Threshold Dynamics in a Delayed SIS Epidemic Model[1]

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An SIS epidemic model with maturation delay is analysed. It is shown that the disease dies out when the basic reproduction number $R_0 < 1$, and the disease remains endemic when $R_0 > 1$ in the sense of uniform persistence. When the disease induced death rate is sufficiently small, the global attractivity of the endemic equilibrium is also proved. © 2001 Academic Press

Key Words: maturation delay; epidemic model; threshold dynamics; persistence; global attractivity.

1. INTRODUCTION

In their recent paper, Cooke *et al.* [1] derived a population growth model for single-species with multiple life stages and came up with a delay differential equation

$$N'(t) = B(N(t-T))N(t-T)e^{-d_1 T} - dN(t), \qquad (1.1)$$

where $' = \frac{d}{dt}$, $N(t)$ is the adult (matured) population size at time t, $d > 0$ is the death rate constant at the adult stage, $B(N)$ is a birth rate function, T is the developmental or maturation time, and d_1 is the death rate constant for each life stage prior to the adult stage. Typical examples of birth rate functions $B(N)$ found in the biological literature are:

(B1) $B_1(N) = be^{-aN}$, with $a > 0$, $b > d$;

(B2) $B_2(N) = p/(q + N^n)$, with $p, q, n \geq 0$, and $\frac{p}{q} > d$;

(B3) $B_3(N) = A/N + c$, with $A > 0$, $d > c > 0$.

Functions B_1 and B_2 with $n = 1$ are used in fisheries and are known as the Ricker function and the Beverton−Holt function, respectively. Function $B_3(N)N$ represents a constant immigration rate A together with a linear birth term cN.

There have been many models for single-species population growth, which have taken into consideration the maturation delay, and most of these models basically fall into the following two types:

$$N'(t) = N(t)f(N(t), N(t - T)), \tag{1.2}$$

$$N'(t) = B(N(t - T))N(t - T) - dN(t) \tag{1.3}$$

(e.g., see Nisbet and Gurney [9, Sect. 8.3] and Freedman and Gopalsamy [4]). Equation (1.1) is different from (1.2) and (1.3) in that not only the maturation delay but also the death rate ($d_1 > 0$) in life stages prior to the adult stage is incorporated into the model. It has been shown that $d_1 > 0$ does make a difference in the dynamics of the population. See Cooke *et al.* [1, Sect. 3] for details.

Based on (1.1), Cooke *et al.* [1] also established an SIS epidemic model

$$
\begin{aligned}
I'(t) &= A(N - I)\frac{I}{N} - (d + \epsilon + \gamma)I \\[2mm]
S'(t) &= B(N(t - T))N(t - T)e^{-d_1T} - dS - \frac{\lambda SI}{N} + \gamma I \\[2mm]
N'(t) &= B(N(t - T))N(t - T)e^{-d_1T} - dN - \epsilon I,
\end{aligned}
\tag{1.4}
$$

where I is the infective population, S is the susceptible population, and $N = I + S$ is the total population. Here $\epsilon \geq 0$ is the disease induced death rate constant, $\gamma \geq 0$ is the recovery rate constant ($\frac{1}{\gamma}$ is the average infective time), and $\lambda > 0$ is the contact rate constant. The standard incidence function is used with $\frac{\lambda I}{N}$ giving the average number of adequate contacts with infectives of one susceptible per unit time. For some diseases, this incidence function seems to fit the data better than mass action incidence; see Mena-Lorca and Hethcote [8], de Jong *et al.* [2], and the references therein. This model is obtained under the following assumptions:

(A1) transmission of the disease occurs due to contact between susceptibles and infectives;

(A2) there is no vertical transmission;

(A3) the disease confers no immunity, and thus upon recovery an infective individual returns to the susceptible class (hence the name SIS model).

This type of model is appropriate for some bacterial infections. For a fatal disease, the recovery rate constant is set to zero, giving an SI model.

