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SVEIR EPIDEMIOLOGICAL MODEL WITH VARYING INFECTIVITY AND DISTRIBUTED DELAYS

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Abstract. In this paper, based on an SEIR epidemiological model with distributed delays to account for varying infectivity, we introduce a vaccination compartment, leading to an SVEIR model. By employing direct Lyapunov method and LaSalle's invariance principle, we construct appropriate functionals that integrate over past states to establish global asymptotic stability conditions, which are completely determined by the basic reproduction number $\mathcal{R}_0^V$. More precisely, it is shown that, if $\mathcal{R}_0^V \leq 1$, then the disease free equilibrium is globally asymptotically stable; if $\mathcal{R}_0^V > 1$, then there exists a unique endemic equilibrium which is globally asymptotically stable. Mathematical results suggest that vaccination is helpful for disease control by decreasing the basic reproduction number. However, there is a necessary condition for successful elimination of disease. If the time for the vaccinees to obtain immunity or the possibility for them to be infected before acquiring immunity can be neglected, this condition would be satisfied and the disease can always be eradicated by some suitable vaccination strategies. This may lead to overevaluating the effect of vaccination.

1. **Introduction.** Communicable disease models describing a directly transmitted viral or bacterial agent in a closed population and consisting of susceptibles (S), infectives (I), and recovers (R) were considered by Kermack and Mckendrick (1927). For some diseases, such as influenza and tuberculosis, on adequate contact with an infectious individual, a susceptible becomes exposed for a while; that is, infected but not yet infectious. Thus it is realistic to introduce a latent compartment (usually denoted by E), leading to an SEIR model. Such type of models with or without time delays have been widely discussed in recent decades. Local and global stability analysis of the disease-free and endemic equilibria have been carried out using different assumptions and contact rates (see [2, 14, 15, 17] and references therein).

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Vaccination is important for the elimination of infectious disease. Usually, the vaccination process are different schedules for different disease and vaccines. For some disease, such as hepatitis B virus infection [4], doses should be taken by vaccinees several times and there must be some fixed time intervals between two does. Considering the time for vaccinees to obtain immunity and possibility to be infected before vaccination, Liu et al. [18] studied the vaccination effects via two SVIR models according to continuous vaccination strategy and pulse vaccination strategy (PVS), respectively. Their models assumed that susceptible individuals need some time to obtain immunity after vaccinated, and then join into the recovered individuals. Those distinguished from the earlier vaccination models in which vaccinees gain immunity immediately. The results in [18] described that both systems exhibit strict threshold dynamics which depend on the basic reproduction number. When this number is below unity, the disease can be eradicated. And if it exceeds unity, the disease is endemic in the sense of global asymptotic stability of a positive equilibrium for continuous vaccination strategy and disease permanence for PVS. The qualitative analysis suggest that vaccination is helpful for disease control by decreasing the basic reproduction number.

Recently, Röst and Wu [23] presented an SEIR model for an infectious disease that includes infected individuals with infection-age structure to allow for varying infectivity. The incidence is of mass action type, because of the varying infectivity, has the form $\beta S(t)\int_0^\infty k(a)i(t,a)da$. The authors established the basic reproduction number as a threshold quantity regarding the local asymptotic stability of the disease free equilibrium and endemic equilibrium. They also proved disease free equilibrium is globally asymptotically stable and the uniform persistence when the endemic equilibrium exists. However, the global stability of the endemic equilibrium was left as an open problem. McCluskey [21] resolved elegantly the issue proposed by [23] using Lyapunov functional which includes an integral over all previous states. Such type of Lyapunov functions has also been used for infection-age epidemiological models [20]. Recently, this kind of Lyapunov functions are extensively used to nonlinear delay differential equations describing the disease spread and virus infection (see, McCluskey [21, 22], Liu and Wang [19], Li and Shu [16] and Huang et al. [9, 10]).

Motivated by these works, in this paper, we consider an SVEIR epidemiological model with varying infectivity. The model also assumes that individuals obtain partial immunity just after vaccinated and need the time for them to obtain complete immunity. In fact, as soon as the susceptible individuals enter the vaccination process, they are different from susceptible individuals. And they should also be distinguished from recovered individuals who has complete immunity against the disease. Hence when the vaccinees gain immunity, they would be considered as recovered individuals. By transforming the model to distributed delays differential equations, we establish the global dynamics by constructing suitable Lyapunov functionals.

The rest of the paper is organized as follows. In Section 2, taking into account the age of infection as a parameter, we formulate a new SVEIR model with distributed delays. The basic reproduction number $\mathcal{R}_0^V$ and the existence of the equilibria are presented in the Section 3. In Section 4, by constructing suitable Lynapunov functionals, we identify the basic reproduction number $\mathcal{R}_0^V$ as a threshold quantity regarding the global asymptotic stability of the equilibria. In section 5, we give two special case of probability distribution function $k(a)$ for reducing the system.

Vaccination effects implied by the mathematical analysis are considered in Section 6. In the last section, we give some briefly summaries and discussions on our results.

2. **Model derivation and well-posedness.** A population is divided into the following categories: susceptible (those who are capable of contracting the disease); vaccinees (those who are vaccinated to defeat disease); exposed (those who are infected but not yet infectious); infectious (those who are infected and capable of transmitting the disease); and recovered (those who are permanently immune), denoted by $S(t), V(t), E(t), I(t), R(t)$, respectively. The infectious class is structured by age of infection (i.e., time since entry into class $I(t)$). The density of individuals with infection-age a at time t is given by $i(t,a)$ with $I(t) = \int_0^\infty i(t,a)da$. The relative infectivity of individuals of infection-age a is $k(a)$, where $k(a)$ is a kernel function taking values in the interval $[0,1]$. In what follows, Λ denotes the constant recruitment rate. β, β_1 are the baseline transmission rates for susceptibles or vaccinees, respectively. We assume that before obtaining immunity the vaccinees still have the possibility of infection with a disease transmission rate β_1 while contacting with infected individuals. β_1 be assumed to be less than β because the vaccinating individuals may have some partial immunity during the vaccination process or they may recognize the transmission characters of the disease and hence decrease the effective contacts with infected individuals. We also assume that only susceptibles receive vaccination in this model, and exposed and recovered individuals not. d is the natural death rate, δ is the disease-induced death rate, $1/\mu$ is the average latency period and $1/\gamma$ is the average recovery period. Let α be the rate at which susceptible individuals are moved into the vaccination process. They will obtain vaccine-induced immunity during or after the process. Let γ_1 be the average recovery rate (and hence $1/\gamma_1$ is the average recovery period) for vaccinees to obtain immunity and move into recovered population. All these constants are assumed to be positive. Then, we arrive at the following system of differential equations

