

## SEIR EPIDEMIOLOGICAL MODEL WITH VARYING INFECTIVITY AND INFINITE DELAY

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**ABSTRACT.** A new SEIR model with distributed infinite delay is derived when the infectivity depends on the age of infection. The basic reproduction number  $\mathcal{R}_0$ , which is a threshold quantity for the stability of equilibria, is calculated. If  $\mathcal{R}_0 < 1$ , then the disease-free equilibrium is globally asymptotically stable and this is the only equilibrium. On the contrary, if  $\mathcal{R}_0 > 1$ , then an endemic equilibrium appears which is locally asymptotically stable. Applying a permanence theorem for infinite dimensional systems, we obtain that the disease is always present when  $\mathcal{R}_0 > 1$ .

**1. Introduction.** Most traditional compartmental models in mathematical epidemiology descend from the classical SIR model of Kermack and McKendrick, where the population is divided into the classes of susceptible, infected, and recovered individuals. 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, leading to an SEIR-model. Such models have been widely discussed in the literature. Local and global stability analyses of the disease-free and endemic equilibria have been carried out using different assumptions and contact rates in [14],[15],[18],[19],[20],[21],[22],[29], and [30]. Certain delayed effects have been also taken into account in some models (see [6],[27], and [28]).

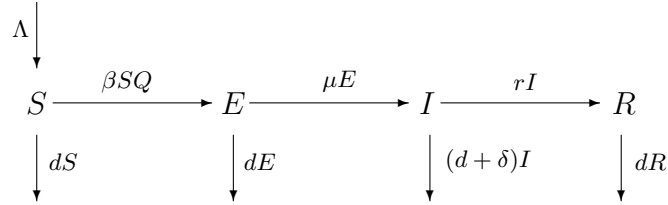
All of the models cited above assume the homogeneity of the infected class: all individuals in that compartment share the same epidemiological parameters. In reality, however, as time elapses and the disease develops within the host, its infectivity might continuously change. The purpose of this paper is to incorporate

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**Figure 1.** Disease transmission ( $Q = \int_0^\infty k(a)i(t, a)da$ )

this feature into the SEIR model. Models keeping track of an individual's infection-age have existed for particular diseases, for instance tuberculosis [7], HIV/AIDS [5],[26], Chagas disease [13], or pandemic influenza [1]. However, our general SEIR model is formulated as a system of delay differential equations with infinite delay.

The paper is organized as follows. In section 2, taking into account the age of infection as a parameter, we formulate a new SEIR model with distributed and infinite delay. We identify the basic reproduction number  $\mathcal{R}_0$  as a threshold quantity regarding the local asymptotic stability of the disease free equilibrium in section 3. In section 4 we show that a stable endemic equilibrium exists if and only if  $\mathcal{R}_0 > 1$ . Section 5 concerns the global stability of the disease-free equilibrium. In section 6 we show that the disease is endemic in the sense of permanence whenever  $\mathcal{R}_0 > 1$ . Disregarding the demographic effects, we derive a final size relation in section 7. Finally, sections 8 and 9 contain several examples and some discussions.

**2. Model derivation.** Assume that a given population may be divided into the following categories: susceptibles (those who are capable of contracting the disease); exposed (those who are infected but not yet infectious); infectives (those who are infected and capable of transmitting the disease); and recovered (those who are permanently immune). Denote the number of individuals at time  $t$  in these classes by  $S(t), E(t), I(t), R(t)$ , respectively. Let  $i(t, a)$  represent the density of infected individuals with respect to the age of infection  $a$  at the current time  $t$ , then  $I(t) = \int_0^\infty i(t, a)da$ . We introduce the kernel function  $0 \leq k(a) \leq 1$  to express the infectivity according to the age of infection  $a$ . In what follows,  $\Lambda$  denotes the constant recruitment rate,  $\beta$  is the baseline transmission rate,  $d$  is the natural death rate,  $\delta$  is the disease-induced death rate,  $1/\mu$  is the average latency period and  $1/r$  is the average infectivity period. All these constants are assumed to be positive. Then, using bilinear incidence in the force of infection corrected by the infectivity factor due to the age of infection, we arrive at the following SEIR model:

$$\begin{aligned}\frac{dS(t)}{dt} &= \Lambda - \beta S(t) \int_0^\infty k(a)i(t,a)da - dS(t), \\ \frac{dE(t)}{dt} &= \beta S(t) \int_0^\infty k(a)i(t,a)da - (\mu + d)E(t), \\ \frac{dI(t)}{dt} &= \mu E(t) - (d + \delta + r)I(t), \\ \frac{dR(t)}{dt} &= rI(t) - dR(t).\end{aligned}$$

The disease transmission diagram is depicted in Figure 1. The evolution of the density is given by

