

Analysis of an SEIRS epidemic model with two delays

K. L. Cooke¹, P. van den Driessche²

¹ Pomona College, Claremont, CA 91711-6348, USA

² University of Victoria, Victoria, B.C., Canada V8W 3P4

Received 8 May 1995; received in revised form 7 November 1995

Abstract. A disease transmission model of SEIRS type with exponential demographic structure is formulated. All newborns are assumed susceptible, there is a natural death rate constant, and an excess death rate constant for infective individuals. Latent and immune periods are assumed to be constants, and the force of infection is assumed to be of the standard form, namely proportional to $I(t)/N(t)$ where $N(t)$ is the total (variable) population size and $I(t)$ is the size of the infective population. The model consists of a set of integro-differential equations. Stability of the disease free proportion equilibrium, and existence, uniqueness, and stability of an endemic proportion equilibrium, are investigated. The stability results are stated in terms of a key threshold parameter. More detailed analyses are given for two cases, the SEIS model (with no immune period), and the SIRS model (with no latent period). Several threshold parameters quantify the two ways that the disease can be controlled, by forcing the number or the proportion of infectives to zero.

Key words: Epidemic model – Integro-differential equation – Delay equation – Epidemic threshold

1 Introduction

In modeling disease transmission, it is often convenient to divide the population being considered into disjoint classes of susceptible, exposed, infective and recovered individuals, with numbers at time t denoted by $S(t)$, $E(t)$, $I(t)$, $R(t)$, respectively. For some diseases (e.g. tuberculosis, influenza, measles), on adequate contact with an infective, a susceptible individual becomes infected but is not yet infective. This individual remains in the exposed class for a certain latent period before becoming infective. Once infective, an individual may either die due to the disease or, after an infective period, pass into the recovered class. Some diseases confer temporary immunity, and the individual cycles back into the susceptible class after an immune period. The common

cold may be considered an example, although the frequently repeated attacks may be due to the multiplicity of agents or to other causes.

We formulate and analyze an SEIRS disease transmission model that also has exponential demographic structure. All newborns are assumed susceptible, and the natural disease-independent death rate constant is the same throughout the population. A constant disease-related death rate of infectives is included. We assume that the latent and immune periods are constants, denoted by ω and τ , respectively. Thus the probability that an individual remains in the exposed group t units after becoming exposed is given by the step function with value 1 for $t \leq \omega$, and 0 for $t > \omega$. For a recovered individual the corresponding probability has value 1 for $t \leq \tau$, and 0 for $t > \tau$. The waiting time in the infective class is assumed to be exponentially distributed (probability $e^{-\gamma t}$) with mean waiting time $\frac{1}{\gamma}$. Thus our model is formulated as an integro-differential equation system. By contrast, the more common assumption that the waiting times in the exposed, infective and recovered classes are all exponentially distributed, leads to an ordinary differential equation system.

As the total population $N(t) = S(t) + E(t) + I(t) + R(t)$ varies and we assume the standard incidence, it is convenient to work with proportional variables, for example the proportion of infective individuals is $i(t) = I(t)/N(t)$. We show that the proportional variables satisfy an integro-differential equation system, which is equivalent to a differential-difference system subject to certain initial integral conditions. For the importance of proper integral conditions in such systems, see Busenberg and Cooke (1980).

We identify a threshold parameter θ , such that the disease free proportion equilibrium is locally asymptotically stable if $\theta < 1$, but unstable if $\theta > 1$. In the case of no disease related deaths, there is a unique endemic equilibrium of the proportions exactly when $\theta > 1$. To examine stability of the endemic equilibrium, we consider two special cases. For a disease conferring no immunity, $\tau = 0$, an SEIS model is appropriate, and in this case (Sect. 5) the endemic equilibrium is locally asymptotically stable. For a disease with no latent period, $\omega = 0$, the SIRS model (Sect. 6) can have periodic solutions arising from Hopf bifurcation. Control of a disease "to extinction," obviously a desirable goal, may be interpreted to mean either that $i(t)$ or $I(t)$ approaches zero. In a population of varying size these are not always equivalent, and we also study the relation between these in our models, giving a summary in Sect. 7.

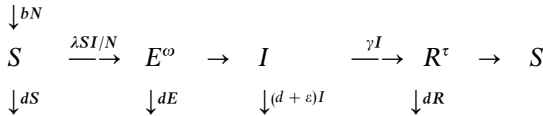
We believe that this is the first time that an SEIRS model has been formulated and analyzed for a variable population size with step functions giving constant latent and immune periods. Distributed delays (with step functions as special cases) have been included in a variety of *constant* population models. For example, SIS models with a time delay in the infective class were analyzed by Cooke and Yorke (1973), and Greenberg and Hoppensteadt (1975). Several SEIS models with time delays in the exposed class and/or infective class have been analyzed by Busenberg and Cooke (1980), and Hethcote et al. (1981b). In all these cases the disease either dies out or approaches an endemic steady state. By contrast, a constant population

SIRS model with time delay in the removed class (i.e. a constant period of temporary immunity) can exhibit periodic solutions for some parameter values, see Hethcote et al. (1981a, 1989).

A delay has been incorporated into a few *variable* population disease models. For example, Busenberg et al. (1983) found some periodic solutions in an SIR model with a maturation delay and vertical disease transmission. Some models incorporating vertical disease transmission and delays are given in Busenberg and Cooke (1993, Ch. 4). With generalized logistic demographics, Brauer found indications of periodic solutions in some models with delays, see Brauer (1990, 1991). An SIS model with exponential demographic structure, disease related deaths and a delay corresponding to the infective period was analyzed by Hethcote and van den Driessche (1995). In this model, which is closely related to ours, periodic solutions of the proportional variables occur for some parameter values (albeit only when death due to the disease is unrealistically large and the contact rate is very high). For a survey of some epidemiological models with delays, see van den Driessche (1996).

2 Model formulation

A population of size $N(t)$ is divided into disjoint classes of individuals who are susceptible, exposed (i.e. infected but not yet infective), infective, and recovered with temporary immunity; with sizes denoted by $S(t), E(t), I(t)$ and $R(t)$, respectively. The flow of individuals is depicted in the transfer diagram:



The parameter $b > 0$ is the birth rate constant (all newborns are assumed susceptible and vertical transmission is ignored), $d > 0$ is the natural death rate constant, $\varepsilon \geq 0$ is the disease related death rate constant in the infective class, and $\gamma \geq 0$ is the rate constant for recovery.

The force of infection is assumed to be of the standard type, namely $\lambda I/N$, with $\lambda > 0$ the effective per capita contact rate constant of infective individuals. Here λ is the product of the average number of contacts of an individual per unit time and the probability of transmitting the disease during one contact by an infective. Thus individuals leave the susceptible class at a rate $\lambda SI/N$. There is a constant $\omega \geq 0$ period of latency and a constant $\tau \geq 0$ period of temporary immunity.

In the limit when $\omega = 0$, an SIRS model results; in the limit when $\tau = 0$, an SEIS model results. Both periods equal to zero gives an SIS model with no delays. The total variable population size is

$$N(t) = S(t) + E(t) + I(t) + R(t) . \tag{2.1}$$

The disease is assumed to have been in the population for at least a time $\bar{\tau} = \max\{\omega, \tau\}$, so that initial perturbations have died out. The equations for the model thus take the following forms for $t > \bar{\tau}$.

$$S'(t) = bN(t) - dS(t) - \frac{\lambda S(t)I(t)}{N(t)} + \gamma I(t - \tau)e^{-d\tau}, \quad (2.2)$$

$$E(t) = \int_{t-\omega}^t \frac{\lambda S(u)I(u)}{N(u)} e^{-d(t-u)} du, \quad (2.3)$$

$$I'(t) = \frac{\lambda S(t - \omega)I(t - \omega)}{N(t - \omega)} e^{-d\omega} - (\varepsilon + \gamma + d)I(t), \quad (2.4)$$

$$R(t) = \int_{t-\tau}^t \gamma I(u) e^{-d(t-u)} du. \quad (2.5)$$

It is convenient to shift time by $\bar{\tau}$, so that (2.2)–(2.5) hold for the new time $t > 0$, with given nonnegative initial conditions,

$$S(t) \geq 0 \quad \text{on } [-\omega, 0], \quad E(t) \geq 0 \quad \text{on } [-\omega, 0],$$

$$I(t) \geq 0 \quad \text{on } [-\bar{\tau}, 0], \quad R(t) \geq 0 \quad \text{on } [-\tau, 0], \quad \text{and} \quad N(t) > 0 \quad \text{on } [-\bar{\tau}, 0].$$

System (2.2)–(2.5) is an integro-differential equation system. Differentiating (2.3), (2.5) gives

$$E'(t) = \frac{\lambda S(t)I(t)}{N(t)} - \frac{\lambda S(t - \omega)I(t - \omega)}{N(t - \omega)} e^{-d\omega} - dE(t), \quad (2.6)$$

$$R'(t) = \gamma I(t) - \gamma I(t - \tau) e^{-d\tau} - dR(t). \quad (2.7)$$

System (2.2), (2.4), (2.6), (2.7) is a differential-difference equation system. The relationship of these two systems is given in the following.