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - \beta S(t)\int_0^\infty k(a)i(t,a)da - (d+\alpha)S(t),\\
\frac{dV(t)}{dt} &= \alpha S(t) - \beta_1 V(t)\int_0^\infty k(a)i(t,a)da - (d+\gamma_1)V(t),\\
\frac{dE(t)}{dt} &= [\beta S(t) + \beta_1 V(t)]\int_0^\infty k(a)i(t,a)da - (d+\mu)E(t),\\
\frac{dI(t)}{dt} &= \mu E(t) - (d+\delta+\gamma)I(t),\\
\frac{dR(t)}{dt} &= \gamma_1 V(t) + \gamma I(t) - dR(t).
\end{aligned} \tag{1}$$

The evolution of the density of the infected is given by

$$(\frac{\partial}{\partial t} + \frac{\partial}{\partial a})i(t,a) = -(d+\delta+\gamma)i(t,a), \tag{2}$$

subject to the boundary condition $i(t,0) = \mu E(t)$. Solving (2) gives

$$i(t,a) = \mu e^{-(d+\delta+\gamma)a}E(t-a). \tag{3}$$

Substituting (3) into system (1), we can rewrite system (1) as

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - \beta S(t)\int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\alpha)S(t),\\
\frac{dV(t)}{dt} &= \alpha S(t) - \beta_1 V(t)\int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\gamma_1)V(t),\\
\frac{dE(t)}{dt} &= [\beta S(t) + \beta_1 V(t)]\int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\mu)E(t),\\
\frac{dI(t)}{dt} &= \mu E(t) - (d+\delta+\gamma)I(t),\\
\frac{dR(t)}{dt} &= \gamma_1 V(t) + \gamma I(t) - dR(t).
\end{aligned} \tag{4}$$

Since the variables $I(t)$ and $R(t)$ do not appear in the first three equations of (4), we can consider the following reduced system with distributed time delays and general kernel function

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda - \beta S(t)\int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\alpha)S(t),\\
\frac{dV(t)}{dt} &= \alpha S(t) - \beta_1 V(t)\int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\gamma_1)V(t),\\
\frac{dE(t)}{dt} &= [\beta S(t) + \beta_1 V(t)]\int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\mu)E(t).
\end{aligned} \tag{5}$$

We will establish the global dynamics of system (5).

Since system (5) contains terms with infinite delays, it is necessary to address the question of well-posedness of system (5). We introduce the following notation. Given a non-negative function E defined on the interval $(-\infty, T]$, for any $t < T$, we define the function $E_t : \mathbf{R}_{\le 0} \to \mathbf{R}_{\ge 0}$ by $E_t(\theta) = E(t+\theta)$ for $\theta \le 0$. For system (5), an equation with infinite delays, the initial condition should satisfy $S(0) \ge 0$, $V(0) \ge 0$ and $E_0 : \mathbf{R}_{\le 0} \to \mathbf{R}_{\ge 0}$. Due to the infinite delays, it is necessary to determine an appropriate phase space. For any $\triangle \in (0, d+\delta+\gamma)$, let

$$C_\Delta = \{\varphi : \mathbf{R}_{\le 0} \to \mathbf{R} \text{ such that } \varphi(\theta)e^{\Delta\theta} \text{ is uniformly continuous for } \theta \in (-\infty, 0], \text{and} \sup_{\theta\le 0}|\varphi(\theta)|e^{\Delta\theta} < \infty\}$$

and

$$Y_\Delta = \{\varphi \in C_\Delta : \varphi(\theta) \ge 0 \text{ for all } \theta \le 0\}.$$

Define the norm on C_Δ and Y_Δ by

$$\| \varphi \| = \sup_{\theta\le 0} | \varphi(\theta)e^{\Delta\theta} | .$$

We consider solutions of system (5), $(S(t), V(t), E_t)$ with the initial condition

$$(S(0), V(0), E_0) \in \mathbf{R}_{\ge 0} \times \mathbf{R}_{\ge 0} \times Y_\triangle. \tag{6}$$

Standard theory of functional differential equation [6] implies $E_t \in Y_\triangle$ for $t > 0$. Moreover, if $(S(t), V(t), E(t))$ is bounded for $t \ge 0$, then the positive orbit $\Gamma_+ = (S(t), V(t), E_t) : t \ge 0$ has compact closure in $\mathbf{R}_{\ge 0} \times \mathbf{R}_{\ge 0} \times Y_\triangle$. For the general theory and application, see ([1], [5], [6]) and references found therein.

We consider system (5) in the phase space

$$X = (\mathbf{R}_{\ge 0} \times \mathbf{R}_{\ge 0} \times Y_\triangle). \tag{7}$$

It can be verified that solution of (5) in X with initial condition (6) remains nonnegative. In particular, from the first equation of (5), we obtain $S'(t) \leq \Lambda - (d+\alpha)S(t)$. Hence, $\limsup_{t\to\infty} S(t) \leq \frac{\Lambda}{d+\alpha}$. Adding the three equations in (5) gives $(S'(t)+V'(t)+E_t'(0)) \leq \Lambda - d(S(t)+V(t)+E_t(0))$. Hence $\limsup_{t\to\infty}(S(t)+V(t)+E_t(0)) \leq \frac{\Lambda}{d}$. Moreover, let K be the maximum of $E(t)$ on $[0,T]$. For any $t > T$, we have $\|E_t\| = \sup_{s\leq 0} E_t(s)e^{\Delta s} = \sup_{u\leq t} E(u)e^{\Delta u}e^{-\Delta t} \leq M$, where $M := \max\{e^{-\Delta t}\|\phi\|, Ke^{\Delta T}e^{-\Delta t}\}$. Therefore, the following set is positively invariant for system (5),

$$\begin{aligned}\Theta =&\{(S(t),V(t),E_t) \in X \mid \\ &0 \leq S(t) \leq \frac{\Lambda}{d+\alpha}, 0 \leq S(t)+V(t)+E_t(0) \leq \frac{\Lambda}{d}, \|E_t\| \leq M, \text{for all } t\}.\end{aligned}$$

