Journal of Mathematical Biology (2023) 86:80
https://doi.org/10.1007/s00285-023-01918-4

Mathematical Biology

Global stability of latency-age/stage-structured epidemic models with differential infectivity

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Received: 6 July 2022 / Revised: 2 April 2023 / Accepted: 3 April 2023 /
Published online: 24 April 2023

Abstract
In this paper, we first formulate a system of ODEs–PDE to model diseases with latency-age and differential infectivity. Then, based on the ways how latent individuals leave the latent stage, one ODE and two DDE models are derived. We only focus on the global stability of the models. All the models have some similarities in the existence of equilibria. Each model has a threshold dynamics for global stability, which is completely characterized by the basic reproduction number. The approach is the Lyapunov direct method. We propose an idea on constructing Lyapunov functionals for the two DDE and the original ODEs–PDE models. During verifying the negative (semi-)definiteness of derivatives of the Lyapunov functionals along solutions, a novel positive definite function and a new inequality are used. The idea here is also helpful in applying the Lyapunov direct method to prove the global stability of some epidemic models with age structure or delays.

Xiaogang Liu, Yuming Chen and Xiaomin Li have contributed equally to this work.

In memory of Professor Fred Brauer.

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Keywords Epidemic model · Latency-age · Time delay · Global stability · Lyapunov function/functional

Mathematics Subject Classification 34A08 · 34D23 · 39B82 · 92D30

1 Introduction

Epidemiological models reflect the processes of disease transmissions and the transitions of individuals among different disease statuses. They have played an important role in understanding transmission mechanisms of infectious diseases, controlling their spread, and predicting their development (Brauer and Castillo-Chavez 2001; Ma and Li 2009). Many diseases (such as tuberculosis, Hepatitis C, influenza, COVID-19, chicken pox, and so on) are known to have an exposed or latent phase, where individuals are infected but not yet infectious. Furthermore, the infected individuals of some diseases (such as malaria, dengue fever, AIDS, and other sexually transmitted diseases) may have different abilities to transmit these infections in different infectious stages since their infectivity usually depends on the level of the parasite or viral loads of infected individuals or vectors (Anderson and May 1991; Nowak and May 2000; Paul and Kuddus 2022). There have been many epidemic models incorporated latency (Demasse et al. 2016; Li and Fang 2008; Wang et al. 2012; Zhong et al. 2019; Mccluskey 2016; McCluskey 2012; Liu et al. 2015; Asamoah et al. 2021; Korobeinikov and Melnik 2013; Alshorman et al. 2016; Qiu et al. 2022 and references therein) and differential infectivity (Fall et al. 2007; Kuzmina et al. 2021; Liu and Chen 2015; Bonzi et al. 2011; Asamoah et al. 2021; Hyman and Li 2006; Hyman et al. 1999; Ma et al. 2003; Bowong and Tewa 2009; Skakauskas 2022; Kouenkam et al. 2020 and references therein). However, there are few considering both latency and differential infectivity. The goal of this paper is to propose and analyze some epidemic models incorporating both latency and differential infectivity.

For diseases that go through a latent stage, it is possible that certain disease-related parameters (for example, the transfer rate from latent individuals to infectious or recovered ones) depend on the latency-age, i.e., the duration when the individual has been in the latent stage. Usually, to model such a phenomenon will lead to systems involving partial differential equations (PDEs) (McCluskey 2012; Demasse and Ducrot 2013; Magal et al. 2010; Magal and McCluskey 2013; Mccluskey 2016; Blyuss and Kyrychko 2021; Ren 2017). When the parameters are independent of the latency-age, the PDEs will reduce to ordinary differential equations (ODEs) (Li and Muldowney 1995; Korobeinikov and Maini 2004; Zhang and Ma 2003; Lu and Lu 2017; Sigdel and McCluskey 2014; Gómez and Mondragon 2021; Bame et al. 2008); while when latent individuals have certain stage characteristics, we may subdivide the latent stage into two phases, an initial phase where the individuals stay at the phase and do not transfer to other states and a phase where individuals can transfer to other states. This situation is suitably described by delayed differential equations (DDEs) (see, for example, Liu and Zhang (2019); Huang et al. (2015) and references therein). In addition, there is also a case where all the latent individuals leave the stage at the same latency-age. This can also lead to a DDE for the change in the number of latent individuals, which is different from the two-stage situation mentioned above (Rst et al. 2013; Liu et al. 2018; Bajiya et al. 2021; Zhou et al. 2021b). Though there are extensive studies for the latter, the former seems more realistic. In this paper, we consider theoretically the above four cases for the transmissions of the same diseases, namely, we investigate the four classes of epidemic models with different interpretations of the latent phase.

In Sect. 2, we first formulate a model consisting of ODEs and PDE to describe infectious diseases with latency and differential infectivity. Then based on the different assumptions on how latent individuals leave the latent stage, an ODE model and two DDE models are resulted. The well-posedness of the four models is not difficult to obtain. Thus we leave out the detail. Our main goal is to establish global stability of equilibria of the models by the Lyapunov direct method. See Sect. 3 for the statement on the threshold dynamics and Sect. 4 for the proof.

For the endemic equilibrium of the ODE model, the commonly used linear combination of the Volterra-type function,

$$L = \sum_{i=0}^{n} a_i \left(u_i - 1 - \ln u_i\right), \qquad a_i > 0 \tag{1}$$

serves the candidate of Lypunov functions and that for the disease-free equilibrium is an obvious modification of (1). We mention that the integral form of (1) (i.e., Lyapunov functionals) has been extensively used to prove global stability of positive equilibria of some epidemic models with age-structure (Li et al. 2016, 2012b; Huang et al. 2010, 2012; McCluskey 2012; Mccluskey 2016) or delay (Li et al. 2016; Yan and Zhang 2021; Zhou et al. 2021a; McCluskey 2015). In either situation, on the one hand, it is important to determine the appropriate coefficients (a_i) of the Lyapunov function/functional; On the other hand, for given coefficients, sometimes it may be difficult to determine whether the derivative of the Lyapunov function/functional along solutions of the model is negative (semi-)definite.

For the Lyapunov function of the form (1) for endemic equilibria of ODE models, based on the method of proving global stability in Korobeinikov (2004), a systematic algebraic approach is proposed in Li et al. (2011, 2012a) to determine the coefficients and to show the negative (semi-)definiteness of the derivative. The main idea is to express the derivative in terms of expressions such that the AM(arithmetic mean)-GM(geometric mean) inequality can be applied. This approach has certain generality and is suitable for many types of models. Also, a method based on graph theory is established to prove the global stability of the endemic equilibria of some multigroup epidemic models in Guo et al. (2006, 2008).

As we have seen, models of DDEs and PDEs for age structured populations are closely related to some models of ODEs. By treating DDE models as perturbation of ODEs, McCluskey (McCluskey 2015) proposed an approach to constructing Lyapunov functionals based on those for the corresponding ODE models, where an integral term is added. The Lyapunov functionals for the DDE models are constructed directly in this way. But, PDE models are not considered in McCluskey (2015), by analogy with ODE models and DDE models, we give similar idea on constructing Lyapunov functionals for ODEs-PDE models.

The paper concludes with a brief discussion.

2 Formulation of the models

In this section, we formulate four classes of epidemic models with differential infectivity to describe the same process of a disease transmission, where the development of latent individuals is reflected in four forms and it is assumed that infectious individuals with two-stage feature have differential infectivity.

We divide the population into five classes, susceptible, latent, infectious-1, infectious-2, and recovered. Here infectious-1 individuals have different infectivity from infectious-2 individuals and may develop into infectious-2 individuals. For example, after a susceptible individual is infected, he/she first enters the latent stage, and then becomes asymptomatic, symptomatic or recovered. Generally, the infectivities of asymptomatic and symptomatic individuals are different, so they are referred to as the infectious-1 individuals and the infectious-2 individuals, respectively.

Let $S(t)$, $I_1(t)$, $I_2(t)$, and $R(t)$ denote the numbers of the susceptible, infectious-1, infectious-2, and removed individuals at time t, respectively, and $v(t,a)$ denote the density of the latent individuals with latency-age a at time t. Then an epidemic model with latency-age structure can be described by the following ODEs-PDE system:

$$\begin{cases} \frac{dS}{dt} = A - \mu S(t) - S(\beta_1 I_1(t) + \beta_2 I_2(t)), \qquad t > 0, \\ \frac{\partial v(t,a)}{\partial t} + \frac{\partial v(t,a)}{\partial a} = -[\mu + \varepsilon(a)]v(t,a), \qquad a > 0, \\ \frac{dI_1}{dt} = k_1 \int_0^\infty \varepsilon(a)v(t,a)da - (\mu + \gamma + \alpha_1 + \delta_1)I_1(t), \\ \frac{dI_2}{dt} = k_2 \int_0^\infty \varepsilon(a)v(t,a)da + \gamma I_1(t) - (\mu + \alpha_2 + \delta_2)I_2(t), \\ \frac{dR}{dt} = k_3 \int_0^\infty \varepsilon(a)v(t,a)da + \delta_1 I_1(t) + \delta_2 I_2(t) - \mu R(t), \end{cases} \tag{2}$$

with the boundary condition

$$v(t,0) = S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) \tag{3}$$

and the initial conditions

$$\begin{aligned} &S(0) = S_b \geq 0, v(0,a) = v_b(a) \in L_+^1(0,\infty), \\ &I_1(0) = I_{1b} \geq 0, I_2(0) = I_{2b} \geq 0, R(0) = R_b \geq 0. \end{aligned} \tag{4}$$

