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GLOBAL STABILITY OF AN AGE-STRUCTURED VIRUS DYNAMICS MODEL WITH BEDDINGTON-DEANGELIS INFECTION FUNCTION

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Dedicated to Professor Glenn Webb on the occasion of his 70th birthday.

Abstract. In this paper, we study an age-structured virus dynamics model with Beddington-DeAngelis infection function. An explicit formula for the basic reproductive number $\mathcal{R}_0$ of the model is obtained. We investigate the global behavior of the model in terms of $\mathcal{R}_0$: if $\mathcal{R}_0 \leq 1$, then the infection-free equilibrium is globally asymptotically stable, whereas if $\mathcal{R}_0 > 1$, then the infection equilibrium is globally asymptotically stable. Finally, some special cases, which reduce to some known HIV infection models studied by other researchers, are considered.

1. **Introduction.** Various mathematical models of within-host virus dynamics with or without delay have been studied by many authors over the past two decades (Culshaw and Ruan[4], De Leenheer and Smith [8], Huang et al. [13], Li and Shu [17], Nowak and Bangham [25], Nowak and May [26], Perelson and Nelson [27]). Since age structure is an important characteristic in modeling of infectious diseases, Kirschner and Webb [16] proposed an HIV-1 infection model that incorporated age structure into the infected cells to account for the mechanism of AZT (zidovudine) treatment. Nelson et al. [24] proposed an age-structured model for HIV-1 infection with bilinear interactions between the uninfected target cells and the virus, which is a generalization of the standard delay differential equation models previously used

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to describe HIV-1 infection. Rong et al. [28] considered two age-structured models to study HIV-1 infection dynamics which extend the existing age-structured models of Kirschner and Webb [16] and Nelson et al. [24] by incorporating combination therapies. The age-related models are normally in the form of partial differential equations (PDEs). It is difficult to investigate the global dynamical properties of PDEs. Magal et al. [20] used Liapunov functional method to study global stability of the endemic equilibrium for an infection-age model of disease transmission. Motivated by this, Huang et al. [14] considered the global stability of equalibria in Nelson et al.'s [24] age-structured model by constructing suitable Liapunov functions. Recently the global dynamical properties of PDEs have also attracted some interests in the literature (Brauer et al. [2], Browne and Pilyugin [3], Magal and McCluskey [21], McCluskey [23]).

In modeling virus dynamics (Nowak and May [26]), the interaction between the virus and uninfected cells is usually regarded as a consumer-resource (predator-prey) relationship, with the virus as consumers (predators) while the uninfected cells as the resource (prey), and is described by a linear (mass action) function or the saturated Michaelis-Menten (Holling type II) function. The Michaelis-Menten function was derived based on the assumption that consumers do not interference with one another's activities, so the only competition among consumers occurs in the depletion of resource. To describe mutual interference among consumers, the Beddington-DeAngelis function, depending on both the resource and consumer densities, was proposed (Cosner et al. [5], Huisman and De Boer [15]) to describe the fact that individuals from a population of more than two consumers not only allocate time in searching for and processing their resource but also take time in encountering with other consumers. De Boer and Perelson [6] used Beddington-DeAngelis function to model the interaction between immune cells and virus. Althaus and De Boer [1] used a Beddington-DeAngelis function to describe the infection of uninfected T-cells by HIV particles. Based on these, we think that it is reasonable to consider virus dynamics models with Beddington-DeAngelis infection function. On the other hand, based on a delay differential equation model Culshaw and Ruan [4] illustrated that the CD4+ T-cells and HIV populations fluctuate in the early stage of the infection and converge to the infected equilibrium values in a longer term. Recently, Huang et al. [11] considered a virus dynamics model with Beddington-DeAngelis infection function and analyzed the global properties by constructing Liapunov functions. Huang et al. [12] also considered a delay virus dynamics model with Beddington-DeAngelis infection function and, by constructing suitable Liapunov functionals, gave complete global stability analysis for the model.

In this paper, we aim to study the global behavior of the following age-structured virus dynamics model with Beddington-DeAngelis infection function:

$$\begin{cases} \dfrac{\mathrm{d}x(t)}{\mathrm{d}t} = s - dx(t) - \dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)}, \\ \dfrac{\partial i(t,a)}{\partial t} + \dfrac{\partial i(t,a)}{\partial a} = -\delta(a) i(t,a), \\ \dfrac{\mathrm{d}v(t)}{\mathrm{d}t} = \displaystyle\int_0^\infty p(a) i(t,a)\,da - cv(t) \end{cases} \tag{1}$$

with the boundary condition

$$i(t,0) = \frac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)}$$

and initial conditions

$$x(0) = x_0, \quad i(0,a) = i_0(a), \quad \text{and} \quad v(0) = v_0.$$

Here, $x(t)$, $i(t,a)$, and $v(t)$ represent the populations of uninfected target cells, infected cells of infection age a, and free virus particles at time $t > 0$, respectively. s is the recruitment rate of uninfected cells, d is the per capita death rate of uninfected cells. The Beddington-DeAngelis function $\dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)}$, where $\alpha_1,\ \alpha_2 \geq 0$ are constants, describes the infection of healthy target cells by the free virus. $\delta(a)$ is the age-dependent per capita death rate of infected cells. c is the clearance rate of virus, $p(a)$ is the viral production rate of an infected cell with age a. The function $\delta(a)$ belongs to $L^\infty_+((0,+\infty),\mathbb{R})$, and $p(a)$ belongs to $L^\infty_+((0,+\infty),\mathbb{R}) \setminus \{0_{L^\infty}\}$. Moreover, there exists a $\delta_{\min} > 0$ such that $\delta(a) \geq \delta_{\min}$ for almost every $a \geq 0$.

The paper is organized as follows. In section 2, we present some preliminary results. In section 3, the local stabilities of the infection-free equilibrium and the infection equilibrium are established. In section 4, we present the results about uniform persistence. In section 5, by constructing a suitable Liapunov function, we conclude that the global asymptotic stability of the model depends only on the basic reproductive number. In section 6, some special cases and numerical simulations are discussed. The papers ends with a brief discussion in section 7.