Lemma 2.1. *System (5) is positively invariant in Θ. Moreover, there exists a positive constant $\overline{\Delta}$ such that $0 < S(t), V(t), E(t) \leq \overline{\Delta}$ for all $t > 0$.*

3. **Basic reproduction number and equilibria.** System (5) always has a disease-free equilibrium $P_0 = (S_0, V_0, 0)$, where $S_0 = \frac{\Lambda}{d+\alpha}$ and $V_0 = \frac{\alpha\Lambda}{(d+\alpha)(d+\gamma_1)}$. Following the theory of van den Driessche and Watmough [24], Introducing a single exposed individual into a totally susceptible or vaccinated population in the disease-free equilibrium at $t = 0$, the survival probability of this individual in the E-class after time t is given by $e^{-(\mu+d)t}$. So the expected number of generated secondary infections can be calculated by

$$\mathcal{R}_0^V = (\beta S_0 + \beta_1 V_0)\int_0^\infty \int_0^\infty k(a)\mu e^{-(d+\delta+\gamma)a}e^{-(\mu+d)t}dadt,$$

which is reduced to

$$\mathcal{R}_0^V = \frac{\beta S_0 + \beta_1 V_0}{\mu+d}\int_0^\infty k(a)\mu e^{-(d+\delta+\gamma)a}da. \tag{8}$$

We denote $\mu\int_0^\infty k(a)e^{-(d+\delta+\gamma)a}da$ as Φ, then

$$\mathcal{R}_0^V = \frac{(\beta S_0 + \beta_1 V_0)}{\mu+d}\Phi.$$

Next, we prove the existence of the endemic equilibrium. If the constant solution $P^*(S^*, V^*, E^*)$ is the endemic equilibrium of (5), the positive constants, S^*, V^* and E^* should satisfy the algebraic equations

$$0 = \Lambda - (d+\alpha)S^* - \beta\Phi S^* E^*, \tag{9}$$

$$0 = \alpha S^* - (d+\gamma_1)V^* - \beta_1\Phi V^* E^*, \tag{10}$$

$$0 = [\beta S^* + \beta_1 V^*]\Phi E^* - (d+\mu)E^*. \tag{11}$$

After simple computation, it has $S^* = \frac{\Lambda}{d+\alpha+\beta\Phi E^*}$, $V^* = \frac{\Lambda\alpha}{(d+\alpha+\beta\Phi E^*)(d+\gamma_1+\beta_1\Phi E^*)}$, which are determined by E^*. E^* is the positive root of the following equation

$$G(E) = a_0E^2 + a_1E + a_2, \tag{12}$$

where

$$\begin{aligned}a_0 =&\beta\beta_1\Phi^2(d+\mu);\\ a_1 =&\Phi[\beta(d+\mu)(d+\alpha)+\beta(d+\mu)(d+\gamma_1)-\beta\beta_1\Lambda\Phi];\\ a_2 =&(d+\mu)(d+\alpha)(d+\gamma_1)(1-\mathcal{R}_0^V).\end{aligned}$$

Since $a_0 > 0$, it has $G(\pm\infty) = +\infty$. When $\mathcal{R}_0^V \leq 1$, we know $G(0) \geq 0$ and have

$$G'(E) = 2a_0E + a_1 = 2a_0E + \beta\beta_1\Phi(d+\mu)\left\{\frac{d+\alpha}{\beta} + \frac{d+\gamma_1}{\beta_1} - \frac{\Lambda\Phi}{d+\mu}\right\}.$$

And $\mathcal{R}_0^V \leq 1$ is equivalent to

$$\frac{\Lambda\Phi}{d+\mu} \leq \frac{d+\alpha}{\beta+\varepsilon}, \quad \text{where} \quad \varepsilon = \frac{\alpha\beta_1}{d+\gamma_1},$$

which implies that $\frac{\Lambda\Phi}{d+\mu} < \frac{d+\alpha}{\beta}$. Therefore, $G'(E) > 0$ for any $E \geq 0$ when $\mathcal{R}_0^V \leq 1$. In this case, it is obvious that equation (12) has not positive root.

On the other hand, when $\mathcal{R}_0^V > 1$, it has that $G(0) = a_2 < 0$. From the second order function properties of $G(E)$, equation (12) has a unique positive real root E^*. We have the following Proposition for system (5).

Proposition 1. *System (5) has an endemic equilibrium $P^*(S^*, V^*, E^*)$ if and only if $\mathcal{R}_0^V > 1$.*

For a solution for which disease is present under the initial condition, we say the disease is *initially present*.

Theorem 3.1. *Consider system (5). Assume that $\mathcal{R}_0^V > 1$ and the disease is initially present, then system (5) is uniformly persistent; that is, there exists $\eta > 0$ such that $\liminf_{t\to\infty} S(t) \geq \eta$, $\liminf_{t\to\infty} V(t) \geq \eta$ and $\liminf_{t\to\infty} E(t) \geq \eta$.*

Since there are similar methods and techniques which have been recently employed in Theorem 6.1 of [23], we omit the proof of the above theorem.

4. **Global asymptotic stability.** It is important to analyze the stability of these equilibria, as it will indicate whether the disease will die out eventually, or it will persist for all time. In this section , we will establish the global stability of disease-free equilibrium and endemic equilibrium.

Theorem 4.1. *If $\mathcal{R}_0^V \leq 1$, then the disease free equilibrium P_0 is globally asymptotically stable.*

Proof. Let $\overline{a} = \inf\{a : \int_a^\infty k(\sigma)d\sigma = 0\}$. For a system with infinite delays, we have $\overline{a} = \infty$, however, for a system with a bounded distributed delays, we have $0 < \overline{a} < \infty$. Let

$$\rho(a) = \mu(\beta S_0 + \beta_1 V_0)\int_a^\infty k(\sigma)e^{-(d+\delta+\gamma)\sigma}d\sigma. \tag{13}$$

