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GLOBAL PROPERTIES OF A DELAYED SIR EPIDEMIC MODEL WITH MULTIPLE PARALLEL INFECTIOUS STAGES

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Abstract. In this paper, we study the global properties of an SIR epidemic model with distributed delays, where there are several parallel infective stages, and some of the infected cells are detected and treated, which others remain undetected and untreated. The model is analyzed by determining a basic reproduction number R_0, and by using Lyapunov functionals, we prove that the infection-free equilibrium E^0 of system (3) is globally asymptotically attractive when $R_0 \leq 1$, and that the unique infected equilibrium E^* of system (3) exists and it is globally asymptotically attractive when $R_0 > 1$.

1. **Introduction.** It is well known that many infectious diseases in a population are often described by an SIR model where the population is divided into three species: susceptible individuals (S), infectious individuals (I) and recovered individuals (R). The basic forms of these models are ordinary differential equations (ODEs) (see [5, 6], [10, 11, 12]), where the models do not have a prolonged infectious period. However, the infection of the disease may have different consequences. For example, some infected hosts can be properly detected and treated. Based on this fact, Korobeinikov [9] proposed an SIR model of infectious diseases with several parallel infective stages. In [9], he considered the SIR model with n alternative infectious pathways and n noninteracting infective subclasses $I_i,\ i = 1, 2, \cdots, n$, and assumed that after infection an individual immediately moves from the susceptible compartment into one of the infective compartments, and then entered into the

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recovered compartment where remains thereafter. In addition, the transmission of the infection is denoted by $\beta_i S I_i$ in [9], so the SIR model can be written as follows:

$$\begin{cases} \dot{S}(t) = \lambda - \sum_{j=1}^{n} \beta_j I_j(t) S(t) - \mu S(t), \\ \dot{I}_i(t) = p_i \sum_{j=1}^{n} \beta_j I_j(t) S(t) - \delta_i I_i(t), \ i = 1, 2, \cdots, n. \\ \dot{R}_i(t) = \sum_{j=1}^{n} r_j I_j(t) - \sigma_i R_i(t), \end{cases} \tag{1}$$

where

(A_1) $p_i \in (0, 1)$ is the probability for an infected individual to enter the ith infective compartment;

(A_2) λ is the recruitment rate of the susceptible class;

(A_3) μ is the natural death rate of the susceptible individuals, and δ_i is the rate of the infectious individuals of the ith compartment leave this compartment (that is, $\delta_i = r_j + \mu$), where r_j denotes the recovery rate;

(A_4) σ_i is the remove rate of the recovered individuals.

In [1], in order to account for transmission by mosquitoes, Cooke investigated a discrete delay model, where the delay is used to denote a latent period in the vector. Takeuchi et al. [23] presented the equations for epidemics (e.g. malaria) spread by vectors (mosquitoes) which have an incubation time to become infectious. Their model would give rise to a system of distributed delay differential equations, and McCluskey [17] considered the equations with a bounded distributed delay and a general nonlinear incidence function to study the properties of the SIR epidemic model, respectively. In view of the complexity of delay differential equations (DDEs), many scholars have studied their mathematical models without delays. In fact, many biological processes have inherent delays, and it may lead to additional insights in the study of complicated biological processes. Herz et al. [7] first proposed and studied an HIV-1 model with delay in 1996. Henceforth, some authors developed their models with discrete or distributed delays (see [2, 4, 14, 24, 15, 22, 25]). This paper extends the results of Korobeinikov [9] adding a distributed delay. The direct Lyapunov method and the notion of an auxiliary function have found a wider range of application and Lyapunov functions may be used to achieve a multitude of diverse tasks. For example, this method may be applied to estimate the rate of convergence to a steady state, or the size of a basin of attraction in ODEs (see [9], [10, 11, 12]). The approach here is to use a Lyapunov functional of the type used by McCluskey [17]. Recently, [16, 18, 19, 20, 21] which used a similar Lyapunov functional.