2. **Preliminary results.** Consider

$$x(t) + \int_0^\infty i(t,a)da,$$

then

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(x(t) + \int_0^\infty i(t,a)da\right) \leq s - \gamma\left(x(t) + \int_0^\infty i(t,a)da\right),$$

where $\gamma = \min\{d, \delta_{\min}\}$. Therefore, we have

$$\limsup_{t\to+\infty}\left(x(t) + \int_0^\infty i(t,a)da\right) \leq \frac{s}{\gamma}.$$

From the third equation of system (1), we have

$$\frac{\mathrm{d}v(t)}{\mathrm{d}t} \leq p_{\max}\int_0^\infty i(t,a)da - cv(t),$$

where $p_{\max} = \operatorname{ess\,sup}_{\theta\in(0,+\infty)} p(\theta)$. Thus

$$\limsup_{t\to+\infty} v(t) \leq \frac{sp_{\max}}{c\gamma}.$$

It is clear to show that the following set is positively invariant for system (1)

$$\Omega = \left\{(x,i,v) \in \mathbb{R}_+ \times L^1_+((0,+\infty),\infty) \times \mathbb{R}_+ \middle| \left(x(t) + \int_0^\infty i(t,a)da\right) \leq \frac{s}{\gamma}, \right.$$

$$\left. v(t) \leq \frac{sp_{\max}}{c\gamma}\right\}.$$

Let

$$N = \int_0^\infty p(a)\sigma(a)da,$$

where $\sigma(a) = e^{-\int_0^a \delta(s)ds}$ is the probability that an infected cell survives to age a. Here, we assume that N is finite.

Now, we consider the existence of equilibria. System (1) always has an infection-free equilibrium $E^0 = (x^0, 0, 0)$, where $x^0 = s/d$. There may exist an infection equilibrium $E^* = (x^*, i^*(a), v^*)$ satisfying the following equations

$$\begin{aligned} & s - dx^* - \frac{kx^*v^*}{1 + \alpha_1 x^* + \alpha_2 v^*} = 0, \\ & \frac{\mathrm{d}i^*(a)}{\mathrm{d}a} = -\delta(a)i^*(a), \\ & \int_0^\infty p(a)i^*(a)da - cv^* = 0, \\ & i^*(0) = \frac{kx^*v^*}{1 + \alpha_1 x^* + \alpha_2 v^*}. \end{aligned} \tag{2}$$

Solving the second equation of (2) yields

$$i^*(a) = i^*(0)e^{-\int_0^a \delta(s)ds} = \frac{kx^*v^*}{1 + \alpha_1 x^* + \alpha_2 v^*}\sigma(a).$$

Then, from the third equation of (2), we have

$$\int_0^\infty p(a)i^*(a)da = \frac{kx^*v^*}{1 + \alpha_1 x^* + \alpha_2 v^*}N = cv^*,$$

which implies that

$$x^* = \frac{c(1 + \alpha_2 v^*)}{Nk - c\alpha_1}.$$

Substituting it into the first equation of (2), we get

$$v^* = \frac{N(sNk - c(d + \alpha_1 s))}{cdN\alpha_2 + c(Nk - c\alpha_1)}.$$

Thus, system (1) has a unique infection equilibrium $E^* = (x^*, i^*(a), v^*)$ if and only if $\mathcal{R}_0 > 1$, where

$$\mathcal{R}_0 = \frac{sNk}{c(d + \alpha_1 s)}.$$

According to the boundary condition and initial conditions of system (1), we obtain

$$i(t,a) = \begin{cases} \dfrac{kx(t-a)v(t-a)}{1 + \alpha_1 x(t-a) + \alpha_2 v(t-a)}\sigma(a), & 0 \le a < t, \\ i_0(a-t)\dfrac{\sigma(a)}{\sigma(a-t)}, & 0 < t \le a. \end{cases} \tag{3}$$

In the following, we use the approach introduced by Thieme [29]. Consider

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

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

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

and

$$\mathcal{X}_{0+} = \mathcal{X}_+ \cap \mathcal{X}_0.$$

Let $A : D(A) \subset \mathcal{X} \to \mathcal{X}$ be the linear operator defined by

$$A\begin{pmatrix} x \\ v \\ \begin{pmatrix} 0 \\ i \end{pmatrix} \end{pmatrix} = \begin{pmatrix} -dx \\ -cv \\ \begin{pmatrix} -i(0) \\ -i' - \delta(a)i \end{pmatrix} \end{pmatrix}$$

with $D(A) = \mathbb{R} \times \mathbb{R} \times \{0\} \times W^{1,1}((0,+\infty),\mathbb{R})$. We define a non-linear map $F : \mathcal{X}_0 \to \mathcal{X}$ by

$$F\begin{pmatrix} x \\ v \\ \begin{pmatrix} 0 \\ i \end{pmatrix} \end{pmatrix} = \begin{pmatrix} s - \dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)} \\ \displaystyle\int_0^\infty p(a)i(t,a)da \\ \begin{pmatrix} \dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)} \\ 0_{L^1} \end{pmatrix} \end{pmatrix}.$$

Define

$$u(t) = \begin{pmatrix} x(t) \\ v(t) \\ \begin{pmatrix} 0 \\ i(t,.) \end{pmatrix} \end{pmatrix},$$

then we can rewrite system (1) with the boundary and initial conditions as the following abstract Cauchy problem:

$$\frac{\mathrm{d}u(t)}{\mathrm{d}t} = Au(t) + F(u(t)), \quad \text{for} \quad t \geq 0, \quad \text{with} \quad u(0) = u_0 \in \mathcal{X}_{0+}. \tag{4}$$

By applying the results in Hale [9], Magal [19], and Magal and Thieme [22], we obtain the following theorem.

Theorem 2.1. *System (4) generates a unique continuous semiflow $\{U(t)\}_{t\geq 0}$ on $\mathcal{X}_{0+}$ that is bounded dissipative and asymptotically smooth. Furthemore, the semiflow $\{U(t)\}_{t\geq 0}$ has a global attractor $\mathcal{A}$ in $\mathcal{X}_{0+}$, which attracts the bounded sets of $\mathcal{X}_{0+}$.*

3. **Local stability.** In this section, we investigate the local stability of equalibria for system (1) and have the following results.

Theorem 3.1. (i) *If $\mathcal{R}_0 < 1$, then the infection-free equilibrium E^0 of system (1) is locally asymptotically stable; if $\mathcal{R}_0 > 1$, then E^0 is unstable;*

(ii) *If $\mathcal{R}_0 > 1$, then the unique infection equilibrium E^* of system (1) is locally asymptotically stable.*

Proof. First, we study the local stability of E^0. Let $x(t) = x_1(t) + x^0$, $i_1(t,a) = i(t,a)$ and $v_1(t) = v(t)$. Linearizing system (1) about E^0, we obtain

$$\begin{cases} \dfrac{\mathrm{d}x_1(t)}{\mathrm{d}t} = -dx_1(t) - \dfrac{kx^0}{1+\alpha_1 x^0}v_1(t), \\ \dfrac{\partial i_1(t,a)}{\partial t} + \dfrac{\partial i_1(t,a)}{\partial a} = -\delta(a)i_1(t,a), \\ \dfrac{\mathrm{d}v_1(t)}{\mathrm{d}t} = \displaystyle\int_0^\infty p(a)i_1(t,a)da - cv_1(t), \\ i_1(t,0) = \dfrac{kx^0}{1+\alpha_1 x^0}v_1(t). \end{cases} \tag{5}$$

