different ages indicate different reproduction and survival abilities and different behaviors. Generally, the progress of disease propagation and individual interactions are modeled by using an ODE system [3, 9] or DDE system [4, 5, 11]. When age structure is introduced into individual interactions, population dynamical models become considerably intricate. Recently, as the significance of age structure in populations has become increasingly prevalent, there has been explosively growing literature dealing with all kinds of aspects of interacting populations with age structure [6, 12–19]. In particular, [14–19] considered the age-structured model as a non-densely defined Cauchy problem and discussed the existence of Hopf bifurcation.

[3] considered the proliferation of uninfected T cells by a logistic function and formulated the following model

\[
\begin{align*}
\frac{dT}{dt} &= \Lambda + rT \left(1 - \frac{T}{K}\right) - \mu T - \beta_1 VT, \\
\frac{dI}{dt} &= \beta_1 VT - \sigma I, \\
\frac{dV}{dt} &= N\sigma I - cV,
\end{align*}
\]

where \(T, I\) and \(V\) denote the population of uninfected CD4\(^+\) T cells, productively infected CD4\(^+\) T cells and virus, respectively. They treated the logistic proliferation term \(rT \left(1 - \frac{T+I}{K}\right)\) in which \(r\) is the maximum proliferation rate and \(K\) is the uninfected CD4\(^+\) T cells population density at which proliferation shuts off. Since the proportion of productively infected CD4\(^+\) T cells \(I\) is very small and thus it is reasonable to ignore this correction. They eventually represented the proliferation of uninfected CD4\(^+\) T cells by a logistic function \(rT \left(1 - \frac{T}{K}\right)\). However, the authors only consider the classical virus-to-cell infection and neglect the direct cell-to-cell transmission.

[12] incorporated the two modes (virus-to-cell infection and cell-to-cell transmission) of transmission into a classic model and considered the following model system

\[
\begin{align*}
\frac{dT(t)}{dt} &= \Lambda - \mu T(t) - \beta_1 T(t)V(t) - \beta_2 T(t) \int_0^{+\infty} q(a)i(t,a)da, \\
\frac{\partial i(t,a)}{\partial t} + \frac{\partial i(t,a)}{\partial a} &= -\sigma(a)i(t,a), \\
\frac{dV(t)}{dt} &= \int_0^{+\infty} p(a)i(t,a)da - cV(t),
\end{align*}
\]
with the boundary and initial conditions

\[
\begin{align*}
    i(t, 0) &= \beta_1 T(t)V(t) + \beta_2 T(t) \int_0^{+\infty} q(a)i(t, a)da, \\
    T(0) &= x_0 > 0, \quad i(0, a) = i_0(a) \in L^1_{+}(0, \infty), \quad V(0) = V_0 > 0,
\end{align*}
\]

where \(T(t)\) and \(V(t)\) denote the concentration of uninfected CD4\(^{+}\) T cells and infectious virus at \(t\), respectively; \(i(t, a)\) denotes the concentration of infected CD4\(^{+}\) T cells of infection age \(a\) at time \(t\), \(\Lambda\) is the constant recruitment rate, \(\mu\) is the natural death rate of uninfected CD4\(^{+}\) T cells, \(\beta_1\) is the rate at which an uninfected CD4\(^{+}\) T cell becomes infected by an infectious virus, \(c\) is the clearance rate of virions, \(\sigma(a)\) is the death rate of infected CD4\(^{+}\) T cells related to infection age \(a\), and \(p(a)\) is the viral production rate of an infected CD4\(^{+}\) T cell with infection age \(a\), \(q(a)\) measures variance of the infectivity of infected CD4\(^{+}\) T cells with respect to the infection age \(a\). They analysed the relative compactness and persistence of the solution semiflow and existence of a global attractor and investigated how the rate functions \(p(a), q(a),\) and \(\sigma(a)\) affected the global dynamics. They do not take into account any more dynamical behaviors such as bifurcation behaviors.

Just as described above, few scholars simultaneously considered the logistic proliferation function of uninfected CD4\(^{+}\) T cells and the two predominant infection modes of HIV in a model. As is known that the age structure model can be considered as abstract Cauchy problems with non-dense domain. Inspired by the papers [3][12][15][16], we attempt to investigate the following HIV infection-age structured model (1.1) by applying the theory of integrated semigroup and Hopf bifurcation theory [20]. A schematic diagram of the model (1.1) is shown in Figure 1 and the dynamics of such a model can be written as

\[
\begin{align*}
    \frac{dT(t)}{dt} &= \Lambda - \mu T(t) + r T(t) \left(1 - \frac{T(t) + \int_0^{+\infty} i(t, a)da}{K}\right) - \beta_1 T(t)V(t) \\
    \frac{dV(t)}{dt} &= N \sigma \int_0^{+\infty} i(t, a)da - cV(t), \\
    \frac{di(t, a)}{dt} &= -\sigma i(t, a), \\
    i(t, 0) &= \beta_1 T(t)V(t) + \beta_2 T(t) \int_0^{+\infty} \beta(a)i(t, a)da, \quad t > 0, \\
    T(0) &= T_0 \geq 0, \quad V(0) = V_0 \geq 0, \quad i(0, \cdot) = i_0 \in L^1_{+}((0, +\infty), \mathbb{R}),
\end{align*}
\] (1.1)
Table 1: The parameters description of the HIV model (1.1).

| Parameter | Description |
|-----------|-------------|
| $\Lambda$ | the rate at which new CD4$^+$ T cells are created from sources within the body. |
| $r$       | the maximum proliferation rate of uninfected CD4$^+$ T cells. |
| $K$       | the CD4$^+$ T cells population density at which proliferation shuts off. |
| $N$       | the number of virons produced the infected CD4$^+$ T cells during its lifetime. |
| $\beta_1$ | the rate at which an uninfected CD4$^+$ T cell becomes infected by an infectious virus. |
| $\beta_2$ | the infection rate of productively infected CD4$^+$ T cells. |
| $\mu$     | the natural death rate of uninfected CD4$^+$ T cells. |
| $c$       | the clearance rate of virions. |
| $\sigma$  | the death rate of infected CD4$^+$ T cells. |

where $T(t)$ denotes the concentration of uninfected CD4$^+$ T cells at time $t$, $i(t,a)$ denotes the concentration of infected CD4$^+$ T cells of infection age $a$ at time $t$, and $V(t)$ denotes the concentration of infectious virus at $t$. All parameters of model (1.1) are positive constants and the parameters description are presented in Table 1. Throughout the paper, $\beta(a)$ is an age-specific fertility function related to infection age $a$ and satisfies the following assumption 1.1.

**Assumption 1.1.** Assume that

$$\beta(a) := \begin{cases} 
\beta^*, & \text{if } a \geq \tau, \\
0, & \text{if } a \in (0, \tau), 
\end{cases}$$

where $\tau > 0$ and $\beta^* > 0$. Moreover, it is reasonable and favorable for the infected CD4$^+$ T cells to show a stable trend to assume that $\int_0^{+\infty} \beta(a)e^{-\sigma a}da = 1$, where $e^{-\sigma a}$ denotes the probability for an infected T cell to survive to age $a$.

