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Global Analysis on Delay Epidemiological Dynamic Models with Nonlinear Incidence

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Abstract In this paper, we derive and study the classical SIR, SIS, SEIR and SEI models of epidemiological dynamics with time delays and a general incidence rate. By constructing Lyapunov functionals, the global asymptotic stability of the disease-free equilibrium and the endemic equilibrium is shown. This analysis extends and develops further our previous results and can be applied to the other biological dynamics, including such as single species population delay models and chemostat models with delay response.

Keyword Epidemic model, nonlinear incidence rate, time delay, Lyapunov functional, global stability

1 Introduction

The mechanism of transmission of infections is now known for most diseases. Generally, diseases transmitted by viral agents, such as influenza, measles, rubella, and chicken pox, confer immunity against reinfection, while diseases transmitted by bacteria, such as tuberculosis, meningitis, and gonorrhea, confer no immunity against reinfection. Other diseases, such as malaria, are transmitted not directly from human to human but by vectors, agents (usually insects) who are infected by humans and who then transmit the disease to humans. Mathematical modeling in epidemiology provides understanding of the underlying mechanisms that influence the spread and control of the disease.

One of the early triumphs of mathematical epidemiology was Kermack-McKendrick model. It divided the population being studied into three classes labeled s, i and r, where s denotes the number of individuals who are susceptible to the disease, i denotes the number of infected individuals, assumed infectious and able to spread the disease by contact with susceptible, r denotes the number of individuals who had been infected and were removed from the possibility of being infected again or of spreading infection. Thereafter, various epidemiological models have been developed in recent decades, such as SIR models, SIS models, SEIR models with or without time delays.

In most epidemiological models, bilinear incidence rate βsi and standard incidence rate $\beta si/N$ are frequently used. Here N is the total number of the population ($N = s + i + r$)

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and β is a positive constant. These incidences imply that the contact number between s and i is proportional to si or si/N. But also the infection probability per contact is likely influenced by the number of infective and susceptible individuals, because more infective individuals can increase the infection risk and susceptible individuals would avoid the contact with infectives. Nonlinear incidence rates of the form $\beta I^p S^q$ in ordinary differential equation SEIRS models with vital dynamics were investigated by Liu et al. [22, 23]. They discovered that the model can yield rich dynamical behaviors including bistable equilibria, saddle-node bifurcation and Hopf bifurcation, etc. Functional form of the incidence rate can have a crucial role for modeling of epidemic dynamics. Hethcote and van den Driessche [11] consider some epidemiological models with a general incidence rate $g(i)s$. As a special case, Ruan and Wang [28] studied the global dynamics of an epidemic model with vital dynamics and nonlinear incidence rate of saturated mass action. They mostly discussed an SIRS model with the incidence rate $ki^2s/(1 + \beta i^2)$ and obtained rich bifurcation phenomena. The first most general case described as function $f(s, i)$ was introduced by Feng and Thieme [9, 10]. Then Korobeinikov studied on global properties for epidemiological models with various nonlinear incidence rate, such as $\beta i^p s^q$ in [14], $f(s)g(i)$ in [16], $f(s, i)$ in [17, 18, 19]. By constructing Lyapunov functions, Korobeinikov [17, 18] established global stability for ordinary differential equations models of epidemiological dynamics with nonlinear incidence rate $f(s, i)$, where the function $f(s, i)$ satisfies some conditions.

Various biological reasons lead to the introduction of time delays in models of disease transmission. Time delays are used to model the mechanisms in the disease dynamics (van den Diressche [29]; Beretta et al. [2, 3]; Cooke et al. [5, 6]; Arino and van den Driessche [1]). Usually, the following several different biological mechanisms have been modeled by the introduction of time delays in epidemiological models:

(i) Delay due to temporary immunity; Some infections provide recovered individuals with a short or long immunity against re-infection. This means that it is natural to include the effects of immunity into the mathematical models in order to represent the actual dynamics of epidemic spread and predict future outbreaks. Immunity can be attained through targeted immunization; it can be naturally acquired after an individual has successfully recovered from an infection, and in some cases maternal antibodies can be transmitted to a newborn providing a certain level of immunity. In each case, the immunity period will vary, as some diseases provide almost life-long immunity while others give only a very short-lived non-susceptibility. Kyrychko and Blyuss [21], and Blyuss and Kyrychko [4] considered delay models with fixed immune period and varying immune period, and with incidence rate $f(i)s$, respectively. It was proved that the disease-free equilibrium is locally and globally asymptotically stable. Under some conditions, the endemic equilibrium is globally asymptotically stable, and bifurcation analysis is performed using traceDDE to investigate different dynamical regimes in the model using numerical continuation for different values of system parameters and different integral kernels.