Theorem 2.1 *A solution of the integro-differential system (2.2)–(2.5) satisfies (2.6) and (2.7). Conversely, let $S(t)$, $E(t)$, $I(t)$, $R(t)$ be a solution of the differential-difference equation system (2.2), (2.4), (2.6), (2.7), with $N(t)$ given by (2.1), and initial conditions given on the intervals as stated above. If, in addition,*

$$E(0) = \int_{-\omega}^0 \frac{\lambda S(u)I(u)}{N(u)} e^{du} du, \quad (2.8)$$

$$R(0) = \int_{-\tau}^0 \gamma I(u) e^{du} du, \quad (2.9)$$

then this solution satisfies the integro-differential equation system (2.2)–(2.5). Moreover, for all $t \geq 0$, the solution exists, is unique, has $S(t) \geq 0$, $E(t) \geq 0$, $I(t) \geq 0$, $R(t) \geq 0$ and $N(t) > 0$.

Proof. The first assertion is clear. Conversely, from (2.6)

$$e^{dt}(E'(t) + dE(t)) = e^{dt} \left(\frac{\lambda S(t)I(t)}{N(t)} - \frac{\lambda S(t - \omega)I(t - \omega)}{N(t - \omega)} e^{-d\omega} \right),$$

which, on integrating, gives

$$e^{dt}E(t) = E(0) - \int_{-\omega}^0 \frac{\lambda S(u)I(u)}{N(u)} e^{du} du + \int_{t-\omega}^t \frac{\lambda S(u)I(u)}{N(u)} e^{du} du .$$

By (2.8), equation (2.3) results. Similarly, on integrating (2.7) and using (2.9), equation (2.5) results for $R(t)$, completing the integro-differential equation system. The system of differential-difference equations is of standard form, and so standard results (Bellman and Cooke (1963), Hale and Verduyn Lunel (1993)) ensure the local existence and uniqueness of solutions, provided the denominators $N(t)$ and $N(t - \omega)$ do not go to zero. To show this, add equations (2.2), (2.4), (2.6), (2.7), and use (2.1) to obtain

$$\begin{aligned} N'(t) &= (b - d)N(t) - \varepsilon I(t) \\ &\geq (b - d - \varepsilon)N(t) . \end{aligned} \tag{2.10}$$

Thus

$$N(t) \geq N(0)\exp\{(b - d - \varepsilon)t\} .$$

Since $N(t) > 0$ on $[-\bar{\tau}, 0]$ by assumption, $N(t) > 0$ for all $t \geq 0$.

On the face $S(t) = 0, S'(t) \geq 0$ by (2.2); on $I(t) = 0, I'(t) \geq 0$ by (2.4). From (2.3) and (2.5), it is clear that $E(t) \geq 0$, and $R(t) \geq 0$; thus the nonnegative orthant is invariant. Also from (2.10)

$$N(t) \leq N(0)\exp\{(b - d)t\} ,$$

and thus $N(t)$ cannot blow up to ∞ in finite time. Consequently, the solution exists globally for all $t > 0$ and is unique. □

From (2.10), a nontrivial equilibrium solution of (2.2), (2.4), (2.6), (2.7) with constant population is possible only when the parameters of the model satisfy a special relation. Since this does not hold in general, interest is in variable population size, so it is convenient to work with proportions of individuals in each class by defining

$$s(t) = \frac{S(t)}{N(t)}, \quad e(t) = \frac{E(t)}{N(t)}, \quad i(t) = \frac{I(t)}{N(t)} \quad \text{and} \quad r(t) = \frac{R(t)}{N(t)} .$$

System (2.2)–(2.5) leads to the following integro-differential equation system for $t > 0$

$$s'(t) = b - \lambda s(t)i(t) + \gamma i(t - \tau) \exp\left(-\int_{t-\tau}^t m(p) dp\right) - m(t)s(t), \tag{2.11}$$

$$e(t) = \int_{t-\omega}^t \lambda s(u) i(u) \exp\left(-\int_u^t m(p) dp\right) du, \tag{2.12}$$

$$i'(t) = \lambda s(t - \omega) i(t - \omega) \exp\left(-\int_{t-\omega}^t m(p) dp\right) - (\varepsilon + \gamma) i(t) - m(t) i(t), \tag{2.13}$$

$$r(t) = \int_{t-\tau}^t \gamma i(u) \exp\left(-\int_u^t m(p) dp\right) du, \tag{2.14}$$

with

$$m(t) = b - \varepsilon i(t), \tag{2.15}$$

and

$$N'(t) = (b - d - \varepsilon i) N(t). \tag{2.16}$$

The expression in (2.15) appears in the solution of (2.16), namely

$$N(t) = N(0) \exp\left(-dt + \int_0^t m(p) dp\right), \tag{2.17}$$

thus

$$\frac{N(u)}{N(t)} = \exp\left\{-d(u - t) - \int_u^t m(p) dp\right\}, \quad u \leq t.$$

The corresponding differential-difference equation system is (2.11), (2.13) together with

$$e'(t) = \lambda s(t) i(t) - \lambda s(t - \omega) i(t - \omega) \exp\left(-\int_{t-\omega}^t m(p) dp\right) - m(t) e(t), \tag{2.18}$$

$$r'(t) = \gamma i(t) - \gamma i(t - \tau) \exp\left(-\int_{t-\tau}^t m(p) dp\right) - m(t) r(t). \tag{2.19}$$

Corollary 2.1 *Let $S(t)$, $E(t)$, $I(t)$, $R(t)$ be the solution of (2.2)–(2.5) on $t \geq 0$ with initial conditions nonnegative and $N(t) > 0$ on the initial interval. Then $s(t)$, $e(t)$, $i(t)$, $r(t)$ is the solution of (2.11)–(2.14) with initial conditions corresponding to those for the above system, and is also the solution of the differential-difference equation system (2.11), (2.13), (2.18) (2.19) with*

$$e(0) = \int_{-\omega}^0 \lambda s(u) i(u) \exp\left(-\int_u^0 m(p) dp\right) du, \tag{2.20}$$

$$r(0) = \int_{-\tau}^0 \gamma i(u) \exp\left(-\int_u^0 m(p) dp\right) du. \tag{2.21}$$

Also $s(t)$, $e(t)$, $i(t)$, $r(t) \geq 0$. If $s(t)$ and $i(t)$ are positive on the initial interval, then $s(t)$ and $i(t)$ are positive for all finite $t \geq 0$. □

Proof. The first assertion and the fact that the variables are nonnegative follow from Theorem 2.1. If $s(t) > 0$, $i(t) > 0$ on the initial interval, define

$$t_1 = \inf\{t > 0: s(t)i(t) = 0\}.$$

If t_1 is finite, either $s(t_1) = 0$ or $i(t_1) = 0$. If $s(t_1) = 0$ then $s'(t_1) > b > 0$ by (2.11), which is a contradiction. If $i(t_1) = 0$ then $i'(t_1) > 0$ by (2.13), also a contradiction. \square

