Global dynamics of a delayed epidemic model with latency and relapse*

Rui Xu

Institute of Applied Mathematics
Shijiazhuang Mechanical Engineering College
Shijiazhuang 050003, China
rxu88@yahoo.com.cn

Received: 18 June 2012 / **Revised:** 30 November 2012 / **Published online:** 18 April 2013

Abstract. A mathematical model describing the transmission dynamics of an infectious disease with an exposed (latent) period, relapse and a saturation incidence rate is investigated. By analyzing the corresponding characteristic equations, the local stability of a disease-free equilibrium and an endemic equilibrium is established. By using suitable Lyapunov functionals and LaSalle's invariance principle, it is proven that if the basic reproduction number is less than unity, the disease-free equilibrium is globally asymptotically stable and therefore the disease fades out; and if the basic reproduction number is greater than unity, the endemic equilibrium is globally asymptotically stable and the disease becomes endemic.

Keywords: epidemic model, latent period, relapse, saturation incidence, time delay, stability.

1 Introduction

Mathematical modelling has become important tools in analyzing the spread and control of infectious diseases. Recently, a great deal of attention has been paid to developing realistic mathematical models for the transmission dynamics of infectious diseases. There has been a large body of work on modelling epidemic models described by ordinary differential equations (see, for example, [1–9] and the references cited therein). In most of the literatures, it was frequently assumed that the disease incubation is negligible. In this case, once infected, each susceptible individual becomes infectious instantaneously and later recovers with a temporary acquired immunity. An epidemic model based on these assumptions is called SIR (susceptible, infectious, recovered) model. However, for some diseases, such as tuberculosis, influenza and measles, on adequate contact with an infective, a susceptible individual becomes exposed, that is, infected but not infective. This individual remains in the exposed class for a certain latent period before becoming infective (see, for example, [5, 10, 11]). Hence, it is realistic to introduce a time delay to describe the latent period. The resulting model is called SEIR (susceptible, exposed,

*This work was supported by the National Natural Science Foundation of China (No. 11071254) and the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry.

infectious, recovered) model (see, for example, [12, 13]). In [12], Gao et al. considered the following delayed SEIR epidemic model

$$\begin{aligned}
\dot{S}(t) &= \mu\big(1 - S(t)\big) - \beta S(t)I(t),\\
\dot{E}(t) &= \beta S(t)I(t) - \beta \mathrm{e}^{-\mu\tau} S(t-\tau)I(t-\tau) - \mu E(t),\\
\dot{I}(t) &= \beta \mathrm{e}^{-\mu\tau} S(t-\tau)I(t-\tau) - (\mu+\gamma)I(t),\\
\dot{R}(t) &= \gamma I(t) - \mu R(t),
\end{aligned} \tag{1}$$

where $S(t)$ represents the number of individuals who are susceptible to the disease, that is, who are not yet infected at time t; $I(t)$ represents the number of infected individuals who are infectious and are able to spread the disease by contact with susceptible individuals; $E(t)$ represents the number of exposed (in the latent period) individuals; and $R(t)$ represents the number of individuals who have been infected and temporarily recovered at time t. In (1), the parameters β, γ and μ are positive constants in which β is the contact rate, μ is the birth and death rate, γ is the removal rate. $\tau \geqslant 0$ represents a time delay describing the latent period of the disease, the term $\beta \mathrm{e}^{-\mu\tau} S(t-\tau)I(t-\tau)$ represents the individuals surviving in the latent period τ and becoming infective at time t.

In [14], van den Driessche and Zou pointed out that for some diseases, recovered individuals may relapse with reactivation of latent infection and revert back to the infective class. This recurrence of disease is an important feature of some animal and human diseases, for example, tuberculosis, including human and bovine [15, 16], and herpes [15, 17]. For human tuberculosis, incomplete treatment can lead to relapse, but relapse can also occur in patients who took a full course of treatment and were declared cured. Most tuberculosis in human adults (caused by Mycobacterium tuberculosis) in the USA results from reactivation of latent infection [15]. In [14], van den Driessche and Zou formulated and analyzed a model including a general exposed distribution and the possibility of relapse in which a constant exposed period was assumed, for the spread of bovine tuberculosis (Mycobacterium bovis) in a cattle herd. For this model with a general probability of remaining in the exposed class, the basic reproduction number was identified and its threshold property was discussed. A model for herpes with a general relapse distribution, but ignoring the exposed class, was formulated in [18] and shown to exhibit a threshold phenomenon.

Incidence plays an important role in the modelling of epidemic dynamics. It has been suggested by several authors that the disease transmission process may have a saturation incidence rate (see, for example, [4, 19, 20]). After studying the cholera epidemic spread in Bari in 1973, Capasso and Serio [4] introduced a saturated incidence rate $g(I)S$ into epidemic models, where $g(I)$ tends to a saturation level when I gets large, i.e., $g(I) = \beta I/(1+\alpha I)$, where βI measures the infection force of the disease and $1/(1+\alpha I)$ measures the inhibition effect from the behavioral change of the susceptible individuals when their number increases or from the crowding effect of the infective individuals. This incidence rate seems more reasonable than the bilinear incidence rate βIS, because it includes the behavioral change and crowding effect of the infective individuals and prevents the unboundedness of the contact rate by choosing suitable parameters.

Motivated by the works of Capasso and Serio [4], Gao et al. [12] and van den Driessche and Zou [14], in this paper, we consider the following delayed SEIR epidemic model with nonlinear incidence rate and relapse

$$\begin{aligned}
\dot{S}(t) &= A - \mu S(t) - \frac{\beta S(t) I(t)}{1+\alpha I(t)},\\
\dot{E}(t) &= \frac{\beta S(t) I(t)}{1+\alpha I(t)} - \mu E(t) - \frac{\beta \mathrm{e}^{-\mu\tau} S(t-\tau) I(t-\tau)}{1+\alpha I(t-\tau)},\\
\dot{I}(t) &= \frac{\beta \mathrm{e}^{-\mu\tau} S(t-\tau) I(t-\tau)}{1+\alpha I(t-\tau)} + \delta R(t) - (\mu+\gamma+\varepsilon) I(t),\\
\dot{R}(t) &= \gamma I(t) - (\mu+\delta) R(t),
\end{aligned} \tag{2}$$

where the parameters A, α, β, γ, μ, ε and τ are positive constants in which A is the constant recruitment rate into the population, μ is the natural death rate of the population, ε is the disease-induced death rate, β is the average number of adequate contacts of an infectious individuals per unit time, γ is the recovery rate of infectious individuals, τ is a time delay representing the latent period of the disease. The parameter δ is a nonnegative constant representing the rate at which an individual in the recovered class reverts to the infective class, and $\delta > 0$ implies that the recovered individuals would lose the immunity, $\delta = 0$ implies that the recovered individuals acquire permanent immunity.