Consider the exponential solutions $x_1(t) = x_1 e^{\lambda t}$, $i_1(t,a) = i_1(a)e^{\lambda t}$ and $v_1(t) = v_1 e^{\lambda t}$ of system (5). Then, we have

$$\begin{cases} (\lambda + d)x_1 = -\dfrac{kx^0}{1+\alpha_1 x^0} v_1, \\ i_1(a) = i_1(0)e^{-\lambda a} e^{-\int_0^a \delta(\omega)d\omega} da, \\ \lambda v_1 = \displaystyle\int_0^\infty p(a) i_1(a) da - c v_1, \\ i_1(0) = \dfrac{kx^0}{1+\alpha_1 x^0} v_1. \end{cases} \tag{6}$$

Substituting the second and fourth equations into the third equation of (6), we obtain

$$\lambda + c = \frac{kx^0}{1+\alpha_1 x^0} \int_0^\infty p(a) e^{-\lambda a} e^{-\int_0^a \delta(\omega)d\omega} da,$$

which implies that

$$\frac{\lambda}{c} + 1 = \mathcal{R}_0 \frac{\displaystyle\int_0^\infty p(a)\sigma(a)e^{-\lambda a} da}{\displaystyle\int_0^\infty p(a)\sigma(a) da}. \tag{7}$$

Define

$$\mathcal{H}(\lambda) = \mathcal{R}_0 \frac{\displaystyle\int_0^\infty p(a)\sigma(a)e^{-\lambda a} da}{\displaystyle\int_0^\infty p(a)\sigma(a) da} - \frac{\lambda}{c} - 1.$$

It is clear that $\lim\limits_{\lambda \to +\infty} \mathcal{H}(\lambda) = -\infty$, $\mathcal{H}(0) = \mathcal{R}_0 - 1$ and $\mathcal{H}'(\lambda) < 0$. Hence, equation (7) has no positive real root if $\mathcal{R}_0 < 1$. If all complex roots have non-negative real parts, then the modulus of the right hand side of equation (7) is always less than 1 when $\mathcal{R}_0 < 1$. Then, we have shown that all roots of (7) have negative real parts when $\mathcal{R}_0 < 1$.

If $\mathcal{R}_0 > 1$, then we have

$$\lim_{\lambda \to +\infty} \mathcal{H}(\lambda) = -\infty, \quad \mathcal{H}(0) = \mathcal{R}_0 - 1 > 0 \quad \text{and} \quad \mathcal{H}'(\lambda) < 0.$$

This implies that equation (7) has at least one positive root. Hence, E^0 is unstable.

To show the local stability of E^*, we take $x_(t) = x(t) + x^*$, $i_1(t,a) = i(t,a) + i^*(a)$ and $v_1(t) = v(t) + v^*$. Then solutions of the linearized system in exponential form $x_1(t) = x_1 e^{\lambda t}$, $i_1(t,a) = i_1(a)e^{\lambda t}$ and $v_1(t) = v_1 e^{\lambda t}$ yield the following equations:

$$\begin{cases} \left(\lambda + d + \dfrac{kv^*(1+\alpha_2 v^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2}\right) x_1 = -\dfrac{kx^*(1+\alpha_1 x^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2} v_1, \\ i_1(a) = i_1(0)e^{-\lambda a} e^{-\int_0^a \delta(\omega)d\omega}, \\ \lambda v_1 = \displaystyle\int_0^\infty p(a) i_1(a) da - c v_1, \\ i_1(0) = \dfrac{kv^*(1+\alpha_2 v^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2} x_1 + \dfrac{kx^*(1+\alpha_1 x^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2} v_1. \end{cases} \tag{8}$$

From the first equation of (8), we have

$$v_1 = -\frac{\lambda + d + \dfrac{kv^*(1+\alpha_2 v^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2}}{\dfrac{kx^*(1+\alpha_1 x^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2}} x_1.$$

Substituting $i_1(a)$, v_1 and $i_1(0)$ into the third equation, we obtain

$$\begin{aligned}\left(\lambda + d + \frac{kv^*(1+\alpha_2 v^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2}\right)(\lambda + c)\\ = (\lambda + d)\frac{kx^*(1+\alpha_1 x^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2}\int_0^\infty p(a)\sigma(a)e^{-\lambda a}da.\end{aligned}$$

This implies that

$$\begin{aligned}\left(\lambda + d + \frac{kv^*(1+\alpha_2 v^*)}{(1+\alpha_1 x^* + \alpha_2 v^*)^2}\right)\left(\frac{\lambda}{c} + 1\right)\\ = (\lambda + d)\frac{1+\alpha_1 x^*}{1+\alpha_1 x^* + \alpha_2 v^*}\frac{\displaystyle\int_0^\infty p(a)\sigma(a)e^{-\lambda a}da}{\displaystyle\int_0^\infty p(a)\sigma(a)da}.\end{aligned} \tag{9}$$

For all complex roots of λ with non-negative real parts, the modulus of left hand side of (9) is greater than the modulus of the right hand side when $\mathcal{R}_0 > 1$. Hence, we conclude that all roots of (1) have negative real parts when $\mathcal{R}_0 > 1$. □

4. **Uniform persistence.** In this section, we study the uniform persistence of system (1). Define

$$\mathcal{M}_0 = \left\{(x, v, 0, i)^{\mathrm{T}} \in \mathcal{X}_{0+} : v + \int_0^\infty i(a)da > 0\right\}$$

and

$$\partial\mathcal{M}_0 = \mathcal{X}_{0+} \setminus \mathcal{M}_0.$$

Theorem 4.1. *$\mathcal{M}_0$ and $\partial\mathcal{M}_0$ are both positively invariant under the semiflow $\{U(t)\}_{t\geq 0}$ generated by system (4) on $\mathcal{X}_{0+}$. Moreover, the infection-free equilibrium $\bar{E}_0 = (x^0, 0, 0, 0_{L^1})$ is globally asymptotically stable for the semiflow $\{U(t)\}_{t\geq 0}$ restricted to $\partial\mathcal{M}_0$.*

Proof. Let $(x_0, v_0, 0, i_0) \in \mathcal{M}_0$ and set $\kappa(t) = v(t) + \displaystyle\int_0^\infty i(t, a)da$. It follows that

$$\kappa'(t) \geq -\max\{c, \delta_{\max}\}\kappa(t),$$

where $\delta_{\max} = \operatorname{ess\,sup}_{\theta\in(0,+\infty)} \delta(\theta)$. That is

$$v(t) + \int_0^\infty i(t, a)da \geq e^{-\max\{c,\delta_{\max}\}t}\left(v_0 + \int_0^\infty i_0(a)da\right).$$

This completes the fact that $U(t)\mathcal{M}_0 \subset \mathcal{M}_0$.