(ii) Delay caused by the latency in a vector; A number of the most dangerous infections are spread by vectors, that is agents (usually insects) by which infections are transmitted from one host to another. The most notorious examples of such vector-born infections and the vectors are: human malaria transmitted by mosquitoes of the

Anopheles genus; *Aedes aegypti* mosquitoes that are vectors of avian malaria, Dengue fever and yellow fever; tsetse flies are vectors of human African trypanosomiasis ("African sleeping sicknes"); Chagas' disease is spread by triatomine bugs; ticks of the genus *Ixodes* are vectors of Lyme disease and babesiosis; phlebotomine sand flies transmit leishmaniasis, bartonellosis and pappataci fever; fleas, such as *Pulex* and *Xenopsylla* transmit bubonic plague. One of the major reasons for delay in the vector-born diseases is that some time needs before the infective organism develops in the vector to the level that is sufficient to pass the infection further.

(iii) Delay caused by latent period in host; The major reason for time delay in epidemic modeling is that all infectious diseases have so-called latent period. The latent period is the time elapsed between exposure of a host to a pathogenic organism, and the infectiousness of this host. It is assumed that this time is needed for the pathogenic organism to reproduce within the infected host in sufficient number to become infectious for the others.

Inclusion of time delay means that the models can be formulated as functional differential equations. One important aim is to investigate the effect of time delays on global properties of models. Lyapunov-LaSalle type theorem for delay differential equations [20] provides a useful method to establish global stability by suitable Lyapunov functionals. Huang et al. [12] have considered two epidemiological models with the last two case delays and nonlinear incidence rate $f(s)g(i)$.

In this paper, we would extend some results in Huang et al. [12]. A more general nonlinear incidence rate $f(s,i)$ in various delay epidemiological dynamical models is considered. By constructing different Lyapunov functionals, we establish the global properties of these models to study the effect of different delays which express different biological meanings. In Section 2, we mainly analyze a delayed SIR model and obtain global stability of disease free equilibrium and endemic equilibrium, respectively. In Section 3, we generalize the type of Lyapunov functionals constructed in Sec.2 to the other delay epidemiological models and chemostat models.

2 Delay SIR models of epidemiological dynamics

In this section, based on delay due to a latency in a vector, we further develop the nonlinear incidence rate $f(s)g(i)$ in delay SIR epidemiological models in [12] to a more general function $f(s,i)$. We assume that

(i) the infection is transmitted to an individual by a vector, such as mosquito. That is, susceptible persons receive the infection from infectious vectors, and susceptible vectors receive the infection from infectious individuals. When a susceptible vector is infected by a person, there is a fixed time τ during which the infectious agent develops in the vector. At the end of this time, the vector can infect a susceptible human [7].

(ii) the incidence rate depends on the number of the susceptible host at a given moment t, and on the number of the infected host at the pervious moment $t-\tau$. Here $\tau > 0$ is a time delay for latency in a vector.

(iii) there is a nonlinear incidence rate which is governed by the function $f(s,i)$. Here

the function $f(s,i)$ is assumed to be always positive, continuous and monotonically increasing for all $s>0$ and $i>0$ and $f(0,i)=f(s,0)=0$.

The delay SIR epidemiological model we consider is described as

$$\begin{aligned} s'(t) &= \mu - \mu s(t) - f(s(t), i(t-\tau)), \\ i'(t) &= f(s(t), i(t-\tau)) - (\sigma+\mu) i(t), \end{aligned} \tag{1}$$

and

$$r'(t) = \sigma i(t) - \mu r(t).$$

where the parameters μ is a natural death rate and σ is a recovery rate. Note that $s'(t)+i'(t)+r'(t) = \mu - \mu(s(t)+i(t)+r(t))$ implies that $s(t)+i(t)+r(t) \to 1$ as $t \to \infty$. That is, $s(t)$, $i(t)$ and $r(t)$ are the ratio of susceptible, infective and recovered respectively.

