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Research article

Dynamical analysis for an age-structured hepatitis B infection model with latency and HBV DNA-containing capsids

Xiu Dong[1], **Ran Zhang**[2] **and Xue Ren**[2,*]

[1] School of Science, Shandong Jianzhu University, Jinan 250100, China
[2] School of Mathematical Sciences, Heilongjiang University, Harbin 150080, China

* **Correspondence:** Email: xueren@hlju.edu.cn.

Abstract: In this paper, we propose an HBV infection model with DNA-containing capsids and age structures in both the latent and infected compartments. We derive the basic reproduction number $\Re_0$ and prove, via Lyapunov functions and LaSalle's invariance principle, that the global dynamics are fully determined by $\Re_0$: viral clearance when $\Re_0 < 1$ and endemic persistence when $\Re_0 > 1$. The local stability of each equilibrium is rigorously established by employing linearization techniques and analyzing the associated characteristic equations. Compared to the previous age-structured HBV models without a latent compartment, our results reveal the significant impact of latent age structure on infection thresholds and disease progression.

Keywords: hepatitis B virus; HBV DNA-containing capsids; age structure; latency; basic reproduction number

1. Introduction

Viral hepatitis persists as a major public health crisis worldwide. The World Health Organization [1] reported that viral hepatitis has become the second leading infectious cause of death globally, claiming approximately 1.3 million lives in 2022. The vast majority (96%) of these fatalities are attributable to the long-term complications of chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. The scale of infection is immense, with an estimated 254 million individuals living with chronic HBV and 50 million with chronic HCV in 2022. The liver disease is not merely an individual health issue; it also places a significant dual burden on families and the healthcare system. Patients endure prolonged suffering, and their households risk vast expenditure on treatment, which can lead to medical impoverishment. This phenomenon translates into a serious public health challenge, placing sustained financial strain on social insurance schemes and government budgets. Hence, a detailed understanding of HBV transmission dynamics is imperative to inform and strengthen public health interventions.

In 1996, Nowak et al. [2] proposed a three-dimensional HBV model based on ordinary differential equations (ODEs), which included uninfected cells, infected cells, and viral particles. Their analysis quantitatively characterized in vivo HBV dynamics, highlighted differences from HIV infection, and showed no evidence of drug resistance in HBV patients treated for up to 24 weeks. Based on this foundational work, many researchers have expanded the model, resulting in a series of rich and significant findings. For further details, please refer to [3–8].

In the traditional sense, classical ODE-based HBV models implicitly assume that all infected cells are homogeneous and ignore the infection-age of the viral life cycle. Age-structured, within-host cell-virus infection models provide a refined mathematical framework for describing viral dynamics by explicitly accounting for the time since a cell becomes infected. Unlike classical ODE models that treat infected cells as a homogeneous population, age-structured formulations capture the progressive intracellular processes of viral replication, maturation, and virus production, as well as age-dependent cell death and treatment effects. This approach naturally yields a more realistic coupling viral dynamic, enabling a rigorous analysis of persistence, stability, and long-term infection outcomes. Nelson et al. [9] incorporated the infection age into the modeling framework and revealed how infection-age-dependent viral production and cell death shape steady states and viral peak timing, and highlighted that viral load data alone are insufficient to identify these age-dependent mechanisms. Furthermore, Huang et al. [10] established global stability results via Lyapunov methods based solely on the basic reproduction number. Since then, an increasing number of age-structured viral infection models have been extensively studied (see, [11,12] and the references therein). Indeed, age-structured models offer deeper mechanistic insight into chronic viral infections and improve the theoretical foundation for evaluating antiviral and immunotherapeutic strategies.

As is well known, the HBV virion is primarily composed of an internal nucleic acid and a protein shell. The nucleic acid within the virion is referred to as the core, which is encapsulated by the protein shell to form the capsid. The core and the capsid together constitute the nucleocapsid. The interior of the nucleocapsid serves as the exclusive site where pregenomic RNA (pgRNA) is reverse transcribed into DNA. The pgRNA, along with the viral polymerase, is packaged into newly assembled nucleocapsids, where the reverse transcription process takes place. Upon maturation, a portion of nucleocapsids containing relaxed circular DNA (rcDNA) is enveloped and released from the cell as new viral particles. In [13–19], HBV DNA-containing capsids are also considered as a distinct topic for research purposes.

Given the indispensable role of the nucleocapsid in virion production, we incorporate it as a separate compartment in our study. As noted in [20], following the infection of a healthy hepatocyte, there exists a latent phase during which no capsid synthesis occurs, and no virions are released. Taking this biological observation into account, we consider the introduction of a latent compartment to be both highly reasonable and necessary. Different from healthy hepatocytes, cells in the latent stage are characterized by a latent age, which denotes the time elapsed since the initial infection. To better characterize the process of HBV infection, we construct a mathematical model that incorporates DNA-containing capsids and age structures in both the latent and infected compartments. It is largely different from [13–19], in which the latency age is not considered.

We consider the infection term of healthy hepatocytes by HBV virions to be bilinear, taking the form βTV, which governs the influx of newly infected cells into both the latent and productively infected compartments, respectively. Upon attack by viral particles, a fraction f of healthy hepatocytes enter the latent compartment; thus, the boundary condition of e is

$$e(t,0) = f\beta TV.$$

The remaining fraction $1 - f$ directly enters the productively infected cell compartment, which is $(1 - f)\beta TV$. The total number of latently infected cells at time t is $\int_0^\infty \xi(a)e(t,a)\mathrm{d}a$. Also, latently infected cells then progress to the productively infected state at an age-dependent rate $\xi(a)$. Thus, the boundary condition of i is

$$i(t,0) = (1 - f)\beta T(t)V(t) + \int_0^\infty \xi(a)e(t,a)\mathrm{d}a.$$

At time t, the total production of HBV DNA-containing capsids per unit time, contributed by all infected cells across all infection ages b, is given by $\int_0^\infty p(b)i(t,b)\mathrm{d}b$, where $p(b)$ is the production rate of HBV DNA-containing capsids from hepatocytes with infection age b.

2. Model formulation

Based on the above analysis, we arrive at the model to be studied in this paper.

$$\begin{cases} \dfrac{\mathrm{d}T}{\mathrm{d}t} = \Lambda - \mu_1 T(t) - \beta T(t)V(t), \\ \dfrac{\partial e}{\partial t} + \dfrac{\partial e}{\partial a} = -\theta_1(a)e(t,a), \\ \dfrac{\partial i}{\partial t} + \dfrac{\partial i}{\partial b} = -\theta_2(b)i(t,b), \\ \dfrac{\mathrm{d}D}{\mathrm{d}t} = \displaystyle\int_0^\infty p(b)i(t,b)\mathrm{d}b - (\mu_2 + k)D, \\ \dfrac{\mathrm{d}V}{\mathrm{d}t} = kD(t) - \mu_3 V(t), \end{cases} \tag{2.1}$$

with boundary conditions

$$\begin{cases} e(t,0) = f\beta T(t)V(t), \\ i(t,0) = (1 - f)\beta T(t)V(t) + \displaystyle\int_0^\infty \xi(a)e(t,a)\mathrm{d}a, \end{cases} \tag{2.2}$$

and initial conditions

$$T(0) = T_0 \geq 0,\ e(0,a) = e_0(a),\ i(0,b) = i_0(b),\ D(0) = D_0 \geq 0,\ V(0) = V_0 \geq 0, \tag{2.3}$$

where $e_0(a),\ i_0(b) \in L^1_+(0,\infty)$. $T(t)$, $D(t)$, and $V(t)$ respectively represent the concentrations of uninfected hepatocytes, HBV DNA-containing capsids, and free viruses at time t. μ_1, μ_2, and μ_3 stand for the natural death rate of uninfected hepatocytes, HBV DNA-containing capsids, and free viruses, respectively.

The description of parameters not mentioned above are listed in Table 1.

Table 1. Description of parameters in Model (2.1).

Parameter	Description
Λ	The recruitment rate of uninfected hepatocytes
β	The infection rate between virus and uninfected hepatocytes
$e(t,a)$	The concentration of latency hepatocytes with latency age a at time t
$i(t,b)$	The concentration of infected hepatocytes with infection age b at time t
$\theta_1(a)$	The removal rate of latency hepatocytes
$\theta_2(b)$	The removal rate of infected hepatocytes
k	The production rate of viral particles from an HBV DNA-containing capsid

We make some assumptions about the coefficients.

(A1) Let functions $\theta_1(a), \theta_2(b), \xi(a), p(b) \in L^\infty_+(0,+\infty)$. Denote

$$\bar{\Theta} = \mathrm{esssup}_{\mathbb{R}_+}\Theta(\cdot) \text{ and } \underline{\Theta} = \mathrm{essinf}_{\mathbb{R}_+}\Theta(\cdot),$$

where $\Theta(\cdot) = \{\theta_1(\cdot), \theta_2(\cdot), \xi(\cdot), p(\cdot)\}$.

(A2) There exist constants $0 < a_\dagger < \infty$ and $0 < b_\dagger < \infty$ such that for all $a \geq a_\dagger$, $e(t,a) = 0$ holds, and for all $b \geq b_\dagger$, $i(t,b) = 0$ holds.

Biologically, Assumption **(A2)** suggests that no individual can live indefinitely. To simplify the notations, denote

$$\phi(a) = \int_a^\infty \xi(s)\mathrm{e}^{-\int_a^s \theta_1(\omega)\mathrm{d}\omega}\mathrm{d}s,\ \Omega(a) = \mathrm{e}^{-\int_0^a \theta_1(\tau)\mathrm{d}\tau},\ K = \int_0^\infty \xi(a)\Omega(a)\mathrm{d}a, \tag{2.4}$$

$$\psi(b) = \int_b^\infty p(s)\mathrm{e}^{-\int_b^s \theta_2(\omega)\mathrm{d}\omega}\mathrm{d}s,\ \Gamma(b) = \mathrm{e}^{-\int_0^b \theta_2(\tau)\mathrm{d}\tau},\ J = \int_0^\infty p(b)\Gamma(b)\mathrm{d}b. \tag{2.5}$$

Biologically, $\Omega(a)$ means the probability of a latency hepatocyte remaining alive with latency age a, and $\Gamma(b)$ denotes the probability of hepatocyte remaining alive with infection age b. It is obvious that

$$\frac{\mathrm{d}\phi(a)}{\mathrm{d}a} = \theta_1(a)\phi(a) - \xi(a),\ \frac{\mathrm{d}\Omega(a)}{da} = -\theta_1(a)\Omega(a),$$
$$\frac{\mathrm{d}\psi(b)}{\mathrm{d}b} = \theta_2(b)\psi(b) - p(b),\qquad \frac{\mathrm{d}\Gamma(b)}{\mathrm{d}b} = -\theta_2(b)\Gamma(b).$$