Now, let $(x_0, v_0, 0, i_0) \in \partial\mathcal{M}_0$. Using (3), we easily find that $v(t) = 0$ for all $t \geq 0$ and

$$\begin{aligned}\int_0^\infty i(t,a)da =& \int_0^t \frac{kx(t-a)v(t-a)}{1+\alpha_1 x(t-a)+\alpha_2 v(t-a)}\sigma(a)da + \int_t^\infty i_0(a-t)\frac{\sigma(a)}{\sigma(a-t)}da\\ \leq& k\int_0^t x(t-a)v(t-a)\sigma(a)da + e^{-\delta_{\min}t}\|i_0\|_{L^1}\\ =& 0.\end{aligned}$$

Thus, $U(t)\partial\mathcal{M}_0 \subset \partial\mathcal{M}_0$.

Let $(x_0, v_0, 0, i_0) \in \partial\mathcal{M}_0$, we obtain that

$$\begin{cases}\dfrac{\mathrm{d}v(t)}{\mathrm{d}t} = \displaystyle\int_0^\infty p(a)i(t,a)da - cv(t),\\ \dfrac{\partial i(t,a)}{\partial t} + \dfrac{\partial i(t,a)}{\partial a} = -\delta(a)i(t,a),\\ i(t,0) = \dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)},\\ v(0) = 0, \quad i(0,a) = i_0(a).\end{cases}$$

Since $x(t) \leq x^0$ as t is large enough, we have

$$v(t) \leq \tilde{v}(t) \quad \text{and} \quad i(t,a) \leq \tilde{i}(t,a), \tag{10}$$

where

$$\begin{cases}\dfrac{\mathrm{d}\tilde{v}(t)}{\mathrm{d}t} = \displaystyle\int_0^\infty p(a)\tilde{i}(t,a)da - c\tilde{v}(t),\\ \dfrac{\partial \tilde{i}(t,a)}{\partial t} + \dfrac{\partial \tilde{i}(t,a)}{\partial a} = -\delta(a)\tilde{i}(t,a),\\ \tilde{i}(t,0) = kx^0\tilde{v}(t),\\ \tilde{v}(0) = 0, \quad \tilde{i}(0,a) = i_0(a).\end{cases} \tag{11}$$

By the formulation (3), we have

$$\tilde{i}(t,a) = \begin{cases} kx^0\tilde{v}(t-a)\sigma(a), & 0 \leq a < t,\\ i_0(a-t)\dfrac{\sigma(a)}{\sigma(a-t)}, & 0 < t \leq a.\end{cases} \tag{12}$$

Substituting (12) into the first equation of (11), we can get

$$\begin{cases}\dfrac{\mathrm{d}\tilde{v}(t)}{\mathrm{d}t} = kx^0\displaystyle\int_0^t p(a)\tilde{v}(t-a)\sigma(a)da + F_v(t) - c\tilde{v}(t),\\ \tilde{v}(0) = 0,\end{cases} \tag{13}$$

where

$$F_v(t) = \int_t^{+\infty} p(a)i_0(a-t)\frac{\sigma(a)}{\sigma(a-t)}da.$$

Thus, we can obtain that $F_v(t) \equiv 0$. Then, equation (13) has a unique solution $\tilde{v}(t) = 0$. If $0 \leq a \leq t$, according to (12), we have $\tilde{i}(t,a) = 0$. If $t < a$, then we have

$$\|\tilde{i}(t,a)\|_{L^1} = \left\| i_0(a-t)\frac{\sigma(a)}{\sigma(a-t)} \right\|_{L^1} \leq e^{-\delta_{\min}t}\|i_0\|_{L^1},$$

which yields that $\tilde{i}(t,a) \to 0$ as $t \to \infty$. By using (10), we obtain that $i(t,a) \to 0$ and $v(t) = 0$ as $t \to \infty$. This completes the proof. □

Therefore, we have the following theorem.

Theorem 4.2. *Assume $\mathcal{R}_0 > 1$, the semiflow $\{U(t)\}_{t\geq 0}$ generated by system (4) is uniformly persistent with respect to the pair $(\partial\mathcal{M}_0, \mathcal{M}_0)$; that is, there exists $\varepsilon > 0$, such that for each $y \in \mathcal{M}_0$,*

$$\liminf_{t\to+\infty} d(U(t)y, \partial\mathcal{M}_0) \geq \varepsilon.$$

Furthermore, there exists a compact subset $\mathcal{A}_0 \subset \mathcal{M}_0$ which is a global attractor for $\{U(t)\}_{t\geq 0}$ in $\mathcal{M}_0$.

Proof. Since the infection-free equilibrium $\bar{E}_0 = (x^0, 0, 0, 0_{L^1})$ is globally asymptotically stable in $\partial\mathcal{M}_0$, applying Theorem 4.2 in Hale and Waltman [10], we only need to investigate the behavior of the solution starting in $\mathcal{M}_0$ in some neighborhood of $\bar{E}_0$. Then, we will show that

$$W^s(\{\bar{E}_0\}) \cap \mathcal{M}_0 = \emptyset,$$

where

$$W^s(\{\bar{E}_0\}) = \{y \in \mathcal{X}_{0+} : \lim_{t\to+\infty} U(t)y = \bar{E}_0\}.$$

Assume by contradiction that there exists $y \in W^s(\{\bar{E}_0\}) \cap \mathcal{M}_0$, it follows that there exists $t_0 > 0$ such that $v(t_0) + \displaystyle\int_0^\infty i(t_0, a)da > 0$. Using the same argument in the proof of Lemma 3.6(i) in Demasse and Ducrot [7], we have that $v(t) > 0$ for $t \geq 0$ and $i(t,a) > 0$ for any $(t,a) \in [0,\infty) \times [0,\infty)$. Define a function

$$\alpha(a) = \int_a^\infty p(\theta) e^{-\int_a^\theta \delta(s)ds} d\theta.$$

Note that $\alpha(a)$ is bounded and satisfies $\alpha'(a) = \delta(a)\alpha(a) - p(a)$ a.e. $a \geq 0$. Consider the function

$$\Phi(t) = \int_0^\infty \alpha(a) i(t,a) da + v(t),$$

which satisfies

$$\frac{\mathrm{d}\Phi(t)}{\mathrm{d}t} = cv\left(\frac{Nkx}{c(1+\alpha_1 x + \alpha_2 v)} - 1\right).$$

Since $y \in W^s(\{\bar{E}_0\})$, we have that $x(t) \to x^0$ and $v(t) \to 0$ as $t \to \infty$. When $\mathcal{R}_0 > 1$, we obtain that the function $\Phi(t)$ is not decreasing for t large enough. Thus, there exists $t_0 > 0$ such that $\Phi(t) \geq \Phi(t_0)$ for all $t \geq t_0$. Since $\Phi(t_0) > 0$, this prevents the function $(v(t), i(t,a))$ from converging to $(0, 0_{L^1})$ as $t \to \infty$. A contradiction with $x(t) \to x^0$. This completes the proof. □

5. Global stability.

In this section, we construct suitable Liapunov functions to investigate the global stability of the infection-free equilibrium and infection equilibrium for system (1).