The paper is organized as follows. In Section 2, we reformulate system (1.1) as an abstract non-densely defined Cauchy problem and study the equilibrium, linearized equation and characteristic equation. The existence of Hopf bifurcation is proved in Section 3. Some numerical simulations and conclusions are presented in Section 4.

## 2 Preliminaries

### 2.1 Rescaling time and age

In this section, we first normalize $\tau$ in the system (1.1) for the purpose of obtaining the smooth dependency of (1.1) related to $\tau$ (i.e., in order to consider the parameter $\tau$ as a bifur-
cation parameter). By applying the following time-scaling and age-scaling
\[
\hat{a} = \frac{a}{\tau} \quad \text{and} \quad \hat{t} = \frac{t}{\tau},
\]
and the following distribution
\[
\hat{T}(\hat{t}) = T(\tau \hat{t}), \hat{V}(\hat{t}) = V(\tau \hat{t}) \quad \text{and} \quad \hat{i}(\hat{t}, \hat{a}) = \tau i(\tau \hat{t}, \tau \hat{a}),
\]
after the change of variables and dropping the hat notation, the new system is given by
\[
\begin{cases}
\frac{dT(t)}{dt} = \tau \left[ \Lambda - \mu T(t) + r T(t) \left( 1 - \frac{T(t) + \int_0^{+\infty} i(t, a) da}{K} \right) - \beta_1 T(t)V(t) \
- \beta_2 T(t) \int_0^{+\infty} i(t, a) da, \right], \\
\frac{dV(t)}{dt} = \tau \left( N \sigma \int_0^{+\infty} i(t, a) da - cV(t) \right), \\
\frac{\partial i(t, a)}{\partial t} + \frac{\partial i(t, a)}{\partial a} = -\tau \sigma i(t, a), \\
i(t, 0) = \tau \left( \beta_1 T(t)V(t) + \beta_2 T(t) \int_0^{+\infty} \beta(a) i(t, a) da \right), \quad t > 0, \\
T(0) = T_0 \geq 0, \quad V(0) = V_0 \geq 0, \quad i(0, \cdot) = i_0 \in L^1_+((0, +\infty), \mathbb{R}),
\end{cases}
\tag{2.1}
\]
where the new function \( \beta(\cdot) \) is defined by
\[
\beta(a) = \begin{cases} 
\beta^*, & \text{if } a \geq 1, \\
0, & \text{otherwise},
\end{cases}
\]
and
\[
\int_{\tau}^{+\infty} \beta^* e^{-\sigma a} da = 1 \iff \beta^* = \sigma e^{\sigma \tau},
\]
where \( \tau \geq 0, \beta^* > 0 \).

Define \( U(t) := \int_0^{+\infty} u(t, a) da \) in system (2.1), where \( U(t) = \begin{pmatrix} T(t) \\ V(t) \end{pmatrix} \) and \( u(t, a) = \begin{pmatrix} \rho(t, a) \\ v(t, a) \end{pmatrix} \), the ordinary differential equations in (2.1) can easily be rewritten as an age-structured model
\[
\begin{cases}
\frac{\partial u(t, a)}{\partial t} + \frac{\partial u(t, a)}{\partial a} = -\tau C u(t, a), \\
u(t, 0) = \tau G(\rho(t, a), v(t, a)), \\
u(0, a) = u_0 \in L^1_+((0, +\infty), \mathbb{R}^2),
\end{cases}
\]
where
\[
C = \begin{pmatrix} \mu & 0 \\ 0 & c \end{pmatrix} \quad \text{and} \quad G(\rho(t, a), v(t, a)) = \left( N \sigma \int_0^{+\infty} i(t, a) da \right).
\]
with
\[ G_{11} = \Lambda + r \int_0^{+\infty} \rho(t, a) da \left( 1 - \frac{\int_0^{+\infty} \rho(t, a) da + \int_0^{+\infty} i(t, a) da}{K} \right) - \beta_1 \int_0^{+\infty} \rho(t, a) da \int_0^{+\infty} v(t, a) da - \beta_2 \int_0^{+\infty} \rho(t, a) da \int_0^{+\infty} i(t, a) da. \]

In what follows, with the notation \( w(t, a) = \left( \begin{array}{c} u(t, a) \\ i(t, a) \end{array} \right) \), we obtain the equivalent system of model (2.1)

\[
\begin{aligned}
\frac{\partial w(t, a)}{\partial t} + \frac{\partial w(t, a)}{\partial a} &= -\tau Q w(t, a), \\
w(t, 0) &= \tau B(w(t, a)), \\
w(0, \cdot) &= w_0 = \left( \begin{array}{c} \rho_0 \\ v_0 \\ u_0 \end{array} \right) \in L^1((0, +\infty), \mathbb{R}^3),
\end{aligned}
\]

where

\[ Q = \left( \begin{array}{ccc} \mu & 0 & 0 \\ 0 & c & 0 \\ 0 & 0 & \sigma \end{array} \right) \]

and

\[ B(w(t, a)) = \left( \begin{array}{c} G(\rho(t, a), v(t, a)) \\ \beta_1 \int_0^{+\infty} \rho(t, a) da \int_0^{+\infty} v(t, a) da + \beta_2 \int_0^{+\infty} \rho(t, a) da \int_0^{+\infty} \beta(a) i(t, a) da \end{array} \right). \]

Subsequently, we consider the following Banach space

\[ X = \mathbb{R}^3 \times L^1((0, +\infty), \mathbb{R}^3) \]

with \( \left\| \begin{array}{c} \alpha \\ \psi \end{array} \right\| = \|\alpha\|_{\mathbb{R}^3} + \|\psi\|_{L^1((0, +\infty), \mathbb{R}^3)}. \) Define the linear operator \( A_\tau : D(A_\tau) \to X \) by

\[ A_\tau \left( \begin{array}{c} 0_{\mathbb{R}^3} \\ \varphi \end{array} \right) = \left( \begin{array}{c} -\varphi(0) \\ -\varphi' - \tau Q \varphi \end{array} \right) \]

with \( D(A_\tau) = \{0_{\mathbb{R}^3}\} \times W^{1,1}((0, +\infty), \mathbb{R}^3) \subset X, \) and the operator \( H : D(A_\tau) \to X \) by

\[ H \left( \begin{array}{c} 0_{\mathbb{R}^3} \\ \varphi \end{array} \right) = \left( \begin{array}{c} B(\varphi) \\ 0_{L^1} \end{array} \right). \]

The linear operator \( A_\tau \) is non-densely defined owing to

\[ X_0 := \overline{D(A_\tau)} = \{0_{\mathbb{R}^3}\} \times L^1((0, +\infty), \mathbb{R}^3) \neq X. \]

Let

\[ x(t) = \left( \begin{array}{c} 0_{\mathbb{R}^3} \\ w(t, \cdot) \end{array} \right), \]
system (2.2) can be rewritten as the following non-densely defined abstract Cauchy problem

\[
\begin{aligned}
\frac{dx(t)}{dt} &= A_\tau x(t) + \tau H(x(t)), \quad t \geq 0, \\
x(0) &= \left( \begin{array}{c}
0_{\mathbb{R}^3} \\
w_0
\end{array} \right) \in D(A_\tau).
\end{aligned}
\] (2.3)

The global existence and uniqueness of solution of system (2.3) follow from the results of [21] and [22].