Inspired by [21], we write (2.1) as a semi-linear Cauchy problem with boundary condition (2.2) and initial condition (2.3). Let $\mathcal{X}$, $\mathcal{X}_0$, and $\mathcal{X}_+$ be Banach spaces, where

$$\mathcal{X} = \mathbb{R}\times\mathbb{R}\times L^1(\mathbb{R}_+,\mathbb{R})\times\mathbb{R}\times L^1(\mathbb{R}_+,\mathbb{R})\times\mathbb{R}\times\mathbb{R},$$
$$\mathcal{X}_0 = \mathbb{R}\times\{0\}\times L^1(\mathbb{R}_+,\mathbb{R})\times\{0\}\times L^1(\mathbb{R}_+,\mathbb{R})\times\mathbb{R}\times\mathbb{R},$$
$$\mathcal{X}_+ = \mathbb{R}_+\times\mathbb{R}_+\times L^1_+(\mathbb{R}_+,\mathbb{R})\times\mathbb{R}_+\times L^1_+(\mathbb{R}_+,\mathbb{R})\times\mathbb{R}_+\times\mathbb{R}_+.$$

At the same time, $\mathcal{X}_{0+} = \mathcal{X}_0 \cap \mathcal{X}_+$. The norm is

$$\|(\phi_1, \varphi_1(\cdot), \varphi_2(\cdot), \phi_2, \phi_3)\|_{\mathcal{Y}} = |\phi_1| + \int_0^\infty |\varphi_1(a)|\mathrm{d}a + \int_0^\infty |\varphi_2(b)|\mathrm{d}b + |\phi_2| + |\phi_3|,$$

where $\mathcal{Y} = \mathbb{R}_+ \times L^1_+(\mathbb{R}_+) \times L^1_+(\mathbb{R}_+) \times \mathbb{R}_+ \times \mathbb{R}_+$. In order to write System (2.1) as an abstract Cauchy problem, two operators are defined on $\mathcal{X}_0$, which are the linear operator B and the nonlinear operator F. The linear operator B : Dom(B)$\subset \mathcal{X} \to \mathcal{X}$ is defined as below:

$$B\begin{pmatrix} \phi_1 \\ \begin{pmatrix} 0 \\ \varphi_1 \end{pmatrix} \\ \begin{pmatrix} 0 \\ \varphi_2 \end{pmatrix} \\ \phi_2 \\ \phi_3 \end{pmatrix} = \begin{pmatrix} -\mu_1\phi_1 \\ \begin{pmatrix} -\varphi_1(0) \\ -\varphi_1' - \theta_1(a)\varphi_1 \end{pmatrix} \\ \begin{pmatrix} -\varphi_2(0) \\ -\varphi_2' - \theta_2(b)\varphi_2 \end{pmatrix} \\ -(\mu_2 + k)\phi_2 \\ -\mu_3\phi_3 \end{pmatrix},$$

and

$$\mathrm{Dom}(B) = \mathbb{R} \times \{0\} \times W^{1,1}(\mathbb{R}_+, \mathbb{R}) \times \{0\} \times W^{1,1}(\mathbb{R}_+, \mathbb{R}) \times \mathbb{R} \times \mathbb{R},$$

where $W^{1,1}$ denotes a Sobolev space.

Define the nonlinear operator $F : \overline{\mathrm{Dom}(B)} \subset \mathcal{X} \to \mathcal{X}$ as follows:

$$F\begin{pmatrix} \phi_1 \\ \begin{pmatrix} 0 \\ \varphi_1 \end{pmatrix} \\ \begin{pmatrix} 0 \\ \varphi_2 \end{pmatrix} \\ \phi_2 \\ \phi_3 \end{pmatrix} = \begin{pmatrix} \Lambda - \beta\phi_1\phi_3 \\ \begin{pmatrix} f\beta\phi_1\phi_3 \\ 0_{L^1} \end{pmatrix} \\ \begin{pmatrix} (1-f)\beta\phi_1\phi_3 + M(t) \\ 0_{L^1} \end{pmatrix} \\ N(t) \\ k\phi_2 \end{pmatrix},$$

where

$$M(t) = \int_0^\infty \xi(a)\varphi_1(a)\mathrm{d}a, \quad N(t) = \int_0^\infty p(b)\varphi_2(b)\mathrm{d}b.$$

Obviously, F is Lipschitz continuous on Dom(B), and $\overline{\mathrm{Dom}(B)} = \mathcal{X}_0$ is not dense in $\mathcal{X}$. Set $u(t) = \left(T(t), \begin{pmatrix} 0 \\ e(\cdot,t) \end{pmatrix}, \begin{pmatrix} 0 \\ i(\cdot,t) \end{pmatrix}, D(t), V(t)\right)^{\mathrm{T}}$, where v^{T} implies the transpose of vector v. Hence, we can write Eq (2.1) with initial and boundary conditions as the abstract Cauchy problem

$$\begin{cases} \frac{\mathrm{d}u(t)}{\mathrm{d}t} = Bu(t) + F(u(t)) \;\; t \geq 0, \\ u(0) = u_0 \in \mathcal{X}_0 \bigcap \mathcal{X}_{0+}. \end{cases} \tag{2.6}$$

To establish the existence and uniqueness of solutions to Eq (2.1) by applying [22, Theorem 5.2.7], it is required to verify that the operator B is a Hille–Yosida operator. Define $\rho(B)$ as the resolvent set of B. The Hille–Yosida operator is defined as follows:

Definition 2.1. *[22] Let B : Dom(B) $\subset \mathcal{X} \to \mathcal{X}$ be a linear operator. B is a Hille–Yosida operator if there exist real comstants $M \geq 1$ and $\omega \in \mathbb{R}$ such that $(\omega, +\infty) \subseteq \rho(B)$, and for all $n \in \mathbb{N}_+$ and $\lambda > \omega$, there holds*

$$\|(\lambda - B)^{-n}\| \leq \frac{M}{(\lambda - \omega)^n}.$$

Lemma 2.1. *The operator B is a Hille–Yosida operator.*

The proof of Lemma 2.1 can be seen in the Appendix.

Let $X_0 = \left(T_0, \begin{pmatrix}0\\e_0\end{pmatrix}, \begin{pmatrix}0\\i_0\end{pmatrix}, D_0, V_0\right)^{\mathrm{T}} \in \mathcal{X}_{0+}$. Considering that the nonlinear operator F is Lipschitz continuous on the bounded set, then by [22, Theorem 5.2.7] (also [23,24]), the following theorem can be obtained.

Theorem 2.1. *There exists a uniquely determined semiflow $\{U(t)\}_{t\geq 0}$ on $\mathcal{X}_{0+}$ such that for every $X_0 \in \mathcal{X}_{0+}$, the unique continuous map $X \in C([0,\infty), \mathcal{X}_{0+})$, denoted by $X = U(t, X_0)$, is an integrated solution of the Cauchy problem of* (2.6)*, that is,*

$$\begin{cases} \int_0^t X(s)\mathrm{d}s \in \mathrm{Dom}(B), & \forall\, t \geq 0, \\ X(t) = X_0 + B\int_0^t X(s)\mathrm{d}s + \int_0^t F(X(s))\mathrm{d}s, & \forall\, t \geq 0. \end{cases}$$

Set

$$\begin{aligned} \Upsilon = &\Big\{(T_0, e_0(a), i_0(b), D_0, V_0) \in \mathcal{X}_{0+} \Big| T_0 \leq \frac{\Lambda}{\mu_1}, \\ &T_0 + \int_0^\infty e_0(a)\mathrm{d}a \leq \frac{\Lambda}{\mu_0}, T_0 + \int_0^\infty e_0(a)\mathrm{d}a + \int_0^\infty i_0(b)\mathrm{d}b \leq \frac{\Lambda}{\mu_0} + \frac{\bar{\xi}\Lambda}{\mu_0^2}, \\ &D_0 \leq \frac{\bar{p}\Lambda}{\mu_0(\mu_2+k)} + \frac{\bar{p}\bar{\xi}\Lambda}{\mu_0^2(\mu_2+k)}, V_0 \leq \frac{\bar{p}k\Lambda}{\mu_0(\mu_2+k)\mu_3} + \frac{\bar{p}\bar{\xi}k\Lambda}{\mu_0^2(\mu_2+k)\mu_3}\Big\}, \end{aligned} \tag{2.7}$$

where $\mu_0 = \min\{\mu_1, \underline{\theta}_1, \underline{\theta}_2\}$. For the set Υ, the following proposition is established.

Proposition 2.1. *The solution Υ is positively invariant under the semiflow $\{U(t)\}_{t\geq 0}$. Furthermore, $\{U(t)\}_{t\geq 0}$ is point-dissipative and attracts every positive solution of System* (2.1) *in $\mathcal{X}_{0+}$.*

The proof of Proposition 2.1 can be seen in the Appendix.

3. Steady states, asymptotically smooth and uniform persistence

3.1. Existence and local stability of steady states

The basic reproduction number of (2.1) is defined as below:

$$\mathfrak{R}_0 = \frac{f\beta\Lambda kKJ + (1-f)\beta\Lambda kJ}{\mu_1\mu_3(\mu_2+k)},$$

which replies the expected number of secondary infections generated by one infected cell during its entire infectious period, and $K = \int_0^\infty \xi(a)\Omega(a)\mathrm{d}a$, $J = \int_0^\infty p(b)\Gamma(b)\mathrm{d}b$.

Mathematically, the basic reproduction number explicitly incorporates the quantity $K = \int_0^\infty \xi(a)\Omega(a)\mathrm{d}a$, which captures the cumulative contribution of the "age-structured latent process". In contrast, models without latent age structure either neglect this term or replace it with a constant transition rate. Therefore, the inclusion of latent age structure modifies $\mathfrak{R}_0$ by introducing a "history-dependent progression mechanism", which can either increase or decrease the infection threshold depending on the distribution of the latency period. The basic reproduction number is derived from next-generation matrix methods, where $\frac{\beta\Lambda}{\mu_1}$ means the number of new infections generated by one virion in the presence of susceptible cells, $\frac{kJ}{\mu_3(\mu_2+k)}$ means the total number of virions produced by one infected cell, $(1-f)+fK$ means the effective infectiousness weight after infection, $1-f$ is the proportion entering the productive infection stage directly, and fK is the proportion entering the latent stage and eventually activating.

Biologically, this means that not only the presence of a latent phase, but also the "distribution of residence time within latency", influences whether infection persists or dies out, which will be determined later. This provides a more refined threshold condition compared to classical models without a latent phase.

Next, we will prove the existence of equilibria of (2.1).

Theorem 3.1. *System* (2.1) *always has a disease-free equilibrium* $E_0 = (T^0, 0, 0, 0, 0)$. *If* $\Re_0 > 1$, *System* (2.1) *also has an endemic equilibrium* $E^*(T^*, e^*(a), i^*(b), D^*, V^*)$, *where* $T^0 = \frac{\Lambda}{\mu_1}$, $T^* = \frac{T^0}{\Re_0}$, $e^*(a) = e^*(0)\Omega(a)$, $i^*(b) = i^*(0)\Gamma(b)$, $D^* = \frac{i^*(0)J}{\mu_2+k}$, $V^* = \frac{i^*(0)kJ}{\mu_3(\mu_2+k)}$, $e^*(0) = \frac{f\mu_1\mu_3(\mu_2+k)}{f\beta kKJ+(1-f)\beta kJ}(\Re_0 - 1)$, $i^*(0) = \frac{\mu_1\mu_3(\mu_2+k)}{\beta kJ}(\Re_0 - 1)$.