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)i(t,a) = -(d + \delta + r)i(t,a), \quad (1)$$

subject to the following boundary condition

$$i(t,0) = \mu E(t).$$

Solving (1) leads to

$$i(t,a) = i(t-a,0)e^{-(d+\delta+r)a} = \mu E(t-a)e^{-(d+\delta+r)a},$$

and we obtain the following deterministic model of delay differential equations:

$$\frac{dS(t)}{dt} = \Lambda - \beta S(t) \int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+r)a}da - dS(t), \quad (2)$$

$$\frac{dE(t)}{dt} = \beta S(t) \int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+r)a}da - (\mu + d)E(t), \quad (3)$$

$$\frac{dI(t)}{dt} = \mu E(t) - (d + \delta + r)I(t), \quad (4)$$

$$\frac{dR(t)}{dt} = rI(t) - dR(t). \quad (5)$$

Since our model contains terms with infinite delay, it is necessary to address the question of well-posedness of system (2-5). To specify a solution for all future time  $t \geq 0$ , we need to know the history of the  $E$ -class on  $(-\infty, 0]$ . From a biological point of view, it may seem natural to choose the space  $BC$  of bounded continuous functions on  $(-\infty, 0]$ ; however, this space may not be desirable for the qualitative theory of functional-differential equations with unbounded delay. See [25], where this issue has been discussed. Therefore, following the standard procedure, we use the phase space  $UC_g$  of fading memory type, see the definition below. Let  $g : (-\infty, 0] \rightarrow [1, \infty)$  be a continuous nonincreasing function with

- (g1)  $g(0) = 1$ ;
- (g2)  $g(s+u)/g(s) \rightarrow 1$  uniformly on  $(-\infty, 0]$  as  $u \rightarrow 0^-$ ; and
- (g3)  $g(s) \rightarrow \infty$  as  $s \rightarrow -\infty$ . Then we can define

$UC_g : \{\phi : (-\infty, 0] \rightarrow R, \phi/g \text{ is bounded and uniformly continuous on } (-\infty, 0]\}$ ,

which is a Banach-space equipped with the norm

$$\|\phi\| = \sup_{s \leq 0} \left| \frac{\phi(s)}{g(s)} \right|.$$

It is well known (see [3], [10]) that standard uniqueness, continuation, and continuous dependence theorems hold in the space  $UC_g$ . Moreover, the bounded solutions

corresponding to initial values from  $BC$  have precompact orbits in  $UC_g$ . For the general theory and applications, see [3], [8], [9], [10], [16], [17], [23] and references thereof.

For our purposes the exponential fading memory is suitable with  $g(s) = \exp(-\Delta s)$ , where  $0 < \Delta < d + \delta + r$ . It is easy to see that (g1), (g2) and (g3) hold with this choice of  $g$ . Denote the space  $UC_g$  with  $g(s) = \exp(-\Delta s)$  by  $C_\Delta$ . Then

$$\int_0^\infty k(a)e^{-(d+\delta+r)a}g(-a)da = \int_0^\infty k(a)e^{(\Delta-d+\delta+r)a}da < \infty$$

is satisfied and our norm on  $C_\Delta$  becomes

$$\|\phi\| = \sup_{s \leq 0} |\phi(s)e^{\Delta s}|.$$

Any  $\phi \in C_\Delta$  can be estimated by  $\phi(s) \leq \|\phi\|e^{-\Delta s}$ ,  $s \leq 0$ . For system (2-5),  $R \times C_\Delta \times \mathbb{R}^2$  serves as the phase space. Let  $E_t$  denote the state of the solution  $E(t)$  at time  $t$ ; i.e.  $E_t(s) = E(t+s)$ , where  $s \leq 0$ . We are interested only in the nonnegative solutions, the corresponding cone of non-negative functions in  $C_\Delta$  is denoted by  $Y$ ; i.e.

$$Y := \{\phi \in C_\Delta : \phi(s) \geq 0 \text{ for } s \leq 0\}.$$

Therefore, the initial conditions to (2-5) take the form

$$S(0) = s_0, E_0 = \phi, I(0) = i_0, R(0) = r_0, \tag{6}$$

where  $s_0, i_0, r_0 \in \mathbb{R}_0^+$  and  $\phi \in Y$ . It is straightforward to see that solutions with such initial conditions remain non-negative.

**Proposition 1.** *The system (2-5) is point dissipative; that is there exists an  $M > 0$  such that for any solution of (2-5) with initial condition (6), there exists a  $T_0 > 0$  such that  $S(t) \leq M, I(t) \leq M, R(t) \leq M$  and  $\|E_t\| \leq M$  for all  $t \geq T$ .*