Here A is the recruitment rate of susceptible individuals; μ is the per capita natural death rate; β_i $(i = 1, 2)$ is the transmission coefficient of infectious-i individuals; $\varepsilon(a)$ is the per capita transfer rate of latent individuals with latency-age a; k_1, k_2, and k_3 $(k_1 + k_2 + k_3 = 1)$ are the proportions of the latent individuals transferring to infectious-1, infectious-2, and recovered individuals, respectively; γ is the per capita transfer rate of infectious-1 individuals to infectious-2 individuals; α_i and δ_i $(i = 1, 2)$ are the disease-induced death rates and the recovery rates of infectious-i individuals, respectively. All the parameters are positive except for $k_3 \geq 0$ and $\varepsilon(a)$ is assumed to be nonnegative, continuous, and bounded for $a \geq 0$. Since it is impossible that the age of a latent individual is infinite, it is natural to impose the condition on $v(t, a)$ that

$$v(0, \infty) = v_b(\infty) = 0. \tag{5}$$

Note that the equations of $S(t)$, $v(t, a)$, $I_1(t)$, and $I_2(t)$ in (2) are independent of R. Thus we will focus on the following subsystem with the above corresponding assumptions,

$$\begin{cases} \frac{dS}{dt} = A - \mu S(t) - S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)), \qquad t > 0, \\ \frac{\partial v(t,a)}{\partial t} + \frac{\partial v(t,a)}{\partial a} = -[\mu + \varepsilon(a)]v(t, a), \qquad a > 0, \\ \frac{dI_1}{dt} = k_1 \int_0^\infty \varepsilon(a)x(t, a)da - \mu_1 I_1(t), \\ \frac{dI_2}{dt} = k_2 \int_0^\infty \varepsilon(a)x(t, a)da + \gamma I_1(t) - \mu_2 I_2(t) \end{cases} \tag{6}$$

with the associated conditions (3) and (4). Here $\mu_1 = \mu + \gamma + \alpha_1 + \delta_1$ and $\mu_2 = \mu + \alpha_2 + \delta_2$. The phase space of (6) with conditions (3) and (4) is $\mathbb{X}_p \triangleq \mathbb{R}_+ \times L^1_+(0, \infty) \times \mathbb{R}_+ \times \mathbb{R}_+$ with $\mathbb{R}_+ = [0, \infty)$, which is a nonnegative cone of the Banach space $\mathbb{R} \times L^1_+(0, \infty) \times \mathbb{R} \times \mathbb{R}$ equipped with the product norm.

In the following, we consider a few special cases of (6) according to different features of latent individuals.

Firstly, we assume that the transfer rate of the individuals leaving the latent stage does not depend on the latency-age, i.e., $\varepsilon(a)$ is a constant (denoted by ε). Let $E(t) = \int_0^\infty v(t, a)da$, which is the number of latent individuals at time t. Then one can get from the equation satisfied by $v(t, a)$ in (6) and the conditions (3) and (5) that E satisfies

$$\frac{dE}{dt} = S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) - (\mu + \varepsilon)E(t)$$

and hence (6) with (3) reduces to the following ODE model

$$\begin{cases} \frac{dS}{dt} = A - \mu S - S(\beta_1 I_1 + \beta_2 I_2), \\ \frac{dE}{dt} = S(\beta_1 I_1 + \beta_2 I_2) - (\mu + \varepsilon)E, \\ \frac{dI_1}{dt} = k_1 \varepsilon E - \mu_1 I_1, \\ \frac{dI_2}{dt} = k_2 \varepsilon E + \gamma I_1 - \mu_2 I_2. \end{cases} \tag{7}$$

Then the phase space for (7) becomes $\mathbb{X}_1 = \mathbb{R}^4_+$ and it is positively invariant for (7).

Next, we assume that a latent individual must pass through a certain period (denoted by τ) before gradually leaving this stage and transferring to infectious-1, or infectious-2, or recovered. We also assume that the transfer rate after τ is independent of the latency-age. Thus $\varepsilon(a)$ is a step function,

$$\varepsilon(a) = \begin{cases} 0, & a < \tau; \\ \varepsilon, & a \geq \tau. \end{cases}$$

This time, denote $E_0(t) = \int_0^\tau v(t,a)da$ and $E(t) = \int_\tau^\infty v(t,a)da$, which represent the numbers of latent individuals in the initial stage and the stage capable of leaving the stage, respectively. Then system (6) with conditions (3) and (5) reduces to the following DDE model,

$$\begin{cases} \frac{dS}{dt} = A - \mu S(t) - S(\beta_1 I_1(t) + \beta_2 I_2(t)), \\ \frac{dE_0}{dt} = S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) - \mu E_0(t) \\ \qquad\qquad -S(t)(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau}, \\ \frac{dE}{dt} = S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau} - (\mu+\varepsilon)E(t), \\ \frac{dI_1}{dt} = k_1\varepsilon E(t) - \mu_1 I_1(t), \\ \frac{dI_2}{dt} = k_2\varepsilon E(t) + \gamma I_1(t) - \mu_2 I_2(t). \end{cases} \tag{8}$$

We refer to "Appendix A" for the derivation of the equations for E_0 and E. Note that the variable E_0 does not appear in the other equations of (8). Thus we will only focus on the following subsystem

$$\begin{cases} \frac{dS}{dt} = A - \mu S(t) - S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)), \\ \frac{dE}{dt} = S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau} - (\mu+\varepsilon)E(t), \\ \frac{dI_1}{dt} = k_1\varepsilon E(t) - \mu_1 I_1(t), \\ \frac{dI_2}{dt} = k_2\varepsilon E(t) + \gamma I_1(t) - \mu_2 I_2(t). \end{cases} \tag{9}$$

Obviously, when $\tau = 0$, system (9) becomes system (7). Without loss of generality, the initial conditions for system (9) can take the form

$$S(\theta) = \phi_1(\theta),\ E(\theta) = \phi_2(\theta),\ I_1(\theta) = \phi_3(\theta),\ I_2(\theta) = \phi_4(\theta),\ \theta \in [-\tau, 0],$$

where $(\phi_1, \phi_2, \phi_3, \phi_4) \in \mathbb{X}_2 \triangleq C\left([-\tau, 0], \mathbb{R}_+^4\right)$, the nonnegative cone of the Banach space $C([-\tau, 0], \mathbb{R}^4)$ of continuous functions from $[-\tau, 0]$ into $\mathbb{R}^4$ equipped with the supremum norm.

Finally, we assume that all the latent individuals have the same latent period (denoted by τ), that is, they all leave the latent stage at the same latent age τ. Then the transfer rate can be expressed by a delta function, *i.e.*, $\varepsilon(a) = 0$ for $a \neq \tau$, and $\varepsilon(a) \neq 0$ for

$a = \tau$. Thus system (6) with condition (3) becomes the following DDE system,

$$\begin{cases} \frac{dS}{dt} = A - \mu S(t) - S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)), \\ \frac{dE}{dt} = S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) - \mu E(t) \\ \qquad -S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau}, \\ \frac{dI_1}{dt} = k_1 e^{-\mu\tau} S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)] - \mu_1 I_1(t), \\ \frac{dI_2}{dt} = k_2 e^{-\mu\tau} S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)] \\ \qquad +\gamma I_1(t) - \mu_2 I_2(t), \end{cases} \tag{10}$$

where as before $E = E(t)$ is the number of latent individuals at time t. See "Appendix B" for the derivation of the equation for E. Again, noting that the variable E is decoupled from the other equations, we only consider the related subsystem

$$\begin{cases} \frac{dS}{dt} = A - \mu S(t) - S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)), \\ \frac{dI_1}{dt} = k_1 S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)] - \mu_1 I_1(t), \\ \frac{dI_2}{dt} = k_2 S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)] + \gamma I_1(t) - \mu_2 I_2(t), \end{cases} \tag{11}$$

where k_1 and k_2 still denote $k_1 e^{-\mu\tau}$ and $k_2 e^{-\mu\tau}$, respectively. Similar to model (9), the initial conditions for system (11) take the form

$$S(\theta) = \phi_0(\theta), I_1(\theta) = \phi_1(\theta), I_2(\theta) = \phi_2(\theta), \theta \in [-\tau, 0],$$

where $(\phi_0, \phi_1, \phi_2) \in \mathbb{X}_3 \triangleq C\left([-\tau, 0], \mathbb{R}^3_+\right)$.

For the original model (6) with conditions (3) and (4), the existence and uniqueness of solutions can be established by using the standard theory for age-dependent models (Webb 1985). For models (9) and (11), by the fundamental theory of functional differential equations (Hale 2003), there are global and unique solutions through available initial conditions. Moreover, all solutions of the four models, (6), (7), (9), and (11), with available nonnegative initial conditions will remain nonnegative. Therefore, we only concentrate on their global stability in the sequel, which is discussed with the Lyapunov direct method. Here, by observing some common features regarding constructing Lyapunov functions/functionals for the four models, we provide an idea on how to construct appropriate Lyapunov functions/functionals for age-dependent/delayed models.

3 Main results

It is easy to see that all the four models always have the disease-free equilibrium $P_0\,(S_0, 0, 0, 0)$, where $S_0 = \frac{A}{\mu}$.

For simplicity of notations, we denote $\frac{\mu_1\mu_2}{\beta_1 k_1\mu_2+\beta_2(k_1\gamma+k_2\mu_1)}$ by Λ. Then the basic reproduction numbers of the four models are as follows. For model (7), $R_{01}=\frac{S_0\varepsilon}{\Lambda(\mu+\varepsilon)}$; for model (9), $R_{02}=\frac{S_0\varepsilon e^{-\mu\tau}}{\Lambda(\mu+\varepsilon)}$; for (11), $R_{03}=\frac{S_0}{\Lambda}$; for model (6) with (3), $R_{04}=\left[S_0\int_0^\infty \varepsilon(a)e^{-\int_0^a[\mu+\varepsilon(\theta)]d\theta}da\right]/\Lambda$.