Proof. Denote $(\hat{T}, \hat{e}(a), \hat{i}(b), \hat{D}, \hat{V})$ as an equilibrium of System (2.1), that is,

$$\begin{cases} \Lambda - \mu_1\hat{T} - \beta\hat{T}\hat{V} = 0, \\ \dfrac{\mathrm{d}\hat{e}(a)}{\mathrm{d}a} = -\theta_1(a)\hat{e}(a), \\ \dfrac{\mathrm{d}\hat{i}(b)}{\mathrm{d}b} = -\theta_2(b)\hat{i}(b), \\ \displaystyle\int_0^\infty p(b)\hat{i}(b)\mathrm{d}b - (\mu_2 + k)\hat{D} = 0, \\ k\hat{D} - \mu_3\hat{V} = 0, \end{cases} \tag{3.1}$$

with initial conditions

$$\hat{e}(0) = f\beta\hat{T}\hat{V} \tag{3.2}$$

and

$$\hat{i}(0) = (1-f)\beta\hat{T}\hat{V} + \int_0^\infty \xi(a)\hat{e}(a)\mathrm{d}a. \tag{3.3}$$

From the second and third equations of (3.1), it follows that $\hat{e}(a) = \hat{e}(0)\Omega(a)$, $\hat{i}(b) = \hat{i}(0)\Gamma(b)$. Using the remaining equations in (3.1), we obtain

$$\begin{aligned} \hat{D} &= \frac{\hat{i}(0)J}{\mu_2 + k}, \\ \hat{V} &= \frac{k\hat{D}}{\mu_3} = \frac{\hat{i}(0)kJ}{\mu_3(\mu_2 + k)}, \\ \hat{T} &= \frac{\Lambda}{\mu_1 + \beta\hat{V}} = \frac{\mu_3(\mu_2 + k)\Lambda}{\mu_1\mu_3(\mu_2 + k) + \beta kJ\hat{i}(0)}. \end{aligned}$$

Substituting $\hat{T}$ and $\hat{V}$ into (3.2) and (3.3) yields

$$\hat{e}(0) = \frac{f\beta\Lambda kJ\hat{i}(0)}{\mu_1\mu_3(\mu_2 + k) + \beta kJ\hat{i}(0)}, \tag{3.4}$$

$$\hat{i}(0) = \frac{(1 - f)\beta\Lambda kJ\hat{i}(0)}{\mu_1\mu_3(\mu_2 + k) + \beta kJ\hat{i}(0)} + \hat{e}(0)K. \tag{3.5}$$

Substituting (3.4) into (3.5), we obtain

$$\hat{i}(0) = \frac{(1 - f)\beta\Lambda kJ\hat{i}(0) + f\beta\Lambda kKJ\hat{i}(0)}{\mu_1\mu_3(\mu_2 + k) + \beta kJ\hat{i}(0)}.$$

The following two cases are considered:
(i) If $\hat{i}(0) = 0$, then $\hat{D} = \hat{V} = \hat{e}(a) = \hat{i}(b) = 0, \hat{T} = \frac{\Lambda}{\mu_1}$, which means System (2.1) has a disease-free equilibrium $E_0(T^0, 0, 0, 0, 0)$.
(ii) If $\hat{i}(0) \neq 0$, it can be calculated that

$$\hat{i}(0) = \frac{\mu_1\mu_3(\mu_2 + k)}{\beta kJ}\left(\frac{f\beta\Lambda kKJ + (1 - f)\beta\Lambda kJ}{\mu_1\mu_3(\mu_2 + k)} - 1\right) = \frac{\mu_1\mu_3(\mu_2 + k)}{\beta kJ}(\Re_0 - 1).$$

Therefore, if $\Re_0 > 1$, the unique endemic equilibrium $E^* = (T^*, e^*(a), i^*(b), D^*, V^*)$ of System (2.1) exists. This completes the proof. □

Theorem 3.2. *(i) The disease-free equilibrium E_0 is locally asymptotically stable when $\Re_0 < 1$ and unstable when $\Re_0 > 1$.*
(ii) The endemic equilibrium E^* is locally asymptotically stable when $\Re_0 > 1$.

Proof. (i) Consider the following perturbation of the variables:

$$T_1(t) = T(t) - T^0, e_1(t, a) = e(t, a), i_1(t, b) = i(t, b), D_1(t) = D(t), V_1(t) = V(t).$$

Linearizing System (2.1) at the disease-free equilibrium E_0 yields

$$\begin{cases} \dfrac{dT_1}{dt} = -\mu_1 T_1(t) - \beta T^0 V_1(t), \\ \dfrac{\partial e_1}{\partial t} + \dfrac{\partial e_1}{\partial a} = -\theta_1(a)e_1(t, a), \\ \dfrac{\partial i_1}{\partial t} + \dfrac{\partial i_1}{\partial b} = -\theta_2(b)i_1(t, b), \\ \dfrac{dD_1}{dt} = \displaystyle\int_0^\infty p(b)i_1(t, b)db - (\mu_2 + k)D_1(t), \\ \dfrac{dV_1}{dt} = kD_1(t) - \mu_3 V_1(t), \end{cases}$$

with boundary condition

$$\begin{cases} e_1(t, 0) = f\beta T^0 V_1(t), \\ i_1(t, 0) = (1 - f)\beta T^0 V_1(t) + \displaystyle\int_0^\infty \xi(a)e_1(t, a)da. \end{cases}$$

Thus, we obtain the characteristic equation for System (2.1) at the disease-free equilibrium

$$\begin{vmatrix} \lambda+\mu_1 & 0 & 0 & 0 & \beta T^0 \\ 0 & 1 & 0 & 0 & -f\beta T^0 \\ 0 & 0 & 1 & 0 & -(1-f)\beta T^0 - f\beta T^0 K \\ 0 & 0 & -\int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\lambda b}\mathrm{d}b & \lambda+\mu_2+k & 0 \\ 0 & 0 & 0 & -k & \lambda+\mu_3 \end{vmatrix} = 0.$$

After calculation and simplification, we obtain

$$(\lambda+\mu_1)\Delta(\lambda) = 0,$$

where $\Delta(\lambda) = [f\beta T^0 k\, K + (1-f)\,\beta T^0 k]\int_0^\infty p(b)\Gamma(b)e^{-\lambda b}\mathrm{d}b - (\lambda+\mu_2+k)(\lambda+\mu_3)$. It follows that the stability of E_0 is determined by the roots of $\Delta(\lambda) = 0$. If $\mathfrak{R}_0 > 1$, then there exist $\Delta(0) = \mu_3(\mu_2+k)(\mathfrak{R}_0 - 1) > 0$ and $\lim_{\lambda\to+\infty}\Delta(\lambda) = -\infty$. It follows from the intermediate value theorem that $\Delta(\lambda) = 0$ has at least one positive root. Hence, if $\mathfrak{R}_0 > 1$, then E_0 is unstable. If $\mathfrak{R}_0 < 1$, it can be verified that all roots of $\Delta(\lambda) = 0$ have negative real parts. We provide a proof by contradiction below. Without loss of generality, we assume that λ_0 is an arbitrary root of $\Delta(\lambda) = 0$, and $\mathrm{Re}(\lambda_0) \geq 0$. Then

$$\frac{(\lambda_0+\mu_3)(\lambda_0+\mu_2+k)}{k} = [f\beta T^0 K + (1-f)\beta T^0]\int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\lambda_0 b}\mathrm{d}b.$$

Thus, we have

$$\begin{aligned} \frac{\mu_3(\mu_2+k)}{k} &\leq \left|\frac{(\lambda_0+\mu_3)(\lambda_0+\mu_2+k)}{k}\right| \\ &= [f\beta T^0 K + (1-f)\beta T^0]\left|\int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\lambda_0 b}\mathrm{d}b\right| \\ &\leq f\beta T^0 KJ + (1-f)\beta T^0 J. \end{aligned}$$

This leads to the contradiction that $\mathfrak{R}_0 \geq 1$ while we assume that $\mathfrak{R}_0 < 1$. Hence, the assumption cannot hold. Therefore, all roots of $\Delta(\lambda) = 0$ have negative real parts if $\mathfrak{R}_0 < 1$. Therefore, the disease-free equilibrium E_0 is locally asymptotically stable when $\mathfrak{R}_0 < 1$.

(ii) Applying a similar method as in situation (i), we obtain the characteristic equation of System (2.1) at the endemic equilibrium E^*.

$$\begin{vmatrix} \gamma+\mu_1+\beta V^* & 0 & 0 & 0 & \beta T^* \\ f\beta V^* & -1 & 0 & 0 & f\beta T^* \\ (1-f)\beta V^* & \int_0^\infty \xi(a)\Omega(a)\mathrm{e}^{-\gamma a}\mathrm{d}a & -1 & 0 & (1-f)\beta T^* \\ 0 & 0 & \int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\gamma b}\mathrm{d}b & -\gamma-\mu_2-k & 0 \\ 0 & 0 & 0 & -k & \gamma+\mu_3 \end{vmatrix} = 0.$$

It can be calculated that

$$\begin{aligned} &(\gamma+\mu_3)(\gamma+\mu_2+k)(\gamma+\mu_1+\beta V^*) \\ &= (\gamma+\mu_1)\left[(1-f)\beta T^* k + f\beta T^* k\int_0^\infty \xi(a)\Omega(a)\mathrm{e}^{-\gamma a}\mathrm{d}a\right]\int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\gamma b}\mathrm{d}b. \end{aligned} \tag{3.6}$$

Note that $\gamma = -\mu_3$ and $\gamma = -(\mu_2 + k)$ are not roots of (3.6). Rewrite (3.6) as

$$\begin{aligned}&\gamma + \mu_1 + \beta V^* \\ =&\frac{(\gamma + \mu_1)\left[(1-f)\beta T^* k + f\beta T^* k \int_0^\infty \xi(a)\Omega(a)\mathrm{e}^{-\gamma a}\mathrm{d}a\right]\int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\gamma b}\mathrm{d}b}{(\gamma + \mu_3)(\gamma + \mu_2 + k)}.\end{aligned} \tag{3.7}$$

From the preceding analysis, we have $\int_0^\infty p(b)i^*(b)\mathrm{d}b = (\mu_2 + k)D^*$, $D^* = \frac{\mu_3 V^*}{k}$, $i^*(0) = (1-f)\beta T^* V^* + \int_0^\infty \xi(a)e^*(a)\mathrm{d}a$ if $\mathfrak{R}_0 > 1$. Then, if γ_0 is a root of (3.7) with $\mathrm{Re}(\gamma_0) \geq 0$, there holds

$$|\gamma_0 + \mu_1 + \beta V^*| > |\gamma_0 + \mu_1|,$$

and

$$\begin{aligned}&\left|\frac{(\gamma_0 + \mu_1)\left[(1-f)\beta T^* k + f\beta T^* k \int_0^\infty \xi(a)\Omega(a)\mathrm{e}^{-\gamma_0 a}\mathrm{d}a\right]\int_0^\infty p(b)\Gamma(b)\mathrm{e}^{-\gamma_0 b}\mathrm{d}b}{(\gamma_0 + \mu_3)(\gamma_0 + \mu_2 + k)}\right| \\ \leq&\left|\frac{[(1-f)\beta T^* k + f\beta T^* kK]\int_0^\infty p(b)\Gamma(b)i^*(0)\mathrm{d}b}{i^*(0)\mu_3(\mu_2 + k)}\right||\gamma_0 + \mu_1| \\ =&\left|\frac{[(1-f)\beta T^* k + f\beta T^* kK]\int_0^\infty p(b)i^*(b)\mathrm{d}b}{i^*(0)\mu_3(\mu_2 + k)}\right||\gamma_0 + \mu_1| \\ =&|\gamma_0 + \mu_1|.\end{aligned}$$

This contradicts with (3.7), which implies that our assumption is invalid, and thus, all roots of (3.6) have negative real parts. Therefore, if $\mathfrak{R}_0 > 1$, the endemic equilibrium E^* is locally asymptotically stable. □

3.2. Asymptotically smooth and uniform persistence

In this section, we prove that the semi-flow $\{U(t)\}_{t\geq 0}$ is asymptotically smooth and uniformly persistent. In the next section, we will prove the global asymptotic stability of the equilibria by constructing suitable Lyapunov functions and applying LaSalle's invariance principle.