Note that $\rho(a) > 0$ for each $a \in [0, \overline{a})$. Using the fact that $h(z) = z - 1 - \ln z$ for all $z > 0$, has the global minimum at $z = 1$ and $h(1) = 0$, we have $S_0h(\frac{S(t)}{S_0}) \geq 0$, $V_0h(\frac{V(t)}{V_0}) \geq 0$. We will study the behavior of the Lyapunov functional

$$U = U_1 + U_2,$$

where

$$U_1 = S_0h\left(\frac{S(t)}{S_0}\right) + V_0h\left(\frac{V(t)}{V_0}\right) + E(t), \tag{14}$$

$$U_2 = \int_0^\infty \rho(a)E(t-a)da. \tag{15}$$

The Lyapunov functional U is nonnegative and defined with respect to the disease free equilibrium $P_0 = (S_0, V_0, 0)$, which is a global minimum. Differentiating U_1 along the solution of system (5), we obtain

$$\begin{aligned}\frac{dU_1(t)}{dt} &= \Lambda - dS(t) - (d+\gamma_1)V(t) - (d+\mu)E(t)\\ &\quad - \frac{\Lambda S_0}{S(t)} + \mu\beta S_0\int_0^\infty k(a)E(t-a)e^{-(d+\delta+\gamma)a}da + (d+\alpha)S_0\\ &\quad - \frac{\alpha S V_0}{V(t)} + \mu\beta_1 V_0\int_0^\infty k(a)E(t-a)e^{-(d+\delta+\gamma)a}da + (d+\gamma_1)V_0\\ &= dS_0\left[2 - \frac{S(t)}{S_0} - \frac{S_0}{S(t)}\right] + \alpha S_0\left[3 - \frac{V(t)}{V_0} - \frac{S_0}{S(t)} - \frac{S(t)V_0}{S_0V(t)}\right]\\ &\quad + (\mu\beta S_0 + \mu\beta_1 V_0)\int_0^\infty k(a)E(t-a)e^{-(d+\delta+\gamma)a}da - (d+\mu)E(t). \quad (16)\end{aligned}$$

Differentiating U_2 along the solution of system (5) and using integration by parts, we obtain

$$\begin{aligned}\frac{dU_2(t)}{dt} &= \frac{d}{dt}\int_0^\infty \rho(a)E(t-a)da\\ &= \int_0^\infty \rho(a)\frac{d}{dt}(E(t-a))da\\ &= -\int_0^\infty \rho(a)\frac{d}{da}(E(t-a))da\\ &= -\rho(a)E(t-a)\,|_{a=0}^{\infty} + \int_0^\infty \frac{d}{da}(\rho(a))E(t-a)da.\end{aligned}$$

Noting that

$$0 \le \rho(a) \le (\mu\beta S_0 + \mu\beta_1 V_0)\int_a^\infty e^{-(d+\delta+\gamma)\sigma}d\sigma = \frac{(\mu\beta S_0 + \mu\beta_1 V_0)}{(d+\delta+\gamma)}e^{-(d+\delta+\gamma)a}$$

and $E(t-a)$ is bounded above and below, it follows that $\lim_{a\to\infty}\rho(a)E(t-a) = 0$. Also, by $\frac{d}{da}\rho(a) = -(\mu\beta S_0 + \mu\beta_1 V_0)k(a)e^{-(d+\delta+\gamma)a}$, we obtain

$$\frac{dU_2(t)}{dt} = (\mu\beta S_0 + \mu\beta_1 V_0)\int_0^\infty k(a)\left[E(t) - E(t-a)\right]e^{-(d+\delta+\gamma)a}da. \quad (17)$$

Combining (16) and (17), we obtain

$$\begin{aligned}\frac{dU(t)}{dt} &= dS_0\left[2 - \frac{S(t)}{S_0} - \frac{S_0}{S(t)}\right] + \alpha S_0\left[3 - \frac{V(t)}{V_0} - \frac{S_0}{S(t)} - \frac{S(t)V_0}{S_0V(t)}\right]\\ &\quad + (d+\mu)(R_0^V - 1)E(t). \quad (18)\end{aligned}$$

Since the arithmetic mean is greater than or equal to the geometric mean, it is clear that

$$2 - \frac{S(t)}{S_0} - \frac{S_0}{S(t)} \le 0 \quad \text{and} \quad 3 - \frac{V(t)}{V_0} - \frac{S_0}{S(t)} - \frac{S(t)V_0}{S_0V(t)} \le 0. \quad (19)$$

The above equalities strictly hold only at $S(t) = S_0$ and $V(t) = V_0$.

Therefore, it follows from $\mathcal{R}_0^V \le 1$ that $U'(t) \le 0$. Define $\Psi = \{(S(t), V(t), E(t)) \mid U' = 0\}$ and let $\mathcal{M}$ be the largest invariant set in Ψ. It is easy to show $\mathcal{M} = \{P_0\}$. In fact, when $\mathcal{R}_0^V < 1$, $\Psi = \{(S(\theta), V(\theta), E(\theta)) \mid S(\theta) = S_0, V(\theta) = V_0, E(\theta) = 0\}$. When $\mathcal{R}_0^V = 1$, $\Psi = \{(S(\theta), V(\theta), E(\theta)) \mid S(\theta) = S_0, V(\theta) = V_0\}$ and $E(\theta) = 0$

from the first equation of (5). Again we have $\mathcal{M} = \{P_0\}$. Note that $\mathcal{M}$ is invariant, by the LaSalle's invariance principle for delay systems (see [7], [8]), P_0 is globally asymptotically stable in Θ when $\mathcal{R}_0^V \leq 1$. This completes the proof of Theorem 4.1. □

Theorem 4.2. *If $\mathcal{R}_0^V > 1$, then the endemic equilibrium P^* is globally asymptotically stable.*

Proof. Let

$$\alpha(a) = (\mu\beta S^* E^* + \mu\beta_1 V^* E^*) \int_a^\infty k(\sigma) e^{-(d+\delta+\gamma)\sigma} d\sigma. \tag{20}$$

Similarly, it has that $\alpha(a) > 0$ for each $a \in [0, \overline{a})$. Using the fact that $h(z) = z - 1 - \ln z$ for all $z > 0$, has the global minimum at $z = 1$ and $h(1) = 0$, we note that $S^* h\left(\frac{S(t)}{S^*}\right) \geq 0$, $V^* h\left(\frac{V(t)}{V^*}\right) \geq 0$, $E^* h\left(\frac{E(t)}{E^*}\right) \geq 0$ and $h\left(\frac{E(t-a)}{E^*}\right) \geq 0$. Define a Lyapunov functional for P^*,

$$W = V_1 + V_2,$$

where

$$V_1 = S^* h\left(\frac{S(t)}{S^*}\right) + V^* h\left(\frac{V(t)}{V^*}\right) + E^* h\left(\frac{E(t)}{E^*}\right), \tag{21}$$

$$V_2 = \int_0^\infty \alpha(a) h\left(\frac{E(t-a)}{E^*}\right) da. \tag{22}$$

So the Lyapunov functional W is nonnegative and defined with respect to the infected equilibrium $P^* = (S^*, V^*, E^*)$, which is a global minimum.