Since $r(t)$ does not appear in the equations for $s(t)$ and $i(t)$, it is enough to consider only the first two equations. When $\tau = 0$, model (1) is represented as an ordinary differential equations model. Korobeinikov [17, 18] proves the global properties for the model (1) without delay, which only depend on the basic reproductive number.

The initial condition of delay differential equations (1) is given as

$$s(\theta) = \varphi_1(\theta), \quad i(\theta) = \varphi_2(\theta), \quad \theta \in [-\tau, 0], \tag{2}$$

where $\varphi = (\varphi_1, \varphi_2) \in C^+ \times C^+$, such that $\varphi_i(\theta) \geq 0$ $(-\tau \leq \theta \leq 0,\ i = 1,2)$. Here C denotes the Banach space $C([-\tau, 0],\ R)$ of continuous functions mapping the interval $[-\tau, 0]$ into R equipped with the sup-norm. The nonnegative cone of C is defined as $C^+ = C([-\tau, 0],\ R_+)$.

Since $(s(t)+i(t))' \leq \mu - \mu(s(t)+i(t))$, we have that $\limsup(s(t)+i(t)) \leq 1$. Hence we discuss system (1) in the closed set

$$\Omega = \left\{ (s(t), i(t)) \in C^+ \times C^+ :\ \| s(t) + i(t) \| \leq 1 \right\}.$$

It is easy to show that Ω is positively invariant with respect to system (1).

The basic reproductive number for (1) is

$$R_0 = \frac{1}{\sigma+\mu} \frac{\partial f(s_0, 0)}{\partial i},$$

where $s_0 = 1$. System (1) always has a disease-free equilibrium $E_0(s_0, i_0)$, where $i_0 = 0$, and may also admit a unique endemic equilibrium $E^*(s^*, i^*)$ which depends on R_0, where s^*, i^* satisfy

$$\mu = f(s^*, i^*) + \mu s^*, \quad f(s^*, i^*) = (\sigma+\mu) i^*. \tag{3}$$

The existence of a positive equilibrium of system (1) is shown by the following lemma in [18].

Lemma 1 *If the following is satisfied,*

$$\lim_{i \to 0} \frac{f(s_0, i)}{f(s, i)} > 1 \quad for\ all \quad s \in (0, s_0),$$

then, if $R_0 > 1$, system (1) has positive equilibrium states $E^*(s^*, i^*)$.

Next we consider the global asymptotic stability of two steady states of (1) by Lyapunov functionals, respectively.

Theorem 1. *If the function $f(s,i)$ is concave with respect to the variable i, then the disease-free equilibrium $E_0(s_0, 0)$ is globally asymptotically stable for any $\tau > 0$ when $R_0 \leq 1$.*

Proof. Define a Lyapunov functional

$$V_1 = s(t) - s_0 - \int_{s_0}^{s(t)} \lim_{i\to 0} \frac{f(s_0,i)}{f(\sigma,i)} d\sigma + i(t) + (\sigma+\mu)\int_0^\tau i(t-\theta)d\theta. \tag{4}$$

Here the functional $\int_0^\tau i(t-\theta)d\theta$ satisfies

$$\frac{d}{dt}\int_0^\tau i(t-\theta)d\theta = \int_0^\tau \frac{d}{dt} i(t-\theta)d\theta = -i(t-\tau) + i(t).$$

The time derivative of V_1 satisfies

$$\begin{aligned}
\frac{dV_1}{dt} =& \left(1 - \lim_{i\to 0}\frac{f(s_0,i)}{f(s(t),i)}\right)(\mu s_0 - \mu s(t) - f(s(t), i(t-\tau))) + f(s(t), i(t-\tau)) - (\sigma+\mu)i(t) \\
& - (\sigma+\mu)i(t-\tau) + (\sigma+\mu)i(t) \\
=& \mu s_0 \left(1 - \frac{s(t)}{s_0}\right)\left(1 - \lim_{i\to 0}\frac{f(s_0,i)}{f(s(t),i)}\right) \\
& + (\sigma+\mu)i(t-\tau)\left(\frac{f(s(t),i(t-\tau))}{(\sigma+\mu)i(t-\tau)}\lim_{i\to 0}\frac{f(s_0,i)}{f(s,i)} - 1\right).
\end{aligned}$$

Since the monotonicity of the function $f(s,i)$ with respect to s, we have

$$\left(1 - \frac{s(t)}{s_0}\right)\left(1 - \lim_{i\to 0}\frac{f(s_0,i)}{f(s(t),i)}\right) \leq 0.$$