Given that the state space $\mathcal{X}_{0+}$ is an infinite-dimensional Banach space, it is necessary to ensure that the semi-flow generated by System (2.1) is asymptotically smooth. Furthermore, a well-defined Lyapunov function requires the semi-flow to be uniformly persistent. First, we establish the asymptotic smoothness of the semi-flow $\{U(t)\}_{t\geq 0}$. Note $U := \Phi + \Psi$, where

$$\Phi(t, X_0) := (0, \tilde{e}(\cdot, t), \tilde{i}(\cdot, t), 0, 0), \tag{3.8}$$
$$\Psi(t, X_0) := (T(t), \tilde{\psi}_1(\cdot, t), \tilde{\psi}_2(\cdot, t), D(t), V(t)), \tag{3.9}$$

with

$$\tilde{e}(\cdot, t) = \begin{cases} 0, & t > a \geq 0, \\ e(t, a), & a \geq t \geq 0, \end{cases} \quad \tilde{i}(\cdot, t) = \begin{cases} 0, & t > b \geq 0, \\ i(t, b), & b \geq t \geq 0, \end{cases}$$

$$\tilde{\psi}_1(\cdot, t) = \begin{cases} e(t, a), & t > a \geq 0, \\ 0, & a \geq t \geq 0, \end{cases} \quad \tilde{\psi}_2(\cdot, t) = \begin{cases} i(t, b), & t > b \geq 0, \\ 0, & b \geq t \geq 0. \end{cases}$$

Based on the above content, the asymptotic smoothness of the semi-flow will be proved below.

Theorem 3.3. *Let Υ, Φ, and Ψ be as defined in* (2.7), (3.8), *and* (3.9), *respectively. For any $X_0 \in \Upsilon$, semi-flow $\{U(t, X_0) : t \geq 0\}$ has compact closure in $\mathcal{X}$ if Conditions (i) and (ii) hold true.*
(i) There exists a function $\Delta : \mathbb{R}_+ \times \mathbb{R}_+ \to \mathbb{R}_+$ such that for each $s > 0$, $\lim_{t\to\infty} \Delta(t, s) = 0$. Moreover, if $X_0 \in \Upsilon$, and $\|X_0\|_{\mathcal{X}} \leq s$, then for any $t \geq 0$, $\|\Phi(t, X_0)\|_{\mathcal{X}} \leq \Delta(t, s)$.
(ii) For any $t \geq 0$, $\Psi(t, X_0)$ maps any bounded subsets of Υ into sets with compact closure in $\mathcal{X}$.

Proof. First, we show that Condition (i) holds. Take $\Delta(t, s) = 2e^{-\delta t}s$, where $\delta = \min\{\underline{\theta}_1, \underline{\theta}_2\}$. Obviously, $\lim_{t\to\infty} \Delta(t, s) = 0$; then, for any $X_0 \in \Upsilon$ with $\|X_0\|_{\mathcal{X}} \leq s$, we have

$$\begin{aligned}
\|\Phi(t, X_0)\|_{\mathcal{X}} &= \int_t^\infty \left| e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)} \right| \mathrm{d}a + \int_b^\infty \left| i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)} \right| \mathrm{d}b \\
&= \int_0^\infty \left| e_0(\sigma)\frac{\Omega(\sigma+t)}{\Omega(\sigma)} \right| \mathrm{d}\sigma + \int_0^\infty \left| i_0(\sigma)\frac{\Gamma(\sigma+t)}{\Gamma(\sigma)} \right| \mathrm{d}\sigma \\
&\leq \mathrm{e}^{-\underline{\theta}_1 t}\|e_0\|_{L^1} + \mathrm{e}^{-\underline{\theta}_2 t}\|i_0\|_{L^1} \\
&\leq 2\mathrm{e}^{-\delta t}\|X_0\|_{\mathcal{X}} \leq \Delta(t, s), \qquad t \geq 0.
\end{aligned}$$

The proof of Condition (i) is completed.

Second, we prove that Condition (ii) is valid. By Proposition 2.1, $T(t)$, $D(t)$, and $V(t)$ remain in a compact set. It suffices to prove that $\tilde{\psi}_1$ and $\tilde{\psi}_2$ remain in a precompact subset of $L^1_+(0, \infty)$. To prove this conclusion, we need to show that the following conditions hold (see [25]).
(a) The supremum of $\int_0^\infty \tilde{\psi}_1(t, a)\mathrm{d}a$ is finite with respect to $X_0 \in \Upsilon$.
(b) $\lim_{u\to\infty} \int_u^\infty \tilde{\psi}_1(t, a)\mathrm{d}a = 0$ holds uniformly with respect to $X_0 \in \Upsilon$.
(c) $\lim_{u\to 0^+} \int_0^\infty (\tilde{\psi}_1(t, a+u) - \tilde{\psi}_1(t, a))\mathrm{d}a = 0$ holds uniformly with respect to $X_0 \in \Upsilon$.
(d) $\lim_{u\to 0^+} \int_u^\infty \tilde{\psi}_1(t, a)\mathrm{d}a = 0$ holds uniformly with respect to $X_0 \in \Upsilon$.
By (2.7), it is easy to verify that Conditions (a), (b), and (d) hold. In the following, we prove that Condition (c) also holds. For sufficiently small $u \in (0, t)$, we have

$$\begin{aligned}
&\int_0^\infty |\tilde{\psi}_1(t, a+u) - \tilde{\psi}_1(t, a)|\mathrm{d}a \\
&\leq \int_0^{t-u} f\beta T(t-a-u)V(t-a-u)|\Omega(a+u) - \Omega(a)|\mathrm{d}a \\
&\quad + \int_0^{t-u} |f\beta T(t-a-u)V(t-a-u) - f\beta T(t-a)V(t-a)|\Omega(a)\mathrm{d}a \\
&\quad + uf\beta\left(\frac{\Lambda}{\mu_0}\right)^2\left(\frac{\bar{p}k}{(\mu_2+k)\mu_3} + \frac{\bar{p}\bar{\xi}k}{\mu_0(\mu_2+k)\mu_3}\right).
\end{aligned}$$

Obviously, $\Omega(a)$ is nonincreasing with respect to a and $0 \leq \Omega(a) \leq 1$, so then,

$$\int_0^{t-u} |\Omega(a+u) - \Omega(a)|\mathrm{d}a = \int_0^{t-u} \Omega(a)\mathrm{d}a - \int_u^t \Omega(a)\mathrm{d}a = \int_0^u \Omega(a)\mathrm{d}a - \int_{t-u}^t \Omega(a)\mathrm{d}a \leq u.$$

It follows that

$$\int_0^\infty |\tilde{\psi}_1(t, a+u) - \tilde{\psi}_1(t, a)|\mathrm{d}a \leq 2uf\beta\left(\frac{\Lambda}{\mu_0}\right)^2\left(\frac{\bar{p}k}{(\mu_2+k)\mu_3} + \frac{\bar{p}\bar{\xi}k}{\mu_0(\mu_2+k)\mu_3}\right) + \varrho,$$

where

$$\varrho = \int_0^{t-u} |f\beta T(t-a-u)V(t-a-u) - f\beta T(t-a)V(t-a)|\Omega(a)\mathrm{d}a.$$

According to [26, Proposition 6], $T(\cdot)V(\cdot)$ is Lipschitz continuous on $\mathbb{R}_+$. Let M_1 be the Lipschitz constant of $T(\cdot)V(\cdot)$; then,

$$\varrho \leq f\beta M_1 u \int_0^u \Omega(a)\mathrm{d}a \leq \frac{f\beta M_1 u}{\underline{\theta}_1}.$$

Therefore,

$$\int_0^\infty |\tilde{\psi}_1(t,a+u) - \tilde{\psi}_1(t,a)|\mathrm{d}a \leq 2uf\beta\left(\frac{\Lambda}{\mu_0}\right)^2\left(\frac{\bar{p}k}{(\mu_2+k)\mu_3} + \frac{\bar{p}\bar{\xi}k}{\mu_0(\mu_2+k)\mu_3}\right) + \frac{f\beta M_1 u}{\underline{\theta}_1},$$

which implies that when $u \to 0^+$, $\int_0^\infty |\tilde{\psi}_1(t,a+u) - \tilde{\psi}_1(t,a)|\mathrm{d}a \to 0$, Condition (c) holds. Similarly, it can be proved that $\int_0^\infty |\tilde{\psi}_2(t,b+u) - \tilde{\psi}_2(t,b)|\mathrm{d}b \to 0$ when $u \to 0^+$. The proof is finished. □

From Theorem 3.3, we can obtain the following proposition.

Proposition 3.1. *Let Assumptions* **(A1)** *and* **(A2)** *hold. The solution semi-flow* $\{U(t)\}_{t\geq 0}$ *of* (2.1) *is asymptotically smooth.*

Next, we prove that the solution semi-flow of (2.1) is uniformly persistent. Following the approaches in [27, 28], we define

$$\widehat{M} = \left\{ \begin{pmatrix} T \\ \begin{pmatrix} 0 \\ e \end{pmatrix} \\ \begin{pmatrix} 0 \\ i \end{pmatrix} \\ D \\ V \end{pmatrix} \in \mathcal{X}_{0+} : \int_0^\infty e(s)\mathrm{d}s + \int_0^\infty i(s)\mathrm{d}s + D + V > 0 \right\}$$

and

$$\partial\widehat{M} = \mathcal{X}_{0+} \setminus \widehat{M}.$$

Lemma 3.1. $\widehat{M}$ *and* $\partial\widehat{M}$ *are both positively invariant under the semi-flow* $\{U(t)\}_{t\geq 0}$ *generated by* (2.1) *on* $\mathcal{X}_{0+}$.