Because of the relation $N = I + S$, for (1.4) it is sufficient to consider

$$I'(t) = \lambda(N - I)\frac{I}{N} - (d + \epsilon + \gamma)I \tag{1.5}$$

$$N'(t) = B(N(t - T))N(t - T)e^{-d_1 T} - dN - \epsilon I.$$

The global dynamics of Eq. (1.1) and system (1.5) were studied in Cooke *et al.* [1]. For (1.5), a basic reproduction number was identified, that is,

$$R_0 = \frac{\lambda}{d + \epsilon + \gamma}, \tag{1.6}$$

which gives the average number of new infectives produced by one infective during the mean death adjusted infective period. When there is no delay ($T = 0$), R_0 acts as a sharp threshold, as shown in Cooke *et al.* [1, Theorem 4.1]. When $T > 0$, $R_0 < 1$ implies the existence of an unique non-trivial equilibrium called disease free equilibrium, which is globally asymptotically stable (Cooke *et al.* [1, Theorems 4.2–4.3]). In the case of $R_0 > 1$, there exists also an endemic equilibrium, in addition to the disease free one, and analysing the dynamics of (1.5) in this case becomes quite hard in general. For those $B(N)$ with $\frac{d}{dN}(B(N)N) > 0$, Cooke *et al.* [1, Theorems 4.4–4.5] obtained the globally asymptotic stability of the endemic equilibrium for $\epsilon = 0$ and established the locally asymptotic stability for $\epsilon > 0$ but with either $B(N) = B_2(N)$ or $B(N) = B_3(N)$. As for the general $B(N)$ and $\epsilon > 0$, the dynamics of (1.5) remains undetermined, and this paper makes an attempt in this direction. In other words, we will investigate the threshold dynamics of system (1.5) for more general $B(N)$ satisfying some biologically reasonable conditions, and we will allow $\epsilon > 0$. Our approach will be a combination of the theory of monotone dynamical systems, theory of asymptotically autonomous semiflows, some abstract persistence theorems, and a perturbation technique.

2. THRESHOLD DYNAMICS

We first impose the following conditions on (1.5):

(H1) $B(\cdot) \in C'((0, \infty), (0, \infty))$ with $B'(N) < 0$, $\forall N \in (0, \infty)$, $B(0^+) > (d + \epsilon)e^{d_1 T}$ and $de^{d_1 T} > B(\infty)$; and there exists a $G(.) \in C^1([0, \infty), R)$ such that $G(N) = B(N)N$, $\forall N > 0$.

(H2)   *Either* $(B(N)N)' > 0$, $\forall N \in (0, \infty)$, *or* $B(N)N$ is bounded on $(0, \infty)$ and the positive equilibrium $N_e = B^{-1}(de^{d_1 T})$ of (1.1) is globally asymptotically stable for initial values in $C([-T, 0], R^+)\backslash\{0\}$.

Note that the condition $(B(N)N)' > 0$, $\forall N \in (0, \infty)$, is sufficient for the global asymptotic stability of N_e for (1.1) with initial values in $C([-T, 0], R^+) \setminus \{0\}$ (see Cooke *et al.* [1, Theorem 3.1]). For other sufficient conditions, we refer to Cooke *et al.* [1, Theorem 3.3 (iii) and (iv)].

In order to get the existence, uniqueness, and positive invariance of solutions of (1.5), we define a function $F \in C(R_+^2, R)$ by

$$F(0, 0) = 0, \quad F(x, y) = \frac{xy}{x + y} \quad \text{if } (x, y) \in R_+^2 \setminus \{(0, 0)\}.$$

It is easy to verify that F is globally Lipschitz on R_+^2,

$$|F(x_1, y_1) - F(x_2, y_2)| \leq |x_1 - x_2| + |y_1 - y_2|,$$
$$\forall (x_i, y_i) \in R_+^2, i = 1, 2.$$

Using $S = N - I$, system (1.5) is transformed into the following nonlinear delayed system

$$\begin{aligned}
I'(t) &= -(d + \epsilon + \gamma)I + \lambda F(I, S) \\
S'(t) &= \gamma I - dS - \lambda F(I, S) \\
&\quad + G(I(t - T) + S(t - T))e^{-d_1 T}.
\end{aligned} \tag{2.1}$$