Differentiating V_1 along the solution of system (5) and using equilibrium equations (9)-(11), we obtain

$$\begin{aligned}
V_1' &= \Lambda - dS(t) - (d+\gamma_1)V(t) - (d+\mu)E(t) \\
&\quad - \frac{\Lambda S^*}{S(t)} + \mu\beta S^* \int_0^\infty k(a)E(t-a)e^{-(d+\delta+\gamma)a} da + (d+\alpha)S^* \\
&\quad - \frac{\alpha S V^*}{V(t)} + \mu\beta_1 V^* \int_0^\infty k(a)E(t-a)e^{-(d+\delta+\gamma)a} da + (d+\gamma_1)V^* \\
&\quad - \left[\frac{\mu\beta S(t)E^*}{E(t)} + \frac{\mu\beta_1 V(t)E^*}{E(t)}\right] \int_0^\infty k(a)E(t-a)e^{-(d+\delta+\gamma)a} da + (d+\mu)E^* \\
&= dS^* \left[2 - \frac{S(t)}{S^*} - \frac{S^*}{S(t)}\right] + \alpha S^* \left[3 - \frac{V(t)}{V^*} - \frac{S^*}{S(t)} - \frac{S(t)V^*}{S^* V(t)}\right] \\
&\quad + (\mu\beta S^* + \mu\beta_1 V^*) \int_0^\infty k(a)[-E(t) + E(t-a)]e^{-(d+\delta+\gamma)a} da \\
&\quad + \mu\beta S^* E^* \int_0^\infty k(a) \left[2 - \frac{S^*}{S(t)} - \frac{S(t)E(t-a)}{S^* E(t)}\right] e^{-(d+\delta+\gamma)a} da \\
&\quad + \mu\beta_1 V^* E^* \int_0^\infty k(a) \left[\frac{V(t)}{V^*} - \frac{V(t)E(t-a)}{V^* E(t)}\right] e^{-(d+\delta+\gamma)a} da.
\end{aligned} \tag{23}$$

Differentiating V_2 along the solution of system (5) and using integration by parts, we obtain

$$\begin{aligned} V_2' &= \frac{d}{dt}\int_0^\infty \alpha(a)h\left(\frac{E(t-a)}{E^*}\right)da \\ &= -\int_0^\infty \alpha(a)\frac{d}{da}h\left(\frac{E(t-a)}{E^*}\right)da \\ &= -\alpha(a)h\left(\frac{E(t-a)}{E^*}\right)|_{a=0}^{\infty} + \int_0^\infty \frac{d}{da}(\alpha(a))h\left(\frac{E(t-a)}{E^*}\right)da. \end{aligned}$$

Noting that

$$0 \le \alpha(a) \le \mu(\beta S^* + \beta_1 V^*)E^* \int_a^\infty e^{-(d+\delta+\gamma)\sigma}d\sigma = \frac{\mu(\beta S^* + \beta_1 V^*)E^*}{d+\delta+\gamma}e^{-(d+\delta+\gamma)a}.$$

Further, $h\left(\frac{E(t-a)}{E^*}\right)$ is bounded above from the persistence of system, it follows that

$$\lim_{a\to\infty} \alpha(a)h\left(\frac{E(t-a)}{E^*}\right) = 0.$$

Also, we have $\frac{d}{da}\alpha(a) = -(\mu\beta S^*E^* + \mu\beta_1 V^*E^*)k(a)e^{-(d+\delta+\gamma)a}$, this implies that

$$\begin{aligned} \frac{dV_2(t)}{dt} &= (\mu\beta S^*E^* + \mu\beta_1 V^*E^*) \\ &\quad \cdot \int_0^\infty k(a)\left[\frac{E(t)}{E^*} - \frac{E(t-a)}{E^*} + \ln\frac{E(t-a)}{E(t)}\right]e^{-(d+\delta+\gamma)a}da. \end{aligned} \tag{24}$$

Combining (23) and (24), we obtain

$$\begin{aligned} \frac{dW}{dt} &= dS^*\left[2 - \frac{S(t)}{S^*} - \frac{S^*}{S(t)}\right] + (d+\gamma_1)V^*\left[3 - \frac{V(t)}{V^*} - \frac{S^*}{S(t)} - \frac{S(t)V^*}{S^*V(t)}\right] \\ &\quad + (\mu\beta S^*E^* + \mu\beta_1 V^*E^*)\int_0^\infty k(a)\left[1 - \frac{S^*}{S(t)} + \ln\frac{S^*}{S(t)}\right]e^{-(d+\delta+\gamma)a}da \\ &\quad + \mu\beta S^*E^*\int_0^\infty k(a)\left[1 - \frac{S(t)E(t-a)}{S^*E(t)} + \ln\frac{S(t)E(t-a)}{S^*E(t)}\right]e^{-(d+\delta+\gamma)a}da \\ &\quad + \mu\beta_1 V^*E^*\int_0^\infty k(a)\left[1 - \frac{S(t)V^*}{S^*V(t)} + \ln\frac{S(t)V^*}{S^*V(t)}\right]e^{-(d+\delta+\gamma)a}da \\ &\quad + \mu\beta_1 V^*E^*\int_0^\infty k(a)\left[1 - \frac{V(t)E(t-a)}{V^*E(t)} + \ln\frac{V(t)E(t-a)}{V^*E(t)}\right]e^{-(d+\delta+\gamma)a}da. \end{aligned}$$

Since the arithmetic mean is greater than or equal to the geometric mean, it is clear that

$$2 - \frac{S(t)}{S^*} - \frac{S^*}{S(t)} \le 0 \quad \text{and} \quad 3 - \frac{V(t)}{V^*} - \frac{S^*}{S(t)} - \frac{S(t)}{S^*}\frac{V^*}{V(t)} \le 0. \tag{25}$$

Further, since the function $h(z) = 1 - z(t) + \ln z(t)$ is always non-positive for any function $z(t) > 0$, and $h(z) = 0$ if and only if $z(t) = 1$. Thus, $dW/dt \le 0$ with the equality if and only if $S(t) = S^*$, $V(t) = V^*$ and $E(t-a) = E(t)$ for almost all $a \in [0, \bar{a})$. By Theorem 5.3.1 of Kuang [13], solutions tend to the largest invariant subset of $\mathcal{M} = \{dW/dt = 0\}$.