2.2 Equilibria and linearized equation

In this section, we will discuss the equilibria of the system (2.3) and the linearized equation of (2.3) around the positive equilibrium.

2.2.1 Existence of equilibria

Assume that \( \overline{x}(a) = \left( \begin{array}{c} 0_{\mathbb{R}^3} \\ \overline{w}(a) \end{array} \right) \in X_0 \) is a steady state of system (2.3). Then

\[
\left( \begin{array}{c} 0_{\mathbb{R}^3} \\ \overline{w}(a)
\end{array} \right) \in D(A_\tau) \quad \text{and} \quad A_\tau \left( \begin{array}{c} 0_{\mathbb{R}^3} \\ \overline{w}(a)
\end{array} \right) + \tau \left( \begin{array}{c} 0_{\mathbb{R}^3} \\ \overline{w}(a)
\end{array} \right) = 0,
\]

which is equivalent to

\[
\begin{aligned}
-\overline{w}(0) + \tau B(\overline{w}(a)) &= 0, \\
-\overline{w}'(a) - \tau Q \overline{w}(a) &= 0.
\end{aligned}
\]

Solving the above equations, we obtain

\[
\overline{w}(a) = \left( \begin{array}{c}
\overline{p}(a) \\
\overline{v}(a) \\
\overline{i}(a)
\end{array} \right) = \left( \begin{array}{c}
\tau \left[ \Lambda + r\overline{T} \left( 1 - \frac{\overline{T} + \int_0^{+\infty} \overline{v}(a)da}{R} \right) - \beta_1 \overline{T} \overline{V} - \beta_2 \overline{T} \int_0^{+\infty} \overline{i}(a)da \right] e^{-\rho\overline{a}}, \\
\tau \left( N\sigma \int_0^{+\infty} \overline{v}(a)da \right) e^{-\tau c a}, \\
\tau \left( \beta_1 \overline{T} \overline{V} + \beta_2 \overline{T} \int_0^{+\infty} \beta(a) \overline{i}(a)da \right) e^{-\tau c a}
\end{array} \right)
\] (2.4)

with \( \overline{T} = \int_0^{+\infty} \overline{p}(a)da \) and \( \overline{V} = \int_0^{+\infty} \overline{v}(a)da \).

It follows from the third equation of (2.4) that

\[
\overline{i}(a) = \tau \left( \beta_1 \overline{T} \overline{V} + \beta_2 \overline{T} \int_0^{+\infty} \beta(a) \overline{i}(a)da \right) e^{-\tau c a}.
\] (2.5)

Integrating the equation (2.5), we have

\[
\int_0^{+\infty} \beta(a) \overline{i}(a)da = \frac{\beta_1 \overline{T} \overline{V}}{1 - \beta_2 \overline{T}} \quad \text{and} \quad \int_0^{+\infty} \overline{i}(a)da = \frac{1}{\sigma} \int_0^{+\infty} \beta(a) \overline{i}(a)da.
\] (2.6)
It follows from the second equation of (2.4) that
\[ \nabla = \int_0^{+\infty} \eta(a) da = \tau \left( N\sigma \int_0^{+\infty} \overline{\eta}(a) da \right) \int_0^{+\infty} e^{-\tau c a} da = \frac{N}{c} \int_0^{+\infty} \beta(a) \overline{\eta}(a) da. \] (2.7)

By substituting (2.6) and (2.7) into the first equation of (2.4), we get
\[ \Lambda - \mu T + r T \left( 1 - \frac{T + \int_0^{+\infty} \overline{\eta}(a) da}{K} \right) - \beta_1 T \nabla - \beta_2 T \int_0^{+\infty} \overline{\eta}(a) da = 0. \] (2.8)

Solving the above equations (2.7) and (2.8), we obtain
\[ \begin{aligned}
\frac{T}{V} &= \frac{K(r-\mu) \pm \sqrt{K^2(\mu-\mu)r^2 + 4rK}}{2r}, \quad \text{and} \quad \frac{T}{V} = \frac{c}{N\beta_1 + c\beta_2}, \quad \frac{V}{V} = \frac{\sigma N(\Lambda(N\beta_1 + c\beta_2) + c(r-\mu) - c^2 r)}{c(N\beta_1 + c\beta_2)|K(N\sigma\beta_1 + c\beta_2) + cr|}. \\
\end{aligned} \] (2.9)

Therefore, in accordance with (2.5) and (2.9), we derive the following lemma.

**Lemma 2.1.** System (2.3) has always the equilibrium
\[ \bar{x}_{01}(a) = \left( \begin{array}{c}
0 \mathbb{R}^3 \\
\tau \mu \bar{T} + e^{-\tau \mu a} \\
0_{L_1}
\end{array} \right) \] and \[ \bar{x}_{02}(a) = \left( \begin{array}{c}
0 \mathbb{R}^3 \\
\tau \mu \bar{T} - e^{-\tau \mu a} \\
0_{L_1}
\end{array} \right). \]

Furthermore, there exists a unique positive equilibrium of system (2.3)
\[ \bar{x}_r = \left( \begin{array}{c}
0 \mathbb{R}^3 \\
\bar{w}_r
\end{array} \right) = \left( \begin{array}{c}
0 \mathbb{R}^3 \\
\tau \frac{c\mu}{N\beta_1 + c\beta_2} e^{-\tau \mu a} \\
\tau \frac{\sigma N(\Lambda(N\beta_1 + c\beta_2) + c(r-\mu) - c^2 r)}{c(N\beta_1 + c\beta_2)|K(N\sigma\beta_1 + c\beta_2) + cr|} e^{-\tau \sigma a}
\end{array} \right) \]

if and only if
\[ K(N\beta_1 + c\beta_2)[\Lambda(N\beta_1 + c\beta_2) + c(r-\mu)] - c^2 r > 0. \]

Correspondingly, there exists a unique positive equilibrium of system (1.1)
\[ \left( \begin{array}{c}
\bar{T} \\
\bar{V} \\
\bar{l}_r(a)
\end{array} \right) = \left( \begin{array}{c}
\tau \frac{c\mu}{N\beta_1 + c\beta_2} \\
\tau \frac{\sigma N(\Lambda(N\beta_1 + c\beta_2) + c(r-\mu) - c^2 r)}{c(N\beta_1 + c\beta_2)|K(N\sigma\beta_1 + c\beta_2) + cr|} e^{-\tau \sigma a}
\end{array} \right) \]

if and only if
\[ K(N\beta_1 + c\beta_2)[\Lambda(N\beta_1 + c\beta_2) + c(r-\mu)] - c^2 r > 0. \]

In the following, we always assume that \( K(N\beta_1 + c\beta_2)[\Lambda(N\beta_1 + c\beta_2) + c(r-\mu)] - c^2 r > 0. \)
2.2.2 Linearized equation

In order to obtain the linearized equation of (2.3) around the positive equilibrium \( \bar{x}_\tau \), we first make the following change of variable

\[
y(t) := x(t) - \bar{x}_\tau,
\]

and then, (2.3) becomes

\[
\begin{align*}
\frac{dy(t)}{dt} &= A_\tau y(t) + \tau H(y(t) + \bar{x}_\tau) - \tau H(\bar{x}_\tau), \quad t \geq 0, \\
y(0) &= \left( \begin{array}{c} 0_{R^3} \\ w_0 - \bar{w}_\tau \end{array} \right) =: y_0 \in D(A_\tau).
\end{align*}
\]