The system (2.11), (2.13), (2.18), (2.19) defines a functional differential equation for $v = (s, e, i, r)^T$;

$$v'(t) = F(v_t) \tag{2.22}$$

where v_t has the usual meaning, $v_t(\phi) = v(t + \phi)$ for $-\bar{\tau} \leq \phi \leq 0, t \geq 0$. If it is assumed that S, E, I, R are solutions of system (2.2)–(2.5) or of (2.2), (2.4), (2.6), (2.7), and s, e, i, r are defined as above, then the equation

$$s(t) + e(t) + i(t) + r(t) = 1 \tag{2.23}$$

holds for $t \geq 0$, by definition. On the other hand, since we will be doing much of our analysis on system (2.22) or on the integro-differential system (2.11)–(2.14), we need to know which solutions of those systems satisfy the biologically meaningful condition (2.23). It is not true that every solution of (2.22) satisfies (2.23). The following theorem answers this question. Let v_0 denote the initial function for (2.22) on $[-\bar{\tau}, 0]$. Although the initial conditions for some of the variables may be given on a smaller interval, we may extend these initial functions over $[-\bar{\tau}, 0]$ without affecting the solution. Let

$$D = \{ (s, e, i, r) : s \geq 0, e \geq 0, i \geq 0, r \geq 0, s + e + i + r = 1 \} .$$

We will say that v_t is in D if $v(t + \phi)$ is in D for $-\bar{\tau} \leq \phi \leq 0$.

Theorem 2.2 *Let $v(t) = (s(t), e(t), i(t), r(t))^T$ be a solution of (2.22) with initial conditions v_0 on $[-\bar{\tau}, 0]$ that are nonnegative and for which v_0 is in D . Moreover, assume that (2.20) and (2.21) hold. Then the solution of (2.22) exists for all $t \geq 0$ and v_t lies in D for all $t \geq 0$. Furthermore, a solution of the integro-differential system (2.11)–(2.14) with initial condition in D is a solution of (2.22) for which (2.20) and (2.21) are satisfied, so that if the initial function is in D then the solution exists for $t \geq 0$ and remains in D .*

Proof. Let $v(t) = (s(t), e(t), i(t), r(t))^T$ be a solution of (2.22), that is, of (2.11), (2.13), (2.18), (2.19). Let $n(t) = s(t) + e(t) + i(t) + r(t)$. Adding the four equations, we obtain $n'(t) = m(t) [1 - n(t)]$. Since $n(0) = 1$, we conclude that $n(t) = 1$ for all t for which $n(t)$ exists. Because (2.20) and (2.21) have been assumed to hold, it can be proved that $v(t)$ is also a solution of the system (2.11)–(2.14), by using the kind of argument that was used in the proof of Theorem 2.1. Non-negativity of $s(t), e(t), i(t),$ and $r(t)$ follows from (2.11)–(2.14). Then since $n(t) = 1$, it follows that $s(t), e(t), i(t),$ and $r(t)$ are bounded. Therefore, the solution exists for all $t \geq 0$ and v_t is in D . To establish the last statement of the theorem, suppose that $v(t)$ is a solution of (2.11)–(2.14) with v_0 lying in D . From (2.12), (2.14) it follows that (2.20), (2.21) hold, and (2.22) is satisfied. By the first part of the proof, the solution exists and is in D for $t \geq 0$. \square

The above theorem says that we can be sure that the solution remains in the biologically meaningful set $s + e + i + r = 1$ provided (2.20) and (2.21) are satisfied.

3 Disease-free equilibrium

When the infective fraction $i = 0$, then $e = r = 0$, and $s = 1$; this is the disease free equilibrium (DFE) for proportions. This is the only equilibrium on the boundary of D . The following theorem determines linear stability of the DFE in terms of a threshold parameter

$$\theta = \frac{\lambda \exp(-b\omega)}{(\varepsilon + \gamma + b)}. \quad (3.1)$$

The standard approach to studying stability of an equilibrium for a system of functional differential equations (2.22) is to compute the ‘‘Jacobian matrix’’, or rather the linearized operator, and to study the eigenvalues of the operator. This is equivalent to allowing arbitrary small perturbations near the equilibrium. Here, however, only perturbations within the set D are relevant, not arbitrary perturbations, and the linear system obtained by the standard method does not have the property that its solutions remain in D . It will be convenient to use a slightly modified approach here.

Theorem 3.1 *The system (2.11)–(2.15) always has the disease free proportion equilibrium $(s(t), e(t), i(t), r(t)) = (1, 0, 0, 0)$. If $\theta < 1$, then it is locally asymptotically stable; if $\theta > 1$, then it is unstable.*

Proof. Equations (2.11), (2.13), (2.18) are decoupled from the equations for r . Suppose that $s(t), e(t), i(t), r(t)$ is a solution of the full system, with initial condition in D and close to the DFE. Then $s(t), e(t), i(t)$ satisfy the reduced system (2.11), (2.13), (2.18), with initial conditions near the equilibrium $(1, 0, 0)$. Moreover, any such solution determines $r(t)$ by (2.14) in such a way that $(s(t), e(t), i(t), r(t))$ is in D (see Theorem 2.2). If we compute the linearization of the reduced system near $(1, 0, 0)$, we find that the characteristic equation has a double root $-b$ and solutions z of the quasipolynomial equation

$$z + \varepsilon + \gamma + b - \lambda \exp(-\omega(b + z)) = 0. \quad (3.2)$$

It is shown in Theorem A.2 in the Appendix that (3.2) (with $a = \varepsilon + \gamma + b$) has a positive root $z = x > 0$ if and only if $\lambda \exp(-b\omega) > \varepsilon + \gamma + b$, but has no root $z = x + iy$ with $x \geq 0$ if $\lambda \exp(-b\omega) < \varepsilon + \gamma + b$.

Now suppose that $\theta < 1$. Then $\lambda \exp(-b\omega) < \varepsilon + \gamma + b$, and consequently $(1, 0, 0)$ is locally asymptotically stable for the reduced system, that is, $s(t) \rightarrow 1, i(t) \rightarrow 0, e(t) \rightarrow 0$ as $t \rightarrow \infty$. It follows from (2.14) that $r(t) \rightarrow 0$. Hence the first part of the conclusion has been proved.

On the other hand, suppose that $\theta > 1$. Then $\lambda \exp(-b\omega) > \varepsilon + \gamma + b$, from which it follows that $(1, 0, 0)$ is unstable for (2.11), (2.13), (2.18). In fact,

there is a positive x and a manifold of solutions, growing locally like $\exp(xt)$ (for the linear system), of the form $(s, e, i)^T = (1, 0, 0)^T + \exp(xt) (c_1, c_2, c_3)^T$ where the eigenvector (c_1, c_2, c_3) is determined from the equations

$$\begin{aligned} -(b+x)c_1 + [- (\lambda - \varepsilon) + \gamma \exp(- (b+x)\tau)]c_2 &= 0 \\ [- (\varepsilon + \gamma + b+x) + \lambda \exp(- (b+x)\omega)]c_2 &= 0 \\ \lambda[1 - \exp(- (b+x)\omega)]c_2 - (b+x)c_3 &= 0 . \end{aligned}$$

The middle equation is satisfied by definition of x . The last equation shows that c_2 and c_3 have the same sign, say positive, and the first equation gives

$$(b+x)c_1 = [- (\lambda - \varepsilon) + \gamma \exp(- (b+x)\tau)]c_2 .$$

Since $\theta > 1$, we have $\gamma + \varepsilon < \lambda$, hence the expression in brackets is negative and $c_1 < 0$. We claim that the vector (c_1, c_2, c_3) from the point $(s, e, i) = (1, 0, 0)$ points into the tetrahedron

$$\{(s, e, i): s \geq 0, e \geq 0, i \geq 0, s + e + i \leq 1\} .$$

Then the unstable direction of solutions projects onto an unstable direction of solutions lying on the set $s + e + i + r = 1$, proving the second part of the theorem. To prove the claim, note that the equation for x implies

$$\lambda \exp(- (b+x)\omega) = b+x+\varepsilon+\gamma > \varepsilon + \gamma \exp(- (b+x)\tau) ,$$

hence $c_2/|c_1| < 1$. Also, it is clear that

$$\lambda - \varepsilon - \gamma \exp(- (b+x)\tau) > \lambda \exp(- (b+x)\omega) - \varepsilon - \gamma = b+x ,$$

so that $c_2/|c_1| < 1$. These inequalities and the sign conditions $c_1 < 0, c_2 > 0, c_3 > 0$, establish the claim. □

This threshold parameter θ is a measure of the relative strength of the disease transmission versus dilution of infectives. The quantity $1/(\varepsilon + \gamma + b)$ is the mean waiting time in the infective class i , thus θ is the average number of adequate contacts of an infective during the average time in the i class. The contact rate λ is modified by the lag ω and births, $\exp(- b\omega)$ is the fraction surviving the e class. The mean waiting time in I is $1/(\varepsilon + \gamma + d)$, for $b \neq d$ this is not the same as in i because the population size is changing. In a constant size population ($b = d, \varepsilon = 0$) the threshold parameter is $\lambda \exp(- d\omega)/(\gamma + d)$.