The concavity of $f(s,i)$ with respect to i ensures that $f(s,i) \leq i\frac{\partial f(s,0)}{\partial i}$, we have

$$f(s(t), i(t-\tau)) \leq i(t-\tau)\frac{\partial f(s,0)}{\partial i}.$$

Hence

$$\frac{f(s(t),i(t-\tau))}{(\sigma+\mu)i(t-\tau)}\lim_{i\to 0}\frac{f(s_0,i)}{f(s,i)} = \frac{f(s(t),i(t-\tau))}{(\sigma+\mu)i(t-\tau)}\frac{\frac{\partial f(s_0,0)}{\partial i}}{\frac{\partial f(s,0)}{\partial i}} \leq \frac{1}{\sigma+\mu}\frac{\partial f(s_0,0)}{\partial i} = R_0.$$

Therefore, $R_0 < 1$ ensures that $dV_1/dt \leq 0$ for all $s(t) > 0$ and $i(t) > 0$ and the equality holds only at $s = s_0, i = 0$. Hence, from Corollary 5.2 of Kuang ([20], p.30), we have that E_0 is globally stable. Furthermore, for $R_0 = 1$, $dV_1/dt = 0$ implies that $s(t) = s_0$. Hence,

it is easy to show that $E_0(s_0, 0)$ is the largest invariant set in $\{(s(t), i(t))|\dot{V}_1 = 0\}$. By the classical Lyapunov-LaSalle invariance principle (Theorem 5.3 of Kuang ([20], p.30)), E_0 is also globally stable.

Theorem 2. *Suppose that there exists a positive equilibrium point $E^*(s^*, i^*)$, if the function $f(s, i)$ is satisfied with*

$$\frac{i}{i^*} \leq \frac{f(s,i)}{f(s,i^*)} \leq 1 \quad for \quad 0 < i \leq i^*, \tag{5}$$

$$1 \leq \frac{f(s,i)}{f(s,i^*)} \leq \frac{i}{i^*} \quad for \quad i > i^*, \tag{6}$$

then $E^*(s^*, i^*)$ is globally asymptotically stable for any $\tau > 0$ when $R_0 > 1$.

Proof. To prove global stability of the endemic equilibrium, we define a Lyapunov functional

$$V_2 = s(t) - s^* - \int_{s^*}^{s(t)} \frac{f(s^*, i^*)}{f(\eta, i^*)} d\eta + \left(i(t) - i^* - i^* \ln \frac{i(t)}{i^*} \right) + f(s^*, i^*)\ U_t, \tag{7}$$

where

$$U_t = \int_0^\tau \left(\frac{i(t-\theta)}{i^*} - 1 - \ln \frac{i(t-\theta)}{i^*} \right) d\theta.$$

Then, the derivative of U_t satisfies

$$\begin{aligned}
\frac{dU_t}{dt} =& \frac{d}{dt} \int_0^\tau \left(\frac{i(t-\theta)}{i^*} - 1 - \ln \frac{i(t-\theta)}{i^*} \right) d\theta \\
=& \int_0^\tau \frac{d}{dt} \left(\frac{i(t-\theta)}{i^*} - 1 - \ln \frac{i(t-\theta)}{i^*} \right) d\theta \\
=& - \int_0^\tau \frac{d}{d\theta} \left(\frac{i(t-\theta)}{i^*} - 1 - \ln \frac{i(t-\theta)}{i^*} \right) d\theta \\
=& - \frac{i(t-\tau)}{i^*} + \frac{i(t)}{i^*} + \ln \frac{i(t-\tau)}{i(t)}.
\end{aligned}$$

The time derivative of V_2 along solution of (1) is given by

$$\begin{aligned}
\frac{dV_2}{dt} =& \mu s^* \left(1 - \frac{s(t)}{s^*} \right) \left(1 - \frac{f(s^*, i^*)}{f(s(t), i^*)} \right) + f(s^*, i^*) \ln \frac{i(t-\tau)}{i(t)} \\
&+ f(s^*, i^*) \left(2 - \frac{f(s^*, i^*)}{f(s(t), i^*)} - \frac{i^*}{i(t)} \frac{f(s(t), i(t-\tau))}{f(s^*, i^*)} - \frac{i(t-\tau)}{i^*} + \frac{f(s(t), i(t-\tau))}{f(s(t), i^*)} \right)
\end{aligned}$$