(2.10)

Therefore the linearized equation (2.10) around the equilibrium 0 is given by

\[
\frac{dy(t)}{dt} = A_\tau y(t) + \tau D\bar{H}(\bar{x}_\tau) y(t) \quad \text{for} \quad t \geq 0, \quad y(t) \in X_0,
\]

(2.11)

where

\[
\tau D\bar{H}(\bar{x}_\tau) \left( \begin{array}{c} 0_{R^3} \\ \varphi \end{array} \right) = \left( \tau D\bar{B}(\bar{w}_\tau)(\varphi) \right) \quad \text{for all} \quad \left( \begin{array}{c} 0_{R^3} \\ \varphi \end{array} \right) \in D(A_\tau)
\]

with

\[
D\bar{B}(\bar{w}_\tau)(\varphi) = \left( \begin{array}{cc}
\left( r - \frac{2a_T}{K} - (\frac{r}{K} + \beta_2) \int_0^{+\infty} i(a)da - \beta_1 V - \beta_1 T - \beta_1 T \right) & 0 \\
0 & N\sigma \\
\beta_1 V + \beta_2 \int_0^{+\infty} \beta_1 i(a)da & 0 \\
0 & \beta_1 T
\end{array} \right) \times \int_0^{+\infty} \varphi(a)da + \left( \begin{array}{ccc}
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & \beta_2 T
\end{array} \right) \int_0^{+\infty} \beta_1 \varphi(a)da.
\]

Then we can rewrite system (2.10) as

\[
\frac{dy(t)}{dt} = B_\tau y(t) + \mathcal{H}(y(t)) \quad \text{for} \quad t \geq 0,
\]

(2.12)

where

\[
B_\tau := A_\tau + \tau D\bar{H}(\bar{x}_\tau)
\]

is a linear operator and

\[
\mathcal{H}(y(t)) = \tau H(y(t) + \bar{x}_\tau) - \tau H(\bar{x}_\tau) - \tau D\bar{H}(\bar{x}_\tau)y(t)
\]

satisfying \( \mathcal{H}(0) = 0 \) and \( D\mathcal{H}(0) = 0 \).
2.3 Characteristic equation

In this section, we will obtain the characteristic equation of (2.3) around the positive equilibrium $\mathbf{r}_\tau$. Denote

$$\nu := \min\{\mu, c, \sigma\} > 0 \quad \text{and} \quad \Omega := \{\lambda \in \mathbb{C} : \text{Re}(\lambda) > -\nu \tau\}.$$  

Applying the results of [20], we obtain the following result.

**Lemma 2.2.** For $\lambda \in \Omega$, $\lambda \in \rho(A_\tau)$ and

$$\left(\lambda I - A_\tau\right)^{-1} \begin{pmatrix} \delta \\ \psi \end{pmatrix} = \begin{pmatrix} 0_{\mathbb{R}^3} \\ \varphi \end{pmatrix} \iff \varphi(a) = e^{-\int_0^a \lambda \tau \psi ds} \delta + \int_0^a e^{-\int_s^a \lambda \tau \psi ds} \psi(s) ds$$

with $\begin{pmatrix} \delta \\ \psi \end{pmatrix} \in X$ and $\begin{pmatrix} 0_{\mathbb{R}^3} \\ \varphi \end{pmatrix} \in D(A_\tau)$. Moreover, $A_\tau$ is a Hille-Yosida operator and

$$\|\left(\lambda I - A_\tau\right)^{-n}\| \leq \frac{1}{\left(\text{Re}(\lambda) + \nu \tau\right)^n}, \quad \forall \lambda \in \Omega, \quad \forall n \geq 1. \quad (2.13)$$

Let $A_0$ be the part of $A_\tau$ in $\overline{D(A_\tau)}$, that is, $A_0 := D(A_0) \subset X \to X$. For $\begin{pmatrix} 0_{\mathbb{R}^3} \\ \varphi \end{pmatrix} \in D(A_0)$, we have

$$A_0 \begin{pmatrix} 0_{\mathbb{R}^3} \\ \varphi \end{pmatrix} = \begin{pmatrix} 0_{\mathbb{R}^3} \\ \hat{A}_0(\varphi) \end{pmatrix},$$

where $\hat{A}_0(\varphi) = -\varphi' - \tau Q \varphi$ with $D(\hat{A}_0) = \{\varphi \in W^{1,1}((0, +\infty), \mathbb{R}^3) : \varphi(0) = 0\}$.

Note that $\tau DH(\tau_\tau) : D(A_\tau) \subset X \to X$ is a compact bounded linear operator. Based on (2.13) we have

$$\|T_{A_0}(t)\| \leq e^{-\nu \tau t} \quad \text{for} \quad t \geq 0.$$  

Furthermore, we get

$$\omega_{0, \text{ess}}(A_0) \leq \omega_0(A_0) \leq -\nu \tau.$$  

Using the perturbation results developed in [23], we obtain

$$\omega_{0, \text{ess}}((A_\tau + \tau DH(\tau_\tau))_0) \leq -\nu \tau < 0.$$  

Hence we conclude the following proposition.

**Lemma 2.3.** The linear operator $B_\tau$ is a Hille-Yosida operator, and its parts $(B_\tau)_0$ in $\overline{D(B_\tau)}$ satisfies

$$\omega_{0, \text{ess}}((B_\tau)_0) < 0.$$
Let \( \lambda \in \Omega \). Since \((\lambda I - A_\tau)\) is invertible, and
\[
(\lambda I - B_\tau)^{-1} = (\lambda I - (A_\tau + \tau DH(\overline{x}_\tau)))^{-1} = (I - \tau DH(\overline{x}_\tau)(\lambda I - A_\tau)^{-1})^{-1},
\]
(2.14)
\(\lambda I - B_\tau\) is invertible if and only if \(I - \tau DH(\overline{x}_\tau)(\lambda I - A_\tau)^{-1}\) is invertible. Set
\[
(I - \tau DH(\overline{x}_\tau)(\lambda I - A_\tau)^{-1}) \left( \begin{array}{c} \delta \\ \varphi \end{array} \right) = \left( \begin{array}{c} \gamma \\ \psi \end{array} \right).
\]
That is
\[
\left( \begin{array}{c} \delta \\ \varphi \end{array} \right) - \tau DH(\overline{x}_\tau)(\lambda I - A_\tau)^{-1} \left( \begin{array}{c} \varphi \\ \delta \end{array} \right) = \left( \begin{array}{c} \gamma \\ \psi \end{array} \right).
\]
It follows that
\[
\begin{cases}
\delta - \tau DB(\overline{w}_\tau) \left( e^{-\int_0^a (\lambda I + \tau Q)dl} + \int_0^a e^{-\int_s^a (\lambda I + \tau Q)dl} \varphi(s) ds \right) = \gamma, \\
\varphi = \psi,
\end{cases}
\]
i.e.,
\[
\begin{cases}
\delta - \tau DB(\overline{w}_\tau) \left( e^{-\int_0^a (\lambda I + \tau Q)dl} \delta \right) = \gamma + \tau DB(\overline{w}_\tau) \left( \int_0^a e^{-\int_s^a (\lambda I + \tau Q)dl} \varphi(s) ds \right), \\
\varphi = \psi.
\end{cases}
\]
Combining with the formula of \(DB(\overline{w}_\tau)\) we conclude that
\[
\begin{cases}
\Delta(\lambda) \delta = \gamma + K(\lambda, \psi), \\
\varphi = \psi,
\end{cases}
\]
where
\[
\Delta(\lambda) = I - \left( \begin{array}{cccc}
r - \frac{2r}{K} & - (r + \beta_1 \overline{V}) & - (r + \beta_1 \overline{V}) & - \beta_1 \overline{T} \\
0 & - \beta_1 \overline{V} & - \beta_2 \overline{T} & - \beta_1 \overline{T} \\
\beta_1 \overline{V} & \beta_2 \int_0^{+\infty} \beta(a) \overline{i}(a) da & \beta_1 \overline{T} & 0 \\
0 & \beta_2 \overline{T} & 0 & N \sigma
\end{array} \right) \times \tau \int_0^{+\infty} e^{-\int_0^a (\lambda I + \tau Q)dl} \beta(a) \overline{i}(a) da
\]
(2.15)
and
\[
K(\lambda, \psi) = \tau DB(\overline{w}_\tau) \left( \int_0^a e^{-\int_s^a (\lambda I + \tau Q)dl} \varphi(s) ds \right).
\]
(2.16)
Whenever \(\Delta(\lambda)\) is invertible, we have
\[
\delta = (\Delta(\lambda))^{-1} (\gamma + K(\lambda, \psi)).
\]
(2.17)
Following the above discussion and the proof of Lemma 3.5 in [16], we derive the lemma as follows.
Lemma 2.4. The following results hold