A global stability result for a restricted set of parameter values can be given by considering the following Lyapunov function V . See, for example, Hale and Verduyn Lunel (1993).

Theorem 3.2 *For $\lambda < \varepsilon + \gamma + b$ all solutions of the system (2.11)–(2.15) starting in D approach the disease free proportion equilibrium as $t \rightarrow \infty$.*

Proof. Let $s(t)$, $e(t)$, $i(t)$, $r(t)$ be a solution of the integro-differential system in D , and let $V(t) = i(t) + e(t)$. From the equations for $e'(t)$ and $i'(t)$, we get

$$\begin{aligned} V'(t) &= \lambda s(t)i(t) - (\varepsilon + \gamma + b)i(t) - be(t) + \varepsilon i(t) [1 - s(t) - r(t)] \\ &= (\lambda - \varepsilon)s(t)i(t) - (\gamma + b)i(t) - be(t) - \varepsilon i(t)r(t) . \end{aligned}$$

If $\lambda \leq \varepsilon$, we have

$$V'(t) \leq -(\gamma + b)i(t) - be(t) \leq -b[i(t) + e(t)] = -bV(t) .$$

If $\lambda > \varepsilon$, we have $(\lambda - \varepsilon)s(t)i(t) \leq (\lambda - \varepsilon)i(t)$, hence

$$V'(t) \leq (\lambda - \varepsilon - \gamma - b)i(t) - be(t) .$$

Assume that $\lambda < \gamma + b + \varepsilon$. Then $V'(t) \leq 0$ and

$$V'(t) \leq -\delta V(t) ,$$

where $\delta = \min\{b, -\lambda + \varepsilon + \gamma + b\}$ is positive. Thus $V(t)$ is nonnegative and nonincreasing with limit zero as $t \rightarrow \infty$. Thus $i(t)$ and $e(t)$ tend to zero, and $r(t) \rightarrow 0$ from (2.14). Hence $s(t) = 1 - e(t) - i(t) - r(t)$ tends to 1. \square

Note that this global stability result is for only a subset of parameters for which local stability has been proved (namely, $\lambda < (\varepsilon + \gamma + b)\exp(b\omega)$) in Theorem 3.1.

4 Endemic equilibria

Let s^* , e^* , i^* , r^* be an endemic equilibrium in the interior of D , with $m^* = b - \varepsilon i^*$ from (2.15). If $\varepsilon = 0$ then $m^* > 0$. If $\varepsilon > 0$ and $m^* = 0$, then $i^* = b/\varepsilon$ with $\varepsilon > b$. So $s^* = \frac{(\gamma + \varepsilon)}{\lambda}$, $e^* = \lambda s^* i^* \omega$, $r^* = \gamma i^* \tau$ from (2.11), (2.12) and (2.14). But, using (2.23), this means that

$$s^* + e^* + i^* + r^* = 1 = \frac{\gamma + \varepsilon}{\lambda} \left(1 + \frac{\lambda b \omega}{\varepsilon} \right) + \frac{b}{\varepsilon} (1 + \gamma \tau)$$

which is in general not true. Thus $i^* = b/\varepsilon$ cannot produce an acceptable equilibrium for the system; therefore $m^* \neq 0$. From the proportion equations, an equilibrium must satisfy

$$0 = b - \lambda s^* i^* + \gamma i^* \exp(-m^* \tau) - m^* s^* , \quad (4.1)$$

$$e^* = \lambda s^* i^* (1 - \exp(-m^* \omega)) / m^* , \quad (4.2)$$

$$0 = \lambda s^* i^* \exp(-m^* \omega) - (\varepsilon + \gamma) i^* - m^* i^* , \quad (4.3)$$

$$r^* = \gamma i^* (1 - \exp(-m^* \tau)) / m^* . \quad (4.4)$$

Adding (4.1) and (4.3) gives

$$0 = m^* (1 - s^* - i^*) - \lambda s^* i^* (1 - \exp(-m^* \omega)) - \gamma i^* (1 - \exp(-m^* \tau)) ,$$

which, as $m^* \neq 0$, can be written as

$$\lambda s^* i^* \frac{(1 - \exp(-m^* \omega))}{m^*} + \gamma i^* \frac{(1 - \exp(-m^* \tau))}{m^*} = 1 - s^* - i^*.$$

Therefore when e^* and r^* are given by (4.2) and (4.4), any equilibrium solution (with $m^* \neq 0$) lies on the required manifold (2.23). From (4.1), note that $b + (\lambda - \varepsilon) i^* \neq 0$ (since that would imply that $b + \gamma i^* \exp(-m^* \tau) = 0$). Thus (4.1) gives

$$s^* = \frac{b + \gamma i^* \exp(-m^* \tau)}{b + (\lambda - \varepsilon) i^*} = g_1(i^*), \tag{4.5}$$

and from (4.3), with $i^* > 0$,

$$s^* = \exp(m^* \omega) [(\varepsilon + \gamma + b) - \varepsilon i^*] / \lambda = g_2(i^*). \tag{4.6}$$

As $s^* < 1$ at endemic equilibrium, (4.5) implies that $\lambda > \varepsilon + \gamma \exp(-m^* \tau) > \varepsilon$ for such an equilibrium to exist.

Study of an endemic equilibrium is complicated by the presence of $m^* = b - \varepsilon i^*$ in the exponential terms in (4.5) and (4.6). Consideration is now restricted to the special case $\varepsilon = 0$, that is, no excess death due to disease. However, for $b \neq d$, the total population $N(t)$ is growing or decaying exponentially (see (2.10)).

Theorem 4.1 *The system (2.11)–(2.15) with $\varepsilon = 0$ has a unique endemic equilibrium (in the interior of D) if $\lambda \exp(-b\omega) / (\gamma + b) = \theta > 1$. If $\theta \leq 1$, then there is no endemic equilibrium.*

Proof. With the assumption $\varepsilon = 0$, the endemic susceptible proportion can be found explicitly from (4.6) as

$$s^* = \frac{\gamma + b}{\lambda \exp(-b\omega)} = \frac{1}{\theta}. \tag{4.7}$$

This is in the interior of D exactly when $1 < \theta = \lambda \exp(-b\omega) / (\gamma + b)$. In this case (4.5) gives

$$i^* = \frac{b[\lambda \exp(-b\omega) - (\gamma + b)]}{\lambda[(\gamma + b) - \gamma \exp(-b(\omega + \tau))]}, \tag{4.8}$$

and e^* and r^* are given by (4.2) and (4.4) respectively. As $\theta \rightarrow 1^+$, this equilibrium tends to the disease free equilibrium. □

Continuing with the assumption $\varepsilon = 0$, and $\theta > 1$, local stability of the unique endemic equilibrium is now investigated. This is governed by the Jacobian matrix in s, i variables from (2.11) and (2.13) with $s = s^*, i = i^*$ and $m^* = b$. This leads to the quasipolynomial equation in the variable z given by

$$0 = \begin{vmatrix} -\lambda i^* - b - z & -\lambda s^* + \gamma \exp(-\tau(b + z)) \\ \lambda i^* \exp(-\omega(b + z)) & \lambda s^* \exp(-\omega(b + z)) - (\gamma + b) - z \end{vmatrix},$$

which can be written as

$$0 = (z + \gamma + b)(z + b + \lambda i^*) - \lambda[zs^* + bs^* + \gamma i^* \exp(-\tau(b + z))]\exp(-\omega(b + z)). \tag{4.9}$$

There is a root $z = 0$ if and only if $\theta = 1$; for $\theta > 1$, the constant term is positive. For general lags ω, τ , equation (4.9) is complicated. Thus, in the next sections, two special cases are considered, the case $\tau = 0$ (the SEIS model), and the case $\omega = 0$ (the SIRS model).