Here by using

$$\ln \frac{i(t-\tau)}{i(t)} = \ln \frac{f(s^*, i^*)}{f(s(t), i^*)} + \ln \frac{i^*}{i(t)} \frac{f(s(t), i(t-\tau))}{f(s^*, i^*)} + \ln \frac{i(t-\tau)}{i^*} \frac{f(s(t), i^*)}{f(s(t), i(t-\tau))},$$

we have

$$\begin{aligned}\frac{dV_2}{dt} =&\mu s^*\left(1-\frac{s(t)}{s^*}\right)\left(1-\frac{f(s^*,i^*)}{f(s(t),i^*)}\right)\\ &+f(s^*,i^*)\left(1-\frac{f(s^*,i^*)}{f(s(t),i^*)}+\ln\frac{f(s^*,i^*)}{f(s(t),i^*)}\right)\\ &+f(s^*,i^*)\left(1-\frac{i^*}{i(t)}\frac{f(s(t),i(t-\tau))}{f(s^*,i^*)}+\ln\frac{i^*}{i(t)}\frac{f(s(t),i(t-\tau))}{f(s^*,i^*)}\right)\\ &+f(s^*,i^*)\left(1-\frac{i(t-\tau)}{i^*}\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}+\ln\frac{i(t-\tau)}{i^*}\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}\right)\\ &+f(s^*,i^*)\left(-1-\frac{i(t-\tau)}{i^*}+\frac{f(s(t),i(t-\tau))}{f(s(t),i^*)}+\frac{i(t-\tau)}{i^*}\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}\right).\end{aligned}$$

By calculating the last term, we have

$$\begin{aligned}\frac{dV_2}{dt} =&\mu s^*\left(1-\frac{s(t)}{s^*}\right)\left(1-\frac{f(s^*,i^*)}{f(s(t),i^*)}\right)\\ &+f(s^*,i^*)\left(1-\frac{f(s^*,i^*)}{f(s(t),i^*)}+\ln\frac{f(s^*,i^*)}{f(s(t),i^*)}\right) &(8)\\ &+f(s^*,i^*)\left(1-\frac{i^*}{i(t)}\frac{f(s(t),i(t-\tau))}{f(s^*,i^*)}+\ln\frac{i^*}{i(t)}\frac{f(s(t),i(t-\tau))}{f(s^*,i^*)}\right) &(9)\\ &+f(s^*,i^*)\left(1-\frac{i(t-\tau)}{i(t)}\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}+\ln\frac{i(t-\tau)}{i(t)}\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}\right) &(10)\\ &+f(s^*,i^*)\left(\frac{i(t-\tau)}{i^*}-\frac{f(s(t),i(t-\tau))}{f(s(t),i^*)}\right)\left(\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}-1\right).\end{aligned}$$

¿From the monotonicity of the function $f(s,i)$ with respect to s, we have

$$\left(1-\frac{s(t)}{s^*}\right)\left(1-\frac{f(s^*,i^*)}{f(s(t),i^*)}\right)\le 0,$$

and from the conditions (5) and (6), we have

$$\left(\frac{i(t-\tau)}{i^*}-\frac{f(s(t),i(t-\tau))}{f(s(t),i^*)}\right)\left(\frac{f(s(t),i^*)}{f(s(t),i(t-\tau))}-1\right)\le 0.$$

Since the function

$$H(h)=1-h+\ln h$$

is always non-positive for any $h>0$, and $H(h)=0$ if and only if $h=1$. Therefore, the terms (8)-(10) are always non-positive.

Hence, the functional V_2 satisfies all the conditions of Corollary 5.2 of Kuang ([20], p.30). This proves that $E^*(s^*,i^*)$ is globally asymptotically stable under the condition $R_0>1$. It completes the proof of Theorem 2.

Remark 1: Korobeinikov [17, 18] used the following Lyapunov function

$$W(t) = s(t) - s^* - \int_{s^*}^{s(t)} \frac{f(s^*, i^*)}{f(\eta, i^*)} d\eta + i(t) - \int_{i^*}^{i(t)} \frac{f(s^*, i^*)}{f(s^*, \eta)} d\eta, \tag{11}$$

to prove the global stability of E^* for model (1) without time delay ($\tau = 0$). Since we incorporate a time delay into (1), our functional V_2 has an additional functional U_t in (7). When we compare V_2 to the above $W(t)$ and the functionals in [12], (7) has a simpler term for $i(t)$. Further note that conditions (5) and (6) are satisfied when $f(s, i)$ is concave with respect to i as indicated in [17] and Theorems 1 and 2 completely solve the global stability of (1) under the concavity. On the other hand, the above two theorems show that the delay τ in (1) does not change the global properties of two equilibria.