In this paper, a delayed SIR model of infectious disease with several parallel infective stages is introduced in Section 2. In Section 3, by constructing Lyapunov functionals, we show that the global asymptotic behaviors of the model relies only on the basic reproduction number R_0. The paper ends with conclusions in Section 4.

2. **The model and equilibria.** In this section, we develop the model give in [9] by the following system of DDEs:

$$\begin{cases} \dot{S}(t) = \lambda - \mu S(t) - \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j, \\ \dot{I}_i(t) = p_i \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j - \delta_i I_i(t), \\ \dot{R}_i(t) = \sum_{j=1}^{n} r_i I_j(t) - \sigma_i R_i(t), \end{cases} \tag{2}$$

where following [8] and [3], the vectors can be omitted from the equations by including a distributed delay τ_j in the incidence term up to a maximum delay $h > 0$. The incidence at time t is $\beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j$(here k_j is a Lebesgue integrable function). We can choose β_j such that $\int_0^h k_j(\tau_j) d\tau_j = 1$.

The variables and the other parameters are defined the same as (1).

Since R_i does not appear in the first two equations, it is sufficient to analyze the behavior of solutions of subsystem as follows:

$$\begin{cases} \dot{S}(t) = \lambda - \mu S(t) - \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j, \\ \dot{I}_i(t) = p_i \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j - \delta_i I_i(t). \end{cases} \tag{3}$$

The initial condition for system (3) is

$$S(0) \in R_{\geq 0}, \ I_i(\theta) = \phi_i(\theta), \quad \text{for } \theta \in [-h, 0], \tag{4}$$

where $\phi_i \in C = C([-h, 0], R_{\geq 0})$, the space of continuous functions from $[-h, 0]$ to $R_{\geq 0}$, equipped with the sup-norm: $\|\phi\| = \sup_{\theta \in [-h,0]} \phi(\theta)$. By the standard theory of functional differential equations [8], we can prove that the solutions of system (3) with initial condition (4) exist and are differentiable for all $t > 0$. Moreover, the phase space $X = R_{\geq 0} \times \overbrace{C \times \cdots \times C}^{n}$ is positively invariant.

Lemma 2.1. *For initial conditions in (4), solutions of system (3) are positive and ultimately uniformly bounded in X.*

Proof. Since the right hand side of system (3) is completely continuous, so the solution $(S(t), I_1(t), \cdots, I_n(t))$ of system (3) with initial condition (4) exists and is unique. Clearly, from system (3), we have

$$\begin{aligned} S(t) &= S(0) e^{-\int_0^t (\mu + \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) I_j(\theta - \tau_j) d\tau_j) d\theta} \\ &\quad + \int_0^t \lambda e^{\int_t^\theta (\mu + \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) I_j(\xi - \tau_j) d\tau_j) d\xi} d\theta > 0, \end{aligned} \tag{5}$$

evidently, we obtain $S(t) > 0$ for all $t \geq 0$ since $S(0) > 0$.

Next, we will prove that $I_i(t) > 0$ for all $t \geq 0,\ i = 1, 2, \cdots, n$. We easily see that disease is initially present when the initial conditions $I_i(\theta_0)$ for some $\theta_0 \in [-h, 0]$; by the continuity, $I_i(t)$ is positive on some interval about θ_0, then there exists $t_1 > 0$ such that $I_i(t_1) > 0$. From the second equation of (3), we have

$$\dot{I}_i(t) \geq -\delta_i I_i(t),\ \text{ for } t \geq t_1,$$

so

$$I_i(t) \geq I_i(t_1)e^{-\delta_i(t-t_1)} > 0,\ \text{ for } t \geq t_1.$$

Let $U(t) = S(t) + I_i(t)$, then we have

$$\begin{aligned}\frac{dU(t)}{dt} &= \lambda - \mu S(t) - (1-p_i)\sum_{j=1}^{n}\beta_j\int_0^h k_j(\tau_j)S(t)I_j(t-\tau_j)d\tau_j - \delta_i I_i(t)\\ &\leq \lambda - \mu S(t) - \delta_i I_i(t)\\ &\leq \lambda - \mu(S(t) + I_i(t)),\end{aligned}$$

noting that $p_i \in (0, 1),\ \delta_i = r_i + \mu$, and so

$$\limsup_{t\to+\infty}(S(t) + I_i(t)) \leq \frac{\lambda}{\mu},\quad i = 1, 2, \cdots, n.$$