Since $S(t) = S^*$, $V(t) = V^*$ and $E(t-a) = E(t)$ in $\mathcal{M}$, from the third equation of (5), we know that $\frac{dE(t)}{dt}$ at each point in $\mathcal{M}$ satisfies

$$\begin{aligned} E'(t) &= (\beta S^* + \beta_1 V^*) \int_0^\infty k(a)\mu E(t) e^{-d+\delta+\gamma} da - (d+\mu)E(t) \\ &= (\beta S^* + \beta_1 V^*)\Phi E(t) - (d+\mu)E(t) \\ &= 0. \end{aligned}$$

It implies that $E(t)$ is a constant in $\mathcal{M}$. From the first equation in (5) and $dS(t)/dt = 0$ in $\mathcal{M}$, it gives $E(t) = E^*$ for all t. Hence, we have $\mathcal{M} = (S^*, V^*, E^*)$. Using a similar argument as that in the proof of Theorem 4.1, by the LaSalle's invariant principle, the global asymptotic stability of P^* follows. This completes the proof. □

Remark 1. The above analysis resolve the global stability of two equilibria of system (5), which is subsystem of (4). When $\mathcal{R}_0^V > 1$, by Theorem 4.2, we know that $E(t)$ converges to positive constant E^*. Now the equation $I'(t) = \mu E(t) - (d+\delta+\gamma)I(t)$ in (4) is an asymptotic autonomous ordinary differential equation for which solutions of the limiting equation go to a hyperbolic equilibrium. Thus,

$$\lim_{t\to+\infty} I(t) = I^* = \mu E^*/(d+\delta+\gamma).$$

Similarly, from the equation $R'(t) = \gamma_1 V(t) + \gamma I(t) - dR(t)$, we also obtain that solutions $R(t)$ approach to equilibrium R^* since $\lim_{t\to+\infty} V(t) = V^*$ and $\lim_{t\to+\infty} I(t) = I^*$, that is

$$\lim_{t\to+\infty} R(t) = R^* = \frac{1}{d}(\gamma_1 V^* + \gamma I^*) = \frac{1}{d}(\gamma_1 V^* + \frac{\gamma\mu E^*}{d+\delta+\gamma}).$$

When $R_0^V \le 1$, similar argument to the above, it has $\lim_{t\to+\infty} I(t) = 0$ and $\lim_{t\to+\infty} R(t) = \gamma V_0/d$. Hence, although system (4) has five variables and (5) just has three ones, the global stability of system (5) implies the global stability of system (4).

5. **Two cases for kernel function** $k(a)$**.** Usually, the kernel function $k(a)$ is assumed to probability distribution function, and satisfies $0 \le k(a) \le 1$ for all $a > 0$. In this section, we study the two special cases for $k(a)$.

Case where $k(a) = 1$ for all $a \ge 0$, then

$$\int_0^\infty k(a)\mu E(t-a) e^{-(d+\delta+\gamma)a} da = \int_0^\infty i(t,a) da = I(t).$$

System (5) is simply reduced to an ordinary differential equation (ODE) model as follows:

$$\begin{aligned} S'(t) &= \Lambda - \beta S(t) I(t) - (d+\alpha) S(t), \\ V'(t) &= \alpha S(t) - \beta_1 V(t) I(t) - (d+\gamma_1) V(t), \\ E'(t) &= (\beta S(t) + \beta_1 V(t)) I(t) - (d+\mu) E(t). \\ I'(t) &= \mu E(t) - (d+\delta+\gamma) I(t). \end{aligned} \tag{26}$$

Now the basic reproduction number for system (26) is rewritten as

$$\bar{\mathcal{R}}_0^V = \frac{(\beta S_0 + \beta_1 V_0)\mu}{(d+\mu)(d+\delta+\gamma)}.$$

The ODE system (26) means the susceptible and vaccinated individuals are infected by infectious individuals with mass action type incidence. Susceptible individuals (regardless of whether they have been previously vaccinated) are further vaccinated at the rate α. Obviously, system (26) has disease free equilibrium $\bar{P}_0(S_0, V_0, 0, 0)$, and the endemic equilibrium $\bar{P}^*(\bar{S}^*, \bar{V}^*, \bar{E}^*, \bar{I}^*)$ (when $\bar{\mathcal{R}}_0^V > 1$). A similar system regard to (26) was considered in [3], which prove the global stability of the endemic equilibrium by using Li-Muldowney techniques. Here we use Lyapunov functions as follows

$$L_1(t) = S_0 h\left(\frac{S}{S_0}\right) + V_0 h\left(\frac{V}{V_0}\right) + E + I,$$
$$L_2(t) = S^* h\left(\frac{S}{S^*}\right) + V^* h\left(\frac{V}{V^*}\right) + E^* h\left(\frac{E}{E^*}\right) + \frac{d+\mu}{\mu} h\left(\frac{I}{I^*}\right).$$

Omitting the proof in detail, we establish the global dynamics for (26).

Corollary 1. *Consider system (26). (i) If $\bar{\mathcal{R}}_0^V \le 1$, then the disease free equilibrium $\bar{P}_0$ of (26) is globally asymptotically stable. (ii) If $\bar{\mathcal{R}}_0^V > 1$, then the endemic equilibrium $\bar{P}^*$ of (26) is globally asymptotically stable.*

Case where $k(a) = \delta(a-r)$, the incidence terms become $\mu\beta e^{-(d+\delta+\gamma)r} S(t)E(t-r)$ and $\mu\beta_1 e^{-(d+\delta+\gamma)r} V(t)E(t-r)$ with discrete delays. Thus, system (5) reduces to

$$\begin{aligned}
S'(t) &= \Lambda - \mu\beta e^{-(d+\delta+\gamma)r} S(t)E(t-r) - (d+\alpha)S(t),\\
V'(t) &= \alpha S(t) - \mu\beta_1 e^{-(d+\delta+\gamma)r} V(t)E(t-r) - (d+\gamma_1)V(t),\\
E'(t) &= [\mu\beta S(t) + \mu\beta_1 V(t)] e^{-(d+\delta+\gamma)r} E(t-r) - (d+\mu)E(t).\\
I'(t) &= \mu E(t) - (d+\delta+\gamma)I(t).
\end{aligned} \tag{27}$$

The basic reproductive number for system (27) is rewritten as

$$\tilde{\mathcal{R}}_0^V = \frac{\mu\beta S_0 + \mu\beta_1 V_0}{(d+\mu)(d+\delta+\gamma)} \cdot e^{-(d+\delta+\gamma)r}.$$

Corollary 2. *Consider system (27). (i) If $\tilde{\mathcal{R}}_0^V \le 1$, then the disease free equilibrium $\bar{P}_0$ of (27) is globally asymptotically stable. (ii) If $\tilde{\mathcal{R}}_0^V > 1$, then the endemic equilibrium $\bar{P}^*$ of (27) is globally asymptotically stable.*

Comparing the above two corollaries, we find that incorporating time delays does not affect the stability of the equilibrium if the sign of $\bar{\mathcal{R}}_0^V - 1$ is uncharged when the delays are set to 0, i.e., if no Hopf bifurcation occurs in a model without delays, incorporating time delays will not produce periodic oscillations.