Proof. Set

$$G(t) = D(t) + V(t) + \int_0^\infty e(t,a)\mathrm{d}a + \int_0^\infty i(t,b)\mathrm{d}b.$$

It follows that

$$\frac{\mathrm{d}G(t)}{\mathrm{d}t} \geq -\mu_2 D(t) - \mu_3 V(t) - \bar{\theta}_1 \int_0^\infty e(t,a)\mathrm{d}a - \bar{\theta}_2 \int_0^\infty i(t,b)\mathrm{d}b \geq -a_1 G(t),$$

where $a_1 = \max\{\mu_2, \mu_3, \bar{\theta}_1, \bar{\theta}_2\}$. For any $\tilde{\zeta} = \left(\tilde{T}, \left(0, \tilde{e}\right), \left(0, \tilde{i}\right), \tilde{D}, \tilde{V}\right)^{\mathrm{T}} \in \widehat{M}$, we have $G(0) > 0$. Consequently, $G(t) \geq G(0)\mathrm{e}^{-a_1 t} > 0$, which implies that $U(t, \widehat{M}) \subset \widehat{M}$, that is, $\widehat{M}$ is positively invariant.

For any $\tilde{\zeta} = \left(T_0, \left(0, e_0\right), \left(0, i_0\right), D_0, V_0\right)^{\mathrm{T}} \in \partial\widehat{M}$, we have $V_0 = V(0) = 0$, $D_0 = D(0) = 0$, $\int_0^\infty e_0(a)\mathrm{d}a = 0$, $\int_0^\infty i_0(b)\mathrm{d}b = 0$. We proceed to prove that $\partial\widehat{M}$ is positively invariant. Noticing (B.1) and (B.2), the fourth equation of system (2.1) can be rewritten as

$$\begin{aligned}\frac{\mathrm{d}G(t)}{\mathrm{d}t} =&(1-f)\beta \int_0^t p(b)T(t-b)V(t-b)\Gamma(b)\mathrm{d}b + \int_0^t p(b)M(t-b)\Gamma(b)\mathrm{d}b \\ &+ \int_t^\infty p(b)i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}\mathrm{d}b - (\mu_2 + k)D(t),\end{aligned} \tag{3.10}$$

where

$$\begin{aligned}\int_0^t p(b)M(t-b)\Gamma(b)\mathrm{d}b =& \int_0^t p(b)\int_0^{t-b} \xi(a)e(t-a-b,0)\Omega(a)\mathrm{d}a\Gamma(b)\mathrm{d}b \\ &+ \int_0^t p(b)\int_{t-b}^\infty \xi(a)e_0(a+b-t)\frac{\Omega(a+b)}{\Omega(a+b-t)}\mathrm{d}a\Gamma(b)\mathrm{d}b.\end{aligned} \tag{3.11}$$

By the fifth equation of system (2.1) and the initial value $V(0) = 0$, we have

$$V(t) = k\int_0^t D(s)\mathrm{e}^{-\mu_3(t-s)}. \tag{3.12}$$

Substituting (3.12) into (3.10) and (3.11), we have

$$\begin{aligned}\frac{\mathrm{d}G(t)}{\mathrm{d}t} =&(1-f)\beta\int_0^t p)b)T(t-b)V(t-b)\Gamma(b)\mathrm{d}b \\ &+ \int_0^t p(b)\int_0^{t-b}\xi(a)e(t-a-b,0)\Omega(a)\mathrm{d}a\Gamma(b)\mathrm{d}b \\ &+ \int_0^t p(b)\int_{t-b}^\infty \xi(a)e_0(a+b-t)\frac{\Omega(a+b)}{\Omega(a+b-t)}\mathrm{d}a\Gamma(b)\mathrm{d}b \\ &+ \int_t^\infty p(b)i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}\mathrm{d}b - (\mu_2+k)D(t).\end{aligned}$$

It can be deduced that $D(t) = V(t) = 0$ for any $t \geq 0$ if $D(0) = V(0) = 0$ (the details can be found in [29, lemma 4.3]). Thus, we observe

$$0 \leq \int_0^\infty e(t,a)\mathrm{d}a = \int_0^t f\beta T(t-a)V(t-a)\Omega(a)\mathrm{d}a + \int_t^\infty e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}\mathrm{d}a \leq 0,$$

which indicates that $\int_0^\infty e(t,a)\mathrm{d}a = 0$. Meanwhile, the following estimate holds:

$$\begin{aligned}0 \leq \int_0^\infty i(t,b)\mathrm{d}b \leq&(1-f)\beta\int_0^t p)b)T(t-b)V(t-b)\Gamma(b)\mathrm{d}b + \int_t^\infty p(b)i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}\mathrm{d}b \\ &+ f\beta\int_0^t p(b)\int_0^{t-b}\xi(a)T(t-a-b)V(t-a-b)\Omega(a)\mathrm{d}a\Gamma(b)\mathrm{d}b\end{aligned}$$

$$+\int_0^t p(b)\int_{t-b}^{\infty}\xi(a)e_0(a+b-t)\frac{\Omega(a+b)}{\Omega(a+b-t)}\mathrm{d}a\Gamma(b)\mathrm{d}b\leq 0,$$

that is, $\int_0^\infty i(t,b)\mathrm{d}b = 0$. Thus, $\partial\widehat{M}$ is positively invariant. Moreover, $\int_0^\infty e(t,a)\mathrm{d}a = 0$ implies $\lim_{t\to\infty}\|e(t,a)\|_{L^1} = 0$, and $\int_0^\infty i(t,b)\mathrm{d}b = 0$ indicates $\lim_{t\to\infty}\|i(t,b)\|_{L^1} = 0$. When $t\to\infty$, $(D(t),V(t))\to(0,0)$. Then, by System (2.1), we have $T(t)\to T^0$ as $t\to\infty$. Thus, for any $\zeta\in\partial\widehat{M}$, $U(t,\zeta)\to E_0$ as $t\to\infty$. □

On the basis of the conclusion in [30, 31], we can derive the following theorem.

Theorem 3.4. *If $\Re_0 > 1$, the solution semi-flow $\{U(t)\}_{t\geq 0}$ generated by System* (2.1) *is uniformly persistent with respect to $(\partial\widehat{M},\widehat{M})$, that is, there exists $\varepsilon > 0$ such that*

$$\liminf_{t\to+\infty} d(U(t)\zeta,\partial\widehat{M})\geq\varepsilon.$$

The proof of Theorem 3.4 can be found in the Appendix.

4. Global stability of steady states

In this section, we mainly investigate the global stability of the equilibria by constructing appropriate Lyapunov functions. The global stability of the disease-free equilibrium and the endemic equilibrium are established in Theorems 4.1 and 4.2, respectively.

Theorem 4.1. *If $\Re_0 < 1$, the disease-free equilibrium E_0 is globally asymptotically stable.*

Proof. Define the following function

$$H(x) = x - 1 - \ln x,\quad \forall\, x > 0.$$

Obviously, it achieves its minimum value of 0 if and only if $x = 1$. Consider the Lyapunov function

$$\mathcal{L}_{IFE}(t) = \mathcal{L}_1(t) + \frac{\beta k T^0 J}{\mu_3(\mu_2+k)}\mathcal{L}_2(t) + \frac{\beta k T^0}{\mu_3(\mu_2+k)}\mathcal{L}_3(t) + \mathcal{L}_4(t) + \mathcal{L}_5(t),$$

where $\mathcal{L}_1(t) = T^0 H\left(\frac{T}{T^0}\right)$, $\mathcal{L}_2(t) = \int_0^\infty \phi(a)e(t,a)\mathrm{d}a$, $\mathcal{L}_3(t) = \int_0^\infty \psi(b)i(t,b)\mathrm{d}b$, $\mathcal{L}_4(t) = \frac{\beta k T^0}{\mu_3(\mu_2+k)}D(t)$, $\mathcal{L}_5(t) = \frac{\beta T^0}{\mu_3}V(t)$.

Calculation gives

$$\frac{\mathrm{d}\mathcal{L}_1(t)}{\mathrm{d}t} = -\frac{\mu_1}{T}(T-T^0)^2 - \beta T V + \beta T^0 V.$$

Applying integration by parts, the derivative of $\mathcal{L}_2$ is obtained as follows:

$$\frac{\mathrm{d}\mathcal{L}_2(t)}{\mathrm{d}t} = -\lim_{a\to\infty}\phi(a)e(t,a) + \phi(0)e(t,0) + \int_0^\infty\Big(\phi'(a) - \phi(a)\theta_1(a)\Big)e(t,a)\mathrm{d}a.$$

By Assumption **(A2)**, we have $\lim_{a\to\infty}\phi(a)e(t,a) = 0$, and then,

$$\frac{\mathrm{d}\mathcal{L}_2(t)}{\mathrm{d}t} = \phi(0)e(t,0) + \int_0^\infty\Big(\phi'(a) - \phi(a)\theta_1(a)\Big)e(t,a)\mathrm{d}a.$$

Following a similar differentiation procedure as for $\mathcal{L}_2$, we obtain

$$\frac{\mathrm{d}\mathcal{L}_3(t)}{\mathrm{d}t} = \psi(0)i(t,0) + \int_0^\infty \Big(\psi'(b) - \psi(b)\theta_2(b)\Big)i(t,b)\mathrm{d}b.$$

Calculating the derivatives of $\mathcal{L}_4$ and $\mathcal{L}_5$, respectively, we have

$$\frac{\mathrm{d}\mathcal{L}_4(t)}{\mathrm{d}t} = \frac{\beta k T^0}{\mu_3(\mu_2+k)}\left(\int_0^\infty p(b)i(t,b)\mathrm{d}b - (\mu_2+k)D(t)\right)$$

and

$$\frac{\mathrm{d}\mathcal{L}_5(t)}{\mathrm{d}t} = \frac{\beta T^0}{\mu_3}\left(kD(t) - \mu_3 V(t)\right).$$

Combining the above equations, we obtain

$$\begin{aligned}\frac{\mathrm{d}\mathcal{L}_{IFE}(t)}{\mathrm{d}t} = & -\frac{\mu_1}{T}(T-T^0)^2 - \beta TV + \phi(0)f\beta TV\frac{\beta k T^0 J}{\mu_3(\mu_2+k)} \\ & + \psi(0)(1-f)\beta TV\frac{\beta k T^0}{\mu_3(\mu_2+k)} \\ & + \int_0^\infty \frac{\beta k T^0}{\mu_3(\mu_2+k)}\Big(\phi'(a) - \phi(a)\theta_1(a) + \xi(a)\Big)e(t,a)\mathrm{d}a \\ & + \int_0^\infty \frac{\beta k T^0 J}{\mu_3(\mu_2+k)}\Big(\psi'(b) - \psi(b)\theta_2(b) + p(b)\Big)i(t,b)\mathrm{d}b,\end{aligned} \tag{4.1}$$

where $\phi(a)$ and $\psi(b)$ are as defined in (2.4), and (2.5), respectively. Obviously, $\phi(0) = K$, $\psi(0) = J$. Moreover,

$$\phi'(a) = \theta_1(a)\phi(a) - \xi(a),\ \psi'(b) = \theta_2(b)\psi(b) - p(b). \tag{4.2}$$