When the basic reproduction number R_{0i} $(i=1,2,3,4)$ of each model is greater than one, it has a unique endemic equilibrium P^*, denoted by $P^*(S^*, v^*(a), I_1^*, I_2^*)$ for (6) with (3), $P^*(S^*, E^*, I_1^*, I_2^*)$ for (7) and (9), and $P^*(S^*, I_1^*, I_2^*)$ for (11). Obviously,

$$I_2^*=\frac{k_1\gamma+k_2\mu_1}{k_1\mu_2}I_1^* \tag{12}$$

from the last two equations of every model. With the help of (12), solving directly the equations satisfied by the endemic equilibrium gives

$$S^*=\frac{\Lambda(\mu+\varepsilon)}{\varepsilon}, \qquad E^*=\frac{\mu_1 I_1^*}{k_1\varepsilon}$$

for (7);

$$S^*=\Lambda(\mu+\varepsilon)e^{\mu\tau}, \qquad E^*=\frac{\mu_1 I_1^*}{k_1\varepsilon}$$

for (9);

$$S^*=\Lambda$$

for (11); and

$$S^*=\frac{\Lambda}{\int_0^\infty \varepsilon(a)e^{-\int_0^a[d+\varepsilon(\theta)]d\theta}da},$$
$$v^*(a)=S^*(\beta_1 I_1^*+\beta_2 I_2^*)e^{-\int_0^a[d+\varepsilon(\theta)]d\theta}$$

for (6) with (3). Furthermore, combining the first equation of each model with the corresponding expression of S^* gives $I_1^*=\frac{\mu k_1\Lambda}{\mu_1}(R_{0i}-1)$ $(i=1,2,3,4)$.

It is routine to show that the disease-free equilibrium P_0 is locally asymptotically stable if the basic reproduction number $R_{0i}<1$ and is unstable if $R_{0i}>1$. Moreover, when $R_{0i}>1$ the corresponding model is persistent. The main result on the global stability of equilibria is summarized below, which is proved in the coming section.

Theorem 1 *For each of the models* (7), (9), (11), *and* (6) *with* (3),

(a) *the disease-free equilibrium P_0 is globally asymptotically stable (GAS) on the feasible region when the corresponding basic reproduction number is less than or equal to unity;*

(b) *the endemic equilibrium P^* is GAS in the feasible region when the corresponding basic reproduction number is greater than unity.*

The corresponding feasible region will be mentioned in the proof.

4 Proof of main results

As mentioned before, the stability stated in Theorem 1 is established by constructing appropriate Lyapunov functions/functionals. For this purpose, we introduce the function $g(u) = u - 1 - \ln u$ for $u > 0$. It is easy to see that $g(u) \geq 0$ and that $g(u) = 0$ if and only if $u = 1$. We discuss the systems one by one with the stability of P^* first. When arranging terms of the derivatives along solutions of the models, we omit some detail in using the equalities satisfied by the equilibria.

4.1 Stability of model (7)

(a) First, we prove the global stability of P^* of model (7) in the feasible region $\mathbb{X}_{10} = \{(S, E, I_1, I_2) \in \mathbb{X}_1 : E + I_1 + I_2 > 0\}$. It is not difficult to see that solutions with initial conditions in $\mathbb{X}_{10}$ will be positive on $(0, \infty)$. Thus we can define a function

$$L_1^* = S^* g\left(\frac{S}{S^*}\right) + \bar{n}_0 E^* g\left(\frac{E}{E^*}\right) + n_1^* I_1^* g\left(\frac{I_1}{I_1^*}\right) + n_2^* I_2^* g\left(\frac{I_2}{I_2^*}\right),$$

where $\bar{n}_0$, n_1^*, and n_2^* are positive constants to be specified later on. Then the derivative of L_1^* with respect to t along solutions of (7) is given by

$$\begin{aligned} D_{(7)} L_1^* = &\left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + \bar{n}_0\left(1 - \frac{E^*}{E}\right)\frac{dE}{dt} \\ &+ n_1^*\left(1 - \frac{I_1^*}{I_1}\right)\frac{dI_1}{dt} + n_2^*\left(1 - \frac{I_2^*}{I_2}\right)\frac{dI_2}{dt}. \end{aligned}$$

According to the approach provided in Li et al. (2011, 2012a), we find that

$$\bar{n}_0 = 1, \quad n_1^* = \frac{\beta_1\mu_2 + \beta_2\gamma}{\mu_1\mu_2} S^*, \quad n_2^* = \frac{\beta_2 S^*}{\mu_2} \tag{13}$$

are appropriate to make $D_{(7)} L_1^*$ negative (semi-)definite with respect to P^*. In fact, with them, we have

$$\begin{aligned} D_{(7)} L_1^* = &\mu S^*\left(2 - x - \frac{1}{x}\right) + \beta_1 S^* I_1^*\left(3 - \frac{1}{x} - \frac{u}{y_1} - \frac{x y_1}{u}\right) \\ &+ n_2^* k_2 \varepsilon E^*\left(2 - \frac{1}{x} - \frac{u}{y_2} - \frac{x y_2}{u}\right) \end{aligned}$$

$$+n_2^*\gamma I_1^*\left(4-\frac{1}{x}-\frac{u}{y_1}-\frac{y_1}{y_2}-\frac{xy_2}{u}\right),$$

where $x=\frac{S}{S^*}$, $u=\frac{E}{E^*}$, $y_1=\frac{I_1}{I_1^*}$, and $y_2=\frac{I_2}{I_2^*}$. Thus $D_{(7)}L_1^*\le 0$ by the AM-GM inequality. Moreover, the equality holds if and only if $x=1$ (i.e., $S=S^*$) and $u=y_1=y_2$ (i.e., $\frac{E}{E^*}=\frac{I_1}{I_1^*}=\frac{I_2}{I_2^*}$), from which we can easily verify that the largest invariant set of (7) in the set

$$\left\{(S,E,I_1,I_2)\in\mathbb{X}_{10}:D_6L_1^*=0\right\}$$

is the singleton $\{P^*\}$. By LaSalle Invariance Principle (LaSalle 1976), we know that P^* is GAS in $\mathbb{X}_{10}$.

(b) Now, for the disease-free equilibrium P_0 of (7), define a function

$$L_1^{(0)}=S_0g\left(\frac{S}{S_0}\right)+\bar{n}_0E+n_1^{(0)}I_1+n_2^{(0)}I_2,$$

where $\bar{n}_0$, $n_1^{(0)}$, and $n_2^{(0)}$ are given by (13) with S^* being replaced by S_0, namely,

$$\bar{n}_0=1,\quad n_1^{(0)}=\frac{\beta_1\mu_2+\beta_2\gamma}{\mu_1\mu_2}S_0,\quad n_2^{(0)}=\frac{\beta_2}{\mu_2}S_0. \tag{14}$$

Note that $L_1^{(0)}$ can be regarded as well-defined as for any solution of (7) with the initial condition in $\mathbb{X}_1$, one has $S(t)>0$ for $t>0$. Then the derivative of $L_1^{(0)}$ with respect to t along solutions of (7) is

$$\begin{aligned}D_{(7)}L_1^{(0)}&=-\frac{\mu(S-S_0)^2}{S}-\left[\bar{n}_0(\mu+\varepsilon)-(n_1^{(0)}k_1+n_2^{(0)}k_2)\varepsilon\right]E\\&=-\frac{\mu(S-S_0)^2}{S}-(\mu+\varepsilon)(1-R_{01})E,\end{aligned}$$

where $A=\mu S_0$ and $\bar{n}_0(\mu+\varepsilon)-(n_1^{(0)}k_1+n_2^{(0)}k_2)\varepsilon=(\mu+\varepsilon)(1-R_{01})$ have been used. Clearly, $D_7L_1^{(0)}\le 0$ when $R_{01}\le 1$. Furthermore, $D_{(7)}L_1^{(0)}=0$ if and only if $S=S_0$ and $E=E_0$ when $R_{01}<1$ while $D_{(7)}L_1^{(0)}=0$ only for $S=S_0$ when $R_{01}=1$. It is not difficult to check that, in either case, the largest invariant set of (7) in $\{(S,E,I_1,I_2)\in\mathbb{X}_1:D_{(7)}L_1^0=0\}$ is $\{P_0\}$. Therefore, by LaSalle Invariance Principle (LaSalle 1976) again, P_0 is GAS in the feasible region $\mathbb{X}_1$ when $R_{01}\le 1$.