Theorem 5.1. *If $\mathcal{R}_0 \leq 1$, then the infection-free equilibrium E^0 of system (1) is globally asymptotically stable.*

Proof. Define a Liapunov function

$$V_1(t) = \frac{1}{N}\int_0^\infty \alpha(a)i(t,a)da + \frac{1}{N}v(t).$$

Calculating the time derivative of $V_1(t)$ along system (1), we have

$$\begin{aligned}
\frac{\mathrm{d}V_1(t)}{\mathrm{d}t} &= \frac{1}{N}\int_0^\infty \alpha(a)\frac{\partial i(t,a)}{\partial t}da + \frac{1}{N}\frac{\mathrm{d}v(t)}{\mathrm{d}t}\\
&= -\frac{1}{N}\int_0^\infty \alpha(a)\left(\frac{\partial i(t,a)}{\partial a} + \delta(a)i(t,a)\right)da + \frac{1}{N}\int_0^\infty p(a)i(t,a)da - \frac{c}{N}v(t)\\
&= -\frac{1}{N}\int_0^\infty \alpha(a)\frac{\partial i(t,a)}{\partial a}da + \frac{1}{N}\int_0^\infty (p(a)-\delta(a)\alpha(a))i(t,a)da - \frac{c}{N}v(t)\\
&= -\frac{1}{N}\alpha(a)i(t,a)|_{a=\infty} + \frac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)} + \frac{1}{N}\int_0^\infty \alpha'(a)i(t,a)da\\
&\quad + \frac{1}{N}\int_0^\infty (p(a)-\alpha(a)\delta(a))i(t,a)da - \frac{c}{N}v(t).
\end{aligned}$$

Note that $\dfrac{\mathrm{d}x(t)}{\mathrm{d}t} \le s - dx(t)$ and so $\limsup\limits_{t\to\infty} x(t) \le \dfrac{s}{d}$. This yields that all omega limit points satisfy $x(t) \le \dfrac{s}{d}$. Hence, it is sufficient to consider solutions for which $x(t) \le \dfrac{s}{d}$. Using $\mathcal{R}_0 = \dfrac{sNk}{c(d+\alpha_1 s)}$, we get

$$\begin{aligned}
\frac{\mathrm{d}V_1(t)}{\mathrm{d}t} &= \frac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)} - \frac{c}{N}v(t)\\
&= \frac{c}{N}v(t)\left(\frac{N}{c}\frac{kx(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)} - 1\right)\\
&\le \frac{c}{N}v(t)\left(\frac{sNk}{c(d+\alpha_1 s)} - 1\right)\\
&\le \frac{c}{N}v(t)\left(\mathcal{R}_0 - 1\right).
\end{aligned}$$

Therefore, we have that $\dfrac{\mathrm{d}V_1(t)}{\mathrm{d}t} = 0$ implies that $v(t) = 0$ or $\mathcal{R}_0 = 1$ and $x(t) = \dfrac{s}{d}$. It is easy to show that the largest invariant set where $\dfrac{\mathrm{d}V_1(t)}{\mathrm{d}t} = 0$ is the singleton $\{E^0\}$. Then, by the Liapunov-LaSalle asymptotic stability theorem, the infection-free equilibrium E^0 of system (1) is globally asymptotically stable for $\mathcal{R}_0 \le 1$. □

Next, we discuss the global stability of the infection equilibrium E^* for system (1) when $\mathcal{R}_0 > 1$. Denote

$$g(x) = x - 1 - \ln x.$$

Therefore, the function g has a global minimum at 1 and satisfies $g(1) = 0$.

Theorem 5.2. *If $\mathcal{R}_0 > 1$, then $\lim\limits_{t\to\infty} U(t)u = u^*$ for each $u \in \mathcal{A}_0$, where $u^* = (x^*, v^*, 0, i^*(a))^{\mathrm{T}}$.*

Proof. From Theorem 4.2, let $u(t) = \{(x(t), v(t), 0, i(t,a))^{\mathrm{T}}\}_{t\in\mathbb{R}} \subset \mathcal{A}_0$ be a given entire solution of $U(t)$. It remains to prove that $\mathcal{A}_0 = \{u^*\}$. Similar to the proof of

Lemma 3.6 and claim 5.3 in Demasse and Ducrot [7], we know that there exist δ_1 and $\delta_2 > 0$ such that

$$\delta_1 \leq x(t) \leq \delta_2, \quad \delta_1 \leq i(t,a) \leq \delta_2, \quad \delta_1 \leq v(t) \leq \delta_2,$$

for all $t \in \mathbb{R}$ and $a \geq 0$. Now let us define the following Liapunov function

$$\begin{aligned} V_2(t) = x(t) - x^* - \int_{x^*}^{x(t)} \frac{1+\alpha_1\theta+\alpha_2 v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\frac{x^*}{\theta}d\theta \\ + \frac{1}{N}\int_0^\infty \alpha(a) i^*(a) g\left(\frac{i(t,a)}{i^*(a)}\right) da + \frac{1}{N} v^* g\left(\frac{v(t)}{v^*}\right). \end{aligned}$$

Using system (1) and calculating the time derivative of $V_2(t)$, we get

$$\begin{aligned} \frac{\mathrm{d}V_2(t)}{\mathrm{d}t} = &\left(1 - \frac{x^*}{x(t)}\frac{1+\alpha_1 x(t)+\alpha_2 v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\right)\left(s - dx(t) - \frac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)}\right) \\ &- \frac{1}{N}\int_0^\infty \alpha(a)\left(1 - \frac{i^*(a)}{i(t,a)}\right)\frac{\partial i(t,a)}{\partial a} da \\ &- \frac{1}{N}\int_0^\infty \alpha(a)\delta(a) i(t,a)\left(1 - \frac{i^*(a)}{i(t,a)}\right) da \\ &+ \frac{1}{N}\left(1 - \frac{v^*}{v(t)}\right)\left(\int_0^\infty p(a) i(t,a) da - cv(t)\right). \end{aligned}$$

Notice that

$$s = dx^* + \frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}, \quad \frac{kx^*}{1+\alpha_1 x^*+\alpha_2 v^*} = \frac{c}{N}.$$