The initial conditions for system (2) take the form

$$\begin{aligned}
&S(\theta) = \phi_1(\theta), \qquad E(\theta) = \phi_2(\theta), \qquad I(\theta) = \phi_3(\theta), \qquad R(\theta) = \phi_4(\theta),\\
&\phi_i(\theta) \geqslant 0, \quad \theta \in [-\tau, 0], \quad \phi_i(0) > 0, \quad i = 1,2,3,4,
\end{aligned} \tag{3}$$

where $(\phi_1(\theta), \phi_2(\theta), \phi_3(\theta), \phi_4(\theta)) \in C([-\tau, 0], \mathbb{R}^4_{+0})$, the Banach space of continuous functions mapping the interval $[-\tau, 0]$ into $\mathbb{R}^4_{+0}$, where $\mathbb{R}^4_{+0} = \{(x_1, x_2, x_3, x_4)\colon\ x_i \geqslant 0, i = 1,2,3,4\}$.

For continuity of the initial conditions, we require

$$E(0) = \int_{-\tau}^{0} \beta \mathrm{e}^{\mu\theta} \frac{\phi_1(\theta)\phi_3(\theta)}{1+\alpha\phi_3(\theta)}\,\mathrm{d}\theta. \tag{4}$$

It is well known by the fundamental theory of functional differential equations [21], system (2) has a unique solution $(S(t), E(t), I(t), R(t))$ satisfying the initial conditions (3) and (4). It is easy to show that all solutions of system (2) with initial conditions (3) and (4) are defined on $[0, +\infty)$ and remain positive for all $t \geqslant 0$.

The organization of this paper is as follows. In the next section, by analyzing the corresponding characteristic equations, the local stability of a disease-free equilibrium and an endemic equilibrium is established. In Section 3, by using suitable Lyapunov functionals and LaSalle's invariance principle, we prove that if the basic reproduction number is less than unity, the disease-free equilibrium is globally asymptotically stable; and if the basic reproduction number is greater than unity, the endemic equilibrium is globally asymptotically stable. A brief discussion is given in Section 4 to conclude this work.

2 Local stability

In this section, we study the local stability of a disease-free equilibrium and an endemic equilibrium of system (2) by analyzing the corresponding characteristic equations, respectively.

System (2) always has a disease-free equilibrium $E_1(A/\mu, 0, 0, 0)$. Using a similar argument as that in [14] one may obtain the basic reproduction number for system (2) as

$$\mathscr{R}_0 = \frac{A\beta \mathrm{e}^{-\mu\tau}}{\mu(\mu+\gamma+\varepsilon-\gamma\delta/(\mu+\delta))}.$$

$\mathscr{R}_0$ is the average number of secondary transmissions of a single infectious individual in a fully susceptible population. It is easy to show that if $\mathscr{R}_0 > 1$, system (2) has a unique endemic equilibrium $E_2(S^*, E^*, I^*, R^*)$, where

$$\begin{aligned} S^* &= \frac{A}{\mu\mathscr{R}_0}(1+\alpha I^*), \qquad E^* = \frac{\beta(1-\mathrm{e}^{-\mu\tau})S^*I^*}{\mu(1+\alpha I^*)}, \\ I^* &= \frac{\mu}{\alpha\mu+\beta}(\mathscr{R}_0-1), \qquad R^* = \frac{\gamma}{\mu+\delta}I^*. \end{aligned} \tag{5}$$

The characteristic equation of system (2) at the disease-free equilibrium $E_1(A/\mu, 0, 0, 0)$ takes the form

$$(\lambda+\mu)^2\big[\lambda^2 + P_1(\tau)\lambda + P_0(\tau) + \big(Q_1(\tau)\lambda + Q_0(\tau)\big)\mathrm{e}^{-\lambda\tau}\big] = 0, \tag{6}$$

where

$$\begin{aligned} P_0(\lambda) &= (\mu+\delta)(\mu+\gamma+\varepsilon) - \gamma\delta, \qquad P_1(\lambda) = \mu+\delta+\mu+\gamma+\varepsilon, \\ Q_0(\lambda) &= -\frac{A\beta\mathrm{e}^{-\mu\tau}(\mu+\delta)}{\mu}, \qquad Q_1(\lambda) = -\frac{A\beta\mathrm{e}^{-\mu\tau}}{\mu}. \end{aligned}$$

Clearly, Eq. (6) always has a negative real root $\lambda = -\mu$. Other roots of Eq. (6) are determined by the following equation:

$$\lambda^2 + P_1(\tau)\lambda + P_0(\tau) + \big(Q_1(\tau)\lambda + Q_0(\tau)\big)\mathrm{e}^{-\lambda\tau} = 0. \tag{7}$$

When $\tau = 0$, Eq. (7) becomes

$$\lambda^2 + \big(P_1(0) + Q_1(0)\big)\lambda + P_0(0) + Q_0(0) = 0. \tag{8}$$

By calculation we derive that

$$\begin{aligned} P_0(0) + Q_0(0) &= (\mu+\delta)\left(\mu+\gamma+\varepsilon-\frac{\gamma\delta}{\mu+\delta}\right)(1-\mathscr{R}_0), \\ P_1(0) + Q_1(0) &= \mu+\delta+\frac{\gamma\delta}{\mu+\delta} + \left(\mu+\gamma+\varepsilon-\frac{\gamma\delta}{\mu+\delta}\right)(1-\mathscr{R}_0). \end{aligned}$$

Hence, if $\mathscr{R}_0 < 1$, the equilibrium E_1 is locally asymptotically stable when $\tau = 0$.