6. **Vaccination effects.** Theorems 4.1 and 4.2 imply that the global dynamics of system (5) is completely determined by the basic reproduction number $\mathcal{R}_0^V$. Hence the vaccination effects depend on whether the basic reproduction number can be reduced to below unity or not. Recall that when vaccination rate $\alpha = 0$, system (5) will become the same model of Röst and Wu [23] with a basic reproduction number $\mathcal{R}_0 = \frac{\beta\Lambda\mu}{d(d+\mu)} \int_0^\infty k(a) e^{-(d+\delta+r)a} da$. By Theorem 5.1 of Röst and Wu [23], when $\mathcal{R}_0 \le 1$, the disease free equilibrium P_0 is globally asymptotically stable and so is the endemic equilibrium $P^* = (S^*, E^*)$ when $R_0 > 1$ by Theorem 4.3 of McCluskey [21]. We now consider the vaccination effects by the continuous vaccination strategy.

Let

$$\mathcal{R}_1^V := \mathcal{R}_0^V \mid_{\beta_1=0 \text{ or } \gamma_1\to\infty} = \frac{\beta\Lambda\mu}{(d+\alpha)(d+\mu)} \int_0^\infty k(a)e^{-(d+\delta+\gamma)a}da,$$

which is the basic reproduction number of system (5) when we neglect the possibility for vaccinees to be infected ($\beta_1 = 0$) or neglect the time for them to obtain immunity ($\gamma_1 \to \infty$). It is obvious that $\mathcal{R}_1^V \le \mathcal{R}_0^V$. Since $\beta \ge \beta_1$, calculating the derivative of $\mathcal{R}_0^V$ with respective to α, we obtain

$$\frac{\partial\mathcal{R}_0^V}{\partial\alpha} = -\frac{\Lambda\mu[(\beta-\beta_1)d+\beta\gamma_1]}{(d+\mu)(d+\gamma_1)(d+\alpha)^2} \int_0^\infty k(a)e^{-(d+\delta+\gamma)a}da < 0.$$

It follows that $\mathcal{R}_0^V \le \mathcal{R}_0^V \mid_{\alpha=0} = \mathcal{R}_0$. Moreover, we have

$$\lim_{\alpha\to\infty} \mathcal{R}_1^V = 0 \quad \text{and} \quad \lim_{\alpha\to\infty} \mathcal{R}_0^V = \frac{\beta_1\Lambda\mu}{(d+\gamma_1)(d+\mu)} \int_0^\infty k(a)e^{-(d+\delta+\gamma)a}da := \mathcal{R}_2.$$

When $\mathcal{R}_0 < 1$, without vaccinations the disease will disappear ultimately. Since $\mathcal{R}_0^V \le \mathcal{R}_0$, Theorem 4.1 implies that the disease also will be extinct when continuous vaccination strategy is executed. To understand the effects of vaccinations, we should suppose that without vaccinations the disease is in endemic state, i.e. $\mathcal{R}_0 > 1$. Since $\frac{\partial\mathcal{R}_0^V}{\partial\alpha} < 0$, vaccination always has a good effect for disease control by decreasing the basic reproduction number. Next, we will discuss this issue in the following two cases:

Case I If we neglect the possibility for vaccinees to be infected $\beta_1 = 0$ or neglect the time for them to obtain immunity $\gamma_1 \to \infty$, then by $\frac{\partial R_1^V}{\partial\alpha} < 0$, $\lim_{\alpha\to\infty} \mathcal{R}_1^V = 0$, we can conclude that the disease always can be eradicated by some suitable vaccination strategy.

Case II If we consider the possibility for vaccinees to be infected $\beta_1 > 0$ and the time for them to obtain immunity (γ_1 is finite), by $\frac{\partial\mathcal{R}_0^V}{\partial\alpha} < 0$ we have $\lim_{\alpha\to\infty} \mathcal{R}_0^V = \mathcal{R}_2$. If $\mathcal{R}_2 < 1$, then there is a unique α_0 for continuous strategy such that $\mathcal{R}_0^V = 1$ for $\alpha = \alpha_0$. Hence $\mathcal{R}_0^V < 1$ for $\alpha > \alpha_0$. By Theorem 4.1, the disease can be eliminated by some suitable vaccination strategies (satisfying $\alpha > \alpha_0$). If $\mathcal{R}_2 \ge 1$, then $\mathcal{R}_0^V > \mathcal{R}_2 \ge 1$. By Theorem 4.2, the situation is so serious that disease cannot be eradicated by any vaccination strategies (for any values of α). Note that $\mathcal{R}_2$ means the average new infections produced by one infected individual during his lifespan when the whole population is vaccinated. And clearly, $\mathcal{R}_2 < 1$ is the necessary condition for disease elimination. The validity of the necessary condition requires that the possibility for the vaccinees to be infected is small (β_1 is small) or the time for them to gain immunity is short (γ_1 is large). These two improvements of the efficacy of vaccines may lead to disease eradication. If the time for the vaccinees to obtain immunity or the possibility for them to be infected before gaining immunity is neglected, this necessary condition is automatically satisfied and the disease can always be eradicated by some suitable vaccination strategies. This warns over-evaluating the effect of vaccination.

7. **Summary and discussion.** We studied the vaccination effects based on an SVEIR epidemic model with distributed delays to account for varying infectivity. By employing direct Lyapunov method and LaSalle's invariance principle, we constructed appropriate functionals that integrate over past states to establish global asymptotic stability results. We have identified the basic reproduction number $\mathcal{R}_0^V$ as threshold quantity for stability of equilibria. More precisely, it is shown that,

if $\mathcal{R}_0^V \leq 1$, then the disease free equilibrium is globally asymptotically stable; if $\mathcal{R}_0^V > 1$, then there exists a unique endemic equilibrium which is globally asymptotically stable.