In particular, for two specific cases, bilinear rate $\beta s(t)i(t-\tau)$ and Holling type II incidence rate $\beta s(t)i(t-\tau)/(1+\alpha i(t-\tau))$ which were introduced by Beretta and Takeuchi [3] and Xu and Ma [31] respectively, the global stability for endemic equilibrium were both established by McCluskey [25, 26] recently. Note that the above incidences satisfy (5) and (6), it is obvious that the functional (7) can also be applied.

3 Delay SIS, SEIR and SEI epidemiological models

3.1 *SIS model*

Since some infectious disease does not have an immune period, and the removed individual would move directly to susceptible immediately after recovery, there is no recovered class and the population is only composed of the susceptible and the infective. Similarly, if we consider the latency in a vector for infective, model (1) becomes a known delay SIS model

$$\begin{aligned} s'(t) &= \mu - \mu s(t) - f(s(t), i(t-\tau)) + \sigma i(t), \\ i'(t) &= f(s(t), i(t-\tau)) - (\sigma + \mu) i(t). \end{aligned} \tag{12}$$

Since $s'(t) + i'(t) = \mu(1 - s(t) - i(t))$, the solution $s(t) + i(t) \to 1$ as $t \to \infty$. Hence we assume that $1 = s(t) + i(t)$ and we have $i(t) = 1 - s(t)$. By letting $\bar{\mu} = \mu + \sigma$, model (12) can be represented as

$$\begin{aligned} s'(t) &= \bar{\mu} - \bar{\mu} s(t) - f(s(t), i(t-\tau)), \\ i'(t) &= f(s(t), i(t-\tau)) - \bar{\mu} i(t), \end{aligned} \tag{13}$$

which is the same as (1). Therefore, (12) has the same global properties as Theorem 1 and Theorem 2.

Remark 2: Here we would extend some results from system (13). If we use $s(t) = 1 - i(t)$, system (13) is transformed to a single species population equation as

$$i'(t) = f(1 - i(t), i(t-\tau)) - \bar{\mu} i(t). \tag{14}$$

(14) is the same as the following scalar delay differential equation

$$y'(t) = f(1 - y(t), y(t - T)) - cy(t), \tag{15}$$

which was introduced by Cooke [7]. For a specific case $f(1-y(t), y(t-T)) = by(t-T)[1-y(t)]$, Cooke [7] gave a Lyapunov stability analysis for equation

$$y'(t) = by(t - T)[1 - y(t)] - cy(t). \tag{16}$$

Eq.(16) has a zero equilibrium $y_0 = 0$ and a positive equilibrium $y^* = 1-\frac{c}{b}$ when $b > c > 0$. Now we can show the global stability of y_0 and y^* by applying two simpler Lyapunov functionals:

(i) For y_0, we choose a functional U_1 and calculate the time derivative of U_1, that is

$$U_1 = -\ln(1 - y(t)) + b\int_0^T y(t - \theta)d\theta, \quad \text{and} \quad \frac{dU_1}{dt}|_{(16)} = -\frac{by^2}{1 - y} + \frac{(b - c)y}{1 - y}.$$

Since $0 \le y(t) \le 1$, it is easy to know that equilibrium y_0 is globally stable when $0 < b < c$.

(ii) For y^*, if it exists we choose a functional

$$U_2 = -(1 - y^*)\ln\frac{1 - y(t)}{1 - y^*} - y^*\ln\frac{y(t)}{y^*} + cy^*\int_0^T \left(\frac{y(t - \theta)}{y^*} - 1 - \ln\frac{y(t - \theta)}{y^*}\right) d\theta.$$

The time derivative of U_2 satisfies

$$\begin{aligned}\frac{dU_2}{dt}|_{(16)} =& - cy^*\left(\frac{(1 - y)y(t - T)}{(1 - y^*)y(t)} - 1 - \ln\frac{(1 - y)y(t - T)}{(1 - y^*)y(t)}\right)\\ & - cy^*\left(\frac{1 - y^*}{1 - y} - 1 - \ln\frac{1 - y^*}{1 - y}\right)\\ & - \frac{c(y - y^*)^2}{(1 - y)}\\ & \le 0.\end{aligned}$$

Note that equation (15) is a generalization of (16), and the global analysis for (15) is given as an open question in [7]. Here it is suggested that our Lyapunov functionals such as (4) and (7) can be applied to (15) under more limited conditions for the function f and parameters. The detailed global anlysis for (15) and for other single species population delay models is currently a work in progress.