If $\mathrm{i}\omega(\omega > 0)$ is a solution of (7), separating real and imaginary parts, it follows that

$$\begin{aligned} \omega^2 - P_0(\tau) &= Q_0(\tau)\cos\omega\tau + Q_1(\tau)\omega\sin\omega\tau, \\ P_1(\tau)\omega &= Q_0(\tau)\sin\omega\tau - Q_1(\tau)\omega\cos\omega\tau. \end{aligned} \tag{9}$$

Squaring and adding the two equations of (9), we obtain that

$$\omega^4 + \big(P_1^2(\tau) - 2P_0(\tau) - Q_1^2(\tau)\big)\omega^2 + P_0^2(\tau) - Q_0^2(\tau) = 0. \tag{10}$$

Clearly, $P_0^2(\tau) - Q_0^2(\tau) > 0$. A direct calculation shows that if $\mathscr{R}_0 < 1$, then

$$P_1^2(\tau) - 2P_0(\tau) - Q_1^2(\tau) = (\mu+\delta)^2 + 2\gamma\delta + (\mu+\gamma+\varepsilon)^2 - \left(\frac{A\beta\mathrm{e}^{-\mu\tau}}{\mu}\right)^2 > 0.$$

Hence, if $\mathscr{R}_0 < 1$, Eq. (10) has no positive roots. Noting that the equilibrium E_1 is locally asymptotically stable when $\tau = 0$, by the general theory on characteristic equations of delay differential equations from [22, Thm. 4.1] we see that if $\mathscr{R}_0 < 1$, E_1 is locally asymptotically stable.

Let

$$f_1(\lambda) = \lambda^2 + P_1(\tau)\lambda + P_0(\tau) + \big(Q_1(\tau)\lambda + Q_0(\tau)\big)\mathrm{e}^{-\lambda\tau}.$$

If $\mathscr{R}_0 > 1$, it is easy to show that, for λ real,

$$f_1(0) = (\mu+\delta)\left(\mu+\gamma+\varepsilon - \frac{\gamma\delta}{\mu+\delta}\right)(1-\mathscr{R}_0) < 0, \qquad \lim_{\lambda\to+\infty} f_1(\lambda) = +\infty.$$

Hence, Eq. (7) has a positive real root, which yields that the disease-free equilibrium E_1 is unstable if $\mathscr{R}_0 > 1$.

The characteristic equation of system (2) at the endemic equilibrium $E_2(S^*, E^*, I^*, R^*)$ is of the form

$$(\lambda+\mu)\big[\lambda^3 + p_2(\tau)\lambda^2 + p_1(\tau)\lambda + p_0(\tau) + \big(q_2(\tau)\lambda^2 + q_1(\tau)\lambda + q_0(\tau)\big)\mathrm{e}^{-\lambda\tau}\big] = 0, \tag{11}$$

where

$$\begin{aligned} p_0(\tau) &= \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)\big[(\mu+\delta)(\mu+\gamma+\varepsilon) - \gamma\delta\big], \\ p_1(\tau) &= \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)(\mu+\gamma+\varepsilon+\mu+\delta) + (\mu+\delta)(\mu+\gamma+\varepsilon) - \gamma\delta, \\ p_2(\tau) &= \mu + \frac{\beta I^*}{1+\alpha I^*} + \mu + \gamma + \varepsilon + \mu + \delta, \\ q_0(\tau) &= -\big[(\mu+\delta)(\mu+\gamma+\varepsilon) - \gamma\delta\big]\frac{\mu}{1+\alpha I^*}, \\ q_1(\tau) &= -\left(\mu+\gamma+\varepsilon - \frac{\gamma\delta}{\mu+\delta}\right)(\mu+\mu+\delta)\frac{1}{1+\alpha I^*}, \\ q_2(\tau) &= -\left(\mu+\gamma+\varepsilon - \frac{\gamma\delta}{\mu+\delta}\right)\frac{1}{1+\alpha I^*}. \end{aligned}$$

Clearly, Eq. (11) always has a negative real root $\lambda = -\mu$. Other roots of Eq. (11) are determined by the following equation:

$$\lambda^3 + p_2(\tau)\lambda^2 + p_1(\tau)\lambda + p_0(\tau) + \big(q_2(\tau)\lambda^2 + q_1(\tau)\lambda + q_0(\tau)\big)\mathrm{e}^{-\lambda\tau} = 0. \tag{12}$$

When $\tau = 0$, Eq. (12) becomes

$$\lambda^3 + \big(p_2(0) + q_2(0)\big)\lambda^2 + \big(p_1(0) + q_1(0)\big)\lambda + p_0(0) + q_0(0) = 0. \tag{13}$$

If $\mathscr{R}_0 > 1$, by calculation we derive that

$$\begin{aligned}
&p_0(\tau) + q_0(\tau) = \frac{(\mu\alpha + \beta)I^*}{1 + \alpha I^*}\big[(\mu + \delta)(\mu + \gamma + \varepsilon) - \gamma\delta\big] > 0,\\
&p_1(\tau) + q_1(\tau)\\
&\quad = \left(\mu + \frac{\beta I^*}{1 + \alpha I^*}\right)(\mu + \gamma + \varepsilon + \mu + \delta) - \mu\left(\mu + \gamma + \varepsilon - \frac{\gamma\delta}{\mu + \delta}\right)\frac{1}{1 + \alpha I^*}\\
&\qquad + \frac{\alpha I^*}{1 + \alpha I^*}\big[(\mu + \delta)(\mu + \gamma + \varepsilon) - \gamma\delta\big] > 0,\\
&p_2(\tau) + q_2(\tau) = \mu + \mu + \delta + \frac{\gamma\delta}{\mu + \delta}\frac{1}{1 + \alpha I^*} + \big[\alpha(\mu + \gamma + \varepsilon) + \beta\big]\frac{I^*}{1 + \alpha I^*} > 0,
\end{aligned}$$