5 The SEIS model

Setting $\tau = 0$ in the model of Sect. 2 gives an SEIS model with no immunity. In this case $s + e + i = 1$ and the positively invariant set is

$$\tilde{D} = \{(s, e, i) : s \geq 0, e \geq 0, i \geq 0, s + e + i = 1\} \tag{5.1}$$

(under the assumption that (2.20) holds). Theorems 3.1 and 3.2 hold as stated for the disease free proportion equilibrium $(s, e, i) = (1, 0, 0)$. To analyze this SEIS model further, assume $b > \varepsilon$, that is the birth rate is greater than the disease related death rate. (This includes the case $\varepsilon = 0$ as assumed near the end of Sect. 4). As before, $m^* > 0$. An endemic equilibrium (s^*, e^*, i^*) is given from (4.5) (with $\tau = 0$) and (4.6), with $\lambda > \varepsilon + \gamma$ being necessary for such an equilibrium to exist. The quantity $i^* + s^* = i^* + g_1(i^*)$ must be < 1 , since $s^* \neq 0$ and $e^* > 0$ by (4.1), (4.2). But by (4.5)

$$i^* + g_1(i^*) = \frac{bi^* + (\lambda - \varepsilon)i^{*2} + b + \gamma i^*}{b + (\lambda - \varepsilon)i^*},$$

which is < 1 exactly when $i^* < c$ where

$$c = 1 - \frac{(b + \gamma)}{(\lambda - \varepsilon)}. \tag{5.2}$$

If $\theta > 1$, then $\lambda > \varepsilon + \gamma + b$, hence $0 < c < 1$. Thus for an endemic equilibrium, $i^* \in (0, c)$. A result analogous to Theorem 4.1 follows.

Theorem 5.1 *Consider the SEIS system (2.11)–(2.15) with $\tau = 0$ (and $r(t) = 0$), under the assumption $b > \varepsilon$. Then there is a unique endemic equilibrium (in the interior of \tilde{D}) if $\theta > 1$. If $\theta \leq 1$, then there is no endemic equilibrium.*

Proof. Define

$$h(i) = \lambda[b + (\lambda - \varepsilon)i]\exp(\varepsilon i\omega)(g_1(i) - g_2(i)), \tag{5.3}$$

where $g_1(i)$ is given by (4.5) with $\tau = 0, i^* = i$, and $g_2(i)$ is given by (4.6) with $i^* = i$. Then

$$h(i) = \lambda(b + \gamma i)\exp(\varepsilon\omega i) - [b + (\lambda - \varepsilon)i][\varepsilon + \gamma + b - \varepsilon i]\exp(b\omega)$$

$$h(0) = b(\varepsilon + \gamma + b)\exp(b\omega)(\theta - 1).$$

If $c < 0$, then $i^* < 0$ by (5.2), which is not a case of interest. Therefore we assume that $c > 0$, and find that $h(c) < 0$ if $b > \varepsilon$, and $h''(i) \geq 0$ (> 0 if $\varepsilon > 0$) if $\lambda > \varepsilon$. Thus if $\theta < 1$, there is no positive root of $h(i) = 0$; if $\theta = 1$, then $i = 0$ is a root; whereas if $\theta > 1$, then there is a unique root $i = i^* \in (0, c)$. From this value, s^* can be obtained from $g_1(i^*)$ or $g_2(i^*)$, and e^* from (4. 2). \square

Local stability of this endemic equilibrium is governed by a complicated quasipolynomial. For the case $\varepsilon = 0$, this is given by (4.9) with $\tau = 0$, and yields the following result.

Theorem 5.2 *Consider the SEIS system (2.11)–(2.15) with $\tau = 0$ and no disease related death ($\varepsilon = 0$). If $\theta = \lambda \exp(-b\omega)/(\gamma + b) > 1$, then the unique endemic equilibrium is locally asymptotically stable.*

Proof. Existence of the unique endemic equilibrium is guaranteed by Theorem 4.1 or Theorem 5.1. Local stability is governed by (4.9) with $\tau = 0$, namely

$$0 = (z + \gamma + b)(z + b + \lambda i^*) - \lambda(zs^* + bs^* + \gamma i^*)\exp(-\omega(b + z)) = H_\omega(z). \tag{5.4}$$

Setting $z = 0$, and using (4.8) gives

$$H_\omega(0) = b\lambda(1 - s^*)\exp(-\omega b) > 0.$$

Setting $\omega = 0$, gives

$$H_0(z) = z^2 + (\gamma + 2b + \lambda i^* - \lambda s^*)z + b(\gamma + b + \lambda i^* - \lambda s^*),$$

wherein s^* and i^* have the values given by (4.7), (4.8) with $\tau = \omega = 0$, thus $s^* = (\gamma + b)/\lambda$. This has all coefficients positive, and so both roots of the polynomial have negative real parts. Therefore in the limit as $\omega \rightarrow 0$, equation (5.4) is stable. By Lemma A.1 in the Appendix, instability can occur for $\omega > 0$ only by roots crossing the finite imaginary axis. Without loss of generality, (here i is the imaginary unit, $i^2 = -1$) assume $z = iy$, $y > 0$ ($y = 0$ has been ruled out above). Then (5.4) can be written as

$$(iy + \gamma + b)(iy + b + \lambda i^*) = s^*\lambda \left(iy + b + \frac{\gamma i^*}{s^*} \right) \exp(-b\omega) [\cos(\omega y) - i \sin(\omega y)].$$

Taking absolute values gives

$$[y^2 + (\gamma + b)^2][y^2 + (b + \lambda i^*)^2] = (s^*\lambda)^2 \left[y^2 + \left(b + \frac{\gamma i^*}{s^*} \right)^2 \right] \exp(-2b\omega),$$

which can be written as

$$Y^2 + AY + B = 0,$$

where $Y = y^2$,

$$A = (\gamma + b)^2 + (b + \lambda i^*)^2 - (s^*\lambda)^2 \exp(-2b\omega),$$

and

$$B = (\gamma + b)^2(b + \lambda i^*)^2 - (s^* \lambda)^2 \left(b + \frac{\gamma i^*}{s^*} \right)^2 \exp(-2b\omega).$$

Using (4.7) to substitute for s^* , we see that the coefficients A and B are positive. Thus the equation for Y can have no positive root, and no pure imaginary root $z = iy$ can exist. It follows that all roots of (5.4) have negative real parts, and the endemic equilibrium is locally asymptotically stable. \square

It is conjectured that for $\theta > 1$, the endemic equilibrium is globally asymptotically stable in $\tilde{D} - \{(1, 0, 0)\}$. If this is true, then θ is a sharp threshold; when $\theta < 1$ the disease dies out, when $\theta > 1$ proportions remain endemic. In the limit $\omega \rightarrow 0$, the model reduces to an (ordinary differential equation) SIS model that has been shown by Busenberg and van den Driessche (1990, 1991) to have this global behavior.

In Theorem 5.1 it has been shown that for $\theta > 1$ there is a unique endemic equilibrium for disease related death small enough ($\varepsilon < b$). As roots of (4.9) with $\tau = 0$ are continuous functions of ε , Theorem 5.2 shows that this equilibrium is locally asymptotically stable for sufficiently small ε . The stability for more general ε remains open.