*Proof.* Consider an arbitrary nonnegative solution, where  $\phi \in Y$  is the initial function for the  $E$ -class. For  $N(t) = S(t) + E(t) + I(t) + R(t)$ , we have

$$\frac{dN(t)}{dt} = \Lambda - dN(t) - \delta I(t) \leq \Lambda - dN(t).$$

Since any nonnegative solution of  $n'(t) = \Lambda - dn(t)$  satisfies  $\lim_{t \rightarrow \infty} n(t) = \Lambda/d$ , by a standard comparison argument we obtain

$$\limsup_{t \geq 0} N(t) \leq \frac{\Lambda}{d}.$$

We conclude that for any  $\varepsilon > 0$ , there is a  $T > 0$  such that the nonnegative solution of (2-5) satisfies

$$S(t) \leq \frac{\Lambda}{d} + \varepsilon, E(t) \leq \frac{\Lambda}{d} + \varepsilon, I(t) \leq \frac{\Lambda}{d} + \varepsilon, R(t) \leq \frac{\Lambda}{d} + \varepsilon,$$

whenever  $t \geq T$ . We still have to estimate  $\|E_t\|$ . Let  $K$  be the maximum of  $E(t)$  on  $[0, T]$ . For any  $t > T$ ,

$$\begin{aligned} \|E_t\| &= \sup_{s \leq 0} E_t(s)e^{\Delta s} = \sup_{u \leq t} E(u)e^{\Delta u}e^{-\Delta t} \\ &\leq \max\{e^{-\Delta t}\|\phi\|, Ke^{\Delta T}e^{-\Delta t}, \frac{\Lambda}{d} + \varepsilon\}, \end{aligned}$$

where the last estimation was obtained by separation to  $u \leq 0, 0 \leq u \leq T$  and  $T \leq u \leq t$ . Consequently, we can choose any  $M > \frac{\Lambda}{d}$ . □

**3. Basic reproduction number and the disease-free equilibrium.** Clearly our model has a disease-free equilibrium  $P_0 = (S_0, 0, 0, 0)$  where  $S_0 = \Lambda/d$ . To find the basic reproduction number  $\mathcal{R}_0$ , we introduce a single exposed individual into a totally susceptible population in the disease-free equilibrium at  $t = 0$ . The probability of the presence 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

$$\mathcal{R}_0 = \beta S_0 \int_0^\infty \int_0^\infty k(a) \mu e^{-(d+\delta+r)a} e^{-(\mu+d)t} da dt,$$

which reduces to

$$\mathcal{R}_0 = \frac{\beta S_0 \mu}{\mu + d} \int_0^\infty k(a) e^{-(d+\delta+r)a} da, \quad (7)$$

after interchanging the integrals. Next we show that  $\mathcal{R}_0$  determines the stability of the disease-free equilibrium.

**Theorem 3.1.** *The disease-free equilibrium is locally asymptotically stable if  $\mathcal{R}_0 < 1$  and unstable if  $\mathcal{R}_0 > 1$ .*

*Proof.* By Chapter 5 of [12] (in particular Corollary 5.3.5), it is sufficient to check that each characteristic root has negative real part. Let  $V(t) = S(t) - S_0$ . Linearizing the system about  $(V, E, I, R) = (0, 0, 0, 0)$  gives, using  $\Lambda = dS_0$ ,

$$\begin{aligned} \frac{dV(t)}{dt} &= -\beta S_0 \mu \int_0^\infty k(a) E(t-a) e^{-(d+\delta+r)a} da - dV(t), \\ \frac{dE(t)}{dt} &= \beta S_0 \mu \int_0^\infty k(a) E(t-a) e^{-(d+\delta+r)a} da - (\mu + d)E(t), \\ \frac{dI(t)}{dt} &= \mu E(t) - (d + \delta + r)I(t), \\ \frac{dR(t)}{dt} &= rI(t) - dR(t). \end{aligned}$$

Substituting the Ansatz  $\underline{w}e^{\lambda t}$ , where  $\underline{w} = (v_0, l_0, i_0, r_0)$ , leads to the relations

$$\begin{aligned} \lambda e^{\lambda t} v_0 &= -\beta S_0 \mu \int_0^\infty k(a) e^{\lambda(t-a)} l_0 e^{-(d+\delta+r)a} da - d e^{\lambda t} v_0, \\ \lambda e^{\lambda t} l_0 &= \beta S_0 \mu \int_0^\infty k(a) e^{\lambda(t-a)} l_0 e^{-(d+\delta+r)a} da - (\mu + d) e^{\lambda t} l_0, \\ \lambda e^{\lambda t} i_0 &= \mu e^{\lambda t} l_0 - (d + \delta + r) e^{\lambda t} i_0, \\ \lambda e^{\lambda t} r_0 &= r e^{\lambda t} i_0 - d e^{\lambda t} r_0. \end{aligned}$$

Without loss of generality, we may assume  $l_0 = 1$ . Simplifying by  $e^{\lambda t}$ , we obtain

$$\begin{aligned} v_0 &= -\frac{\beta S_0 \mu}{\lambda + d} \int_0^\infty k(a) e^{-(\lambda+d+\delta+r)a} da, \\ i_0 &= \frac{\mu}{\lambda + d + \delta + r}, \\ r_0 &= \frac{\mu r}{(\lambda + d + \delta + r)(\lambda + d)}, \end{aligned}$$

where  $\lambda$  is a root of the characteristic function

$$h(\lambda) = \beta S_0 \mu \int_0^\infty k(a) e^{-(\lambda+d+\delta+r)a} da - (\lambda + \mu + d). \quad (8)$$