After some computations, we obtain that

$$\begin{aligned} &\int_0^\infty \alpha(a)\left(1 - \frac{i^*(a)}{i(t,a)}\right)\frac{\partial i(t,a)}{\partial a} da + \int_0^\infty \alpha(a)\delta(a) i(t,a)\left(1 - \frac{i^*(a)}{i(t,a)}\right) da \\ &\quad = \alpha(a) i^*(a)\left(\frac{i(t,a)}{i^*(a)} - 1 - \ln\frac{i(t,a)}{i^*(a)}\right)\Big|_{a=\infty} \\ &\qquad - N\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\left(\frac{x(t)v(t)(1+\alpha_1 x^*+\alpha_2 v^*)}{x^*v^*(1+\alpha_1 x(t)+\alpha_2 v(t))} - 1\right. \\ &\qquad \left. - \ln\frac{x(t)v(t)(1+\alpha_1 x^*+\alpha_2 v^*)}{x^*v^*(1+\alpha_1 x(t)+\alpha_2 v(t))}\right) \\ &\qquad + \int_0^\infty p(a) i^*(a)\left(\frac{i(t,a)}{i^*(a)} - 1 - \ln\frac{i(t,a)}{i^*(a)}\right) da. \end{aligned}$$

Then, we have

$$\begin{aligned}
\frac{\mathrm{d}V_2(t)}{\mathrm{d}t} &= -\frac{d(1+\alpha_2 v^*)(x(t)-x^*)^2}{x(t)(1+\alpha_1 x^*+\alpha_2 v^*)} - \frac{1}{N}\alpha(a)i^*(a)g\left(\frac{i(t,a)}{i^*(a)}\right)\Big|_{a=\infty} \\
&\quad -\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\left(\frac{1+\alpha_1 x(t)+\alpha_2 v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\frac{x^*}{x(t)}-1\right) \\
&\quad +\frac{kx^*(1+\alpha_1 x(t)+\alpha_2 v^*)v(t)}{(1+\alpha_1 x^*+\alpha_2 v^*)(1+\alpha_1 x(t)+\alpha_2 v(t))} - \frac{c}{N}v(t) \\
&\quad -\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\ln\frac{x(t)v(t)(1+\alpha_1 x^*+\alpha_2 v^*)}{x^*v^*(1+\alpha_1 x(t)+\alpha_2 v(t))} \\
&\quad +\frac{1}{N}\int_0^\infty p(a)i^*(a)\left(1+\ln\frac{i(t,a)}{i^*(a)}-\frac{v^*i(t,a)}{v(t)i^*(a)}\right)da \\
&= -\frac{d(1+\alpha_2 v^*)(x(t)-x^*)^2}{x(t)(1+\alpha_1 x^*+\alpha_2 v^*)} - \frac{1}{N}\alpha(a)i^*(a)g\left(\frac{i(t,a)}{i^*(a)}\right)\Big|_{a=\infty} \\
&\quad -\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}g\left(\frac{1+\alpha_1 x(t)+\alpha_2 v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\frac{x^*}{x(t)}\right) \\
&\quad -\frac{1}{N}\int_0^\infty p(a)i^*(a)g\left(\frac{v^*i(t,a)}{v(t)i^*(a)}\right)da \\
&\quad +\frac{kx^*(1+\alpha_1 x(t)+\alpha_2 v^*)v(t)}{(1+\alpha_1 x^*+\alpha_2 v^*)(1+\alpha_1 x(t)+\alpha_2 v(t))} - \frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\frac{v(t)}{v^*} \\
&\quad -\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\ln\frac{1+\alpha_1 x(t)+\alpha_2 v^*}{1+\alpha_1 x(t)+\alpha_2 v(t)} \\
&= -\frac{d(1+\alpha_2 v^*)(x(t)-x^*)^2}{x(t)(1+\alpha_1 x^*+\alpha_2 v^*)} - \frac{1}{N}\alpha(a)i^*(a)g\left(\frac{i(t,a)}{i^*(a)}\right)\Big|_{a=\infty} \\
&\quad -\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}g\left(\frac{1+\alpha_1 x(t)+\alpha_2 v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\frac{x^*}{x(t)}\right) \\
&\quad -\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}g\left(\frac{1+\alpha_1 x(t)+\alpha_2 v(t)}{1+\alpha_1 x(t)+\alpha_2 v^*}\right) \\
&\quad -\frac{1}{N}\int_0^\infty p(a)i^*(a)g\left(\frac{v^*i(t,a)}{v(t)i^*(a)}\right)da \\
&\quad +\frac{kx^*v^*}{1+\alpha_1 x^*+\alpha_2 v^*}\left(-1-\frac{v(t)}{v^*}+\frac{(1+\alpha_1 x(t)+\alpha_2 v^*)v(t)}{(1+\alpha_1 x(t)+\alpha_2 v(t))v^*}\right. \\
&\quad \left.+\frac{1+\alpha_1 x(t)+\alpha_2 v(t)}{1+\alpha_1 x(t)+\alpha_2 v^*}\right).
\end{aligned}$$

Some straightforward calculations yield that

$$\begin{aligned}
&-1-\frac{v(t)}{v^*}+\frac{(1+\alpha_1 x(t)+\alpha_2 v^*)v(t)}{(1+\alpha_1 x(t)+\alpha_2 v(t))v^*}+\frac{1+\alpha_1 x(t)+\alpha_2 v(t)}{1+\alpha_1 x(t)+\alpha_2 v^*} \\
&= -\frac{\alpha_2(1+\alpha_1 x(t))}{(1+\alpha_1 x(t)+\alpha_2 v(t))(1+\alpha_1 x(t)+\alpha_2 v^*)v^*}(v(t)-v^*)^2.
\end{aligned}$$

Therefore, $V_2(t)$ is a bounded and decreasing map. Arguing similarly as the end of the proof of Theorem 2.2(i) in Demasse and Ducrot [7], we obtain that $u(t) = u^*$, i.e., $\mathcal{A}_0 = \{u^*\}$. This completes the proof. □

Hence, using Theorem 3.1 and Theorem 5.2, we have the following result.

Theorem 5.3. *If $\mathcal{R}_0 > 1$, then the infection equilibrium E^* of system (1) is globally asymptotically stable.*

6. **Special cases and numerical simulations.** In this section we apply the results obtained in the last two sections to some special cases of the age structured model (1), namely, the ODE and DDE versions of the model studied by Huang et al. [11, 12]. We also perform some numerical simulations on the ODE, DDE, and age structured models.

Example 6.1. (**ODE**) Suppose that $\delta(a) = p$ and $p(a) = \gamma$ for $p,\ \gamma > 0$. Let

$$y(t) = \int_0^\infty i(t,a)da.$$

Then, system (1) becomes

$$\begin{cases} \dot{x}(t) = s - dx(t) - \dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)}, \\ \dot{y}(t) = \dfrac{kx(t)v(t)}{1+\alpha_1 x(t)+\alpha_2 v(t)} - py(t), \\ \dot{v}(t) = \gamma y(t) - cv(t). \end{cases} \tag{14}$$

The global behavior of this system was studied by Huang et al. [11] by constructing Liapunov functions. By Theorems 5.1 and 5.3, we have the following result.