(i) \( \sigma(B_\tau) \cap \Omega = \sigma_p(B_\tau) \cap \Omega = \{ \lambda \in \Omega : \det(\Delta(\lambda)) = 0 \} \);

(ii) If \( \lambda \in \rho(B_\tau) \cap \Omega \), we have the following formula for resolvent

\[
(\lambda I - B_\tau)^{-1} \begin{pmatrix} \delta \\ \varphi \end{pmatrix} = \begin{pmatrix} 0_R^2 \\ \psi \end{pmatrix},
\]

where

\[
\psi(a) = e^{-\int_0^a (\lambda I + \tau Q) dt}(\Delta(\lambda))^{-1} [\gamma + K(\lambda, \varphi)] + \int_0^a e^{-\int_0^s (\lambda I + \tau Q) dt}\varphi(s) ds
\]

with \( \Delta(\lambda) \) and \( K(\lambda, \varphi) \) defined in (2.15) and (2.16).

Under Assumption 1.1, we have

\[
\int_0^{+\infty} e^{-\int_0^a (\lambda I + \tau Q) dt} da = \begin{pmatrix} \frac{1}{\lambda + \mu \tau} & 0 & 0 \\ 0 & \frac{1}{\lambda + c \tau} & 0 \\ 0 & 0 & \frac{1}{\lambda + \sigma \tau} \end{pmatrix}
\]

(2.19)

and

\[
\int_0^{+\infty} \beta(a) e^{-\int_0^a (\lambda I + \tau Q) dt} da = \begin{pmatrix} \beta e^{-(\lambda + \mu \tau)}/\lambda + \mu \tau & 0 & 0 \\ 0 & \beta e^{-(\lambda + c \tau)}/\lambda + c \tau & 0 \\ 0 & 0 & \beta e^{-(\lambda + \sigma \tau)}/\lambda + \sigma \tau \end{pmatrix}
\]

(2.20)

It follows from (2.15), (2.19) and (2.20) that the characteristic equation at the positive equilibrium \( x_\tau \) is

\[
det(\Delta(\lambda)) = \frac{\beta_1 \tau + \frac{2 \tau}{\mu + \lambda} (\beta_2 + \frac{\tau}{\mu + \lambda})}{\mu + \lambda} + \frac{\beta_1 \tau}{c \tau + \lambda} + \frac{\tau \beta_1 \tau}{\sigma + \lambda} + \frac{\tau T (\beta_2 + \frac{\tau}{\mu + \lambda})}{\sigma + \lambda} = 0,
\]

(2.21)
where
\[ T = \int_0^{+\infty} \overline{t}(a) da, \]
\[ V = \int_{0}^{+\infty} \overline{v}(a) da, \]
\[ \xi = \int_0^{+\infty} \beta(a) \overline{t}(a) da = \sigma \int_0^{+\infty} \overline{t}(a) da, \]
\[ p_2 = \beta_1 V + \mu + c + \sigma - r + \frac{\beta_2 T}{\sigma} + \frac{2\sigma T}{K}, \]
\[ p_1 = \beta_1 T(\beta_2 V - \sigma N) + \beta_2 \xi (\beta_2 T + 1) + (c + \sigma)(\beta_1 V + \mu - r) + c\sigma + \frac{\beta_2 T}{K}(\beta_1 V + \beta_2 \xi) + 2(\xi + \frac{\beta_2 T}{K}(\beta_1 V + \beta_2 \xi)), \]
\[ p_0 = N\beta_1 \beta_2 \xi T(\sigma - 1) + \sigma (r - \mu)(N\beta_1 T - c) + c\beta_2 T(\beta_1 V + \beta_2 \xi) + c(\beta_1 V + \beta_2 \xi) - \frac{T}{K} \{ N\beta_1 T - c \} (2\sigma T + \xi) - c\beta_2 T(\beta_1 V + \beta_2 \xi), \]
\[ q_2 = -\sigma \beta_2 T, \]
\[ q_1 = -\beta_2 T[\sigma(\beta_1 V + \mu + c - r) + \beta_2 \xi + \frac{T}{K}(\xi + 2\sigma T)], \]
\[ q_0 = -c\beta_2 T[\sigma(\beta_1 V + \mu - r) + \beta_2 \xi + \frac{T}{K}(2\sigma T + \xi)], \]
\[ \tilde{f}(\lambda) = \lambda^3 + \tau p_2 \lambda^2 + \tau^2 p_1 \lambda + \tau^3 p_0 + (\tau q_2 \lambda^2 + \tau^2 q_1 \lambda + \tau^3 q_0) e^{-\lambda}, \]
\[ \tilde{g}(\lambda) = (\lambda + \tau \mu)(\lambda + \tau c)(\lambda + \tau \sigma). \]

Let \( \lambda = \tau \zeta. \)

Then we get
\[ \tilde{f}(\lambda) = \tilde{f}(\tau \zeta) := \tau^3 g(\zeta) = \tau^3 [\zeta^3 + p_2 \zeta^2 + p_1 \zeta + p_0 + (q_2 \zeta^2 + q_1 \zeta + q_0) e^{-\tau \zeta}]. \tag{2.22} \]

It is straightforward to demonstrate that
\[ \{ \lambda \in \Omega : \det(\Delta(\lambda)) = 0 \} = \{ \lambda = \tau \zeta \in \Omega : g(\zeta) = 0 \}. \]