By Smith [10, Theorem 5.2.1], for any $\phi \in C_+ = C([-T, 0], R_+^2)$, there is a unique solution $(I(t, \phi), S(t, \phi))$ of (2.1) with $(I(\theta, \phi), S(\theta, \phi)) = \phi(\theta)$, $\forall \theta \in [-T, 0]$, and $I(t, \phi) \geq 0$, $S(t, \phi) \geq 0$ for all $t \geq 0$ in its maximal interval of existence. Then $N(t) = S(t) + I(t)$ satisfies the differential inequality

$$N'(t) \leq G(N(t - T))e^{-d_1 T} - dN.$$

By Smith [10, Theorem 5.1.1] and the standard comparison theorem, together with assumption (H2), it then follows that each solution $(I(t, \phi), S(t, \phi))$ exists globally on $[0, \infty)$ and solutions of (2.1) are ultimately bounded. Moreover, if $\phi = (\phi_1, \phi_2) \in C_+$ with $\phi_1(0) > 0$, by using the two equations in (2.1) respectively, we then have $I(t, \phi) > 0$, $S(t, \phi) > 0$, $\forall t \geq 0$.

Let $X = \{(\phi_1, \phi_2) \in C_+ : \phi_2(\theta) \geq \phi_1(\theta), \ \forall \theta = [-T, 0]\}$, $X_0 = \{(\phi_1, \phi_2) \in X : \phi_1(0) > 0\}$ and $\partial X_0 = X \setminus X_0$. Clearly, X_0 is an open set relative to X. To consider the dynamics of (1.5), we extend it to the system

$$\begin{aligned}
I'(t) &= \lambda F(I, N - I) - (d + \epsilon + \gamma)I, \\
N'(t) &= G(N(t - T))^{-d_1 T} - dN - \epsilon I.
\end{aligned} \tag{2.2}$$

By the aforementioned conclusions for (2.1), it then follows that for any $\phi \in X$, the unique solution $(I(t, \phi), N(t, \phi))$ of (2.2) with $(I(\theta, \phi), N(\theta, \phi)) = \phi(\theta)$, $\forall \theta \in [-T, 0]$, satisfies $I(t, \phi) \geq 0$ and $N(t, \phi) \geq I(t, \phi)$, $\forall t \in [0, \infty)$. Let $\Phi(t): X \to X$, $t \geq 0$, be the solution semiflow generated by (2.2), that is, $(\Phi(t)\phi)(\theta) = (I(t + \theta, \phi), N(t + \theta, \phi))$, $\theta \in [-T, 0]$, $t \geq 0$. Thus we further have $\Phi(t): X_0 \to X_0$, $\Phi(t): \partial X_0 \to \partial X_0$, $\forall t \geq 0$, and $\Phi(t): X \to X$ is point dissipative. By the standard theory of FDE (see, e.g., Hale and Verduyn Lunel [6]), $\Phi(t): X \to X$ is compact for each $t > T$, and hence, there is a global attractor A for $\Phi(t): X \to X$ (see Hale [5, Theorem 3.4.8]).

Now we are in the position to state and prove the following result of threshold dynamics for (1.5), determining whether the disease dies out or remains endemic eventually.

THEOREM 2.1. *Assume that* (H1) *and* (H2) *hold. If* $R_0 < 1$, *then every solution* $(I(t, \phi), N(t, \phi))$ *of* (1.5) *with* $\phi \in X_0$ *satisfies* $\lim_{t \to \infty} I(t, \phi) = 0$ *and* $\lim_{t \to \infty} N(t, \phi) = N_e$. *If* $R_0 > 1$, *then there is a* $\beta > 0$ *such that every solution* $(I(t, \phi), N(t, \phi))$ *of* (1.5) *with* $\phi \in X_0$ *satisfies* $\liminf_{t \to \infty} N(t, \phi) \geq \liminf_{t \to \infty} I(t, \phi) \geq \beta$.

Proof. Let $B(\cdot)$, λ, d, d_1, γ, and T be fixed. Then we have the following claim.

Claim 1. For any positive number ϵ_0 with $B(0^+) > (d + \epsilon_0)e^{d_1 T}$, there exists $\delta_1 = \delta_1(\epsilon_0) > 0$ such that for any $\epsilon \in [0, \epsilon_0]$, the solution semiflow $\Phi(t)$ associated with (2.2) satisfies $\limsup_{t \to \infty} \|\Phi(t)\phi\| \geq \delta_1$, $\forall \phi \in X_0$.