Clearly,  $h(\lambda)$  is a monotone decreasing continuous function for nonnegative real  $\lambda$  and  $h(\infty) = -\infty$ . We have

$$h(0) = \beta S_0 \mu \int_0^\infty k(a) e^{-(d+\delta+r)a} da - (\mu + d) = (\mu + d)(\mathcal{R}_0 - 1).$$

If  $\mathcal{R}_0 > 1$ , then there exists a positive real root, and the disease-free equilibrium is unstable. Suppose that  $\lambda = x + iy$  is a root of  $h(\lambda)$  with  $x > 0$ . Then  $|e^{-\lambda a}| < 1$  for any  $a > 0$ , and

$$\begin{aligned} 1 &= \left| \frac{\beta S_0 \mu}{\lambda + \mu + d} \int_0^\infty k(a) e^{-(\lambda+d+\delta+r)a} da \right| \\ &\leq \frac{\beta S_0 \mu}{|\lambda + \mu + d|} \int_0^\infty k(a) |e^{-\lambda a}| e^{-(d+\delta+r)a} da < \mathcal{R}_0. \end{aligned}$$

Therefore, if  $\mathcal{R}_0 < 1$ , then all roots have negative real part and the disease-free equilibrium is locally asymptotically stable.  $\square$

#### 4. The endemic equilibrium.

**Theorem 4.1.** *An endemic equilibrium exists if and only if  $\mathcal{R}_0 > 1$ . Moreover, the endemic equilibrium, if exists, is unique and locally asymptotically stable.*

*Proof.* An endemic equilibrium  $P^* = (S^*, E^*, I^*, R^*)$  must satisfy the algebraic equations

$$dS^* = \Lambda - \beta S^* \mu \int_0^\infty k(a) E^* e^{-(d+\delta+r)a} da, \quad (9)$$

$$(\mu + d)E^* = \beta S^* \mu \int_0^\infty k(a) E^* e^{-(d+\delta+r)a} da, \quad (10)$$

$$\mu E^* = (d + \delta + r)I^*, \quad (11)$$

$$dR^* = rI^*. \quad (12)$$

Since  $E^* \neq 0$ , (10) yields

$$S_0/S^* = \mathcal{R}_0, \quad \text{or} \quad S^* = \frac{\Lambda}{\mathcal{R}_0 d}. \quad (13)$$

Simple calculations on (9) show that

$$\frac{\Lambda}{\mathcal{R}_0} = \Lambda - (d + \mu)E^*;$$

that is

$$E^* = \frac{\Lambda}{d + \mu} \left(1 - \frac{1}{\mathcal{R}_0}\right).$$

So, we conclude that  $E^* > 0$  if and only if  $\mathcal{R}_0 > 1$ . In this case the other two coordinates of  $P^*$  are given by

$$\begin{aligned} I^* &= \frac{\Lambda \mu}{(d + \mu)(d + \delta + r)} \left(1 - \frac{1}{\mathcal{R}_0}\right), \\ R^* &= \frac{\Lambda \mu r}{d(d + \mu)(d + \delta + r)} \left(1 - \frac{1}{\mathcal{R}_0}\right). \end{aligned}$$

Now we show the local asymptotic stability of the endemic equilibrium. Introduce the new variables  $V(t) = S(t) - S^*$ ,  $D(t) = E(t) - E^*$ ,  $J(t) = I(t) - I^*$  and  $Q(t) = R(t) - R^*$ . Notice that

$$\beta\mu \int_0^\infty k(a)E^*e^{-(d+\delta+r)a} da = \mathcal{R}_0 - 1.$$

Linearizing about the endemic equilibrium  $P^* = (S^*, E^*, I^*, R^*)$  gives the system

$$\begin{aligned} \frac{dV(t)}{dt} &= -V(t)(\mathcal{R}_0 - 1) - \beta S^* \mu \int_0^\infty k(a)D(t-a)e^{-(d+\delta+r)a} da - dV(t), \\ \frac{dD(t)}{dt} &= V(t)(\mathcal{R}_0 - 1) + \beta S^* \mu \int_0^\infty k(a)D(t-a)e^{-(d+\delta+r)a} da - (\mu + d)D(t), \\ \frac{dJ(t)}{dt} &= \mu D(t) - (d + \delta + r)J(t), \\ \frac{dQ(t)}{dt} &= rJ(t) - dQ(t). \end{aligned}$$

Substituting the exponential Ansatz, after some elementary calculations, we can derive the characteristic equation

$$h(\lambda) = (\lambda + \mu + d - \mathcal{S}_\lambda)(\mathcal{R}_0 - 1 + d + \lambda) + \mathcal{S}_\lambda(\mathcal{R}_0 - 1) = 0,$$

where, for simplicity, we use the notation

$$\mathcal{S}_\lambda = \beta S^* \mu \int_0^\infty k(a)e^{-\lambda a} e^{-(d+\delta+r)a} da.$$