It follows that the system (3) is point dissipative. Without loss of generality, we assume that

$$S(t) + I_i(t) \leq \frac{2\lambda}{\mu},\ i = 1, 2, \cdots, n \text{ for all } t \geq -h.$$

Hence, we may assume $I_i(t)$ is bounded above, which in turn implies $\dot{S}(t) > 0$ for small $S(t)$, and so $S(t)$ is positive for $t > 0$. □

Now, we consider the equilibria of system (3). Obviously, system (3) always has an infection-free equilibrium $E^0 = (S^0, 0, 0, \cdots, 0)$, where $S^0 = \frac{\lambda}{\mu},\ I_i^0 = 0,\ i = 1, 2, \cdots, n$. Apart from this steady state, system (3) can also has the infected equilibrium $E^* = (S^*, I_1^*, I_2^*, \cdots, I_n^*)$, and satisfies the following algebraic equations:

$$\left.\begin{aligned}0 &= \lambda - \sum_{j=1}^{n}\beta_j I_j^* S^* - \mu S^*,\\ 0 &= p_i\sum_{j=1}^{n}\beta_j I_j^* S^* - \delta_i I_i^*,\end{aligned}\right. \qquad i = 1, 2, \cdots, n.$$

Therefore,

$$S^* = \frac{1}{\sum_{j=1}^{n}\frac{\beta_j p_j}{\delta_j}},\qquad I_i^* = \frac{(\lambda - \mu S^*)p_i}{\delta_i},\ i = 1, 2\cdots, n.$$

The basic reproduction number [3] for the model is

$$R_0 = \sum_{i=1}^{n}\beta_i\frac{p_i}{\delta_i}\frac{\lambda}{\mu}.$$

3. **Global dynamics.** In this section, we shall study the global attractivities of the infection-free equilibrium E^0 and the infected equilibrium E^* of system (3) by constructing the Lyapunov functionals, respectively.

Theorem 3.1.

(i) If $R_0 \le 1$, then the system (3) has no infected (or positive) equilibrium, and the infection-free equilibrium $E^0 = (S^0, 0, 0, \cdots, 0)$ is globally asymptotically attractive in $R^{n+1}_{\geq 0}$.

(ii) If $R_0 > 1$, then the infected equilibrium $E^* = (S^*, I_1^*, I_2^*, \cdots, I_n^*)$ is globally asymptotically attractive in R^{n+1}_{+}.

Proof. (i) Let $g(z) = z - 1 - \ln z,\ z \in R_+$, then $g(z) \ge 0$ for $z > 0$ and $g(z) = 0$ if and only if $z = 1$.

Define a Lyapunov functional,

$$V_1(t) = S^0 g(\frac{S(t)}{S^0}) + \sum_{i=1}^{n} a_i I_i(t) + S^0 U_+(t), \quad a_i = \frac{\beta_i \lambda}{\delta_i \mu}, \tag{6}$$

where

$$U_+(t) = \sum_{j=1}^{n} \beta_j \int_0^h F_j(\tau_j) I_j(t-\tau_j) d\tau_j, \quad F_j(\tau_j) = \int_{\tau_j}^{h} k_j(s) ds, \quad F_j(h) = 0.$$

Noting that $F_j(\tau_j) > 0$ for $0 \le \tau_j < h$ since the support of k_j has positive measure near h, and from $I_i(t) \ge 0$ implies $U_+(t) \ge 0$ with equality if and only if $I_i(t)$ is identically zero on the interval $[t-h, t]$.