Indeed, let $\eta_1 = \frac{1}{2}(B(0^+) - (d + \epsilon_0)e^{d_1 T})$. Note that if $B(0^+) = \infty$, we replace $B(0^+)$ with any positive number $B^+ > (d + \epsilon_0)e^{d_1 T}$. Then there exists a $\delta_1 = \delta_1(\eta_1)$ such that $B(N) > B(0^+) - \eta_1 > 0$, $\forall 0 < N < \delta_1$. Suppose that, by contradiction, $\limsup_{t \to \infty} \|\Phi(t)\phi\| < \delta_1$ for some $\phi \in X_0$ and $\epsilon \in [0, \epsilon_0]$. Then there exists a $T_1 > 0$ such that $\|\Phi(t)\phi\| < \delta_1$, $\forall t \geq T_1$. Let $(I(t), N(t)) = (\Phi(t)\phi)(0)$, $t \geq 0$. Thus $N(t) \geq I(t)$, $\forall t \geq 0$, and hence $N(t)$ satisfies the differential inequality

$$N'(t) \geq (B(0^+) - \eta)N(t - T)e^{-d_1 T} - (d + \epsilon)N(t), \qquad \forall t > T_1.$$

Consider the linear delayed equation

$$N'(t) = (B(0^+) - \eta_1)N(t - T)e^{-d_1 T} - (d + \epsilon)N(t), \qquad t \geq T_1. \tag{2.3}$$

Since $B(0^+) - \eta_1 > 0$, (2.3) is a cooperative and irreducible equation, and hence, by Smith [10, Corollary 5.5.2], the linear stability of $(0, 0)$ for (2.3) is the same as for ordinary differential equation (by ignoring the delay in

$N(t - T))$

$$N'(t) = \big((B(0^+) - \eta_1)e^{-d_1 T} - (d + \epsilon)\big)N(t), \qquad t \geq T_1. \quad (2.4)$$

Note that $\eta_1 < B(0^+) - (d + \epsilon_0)e^{-d_1 T}$ and $\epsilon \in [0, \epsilon_0]$. We then have $(B(0^+) - \eta_1)e^{-d_1 T} - (d + \epsilon) > 0$, and hence, by Smith [10, Corollary 5.5.2], the stability modulus s of (2.3) is positive. Then, by Smith [10, Theorem 5.5.1], (2.3) admits a solution $N^*(t) = e^{st}u$ with $u > 0$. Since $N(t) > 0, \forall t > 0$, we can choose a $k > 0$ such that $N(t) > kN^*(t), \forall t \in [T_1 - T, T_1]$. By the comparison theorem of quasimonotone systems with delays (Smith [10, Theorem 5.1.1]), we get $N(t) \geq kN^*(t), \forall t \geq T_1$, and hence $\lim_{t \to \infty} N(t) = \infty$, which contradicts the boundedness of $(I(t), N(t))$ on $[0, \infty)$.

In the case of $R_0 < 1$, we have $\lambda < d + \epsilon + \gamma$. If $I(0) > 0$, then $N(t) \geq I(t) > 0, \forall t \geq 0$, and hence, by Eq. (1.5), we get

$$I'(t) \leq (\lambda - (d + \epsilon + \gamma))I(t), \qquad t \geq 0.$$

It then follows that

$$I(t) \leq I(0)e^{(\lambda - (d + \epsilon + \gamma))t}, \qquad t \geq 0,$$

and hence $\lim_{t \to \infty} I(t) = 0$ exponentially. Thus $N(t)$ satisfies the following non-autonomous delayed equation

$$N'(t) = B(N(t - T))N(t - T)e^{-d_1 T} - dN - \epsilon I(t),$$

which is asymptotic to the autonomous delayed equation (1.1). By the generalized Markus' theorem for asymptotically autonomous semiflows (see Thieme [14, Theorem 4.1]), together with assumption (H2) and Claim 1 above, it then follows that $\lim_{t \to \infty} N(t) = N_e$.

In the case of $R_0 > 1$, that is, $\lambda > d + \epsilon + \gamma$, let $M_1 = (0, 0)$ and $M_2 = (0, N_e)$. By assumption (H2), we have $\tilde{A}_\partial := \bigcup_{\phi \in \partial X_0} \omega(\phi) = \{M_1, M_2\}$, where $\omega(\phi)$ is the omega limit set of ϕ for the solution semiflow $\Phi(t)$. Clearly, M_1 and M_2 are disjoint, compact, and isolated invariant sets for the semiflow $\Phi(t)|_{\partial X_0}$, and no subset of $\{M_1, M_2\}$ forms a cycle in ∂X_0. We further have the following claim.