Then  $\mathcal{S}_0 = \mu + d$  and  $h(0) = (\mu + d)(\mathcal{R}_0 - 1) > 0$ . Suppose that  $\lambda$  is a root of  $h(\lambda)$  and  $\operatorname{Re} \lambda \geq 0$ , that implies  $|e^{-\lambda a}| \leq 1$  for any  $a \geq 0$ . Now the inequalities

$$|\mathcal{S}_\lambda| \leq \mu + d \leq |\lambda + \mu + d|$$

and

$$|d + \lambda| < |\mathcal{R}_0 - 1 + d + \lambda|$$

follow. But  $h(\lambda) = 0$  is equivalent to

$$\mathcal{S}_\lambda(d + \lambda) = (\lambda + \mu + d)(\mathcal{R}_0 - 1 + d + \lambda),$$

a contradiction. Therefore, every root has negative real part and the endemic equilibrium is locally asymptotically stable if  $\mathcal{R}_0 > 1$ .  $\square$

## 5. Global stability of the disease-free equilibrium.

**Theorem 5.1.** *If  $\mathcal{R}_0 < 1$ , then all solutions converge to the disease-free equilibrium.*

*Proof.* For any  $\varepsilon > 0$ , define

$$\mathcal{R}_\varepsilon = \frac{\beta\mu}{\mu + d} \left( \frac{\Lambda}{d} + \varepsilon \right) \int_0^\infty k(a)e^{-(d+\delta+r)a} da.$$

Then clearly  $\lim_{\varepsilon \rightarrow 0} \mathcal{R}_\varepsilon = \mathcal{R}_0$  and  $\mathcal{R}_\varepsilon < 1$  if  $\mathcal{R}_0 < 1$  and  $\varepsilon$  is sufficiently small. In Proposition 1. we have shown that for any  $\varepsilon > 0$  there is a  $T > 0$  such that  $S(t) \leq \frac{\Lambda}{d} + \varepsilon$  whenever  $t > T$ . Thus, without loss of generality, we can suppose that  $S(t) \leq \frac{\Lambda}{d} + \varepsilon$  for all  $t \geq 0$ . This yields that the exposed population  $E(t)$  is bounded above by the solutions of the linear equation

$$\frac{dE(t)}{dt} = \beta \left( \frac{\Lambda}{d} + \varepsilon \right) \int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+r)a} da - (\mu + d)E(t).$$

Now analogously to the proof of Theorem 3.1, from  $\mathcal{R}_\varepsilon < 1$  we obtain that the characteristic roots of this linear equation have negative real parts and the global stability of the disease-free equilibrium follows from the standard comparison argument.  $\square$

**6. Permanence.** Now we restrict our attention to the subsystem

$$\frac{dS(t)}{dt} = \Lambda - \beta S(t) \int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+r)a} da - dS(t), \quad (14)$$

$$\frac{dE(t)}{dt} = \beta S(t) \int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+r)a} da - (\mu + d)E(t). \quad (15)$$

Denote by  $T(t)$ ,  $t \geq 0$  the family of solution operators corresponding to (14-15). Because of the infinite delay, we can not expect that the solution operator ever becomes completely continuous. However, we can apply a permanence theorem of Hale and Waltman [11], which does not require the compactness of the solution operators. Let  $X = R_0^+ \times Y$ , according to (14-15). We introduce some notations and terminology: the positive orbit  $\gamma^+(x)$  through  $x \in X$  is defined as  $\gamma^+(x) = \cup_{t \geq 0} \{T(t)x\}$ . The  $\omega$ -limit set  $\omega(x)$  of  $x$  consists of  $y \in X$  such that there is a sequence  $t_n \rightarrow \infty$  as  $n \rightarrow \infty$  with  $T(t_n)x \rightarrow y$  as  $n \rightarrow \infty$ . The semigroup  $T(t)$  is said to be asymptotically smooth, if for any bounded subset  $U$  of  $X$ , for which  $T(t)U \subset U$  for any  $t \geq 0$ , there exists a compact set  $\mathcal{M}$  such that  $d(T(t)U, \mathcal{M}) \rightarrow 0$  as  $t \rightarrow \infty$ . The following result is taken from [11, Theorem 4.2]:

**Theorem.** Suppose that we have the following:

- (i)  $X^0$  is open and dense in  $X$  with  $X^0 \cup X_0 = X$  and  $X^0 \cap X_0 = \emptyset$ ;
- (ii) the solution operators  $T(t)$  satisfy

$$T(t) : X^0 \rightarrow X^0, \quad T(t) : X_0 \rightarrow X_0;$$

- (iii)  $T(t)$  is point dissipative in  $X$ ;
- (iv)  $\gamma^+(U)$  is bounded in  $X$  if  $U$  is bounded in  $X$ ;
- (v)  $T(t)$  is asymptotically smooth;
- (vi)  $\mathcal{A} = \bigcup_{x \in A_b} \omega(x)$  is isolated and has an acyclic covering  $N$ , where  $A_b$  is the global attractor of  $T(t)$  restricted to  $X_0$  and  $N = \cup_{i=1}^k N_i$ ;
- (vii) for each  $N_i \in N$ ,

$$W^s(N_i) \cap X^0 = \emptyset,$$

where  $W^s$  refers to the stable set.