### 3 Existence of Hopf bifurcation

In this section, the parameter \( \tau \) will be viewed as a Hopf bifurcation parameter and the existence of Hopf bifurcation for the Cauchy problem (2.3) will be further investigated by applying the Hopf bifurcation theory [20]. On the basis of (2.22), we have
\[ g(\zeta) = \zeta^3 + p_2 \zeta^2 + p_1 \zeta + p_0 + (q_2 \zeta^2 + q_1 \zeta + q_0) e^{-\tau \zeta}, \tag{3.1} \]

where
\[ p_2 = \frac{K(N\beta_1 + c\beta_2)[\Delta(N\beta_1 + c\beta_2)] + c(c + \sigma)] + c^2 r}{cK(N\beta_1 + c\beta_2)}, \]
\[ p_1 = \frac{cK(N\beta_1 + c\beta_2)[\Delta(N\beta_1 + c\beta_2)] + c^2 r}{cK(N\beta_1 + c\beta_2)[\Delta(N\beta_1 + c\beta_2)] + c(c + \sigma)] - N\beta_1 c^2 r}, \]
\[ p_0 = \frac{\sigma K(N\beta_1 + c\beta_2)^2}{\sigma K(N\beta_1 + c\beta_2)^2 [\Delta(N\beta_1 + c\beta_2)] + c^2 r - \sigma N\beta_1 c^2 r}, \tag{3.2} \]
\[ q_2 = \frac{c\sigma \beta_2}{N\beta_1 + c\beta_2}, \]
\[ q_1 = \frac{c\beta_2 \{ K(N\beta_1 + c\beta_2)[\Delta(N\beta_1 + c\beta_2)] + c^2 r \}}{cK(N\beta_1 + c\beta_2)^2}, \]
\[ q_0 = \frac{c\sigma \beta_2 [K(N\beta_1 + c\beta_2)^2 + c^2 r]}{K(N\beta_1 + c\beta_2)^2}. \]
and
\[ \mathcal{P} = K^2\Lambda(N_{\beta_1} + c_2\beta_2)^2[N_{\beta_1}(c + \sigma) + c_2\beta_2(c + 2\sigma)] + K^2N_{\beta_1}\beta_2^2\sigma(c\sigma + r - \mu) + K^2\beta_2^3\sigma(c + r - \mu) + K\Lambda\sigma(N_{\beta_1} + c_2\beta_2)^2(c + 2\sigma) + KN_{\beta_1}\beta_2^2\sigma(c\sigma + r - \mu) + K\beta_2^3\sigma[(c + r - \mu)c\sigma + c\sigma] + c^4r^2. \]

In addition,
\[ p_0 + q_0 = \frac{\sigma(K(N_{\beta_1} + c_2\beta_2)\Lambda(N_{\beta_1} + c_2\beta_2) + c(r - \mu) - c^2r)}{K(N_{\beta_1} + c_2\beta_2)}, \] (3.3)
If \( K(N_{\beta_1} + c_2\beta_2)\Lambda(N_{\beta_1} + c_2\beta_2) + c(r - \mu) - c^2r > 0 \), then \( p_0 + q_0 > 0, p_0 - q_0 > 0 \) and \( \zeta = 0 \) is not a eigenvalue of (3.1).

In what follows, we first let \( \zeta = i\omega(\omega > 0) \) be a purely imaginary root of \( g(\zeta) = 0 \), that is,
\[ -i\omega^3 - p_2\omega^2 + ip_1\omega + p_0 + (-q_2\omega^2 + iq_1\omega + q_0)e^{-i\omega\tau} = 0. \]

Separating the real part and the imaginary part in the above equation, we have
\[
\begin{cases}
p_2\omega^2 - p_0 = (q_0 - q_2\omega^2)\cos(\omega\tau) + q_1\omega\sin(\omega\tau), \\
p_1\omega - \omega^3 = (q_0 - q_2\omega^2)\sin(\omega\tau) - q_1\omega\cos(\omega\tau).
\end{cases} \] (3.4)

Consequently, we can further obtain
\[ (p_2\omega^2 - p_0)^2 + (p_1\omega - \omega^3)^2 = (q_0 - q_2\omega^2)^2 + (q_1\omega)^2, \]
i.e.,
\[ \omega^6 + (p_2^2 - q_2^2 - 2p_1)\omega^4 + (p_1^2 - q_1^2 - 2p_2p_0 + 2q_2q_0)\omega^2 + p_0^2 - q_0^2 = 0. \] (3.5)
Set \( \omega^2 = \theta \). Now (3.5) becomes
\[ \theta^3 + C_2\theta^2 + C_1\theta + C_0 = 0, \] (3.6)
where
\[
C_2 = p_2^2 - q_2^2 - 2p_1, \\
C_1 = p_1^2 - q_1^2 - 2p_2p_0 + 2q_2q_0, \\
C_0 = p_0^2 - q_0^2. \] (3.7)
Let \( \theta_1, \theta_2 \) and \( \theta_3 \) denote the three roots of (3.6). According to the theorem of Vieta, we have
\[ \theta_1 + \theta_2 + \theta_3 = -C_2 \quad \text{and} \quad \theta_1\theta_2\theta_3 = -C_0. \]

Combing with (3.3) and (3.7), we can get that
\[ \theta_1\theta_2\theta_3 = -C_0 = -(p_0 + q_0)(p_0 - q_0) < 0. \] (3.8)
purely imaginary roots

be given by solutions of (3.6) under the condition that the coefficients are real. The solutions of (3.6) can be given by (3.9) and (3.7). Table 2 describes the behavior of the solutions of (3.6) under the condition that the coefficients are real. The solutions of (3.6) can be given by

\[ D := p^3 + q^2, \quad (3.9) \]

where

\[ q = \frac{C_3^3}{27} - \frac{C_2C_1}{6} + \frac{C_0}{2} \quad \text{and} \quad p = \frac{C_1}{3} - \frac{C_2^2}{9}. \]

The quantity (3.9) is named the discriminant of (3.6). Table 2 describes the behavior of the solutions of (3.6) under the condition that the coefficients are real. The solutions of (3.6) can be given by

\[
\begin{align*}
\theta_1 &= \sqrt[3]{-q + \sqrt{D}} + \sqrt[3]{-q - \sqrt{D}}, \\
\theta_2 &= \frac{1 + i\sqrt{3}}{2} \sqrt[3]{-q + \sqrt{D}} + \frac{1 - i\sqrt{3}}{2} \sqrt[3]{-q - \sqrt{D}}, \\
\theta_3 &= \frac{1 - i\sqrt{3}}{2} \sqrt[3]{-q + \sqrt{D}} + \frac{1 + i\sqrt{3}}{2} \sqrt[3]{-q - \sqrt{D}}.
\end{align*} \quad (3.10)
\]