Claim 2. For any positive number ϵ_0 with $\lambda > d + \epsilon_0 + \gamma$, there exists $\delta_2 = \delta_2(\epsilon_0) > 0$ such that for any $\epsilon \in [0, \epsilon_0]$, the solution semiflow $\Phi(t)$ associated with (2.2) satisfies $\limsup_{t \to \infty}\|\Phi(t)\phi - (0, N_e)\| \geq \delta_2, \forall \phi \in X_0$.

Indeed, let $\eta_2 = \frac{1}{2}(1 + (d + \epsilon_0 + \gamma)/\lambda)$. Since $\lim_{(I, N) \to (0, N_e)} \frac{N - I}{N} = 1 > \eta_2$, there exists a $\delta_2 = \delta_2(\eta_2)$ such that $\frac{N - I}{N} > \eta_2, \forall 0 \leq I < \delta_2, |N - N_e| < \delta_2$. Suppose that, by contradiction, $\limsup_{t \to \infty}\|\Phi(t)\phi - (0, N_e)\| < \delta_2$ for some $\phi \in X_0$ and $\epsilon \in [0, \epsilon_0]$. Then there exists a $T_2 > 0$ such that $\|\Phi(t)\phi - (0, N_e)\| < \delta_2, \forall t \geq T_2$. let $(I(t), N(t)) = (\Phi(t)\phi)(0), t \geq 0$. Thus $I(t)$ satisfies the differential inequality

$$I'(t) \geq (\lambda\eta_2 - (d + \epsilon + \gamma))I(t), \qquad \forall t \geq T_2.$$

Then

$$I(t) \geq I(T_2)e^{(\lambda\eta_2 - (d + \epsilon + \gamma))(t - T_2)}, \qquad \forall t \geq T_2.$$

By the choice of η_2, we have $\lambda\eta_2 - (d + \epsilon + \gamma) \geq \lambda\eta_2 - (d + \epsilon_0 + \gamma) > 0$, and hence $\lim_{t \to \infty} I(t) = \infty$, which contradicts the boundedness of $(I(t), N(t))$ on $[0, \infty)$.

In view of Claims 1 and 2 above, it is easy to see that M_1 and M_2 are isolated invariant sets for $\Phi(t)$ in X, and $W^s(M_i) \cap X_0 = \emptyset$, $i = 1, 2$, where $W^s(M_i)$ is the stable set of M_i for $\Phi(t)$. By the acyclicity theorem on uniform persistence (see Hale and Waltman [7, Theorem 4.1]), for any positive ϵ satisfying (H1), the semiflow $\Phi(t)$ is uniformly persistent with respect to $(X_0, \partial X_0)$ in the sense that there is a $\beta_0 > 0$ such that $\lim\inf_{t \to \infty} dist(\Phi(t)\phi, \partial X_0) \geq \beta_0$ for all $\phi \in X_0$. Then, by Smith and Zhao [13, Theorem A.2] with $Z = C([-T, 0], R^2)$ and $e = (1, 1)$, there exists a $\beta > 0$ such that $(I(t, \phi), N(t, \phi)) = (\Phi(t)\phi)(0)$, $t \geq 0$, satisfies $\lim\inf_{t \to \infty} I(t, \phi) \geq \beta$ and $\lim\inf_{t \to \infty} N(t, \phi) \geq \beta$ for all $\phi \in X_0$. ∎

In the case that the disease induced death rate ϵ is sufficiently small and the basic reproduction number $R_0 > 1$, we have the following result on the global attractivity of the endemic equilibrium.

THEOREM 2.2. *Assume that* (H1) *with* $\epsilon = 0$ *and* (H2) *hold. If* $\frac{\lambda}{d + \gamma} > 1$, *then there exists an* $\bar{\epsilon} > 0$ *such that for any* $\epsilon \in [0, \bar{\epsilon}]$, *system* (1.5) *admits a positive equilibrium* $(I^*(\epsilon), N^*(\epsilon))$ *which is globally attractive in* X_0.