and

$$\begin{aligned}
&\big(p_1(\tau) + q_1(\tau)\big)\big(p_2(\tau) + q_2(\tau)\big) - \big(p_0(\tau) + q_0(\tau)\big)\\
&\quad = \left\{\left(\mu + \frac{\beta I^*}{1 + \alpha I^*}\right)(\mu + \gamma + \varepsilon + \mu + \delta) - \mu\left(\mu + \gamma + \varepsilon - \frac{\gamma\delta}{\mu + \delta}\right)\frac{1}{1 + \alpha I^*}\right.\\
&\qquad \left. + \frac{\alpha I^*}{1 + \alpha I^*}\big[(\mu + \delta)(\mu + \gamma + \varepsilon) - \gamma\delta\big]\right\}\\
&\qquad \times \left\{\frac{(\alpha(\mu + \gamma + \varepsilon) + \beta)I^*}{1 + \alpha I^*} + \frac{\gamma\delta}{\mu + \delta}\frac{1}{1 + \alpha I^*}\right\}\\
&\qquad + (\mu + \mu + \delta)\left[\mu(\mu + \gamma + \varepsilon + \mu + \delta) - \mu\left(\mu + \gamma + \varepsilon - \frac{\gamma\delta}{\mu + \delta}\right)\frac{1}{1 + \alpha I^*}\right]\\
&\qquad + (\mu + \mu + \delta)\left\{\frac{\beta I^*}{1 + \alpha I^*}(\mu + \gamma + \varepsilon + \mu + \delta)\right.\\
&\qquad \left. + \frac{\alpha I^*}{1 + \alpha I^*}\big[(\mu + \delta)(\mu + \gamma + \varepsilon) - \gamma\delta\big]\right\}\\
&\qquad - \frac{(\mu\alpha + \beta)I^*}{1 + \alpha I^*}\big[(\mu + \delta)(\mu + \gamma + \varepsilon) - \gamma\delta\big] > 0.
\end{aligned}$$

Therefore, if $\mathscr{R}_0 > 1$, the endemic equilibrium E_2 of system (2) is locally asymptotically stable when $\tau = 0$.

If $\mathrm{i}\omega(\omega > 0)$ is a solution of (12), separating real and imaginary parts, it follows that

$$\begin{aligned}
&p_1(\tau)\omega - \omega^3 = \big(q_0(\tau) - q_2(\tau)\omega^2\big)\sin\omega\tau - q_1(\tau)\omega\cos\omega\tau,\\
&p_2(\tau)\omega^2 - p_0(\tau) = \big(q_0(\tau) - q_2(\tau)\omega^2\big)\cos\omega\tau + q_1(\tau)\omega\sin\omega\tau.
\end{aligned} \tag{14}$$

Squaring and adding the two equations of (14), we obtain that

$$\omega^6 + \big(p_2^2(\tau) - 2p_1(\tau) - q_2^2(\tau)\big)\omega^4 + \big(p_1^2(\tau) - 2p_0(\tau)p_2(\tau) + 2q_0(\tau)q_2(\tau) - q_1^2(\tau)\big)\omega^2 + p_0^2(\tau) - q_0^2(\tau) = 0. \quad (15)$$

Clearly, $p_0^2(\tau) - q_0^2(\tau) > 0$. By direct calculations, it is easy to show that

$$\begin{aligned} &p_2^2(\tau) - 2p_1(\tau) - q_2^2(\tau) \\ &\quad = \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)^2 + (\mu+\delta)^2 + 2\gamma\delta + (\mu+\gamma+\varepsilon)^2 \\ &\qquad - \left(\mu + \gamma + \varepsilon - \frac{\gamma\delta}{\mu+\delta}\right)^2 \frac{1}{(1+\alpha I^*)^2} > 0, \end{aligned}$$

and

$$\begin{aligned} &p_1^2(\tau) - 2p_0(\tau)p_2(\tau) + 2q_0(\tau)q_2(\tau) - q_1^2(\tau) \\ &\quad = \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)^2 (\mu+\delta)^2 + 2\gamma\delta\left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)^2 \\ &\qquad + (\mu+\delta)^2\left(\mu+\gamma+\varepsilon - \frac{\gamma\delta}{\mu+\delta}\right)^2 \frac{\alpha I^*(2+\alpha I^*)}{(1+\alpha I^*)^2} \\ &\qquad + \left(\mu + \frac{\beta I^*}{1+\alpha I^*}\right)^2 (\mu+\gamma+\varepsilon)^2 \\ &\qquad - \left(\mu + \gamma + \varepsilon - \frac{\gamma\delta}{\mu+\delta}\right)^2 \frac{\mu^2}{(1+\alpha I^*)^2} > 0. \end{aligned}$$

Hence, if $\mathscr{R}_0 > 1$, Eq. (15) has no positive roots. Noting that the equilibrium E_2 is locally asymptotically stable when $\tau = 0$, by the general theory on characteristic equations of delay differential equations from [22, Thm. 4.1], we see that if $\mathscr{R}_0 > 1$, the endemic equilibrium E_2 of system (2) exists and is locally asymptotically stable.

We therefore obtain the following results.

Theorem 1. *For system* (2)*, we have*:

(i) *If $\mathscr{R}_0 < 1$, the disease-free equilibrium $E_1(A/\mu, 0, 0, 0)$ is locally asymptotically stable*; *if $\mathscr{R}_0 > 1$, E_1 is unstable.*

(ii) *If $\mathscr{R}_0 > 1$, system* (2) *has a unique endemic equilibrium $E_2(S^*, E^*, I^*, R^*)$ which is locally asymptotically stable.*

3 Global stability

In this section, we are concerned with the global stability of the disease-free equilibrium $E_1(A/\mu, 0, 0, 0)$ and the endemic equilibrium $E_2(S^*, E^*, I^*, R^*)$ of system (2). The technique of the proofs is to use suitable Lyapunov functionals and LaSalle's invariance principle.