And then, it follows from (3.8), Table 2 and (3.10) that when \( D = 0 \) and \( q > 0 \), (3.6) has only one double positive real root \( \theta_0 \). Therefore (3.5) has only one positive real root \( \omega_0 = \sqrt{\theta_0} \). On the basis of (3.4), we can further conclude that \( g(\zeta) = 0 \) with \( \tau = \tau_k, k = 1, 2, \cdots \) has a pair of purely imaginary roots \( \pm i\omega_0 \), where

\[ \omega_0 = \sqrt{-\sqrt[3]{-q}} \]

and

\[
\tau_k = \begin{cases} 
\frac{1}{\omega_0} \left\{ \arccos \left( -\frac{(p_2q_2-q_1)\omega_0^2 - (p_2q_0+p_0q_2-p_1q_1)\omega_0 + p_0q_0}{q_2^2\omega_0^4 + (q_1^2 - 2q_2q_0)\omega_0 + q_0^2} \right) + 2k\pi \right\}, & \text{if } \Theta \geq 0, \\
\frac{1}{\omega_0} \left\{ 2\pi - \arccos \left( -\frac{(p_2q_2-q_1)\omega_0^2 - (p_2q_0+p_0q_2-p_1q_1)\omega_0 + p_0q_0}{q_2^2\omega_0^4 + (q_1^2 - 2q_2q_0)\omega_0 + q_0^2} \right) + 2k\pi \right\}, & \text{if } \Theta < 0,
\end{cases} \quad (3.11)
\]

for \( k = 1, 2, \cdots \) with

\[ \Theta := \frac{\omega_0(q_2\omega_0^4 + (p_2q_1 - p_1q_2 - q_0)\omega_0^2 + p_1q_0 - p_0q_0)}{q_2^2\omega_0^4 + (q_1^2 - 2q_2q_0)\omega_0^2 + q_0^2}. \]

**Assumption 3.1.** Assume that \( \Lambda(N\beta_1 + c\beta_2)[\Lambda(N\beta_1 + c\beta_2) + c(r - \mu)] - c^2r > 0, D = 0, q > 0, C_2 > 0 \) and \( C_1 > 0 \) where \( D, q, C_2 \) and \( C_1 \) are given by (3.9) and (3.7).
Lemma 3.1. Let Assumption 1.1 and 3.1 hold, then

\[ \frac{dg(\zeta)}{d\zeta} \bigg|_{\zeta = i\omega_0} \neq 0. \]

Therefore \( \zeta = i\omega_0 \) is a simple root of (3.1).

Proof. On the basis of (3.1), we obtain

\[ \frac{dg(\zeta)}{d\zeta} \bigg|_{\zeta = i\omega_0} = \{ 3\zeta^2 + 2p_2\zeta + p_1 + [2q_2\zeta + q_1 - \tau(q_2\zeta^2 + q_1\zeta + q_0)]e^{-\tau\zeta} \} \bigg|_{\zeta = i\omega_0} \]

and

\[ \{ 3\zeta^2 + 2p_2\zeta + p_1 + [2q_2\zeta + q_1 - \tau(q_2\zeta^2 + q_1\zeta + q_0)]e^{-\tau\zeta} \} \frac{d\zeta(\tau)}{d\tau} = \zeta(q_2\zeta^2 + q_1\zeta + q_0)e^{-\tau\zeta}. \]

Suppose that \( \frac{dg(\zeta)}{d\zeta} \bigg|_{\zeta = i\omega_0} = 0 \), then

\[ i\omega_0(-q_2\omega_0^2 + iq_1\omega_0 + q_0)e^{-i\omega_0\tau} = 0. \]

Separating real and imaginary parts in the above equation, we have

\[ \begin{cases} (q_0\omega_0 - q_2\omega_0^3)\sin(\omega_0\tau) - q_1\omega_0^2\cos(\omega_0\tau) = 0, \\ (q_0\omega_0 - q_2\omega_0^3)\cos(\omega_0\tau) + q_1\omega_0^2\sin(\omega_0\tau) = 0. \end{cases} \quad (3.12) \]

That is,

\[ (q_0\omega_0 - q_2\omega_0^3)^2 + (q_1\omega_0^2)^2 = 0, \]

which implies

\[ q_0\omega_0 - q_2\omega_0^3 = 0 \quad \text{and} \quad q_1\omega_0^2 = 0. \]

Since \( \omega_0 > 0 \), it follows that

\[ q_0 - q_2\omega_0^2 = 0 \quad \text{and} \quad q_1 = 0. \]

However, \( q_1 = -\frac{\sigma\beta_2(K(N\beta_1 + c\beta_2)[\Delta(N\beta_1 + c\beta_2) + e] + e^2)}{K(N\beta_1 + c\beta_2)^2} < 0 \) which leads to a contradiction. Hence

\[ \frac{dg(\zeta)}{d\zeta} \bigg|_{\zeta = i\omega_0} \neq 0. \]

This completes the proof. \( \square \)

Lemma 3.2. Let Assumption 1.1 and 3.1 hold. Denote the root \( \zeta(\tau) = \alpha(\tau) + i\omega(\tau) \) of \( g(\zeta) = 0 \) satisfying \( \alpha(\tau_k) = 0 \) and \( \omega(\tau_k) = \omega_0 \), where \( \tau_k \) is defined in (3.11). Then

\[ \alpha'(\tau_k) = \frac{d\text{Re}(\zeta)}{d\tau} \bigg|_{\tau = \tau_k} > 0. \]
Proof. For simplicity, we discuss \( \frac{dv}{dc} \) instead of \( \frac{dc}{d\tau} \). Based on the expression of \( g(\zeta) = 0 \), we obtain

\[
\frac{dv}{dc} \bigg|_{\zeta = i\omega_0} = \frac{3\zeta^2 + 2p_2\zeta + p_1 + (2p_2\zeta + q_1)e^{-\tau\zeta} - \zeta(2p_2\zeta + q_1\zeta + q_0)e^{-\tau\zeta}}{(2p_2\zeta + q_1\zeta + q_0)e^{-\tau\zeta}} \bigg|_{\zeta = i\omega_0}
\]

Consequently, we can further get

\[
\text{Re}\left(\frac{dv}{dc} \bigg|_{\zeta = i\omega_0}\right) = \frac{-\omega_0^2 - p_1 - 3\omega_0^2 + 2p_2(p_0 - p_2\omega_0^2)}{(\omega_0^2(p_0 - p_2\omega_0^2))^2} - \frac{q_1^2 - 2q_2(q_0 - q_2\omega_0^2)}{(q_1\omega_0)^2 + (q_0 - q_2\omega_0^2)}
\]

Since

\[
C_2 = p_2^2 - q_2^2 - 2p_1 > 0 \quad \text{and} \quad C_1 = p_1^2 - q_1^2 - 2p_2p_0 + 2q_2q_0 > 0,
\]

we conclude that

\[
\text{sign}\left(\frac{d\text{Re}(\zeta)}{d\tau} \bigg|_{\tau = \tau_k}\right) = \text{sign}\left(\text{Re}\left(\frac{dv}{dc} \bigg|_{\zeta = i\omega_0}\right)\right)
\]

\[
= \text{sign}\left(\frac{-\omega_0^2 - p_1 - 3\omega_0^2 + 2p_2(p_0 - p_2\omega_0^2) - q_1^2 - 2q_2(q_0 - q_2\omega_0^2)}{(q_0 - q_2\omega_0^2)^2 + (q_1\omega_0)^2}\right) > 0.
\]

Summarizing the results presented above, we derive the following theorem.

**Theorem 3.1.** Let Assumption 3.1 and 3.2 be satisfied. Then there exist \( \tau_k > 0, k = 1, 2, \cdots (\tau_k \text{ is defined in (3.11))}, \) such that when \( \tau = \tau_k \), the HIV model (1.1) undergoes a Hopf bifurcation at the equilibrium \( (\tilde{T}, \tilde{V}, \tilde{r}_{\tau_k}(a)) \). In particular, a non-trivial periodic solution bifurcates from the equilibrium \( (\tilde{T}, \tilde{V}, \tilde{r}_{\tau_k}(a)) \) when \( \tau = \tau_k \).