Proof. By assumption, we can choose an $\epsilon_0 > 0$ sufficiently small such that $B(0^+) > (d + \epsilon)e^{-d_1 T}$ and $R_0 := \lambda/(d + \epsilon_0 + \gamma) > 1$. Note that for any $\phi \in X$, the solution $(I(t, \phi), N(t, \phi))$ of (2.2) satisfies $N(t) \geq I(t) \geq 0$, $t \geq 0$, and

$$N'(t) \leq G(N(t - T))e^{-d_1 T} - dN(t), \qquad t \geq 0. \qquad (2.5)$$

Since $B(\infty) < de^{d_1 T}$, there exists a $K_0 > 0$ such that $B(N)e^{-d_1 T} - d < 0$, $\forall N \geq K_0$. Then Smith [10, Theorem 5.2.1 and Remark 5.2.1] imply that any interval $[0, K]$, $K \geq K_0$, is positively invariant for the scalar delayed equation

$$N'(t) = G(N(t - T))e^{-d_1 T} - dN(t), \qquad t \geq 0. \qquad (2.6)$$

In the case that $B(N)N$ is bounded by K_1 on $(0, \infty)$, $N(t, \phi)$ also satisfies

$$N'(t) \leq K_1 e^{-d_1 T} - dN(t), \qquad t \geq 0. \qquad (2.7)$$

By the comparison theorem for quasimonotone systems with delays (Smith [10, Theorem 5.1.1]) and the standard comparison theorem for scalar ordinary differential equations, it then follows that solutions of (2.2) are uniformly bounded and ultimately bounded uniformly for $\epsilon \in [0, \epsilon_0]$. Let

$\Phi(\epsilon, t)$ be the solution semiflow generated by (2.2). As mentioned before, for each $\epsilon \in [0, \epsilon_0]$ and $t > T$, $\Phi(\epsilon, t): X \to X$ is compact. It then easily follows that for any fixed $t > T$, $\Phi(\cdot, t)\phi : [0, \epsilon_0] \to X$ is continuous uniformly for ϕ in any bounded subset B of X, and hence, $\overline{\bigcup_{\epsilon \in [0, \epsilon_0]} \Phi(\epsilon, t)B}$ is compact in X (see, e.g., the Claim in the proof of Smith and Zhao [12, Theorem 3.1]). Moreover, there is a bounded and closed subset B_0 of X, independent of $\epsilon \in [0, \epsilon_0]$, such that for any $\phi \in X$, $\epsilon \in [0, \epsilon_0]$, there exists $t_0 = t_0(\phi, \epsilon) > 0$ such that $\Phi(\epsilon, t)\phi \in B_0$ for all $t \geq t_0$. Let $\omega_\epsilon(\phi)$ be the omega limit set of $\phi \in X$ for $\Phi(\epsilon, t): X \to X$. Clearly, $\omega_\epsilon(\phi)$ is invariant for $\Phi(\epsilon, t)$ and is a subset of B_0. Then,

$$\overline{\bigcup_{\epsilon \in [0, \epsilon_0], \, \phi \in X} \omega_\epsilon(\phi)} \subset \overline{\bigcup_{\epsilon \in [0, \epsilon_0], \, \phi \in X} \Phi(\epsilon, t)(\omega_\epsilon(\phi))}$$
$$\subset \overline{\bigcup_{\epsilon \in [0, \epsilon_0]} \Phi(\epsilon, t)B_0}, \qquad \forall t > T,$$

and hence $\overline{\bigcup_{\epsilon \in [0, \epsilon_0], \, \phi \in X} \omega_\epsilon(\phi)}$ is compact in X. By Theorem 2.1, for each $\epsilon \in [0, \epsilon_0]$, $\Phi(\epsilon, t)$ is uniformly persistent with respect to $(X_0, \partial X_0)$, and hence, by Hale and Waltman [7, Theorem 3.2], there is a global attractor A_ϵ^0 for $\Phi(\epsilon, t): X_0 \to X_0$. By the theorem on the uniform persistence uniform in parameters (see Smith and Zhao [12, Theorem 4.3 and Remark 4.2]), together with Claims 1 and 2 in the proof of Theorem 2.1, it then follows that there exist $\epsilon_1 \in (0, \epsilon_0]$ and $\beta_1 > 0$ such that $\liminf_{t \to \infty} dist(\Phi(\epsilon, t)\phi, \partial X_0) \geq \beta_1$ for all $\phi \in X_0$, $\epsilon \in [0, \epsilon_1]$. Thus there exists a bounded and closed subset B_0^* of X_0 such that $A_\epsilon^0 \subset B_0^*$ for all $\epsilon \in [0, \epsilon_1]$. For any $t > T$,