4.2 Stability of model (9)

(a) For the endemic equilibrium P^* of (9), we first define a function

$$L_{21}^* = S^* g\left(\frac{S(t)}{S^*}\right) + n_0 E^* g\left(\frac{E(t)}{E^*}\right) + n_1^* I_1^* g\left(\frac{I_1(t)}{I_1^*}\right) + n_2^* I_2^* g\left(\frac{I_2(t)}{I_2^*}\right)$$

in the feasible region $\mathbb{X}_{20} = \{(\phi_1, \phi_2, \phi_3, \phi_4) \in \mathbb{X}_2 : \phi_2(0)+\phi_3(0)+\phi_4(0) > 0\}$, where $n_0 = e^{\mu\tau}$, n_1^* and n_2^* are the same as those in (13). For any initial condition in $\mathbb{X}_{20}$, one can show that the corresponding solution is positive on $[\tau, \infty)$. As a result, L_{21}^* is well-defined, without loss of generality. Then the derivative of L_{21}^* with respect to t along solutions of (9) is

$$\begin{aligned} D_{(9)} L_{21}^* = &\left(1 - \frac{S^*}{S(t)}\right)\frac{dS}{dt} + n_0\left(1 - \frac{E^*}{E(t)}\right)\frac{dE}{dt} \\ &+ n_1^*\left(1 - \frac{I_1^*}{I_1(t)}\right)\frac{dI_1}{dt} + n_2^*\left(1 - \frac{I_2^*}{I_2(t)}\right)\frac{dI_2}{dt}. \end{aligned}$$

For simplicity, denote $x(t) = \frac{S(t)}{S^*}$, $u(t) = \frac{E(t)}{E^*}$, $y_1(t) = \frac{I_1(t)}{I_1^*}$, and $y_2(t) = \frac{I_2(t)}{I_2^*}$. We rewrite $D_9 L_{21}^*$ as

$$\begin{aligned} D_{(9)} L_{21}^* = &\left(A + \mu S^*\right) + \left[n_0(\mu + \varepsilon) + n_1^*\mu_1 + n_2^*\mu_2\right] E^* \\ &- \frac{A}{x(t)} - \mu S^* x(t) - \frac{S^* x(t-\tau)\left[\beta_1 I_1^* y_1(t-\tau) + \beta_2 I_2^* y_2(t-\tau)\right]}{u(t)} \\ &- n_1^* k_1 \varepsilon E^* \frac{u(t)}{y_1(t)} - n_2^* k_2 \varepsilon E^* \frac{u(t)}{y_2(t)} - n_2^* \gamma I_1^* \frac{y_1(t)}{y_2(t)} + \Phi, \end{aligned}$$

where

$$\begin{aligned} \Phi = &\beta_1 S^* I_1^* [x(t-\tau) y_1(t-\tau) - x(t) y_1(t)] \\ &+ \beta_2 S^* I_2^* [x(t-\tau) y_2(t-\tau) - x(t) y_2(t)]. \end{aligned} \tag{15}$$

In order to cancel out Φ in $D_{(9)} L_{21}^*$ and ensure the positive definiteness of the constructed Lyapunov functionals, we define a functional

$$L_{22}^* = \beta_1 S^* I_1^* \int_{t-\tau}^{t} g\left(\frac{S(\theta) I_1(\theta)}{S^* I_1^*}\right) d\theta + \beta_2 S^* I_2^* \int_{t-\tau}^{t} g\left(\frac{S(\theta) I_2(\theta)}{S^* I_2^*}\right) d\theta,$$

that is,

$$L_{22}^* = \beta_1 S^* I_1^* \int_{t-\tau}^{t} g\left(x(\theta) y_1(\theta)\right) d\theta + \beta_2 S^* I_2^* \int_{t-\tau}^{t} g\left(x(\theta) y_2(\theta)\right) d\theta.$$

Then, for $L_2^* = L_{21}^* + L_{22}^*$, we have

$$D_{(9)}L_2^* = \mu S^* \left(2 - x(t) - \frac{1}{x(t)}\right) + \beta_1 S^* I_1^* \Phi_{21} + n_2 k_2 E^* \Phi_{22} + n_2 \gamma I_1^* \Phi_{23},$$

where

$$\Phi_{21} = 3 - \frac{1}{x(t)} - \frac{u(t)}{y_1(t)} - \frac{x(t-\tau)y_1(t-\tau)}{u(t)} + \ln \frac{x(t-\tau)y_1(t-\tau)}{x(t)y_1(t)},$$
$$\Phi_{22} = 3 - \frac{1}{x(t)} - \frac{u(t)}{y_2(t)} - \frac{x(t-\tau)y_2(t-\tau)}{u(t)} + \ln \frac{x(t-\tau)y_2(t-\tau)}{x(t)y_2(t)},$$
$$\Phi_{23} = 4 - \frac{1}{x(t)} - \frac{u(t)}{y_1(t)} - \frac{y_1(t)}{y_2(t)} - \frac{x(t-\tau)y_2(t-\tau)}{u(t)} + \ln \frac{x(t-\tau)y_2(t-\tau)}{x(t)y_2(t)}.$$

From Lemma 1 in "Appendix A", we know that $\Phi_{2i} \le 0$ $(i = 1, 2, 3)$; moreover, $\Phi_{21} = 0$ if and only if $x(t) = 1$ and $y_1(t) = y_1(t-\tau) = u(t)$; $\Phi_{22} = 0$ if and only if $x(t) = 1$ and $y_2(t) = y_2(t-\tau) = u(t)$; and $\Phi_{23} = 0$ if and only if $x(t) = 1$ and $y_1(t) = y_2(t) = y_2(t-\tau) = u(t)$. Therefore, the largest invariant set of (9) in the region making $D_{(9)}L_2^* = 0$ is the singleton $\{P^*\}$. It follows that P^* is GAS in the feasible region $\mathbb{X}_{20}$ by LaSalle Invariance Principle (LaSalle 1976).

(b) Next, we prove the global stability of P_0 of (9) in the feasible region $\mathbb{X}_2$. Note that any solution of (9) with the initial condition in $\mathbb{X}_2$ satisfies $S(t) > 0$ for $t > 0$. We first define

$$L_{21}^{(0)} = S_0 g\left(\frac{S(t)}{S_0}\right) + n_0 E(t) + n_1^{(0)} I_1(t) + n_2^{(0)} I_2(t)$$

with $n_0 = e^{\mu\tau}$, $n_1^{(0)}$ and $n_2^{(0)}$ are the same as those in (14). Without loss of generality, we can assume that $L_{21}^{(0)}$ is well-defined on $\mathbb{X}_2$. Then the derivative of $L_{21}^{(0)}$ with respect to t along solutions of (9) is

$$\begin{aligned} D_{(9)}L_{21}^{(0)} &= -\frac{\mu(S(t)-S_0)^2}{S(t)} - \left[n_0(\mu+\varepsilon) - (n_1^{(0)}k_1 + n_2^{(0)}k_2)\varepsilon\right]E(t) \\ &\quad + S(t-\tau)\left[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)\right] - S(t)\left[\beta_1 I_1(t) + \beta_2 I_2(t)\right], \end{aligned}$$

where $A = \mu S_0$ was used.
Further, define

$$L_2^{(0)} = L_{21}^{(0)} + \int_{t-\tau}^{t} S(\theta)\left[\beta_1 I_1(\theta) + \beta_2 I_2(\theta)\right] d\theta.$$

Then the derivative of $L_2^{(0)}$ with respect to t along solutions of (9) is

$$D_{(9)}L_2^{(0)} = -\frac{\mu(S(t)-S_0)^2}{S(t)} - \left[n_0(\mu+\varepsilon) - (n_1^{(0)}k_1 + n_2^{(0)}k_2)\varepsilon\right]E(t).$$

A straightforward calculation shows that $n_0(\mu+\varepsilon)-(n_1^{(0)}k_1+n_2^{(0)}k_2)\varepsilon = e^{\mu\tau}(\mu+\varepsilon)(1-R_{02})$. Then, similar to the case for (7) in the previous subsection, P_0 is GAS in the feasible region $\mathbb{X}_2$ when $R_{02} \le 1$ by LaSalle Invariance Principle (LaSalle 1976).

4.3 Stability of model (11)

(a) In order to prove the global stability of the endemic equilibrium P^* of (11) in the feasible region $\mathbb{X}_{30} = \{(\phi_0, \phi_1, \phi_2 \in \mathbb{X}_3 : \phi_1(0)+\phi_2(0) > 0\}$, as for (9), we first define a function

$$L_{31}^* = S^* g\left(\frac{S(t)}{S^*}\right) + n_1^* I_1^* g\left(\frac{I_1(t)}{I_1^*}\right) + n_2^* I_2^* g\left(\frac{I_2(t)}{I_2^*}\right)$$

where n_1^* and n_2^* are the same as those in (13). Then its derivative along solutions of (11) is

$$\begin{aligned} D_{(11)}L_{31}^* &= \left(1-\frac{S^*}{S}\right)\frac{dS}{dt} + n_1^*\left(1-\frac{I_1^*}{I_1}\right)\frac{dI_1}{dt} + n_2^*\left(1-\frac{I_2^*}{I_2}\right)\frac{dI_2}{dt} \\ &= \left(A^* + \mu S^* + n_1^*\mu_1 I_1^* + n_2^*\mu_2 I_2^*\right) - \frac{A}{x} - \mu S^* x - \frac{n_2^*\gamma I_1^* y_1}{y_2} \\ &\quad - \left(\frac{n_1^* k_1}{y_1} + \frac{n_2^* k_2}{y_2}\right) S^* x(t-\tau)\left[\beta_1 I_1^* y_1(t-\tau) + \beta_2 I_2 y_2(t-\tau)\right] \\ &\quad + \Phi_0, \end{aligned}$$

where $x(t) = \frac{S(t)}{S^*}$, $y_1(t) = \frac{I_1(t)}{I_1^*}$, $y_2(t) = \frac{I_2(t)}{I_2^*}$, and

$$\begin{aligned} \Phi_0 = {} & \beta_1 S^* I_1^*[(n_1^*k_1 + n_2^*k_2)x(t-\tau)y_1(t-\tau) - x(t)y_1(t)] \\ & + \beta_2 S^* I_2^*[(n_1^*k_1 + n_2^*k_2)x(t-\tau)y_2(t-\tau) - x(t)y_2(t)]. \end{aligned}$$