We note that the variable $E(t)$ does not appear in the first, the third and the fourth equations of system (2). Therefore, we first consider the following subsystem of system (2):

$$\begin{aligned}
\dot{S}(t) &= A - \mu S(t) - \frac{\beta S(t)I(t)}{1+\alpha I(t)},\\
\dot{I}(t) &= \frac{\beta \mathrm{e}^{-\mu\tau} S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)} + \delta R(t) - (\mu+\gamma+\varepsilon)I(t),\\
\dot{R}(t) &= \gamma I(t) - (\mu+\delta)R(t).
\end{aligned} \tag{16}$$

Clearly, system (16) always has a semi-trivial equilibrium $E_1^0(A/\mu, 0, 0)$. Further, if $\mathscr{R}_0 > 1$, system (16) has a unique positive equilibrium $E_2^0(S^*, I^*, R^*)$, where S^*, I^* and R^* are determined in (5). From Section 2, we see that if $\mathscr{R}_0 < 1$, the equilibrium E_1^0 is locally asymptotically stable; and if $\mathscr{R}_0 > 1$, E_1^0 is unstable and the positive equilibrium E_2^0 is locally asymptotically stable.

We now first give a result on the global stability of the semi-trivial equilibrium E_1^0 of system (16).

Theorem 2. *If $\mathscr{R}_0 < 1$, the semi-trivial equilibrium $E_1^0(A/\mu, 0, 0)$ of system* (16) *is globally asymptotically stable.*

Proof. Let $(S(t), I(t), R(t))$ be any positive solution of system (16) with initial conditions (3). Denote $S_0 = A/\mu$. Define

$$V_{11}(t) = S - S_0 - S_0 \ln \frac{S}{S_0} + \mathrm{e}^{\mu\tau} I + \frac{\delta \mathrm{e}^{\mu\tau}}{\mu+\delta} R.$$

Calculating the derivative of $V_{11}(t)$ along positive solutions of system (16), it follows that

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} V_{11}(t) &= \left(1 - \frac{S_0}{S(t)}\right)\left[A - \mu S(t) - \frac{\beta S(t)I(t)}{1+\alpha I(t)}\right]\\
&\quad + \mathrm{e}^{\mu\tau}\left[\frac{\beta \mathrm{e}^{-\mu\tau} S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)} + \delta R(t) - (\mu+\gamma+\varepsilon)I(t)\right]\\
&\quad + \frac{\delta \mathrm{e}^{\mu\tau}}{\mu+\delta}\big[\gamma I(t) - (\mu+\delta)R(t)\big]\\
&= \left(1 - \frac{S_0}{S(t)}\right)\left[A - \mu S(t) - \frac{\beta S(t)I(t)}{1+\alpha I(t)}\right] + \frac{\beta S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)}\\
&\quad - \mathrm{e}^{\mu\tau}\left[\mu+\gamma+\varepsilon - \frac{\gamma\delta}{\mu+\delta}\right] I(t).
\end{aligned} \tag{17}$$

On substituting $A = \mu S_0$ into (17), we derive that

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} V_{11}(t) &= \left(1 - \frac{S_0}{S(t)}\right)\big[-\mu(S(t) - S_0)\big] - \frac{\beta S(t)I(t)}{1+\alpha I(t)} + \frac{\beta S_0 I(t)}{1+\alpha I(t)}\\
&\quad + \frac{\beta S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)} - \mathrm{e}^{\mu\tau}\left[\mu+\gamma+\varepsilon - \frac{\gamma\delta}{\mu+\delta}\right] I(t).
\end{aligned} \tag{18}$$

Define

$$V_1(t) = V_{11}(t) + \int_{t-\tau}^{t} \frac{\beta S(u)I(u)}{1+\alpha I(u)}\,\mathrm{d}u. \tag{19}$$

It then follows from (18) and (19) that

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}V_1(t) &= \left(1-\frac{S_0}{S(t)}\right)\left[-\mu(S(t)-S_0)\right] + \frac{\beta S_0 I(t)}{1+\alpha I(t)} \\ &\quad - \mathrm{e}^{\mu\tau}\left[\mu+\gamma+\varepsilon-\frac{\gamma\delta}{\mu+\delta}\right]I(t) \\ &= \left(1-\frac{S_0}{S(t)}\right)\left[-\mu(S(t)-S_0)\right] + \frac{\beta S_0 I(t)}{1+\alpha I(t)} \\ &\quad - \beta S_0 I(t) + \beta S_0 I(t) - \mathrm{e}^{\mu\tau}\left[\mu+\gamma+\varepsilon-\frac{\gamma\delta}{\mu+\delta}\right]I(t) \\ &= -\mu\frac{(S(t)-S_0)^2}{S(t)} - \frac{\alpha\beta S_0 I^2(t)}{1+\alpha I(t)} \\ &\quad + \mathrm{e}^{\mu\tau}\left(\mu+\gamma+\varepsilon-\frac{\gamma\delta}{\mu+\delta}\right)(\mathscr{R}_0-1)I(t). \end{aligned} \tag{20}$$

Clearly, if $\mathscr{R}_0 < 1$, then we obtain from (20) that $V_1'(t) \leqslant 0$. By Theorem 5.3.1 in [21], solutions limit to $\mathcal{M}$, the largest invariant subset of $\{V_1'(t) = 0\}$. Clearly, it follows from (20) that $V_1'(t) = 0$ if and only if $S = S_0$, $I = 0$. Noting that $\mathcal{M}$ is invariant, for each element in $\mathcal{M}$, we have $I = 0$, $I'(t) = 0$. We therefore obtain from the second equation of system (16) that

$$0 = I'(t) = \delta R(t),$$

which leads to $R = 0$. Hence, $V_1'(t) = 0$ if and only if $(S, I, R) = (S_0, 0, 0)$. Note that if $\mathscr{R}_0 < 1$, the equilibrium E_1^0 is locally asymptotically stable. Therefore, the global asymptotic stability of $E_1^0(A/\mu, 0, 0)$ follows from LaSalle's invariance principle for delay differential systems (see, for example, [23]). This completes the proof. □

Corollary 1. *If $\mathscr{R}_0 < 1$, the disease-free equilibrium $E_1(A/\mu, 0, 0, 0)$ of system* (2) *is globally asymptotically stable in the interior of $\mathbb{R}_+^4$ and the disease dies out.*

Proof. Let $(S(t), E(t), I(t), R(t))$ be a positive solution of system (2) with initial conditions (3) and (4).