In particular, when $\alpha = 0$, it means there are no vaccinations, then we have $\lim_{t\to\infty} V(t) = 0$ in system (1). And system (1) is reduced to the same model of [23], of which global asymptotic stability was given in [21]. On the other hand, when $\alpha \to \infty$ in system (1), then the vaccination is executed so fast at any time such that all susceptible population will become vaccinated immediately. And system (1) is reduced to the continuous VEIR model, which has similar global properties as SEIR model in [23].

The proofs in this paper use the function of the form $V_1(x) = x - x^* - x^* \ln(x/x^*)$. This function was applied to Lyapunov functions for the Lotka-Volterra system at first. Recently, it is extremely successful for a broad variety of epidemics models by Korobenikov [11, 12]. McCluskey ([21],[22]) extended it as $V_2 = \int_0^\infty \alpha(\theta)\{x_\theta - x^* - x^* \ln(x_\theta/x^*)\}d\theta$ to some delay model, it appears to be a sound basis to construct Lyapunov functions for more advanced problem that arise in mathematical biology. Obviously, here $V_2 \geq 0$ for all $x \geq 0$, and $V_2 = 0$ if and only if $x_\theta = x^*$. It should be pointed out here that uniform persistence result of Theorem 3.1 implies the existence of integral V_2. Thus, combined with the boundedness of solutions in Θ, the Lyapunov functional calculation for solutions are separated away from zero, lying in the omega limit sets. As incorporating infinite delays into our model, kernal function $k(\cdot)$ is bounded above by a decaying exponential function, we choose fading memory space C_Δ as the phase space. Mathematical results suggest that vaccination is helpful for disease control by decreasing the basic reproduction number. However, this model gives a necessary condition for successful elimination of disease. If the time for the vaccinees to obtain immunity or the possibility for them to be infected before acquiring immunity can be neglected, this necessary condition will be satisfied and the disease can always be eradicated by some suitable vaccination strategies. This warns over-evaluating the effect of vaccination.

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REFERENCES

[1] F. V. Atkinson and J. R. Haddock, *On determining phase spaces for functional differential equations*, Funkcial. Ekvac., **31** (1988), 331–347.

[2] E. Beretta, T. Hara, W. Ma and Y. Takeuchi, *Global asymptotic stability of an SIR epidemic model with distributed time delay*, Nonlinear Anal., **47** (2001), 4107–4115.

[3] A. B. Gumel, C. C. MuCluskey and J. Watmough, *An SVEIR model for assessing potential impact of an imperfect anti-SARS vaccine*, Math. Biosci. Eng., **3** (2006), 485–512.

[4] A. Gabbuti, L. Romano, P. Blanc, et al., *Long-term immunogenicity of hepatitis B vaccination in a cohort of Italian healthy adolescents*, Vaccine, **25** (2007), 3129–3132.

[5] J. K. Hale and J. Kato, *Phase space for retarded equations with infinite delay*, Funkcial. Ekvac., **21** (1978), 11–41.

[6] Y. Hino, S. Murakami and T. Naito, "Functional-Differential Equations with Infinite Delay," Lecture Notes in Mathematics, **1473**, Springer-Verlag, 1991.
[7] J. R. Haddock and J. Terjéki, *Liapunov-Razumikhin functions and an invariance principle for functional-differential equations*, J. Differential Equations, **48** (1983), 95–122.
[8] J. R. Haddock, T. Krisztin and J. Terjéki, *Invariance principles for autonomous functional-differential equations*, J. Integral equations, **10** (1985), 123–136.
[9] G. Huang, Y. Takeuchi, W. Ma and D. Wei, *Global stability for delay SIR and SEIR epidemic models with nonlinear incidence rate*, Bull. Math. Biol., **72** (2010), 1192–1207.
[10] G. Huang, Y. Takeuchi and W. Ma, *Lyapunov functionals for delay differential equations model of viral infections*, SIAM J. Appl. Math., **70** (2010), 2693–2708.
[11] A. Korobeinikov and P. K. Maini, *A Lyapunov function and global properties for SIR and SEIR epidemiological models with nonlinear incidence*, Math. Biosci. Eng., **1** (2004), 57–60.
[12] A. Korobeinikov, *Global properties of infectious disease models with nonlinear incidence*, Bull. Math. Biol., **69** (2007), 1871–1886.
[13] Y. Kuang, "Delay Differential Equations with Applications in Population Dynamics," Mathematics in Science and Engineering, **191**, Academic Press, Boston, MA, 1993.
[14] G. Li and Z. Jin, *Global stability of a SEIR epidemic model with infectious force in latent, infected and immune period*, Chaos Solitons Fractals, **25** (2005), 1177–1184.
[15] M. Y. Li, J. R. Graef, L. Wang and J. Karsai, *Global dynamics of a SEIR model with varying total population size*, Math. Biosci., **160** (1999), 191–213.
[16] M. Y. Li and H. Shu, *Impact of intracellular delays and target-cell dynamics on in vivo viral infections*, SIAM J. Appl. Math., **70** (2010), 2434–2448.
[17] M. Y. Li and J. S. Muldowney, *Global stability for the SEIR model in epidemiology*, Math. Biosci., **125** (1995), 155–164.
[18] X. Liu, Y. Takeuchi and S. Iwami, *SVIR epidemic models with vaccination strategies*, J. Theo. Biol., **253** (2008), 1–11.
[19] S. Liu and L. Wang, *Global stability of an HIV-1 model with distributed intracellular delays and a combination therapy*, Math. Biosci. Eng., **7** (2010), 675–685.
[20] P. Magal, C. C. McCluskey and G. Webb, *Lyapunov functional and global asymptotic stability for an infection-age model*, Applicable Analysis, **89** (2010), 1109–1140.
[21] C. C. McCluskey, *Global stability for an SEIR epidemiological model with varying infectivity and infinite delay*, Math. Biosci. Eng., **6** (2009), 603–610.
[22] C. C. McCluskey, *Complete global stability for an SIR epidemic model with delay–distributed or discrete*, Nonlinear Anal. RWA., **11** (2010), 55–59.
[23] G. Röst and J. Wu, *SEIR epidemiological model with varying infectivity and infinite delay*, Math. Biosci. Eng., **5** (2008), 389–402.
[24] P. van den Driessche and J. Watmough, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Math. Biosci., **180** (2002), 29–48.

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