Note that $S^* = \Lambda$ implies that $n_1^*k_1 + n_2^*k_2 = 1$. Thus

$$\begin{aligned} \Phi_0 = {} & \beta_1 S^* I_1^*[x(t-\tau)y_1(t-\tau) - x(t)y_1(t)] \\ & + \beta_2 S^* I_2^*[x(t-\tau)y_2(t-\tau) - x(t)y_2(t)], \end{aligned}$$

which is the same as that defined in (15). Then, similarly as for L_2^*, we now define

$$L_3^* = L_{31}^* + \beta_1 S^* I_1^* \int_{t-\tau}^{t} g\left(\frac{S(\theta)I_1(\theta)}{S^* I_1^*}\right) d\theta + \beta_2 S^* I_2^* \int_{t-\tau}^{t} g\left(\frac{S(\theta)I_2(\theta)}{S^* I_2^*}\right) d\theta,$$

whose derivative with respect to t along solutions of (11) is

$$D_{(11)}L_3^* = \left(A + \mu S^* + n_1^*\mu_1 I_1^* + n_2^*\mu_2 I_2^*\right) - \frac{A}{x} - \mu S^* x$$

$$+ S^*\left[\beta_1 I_1^* \ln \frac{x(t-\tau)y_1(t-\tau)}{x(t)y_1(t)} + \beta_2 I_2^* \ln \frac{x(t-\tau)y_2(t-\tau)}{x(t)y_2(t)}\right] - n_2^*\gamma I_1^* \frac{y_1(t)}{y_2(t)} - n_1 k_1 \frac{S^* x(t-\tau)[\beta_1 I_1^* y_1(t-\tau) + \beta_2 I_2^* y_2(t-\tau)]}{y_1(t)} - n_2^* k_2 \frac{S^* x(t-\tau)[\beta_1 I_1^* y_1(t-\tau) + \beta_2 I_2^* y_2(t-\tau)]}{y_2(t)}.$$

Further, by applying the equalities satisfied by $P^*(S^*, I_1^*, I_2^*)$, we can reexpress $D_{(11)}L_3^*$ as

$$\begin{aligned} D_{(11)}L_3^* &= \mu S^*\left(2 - x(t) - \frac{1}{x(t)}\right) + n_1^* k_1 \beta_1 S^* I_1^* \Phi_{31} \\ &\quad + n_2^* \gamma I_1^* \Phi_{32} + n_2^* k_2 \beta_2 S^* I_2^* \Phi_{33}, \end{aligned} \tag{16}$$

where

$$\begin{aligned} \Phi_{31} &= 2 - \frac{1}{x(t)} - \frac{x(t-\tau)y_1(t-\tau)}{y_1(t)} + \ln \frac{x(t-\tau)y_1(t-\tau)}{x(t)y_1(t)}, \\ \Phi_{32} &= 3 - \frac{1}{x(t)} - \frac{y_1(t)}{y_2(t)} - \frac{x(t-\tau)y_1(t-\tau)}{y_2(t)} + \ln \frac{x(t-\tau)y_2(t-\tau)}{x(t)y_2(t)}, \\ \Phi_{33} &= 6 - \frac{3}{x(t)} - \frac{x(t-\tau)y_2(t-\tau)}{y_1(t)} - \frac{x(t-\tau)y_1(t-\tau)}{y_2(t)} \\ &\quad - \frac{x(t-\tau)y_2(t-\tau)}{y_2(t)} + \ln \frac{x^3(t-\tau)y_1(t-\tau)y_2^2(t-\tau)}{x^3(t)y_1(t)y_2^2(t)}. \end{aligned}$$

By Lemma 1 in "Appendix C", $\Phi_{3i} \leq 0$ $(i = 1, 2, 3)$ and

$$\begin{aligned} &\Phi_{31} = 0 \text{ if and only if } x(t) = 1 \text{ and } \frac{y_1(t-\tau)}{y_1(t)} = 1; \\ &\Phi_{32} = 0 \text{ if and only if } x(t) = 1 \text{ and } \frac{y_1(t)}{y_2(t)} = \frac{y_1(t-\tau)}{y_2(t)} = 1; \\ &\Phi_{33} = 0 \text{ if and only if } x(t) = 1 \text{ and } y_1(t) = y_2(t). \end{aligned}$$

Thus $D_{(11)}L_3^* \leq 0$ and the equality holds if and only if $x(t) = y_1(t) = y_2(t) = 1$, that is, $S = S^*$, $I_1 = I_2^*$, and $I_2 = I_2^*$. Therefore, by Lyapunov Theorem (Hale 2003), P^* of (11) is GAS in the feasible region $\mathbb{X}_{30}$.

(b) Now we prove the global stability of P_0 in the feasible region $\mathbb{X}_3$. For this end, we first define

$$L_{31}^{(0)} = S_0 g\left(\frac{S(t)}{S_0}\right) + n_1^{(0)} I_1(t) + n_2^{(0)} I_2(t),$$

where $n_1^{(0)}$ and $n_2^{(0)}$ are the same as those in (14). Note that

$$n_1^{(0)}k_1 + n_2^{(0)}k_2 = \frac{\beta_1 k_1 \mu_2 + \beta_2(k_1\gamma + k_2\mu_1)}{\mu_1\mu_2} S_0 = R_{03}.$$

Then the derivative of $L_{31}^{(0)}$ along solutions of (11) is

$$\begin{aligned}
D_{(11)}L_{31}^{(0)} &= -\frac{\mu(S(t)-S_0)^2}{S(t)} - S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) \\
&\quad + (n_1k_1 + n_2k_2)S(t-\tau)\left[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)\right] \\
&= -\frac{\mu(S(t)-S_0)^2}{S(t)} - S(\beta_1 I_1(t) + \beta_2 I_2(t)) \\
&\quad + R_{03}S(t-\tau)\left[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)\right],
\end{aligned}$$

where $A = \mu S_0$ was used. In order to remove the term $R_{03}S(t-\tau)$ $[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]$, we again define a functional

$$L_3^{(0)} = L_{31}^{(0)} + R_{03}\int_{t-\tau}^{t} S(\theta)\left[\beta_1 I_1(\theta) + \beta_2 I_2(\theta)\right] d\theta.$$

The derivative of $L_3^{(0)}$ along solutions of (11) is

$$D_{(11)}L_3^{(0)} = -\frac{\mu(S(t)-S_0)^2}{S(t)} + (R_{03}-1)S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)).$$

Therefore, similar to the cases in the above two subsections, we can show that the equilibrium P_0 of model (11) is GAS in the feasible region $\mathbb{X}_3$ when $R_{03} < 1$ by Lyapunov Theorem (Hale 2003) and when $R_{03} = 1$ by LaSalle Invariance Principle (LaSalle 1976).

4.4 Stability of model (6)

Let

$$\mathbb{X}_{p0} = \{(S, v, I_1, I_2) \in \mathbb{X}p : \text{ there exists } t_0 \geq 0 \text{ such that } \beta_1 I(t_0) + \beta I_2(t_0) > 0\}.$$

When $R_{04} > 1$, model (6) has global attractor $\mathscr{A}$ in $\mathbb{X}_{p0}$. Moreover, there exists $\eta > 0$ such that for a total trajectory $(S(t), v(t,\cdot), I_1(t), I_2(t))$ in $\mathscr{A}$, $S(t)$, $v(t,0)$, $I_1(t)$, $I_2(t) \geq \eta$. Also, note that $\frac{v(t,a)}{v^*(a)} = \frac{v(t-a,0)}{v^*(0)}$. The proofs are standard. See, for example, (Liu et al. 2015; Zhong et al. 2019).

(a) For the endemic equilibrium P^* of (6), according to the above cases, the function

$$L_{41}^* = S^* g\left(\frac{S(t)}{S^*}\right) + n_1^* I_1^* g\left(\frac{I_1(t)}{I_1^*}\right) + n_2^* I_2^* g\left(\frac{I_2(t)}{I_2^*}\right)$$

is still used, where n_1^* and n_2^* are the same as those in (13). We only need to consider L_{41}^* on $\mathscr{A}$, which is well-defined by the discussion above. The derivative of L_{41}^* with respect to t along solutions of (6) with (3) is calculated to be

$$\begin{aligned}D_{(6)}L_{41}^* = &\left(1-\frac{S^*}{S(t)}\right)[A-\mu S(t)-S(t)(\beta_1 I_1(t)+\beta_2 I_2(t))]\\ &+n_1^*\left(1-\frac{I_1^*}{I_1(t)}\right)\left[k_1\int_0^\infty \varepsilon(a)v(t,a)da-\mu_1 I_1(t)\right]\\ &+n_2^*\left(1-\frac{I_2^*}{I_2(t)}\right)\left[k_2\int_0^\infty \varepsilon(a)v(t,a)da+\gamma I_1(t)-\mu_2 I_2(t)\right].\end{aligned}$$