Theorem 6.2. (i) *The infection-free equilibrium E^0 of system (14) is globally asymptotically stable if $\mathcal{R}_0 \le 1$;*

(ii) *The infection equilibrium E^* of system (14) is globally asymptotically stable if $\mathcal{R}_0 > 1$.*

We can choose some parameters values so that $\mathcal{R}_0 < 1$ and some other parameter values so that $\mathcal{R}_0 = 1$. In both cases, the infection-free equilibrium E^0 is globally asymptotically stable (see Figures 1-2). When $\mathcal{R}_0 > 1$ for the third set of parameters values, the infection equilibrium E^* is globally asymptotically stable (see Figure 3).

Example 6.3. (**DDE**) Suppose that

$$\delta(a) = \begin{cases} p, & a \ge \tau, \\ 0, & 0 \le a < \tau \end{cases}$$

and $p(a) = \gamma$ for $p,\ \gamma > 0$. Let

$$y(t) = \int_0^\infty i(t,a)da.$$

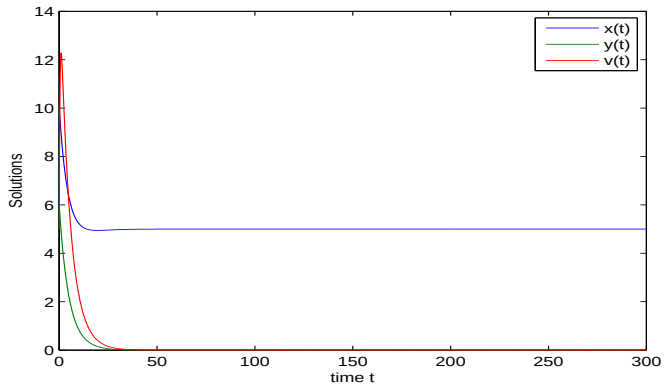

FIGURE 1. Taking $s = 1$, $d = 0.2$, $k = 0.01$, $\alpha_1 = 0.15$, $\alpha_2 = 0.2$, $p = 0.25$, $\gamma = 6$, $c = 2.4$, then $\mathcal{R}_0 = 0.2857 < 1$, the solution $(x(t), y(t), v(t))$ approaches to the infection-free equilibrium $E^0 = (5, 0, 0)$ as $t \to +\infty$.

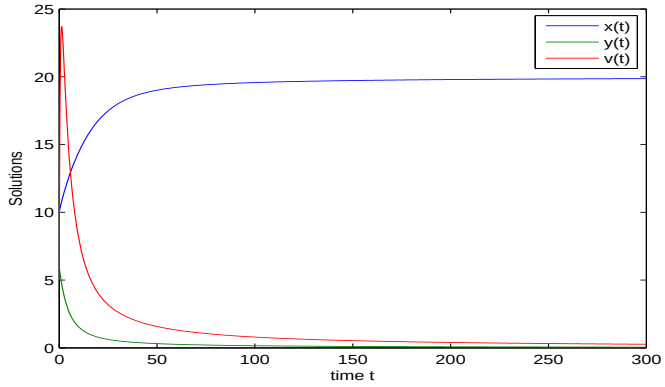

FIGURE 2. Taking $s = 2$, $d = 0.1$, $k = 0.01$, $\alpha_1 = 0.15$, $\alpha_2 = 0.2$, $p = 0.25$, $\gamma = 10$, $c = 2$, then $\mathcal{R}_0 = 1$, the solution $(x(t), y(t), v(t))$ approaches to the infection-free equilibrium $E^0 = (20, 0, 0)$ as $t \to +\infty$.

Then, system (1) becomes

$$\begin{cases} \dot{x}(t) = s - dx(t) - \dfrac{kx(t)v(t)}{1 + \alpha_1 x(t) + \alpha_2 v(t)}, \\ \dot{y}(t) = \dfrac{kx(t-\tau)v(t-\tau)}{1 + \alpha_1 x(t-\tau) + \alpha_2 v(t-\tau)} e^{-p\tau} - py(t), \\ \dot{v}(t) = \gamma y(t) - cv(t). \end{cases} \tag{15}$$

The global stability analysis for this system was completed by Huang et al. [12] utilizing the technology of constructing Liapunov functionals. From Theorems 5.1 and 5.3, we have the following result.

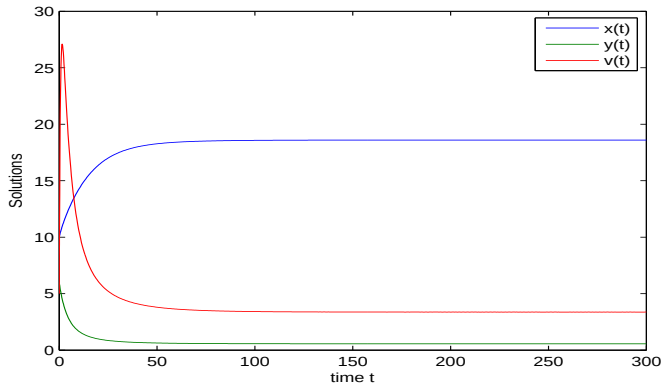

FIGURE 3. Taking $s = 2$, $d = 0.1$, $k = 0.01$, $\alpha_1 = 0.15$, $\alpha_2 = 0.2$, $p = 0.25$, $\gamma = 9$, $c = 1.5$, then $\mathcal{R}_0 = 1.2 > 1$, the solution $(x(t), y(t), v(t))$ approaches to the infection equilibrium $E^* = (18.5965, 0.5614, 3.3684)$ as $t \to +\infty$.

Theorem 6.4. (i) *If $\mathcal{R}_0 \leq 1$, then the infection-free equilibrium E^0 of system (15) is globally asymptotically stable for any time delay $\tau \geq 0$.*

(ii) *If $\mathcal{R}_0 > 1$, then the infection equilibrium E^* of system (15) is globally asymptotically stable for any time delay $\tau \geq 0$.*

We choose $s = 3$, $d = 0.15$, $k = 0.02$, $\alpha_1 = 0.15$, $\alpha_2 = 0.2$, $p = 0.25$, $\gamma = 8$, $c = 1.6$ with different τ values to simulate the asymptotic dynamics of system (15) (see Figures 4-6).