We calculate the time derivative of $U_+(t)$,

$$\begin{aligned} \dot{U}_+(t) &= \frac{d}{dt} \sum_{j=1}^{n} \beta_j \int_0^h F_j(\tau_j) I_j(t-\tau_j) d\tau_j \\ &= \sum_{j=1}^{n} \beta_j \int_0^h \frac{d}{dt} F_j(\tau_j) I_j(t-\tau_j) d\tau_j \\ &= -\sum_{j=1}^{n} \beta_j \int_0^h F_j(\tau_j) \frac{d}{d\tau_j} I_j(t-\tau_j) d\tau_j. \end{aligned}$$

Using integration by parts, we obtain:

$$\begin{aligned} \dot{U}_+(t) &= \sum_{j=1}^{n} \beta_j F_j(\tau_j) I_j(t-\tau_j) \Big|_{\tau_j=0}^{h} + \sum_{j=1}^{n} \int_0^h \beta_j I_j(t-\tau_j) \frac{dF_j(\tau_j)}{d\tau_j} d\tau_j \\ &= \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) I_j(t) d\tau_j - \sum_{j=1}^{n} \int_0^h \beta_j k_j(\tau_j) I_j(t-\tau_j) d\tau_j. \end{aligned} \tag{7}$$

By (6), we obtain the time derivative of $V_1(t)$ along a solution of system (3):

$$\begin{aligned}
\dot{V}_1(t)\Big|_{(3)} &= (1-\frac{S^0}{S(t)})\dot{S}(t) + \sum_{i=1}^{n} a_i \dot{I}_i(t) + S^0\dot{U}_+(t) \\
&= \lambda - \mu S(t) - \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j)S(t)I_j(t-\tau_j)d\tau_j \\
&\quad -\frac{S^0}{S(t)}(\lambda - \mu S(t) - \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j)S(t)I_j(t-\tau_j)d\tau_j) \\
&\quad +\sum_{i=1}^{n} a_i(p_i \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j)S(t)I_j(t-\tau_j)d\tau_j - \delta_i I_i(t)) \\
&\quad +S^0\sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j)(I_j(t)-I_j(t-\tau_j))d\tau_j \\
&\overset{S^0=\frac{\lambda}{\mu}}{=} -\mu(S(t)-S^0)(1-\frac{S^0}{S(t)}) \\
&\quad +S(t)(\sum_{i=1}^{n} a_i p_i - 1)\sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j)I_j(t-\tau_j)d\tau_j \\
&\quad +\sum_{i=1}^{n}\beta_i I_i(t)S^0 - \sum_{i=1}^{n} a_i\delta_i I_i(t).
\end{aligned} \tag{8}$$

Using

$$R_0 = \sum_{i=1}^{n}\frac{\beta_i p_i}{\delta_i}\frac{\lambda}{\mu} = S^0\sum_{i=1}^{n}\frac{\beta_i p_i}{\delta_i}, \quad a_i = \frac{\beta_i\lambda}{\delta_i\mu}, \ i=1,2,\cdots,n.$$

Hence, we have

$$\dot{V}_1(t)\Big|_{(2)} = -\frac{\mu(S(t)-S^0)^2}{S(t)} + S(t)(R_0-1)\sum_{j=1}^{n}\beta_j\int_0^h k_j(\tau_j)I_j(t-\tau_j)d\tau_j \le 0$$

when $R_0 \le 1$ and $\dot{V}_1(t)\Big|_{(2)} = 0$ implies that $S(t) = S^0$ and $R_0 = 1$ or $I_i(t) = 0$. Therefore, the largest invariant set in $\{\dot{V}_1(t)\Big|_{(2)} = 0\}$ is the singleton $\{E^0\}$. By the LaSalle invariance principle [8] and [13], E^0 is globally attractive in X.

(ii) From section 2, we know that an infected equilibrium $E^* = (S^*, I_1^*, I_2^*, \cdots, I_n^*)$ exists, we now prove that E^* is globally asymptotically attractive in $\overset{o}{X}$. In particular, this means E^* is unique.