Similarly as before, let $x(t)=\frac{S}{S^*}$, $u(t,a)=\frac{v(t,a)}{v^*(a)}$, $y_1(t)=\frac{I_1(t)}{I_1^*}$, and $y_2(t)=\frac{I_2(t)}{I_2^*}$. Then $D_{(6)}L_{41}^*$ can be rewritten as

$$\begin{aligned}D_{(6)}L_{41}^* = &\left(A+\mu S^*+n_1^*\mu_1 I_1^*+n_2^*\mu_2 I_2^*\right)-\frac{A}{x}\\ &-\mu S^* x-S^* x(\beta_1 I_1^* y_1+\beta_2 I_2^* y_2)\\ &+\int_0^\infty \frac{S^*}{\Lambda}\varepsilon(a)v^*(a)u(t,a)da-n_1^*k_1\int_0^\infty \varepsilon(a)v^*(a)\frac{u(t,a)}{y_1(t)}da\\ &-n_2^*k_2\int_0^\infty \varepsilon(a)v^*(a)\frac{u(t,a)}{y_2(t)}da-n_2^*\gamma I_1^*\frac{y_1}{y_2},\end{aligned}$$

where $n_1^*k_1+n_2^*k_2=\frac{S^*}{\Lambda}$ was used.
Next, define a functional

$$L_{42}^*=\int_0^\infty n^*(a)x^*(a)g\left(\frac{v(t,a)}{v^*(a)}\right)da,$$

where $n^*(a)$ is a nonnegative differentiable and bounded function on $[0,\infty)$ to be specified. With the assistance of the second equation of (6), we get

$$\begin{aligned}D_{(6)}L_{42}^* &= \int_0^\infty n^*(a)\left[1-\frac{v^*(a)}{v(t,a)}\right]\frac{\partial v(t,a)}{\partial t}da\\ &=-\int_0^\infty n^*(a)\left[1-\frac{v^*(a)}{v(t,a)}\right]\left\{\frac{\partial v(t,a)}{\partial a}+[\mu+\varepsilon(a)]v(t,a)\right\}da.\end{aligned}$$

Note that $v^*(a)$ satisfies $\mu+\varepsilon(a)=-\frac{1}{v^*(a)}\cdot\frac{dv^*(a)}{da}$. Then $D_{(6)}L_{42}^*$ can be rewritten as

$$\begin{aligned}D_{(6)}L_{42}^* &= -\int_0^\infty n^*(a)\left[1-\frac{v^*(a)}{v(t,a)}\right]\left[\frac{\partial v(t,a)}{\partial a}-\frac{v(t,a)}{v^*(a)}\cdot\frac{dv^*(a)}{da}\right]da\\ &=-\int_0^\infty n^*(a)v^*(a)\left[1-\frac{v^*(a)}{v(t,a)}\right]\left\{\frac{1}{v^*(a)}\cdot\frac{\partial v(t,a)}{\partial a}\right.\end{aligned}$$

$$
\begin{aligned}
&-\frac{v(t,a)}{[v^*(a)]^2}\cdot\frac{dv^*(a)}{da}\Bigg\}da\\
&=-\int_0^\infty n^*(a)v^*(a)\left[1-\frac{v^*(a)}{v(t,a)}\right]\frac{\partial}{\partial a}\left(\frac{v(t,a)}{v^*(a)}\right)da\\
&=-\int_0^\infty n^*(a)v^*(a)\frac{\partial}{\partial a}\left[\frac{v(t,a)}{v^*(a)}-1-\ln\frac{v(t,a)}{v^*(a)}\right]da\\
&=-\int_0^\infty n^*(a)v^*(a)\frac{\partial}{\partial a}g\left(\frac{v(t,a)}{v^*(a)}\right)da.
\end{aligned}
$$

Further, with integration by parts, we obtain

$$
\begin{aligned}
D_{(6)}L_{42}^* &= n^*(0)v^*(0)g\left(\frac{v(t,0)}{v^*(0)}\right)-\left[n(a)^*v^*(a)g\left(\frac{v(t,a)}{v^*(a)}\right)\right]_{a=\infty}\\
&\quad+\int_0^\infty g\left(\frac{v(t,a)}{v^*(a)}\right)\frac{d\left(n^*(a)v^*(a)\right)}{da}da\\
&\le n^*(0)v^*(0)\left[\frac{v(t,0)}{v^*(0)}-1-\ln\frac{v(t,0)}{v^*(0)}\right]\\
&\quad+\int_0^\infty\left[\frac{v(t,a)}{v^*(a)}-1-\ln\frac{v(t,a)}{v^*(a)}\right]\frac{d\left(n^*(a)v^*(a)\right)}{da}da,
\end{aligned}
$$

where $\left[n^*(a)v^*(a)g\left(\frac{v(t,a)}{v^*(a)}\right)\right]_{a=\infty}\ge 0$ was used. Substituting $v(t,0)=S^*x(\beta_1I_1^*y_1+\beta_2I_2^*y_2)$, $v^*(0)=S^*(\beta_1I_1^*+\beta_2I_2^*)$, and $v(t,a)=v^*(a)u(t,a)$ into the last expression gives

$$
\begin{aligned}
&D_{(6)}L_{42}^*\\
&\le n^*(0)\left[S^*x(\beta_1I_1^*y_1+\beta_2I_2^*y_2)-v^*(0)-v^*(0)\ln\frac{x(\beta_1I_1^*y_1+\beta_2I_2^*y_2)}{\beta_1I_1^*+\beta_2I_2^*}\right]\\
&+\int_0^\infty[u(t,a)-1-\ln u(t,a)]\frac{d\left(n^*(a)v^*(a)\right)}{da}da.
\end{aligned}
$$

To sum up, for the functional $L_4^*=L_{41}^*+L_{42}^*$, we have got

$$
\begin{aligned}
D_{(6)}L_4^*\le{}&\left[A+\mu S^*+n_1^*\mu_1I_1^*+n_2^*\mu_2I_2^*-n^*(0)v^*(0)\right]\\
&-\mu S^*x-\frac{A}{x}+[n^*(0)-1]S^*x(\beta_1I_1^*y_1+\beta_2I_2^*y_2)\\
&+\int_0^\infty\left[\frac{S^*}{\Lambda}\varepsilon(a)v^*(a)+\frac{d\left(n^*(a)v^*(a)\right)}{da}\right]u(t,a)da-n_2^*\gamma I_1^*\frac{y_1}{y_2}\\
&-\int_0^\infty\Bigg\{\left[n_1^*k_1\frac{u(t,a)}{y_1(t)}+n_2^*k_2\frac{u(t,a)}{y_2(t)}\right]\varepsilon(a)v^*(a)\\
&+[1+\ln u(t,a)]\frac{d\left(n^*(a)v^*(a)\right)}{da}\Bigg\}da
\end{aligned}
$$

$$-n^*(0)v^*(0)\ln\frac{x(\beta_1 I_1^* y_1+\beta_2 I_2^* y_2)}{\beta_1 I_1^*+\beta_2 I_2^*}. \tag{17}$$

To make $D_{(6)}L_4^*\le 0$, let $n^*(a)$ satisfy

$$\frac{S^*}{\Lambda}\varepsilon(a)v^*(a)+\frac{d\left(n^*(a)v^*(a)\right)}{da}=0,\qquad n^*(0)=1.$$

Solving it gives

$$n^*(a)=e^{\int_0^a[\mu+\varepsilon(\theta)]d\theta}\frac{\int_a^\infty \varepsilon(\theta)e^{-\int_0^\theta[\mu+\varepsilon(\xi)]d\xi}d\theta}{\int_0^\infty \varepsilon(a)e^{-\int_0^a[\mu+\varepsilon(\theta)]d\theta}d\alpha}.$$

With this choice of $n^*(a)$, (17) becomes

$$\begin{aligned}
D_{(6)}L_4^* \le{} & \left[2\mu S^*+S^*(\beta_1 I_1^*+\beta_2 I_2^*)+n_2^*\gamma I_1^*\right]-\mu S^* x\\
& -\frac{\mu S^*+S^*(\beta_1 I_1^*+\beta_2 I_2^*)}{x}-n_2^*\gamma I_2^*\frac{y_1}{y_2}\\
& -S^*(\beta_1 I_1^*+\beta_2 I_2^*)\ln\frac{x\left(\beta_1 I_1^* y_1+\beta_2 I_2^* y_2\right)}{\beta_1 I_1^*+\beta_2 I_2^*}\\
& -\int_0^\infty\left\{\left[n_1^*k_1\frac{u(t,a)}{y_1(t)}+n_2^*k_2\frac{u(t,a)}{y_2(t)}\right]\right.\\
& \left.-[1+\ln u(t,a)]\frac{S^*}{\Lambda}\right\}\varepsilon(a)v^*(a)da\\
={} & H_0^*+H^*,
\end{aligned}$$

where

$$\begin{aligned}
H_0^* &= \mu S^*\left(2-x-\frac{1}{x}\right)+S^*(\beta_1 I_1^*+\beta_2 I_2^*)\left(1-\frac{1}{x}-\ln x\right),\\
H^* &= n_2^*\gamma I_1^*\left(1-\frac{y_1}{y_2}\right)-S^*(\beta_1 I_1^*+\beta_2 I_2^*)\ln\frac{\beta_1 I_1^* y_1+\beta_2 I_2^* y_2}{\beta_1 I_1^*+\beta_2 I_2^*}\\
&\quad -\int_0^\infty\left\{\left[n_1^*k_1\frac{u(t,a)}{y_1(t)}+n_2^*k_2\frac{u(t,a)}{y_2(t)}\right]\right.\\
&\quad \left.-[1+\ln u(t,a)]\frac{S^*}{\Lambda}\right\}\varepsilon(a)v^*(a)da.
\end{aligned}$$