Then  $T(t)$  is a uniform repeller with respect to  $X^0$ , i.e. there is an  $\eta > 0$  such that for any  $x \in X^0$ ,  $\liminf_{t \rightarrow \infty} d(T(t)x, X_0) \geq \eta$ .

**Theorem 6.1.** *If  $\mathcal{R}_0 > 1$ , then the disease is endemic; more precisely, there exists an  $\eta > 0$  such that*

$$\liminf_{t \rightarrow \infty} E(t) \geq \eta.$$

*Proof.* Let

$$X^0 = \{(S, \phi) : \phi(\theta) > 0 \text{ for some } \theta < 0\}$$

$$X_0 = \{(S, \phi) : \phi(\theta) = 0 \text{ for all } \theta \leq 0, \}.$$

We check all the conditions of the permanence theorem. It is straightforward to see that (i) and (ii) are satisfied. The point dissipativity has been proved in Proposition 1, so we have (iii). Let  $U$  be a bounded set of  $X$ , and  $B > 0$  be such that for any  $(\sigma, \phi) \in U$ ,  $\sigma < B$  and  $\|\phi\| \leq B$ . Let  $\psi(s) := Be^{\Delta s}$ ,  $s \leq 0$ . This function



dominates any other in  $U$ . Consider the solution  $\bar{S}(t), \bar{E}(t)$  with initial condition  $S(0) = B, E_0 = \psi$ . We claim that for any solution  $S(t), E(t)$  with initial data from  $U$ , we have  $S(t) < \bar{S}(t)$  and  $E(t) < \bar{E}(t)$  for  $t \geq 0$ . Indeed, suppose that  $t_0$  is the smallest  $t$  such that  $E(t) = \bar{E}(t)$  and  $S(t) \leq \bar{S}(t)$  for all  $t \in [0, t_0]$ . Then  $E'(t_0) > \bar{E}'(t_0)$  and

$$\beta S(t) \int_0^\infty k(a) \mu E(t-a) e^{-(d+\delta+r)a} da > \beta \bar{S}(t) \int_0^\infty k(a) \mu \bar{E}(t-a) e^{-(d+\delta+r)a} da,$$

a contradiction. Similarly, if  $t_0$  is the smallest  $t$  such that  $S(t) = \bar{S}(t)$  and  $E(t) \leq \bar{E}(t)$  for all  $t \leq t_0$ , then  $S'(t_0) > \bar{S}'(t_0)$  and

$$\int_0^\infty k(a) \mu E(t-a) e^{-(d+\delta+r)a} da > \int_0^\infty k(a) \mu \bar{E}(t-a) e^{-(d+\delta+r)a} da,$$

contradiction again. Thus  $T(t)$  is monotone, and using the arguments of Proposition 1, we can show that  $\bar{S}(t), \bar{E}(t)$  are bounded and dominate every solution with initial data from  $U$ . Hence, we obtain (iv).

Next we show that  $T(t)$  is asymptotically smooth (v). Let  $M > \Lambda/d$  and

$$\mathcal{M} := \{\phi \in C_\Delta : \sup_{s \leq 0} \phi(s) e^{\frac{\Delta}{2}s} \leq M\}.$$

From Lemma 3.2 of [4], we know that  $\mathcal{M}$  is compact in  $C_\Delta$ . Consider an arbitrary bounded set  $U \subset X$ , and let  $E_t$  be the segment of a solution with  $E_0 \in U$ . By Proposition 1, there exists a  $T > 0$  such that  $E(t) \leq M$  for  $t \geq T$  and  $E(T) = M$  or  $E(t) < M$  for all  $t > 0$ . In the first case, let  $K$  be the maximum of  $E(t)$  on  $[0, T]$  and define for  $t > T$  the function  $\psi^t(s)$  such that

$$\psi^t(s) := \begin{cases} E(t+s) e^{-\frac{\Delta}{2}s} & \text{if } T-t \leq s \leq 0, \\ M e^{-\frac{\Delta}{2}s} & \text{if } s \leq T-t. \end{cases}$$

Then, obviously  $\psi^t \in \mathcal{M}$  and

$$d(E_t, \mathcal{M}) \leq d(E_t, \psi^t) = \sup_{s \leq 0} |E_t(s) - \psi^t(s)| e^{\Delta s}.$$

Separating to the intervals  $[T-t, 0]$ ,  $[-t, T-t]$ ,  $(-\infty, -t]$ , we obtain

$$\begin{aligned} \sup_{T-t \leq s \leq 0} |E_t(s) - \psi^t(s)| e^{\Delta s} &= 0, \\ \sup_{-t \leq s \leq T-t} |E_t(s) - \psi^t(s)| e^{\Delta s} &\leq (K e^{\Delta T} + M e^{\frac{\Delta}{2}T}) e^{-\frac{\Delta}{2}t}, \end{aligned}$$

and

$$\sup_{s \leq -t} |E_t(s) - \psi^t(s)| e^{\Delta s} \leq (\|E_0\| + M) e^{-\Delta t}.$$

Summarizing, we get that

$$\lim_{t \rightarrow \infty} d(E_t, \mathcal{M}) = 0,$$

and  $T(t)$  is asymptotically smooth. The case  $E(t) < M$  for all  $t > 0$  is easier and can be treated analogously. Thus, we confirmed (v).