We now determine the asymptotic behavior of $N(t)$ and $I(t)$. The arguments involve other parameters; see Busenberg and van den Driessche (1990) for similar thresholds for an SIRS model without delays. We consider two cases, one in which a positive solution $i(t)$ converges to a positive equilibrium i^* , and the other in which a solution $i(t)$ converges to the DFE $i = 0$. We define

$$R_1 = \begin{cases} \frac{b}{d + \varepsilon i^*} & \text{if } i(t) \rightarrow i^* \text{ as } t \rightarrow \infty, \\ \frac{b}{d} & \text{if } i(t) \rightarrow 0 \text{ as } t \rightarrow \infty. \end{cases} \tag{5.5}$$

If $b > \varepsilon$ and $\theta > 1$, the DFE is unstable and there is a unique endemic equilibrium that is locally asymptotically stable for sufficiently small epsilon, and which we conjecture attracts all solutions in $\tilde{D} - \{(1, 0, 0)\}$. Consider solutions $i(t)$ converging to i^* . The limit equation of (2.16) is $N'(t) = (b - d - \varepsilon i^*) N(t)$, so that $N(t) \rightarrow 0$ as $t \rightarrow \infty$ if $R_1 < 1$, and $N(t) \rightarrow \infty$ if $R_1 > 1$. The rate of decay or growth is asymptotically exponential. Since $I(t) = i(t) N(t)$, $I(t)$ has the same asymptotic limit as $N(t)$. We note that the case $N \rightarrow \infty, I \rightarrow 0$ is impossible.

On the other hand, suppose that $b > \varepsilon$ and $\theta < 1$. In this case there is no endemic equilibrium and the DFE is locally asymptotically stable. We conjecture that it is globally attracting (see Theorem 3.2). Consider a positive solution $i(t)$ for which $i(t) \rightarrow 0$. The limit equation of (2.16) is $N'(t) = (b - d) N(t)$ so that $N(t) \rightarrow 0$ if $R_1 < 1$, and $N(t) \rightarrow \infty$ if $R_1 > 1$. If $N(t) \rightarrow 0$ then also $I(t) = N(t)i(t)$ tends to 0, but if $N(t) \rightarrow \infty$ then the asymptotic behavior of $I(t)$ is not immediately obvious, and indeed another threshold parameter must be introduced.

It remains to determine the behavior of $I(t)$ when $R_1 > 1$ and $N(t) \rightarrow \infty$. From (2.4) we have

$$I'(t) = \left\{ \frac{\lambda S(t - \omega)}{N(t - \omega)} \frac{i(t - \omega)}{i(t)} \frac{N(t - \omega)}{N(t)} \exp(-d\omega) - (\varepsilon + \gamma + d) \right\} I(t)$$

where we have used the facts that $N(t)$ and $i(t)$ are not zero in finite time (see Corollary 2.1). Using the expression for $\frac{N(t-\omega)}{N(t)}$ from (2.17), this becomes

$$I'(t) = f(t)I(t), \tag{5.6}$$

where

$$f(t) = \lambda s(t - \omega) \frac{i(t - \omega)}{i(t)} \exp \left\{ -b\omega + \varepsilon \int_{t-\omega}^t i(p) dp \right\} - (\varepsilon + \gamma + d). \tag{5.7}$$

It is necessary to determine the limiting behavior of $\frac{i(t-\omega)}{i(t)}$ when $i(t) \rightarrow 0$. Since $\theta < 1$ the disease free proportion equilibrium is asymptotically stable. Then by Theorem A.2 there is a characteristic root x_0 satisfying $-(\varepsilon + \gamma + b) < x_0 < 0$, and all other roots z satisfy $\Re(z) < x_0$. Since $i(t) \rightarrow 0$, the asymptotic behavior of $i(t)$ is given by the dominant characteristic root, that is, $i(t) = k \exp(x_0 t)(1 + o(1))$ as $t \rightarrow \infty$. Therefore $\frac{i(t-\omega)}{i(t)} = \exp(-\omega x_0)(1 + o(1))$, with limit $\exp(-\omega x_0)$. Hence

$$\lim_{t \rightarrow \infty} f(t) = \lambda \exp\{-\omega(x_0 + b)\} - (\varepsilon + \gamma + d).$$

We let

$$R_2 = \frac{\lambda \exp\{-\omega(x_0 + b)\}}{(\varepsilon + \gamma + d)} \tag{5.8}$$

and conclude that if $R_2 < 1$ then $I(t) \rightarrow 0$, and if $R_2 > 1$ then $I(t)$ grows exponentially. Note the difference between θ and R_2 . Thus the two ways of controlling the disease, by forcing the *number* of infectives or the *proportion* of infectives to zero, are not always the same in a population of varying size.

These results are summarized in Table 1.

Table 1. Threshold criteria and asymptotic behavior when $b > \varepsilon$, where θ , R_1 and R_2 are given by (3.1), (5.5), and (5.8), respectively. The value of R_2 is relevant only in case $\theta < 1$ and $R_1 > 1$. For precise interpretation of the table, see the text

θ	R_1	R_2	$i \rightarrow$	$N \rightarrow$	$I \rightarrow$
< 1	< 1		0	0	0
< 1	> 1	< 1	0	∞	0
< 1	> 1	> 1	0	∞	∞
> 1	< 1		i^*	0	0
> 1	> 1		i^*	∞	∞

6 The SIRS model

Setting $\omega = 0$ in the model of Sect. 2 gives an SIRS model with no exposed class. In this case $s + i + r = 1$ and the positively invariant set is

$$D' = \{(s, i, r) : s \geq 0, i \geq 0, r \geq 0, s + r + i = 1\} \quad (6.1)$$

(under the assumption that (2.21) holds). Theorems 3.1 and 3.2 hold as stated with $\theta = \frac{\lambda}{(\varepsilon + \gamma + b)}$ for the disease free proportion equilibrium $(s, i, r) = (1, 0, 0)$. Now $V(t) = i(t)$ in the proof of Theorem 3.2, and this global result holds for all parameter values for which $\theta < 1$.

For $t \geq \tau$, this model can be written as a single integro-differential equation for $i(t)$. From (2.13) and (2.14) this is

$$i'(t) = \lambda \left[1 - i(t) - \int_{t-\tau}^t \gamma i(u) \exp\left(-\int_u^t m(p) dp\right) du \right] i(t) - (\varepsilon + \gamma)i(t) - m(t)i(t), \quad (6.2)$$

with $m(t) = b - \varepsilon i(t)$. This is similar to, but more complicated than, equations studied by Hethcote et al. (1981a) and van den Driessche (1983) for the number of infectives in a constant size population.

Theorem 6.1 *Let $\theta = \frac{\lambda}{(\varepsilon + \gamma + b)}$. If $\theta < 1$, then all solutions of the SIRS model starting in D' approach the disease free proportion equilibrium as $t \rightarrow \infty$. If $\theta > 1$ and $b > \varepsilon$, there is a unique positive equilibrium s^*, i^*, r^* in the interior of D' .*

Proof. The first assertion was already discussed in the first paragraph of this section. To complete the proof, consider equations (4.1), (4.3), (4.4) for endemic proportions. Now $g_1(i^*)$ is given by (4.5) and $g_2(i^*) = \frac{\varepsilon + \gamma + b - \varepsilon i^*}{\lambda}$. Assume that $\theta > 1$ and $b > \varepsilon$. As in (5.2), define

$$c = 1 - \frac{(b + \gamma)}{(\lambda - \varepsilon)} = \frac{\lambda - \varepsilon - \gamma - b}{\lambda - \varepsilon}.$$

From $\theta > 1$ we have $\lambda > \varepsilon + \gamma + b$, hence $0 < c < 1$. Then the function

$$i^* + g_2(i^*) = \frac{\varepsilon + \gamma + b + (\lambda - \varepsilon)i^*}{\lambda}$$

is increasing in i^* and $c + g_2(c) = 1$. Thus c is the upper bound for values of i^* for which $i^* + s^* < 1$, just as in Sect. 5. With $h(i)$ as in (5.3) and $\omega = 0$ we have

$$h(i) = \lambda[b + \gamma i \exp(-\tau(b - \varepsilon i))] - [b + (\lambda - \varepsilon)i][\varepsilon + \gamma + b - \varepsilon i].$$

We find that $h(0) = \lambda b(1 - 1/\theta) > 0$ when $\theta > 1$. Also

$$h(c) = \lambda \gamma (\lambda - \varepsilon - \gamma - b) [\exp(-\tau(b - \varepsilon c)) - 1] (\lambda - \varepsilon)^{-1}.$$