Obviously, $H_0^*\le 0$ and $H_0^*=0$ if and only if $x=1$.
Note that $k_1\int_0^\infty \varepsilon(a)v^*(a)da=\mu_1 I_1^*$ implies $\int_0^\infty \frac{k_1\varepsilon(a)v^*(a)}{\mu_1 I_1^*}da=1$. Then H^* can be expressed as

$$H^*=\int_0^\infty \varepsilon(a)v^*(a)H(t,a)da,$$

where

$$\begin{aligned} H(t,a) &= \frac{k_1 n_2^* \gamma}{\mu_1}\left(1-\frac{y_1}{y_2}\right) - \frac{k_1 S^*(\beta_1 I_1^* + \beta_2 I_2^*)}{\mu_1 I_1^*} \ln \frac{\beta_1 I_1^* y_1 + \beta_2 I_2^* y_2}{\beta_1 I_1^* + \beta_2 I_2^*} \\ &\quad - n_1^* k_1 \left[\frac{u(t,a)}{y_1(t)} - 1 - \ln u(t,a)\right] - n_2^* k_2 \left[\frac{u(t,a)}{y_2(t)} - 1 - \ln u(t,a)\right] \\ &= \frac{k_1 n_2^* \gamma}{\mu_1}\left(1-\frac{y_1}{y_2}\right) - (n_1^* k_1 + n_2^* k_2) \ln \frac{\beta_1 I_1^* y_1 + \beta_2 I_2^* y_2}{\beta_1 I_1^* + \beta_2 I_2^*} \\ &\quad - n_1^* k_1 \left[\frac{u(t,a)}{y_1(t)} - 1 - \ln u(t,a)\right] - n_2^* k_2 \left[\frac{u(t,a)}{y_2(t)} - 1 - \ln u(t,a)\right]. \end{aligned}$$

Here we have used $\frac{k_1 S^*(\beta_1 I_1^* + \beta_2 I_2^*)}{\mu_1 I_1^*} = \frac{S^*}{\Lambda} = n_1^* k_1 + n_2^* k_2$. As $I_2^* = \frac{k_1\gamma + k_2\mu_1}{k_1\mu_2} I_1^*$, $n_1^* = \frac{\beta_1 n_2 + \beta_2\gamma}{\mu_1\mu_2} S^*$, and $n_2^* = \frac{\beta_2 S^*}{\mu_2}$, we further have

$$\begin{aligned} &H(t,a) \\ &= \frac{\beta_2 S^*}{\mu_2}\left\{\frac{k_1\gamma}{\mu_1}\left[2 - \frac{y_1(t)}{y_2(t)} - \frac{u(t,a)}{y_1(t)} + \ln\frac{u(t,a)}{y_2(t)}\right]\right. \\ &\quad \left. + k_2\left[1 - \frac{u(t,a)}{y_2(t)} + \ln\frac{u(t,a)}{y_2(t)}\right]\right\} + \frac{k_1\beta_1 S^*}{\mu_1}\left[1 - \frac{u(t,a)}{y_1(t)} + \ln\frac{u(t,a)}{y_1(t)}\right] \\ &\quad + \frac{k_1\beta_1 S^*}{\mu_1} \ln\frac{y_1(\beta_1 I_1^* + b_2 I_2^*)}{\beta_1 I_1^* y_1 + \beta_2 I_2^* y_2} + \frac{\beta_2 S^*}{\mu_2}\left(\frac{k_1\gamma}{\mu_1} + k_2\right) \ln\frac{y_2(\beta_1 I_1^* + b_2 I_2^*)}{\beta_1 I_1^* y_1 + \beta_2 I_2^* y_2} \\ &= H_1 + H_2, \end{aligned}$$

where

$$\begin{aligned} H_1 &= \frac{\beta_2 S^*}{\mu_2}\left\{\frac{k_1\gamma}{\mu_1}\left[2 - \frac{y_1(t)}{y_2(t)} - \frac{u(t,a)}{y_1(t)} + \ln\frac{u(t,a)}{y_2(t)}\right]\right. \\ &\quad \left. + k_2\left[1 - \frac{u(t,a)}{y_2(t)} + \ln\frac{u(t,a)}{y_2(t)}\right]\right\} + \frac{k_1 S^*}{\mu_2 I_1^*}\cdot\beta_1 I_1^*\left[1 - \frac{u(t,a)}{y_1(t)} + \ln\frac{u(t,a)}{y_1(t)}\right] \end{aligned}$$

and

$$H_2 = \frac{k_1\beta_1 S^*}{\mu_1} \ln\frac{y_1(\beta_1 I_1^* + b_2 I_2^*)}{\beta_1 I_1^* y_1 + \beta_2 I_2^* y_2} + \frac{k_1\beta_2 S^* I_2^*}{\mu_1 I_1^*} \ln\frac{y_2(\beta_1 I_1^* + b_2 I_2^*)}{\beta_1 I_1^* y_1 + \beta_2 I_2^* y_2}. \tag{18}$$

It follows from Lemma 1 in "Appendix C" that $H_1 \le 0$ and $H_1 = 0$ if and only if $y_1(t) = y_2(t) = u(t,a)$. Note that the expression H_2 can be rewritten as $H_2 = -\frac{k_1\beta_2 S^* I_2^*}{\mu_1 I_1^*}\phi\left(\frac{\beta_1 I_1^* y_1}{\beta_2 I_2^* y_2}, \frac{\beta_1 I_1^*}{\beta_2 I_2^*}\right)$, where $\phi(u,u^*) = (1+u^*)\ln\frac{1+u}{1+u^*} - u^*\ln\frac{u}{u^*}$ $(u, u^* > 0)$ is positive definite with respect to $u = u^*$ (the function $\phi(u,u^*)$ has been used to prove the global stability of the positive equilibrium of an epidemic model in Li et al. (2021)). Thus $H_2 \le 0$ and $H_2 = 0$ if and only if $y_1 = y_2$.
From the above discussion, we see that $H \le 0$ and $H = 0$ if and only if $y_1(t) = y_2(t) = u(t,a)$, i.e., $\frac{I_1(t)}{I_1^*} = \frac{I_2(t)}{I_2^*} = \frac{v(t,a)}{v^*(a)}$. Similarly as before, the largest invariant

set of (6) in the region where $D_{(6)}L_4^* = 0$ is the singleton $\{P^*\}$. Therefore, the endemic equilibrium P^* of (6) is GAS in the feasible region $\mathbb{X}_{p0}$ when $R_{04} > 1$ according to LaSalle Invariance Principle (LaSalle 1976).

(b) Next, we prove the global stability of the disease-free equilibrium P_0. First, define a function

$$L_{41}^{(0)} = S_0 g\left(\frac{S(t)}{S_0}\right) + n_1^{(0)} I_1(t) + n_2^{(0)} I_2(t),$$

where $n_1^{(0)}$ and $n_2^{(0)}$ are the same as those in (14). Then

$$D_{(6)}L_{41}^{(0)} = -\frac{\mu(S(t)-S_0)^2}{S(t)} - S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) + \frac{S_0}{\Lambda}\int_0^{\infty} \varepsilon(a)v(t,a)da,$$

where $A = \mu S_0$ was used.
Again, let $L_{42}^{(0)} = \int_0^{\infty} n_4^{(0)}(a)v(t,a)da$, where $n_4^{(0)}(a)$ is a nonnegative differentiable and bounded function on $[0,\infty)$ to be determined. Similarly as in (a), we get

$$\begin{aligned}
D_{(6)}L_{42}^{(0)} &= \int_0^{\infty} n_4^{(0)}(a)\frac{v(t,a)}{dt}da \\
&= -\int_0^{+\infty} n_4^{(0)}(a)\left\{[\mu+\varepsilon(a)]\,v(t,a) + \frac{\partial v(t,a)}{\partial a}\right\}da \\
&= -\int_0^{\infty} n_4^{(0)}(a)\,[\mu+\varepsilon(a)]\,v(t,a)da - \left[n_4^{(0)}(a)v(t,a)\right]_{a=\infty} \\
&\quad + n_4^{(0)}(0)x(t,0) + \int_0^{\infty}\frac{dn_4^{(0)}(a)}{da}v(t,a)da \\
&\le n_4^{(0)}(0)S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) \\
&\quad + \int_0^{\infty}\left\{\frac{dn_4^{(0)}(a)}{da} - n_4^{(0)}(a)\,[\mu+\varepsilon(a)]\right\}v(t,a)da
\end{aligned}$$

since $\left[n_4^{(0)}(a)v(t,a)\right]_{a=\infty} \ge 0$ and $x(t,0) = S(t)(\beta_1 I_1(t) + \beta_2 I_2(t))$.
Now, for the functional

$$L_4^{(0)} = L_{41}^{(0)} + L_{42}^{(0)},$$

we have

$$\begin{aligned}
D_{(6)}L_4^{(0)} \le& -\frac{\mu(S(t)-S_0)^2}{S(t)} + [n_4^{(0)}(0) - 1]S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) \\
&+ \int_0^{\infty}\left\{\frac{dn_4^{(0)}(a)}{da} - n(a)\,[\mu+\varepsilon(a)] + \frac{S_0}{\Lambda}\varepsilon(a)\right\}v(t,a)da. \quad (19)
\end{aligned}$$

Obviously, if we choose

$$\begin{aligned} n_4^{(0)}(a) &= e^{\int_0^a [\mu+\varepsilon(\theta)]d\theta} \left\{1 - \frac{S_0}{\Lambda} \int_0^a \varepsilon(\theta) e^{-\int_0^\theta [\mu+\varepsilon(\xi)]d\xi} d\theta \right\} \\ &= e^{\int_0^a [\mu+\varepsilon(\theta)]d\theta} \left\{1 - R_{04} \frac{\int_0^a \varepsilon(\theta) e^{-\int_0^\theta [\mu+\varepsilon(\xi)]d\xi} d\theta}{\int_0^\infty \varepsilon(\theta) e^{-\int_0^\theta [\mu+\varepsilon(\xi)]d\xi} d\theta} \right\}, \end{aligned}$$

then $n_4^{(0)}(a)$ is nonnegative with $n_4^{(0)}(0) = 1$ and $\frac{dn_4^{(0)}(a)}{da} - n_4^{(0)}(a)\,[\mu + \varepsilon(a)] + \frac{S_0}{\Lambda}\varepsilon(a) = 0$. With this choice of $n_4^{(0)}(a)$, (19) becomes

$$D_{(6)} L_4^{(0)} \le -\frac{\mu(S(t) - S_0)^2}{S(t)} \le 0.$$

Further, it is easy to verify that the largest invariant set of (6) with (3) in the set where $D_{(6)} L_4^{(0)} = 0$ is the singleton $\{P_0\}$. Therefore, By LaSalle Invariance Principle (LaSalle 1976), P_0 is GAS in the feasible region $\mathbb{X}_p$ when $R_{04} \le 1$.