Define a Lyapunov functional for E^*,

$$V_2(t) = S^* g(\frac{S(t)}{S^*}) + \sum_{i=1}^{n} b_i g(\frac{I_i(t)}{I^*}) + U^+(t), \quad b_i = \frac{\beta_i S^*}{\delta_i}, \tag{9}$$

here

$$U^+(t) = \sum_{i=1}^{n}\int_0^h \beta_i S^* I_i^* F_i(\tau_i) g(\frac{I_i(t-\tau_i)}{I_i^*})d\tau_i,$$

$$F_i(\tau_i) = \int_{\tau_i}^h k_i(s)ds, \quad F_i(h) = 0.$$

Then we have

$$
\begin{aligned}
\dot{U}^{+}(t) &= \sum_{i=1}^{n}\beta_i S^* I_i^* \int_0^h F_i(\tau_i) g(\frac{I_i(t-\tau_i)}{I_i^*}) d\tau_i \\
&= -\sum_{i=1}^{n}\beta_i S^* I_i^* \int_0^h F_i(\tau_i) \frac{d}{d\tau_i} g(\frac{I_i(t-\tau_i)}{I_i^*}) d\tau_i \\
&= -\sum_{i=1}^{n}\beta_i S^* I_i^* F_i(\tau_i) g(\frac{I_i(t-\tau_i)}{I_i^*})\Big|_{\tau_i=0}^{h} \\
&\quad + \sum_{i=1}^{n}\beta_i S^* I_i^* \int_0^h \frac{dF_i(\tau_i)}{d\tau_i} g(\frac{I_i(t-\tau_i)}{I_i^*}) d\tau_i \\
&= \sum_{i=1}^{n}\beta_i S^* I_i^* \int_0^h (g(\frac{I_i(t)}{I_i^*}) - g(\frac{I_i(t-\tau_i)}{I_i^*})) d\tau_i \\
&= \sum_{i=1}^{n}\beta_i S^* I_i(t) - \sum_{i=1}^{n}\beta_i S^* \int_0^h k_i(\tau_i) I_i(t-\tau_i) d\tau_i \\
&\quad + \sum_{i=1}^{n}\beta_i S^* I_i^* \int_0^h k_i(\tau_i) \ln\frac{I_i(t-\tau_i)}{I_i(t)} d\tau_i.
\end{aligned}
\tag{10}
$$

In the following, we calculate the time derivative of $V_2(t)$ along the solution of (3) is given by

$$
\begin{aligned}
\dot{V}_2(t)\Big|_{(3)} &= (1-\frac{S^*}{S(t)})\dot{S}(t) + \sum_{i=1}^{n} b_i(1-\frac{I_i^*}{I_i(t)})\dot{I}_i(t) + \dot{U}^{+}(t) \\
&= \lambda - \mu S(t) - \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j \\
&\quad - \frac{S^*}{S(t)}(\lambda - \mu S(t) - \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j) \\
&\quad + \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j - \sum_{i=1}^{n} b_i \delta_i I_i(t) \\
&\quad - \sum_{i=1}^{n} b_i p_i \frac{I_i^*}{I_i(t)} \sum_{j=1}^{n}\beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j + \sum_{i=1}^{n} b_i \delta_i I_i^* \\
&\quad + \sum_{i=1}^{n}\beta_i S^* I_i^* \int_0^h k_i(\tau_i) \Big[\frac{I_i(t)}{I_i^*} - \frac{I_i(t-\tau_i)}{I_i^*} + \ln\frac{I_i(t-\tau_i)}{I_i(t)}\Big] d\tau_i.
\end{aligned}
\tag{11}
$$

Noting that

$$
\begin{aligned}
&\lambda = \mu S^* + \sum_{j=1}^{n}\beta_j S^* I_j^*, \\
&p_i \sum_{j=1}^{n}\beta_j I_j^* S^* = \delta_i I_i^*, \\
&b_i \delta_i I_i^* = b_i p_i \sum_{j=1}^{n}\beta_j I_j^* S^* = \beta_i S^* I_i^*.
\end{aligned}
\tag{12}
$$