Since $\lambda > \varepsilon + \gamma + b$, $b > \varepsilon$, and $c < 1$, we see that $h(c) < 0$. Therefore there exists i^* with $0 < i^* < c$ and $h(i^*) = 0$. It is easy to compute $h''(i)$ and to see that $h''(i) > 0$ for $i > 0$, so that i^* is unique. From this value, s^* can be

obtained from $g_1(i^*)$ or $g_2(i^*)$, and r^* from (4.4), which establishes existence of a positive equilibrium. \square

If it is assumed that there is no disease related death (i.e. $\varepsilon = 0$), then the unique endemic proportion equilibrium is explicitly given by setting $\omega = 0$ in (4.7) and (4.8). Stability of the unique equilibrium (s^*, i^*, r^*) when $\varepsilon = 0$ and $\theta > 1$ is governed by (4.9) with $\omega = 0$, namely

$$0 = z^2 + z(b + \lambda i^*) + \lambda b i^* + \lambda \gamma i^* [1 - \exp(-\tau(b + z))] . \tag{6.3}$$

This equation has been considered by van den Driessche (1983) and can have purely imaginary zeros for some parameter values. Thus for some $\tau > 0$, periodic solutions, arising by a Hopf bifurcation, are possible. The SIRS model with finite delay in the removed class can thus have more complicated dynamics than the SEIS model with delay in the latent class, even in the case of no disease related death.

Consider a solution for which $i(t)$ tends to $i^* > 0$. Then from (2.16) the entries in Table 1 for $\theta > 1$ are valid here also. We discuss below the case in which there is a periodic solution. Now suppose that $\theta < 1$. Since $i(t) \rightarrow 0$, we have, just as in Sect. 5, that $N(t) \rightarrow 0$ or ∞ according as $R_1 < 1$ or > 1 , and when $N(t) \rightarrow 0$ also $I(t) \rightarrow 0$. We also have $I'(t) = f(t)I(t)$ where $f(t)$ is given by (5.7) with $\omega = 0$, that is,

$$f(t) = \lambda s(t) - (\varepsilon + \gamma + d) . \tag{6.4}$$

Since $s(t)$ tends to 1, we see that $I(t)$ tends to 0 or ∞ according as $R_2 < 1$ or > 1 where R_2 is given by (5.8) with $\omega = 0$. So the entries in Table 1 for $\theta < 1$ remain valid.

On the other hand, suppose that for some $\tau > 0$ there is a positive periodic solution of the proportional variables, $s = \tilde{s}(t)$, $i = \tilde{i}(t)$, $r = \tilde{r}(t)$, of period T , which attracts all solutions. Then $s(t) = \tilde{s}(t) [1 + o(1)]$ as $t \rightarrow \infty$, where $\tilde{s}(t)$ has period T , and $f(t) = \tilde{f}(t) + o(1)$ where $\tilde{f}(t) = \lambda \tilde{s}(t) - (\varepsilon + \gamma + d)$. Let \bar{s} and \bar{f} be the mean values of $\tilde{s}(t)$ and $\tilde{f}(t)$, respectively, so $\bar{f} = \lambda \bar{s} - (\varepsilon + \gamma + d)$. From $I'(t) = f(t)I(t)$ we obtain

$$I(t) = I(t_0) \exp\left(\int_{t_0}^t f(u) du\right), \quad t \geq t_0 > 0 \tag{6.5}$$

and therefore for any $t \geq t_0$

$$I(t + T) = I(t) \exp\left(\int_t^{t+T} f(u) du\right) . \tag{6.6}$$

Also

$$\frac{1}{T} \int_t^{t+T} f(u) du = \bar{f} + o(1)$$

so

$$I(t + T) = I(t) \exp(T\bar{f} + o(1)) = I(t) \exp(T\bar{f}) [1 + o(1)] . \tag{6.7}$$

Let

$$\bar{R}_2 = \frac{\lambda \bar{s}}{(\varepsilon + \gamma + d)},$$

so that \bar{R}_2 is < 1 , $= 1$, or > 1 according as \bar{f} is < 0 , $= 0$, or > 0 . Then from (6.7) we obtain the following result.

Theorem 6.2 *Assume that $\theta > 1$ in the SIRS model, and that $\tilde{s}(t), \tilde{i}(t), \tilde{r}(t)$, is a T -periodic solution, $0 < \tilde{s}(t) < 1$, that attracts all solutions. Then $I(t)$ is asymptotically T -periodic if and only if $\bar{R}_2 = 1$. If $\bar{R}_2 < 1$, $I(t)$ is eventually decreasing, and if $\bar{R}_2 > 1$ then $I(t)$ is eventually increasing. \bar{f} is the asymptotic rate constant.*

7 Summary

As claimed in the Introduction, we have formulated a variable population SEIRS disease transmission model with constant latent and immune periods. We have begun analysis of the resulting complicated integro-differential equation system. We now summarize results and restrictions with the aim of indicating problems that remain open.

An important threshold parameter θ is identified in (3.1). If $\theta > 1$, the proportion of infectives does not tend to zero; if $\theta < 1$, the disease free proportion equilibrium is locally asymptotically stable, with global stability proved only for the subset $\theta < \exp(-b\omega)$. An endemic proportion equilibrium satisfies (4.5), (4.6); for $\varepsilon = 0$ (i.e., no disease related death) there is no such equilibrium if $\theta \leq 1$, but a unique endemic equilibrium if $\theta > 1$. For a disease that confers no immunity or has no latent period, this result holds under the weaker restriction that $\varepsilon < b$. In both of these special cases local stability of the endemic proportion equilibrium is analyzed under the restriction that $\varepsilon = 0$. This equilibrium is shown to be locally asymptotically stable for the SEIS model, whereas the SIRS model can exhibit periodic solutions.

The results on when periodic solutions exist for the SEIS and SIRS models here are qualitatively the same as those in Hethcote et al. (1981a, b) for corresponding models with constant population size. In the cases with variable population size, global asymptotic stability of the endemic equilibrium remains unproved. The full SEIRS model can exhibit periodic solutions for some parameter values, but appropriate parameter ranges remain to be explored. The asymptotic behavior as $t \rightarrow \infty$ of the *number* of infectives is shown to depend on other threshold parameters R_1, R_2, \bar{R}_2 . These parameters, together with θ , quantify two ways that the disease can be controlled, as summarized in Table 1. We note (from (2.4) and Theorem A.2) that another threshold parameter, namely

$$R_0 = \frac{\lambda \exp(-d\omega)}{(\varepsilon + \gamma + d)},$$

determines whether $I(t)$ initially grows or decays if a small number of infectives is introduced into a population of susceptibles.

Note added in proof. Professor Y. Kuang has pointed out that the Razumikhin function technique (see [11], Theorem 4.2, page 152 or Y. Kuang, *Delay Differential Equations with Applications in Population Dynamics*, Academic Press, 1993, Section 2.6) can be used to prove the following global result from (2.4). If $R_0 < 1$ then $I(t)$, $E(t)$, $R(t)$, and $N(t) - S(t)$ tend to zero as t tends to infinity. Note that if $\theta < 1$ and $b < d$, then $R_0 < \theta < 1$; whereas if $R_0 < 1$ and $b > d$, then $\theta < R_0 < 1$. These results complement those in Table 1. By applying the Razumikhin method to (2.13) it can be shown that $i(t) \rightarrow 0$ if $\varepsilon(\varepsilon + \gamma + b)^{-1} + \theta \exp(\varepsilon\omega) < 1$, and therefore for $\theta < 1$ if ε is sufficiently small.

Acknowledgments. Research of the first author was partially supported by U.S. National Science Foundation grant DMS-9208818, and research of the second author by Natural Sciences and Engineering Research Council of Canada grant A-8965 and by the University of Victoria Committee on Faculty Research and Travel. The authors thank an anonymous referee for several useful comments.

A Appendix

The assertion in Sect. 5 that instability can occur for $\omega > 0$ only by roots crossing the finite imaginary axis can be established as in the following theorem.

Theorem A.1 *Consider an equation of form*

$$P_\omega(z) + Q_\omega(z)\exp(-\omega(b + z)) = 0$$

where $b > 0$, P_ω and Q_ω are relatively prime polynomials in z with coefficients that are continuous functions of ω , and the degree of P_ω is greater than the degree of Q_ω . Suppose that for $\omega = 0$ all roots lie in $\Re(z) < 0$. Assume that for $\omega > 0$ there are no roots on the imaginary axis. Then all roots lie in $\Re(z) < 0$ for $\omega \geq 0$.