Regarding (vi), clearly  $\mathcal{A} = \{P_0\}$  (now  $P_0 = (\Lambda/d, 0) \in X$ ) and isolated. Hence the covering is simply  $N = \{P_0\}$ , which is acyclic (there is no orbit which connects  $P_0$  to itself in  $X_0$ ).

It remains to show that  $W^s(P_0) \cap X^0 = \emptyset$ . Suppose the contrary, that is there exists a solution  $u_t \in X^0$  such that

$$\lim_{t \rightarrow \infty} S(t) = S_0, \quad \lim_{t \rightarrow \infty} E(t) = 0.$$

Now we take advantage of  $\mathcal{R}_0 > 1$ : there exists an  $\varepsilon > 0$  such that

$$\beta(S_0 - \varepsilon) \int_0^\infty k(a)\mu e^{-(d+\delta+r)a} da > \mu + d.$$

There exists a  $t_0$  such that for  $t \geq t_0$ ,  $S(t) > S_0 - \varepsilon$  and

$$E'(t) \geq \beta(S_0 - \varepsilon) \int_0^\infty k(a)\mu E(t-a)e^{-(d+\delta+r)a} da - (\mu + d)E(t).$$

There exists a  $t_1$  such that

$$\beta(S_0 - \varepsilon) \int_0^{t_1} k(a)\mu e^{-(d+\delta+r)a} da > \mu + d.$$

For  $t \geq t^* := \max\{t_0, t_1\}$ ,

$$E'(t) \geq \beta(S_0 - \varepsilon) \int_0^{t^*} k(a)\mu E(t-a)e^{-(d+\delta+r)a} da - (\mu + d)E(t).$$

If  $E(t) \rightarrow 0$ , as  $t \rightarrow \infty$ , then by a standard comparison argument and the nonnegativity, the solution  $n(t)$  of

$$n'(t) = \beta(S_0 - \varepsilon) \int_0^{t^*} k(a)\mu n(t-a)e^{-(d+\delta+r)a} da - (\mu + d)n(t)$$

with initial data  $n_0 = E_0$ , has to converge to 0 as well. By the mean value theorem for integrals we know that for any  $t$  there is a  $\xi_t$  such that

$$\int_0^{t^*} k(a)n(t-a)e^{-(d+\delta+r)a} da = n(\xi_t) \int_0^{t^*} k(a)e^{-(d+\delta+r)a} da$$

and  $t - t^* \leq \xi_t \leq t$ . Define

$$V(t) := n(t) + (\mu + d) \int_{\xi_t}^t n(s) ds.$$

Differentiating with respect to time gives

$$\frac{dV}{dt} = \left( \beta(S_0 - \varepsilon) \int_0^{t^*} k(a)\mu e^{-(d+\delta+r)a} da - (\mu + d) \right) n(\xi_t) \geq 0.$$

Therefore,  $V(t)$  goes to infinity or approaches a positive limit as  $t \rightarrow \infty$ . On the other hand, by the definition of  $V$ ,  $\lim_{t \rightarrow \infty} n(t) = 0$  implies  $\lim_{t \rightarrow \infty} V(t) = 0$ , a contradiction. Thus  $W^s(P_0) \cap X^0 = \emptyset$  and we can apply Theorem 4.2 of [11] to obtain that

$$\liminf_{t \rightarrow \infty} \|E_t\| \geq \eta,$$

and by similar estimates as in the proof of Proposition 1, we get

$$\liminf_{t \rightarrow \infty} E(t) > \eta.$$

Finally, we can use a standard comparison argument to obtain

$$\liminf_{t \rightarrow \infty} I(t) > \eta\mu/(d + \delta + r).$$

□

**7. Final size relation.** It is interesting to check, whether the standard final size relation

$$\ln s_\infty = \mathcal{R}_0(s_\infty - 1) \quad (16)$$

holds for the epidemiological model, where  $s_\infty$  is the portion of susceptibles who have not been infected during the whole course of the epidemics. The generality of final size relations has been studied in detail in [2] and [24]. If the disease runs on a short course, demographic changes might be ignored; hence  $\Lambda = 0$  and  $d = 0$  are assumed. Our model reduces to

$$\frac{dS(t)}{dt} = -\beta S(t) \int_0^\infty k(a)\mu E(t-a)e^{-(\delta+r)a} da, \quad (17)$$

$$\frac{dE(t)}{dt} = \beta S(t) \int_0^\infty k(a)\mu E(t-a)e^{-(\delta+r)a} da - \mu E(t), \quad (18)$$