Since $b_i = \frac{\beta_i S^*}{\delta_i}$, then $\sum\limits_{i=1}^{n} b_i p_i = 1$ and $b_i p_i \beta_j S^* I_j^* = b_j p_j \beta_i S^* I_i^*$. Hence, we get

$$
\begin{aligned}
\dot{V}_2(t)\Big|_{(3)} &= \mu S^* + \sum_{j=1}^{n} \beta_j S^* I_i^* - \mu S(t) - \frac{S^*}{S(t)}(\mu S^* + \sum_{j=1}^{n} \beta_j S^* I_j^*) + \mu S^* \\
&\quad + S^* \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) I_j(t-\tau_j) d\tau_j - \sum_{i=1}^{n} b_i \delta_i I_i(t) \\
&\quad - \sum_{i=1}^{n} b_i p_i \frac{I_i^*}{I_i(t)} \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j + \sum_{i=1}^{n} b_i \delta_i I_i^* \\
&\quad + \sum_{i=1}^{n} \beta_i S^* I_i^* \int_0^h k_i(\tau_i) \Big[\frac{I_i(t)}{I_i^*} - \frac{I_i(t-\tau_i)}{I_i^*} + \ln \frac{I_i(t-\tau_i)}{I_i(t)} \Big] d\tau_i \\
&= \mu S^* (2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*}) + \sum_{j=1}^{n} \beta_j S^* I_j^* (2 - \frac{S^*}{S(t)}) \\
&\quad + \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) (\ln \frac{I_j(t-\tau_j)}{I_j^*} - \ln \frac{I_j(t)}{I_j^*}) d\tau_j \\
&\quad - \sum_{j=1}^{n} b_i p_i \frac{I_i^*}{I_i(t)} \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j \\
&= \mu S^* (2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*}) + \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* (2 - \frac{S^*}{S(t)}) \\
&\quad - \sum_{i=1}^{n} b_i p_i \frac{I_i^*}{I_i(t)} \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j \\
&\quad + \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) \ln \frac{I_j(t-\tau_j)}{I_j^*} d\tau_j \\
&\quad + \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) \ln \frac{I_j^*}{I_j(t)} d\tau_j.
\end{aligned} \tag{13}
$$

Set

$$
\begin{aligned}
&\sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* (2 - \frac{S^*}{S(t)}) - \sum_{i=1}^{n} b_i p_i \frac{I_i^*}{I_i(t)} \sum_{j=1}^{n} \beta_j \int_0^h k_j(\tau_j) S(t) I_j(t-\tau_j) d\tau_j \\
&+ \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) (\ln \frac{I_j(t-\tau_j)}{I_j^*} + \ln \frac{I_j^*}{I_j(t)}) d\tau_j \\
&\triangleq \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) G(\tau_j) d\tau_j,
\end{aligned}
$$

where

$$
\begin{aligned}
G(\tau_j) &= 2 - \frac{S^*}{S(t)} - \frac{I_i^* I_j(t-\tau_j) S(t)}{I_i(t) I_j^* S^*} + \ln \frac{I_j(t-\tau_j)}{I_j^*} + \ln \frac{I_j^*}{I_j(t)} \\
&= 1 - \frac{S^*}{S(t)} + \ln \frac{S^*}{S(t)} + 1 - \frac{I_i^* I_j(t-\tau_j) S(t)}{I_i(t) I_j^* S^*} + \ln \frac{I_i^* I_j(t-\tau_j) S(t)}{I_i(t) I_j^* S^*} \\
&\quad + \ln \frac{I_j^*}{I_j(t)} + \ln \frac{I_i(t)}{I_i^*} \\
&= -g(\frac{S^*}{S(t)}) - g(\frac{I_i^* I_j(t-\tau_j) S(t)}{I_i(t) I_j^* S^*}) + \ln \frac{I_j^* I_i(t)}{I_j(t) I_i^*}.
\end{aligned} \tag{14}
$$