Proof. It is easy to see that each root z varies continuously with ω . Now let $\omega_0 > 0$ be fixed. We claim that all roots z for $0 \leq \omega \leq \omega_0$ with $\Re(z) \geq 0$ lie in a bounded domain. To see this, let n be the degree of P_ω . With no loss of generality we may assume that 1 is the leading coefficient in P_ω . Then

$$\begin{aligned} |z^{-n}P_\omega(z)| &= |z^{-n}Q_\omega(z)\exp(-\omega(b + z))| \\ &= |z^{-n}Q_\omega(z)|\exp(-\omega b)\exp(-\omega\Re(z)). \end{aligned}$$

Choose ρ_1 so large that $|z^{-n}P_\omega(z)| > 1/2$ for $|z| \geq \rho_1$, $0 \leq \omega \leq \omega_0$. Since the degree of Q_ω is less than n , there is $\rho_2 > 0$ such that the right side of the above equation is less than $1/2$ for $0 \leq \omega \leq \omega_0$, $|z| \geq \rho_2$, $\Re(z) \geq 0$. So the equation cannot hold for $|z| \geq \max\{\rho_1, \rho_2\}$, $\Re(z) \geq 0$, hence all roots in $\Re(z) \geq 0$ with $0 \leq \omega \leq \omega_0$ lie in $|z| < \max\{\rho_1, \rho_2\}$. Informally speaking, this shows that a root cannot suddenly appear in the right half plane from infinity, but only by moving onto the imaginary axis. Since, by hypothesis, there are no roots on the imaginary axis for any $\omega > 0$, all roots must remain in $\Re(z) < 0$. \square

In order to complete the discussion of equation (3.2), we consider quasipolynomial equations of the form

$$z + a - \lambda \exp(-\omega(b + z)) = 0. \quad (\text{A.1})$$

This arises from a differential-delay equation with lag $\omega > 0$. Parameters a, λ are positive and independent of ω and $b \geq 0$. The case with $b = 0$ is well known in the literature.

Theorem A.2 *Consider equation (A.1) with $\lambda > 0, a > 0, b \geq 0$. There is a positive zero $z = x > 0$ of (A.1) if and only if $\lambda \exp(-b\omega) > a$. If $\lambda \exp(-b\omega) < a$, then there is a unique real negative zero x_0 ; it is on the interval $(-a, 0)$, and every other zero z satisfies $\Re(z) < x_0 < 0$.*

Proof. Consider $z = x$ as a zero of (A.1), thus

$$x + a = \lambda \exp(-\omega(b + x)) - a. \quad (\text{A.2})$$

By examining the graphs we see that there is a solution $x > 0$ exactly when $\lambda \exp(-b\omega) - a > 0$. There is a solution $x = 0$ exactly when $\lambda \exp(-b\omega) - a = 0$. When $\lambda \exp(-b\omega) - a < 0$, there is a unique real zero x_0 , which satisfies $-a < x_0 < 0$. Assume there is a zero of (A.1) $z = x + iy$ with $x = \Re(z) \geq x_0$. Taking real and imaginary parts gives

$$\begin{aligned} x + a &= \lambda \exp(-\omega(b + x)) \cos(\omega y), \\ y &= -\lambda \exp(-\omega(b + x)) \sin(\omega y). \end{aligned}$$

From the first equation, $x + a \leq \lambda \exp(-\omega(b + x))$. When $x > x_0$ this is less than $\lambda \exp(-\omega(b + x_0)) = x_0 + a$, which is a contradiction. If $x = x_0$ and y is not a multiple of 2π then $\cos \omega y < 1$, so $x + a < \lambda \exp(-\omega(b + x)) = x_0 + a$, again a contradiction. Finally, if $x = x_0$ and y is a multiple of 2π , then the second equation yields $y = 0$ and $z = x_0$. We have shown that every zero $z \neq x_0$ satisfies $\Re(z) < x_0$. \square

We examine the quasipolynomial (A.1) further, by assuming there is a purely imaginary zero, $z = iy, y > 0$. Then

$$a = \lambda \exp(-b\omega) \cos(\omega y), \quad y = -\lambda \exp(-b\omega) \sin(\omega y).$$

Squaring and adding gives

$$y^2 = \lambda^2 \exp(-2b\omega) - a^2.$$

So if $\lambda^2 \exp(-2b\omega) < a^2$, then there are no purely imaginary zeros. As all quantities are positive, this is equivalent to $\lambda \exp(-b\omega) < a$. Computing derivatives from (A.2) on the curve $\lambda \exp(-b\omega) = a$ we find

$$\frac{\partial x}{\partial \omega} < 0, \quad \frac{\partial x}{\partial \lambda} > 0.$$

Thus for fixed, positive a, b , the curve $\omega = \frac{1}{b} \ln(\frac{a}{\lambda})$ in the first quadrant of the (λ, ω) plane separates the region of stability on the left from the region of instability on the right. In the limit $b = 0$, this curve becomes the vertical line $\lambda = a$.

References

1. Bellman, R., Cooke, K. L., *Differential-difference Equations*, Academic Press, New York, 1963
2. Brauer, F., Models for the spread of universally fatal diseases, *J. Math. Biology*, **28** (1990) 451–462
3. Brauer, F., Models for the spread of universally fatal diseases, II, in *Differential Equation Models in Biology, Epidemiology and Ecology*, eds. Busenberg, S., Martelli, M., *Lecture Notes in Biomath.* **92** (1991) 57–69
4. Busenberg, S., Cooke, K. L., The effect of integral conditions in certain equations modelling epidemics and population growth, *J. Math. Biology*, **10** (1980) 13–32
5. Busenberg, S., Cooke, K. L., *Vertically Transmitted Diseases*, *Biomathematics*, **23** Springer-Verlag 1993
6. Busenberg, S., Cooke, K. L., Pozio, A., Analysis of a model of a vertically transmitted disease, *J. Math. Biology*, **17** (1983) 305–329
7. Busenberg, S., van den Driessche, P., Analysis of a disease transmission model in a population with varying size, *J. Math. Biology*, **28** (1990) 257–270
8. Busenberg, S., van den Driessche, P., Nonexistence of periodic solutions of a class of epidemiological models, in *Differential Equation Models in Biology, Epidemiology and Ecology*, eds. Busenberg, S., Martelli, M., *Lecture Notes in Biomath.* **92** (1991) 70–79
9. Cooke, K. L., Yorke, J. A., Some equations modelling growth processes and gonorrhoea epidemics, *Math. Biosci.*, **16** (1973) 75–101
10. Greenberg, J. M., Hoppensteadt, F., Asymptotic behavior of solutions to a population equation, *SIAM J. Appl. Math.*, **28** (1975) 662–674
11. Hale, J. K., Verduyn Lunel, S. M., *Introduction to Functional Differential Equations*, Springer-Verlag 1993
12. Hethcote, H. W., Lewis, M. A., van den Driessche, P., An epidemiological model with a delay and a nonlinear incidence rate, *J. Math. Biology*, **27** (1989) 49–64
13. Hethcote, H. W., Stech, H. W., van den Driessche, P., Nonlinear oscillations in epidemic models, *SIAM J. Appl. Math.*, **40** (1981a) 1–9
14. Hethcote, H. W., Stech, H. W., van den Driessche, P., Stability analysis for models of diseases without immunity, *J. Math. Biology*, **13** (1981b) 185–198
15. Hethcote, H. W., van den Driessche, P., An SIS epidemic model with variable population size and a delay, *J. Math. Biology*, **34** (1995) 177–194
16. van den Driessche, P., A cyclic epidemic model with temporary immunity and vital dynamics, in *Population Biology*, eds. Freedman, H.I., Strobeck, C., *Lecture Notes in Biomath.* **52** (1983) 433–440
17. van den Driessche, P., Some epidemiological models with delays, in *Differential Equations and Applications to Biology and to Industry*, Martelli, M. et al. (eds.) World Scientific (1996) 507–520