3.2 *SEIR model*

For some diseases, such as sexually transmitted infections, it is important to account for the individuals who have been exposed to the infection but have not yet become infected, thus the whole population is split into four classes, including a separate class of exposed

$e(t)$. When we consider latent period in infected host described by a constant delay, we obtain the following delay SEIR model:

$$\begin{aligned}
s'(t) &= \mu - \mu s(t) - f(s(t), i(t)),\\
e'(t) &= f(s(t), i(t)) - e^{-\mu\tau} f(s(t-\tau), i(t-\tau)) - \mu e(t),\\
i'(t) &= e^{-\mu\tau} f(s(t-\tau), i(t-\tau)) - (\sigma+\mu) i(t),\\
r'(t) &= \sigma i(t) - \mu r(t).
\end{aligned}$$

Here, the time delay τ is the latent period of disease in a host. The term $e^{-\mu\tau} f(s(t-\tau), i(t-\tau))$ represents the individuals who were exposed at time $t-\tau$ and survive to time t (with the death rate μ), that is, represents the transformation of the exposed to the infectious group $i(t)$. Since the variables $e(t)$ and $r(t)$ do not appear in the first and third equations of the above system, it is sufficient to consider the following model,

$$\begin{aligned}
s'(t) &= \mu - \mu s(t) - f(s(t), i(t)),\\
i'(t) &= e^{-\mu\tau} f(s(t-\tau), i(t-\tau)) - (\sigma+\mu) i(t).
\end{aligned} \tag{17}$$

Actually, let us define $s(t) = s(t),\ u(t) = i(t+\tau)$, then (17) is equivalent to

$$\begin{aligned}
s'(t) &= \mu - \mu s(t) - f(s(t), u(t-\tau)),\\
u'(t) &= e^{-\mu\tau} f(s(t), u(t-\tau)) - (\sigma+\mu) u(t).
\end{aligned} \tag{18}$$

The basic reproductive number of (18) is

$$R_0^* = \frac{e^{-\mu\tau}}{\sigma+\mu} \frac{\partial f(s_0, 0)}{\partial i},$$

which is a decreasing function on delay τ. Note that (18) is the analogous type delay differential equations as model (1), and only includes an additional survival rate $e^{-\mu\tau}$. The global analysis for (18) is the same as model (1), and it only needs in the first terms of Lyapunov functionals (4) and (7) for $s(t)$ to be multiplied by the term $e^{-\mu\tau}$. We would obtain analogous proposition for (17).

Proposition 1. (i) *If the function $f(s,i)$ is concave with respect to the variable i, then the disease-free equilibrium of (17) is globally asymptotically stable for any $\tau > 0$ when $R_0^* \leq 1$.*

(ii) *Suppose that the endemic equilibrium of (17) exists and the function $f(s,i)$ satisfies the conditions (5) and (6), then the endemic equilibrium is globally asymptotically stable for any $\tau > 0$ when $R_0^* > 1$.*

Remark 3: Since a plenty of delay differential equations models similar to (17) were established in population biology, such as prey-predator with constant birth rate and maturation delays, and chemostat models with delayed response in growth, we would also extend some results from (17). For instance, the Lypunov functionals (4) and (7) can

be applied to chemostat dynamical models with delayed response in growth (Wang and Wolkowicz [30]; EI-Owaidy and Moniem [8]),

$$\begin{aligned} s'(t) &= (s^0 - s)D - \sum_{j=1}^{n} x_j(t) f_j(s(t)), \\ x_j'(t) &= -D_j x_j(t) + e^{-D_j \tau_j} x_j(t-\tau_j) f_j(s(t-\tau_j)), \quad j = 1, 2, ..., n. \end{aligned} \tag{19}$$

where $s(t)$ denotes the concentration of the nutrient at time t; s^0 denotes the input nutrient concentration; D represents the washout rate of the nutrient; $x_j(t)$ represents the biomass of the jth population of microorganisms at time t; D_j represents the specific removal rate of species x_j; $f_j(s(t))$ indicates the consumption rate of nutrient by the jth species; the constant τ_j stands for the time delay in conversion of nutrient to biomass for the jth species. The term $e^{-D_j\tau_j} x_j(t-\tau_j) f_j(s(t-\tau_j))$ represents the biomass of those microorganisms in species x_j that consume nutrient at τ_j units of the time prior to time t and that survive in the chemostat. That is, the τ_j units of time express the time for the species j necessary to complete the nutrient conversion process.