It follows from the second equation of system (2) and (4) that

$$E(t) = \int_{t-\tau}^{t} \frac{\beta I(u)S(u)}{1+\alpha I(u)}\mathrm{e}^{-\mu(t-u)}\,\mathrm{d}u. \tag{21}$$

From Theorem 2, we see that if $\mathscr{R}_0 < 1$, then

$$\lim_{t\to+\infty} S(t) = \frac{A}{\mu}, \qquad \lim_{t\to+\infty} I(t) = 0, \qquad \lim_{t\to+\infty} R(t) = 0. \tag{22}$$

By l'Hôspital's rule, we derive from (21) and (22) that

$$\lim_{t\to+\infty} E(t) = \lim_{t\to+\infty} \int_{t-\tau}^{t} \frac{\beta I(u)S(u)}{1+\alpha I(u)} \mathrm{e}^{-\mu(t-u)}\,\mathrm{d}u$$
$$= \lim_{t\to+\infty} \left[\frac{\beta I(t)S(t)}{1+\alpha I(t)} - \frac{\beta I(t-\tau)S(t-\tau)}{1+\alpha I(t-\tau)}\mathrm{e}^{-\mu\tau}\right] = 0. \tag{23}$$

Noting that if $\mathscr{R}_0 < 1$, the disease-free equilibrium $E_1(A/\mu, 0, 0, 0)$ of system (2) is locally asymptotically stable, we conclude that E_1 is globally asymptotically stable. This completes the proof. □

We are now in a position to study the global stability of the endemic equilibrium E_2 of system (2). To this end, we first consider the global stability of the positive equilibrium $E_2^0(S^*, I^*, R^*)$ of system (16).

Theorem 3. *If $\mathscr{R}_0 > 1$, then the positive equilibrium $E_2^0(S^*, I^*, R^*)$ of system* (16) *is globally asymptotically stable.*

Proof. Let $(S(t), I(t), R(t))$ be a positive solution of system (16) with initial conditions (3).

Define

$$V_{21}(t) = S - S^* - S^* \ln\frac{S}{S^*} + k_1\left(I - I^* - I^* \ln\frac{I}{I^*}\right) + k_2\left(R - R^* - R^* \ln\frac{R}{R^*}\right),$$

here k_1 and k_2 are positive constants to be determined later.

Calculating the derivative of $V_{21}(t)$ along positive solutions of system (16), we derive that

$$\frac{\mathrm{d}}{\mathrm{d}t}V_{21}(t) = \left(1-\frac{S^*}{S}\right)\left[A - \mu S(t) - \frac{\beta S(t)I(t)}{1+\alpha I(t)}\right]$$
$$+ k_1\left(1-\frac{I^*}{I}\right)\left[\frac{\beta\mathrm{e}^{-\mu\tau}S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)} + \delta R(t) - (\mu+\gamma+\varepsilon)I(t)\right]$$
$$+ k_2\left(1-\frac{R^*}{R}\right)\big[\gamma I(t) - (\mu+\delta)R(t)\big]. \tag{24}$$

On substituting $A = \mu S^* + \beta S^* I^*/(1+\alpha I^*)$ into (24), it follows that

$$\frac{\mathrm{d}}{\mathrm{d}t}V_{21}(t) = \left(1-\frac{S^*}{S(t)}\right)\left[-\mu(S(t)-S^*) + \frac{\beta S^* I^*}{1+\alpha I^*}\right] - \frac{\beta S(t)I(t)}{1+\alpha I(t)} + \frac{\beta S^* I(t)}{1+\alpha I(t)}$$
$$+ k_1\left[\frac{\beta\mathrm{e}^{-\mu\tau}S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)} + \delta R(t) - (\mu+\gamma+\varepsilon)I(t)\right]$$
$$+ k_1\left[-\frac{\beta\mathrm{e}^{-\mu\tau}I^*S(t-\tau)I(t-\tau)}{I(t)(1+\alpha I(t-\tau))} - \delta I^*\frac{R(t)}{I(t)} + (\mu+\gamma+\varepsilon)I^*\right]$$
$$+ k_2\left[\gamma I(t) - (\mu+\delta)R(t) - \gamma R^*\frac{I(t)}{R(t)} + (\mu+\delta)R^*\right]. \tag{25}$$

Letting

$$k_1 = \mathrm{e}^{\mu\tau}, \qquad k_2 = \frac{\delta \mathrm{e}^{\mu\tau}}{\mu+\delta},$$

we derive from (25) that

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}V_{21}(t) &= \left(1-\frac{S^*}{S}\right)\left[-\mu(S(t)-S^*)+\frac{\beta S^*I^*}{1+\alpha I^*}\right]-\frac{\beta S(t)I(t)}{1+\alpha I(t)}+\frac{\beta S^*I(t)}{1+\alpha I(t)}\\ &\quad+\frac{\beta S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)}-(\mu+\gamma+\varepsilon)\mathrm{e}^{\mu\tau}I(t)\\ &\quad-\frac{\beta I^*S(t-\tau)I(t-\tau)}{I(t)(1+\alpha I(t-\tau))}-\delta\mathrm{e}^{\mu\tau}I^*\frac{R(t)}{I(t)}+(\mu+\gamma+\varepsilon)\mathrm{e}^{\mu\tau}I^*\\ &\quad+k_2\left[\gamma I(t)-\gamma R^*\frac{I(t)}{R(t)}+(\mu+\delta)R^*\right]. \end{aligned} \tag{26}$$

Define

$$V_2(t) = V_{21}(t) + V_{22}(t), \tag{27}$$

where

$$V_{22}(t) = \beta\int_{t-\tau}^{t}\left[\frac{S(u)I(u)}{1+\alpha I(u)}-\frac{S^*I^*}{1+\alpha I^*}-\frac{S^*I^*}{1+\alpha I^*}\ln\frac{(1+\alpha I^*)S(u)I(u)}{S^*I^*(1+\alpha I(u))}\right]\mathrm{d}u. \tag{28}$$