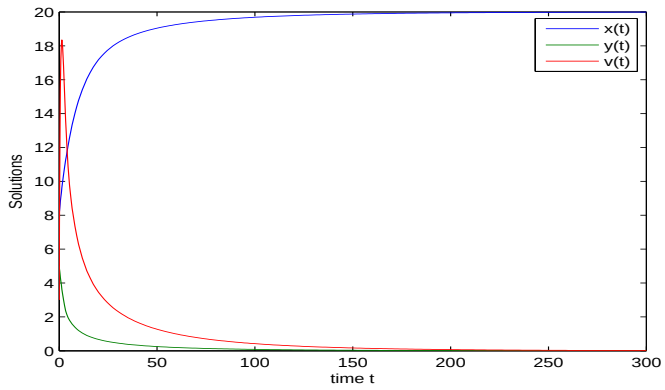

FIGURE 4. When $\tau = 3.3$, $\mathcal{R}_0 = 0.8765 < 1$, the infection-free equilibrium $E^0 = (20, 0, 0)$ is globally asymptotically stable.

Example 6.5. (**Age structured model**) In the following, we provide some numerical simulations to illustrate the global stability of the infection-free equilibrium and the infection equilibrium for system (1). We choose parameters $s = 3$, $d = 0.06$,

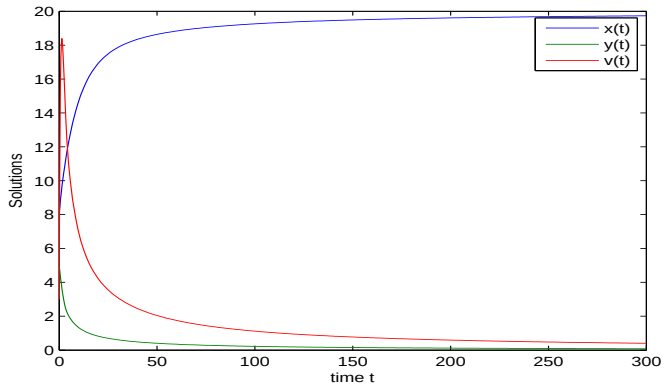

FIGURE 5. When $\tau = 2.7724$, $\mathcal{R}_0 = 1$, the infection-free equilibrium $E^0 = (20, 0, 0)$ is globally asymptotically stable.

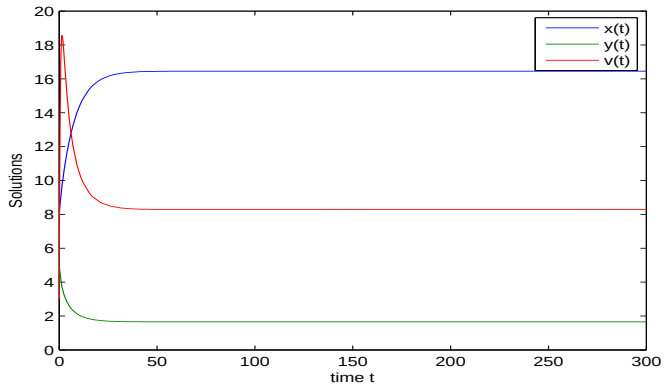

FIGURE 6. When $\tau = 1$, $\mathcal{R}_0 = 1.5576 > 1$, the infection equilibrium $E^* = (16.4529, 1.6575, 8.2874)$ is globally asymptotically stable.

$k = 0.1$, $\alpha_1 = 0.1$, $\alpha_2 = 0.2$, $c = 1$, $\delta(a) = 0.2$, and

$$p(a) := \begin{cases} 0.4, & \text{if } a \geq \tau, \\ 0, & \text{if } a \in (0, \tau). \end{cases}$$

Under the same initial values

$$x(0) = 30, \quad i(0, a) = 6e^{-0.3a}, \quad v(0) = 15,$$

we choose $\tau = 5$ in Figure 7 and $\tau = 1$ in Figure 8, respectively.

7. **Discussion.** Due to the lack of practical tools, it is difficult to study the global properties of age-structured models, which is in the form of PDEs. In 2010, Magal et al. [20] constructed a Liapunov functional to investigate global stability of the endemic equilibrium for an infection-age model of disease transmission. In this paper, we have considered a general class of age-structured virus dynamics models. Based

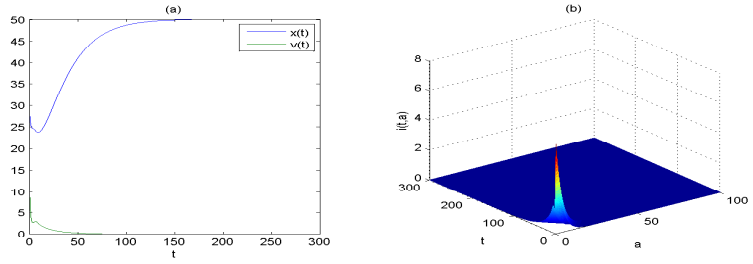

FIGURE 7. We choose $\tau = 5$, then $\mathcal{R}_0 < 1$. (a) Time series of $x(t)$ and $v(t)$ which converge to their equilibrium values. (b) The age distribution and time series of $i(t, a)$.

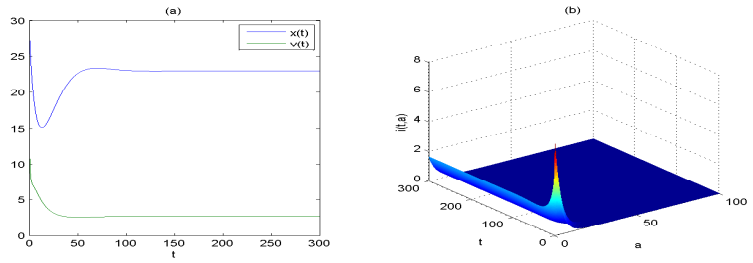

FIGURE 8. We choose $\tau = 1$, then $\mathcal{R}_0 > 1$. (a) Time series of $x(t)$ and $v(t)$ which converge to their equilibrium values. (b) The age distribution and time series of $i(t, a)$.

on the biological meaning, we have incorporated Beddington-DeAngelis function instead of mass action function to describe the infection rate. We have calculated the basic reproduction number $\mathcal{R}_0$ and proved that the global dynamics are completely determined by the value of $\mathcal{R}_0$: if $\mathcal{R}_0 \leq 1$, then the infection-free equilibrium is globally asymptotically stable; if $\mathcal{R}_0 > 1$, then the infection equilibrium is globally asymptotically stable.

For a special case $\alpha_1 = 0$ and $\alpha_2 = 0$, system (1) is similar to that considered by Nelson et al. [24] and Huang et al. [12]. For the case $\alpha_1 = 0$ and $\alpha_2 > 0$, system (1) becomes the virus dynamics model with Holling type II infection function. Thus, our model is a generalization of the ODE model and the DDE model studied by Huang et al. [11, 12] and our results extended theirs to the age-structured model.

Our results further indicate that the incorporation of age-structure does not change the global dynamics of the virus dynamics model. The reason is that our model was based on the HIV infection models which have convergent asymptotic dynamics in the long term. The virus dynamics model could also be improved by further generalizing the infection rate, for example, according to Li and Shu [18]. We leave this for future work.

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