Since system (19) is an n species competition model, and at most one competitor survives at a steady state, the analysis of global stability of the steady states would be reduced to the model with two variables which is similar to model (17).

3.3 *SEI model*

Now we consider the delays caused by vector and latent host described by

$$\begin{aligned} s'(t) &= \mu - \mu s(t) - f(s(t), i(t-\tau_1)), \\ e'(t) &= f(s(t), i(t-\tau_1)) - (\mu + \gamma) e(t), \\ i'(t) &= e^{-\mu\tau_2} \gamma e(t-\tau_2) - (\mu + \sigma) i(t). \end{aligned} \tag{20}$$

Here τ_1 represents the time delay in a vector and τ_2 represents the latent period in host. Note that (20) is a 3-dimensional system including two delays, and it is impossible to reduce any variable in (20). It is difficult to study directly the global properties of (20). By setting

$$S(t) = s(t), \quad E(t) = e(t-\tau_1), \quad I(t) = i(t-\tau_1),$$

system (20) is shown to be equivalent to

$$\begin{aligned} S'(t) &= \mu - \mu S(t) - f(S(t), I(t)), \\ E'(t) &= f(S(t-\tau_1), I(t-\tau_1)) - (\mu + \gamma) E(t), \\ I'(t) &= e^{-\mu\tau_2} \gamma E(t-\tau_2) - (\mu + \sigma) I(t). \end{aligned} \tag{21}$$

The delay differential equations (21) are equivalent to a virus infection model with two intercellular delays which was introduced by Nelson and Perelson [27], and Zhu and Zou [32]. Indeed, $S(t)$ corresponds to the uninfected cells, $E(t)$ to the infected cells which

produce free virus, and $I(t)$ to population of free virus [15]. Specially, time delays τ_1 and τ_2 equal to the periods for free virus to enter the target cell and the period for the infected cell to produce free viruses, respectively. The global properties of model (21) have been established by similar Lyapunov functionals as (7) in [13]. The results in [13] show that the global stability of two equilibria of (21) also depends only on the basic reproductive number.

In conclusion, in this paper we established the global properties of SIR, SIS, SEIR, SEI epidemiological models with delays and nonlinear incidence rate. Generally, the nonlinear incidence rate $f(s, i)$ satisfying with (5) and (6) does not destabilize two equilibria. Comparing with these models without delays, the results show that latency in a vector and the latent period in infected host have no impact for the global stability of equilibria, but long enough latency in host would reduce the value of the basic reproductive number, which can make the disease development slower and the disease has been controlled and disappeared. Mathematically, the Lyapunov functionals in this paper would be successfully applied in epidemiological model with nonlinear incidence and discrete delay, and even with distributed delay (McCluskey, [24, 25]). Finally we should mention that the delayed SIRS model (that is, the model of the removed individuals move back to the susceptible class because of loss of immunity) is not included in the class of (1). In fact, let us add the term $+\alpha r(t)$ in the right hand side of the first equation in (1) and $-\alpha r(t)$ in the third equation in (1). Here $1/\alpha$ is an average length of immunity. Since the new model also satisfies that $s(t) + i(t) + r(t) \to 1$ as $t \to +\infty$, the first equation is rewritten as

$$s'(t) = \bar{\mu} - \bar{\mu}s(t) - f(s(t), i(t-\tau)) - \alpha i(t),$$

where $\bar{\mu} = \mu + \alpha$. Note that the above equation includes new term $-\alpha i(t)$ compared with (1). It looks similar to SIS model (12). But the SIS model discussed in 3.1 does not include the recovered class, since the removed individuals move directly to susceptible class. The delay SIRS model cannot be rewritten as (13) for SIS model. To construct Lyapunov functionals for the delayed SIRS model is left as our future problem.

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