A direct calculation shows that

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}V_{22}(t) &= \frac{\beta S(t)I(t)}{1+\alpha I(t)}-\frac{\beta S^*I^*}{1+\alpha I^*}\ln\frac{(1+\alpha I^*)S(t)I(t)}{S^*I^*(1+\alpha I(t))}\\ &\quad-\frac{\beta S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)}+\frac{\beta S^*I^*}{1+\alpha I^*}\ln\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I^*(1+\alpha I(t-\tau))}. \end{aligned} \tag{29}$$

It then follows from (26)–(29) that

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}V_2(t) &= \left(1-\frac{S^*}{S}\right)\left[-\mu(S(t)-S^*)+\frac{\beta S^*I^*}{1+\alpha I^*}\right]\\ &\quad+\frac{\beta S^*I^*}{1+\alpha I^*}\frac{(1+\alpha I^*)I(t)}{I^*(1+\alpha I(t))}-(\mu+\gamma+\varepsilon)\mathrm{e}^{\mu\tau}I^*\frac{I(t)}{I^*}\\ &\quad-\frac{\beta S^*I^*}{1+\alpha I^*}\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}-\delta\mathrm{e}^{\mu\tau}R^*\frac{I^*}{R^*}\frac{R(t)}{I(t)}\\ &\quad+(\mu+\gamma+\varepsilon)\mathrm{e}^{\mu\tau}I^*+k_2\gamma I^*\frac{I(t)}{I^*}-k_2\gamma I^*\frac{R^*}{I^*}\frac{I(t)}{R(t)}+k_2(\mu+\delta)R^*\\ &\quad+\frac{\beta S^*I^*}{1+\alpha I^*}\ln\frac{S(t-\tau)I(t-\tau)(1+\alpha I(t))}{S(t)I(t)(1+\alpha I(t-\tau))}. \end{aligned} \tag{30}$$

Noting that

$$k_2(\mu+\delta)R^* = k_2\gamma I^* = (\mu+\gamma+\varepsilon)\mathrm{e}^{\mu\tau}I^* - \frac{\beta S^*I^*}{1+\alpha I^*}, \tag{31}$$

we derive from (30) and (31) that

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}V_2(t) &= \left(1-\frac{S^*}{S}\right)\left[-\mu(S(t)-S^*)+\frac{\beta S^*I^*}{1+\alpha I^*}\right]+\frac{\beta S^*I^*}{1+\alpha I^*}\frac{(1+\alpha I^*)I(t)}{I^*(1+\alpha I(t))}\\ &\quad-\frac{\beta S^*I^*}{1+\alpha I^*}\frac{I(t)}{I^*}-\frac{\beta S^*I^*}{1+\alpha I^*}\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}\\ &\quad-k_2\gamma I^*\frac{I^*}{R^*}\frac{R(t)}{I(t)}+k_2\gamma I^*+\frac{\beta S^*I^*}{1+\alpha I^*}-k_2\gamma I^*\frac{R^*}{I^*}\frac{I(t)}{R(t)}+k_2\gamma I^*\\ &\quad+\frac{\beta S^*I^*}{1+\alpha I^*}\ln\frac{S(t-\tau)I(t-\tau)(1+\alpha I(t))}{S(t)I(t)(1+\alpha I(t-\tau))}.\end{aligned} \tag{32}$$

Note that

$$\begin{aligned}&\ln\frac{S(t-\tau)I(t-\tau)(1+\alpha I(t))}{S(t)I(t)(1+\alpha I(t-\tau))}\\ &\quad=\ln\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}+\ln\frac{S^*}{S(t)}+\ln\frac{1+\alpha I(t)}{1+\alpha I^*}.\end{aligned} \tag{33}$$

It therefore follows from (32) and (33) that

$$\begin{aligned}&\frac{\mathrm{d}}{\mathrm{d}t}V_2(t)\\ &\quad=-\mu\frac{(S(t)-S^*)^2}{S(t)}-\frac{\beta S^*I^*}{1+\alpha I^*}\left(\frac{S^*}{S}-1-\ln\frac{S^*}{S}\right)\\ &\qquad-\frac{\beta S^*I^*}{1+\alpha I^*}\left[\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}-1-\ln\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}\right]\\ &\qquad-\frac{\beta S^*I^*}{1+\alpha I^*}\left[\frac{1+\alpha I(t)}{1+\alpha I^*}-1-\ln\frac{1+\alpha I(t)}{1+\alpha I^*}\right]+k_2\gamma I^*\left[2-\frac{I^*}{R^*}\frac{R(t)}{I(t)}-\frac{R^*}{I^*}\frac{I(t)}{R(t)}\right]\\ &\qquad+\frac{\beta S^*I^*}{1+\alpha I^*}\left[\frac{1+\alpha I(t)}{1+\alpha I^*}-1-\frac{I(t)}{I^*}+\frac{(1+\alpha I^*)I(t)}{I^*(1+\alpha I(t))}\right]\\ &\quad=-\mu\frac{(S(t)-S^*)^2}{S(t)}-\frac{\beta S^*I^*}{1+\alpha I^*}\left(\frac{S^*}{S}-1-\ln\frac{S^*}{S}\right)\\ &\qquad-\frac{\beta S^*I^*}{1+\alpha I^*}\left[\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}-1-\ln\frac{(1+\alpha I^*)S(t-\tau)I(t-\tau)}{S^*I(t)(1+\alpha I(t-\tau))}\right]\\ &\qquad-\frac{\beta S^*I^*}{1+\alpha I^*}\left[\frac{1+\alpha I(t)}{1+\alpha I^*}-1-\ln\frac{1+\alpha I(t)}{1+\alpha I^*}\right]\\ &\qquad+\frac{\gamma\delta\mathrm{e}^{\mu\tau}}{\mu+\delta}I^*\left[2-\frac{I^*}{R^*}\frac{R(t)}{I(t)}-\frac{R^*}{I^*}\frac{I(t)}{R(t)}\right]-\frac{\alpha\beta S^*(I-I^*)^2}{(1+\alpha I^*)^2(1+\alpha I(t))}.\end{aligned} \tag{34}$$

Noting that if $\mathscr{R}_0 > 1$, $S^*, I^*, R^* > 0$, we have that $V_2'(t) \leqslant 0$. By Theorem 5.3.1 in [21], solutions limit to $\mathcal{M}$, the largest invariant subset of $\{V_2'(t) = 0\}$. It is readily seen from (34) that $V_2'(t) = 0$ if and only if $S = S^*$, $I = I^*$, $R = R^*$. Note that if $\mathscr{R}_0 > 1$, the equilibrium E_2^0 is locally asymptotically stable. Using a similar argument as that in the proof of Theorem 2 and by LaSalle's invariance principle, the global asymptotic stability of the equilibrium E_2^0 follows. This completes the proof. □

Using a similar argument as that in the proof of Corollary 1, one can obtain the following result.