$$\overline{\bigcup_{\epsilon \in [0, \epsilon_1]} \Phi(\epsilon, t)A_\epsilon^0} \subset \overline{\bigcup_{\epsilon \in [0, \epsilon_1]} \Phi(\epsilon, t)B_0^*}, \qquad \text{and}$$

$$\overline{\bigcup_{\epsilon \in [0, \epsilon_1]} \Phi(\epsilon, t)A_\epsilon^0} = \overline{\bigcup_{\epsilon \in [0, \epsilon_1]} A_\epsilon^0} \subset \overline{B_0^*} = B_0^* \subset X_0.$$

Then $\overline{\bigcup_{\epsilon \in [0, \epsilon_1]} \Phi(\epsilon, t)A_\epsilon^0}$ is compact in X_0. When $\epsilon = 0$, system (2.2) admits a unique positive equilibrium $((1 - \frac{d+\gamma}{\lambda})N_e, N_e)$ which is globally asymptotically stable in X_0 (see Cooke *et al*. [1, Theorem 4.4]). By Smith and Waltman [11, Theorem 2.2] with $U = X_0$ and $B_\epsilon = A_\epsilon^0$, there is an $\bar{\epsilon} \in (0, \epsilon_1]$ such that for each $\epsilon \in [0, \bar{\epsilon}]$, system (2.2) admits a positive equilibrium $(I^*(\epsilon), N^*(\epsilon))$ with $(I^*(0), N^*(0)) = ((1 - \frac{d+\gamma}{\lambda})N_e, N_e)$, and $(I^*(\epsilon), N^*(\epsilon))$ is globally attractive in X_0. ∎

3. DISCUSSION

Under quite general conditions, we have proved that the basic reproduction number R_0 acts as a threshold for the SIS model (1.5): when $R_0 < 1$, the disease dies out, and when $R_0 > 1$ the disease remains endemic in the sense of uniform persistence. For the latter case, if the disease induced
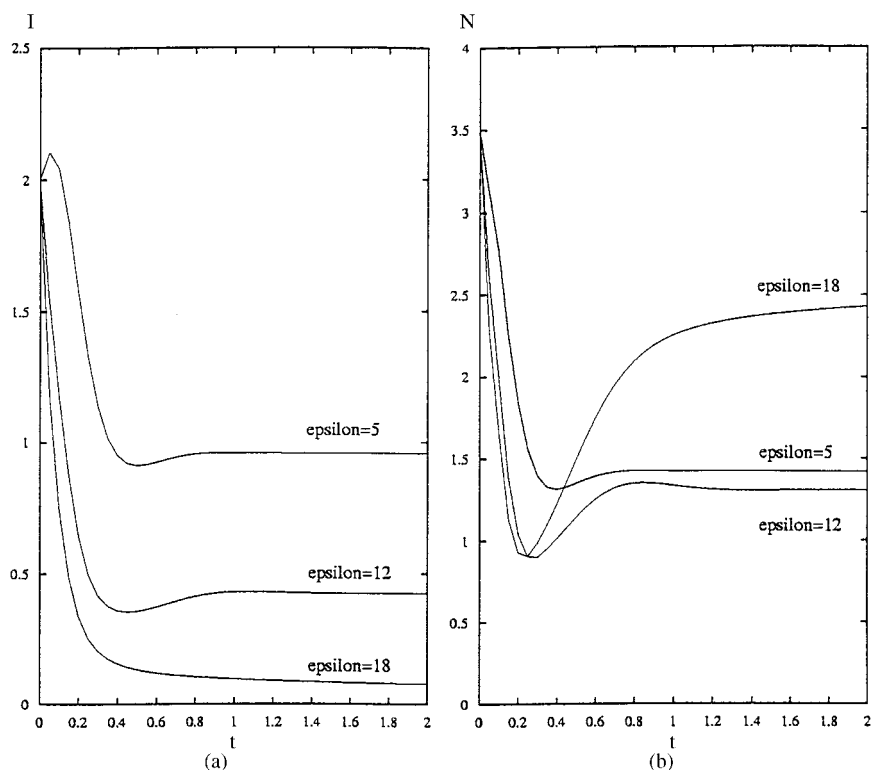
FIG. 1.   Numerical simulations for (1.5) with $B(N) = B_1(N)$, using XPPAUT (Ermentraut [3]). The parameters are chosen as follows: $a = d = d_1 = 1$, $b = 20$, $y = 0.5$, $T = 0.1$, and $\lambda = 20$. It is easy to verify that for these parameter values, the conditions in Theorems 2.1–2.2 are satisfied. Part (a) is for I and (b) is for N. The initial values are $I(s) = 2$, $N(s) = 3.5$ for all $s \in [-0.1, 0]$. Note that the critical value of $\epsilon > 0$ for $R_0 > 1$ is 18.5. Convergence to the endemic equilibrium is observed for values of $\epsilon < 18.5$ ($R_0 > 1$) and is shown in the figure for $\epsilon = 5, 12, 18$. For values of $\epsilon > 18.5$ ($R_0 < 1$), convergence to the disease free equilibrium (see Theorem 2.1) is also confirmed but not given in the figure.