Note that

$$\begin{aligned}
&\sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \ln \frac{I_j^* I_i(t)}{I_j(t) I_i^*} \\
&= \sum_{i=2}^{n} b_i p_i \sum_{j=1}^{i-1} \beta_j S^* I_j^* \ln \frac{I_j^* I_i(t)}{I_j(t) I_i^*} + \sum_{i=1}^{n-1} b_i p_i \sum_{j=i+1}^{n} \beta_j S^* I_j^* \ln \frac{I_j^* I_i(t)}{I_j(t) I_i^*} \\
&= \sum_{i=2}^{n} b_i p_i \sum_{j=1}^{i-1} \beta_j S^* I_j^* \ln \frac{I_j^* I_i(t)}{I_j(t) I_i^*} + \sum_{i=2}^{n} b_i p_i \sum_{j=1}^{i-1} \beta_j S^* I_j^* \ln \frac{I_i^* I_j(t)}{I_i(t) I_j^*} \\
&= 0.
\end{aligned} \tag{15}$$

So, we obtain

$$\begin{aligned}
\dot{V}_2(t) &= \mu S^*(2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*}) + \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) G(\tau_j) d\tau_j \\
&= \mu S^*(2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*}) \\
&\quad - \sum_{i=1}^{n} b_i p_i \sum_{j=1}^{n} \beta_j S^* I_j^* \int_0^h k_j(\tau_j) \Big[g(\frac{S^*}{S(t)}) + g(\frac{I_i^* I_j(t-\tau_j) S(t)}{I_i(t) I_j^* S^*}) \Big] d\tau_j \\
&\leq 0.
\end{aligned}$$

We have $G(\tau_j) \leq 0$, since $g(z) \geq 0$ and

$$2 - \frac{S^*}{S(t)} - \frac{S(t)}{S^*} \leq 0.$$

Then, we have $\dot{V}_2(t)\Big|_{(2)} \leq 0$ for all $(S, I_1, I_2, \cdots, I_n) \in \overset{o}{X}$, and thus omega limit sets of solutions are contained the largest invariant subset of $\{\dot{V}_2(t)\Big|_{(2)} = 0\}$. So $\dot{V}_2(t) \equiv 0$ if and only if

$$S(t) = S^*, \quad \frac{I_i^* I_j(t-\tau_j) S(t)}{I_i(t) I_j^* S^*} = 1.$$

Along a solution in this set, we have

$$S(t) = S^*, \; \dot{S}(t) = \dot{I}_i(t) \equiv 0, \; i = 1, 2, \cdots, n,$$

which means that

$$S(t) = S^*, \; I_i(t) = I_i^*, \; i = 1, 2, \cdots, n,$$

thus, the largest invariant subset is $\{E^*\}$. By the LaSalle invariance principle [8] and [13], we can show that the infected equilibrium E^* is globally asymptotically attractive. □

4. **Conclusions.** A delayed SIR epidemic model with multiple infection stages of infectious individuals such as some of the infected are detected and treated, the others remain undetected and untreated is investigated in our paper. The total target cells are divided into a healthy target cell compartment S, n infected target cell compartments representing different infectious stages. The purpose for this paper is to study how the diversities of stages and pathways can affect the global dynamics of a pathogen population system, and to extend the works in Korobeinikov [9]. The global dynamics of the uninfected and infected steady states of these models are established by direct Lyapunov method. It is shown from the results that the

basic reproduction numbers R_0 determined the global dynamics of our model: the infection-free equilibrium E^0 of system (3) is globally asymptotically attractive when $R_0 \leq 1$; the infected equilibrium E^* of system (3) is globally asymptotically attractive when $R_0 > 1$.

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REFERENCES

[1] K. L. Cooke, *Stability analysis for a vector disease model*, Rocky Mount. J. Math., **9** (1979), 31–42.

[2] R. V. Culshaw and S. Ruan, *A delay-differential equation model of HIV infection of $CD4^+$ T cells*, Math. Biosci., **165** (2000), 27–39.