Noticing that $\Re_0 = \frac{f\beta\Lambda k K J + (1-f)\beta\Lambda k J}{\mu_1\mu_3(\mu_2+k)}$, substitute (4.2) into (4.1) to obtain

$$\frac{\mathrm{d}\mathcal{L}_{IFE}(t)}{\mathrm{d}t} = -\frac{\mu_1}{T}(T-T_0)^2 + (\Re_0 - 1)\beta TV.$$

Obviously, $\frac{\mathrm{d}\mathcal{L}_{IFE}(t)}{\mathrm{d}t} \leq 0$ if $\Re_0 < 1$. Moreover, when $\Re_0 < 1$, that is, $\frac{\mathrm{d}\mathcal{L}_{IFE}(t)}{\mathrm{d}t} = 0$ if and only if $T = T^0, TV = 0$, which implies $V = 0, D = 0, i = 0$, and $e = 0$. Thus, the disease-free equilibrium $\{E_0\}$ is the largest invariant subset of $\{(T, e, i, D, V)|\frac{\mathrm{d}\mathcal{L}_{IFE}(t)}{\mathrm{d}t} = 0\}$. As established in Proposition 3.1, the solution semi-flow is asymptotically smooth. It follows from the results in [22, 32] that the solution semi-flow $U(t)_{t\geq 0}$ possesses a unique global attractor. By the Lyapunov–LaSalle invariance principle, it follows that the disease-free equilibrium E_0 is globally asymptotically stable when $\mathcal{R}_0 < 1$. □

Theorem 4.2. *If* $\Re_0 > 1$*, the endemic equilibrium* E^* *is globally asymptotically stable.*

Proof. Define the function $G(x, y) = x - y - y\ln\frac{x}{y}, x > 0,\ y > 0$. It is clear that G is a non-negative function defined on $\mathbb{R}_+ \times \mathbb{R}_+$ and attains its minimum value of 0 if and only if $x = y$. Consider the following Lyapunov fuctional:

$$\mathcal{L}_{EE}(t) = W_1(t) + W_2(t) + W_3(t) + \frac{\beta k T^*}{\mu_3(\mu_2+k)}W_4(t) + \frac{\beta T^*}{\mu_3}W_5(t),$$

where

$$W_1(t) = G[T, T^*], W_2(t) = \int_0^\infty \tilde{\phi}(a)G[e(t,a), e^*(a)]\mathrm{d}a,$$

$$W_3(t) = \int_0^\infty \tilde{\psi}(b)G[i(t,b), i^*(b)]\mathrm{d}b, W_4(t) = G[D, D^*], W_5(t) = G[V, V^*].$$

Take

$$\tilde{\psi}(b) = \int_b^\infty \frac{\beta k T^*}{\mu_3(\mu_2+k)} p(u) e^{-\int_b^u \theta_2(\omega)\mathrm{d}\omega}\mathrm{d}u,\ \tilde{\phi}(a) = \int_a^\infty \psi(0)\xi(u)e^{-\int_a^u \theta_1(\omega)\mathrm{d}\omega}\mathrm{d}u.$$

Evidently, $\tilde{\phi}(0) = \frac{\beta k T^* K J}{\mu_3(\mu_2+k)}, \tilde{\psi}(0) = \frac{\beta k T^* J}{\mu_3(\mu_2+k)}$. Moreover,

$$\begin{cases} \tilde{\psi}'(b) = \theta_2(b)\tilde{\psi}(b) - \dfrac{\beta k T^*}{\mu_3(\mu_2+k)} p(b), \\ \tilde{\phi}'(a) = \theta_1(a)\tilde{\phi}(a) - \tilde{\psi}(0)\xi(a). \end{cases} \tag{4.3}$$

For W_i, where $i = 1,2,3,4,5$, it can be obtained that

$$\frac{\mathrm{d}W_1(t)}{\mathrm{d}t} = -\frac{\mu_1}{T}(T-T^*)^2 + \frac{1}{f}\left(1 - \frac{T^*}{T}\right)(e^*(0) - e(t,0)).$$

By integration by parts, we obtain

$$\frac{\mathrm{d}W_2(t)}{\mathrm{d}t} = -\tilde{\phi}(a)e^*(a)[e(t,a), e^*(a)]\Big|_{a=0}^{a=\infty} + \int_0^\infty \left(\phi'(a)e^*(a) + \frac{\mathrm{d}e^*(a)}{\mathrm{d}a}\tilde{\phi}(a)\right)\mathrm{d}a. \tag{4.4}$$

We then notice

$$\frac{\mathrm{d}e^*(a)}{\mathrm{d}a} = -\theta_1(a)e^*(a). \tag{4.5}$$

Substituting (4.3) and (4.5) into (4.4), we have

$$\begin{aligned} \frac{\mathrm{d}W_2(t)}{\mathrm{d}t} = &-\tilde{\phi}(a)G[e(t,a), e^*(a)]|_{a=\infty} + \tilde{\phi}(0)G[e(t,0), e^*(0)] \\ &+ \int_0^\infty \tilde{\psi}(0)\xi(a)G[e(t,a), e^*(a)]\mathrm{d}a. \end{aligned}$$

Similarly,

$$\begin{aligned} \frac{\mathrm{d}W_3(t)}{\mathrm{d}t} = &-\tilde{\psi}(b)G[i(t,b), i^*(b)]|_{b=\infty} + \tilde{\psi}(0)G[i(t,0), i^*(0)] \\ &+ \int_0^\infty \frac{\beta k T^*}{\mu_3(\mu_2+k)} p(b)G[i(t,b), i^*(b)]\mathrm{d}b. \end{aligned}$$

By $\int_0^\infty p(\theta)i^*(\theta)\mathrm{d}\theta = (\mu_2+k)D^*, kD^* = \mu_3 V^*$, differentiate $W_4(t)$ and $W_5(t)$, respectively, to get

$$\frac{\mathrm{d}W_4(t)}{\mathrm{d}t} = \int_0^\infty p(b)i^*(b)\left(\frac{i(t,b)}{i^*(b)} - \frac{D}{D^*} - \frac{D^* i(t,b)}{D i^*(b)} + 1\right)\mathrm{d}b$$

and

$$\frac{dW_5(t)}{dt} = \frac{k}{\mu_2 + k}\int_0^\infty p(b)i^*(b)\left(\frac{D}{D^*} - \frac{V}{V^*} - \frac{DV^*}{D^*V} + 1\right)db.$$

Noticing $i(t,0) = (1-f)\beta T(t)V(t) + \int_0^\infty \xi(a)e(a,t)da$, $i^*(0) = (1-f)\beta T^*V^* + \int_0^\infty \xi(a)e^*(a)da$, and

$$\frac{f\beta T^* KJ}{\mu_3(\mu_2+k)} + \frac{(1-f)\beta T^* J}{\mu_3(\mu_2+k)} = \left(\frac{f\beta KJ}{\mu_3(\mu_2+k)} + \frac{(1-f)\beta J}{\mu_3(\mu_2+k)}\right)\frac{T^0}{\Re_0} = 1,$$

integrate the results of the above calculations to obtain that

$$\begin{aligned}\frac{d\mathcal{L}_{EE}(t)}{dt} &= -\frac{\mu_1}{T}(T-T^*)^2 - \tilde{\phi}(a)G[e(t,a),e^*(a)]|_{a=\infty} - \tilde{\psi}(b)G[i(t,b),i^*(b)]|_{b=\infty}\\ &+ \frac{\beta kT^*J}{\mu_3(\mu_2+k)}\left[(1-f)\beta T^*V^*\ln\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)} + \int_0^\infty \xi(a)e^*(a)\ln\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}da\right]\\ &- \frac{\beta kT^*}{\mu_3(\mu_2+k)}\int_0^\infty p(b)i^*(b)\left[\frac{D^*i(t,b)}{Di^*(b)} + \frac{V}{V^*} + \frac{DV^*}{D^*V} - \ln\frac{i(t,b)}{i^*(b)} - 3\right]db.\end{aligned}$$

It is easy to verify that

$$(1-f)\beta T^*V^*\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)} - 1\right) + \int_0^\infty \xi(a)e^*(a)\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)} - 1\right)da = 0.$$

Thus,

$$\begin{aligned}\frac{d\mathcal{L}_{EE}(t)}{dt} = &-\frac{\mu_1}{T}(T-T^*)^2 - \tilde{\phi}(a)G[e(t,a),e^*(a)]|_{a=\infty} - \tilde{\psi}(b)G[i(t,b),i^*(b)]|_{b=\infty}\\ &- \frac{\beta kT^*J}{\mu_3(\mu_2+k)}\left[(1-f)\beta T^*V^*H\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right) + \int_0^\infty \xi(a)e^*(a)H\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right)da\right]\\ &- \frac{\beta kT^*}{\mu_3(\mu_2+k)}\int_0^\infty p(b)i^*(b)\left[H\left(\frac{T^*}{T}\right) + H\left(\frac{DV^*}{D^*V}\right) + H\left(\frac{D^*i(t,b)}{Di^*(b)}\right)\right]db.\end{aligned}$$

Therefore, $\frac{d\mathcal{L}_{EE}(t)}{dt} \le 0$ and $\frac{d\mathcal{L}_{EE}(t)}{dt} = 0$ if and only if $T = T^*$, $G[e(t,a),e^*(a)]|_{a=\infty} = G[i(t,b),i^*(b)]|_{b=\infty} = 0$ and $H\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right) = H\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right) = H\left(\frac{T^*}{T}\right) = H\left(\frac{DV^*}{D^*V}\right) = H\left(\frac{D^*i(t,b)}{Di^*(b)}\right) = 0$. By the property of function H, we have $\frac{D}{D^*} = \frac{V}{V^*} = \frac{i(t,b)}{i^*(b)}$. Set $\eta(t) = \frac{D}{D^*}$, then $i(t,b) = \eta i^*(b)$, $D = \eta D^*$, $V = \eta V^*$. Take $i(t,b) = \eta i^*(b)$ and $i^*(b) = i^*(0)\Gamma(b)$ into the third equation of (2.1), the left side becomes $\dot{\eta}i^*(b) + \eta\frac{di^*(b)}{db} = \dot{\eta}i^*(b) + \eta i^*(b)(-\theta_2(b))$, and the right side becomes $-\theta_2(b)\eta i^*(b)$. Subtract the left side from the right side to obtain $\dot{\eta}i^*(b) = 0$ holds for all $b \ge 0$, so then we have $\dot{\eta} = 0$, which implies η is a constant. Take $\eta = constant$, $T = T^*$, $V = \eta V^*$ into the first equation of (2.1), so that we have $0 = \Lambda - \mu_1 T^* - \beta T^*(\eta V^*)$. Combing with the equilibrium condition $\Lambda = \mu_1 T^* + \beta T^* V^*$, we have $\eta = 1$, which implies $\frac{D}{D^*} = \frac{V}{V^*} = \frac{i(t,b)}{i^*(b)} = 1$. Noticing $e(t,0) = f\beta TV$, $e^* = f\beta T^*V^*$, it can be easily obtained that $e(t,0) = e^*(0)$. Combined with $H\left(\frac{e(t,0)i^*(0)}{e^*(0)i(t,0)}\right) = 0$, we have $i(t,0) = i^*(0)$. Then, by $H\left(\frac{e(t,a)i^*(0)}{e^*(a)i(t,0)}\right) = 0$, we have $e(t,a) = e^*(a)$. By the property of function G, if and only if $a \to \infty$, $e(t,a) = e^*(a)$, there is $G[e(t,a),e^*(a)]|_{a=\infty} = 0$ and $G[i(t,b),i^*(b)]|_{b=\infty} = 0$ if and only if $b \to \infty$, $i(t,b) = i^*(b)$. Hence, $\{E^*\}$ is the largest invariant subset of $\{(T,e,i,D,V)|\frac{d\mathcal{L}_{EE}(t)}{dt} = 0\}$. As shown in Proposition 3.1, the solution semi-flow is asymptotically smooth. By arguments in [22, 32], we have that the solution semi-flow $\{U(t)\}_{t\ge 0}$ admits a unique global attractor. It follows from the Lyapunov–LaSalle invariance principle that the endemic equilibrium E^* is globally asymptotically stable when $\Re_0 > 1$. □