### 4 Numerical simulations and conclusions

In this section, we perform a numerical analysis of the model (1.1) based on the previous results. We choose a set of parameters as follows: \( \Lambda = 0.05, r = 0.95, \mu = 0.0002, \sigma = 0.09, c = 0.4, K = 50, N = 30, \beta_1 = 0.00027, \beta_2 = 0.027 \). System (1.1) becomes
The conditions of Assumption 3.1 can be satisfied. Calculating it further, we can easily obtain that 
\[ D(\tau) \approx 0 \]
\[
\int_0^t \beta(a) i(t,a) da - 0.4V(t),
\]
\[
\int_0^t \beta(a) i(t,a) da > 0,
\]
\[
T(0) = 10 > 0, V(0) = 20 > 0, i(0,\cdot) = 2e^{-\frac{a^2}{2}} \in L^1_t((0, +\infty), \mathbb{R}),
\]
where
\[
\beta(a) := \begin{cases} 
0.09e^{0.09\tau}, & \text{if } a \geq \tau, \\
0, & \text{if } a \in (0, \tau).
\end{cases}
\]

By using the Matlab, we calculate that 
\[ K(N\beta_1+c\beta_2)[0(N\beta_1+c\beta_2)+c(r-\mu)] - c^2r \approx 0.2079, \]
\[ D \approx 2.8735 \times 10^{-8}, q \approx 1.7436 \times 10^{-4}, C_2 \approx 0.2647, C_1 \approx 0.0198. \]

It is obvious that the conditions of Assumption 3.1 can be satisfied. Calculating it further, we can easily obtain that 
\[ \omega_0 \approx 0.2364 \text{ and critical value } \tau_1 \approx 9.3906. \]

For the above parameters, we draw the graph of the solution curve and phase trajectory of model (1.1) and the graph of \(i(t,a)\) with respect to age and time (horizontal axis) by software Matlab when \(\tau = 5 < \tau_1\) (Figure 2) and \(\tau = 50 > \tau_1\) (Figure 3). One can see that positive equilibrium \((T, V, T=5(a)) = (21.1640, 77.6373, 5.1758e^{-0.45a})\) is locally asymptotically stable when \(\tau = 5 \in [0, \tau_1]\). By using Theorem 3.1 we know that, under the set parameters, when \(\tau = \tau_1\), the HIV model (1.1) undergoes a Hopf bifurcation at the equilibrium \((T, V, T=5(a))\). As is shown in Figure 3 when bifurcation parameter \(\tau\) crosses the bifurcation critical value \(\tau_1\), the sustained periodic oscillation phenomenon appears around the positive equilibrium \((T, V, T=50(a)) = (21.1640, 77.6373, 51.7582e^{-4.5a})\). Biologically speaking, for smaller biological maturation period \(\tau\), the stability of the unique positive equilibrium of system (1.1) is barely affected. However, when maturation period \(\tau\) increases continuously, the dynamical behavior of system (1.1) will be resulted in substantial changes. In conclusion, the bifurcation parameter \(\tau\), a measure of a biological maturation period, has an essential impact on the dynamical behavior of system (1.1).

References

[1] Q. Sattentau, The direct passage of animal viruses between cells, Curr. Opin. Virol. 1 (2011) 396-402.
[2] R. J. De Boer and A. S. Perelson, Target cell limited and immune control models of HIV infection: a comparison, J. Theoret. Biol. 190 (1998) 201-214.
[3] A. S. Perelson and P. W. Nelson, Mathematical analysis of HIV-1 dynamics in vivo, SIAM Rev. 41 (1999) 3-44.
[4] X. Zhou, X. Song and X. Shi, Analysis of stability and Hopf bifurcation for an HIV infection model with time delay, Appl. Math. Comput. 199 (2008) 23-38.
[5] X. Song, X. Zhou and X. Zhao, Properties of stability and Hopf bifurcation for a HIV infection model with time delay, Appl. Math. Modelling 34 (2010) 1511-1523.
[6] C. J. Browne, A multi-strain virus model with infected cell age structure: Application to HIV, Nonlinear Anal. Real World Appl. 22 (2015) 354-372.
[7] R. V. Culshaw, S. Ruan and G. Webb, A mathematical model of cell-to-cell spread of HIV-1 that includes a time delay, J. Math. Biol. 46 (2003) 425-444.
[8] N. L. Komarova and D. Wodarz, Virus dynamics in the presence of synaptic transmission, Math. Biosci. 242 (2013) 161-171.
[9] X. Lai and X. Zou, Modeling cell-to-cell spread of HIV-1 with logistic target cell growth, J. Math. Anal. Appl. 426 (2015) 563-584.
[10] X. Lai and X. Zou, Modeling HIV-1 virus dynamics with both virus-to-cell infection and cell-to-cell transmission, SIAM J. Appl. Math. 74 (2014) 898-917.
[11] Q. Hu, Z. Hu and F. Liao, Stability and Hopf bifurcation in a HIV-1 infection model with delays and logistic growth, Math. Comput. Simulation 128 (2016) 26-41.
[12] 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 World Appl. 34 (2017) 75-96.
[13] M. Iannelli, Mathematical theory of age-structured population dynamics, Giardini Editori E Stampatori, Pisa, 1995.
[14] Z. Liu and N. Li, Stability and bifurcation in a predator-prey model with age structure and delays, J. Nonlinear Sci. 25 (2015) 937-957.
[15] H. Tang and Z. Liu, Hopf bifurcation for a predator-prey model with age structure, Appl. Math. Model. 40 (2016) 726-737.
[16] Z. Wang and Z. Liu, Hopf bifurcation of an age-structured compartmental pest-pathogen model, J. Math. Anal. Appl. 385 (2012) 1134-1150.
[17] Z. Liu, P. Magal and S. Ruan, Oscillations in age-structured models of consumer-resource mutualisms, Discrete Contin. Dyn. Syst. Ser. B 21 (2015) 537-555.
[18] Z. Liu, H. Tang and P. Magal, Hopf bifurcation for a spatially and age structured population dynamics model, Discrete Contin. Dyn. Syst. Ser. B 20 (2015) 1735-1757.
[19] X. Fu, Z. Liu and P. Magal, Hopf bifurcation in an age-structured population model with two delays, Commun. Pure Appl. Anal. 14 (2015) 657-676.
[20] Z. Liu, P. Magal and S. Ruan, Hopf bifurcation for non-densely defined Cauchy problems, Z. Angew. Math. Phys. 62 (2011) 191-222.
[21] P. Magal and S. Ruan, On semilinear Cauchy problems with non-dense domain, Adv. Differential Equations 14 (2009) 1041-1084.
[22] P. Magal, Compact attractors for time-periodic age-structured population models, *Electron. J. Differential Equations* **2001** (2001) 1-35.

[23] 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** (2008) 501-518.
Figure 2: Description of the evolution of system (1.1) when \( \tau = 5 \).
Figure 3: Description of the evolution of system (1.1) when $\tau = 50$. 