[3] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, *On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations*, J. Math. Biol., **28** (1990), 365–382.

[4] S. A. Gourley, Y. Kuang and J. D. Nagy, *Dynamics of a delay differential equation model of hepatitis B virus infection*, J. Biol. Dynam., **2** (2008), 140–153.

[5] H. W. Hethcote, *Qualitative analyses of communicable disease models*, Math. Biosci., **28** (1976), 335–356.

[6] H. W. Hethcote, *The mathematics of infectious diseases*, SIAM Rev., **42** (2000), 599–653.

[7] V. Herz, S. Bonhoeffer, R. Anderson, R. M. May and M. A. Nowak, *Viral dynamics in vivo: Limitations on estimations on intracellular delay and virus delay*, Proc. Natl. Acad. Sci. USA, **93** (1996), 7247–7251.

[8] J. Hale and S. Verduyn Lunel, "Introduction to Functional Differential Equations," Applied Mathematical Sciences, **99**, Springer-Verlag, New York, 1993.

[9] A. Korobeinikov, *Global properties of SIR and SEIR epidemic models with multiple parallel infectious stages*, Bull. Math. Biol., **71** (2009), 75–83.

[10] 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.

[11] A. Korobeinikov, *Global asymptotic properties of virus dynamics models with dose-dependent parasite reproduction and virulence and nonlinear incidence rate*, Math. Med. Biol., **26** (2009), 225–239.

[12] A. Korobeinikov, *Lyapunov functions and global stability for SIR and SIRS epidemiological models with non-linear transmission*, Bull. Math. Biol., **68** (2006), 615–626.

[13] Y. Kuang, "Delay Differential Equations with Applications in Population Dynamics," Mathematics in Science and Engineering, **191**, Academic Press, Inc., Boston, MA, 1993.

[14] M. Y. Li and H. Shu, *Global dynamics of an in-host viral model with intracellular delay*, Bull. Math. Biol., **72** (2010), 1492–1505.

[15] S. Liu, S. Wang and L. Wang, *Global dynamics of delay epidemic models with nonlinear incidence rate and relapse*, Nonlinear Anal. Real World Appl., **12** (2011), 119–127.

[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] C. C. McCluskey, *Global stability of an epidemic model with delay and general nonlinear incidence*, Math. Biosci. and Eng., **7** (2010), 837–850.

[18] P. Magal, C. C. McCluskey and G. Webb, *Lyapunov functional and global asymptotic stability for an infection-age model*, Appl. Anal., **89** (2010), 1109–1140.

[19] C. C. McCluskey, *Global stability for an SEIR epidemiological model with varying infectivity and infinite delay*, Math. Biosci. and Eng., **6** (2009), 603–610.

[20] C. C. McCluskey, *Complete global stability for an SIR epidemic model with delay–distributed or discrete*, Nonlinear Anal. Real World Appl., **11** (2010), 55–59.
[21] C. C. McCluskey, *Global stability for an SIR epidemic model with delay and nonlinear incidence*, Nonlinear Anal. Real World Appl., **11** (2010), 3106–3109.
[22] K. A. Pawelek, S. Liu, F. Pahlevani and L. Rong, *A model of HIV-1 infection with two time delays: Mathematical analysis and comparison with patient data*, Math. Biosci., **235** (2012), 98–109.
[23] Y. Takeuchi, W. Ma and E. Beretta, *Global asymptotic properties of a delay SIR epidemic model with finite incubation times*, Nonlinear Anal., **42** (2000), 931–947.
[24] J. Wang, G. Huang, Y. Takeuchi and S. Liu, *Sveir epidemiological model with varying infectivity and distributed delays*, Math. Biosci. and Eng., **8** (2011), 875–888.
[25] X. Wang, Y. D. Tao and X. Y. Song, *A delayed HIV-1 infection model with Beddington-DeAngelis functional response*, Nonlinear Dyn., **62** (2010), 67–72.

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