5. Discussion

We propose and investigate a hepatitis B virus infection model that incorporates both latent delays and age structure. First, based on the standard theory of nondensely defined operators, we reformulate the problem (2.1) as an abstract Cauchy problem and establish the existence and uniqueness of its solution. Next, we derive an explicit expression for the basic reproduction number and analyze the existence conditions for the disease-free equilibrium and the endemic equilibrium. Then, by linearizing the system (2.1) at each equilibrium and studying the corresponding characteristic equations, we prove the local stability of these equilibria. Subsequently, in order to apply the Lyapunov–LaSalle invariance principle to prove the global stability of the equilibria, we demonstrate that the solution semi-flow is asymptotically smooth and uniformly persistent. Finally, by constructing appropriate Lyapunov functions, we establish the following stability results: serving as a threshold for infection dynamics, if the basic reproduction number $\mathfrak{R}_0 < 1$, the disease-free equilibrium is globally asymptotically stable (the virus goes extinct and the disease is eradicated), and unstable otherwise; if $\mathfrak{R}_0 > 1$, the endemic equilibrium exists uniquely and is globally asymptotically stable (the disease persists, leading to chronic infection.).

Compared with models lacking a latent stage, the proposed model introduces two age-structured compartments (latent and productive) with coupled boundary conditions. Consequently, the expressions of the endemic equilibrium and the basic reproduction number $\mathfrak{R}_0$ are modified by latent-stage parameters, including the activation rate $\xi(a)$, the death rate $\theta_1(a)$ of latent cells, and the proportion f of newly infected cells entering the latent stage. Specifically, $\mathfrak{R}_0 = \frac{\beta\Lambda}{\mu_1} \cdot \frac{kJ}{\mu_3(\mu_2+k)} \cdot [(1-f) + fK]$, which generalizes the classical threshold quantity.

Despite these structural changes, the main dynamical properties remain unchanged. Both equilibria exist under the same threshold conditions, and the local stability, asymptotic smoothness, uniform persistence, and global stability of the equilibria are all preserved. The threshold dynamics governed by $\mathfrak{R}_0$ continue to determine the global behavior of the system.

However, the analysis becomes more technically demanding. The construction of Lyapunov functions, the characteristic equation analysis, and the handling of boundary terms all require more intricate procedures due to the coupling of two age-structured compartments.

Numerous researchers have shown great interest in HBV infection models and have conducted extensive studies in this field. However, to the best of our knowledge, this work represents the first attempt to propose an HBV model in which both the latent compartment and the infected compartment are equipped with age structure. In many previous modeling studies, the latent phase has often been neglected or oversimplified. Such an approach, however, fails to capture the biological reality of HBV infection. The inclusion of an age-structured latent compartment is a key distinction of our work and constitutes its main novelty. The latent phase is not merely a delay but a structured process that critically affects infection progression and control. [33] pointed out that in the event of high-risk exposure (e.g., a needlestick injury with a needle or blade contaminated by an HBV patient), the timely administration of hepatitis B immunoglobulin followed by the 0–1–6 month vaccination schedule achieves a high success rate in preventing infection by reducing the basic reproduction number below one. Current hepatitis B vaccines are designed for infection prevention and lack therapeutic efficacy against established chronic infection.

Importantly, the most advanced clinical research efforts focusing on eradicating existing infections are highly consistent with the theoretical framework derived from our model. For instance, [34] demonstrated that GST-HG141, a novel HBV capsid assembly modulator, can not only inhibit viral replication, but also reduce the replenishment of the cccDNA pool by blocking pgRNA packaging and inhibiting capsid uncoating, making it a promising adjunct to NUC therapy for LLV patients. Further, [35] discussed cutting-edge technologies that could lead to noncytolytic direct cccDNA targeting and a cure for infected hepatocytes. Both therapies achieve their therapeutic effects by acting on the latent stage of infection. Our model provides theoretical support for both the interruption of infection following high-risk exposure and the ultimate goal of eradicating HBV, by offering insights into parameters related to the latent stage.

In the present model, we only consider the case that viral particles infect uninfected cells, whereas direct cell-to-cell transmission is not included, which represents another significant route that uninfected cells can become infected. It is worth noting that the bilinear infection term used in the present model to represent the interaction between healthy hepatocytes, and viral particles may be somewhat idealized. In future research, we intend to investigate alternative incidence forms that more accurately reflect the actual infection process. Investigating this mechanism offers a critical direction for our future work.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare there are no conflicts of interest.

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Appendix

A. Proof of Lemma 2.1

Proof. Define the resolvent of the operator B as below:

$$(\lambda - B)^{-1}\begin{pmatrix} \hat{\phi}_1 \\ \begin{pmatrix} \hat{\varphi}_{10} \\ \hat{\varphi}_1 \end{pmatrix} \\ \begin{pmatrix} \hat{\varphi}_{20} \\ \hat{\varphi}_2 \end{pmatrix} \\ \hat{\phi}_2 \\ \hat{\phi}_3 \end{pmatrix} = \begin{pmatrix} \phi_1 \\ \begin{pmatrix} 0 \\ \varphi_1 \end{pmatrix} \\ \begin{pmatrix} 0 \\ \varphi_2 \end{pmatrix} \\ \phi_2 \\ \phi_3 \end{pmatrix}.$$

Thus, it can be inferred that

$$\begin{pmatrix} \phi_1 \\ \varphi_1 \\ \varphi_2 \\ \phi_2 \\ \phi_3 \end{pmatrix} = \begin{pmatrix} \frac{1}{\lambda+\mu_1}\hat{\phi}_1 \\ \hat{\varphi}_{10}e^{-\int_0^a(\lambda+\theta_1(s))ds} + \int_0^a \hat{\varphi}_1 e^{-\int_\tau^a(\lambda+\theta_1(s))ds}d\tau \\ \hat{\varphi}_{20}e^{-\int_0^b(\lambda+\theta_2(s))ds} + \int_0^b \hat{\varphi}_2 e^{-\int_\tau^b(\lambda+\theta_2(s))ds}d\tau \\ \frac{1}{\lambda+\mu_2+k}\hat{\phi}_2 \\ \frac{1}{\lambda+\mu_3}\hat{\phi}_3 \end{pmatrix}.$$

Consequently, we can derive the following estimates.

$$\begin{aligned}
\int_0^\infty \varphi_1(a)da &= \int_0^\infty \hat{\varphi}_{10}e^{-\int_0^a(\lambda+\theta_1(s))ds}da + \int_0^\infty\int_0^a \hat{\varphi}_1(\tau)e^{-\int_\tau^a(\lambda+\theta_1(s))ds}d\tau da \\
&\le \frac{|\hat{\varphi}_{10}|}{|\lambda+\underline{\theta}_1|} + \int_0^\infty\int_0^a \hat{\varphi}_1(\tau)e^{-(\lambda+\underline{\theta}_1)(a-\tau)}d\tau da \\
&= \frac{|\hat{\varphi}_{10}|}{|\lambda+\underline{\theta}_1|} + \int_0^\infty\int_\tau^\infty \hat{\varphi}_1(\tau)e^{-(\lambda+\underline{\theta}_1)(a-\tau)}da d\tau \\
&= \frac{|\hat{\varphi}_{10}|}{|\lambda+\underline{\theta}_1|} + \int_0^\infty \hat{\varphi}_1(\tau)e^{(\lambda+\underline{\theta}_1)\tau}\int_\tau^\infty e^{-(\lambda+\underline{\theta}_1)a}da d\tau \\
&= \frac{|\hat{\varphi}_{10}|}{|\lambda+\underline{\theta}_1|} + \int_0^\infty \hat{\varphi}_1(\tau)e^{(\lambda+\underline{\theta}_1)\tau}\frac{1}{\lambda+\underline{\theta}_1}e^{-(\lambda+\underline{\theta}_1)\tau}d\tau \\
&= \frac{|\hat{\varphi}_{10}|}{|\lambda+\underline{\theta}_1|} + \frac{\|\hat{\varphi}_1\|_{L^1}}{|\lambda+\underline{\theta}_1|}.
\end{aligned}$$

By a similar argument, we can show that

$$\int_0^\infty \varphi_2(b)\mathrm{d}b \le \frac{|\hat{\varphi}_{20}|}{|\lambda+\underline{\theta}_2|} + \frac{\|\hat{\varphi}_2\|_{L^1}}{|\lambda+\underline{\theta}_2|}.$$

Define $\chi = \left(\hat{\phi}_1, \begin{pmatrix}\hat{\varphi}_{10}\\ \hat{\varphi}_1(a)\end{pmatrix}, \begin{pmatrix}\hat{\varphi}_{20}\\ \hat{\varphi}_2(b)\end{pmatrix}, \hat{\phi}_2, \hat{\phi}_3\right)^{\mathrm{T}}$. We have

$$\|(\lambda I - B)^{-1}\chi\|_X \le \frac{|\hat{\phi}_1|}{|\lambda+\mu_1|} + \frac{|\hat{\varphi}_{10}|}{|\lambda+\underline{\theta}_1|} + \frac{\|\hat{\varphi}_1\|_{L^1}}{|\lambda+\underline{\theta}_1|} + \frac{|\hat{\varphi}_{20}|}{|\lambda+\underline{\theta}_2|} + \frac{\|\hat{\varphi}_2\|_{L^1}}{|\lambda+\underline{\theta}_2|} + \frac{|\hat{\phi}_2|}{|\lambda+\mu_2+k|} + \frac{|\hat{\phi}_3|}{|\lambda+\mu_3|}.$$

Select $\mu = \max\{\mu_1, \mu_2+k, \mu_3, \underline{\theta}_1, \underline{\theta}_2\}$; then, for $\lambda > -\mu$, there holds

$$\|(\lambda I - B)^{-1}\chi\|_X \le \frac{\|\chi\|_X}{\lambda+\mu}.$$

Therefore, according to the definition of the Hille–Yosida operator, the operator B is a Hille–Yosida operator. □