5 Discussion

In this paper, we first proposed an epidemic model with latency-age and differential infectivity. Then we made different assumptions on the characteristics of leaving the latent stage by the latent individuals. This leads to models described by either ODEs or DDEs. Thus these models are closely related and so that they have similar threshold dynamics, namely, the basic reproduction numbers completely determine their global stability (see Theorem 1).

The basic reproduction numbers of the four models in this paper are consistent to some extent.

Firstly, when $\tau = 0$, the DDE model (9) reduces to the ODE model (7). Accordingly, the basic reproduction number R_{01} of (7) can be obtained by replacing τ in R_{02} with $\tau = 0$.

Secondly, if $\varepsilon(a)$ is a constant (denoted by ε), which implies that the rate leaving the latent stage of latent individuals does not depend on the latency-age, the model corresponding to the ODEs-PDE model is an ODE one. Then the basic reproduction number R_{01} of the ODE model (7) is a special case of R_{04} of the ODEs-PDE model (6) and R_{01} can be obtained from R_{04} by replacing $\varepsilon(a)$ in R_{04} with the constant ε.

Finally, when establishing model (9), the assumption that $\varepsilon(a)$ is a delta function implies that $\varepsilon(a)$ satisfies $\int_0^\infty \varepsilon(a)da = 1$. Thus the basic reproduction numbers R_{03} for the DDE model (11) and R_{04} for the ODEs-PDE model are unified.

The global stability of the equilibria of the four models is established by applying the Lyapunov direct method. There are some common points about constructing the Lyapunov functions/functionals for models (9), (11), and (6). Each consists of two parts with the first part just being the one for the ODE model (7) and the second part an integral. We provide some detail below.

First, for the ODE model (7), a linear combination of the Volterra-type function, (1), is taken as a candidate of the Lyapunov functions for the endemic equilibrium. The suitable coefficients are found by employing the algebraic approach proposed in Li et al. (2011, 2012a). Then a little obvious modification is made to construct the Lyapunov function for the disease-free equilibrium. It is a surprise that the coefficients except that for the S component are the same.

Next, for the DDE models and the ODEs-PDE model, the used Lyapunov functionals all consist of function parts and functional parts of integral form. Specifically, the two DDE models can be regarded as perturbations of the ODE model (7) and thus the Lyapunov functions for (7) are backbones of their Lyapunov functionals (see McCluskey (2015)), which are the sum of the Lyapunov function and an integral form. The integral is to balance the extra terms arising from just considering the derivative of the Lyapunov function along solutions. But for the ODEs-PDE model, the function parts correspond to the state variables without age feature, while the integral parts are only for the variable with age feature, the integrands (age a as the integral variable) have the same form as those of ODE models and the corresponding coefficient ($n(a)$) equals that of the ODE model at zero age ($a = 0$) (*i.e.*, $n(0) = 1$).

The features of the above Lyapunov functions/functionals indicate a connection between constructed Lyapunov functions/functionals for related different models. Moreover, the relationship between the Lyapunov functions/funnctionals about the different equilibria for the same model certainly provides an idea on how to construct appropriate Lyapunov functions/functionals.

Finally, when applying the Lyapunov direct method, it is required to prove the negative (semi-)definiteness of the derivative. This is a skillful task. Here the inequality in Lemma 1 of "Appendix C" is novel and generalizes some existing ones. With this inequality, it is quite easy to know that the last part of (16) is negative semi-definite. In addition, the introduction of the positive definite function $\phi(u, u^*) = (1 + u^*) \ln \frac{1+u}{1+u^*} - u^* \ln \frac{u}{u^*}$ $(u, u^* > 0)$ proposed in Li et al. (2021) plays a key role in showing that H_2 in (18) is negative definite with respect to $y_1 = y_2$. This suggests that, with new techniques or method, it is possible to prove the negative (semi-)definiteness of the derivative along solutions of a Lyapunov function/functional constructed in the usual way.

Acknowledgements This work is supported partially by the National Natural Science Foundation of PR China (Nos. 11971281, 12071268, 12071418), by NSERC of Canada (No. RGPIN-2019-05892), and by the Natural Science Basic Research Program in Shaanxi Province of China (No. 2022JM-029).

Declarations

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this paper.

Appendix A. Derivations of the equations on E_0 and E in (8)

Firstly, integrate the second equation of (6) with conditions (3) and (5) along its characteristic line $t - a =$ constant gives us

$$v(t,a) = \begin{cases} S(t-a)\,[\beta_1 I_1(t-a) + \beta_2 I_2(t-a)]\, e^{-\int_0^a [\mu+\varepsilon(\theta)]d\theta}, & 0 < a \le t, \\ v_b(a-t)e^{-\int_{a-t}^a [\mu+\varepsilon(\theta)]d\theta}, & a \ge t > 0. \end{cases} \tag{A1}$$

Then $v(t,\infty) = 0$ due to (5) and (A1). Moreover, as $\varepsilon(\theta) = 0$ for $0 < a < \tau$, we get

$$v(t,\tau) = S(t-\tau)\,[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]\, e^{-\mu\tau}. \tag{A2}$$

Next, for $E_0(t) = \int_0^\tau v(t,a)da$ and $E(t) = \int_\tau^\infty v(t,a)da$, integrating both sides of the second equation of (6) on the intervals $[0,\tau]$ and $[\tau,\infty)$, respectively, yields

$$\begin{cases} \frac{dE_0}{dt} & = -\int_0^\tau \frac{\partial v(t,a)}{\partial a}da - \int_0^\tau [\mu+\varepsilon(a)]v(t,a)da \\ & = v(t,\tau) - v(t,0) - \mu E_0(t), \\ \frac{dE}{dt} & = -\int_\tau^\infty \frac{\partial v(t,a)}{\partial a}da - \int_\tau^\infty [\mu+\varepsilon(a)]v(t,a)da \\ & = v(t,\tau) - v(t,\infty) - (\mu+\varepsilon)E(t). \end{cases} \tag{A3}$$

This, combined with (A2), $v(t,\infty) = 0$, and condition (3) to (A3), implies that

$$\begin{cases} \frac{dE_0}{dt} = & S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) \\ & -S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau} - \mu E_0(t), \\ \frac{dE}{dt} = & S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau} - (\mu+\varepsilon)E(t). \end{cases}$$

Appendix B. Derivation of the equation on E in (10)

According to (A1), the number of latent individuals for $t > \tau$ is

$$E(t) = \int_0^\tau S(t-a)\,[\beta_1 I_1(t-a) + \beta_2 I_2(t-a)]\, e^{-\int_0^a [\mu+\varepsilon(\theta)]d\theta} da.$$

As all the latent individuals must stay in the latent stage before latency-age τ and leave the stage at this latency-age, we have $\varepsilon(a) = 0$ for $a < \tau$ and hence

$$E(t) = \int_0^\tau S(t-a)\,[\beta_1 I_1(t-a) + \beta_2 I_2(t-a)]\, e^{-\mu a} da$$

or

$$E(t) = \int_{t-\tau}^t S(\theta)\,[\beta_1 I_1(\theta) + \beta_2 I_2(\theta)]\, e^{-\mu(t-\theta)} d\theta.$$

Differentiating both sides with respect to t yields

$$\begin{aligned}\frac{dE}{dt} &= S(t)(\beta_1 I_1(t) + \beta_2 I_2(t)) \\ &\quad - S(t-\tau)[\beta_1 I_1(t-\tau) + \beta_2 I_2(t-\tau)]e^{-\mu\tau} - \mu E(t).\end{aligned}$$

Appendix C. A generalized inequality

Lemma 1 *Let n be a positive integer. Then, for positive integers $m_1, m_2, \ldots, m_n$ and positive $c_1, c_2, \ldots, c_n$, one has*

$$\left(\sum_{i=1}^{n} m_i\right) - \left(\sum_{i=1}^{n} m_i c_i\right) + \ln\left(\prod_{i=1}^{n} c_i^{m_i}\right) \le 0$$

and the equality holds if and only if $c_1 = c_2 = \cdots = c_n = 1$.

Proof Noting

$$\ln\left(\prod_{i=1}^{n} c_i^{m_i}\right) = \sum_{i=1}^{n}(m_i \ln c_i),$$

we have

$$\begin{aligned}&\left(\sum_{i=1}^{n} m_i\right) - \left(\sum_{i=1}^{n} m_i c_i\right) + \ln\left(\prod_{i=1}^{n} c_i^{m_i}\right) \\ &= \sum_{i=1}^{n} m_i\,(1 - c_i + \ln c_i) \\ &= -\sum_{i=1}^{n} m_i g(c_i).\end{aligned}$$

Here $g(u) = u - 1 - \ln u$ for $u > 0$, which is positive and $g(u) = 0$ if and only if $u = 1$. Then the result follows immediately. □

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