Corollary 2. *If $\mathscr{R}_0 > 1$, then the endemic equilibrium $E_2(S^*, E^*, I^*, R^*)$ of system* (2) *is globally asymptotically stable in the interior of $\mathbb{R}_+^4$ and the disease becomes endemic.*

4 Discussion

In this paper, we have formulated an SEIR epidemic model with disease relapse, a saturation incidence and a time delay describing the latent period of the disease. The global dynamics of system (2) has been completely established. By means of suitable Lyapunov functionals and the LaSalle invariance principle, we have shown that if the basic reproduction number $\mathscr{R}_0$ is less than unity, the disease-free equilibrium of system (2) is globally asymptotically stable and the disease dies out while the endemic equilibrium is not feasible; and if the basic reproduction number $\mathscr{R}_0$ is greater than unity, the endemic equilibrium of system (2) is globally asymptotically stable and therefore the disease becomes endemic. To control the disease, a strategy should reduce the reproduction number to below one. From the expression of $\mathscr{R}_0$, we see that latency period τ and the constant rate δ at which an individual in the recovered class reverts to the infective class do affect the value of the basic reproduction number. Clearly, if τ increases or δ decreases, the basic reproduction number decreases. On the other hand, the contact rate β is also an important parameter for the basic reproduction number. Decreasing the contact rate is helpful for the decrease of the value of $\mathscr{R}_0$.

References

1. E. Beretta, T. Hara, W. Ma, Y. Takeuchi, Global asymptotic stability of an SIR epidemic model with distributed time delay, *Nonlinear Anal., Theory Methods Appl.* **47**:4107–4115, 2001.

2. E. Beretta, Y. Takeuchi, Global stability of an SIR epidemic model with time delays, *J. Math. Biol.* **33**:250–260, 1995.

3. E. Beretta, Y. Takeuchi, Convergence results in SIR epidemic model with varying population sizes, *Nonlinear Anal., Theory Methods Appl.* **28**:1909–1921, 1997.

4. V. Capasso, G. Serio, A generalization of the Kermack–Mckendrick deterministic epidemic model, *Math. Biosci.* **42**:41–61, 1978.

5. K. Cooke, P. van den Driessche, Analysis of an SEIRS epidemic model with two delays, *J. Math. Biol.* **35**:240–260, 1996.

6. Y. Jin, W. Wang, S. Xiao, An SIRS model with a nonlinear incidence rate, *Chaos Solitons Fractals*, **34**:1482–1497, 2007.

7. W. Ma, M. Song, Y. Takeuchi, Global stability of an SIR epidemic model with time delay, *Appl. Math. Lett.*, **17**:1141–1145, 2004.

8. W. Ma, Y. Takeuchi, T. Hara, E. Beretta, Permanence of an SIR epidemic model with distributed time delays, *Tohoku Math. J.*, **54**:581–591, 2002.

9. Y. Takeuchi, W. Ma, E. Beretta, Global asymptotic properties of a SIR epidemic model with finite incubation time, *Nonlinear Anal., Theory Methods Appl.*, **42**:931–947, 2000.

10. H.W. Hethcote, P. van den Driessche, An SIS epidemic model with variable population size and a delay, *J. Math. Biol.*, **34**:177–194, 1995.

11. H.W. Hethcote, P. van den Driessche, Two SIS epidemilogic models with delays, *J. Math. Biol.*, **40**:3–26, 2000.

12. S. Gao, L. Chen, Z. Teng, Pulse vaccination of an SEIR epidemic model with time delay, *Nonlinear Anal., Real World Appl.*, **9**:599–607, 2008.

13. S. Gao, Z. Teng, D. Xie, The effects of pulse vaccination on SEIR model with two time delays, *Appl. Math. Comput.* **201**:282–292, 2008.

14. P. van den Driessche, L. Wang, X. Zou, Modeling diseases with latency and relapse, *Math. Biosci. Eng.*, **4**:205–219, 2007.

15. J. Chin, *Control of Communicable Diseases Manual*, American Public Health Association, Washington, 1999.

16. S.W. Martin, *Livestock Disease Eradication: Evaluation of the Cooperative State-Federal Bovine Tuberculosis Eradication Program*, National Academy Press, Washington, 1994.

17. K.E. VanLandingham, H.B. Marsteller, G.W. Ross, F.G. Hayden, Relapse of herpes simplex encephalitis after conventional acyclovir therapy, *JAMA – J. Am. Med. Asoc.*, **259**:1051–1053, 1988.

18. P. van den Driessche, X. Zou, Modeling relapse in infectious diseases, *Math. Biosci.*, **207**:89–103, 2007.

19. W.M. Liu, H.W. Hethcote, S.A. Levin, Dynamical behavior of epidemiological models with nonlinear incidence rates, *J. Math. Biol.*, **25**:359–380, 1987.

20. W.M. Liu, S.A. Levin, Y. Iwasa, Influence of nonlinear incidence rates upon the behavior of SIRS epidemiological models, *J. Math. Biol.*, **23**:187–204, 1986.

21. J.K. Hale, S. Verduyn Lunel, *Introduction to Functional Differential Equations*, Springer, New York, 1993.

22. Y. Kuang, *Delay Differential Equations with Applications in Population Dynamics*, Academic Press, New York, 1993.

23. J.R. Haddock, J. Terjéki, Liapunov–Razumikhin functions and an invariance principle for functional-differential equations, *J. Differ. Equations*, **48**:95–122, 1983.