death rate ϵ is sufficiently small, we even have proved that the endemic equilibrium is globally attractive. Some numerical simulations are shown in Fig. 1. There arises a natural question: When $R_0 > 1$, does the endemic equilibrium remain globally attractive for large values of $\epsilon > 0$? In proving Theorem 2.2, we made use of a perturbation theorem established in Smith and Waltman [11, Theorem 2.2], and hence our approach fails to answer this question and the problem remains open. We hope to be able to solve this open problem by using some new technique in a forthcoming paper.

REFERENCES

1. K. Cooke, P. van den Driessche, and X. Zou, Interaction of maturation delay and nonlinear birth in population and epidemic models, *J. Math. Biol.* **39** (1999), 332–352.
2. M. C. M. de Jong, O. Diekmann, and H. Heesterbeek, How does transmission of infection depend on population size? *in* "Epidemic Models" (D. Mollison, Ed.), pp. 84–94, Cambridge Univ. Press, Cambridge, UK, 1995.
3. B. Ermentraut, XPPAUT 4.30—The Differential Tool, 2000.
4. H. I. Freedman and K. Gopalsamy, Global stability in time-delayed single-species dynamics, *Bull. Math. Biol.* **48** (1986), 485–492.
5. J. Hale, "Asymptotic Behavior of Dissipative Systems," Math. Surveys and Monographs, Vol. 25, Amer. Math. Soc., Providence, 1988.
6. J. Hale, S. M. Verduyn Lunel, "Introduction to Functional Differential Equations," Springer-Verlag, New York, 1993.
7. J. Hale and P. Waltman, Persistence in infinite-dimensional systems, *SIAM J. Math. Anal.* **20** (1995), 388–395.
8. J. Mena-Lorca and H. W. Hethcote, Dynamic models of infectious diseases as regulators of population sizes, *J. Math. Biol.* **30** (1992), 693–716.
9. R. M. Nisbet and W. S. C. Gurney, "Modelling Fluctuating Populations," Wiley, New York, 1982.
10. H. L. Smith, "Monotone Dynamical Systems: An Introduction to the Theory of Competitive and Cooperative Systems," Mathematical Surveys and Monographs, Vol. 41, Amer. Math. Soc., Providence, 1995.
11. H. L. Smith and P. Waltman, Perturbation of a globally stable steady state, *Proc. Amer. Math. Soc.* **127** (1999), 447–453.
12. H. L. Smith and X.-Q. Zhao, Dynamics of a periodically pulsed bio-reactor model, *J. Differential Equations* **155** (1999), 368–404.
13. H. L. Smith and X.-Q. Zhao, Microbial growth in a plug flow reactor with wall adherence and cell motility, *J. Math. Anal. Appl.* **241** (2000), 134–155.
14. H. R. Thieme, Convergence results and Poincaré–Bendixson trichotomy for asymptotically autonomous differential equations, *J. Math. Biol.* **30** (1992), 755–763.