$$\frac{dI(t)}{dt} = \mu E(t) - (\delta + r)I(t), \quad (19)$$

$$\frac{dR(t)}{dt} = rI(t), \quad (20)$$

and the reproduction number becomes

$$\mathcal{R}_0 = \beta S_0 \int_0^\infty k(a)e^{-(\delta+r)a} da.$$

We have

$$\frac{d}{dt}(S(t) + E(t)) = -\mu E(t), \quad (21)$$

and

$$\frac{d}{dt}(S(t) + E(t) + I(t) + R(t)) = -\delta I(t);$$

therefore  $E(\infty) = I(\infty) = 0$ . Integrating (17) and (21) from 0 to  $\infty$ , we obtain

$$S(\infty) = S_0 \exp\left(-\beta \int_0^\infty \int_0^\infty k(a)\mu E(t-a)e^{-(\delta+r)a} dadt\right),$$

$$S(\infty) - S_0 - E_0 = -\mu \int_0^\infty E(s)ds.$$

Assuming  $E_0 \ll 1$ ,  $E(u) \ll 1$  for  $u < 0$  and interchanging the integrals, we obtain the final size relation

$$S(\infty) = S_0 \exp\left(-\beta(S_0 - S(\infty)) \int_0^\infty k(a)e^{-(\delta+r)a} da\right),$$

which is, for  $s_\infty = \frac{S(\infty)}{S_0}$ , the relation

$$s_\infty = \exp[(s_\infty - 1)\mathcal{R}_0],$$

equivalent with the well-known ‘‘classical’’ final size relation (16).

**8. Some examples.**

8.1. **Constant infectivity.** If  $k(a) = 1$  for all  $a \geq 0$ , then

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

and our model (2)-(5) reduces to the standard SEIR-model

$$\begin{aligned} \frac{dS(t)}{dt} &= \Lambda - \beta S(t)I(t) - dS(t), \\ \frac{dE(t)}{dt} &= \beta S(t)I(t) - (\mu + d)E(t), \\ \frac{dI(t)}{dt} &= \mu E(t) - (d + \delta + r)I(t), \\ \frac{dR(t)}{dt} &= rI(t) - dR(t), \end{aligned}$$

with

$$\mathcal{R}_0 = \frac{\beta\Lambda\mu}{d(\mu + d)(d + \delta + r)}.$$

8.2. **Exponential kernel function.** If the infectivity exponentially decays as time elapses since infection, then  $k(a) = e^{-qa}$  for some  $q > 0$ . Then the basic reproduction number becomes

$$\mathcal{R}_0 = \frac{\beta\Lambda\mu}{d(\mu + d)(d + \delta + r + q)}.$$

Then, with respect to the parameter  $q$ , we can say that the disease is always present and the endemic equilibrium is locally asymptotically stable if

$$\frac{\beta\Lambda\mu}{d(\mu + d)} - (d + \delta + r) > q,$$

and there is no endemic equilibrium and the disease free equilibrium is globally asymptotically stable if

$$\frac{\beta\Lambda\mu}{d(\mu + d)} - (d + \delta + r) < q.$$

8.3. **Linear increasing kernel function.** Suppose that the kernel function is given by

$$k(a) = \begin{cases} ca & \text{if } a \leq 1/c \\ 1 & \text{otherwise.} \end{cases}$$

In this case, by partial integration, we have

$$\begin{aligned} \int_0^\infty k(a)e^{-(d+\delta+r)a} da &= \int_0^{1/c} cae^{-(d+\delta+r)a} da + \int_{1/c}^\infty e^{-(d+\delta+r)a} da \\ &= \frac{c - (c + d + \delta + r)e^{-\frac{d+\delta+r}{c}}}{(d + \delta + r)^2} + \frac{e^{-\frac{d+\delta+r}{c}}}{d + \delta + r} \\ &= \frac{c - ce^{-\frac{d+\delta+r}{c}}}{(d + \delta + r)^2} \end{aligned}$$

and the basic reproduction number is

$$\mathcal{R}_0 = \frac{\beta\Lambda\mu(c - ce^{-\frac{d+\delta+r}{c}})}{d(\mu + d)(d + \delta + r)^2}.$$

Therefore, we can formulate threshold conditions in terms of  $c$ .

**9. Discussion.** The novelty of our model is that we allow varying infectivity of the infected individuals as a function of the age of infection. This assumption leads to a system of differential equations with distributed infinite delay. We have shown that several standard theorems in mathematical epidemiology can be extended to this kind of SEIR model, and the basic reproduction  $\mathcal{R}_0$  has been calculated. If  $\mathcal{R}_0 < 1$ , the disease-free equilibrium is globally asymptotically stable, and this is the only equilibrium. On the contrary, if  $\mathcal{R}_0 > 1$ , then an endemic equilibrium appears which is locally asymptotically stable. Applying a permanence theorem for infinite dimensional systems, we obtain that the disease is always present when  $\mathcal{R}_0 > 1$ . In the future, it would be interesting to prove the global stability of the endemic equilibrium. Besides, we have shown that the standard final size relation holds when the course of the disease is short and the demographic changes are ignored.

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