B. proof of Proposition 2.1

Proof. Integrate the second and third equation of System (2.1) along the characteristic lines $t-a=c$ and $t-b=c$ respectively, and combine them with the boundary condition (2.2) and the initial condition (2.3), where c is a constant. Thus, we have

$$e(a,t) = \begin{cases} f\beta T(t-a)V(t-a)\Omega(a) = e(0,t-a)\Omega(a), & t>a, \\ e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}, & t\le a, \end{cases} \tag{B.1}$$

and

$$i(b,t) = \begin{cases} [(1-f)\beta T(t-b)V(t-b) + M(t-b)]\,\Gamma(b) = i(0,t-b)\Gamma(b), & t>b, \\ i_0(b-t)\frac{\Gamma(b)}{\Gamma(b-t)}, & t\le b, \end{cases} \tag{B.2}$$

where

$$M(t-b) = \int_0^{t-b} \xi(a)e(0,t-b-a)\Omega(a)\mathrm{d}a + \int_{t-b}^\infty \xi(a)e_0(a+b-t)\frac{\Omega(a)}{\Omega(a+b-t)}\mathrm{d}a.$$

Hence,

$$\int_0^\infty e(t,a)\mathrm{d}a \le \int_0^t f\beta T(t-a)V(t-a)\Omega(a)\mathrm{d}a + \int_t^\infty e_0(a-t)\frac{\Omega(a)}{\Omega(a-t)}\mathrm{d}a,$$

and

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty e(t,a)\mathrm{d}a = f\beta T(t)V(t) - \int_0^\infty \theta_1(a)e(t,a)\mathrm{d}a.$$

It then follows from the first and second equations of System (2.1) that

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(T(t) + \int_0^\infty e(t,a)\mathrm{d}a\right) \le \Lambda - \mu_0\left(T(t) + \int_0^\infty e(t,a)\mathrm{d}a\right),$$

which gives

$$T(t)+\int_0^\infty e(t,a)\mathrm{d}a \le \frac{\Lambda}{\mu_0}-\left(\frac{\Lambda}{\mu_0}-x(0)\right)\mathrm{e}^{-\mu_0 t},$$

where $x(0)=T_0+\int_0^\infty e_0(a)\mathrm{d}a$. Similarly, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty i(t,b)\mathrm{d}b = i(0,t)-\int_0^\infty \theta_2(b)i(t,b)\mathrm{d}b,$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(T(t)+\int_0^\infty e(t,a)\mathrm{d}a+\int_0^\infty i(t,b)\mathrm{d}b\right)\le \Lambda+\frac{\bar{\xi}\Lambda}{\mu_0}-\mu_0\left(T(t)+\int_0^\infty e(t,a)\mathrm{d}a+\int_0^\infty i(t,b)\mathrm{d}b\right),$$

and

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(T(t)+\int_0^\infty e(t,a)\mathrm{d}a+\int_0^\infty i(t,b)\mathrm{d}b\right)\ge -\mu_1 T(t)-\bar{\theta}_1\int_0^\infty e(t,a)\mathrm{d}a-\bar{\theta}_2\int_0^\infty i(t,b)\mathrm{d}b.$$

Hence,

$$y(0)\mathrm{e}^{-\bar{\mu}_0 t}\le T(t)+\int_0^\infty e(t,a)\mathrm{d}a+\int_0^\infty i(t,b)\mathrm{d}b\le\left(\frac{\Lambda}{\mu_0}+\frac{\bar{\xi}\Lambda}{\mu_0^2}\right)-\left(\frac{\Lambda}{\mu_0}+\frac{\bar{\xi}\Lambda}{\mu_0^2}-y_0\right)\mathrm{e}^{-\mu_0 t}, \tag{B.3}$$

where $\bar{\mu}_0=\max\{\mu_1,\bar{\theta}_1,\bar{\theta}_2\}$, $y(0)=T_0+\int_0^\infty e_0(a)\mathrm{d}a+\int_0^\infty i_0(b)\mathrm{d}b$. For the fourth equation of system (2.1), we have

$$-(\mu_2+k)D(t)\le\frac{\mathrm{d}D(t)}{\mathrm{d}t}\le\left(\frac{\bar{p}\Lambda}{\mu_0}+\frac{\bar{p}\bar{\xi}\Lambda}{\mu_0^2}\right)-(\mu_2+k)D(t).$$

It yields that

$$D_0\mathrm{e}^{-(\mu_2+k)t}\le D(t)\le\frac{\bar{p}\Lambda}{\mu_0(\mu_2+k)}+\frac{\bar{p}\bar{\xi}\Lambda}{\mu_0^2(\mu_2+k)}-\left(\frac{\bar{p}\Lambda}{\mu_0(\mu_2+k)}+\frac{\bar{p}\bar{\xi}\Lambda}{\mu_0^2(\mu_2+k)}-D_0\right)\mathrm{e}^{-(\mu_2+k)t}. \tag{B.4}$$

Similarly, by the fifth equation of (2.1), we have

$$V_0\mathrm{e}^{-\mu_3 t}\le V(t)\le\left(\frac{\bar{p}\Lambda k}{\mu_0(\mu_2+k)\mu_3}+\frac{\bar{p}\bar{\xi}\Lambda k}{\mu_0^2(\mu_2+k)\mu_3}\right)-\left(\frac{\bar{p}\Lambda k}{\mu_0(\mu_2+k)\mu_3}+\frac{\bar{p}\bar{\xi}\Lambda k}{\mu_0^2(\mu_2+k)\mu_3}-V_0\right)\mathrm{e}^{-\mu_3 t}. \tag{B.5}$$

Thus,

$$\frac{\mathrm{d}T(t)}{\mathrm{d}t}=\Lambda-\mu_1 T(t)-\beta T(t)V(t)\ge-\tilde{\mu}T(t),$$

where $\tilde{\mu}=\mu_1+\beta\left(\frac{\bar{p}\Lambda k}{\mu_0(\mu_2+k)\mu_3}+\frac{\bar{p}\bar{\xi}\Lambda k}{\mu_0^2(\mu_2+k)\mu_3}\right)$. After calculation, it is easy to obtain $T(t)\ge T_0\mathrm{e}^{-\tilde{\mu}t}$. Therefore,

$$T_0\mathrm{e}^{-\tilde{\mu}t}\le T(t)\le\frac{\Lambda}{\mu_1}-\left(\frac{\Lambda}{\mu_1}-T_0\right)\mathrm{e}^{-\mu_1 t}. \tag{B.6}$$

Similarly, we can get

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(T(t)+\int_0^{\infty}e(t,a)\mathrm{d}a\right)\geq -\mu_1T(t)-\beta TV-\int_0^{\infty}\theta_1(a)e(t,a)\mathrm{d}a\geq -\tilde{\mu}T(t)-\bar{\theta}_1\int_0^{\infty}e(t,a)\mathrm{d}a,$$

which yields that $T(t)+\int_0^{\infty}e(t,a)\mathrm{d}a\geq x(0)\mathrm{e}^{-\hat{\mu}t}$, where $\hat{\mu}=\max\{\tilde{\mu},\bar{\theta}_1\}$. The following estimate holds:

$$x(0)e^{-\hat{\mu}t}\leq T(t)+\int_0^{\infty}e(t,a)\mathrm{d}a\leq\frac{\Lambda}{\mu_0}-\left(\frac{\Lambda}{\mu_0}-x(0)\right)\mathrm{e}^{-\mu_0 t}. \tag{B.7}$$

Thus, $U(t)\Upsilon\subset\Upsilon$, which means Υ is a positively invariant set. Combining with (B.3)–(B.7), it is obvious that Υ attracts each positive solution of (2.1). □

C. The proof of Theorem 3.4

Proof. By Lemma 3.1 and Theorem 2.1, Conditions (i)–(iii) in [30, th4.1] are all satisfied. [30, Theorem 4.1] indicates that $\{U(t)\}_{t\geq 0}$ is uniformly persistent if and only if

$$W^s(E_0)\cap\widehat{M}=\emptyset,$$

where

$$W^s(E_0)=\{\zeta\in\Upsilon:\lim_{t\to+\infty}U(t,\zeta)=E_0\}.$$

We now present a proof by contradiction. Without loss of generality, assume $\zeta_0\in W^s(E_0)\cap\widehat{M}$. Noticing $\zeta_0\in\widehat{M}$, there exists $t_1>0$ such that $D(t_1)+V(t_1)+\int_0^{\infty}e(t_1,s)\mathrm{d}s+\int_0^{\infty}i(t_1,s)\mathrm{d}s>0$. Hence, $D(t)+V(t)+\int_0^{\infty}e(t,s)\mathrm{d}s+\int_0^{\infty}i(t,s)\mathrm{d}s>0$ for all $t\geq t_1$.

On the other hand, when $\mathfrak{R}_0>1$, select $\varepsilon_0>0$ small enough such that

$$\frac{f\beta kKJ(T^0-\varepsilon_0)+(1-f)\beta kJ(T^0-\varepsilon_0)}{\mu_3(\mu_2+k)}>1.$$

As $\zeta_0\in W^s(E_0)$, $\lim_{t\to+\infty}T(t)=T^0$, for ε_0 mentioned above, there exists $t_2\geq 0$ such that $T(t)\geq T^0-\varepsilon_0$ for all $t\geq t_2$.

Take $G_1(t)=kJ\int_0^{\infty}\phi(a)e(t,a)\mathrm{d}a+k\int_0^{\infty}\psi(b)i(t,b)\mathrm{d}b+kD(t)+(\mu_2+k)V(t)$, where $\phi(a)$ and $\psi(b)$ are defined in (2.4) and (2.5): $\phi(0)=K$, $\psi(0)=J$. For $t\geq t_2$, we have

$$\begin{aligned}\left.\frac{\mathrm{d}G_1(t)}{\mathrm{d}t}\right|_{(2.1)}&=-\mu_3(\mu_2+k)V(t)+kf\beta TVKJ+k(1-f)\beta TVJ\\&=[kf\beta KJT(t)+k(1-f)\beta JT(t)-\mu_3(\mu_2+k)]V(t)\\&\geq\left(kf\beta KJ(T^0-\varepsilon_0)+k(1-f)\beta J(T^0-\varepsilon_0)-\mu_3(\mu_2+k)\right)V(t)\\&=\mu_3(\mu_2+k)\left(\frac{kf\beta KJ(T^0-\varepsilon_0)+k(1-f)\beta J(T^0-\varepsilon_0)}{\mu_3(\mu_2+k)}-1\right)V(t)\\&\geq 0,\end{aligned}$$

that is, $G_1(t)$ is nondecreasing with respect to $t \geq t_2$. Hence, $G_1(t) \geq G_1(t_0) > 0$ for $t \geq t_0 := \max\{t_1, t_2\}$. This implies that $(e(t,a), i(t,b), D(t), V(t))$ does not converge to $(0_{L^1}, 0_{L^1}, 0, 0)$ as $t \to +\infty$, which contradicts with the assumption that $\zeta \in W^s(E^0)$. This completes the proof. □

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