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Interaction of maturation delay and nonlinear birth in population and epidemic models

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Abstract. A population with birth rate function $B(N)\ N$ and linear death rate for the adult stage is assumed to have a maturation delay $T > 0$. Thus the growth equation $N'(t) = B(N(t-T))N(t-T)\mathrm{e}^{-d_1 T} - dN(t)$ governs the adult population, with the death rate in previous life stages $d_1 \geqq 0$. Standard assumptions are made on $B(N)$ so that a unique equilibrium N_e exists. When $B(N)\ N$ is not monotone, the delay T can qualitatively change the dynamics. For some fixed values of the parameters with $d_1 > 0$, as T increases the equilibrium N_e can switch from being stable to unstable (with numerically observed periodic solutions) and then back to stable. When disease that does not cause death is introduced into the population, a threshold parameter R_0 is identified. When $R_0 < 1$, the disease dies out; when $R_0 > 1$, the disease remains endemic, either tending to an equilibrium value or oscillating about this value. Numerical simulations indicate that oscillations can also be induced by disease related death in a model with maturation delay.

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1. Introduction

Classical epidemic models assume that the total population size is constant, and concentrate on describing the spread of disease through the population. More recent models consider a variable population size, thus taking into account a longer time scale with disease causing death and reduced reproduction; see, e.g., Zhou and Hethcote (1994). In disease transmission models, time delay can be used to model some mechanisms. For example, in Hethcote and van den Driessche (1995) a delay corresponding to an infective period of constant length is introduced in an SIS model. Periodic solutions of the proportional variables occur for a small range of parameters (that appears to be outside the epidemiologically realistic range).

In the population biology literature, oscillations of the population size are observed from data. Theoretical models with time delay are postulated and analyzed in an attempt to explain these oscillations; see, e.g., Nisbet and Gurney (1982, Chapter 8). Population models with density dependent recruitment incorporating a maturation time delay can give rise to cycles of the general type observed.

It is our aim to formulate and analyze an SIS epidemic model with maturation delay in a varying population of size $N(t)$. To describe disease transmission in non-constant population, assumptions must be made on the demography and epidemiology. We consider a nonlinear birth term $B(N)$, and find that the form $B(N)N$ is important in determining the qualitative dynamics. In Sect. 2, we formulate our population model, state basic assumptions, and give examples of $B(N)$ from the biological literature. In Sect. 3, we study the dynamics of the population model with maturation delay in the absence of disease. Results from monotone dynamical systems theory are used in the global analysis, and the delay is taken as the bifurcation parameter. Periodic solutions are found numerically for some values of delay, and it is found that (for other parameter values fixed and a positive death rate constant in each stage prior to the adult stage) these periodic solutions persist for only a finite positive range of values of the delay. For large and for small values of the delay, there is convergence to equilibrium. In Sect. 4 we formulate and analyze the SIS epidemic model in a variable population. When there is no maturation delay, a sharp threshold parameter R_0 is identified with infectives dying out or tending to an endemic level. With maturation delay, analysis for a disease that does not cause death is given, and numerical simulations on the model that includes disease related death show that this can give rise to oscillations.

2. Population model formulation

In the absence of disease and of maturation delay, we assume that the population size changes according to a population growth equation

$$N' = B(N)N - dN, \tag{2.1}$$

where $' = d/dt$. Here $d > 0$ is the death rate constant, and $B(N)N$ is a birth rate function with $B(N)$ satisfying the following basic assumptions for $N \in (0, \infty)$:

(A1) $B(N) > 0$;
(A2) $B(N)$ is continuously differentiable with $B'(N) < 0$;
(A3) $B(0^+) > d > B(\infty)$.

Note that (A2) and (A3) imply that $B^{-1}(N)$ exists for $N \in (B(\infty), B(0^+))$, and (A3) gives the existence of a carrying capacity K such that $B(N) > d$ for $N < K$, and $B(N) < d$ for $N > K$. Under these assumptions, nontrivial solutions of (2.1) approach $B^{-1}(d)$ as $t \to \infty$. Examples of birth functions $B(N)$ found in the biological literature that satisfy (A1)–(A3) are:

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

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

(B3) $B_3(N) = \dfrac{A}{N} + c$, with $A > 0, \quad d > c > 0$.

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.

For the population model (2.1), it can be postulated that the birth rate function $B(N)N$ should depend on $t - T$, where T is the developmental or maturation time. Thus the population growth equation is

$$N'(t) = B(N(t - T))N(t - T) - dN(t). \tag{2.2}$$

Nisbet and Gurney (1982, Sect. 8.3) use this equation with $B(N) = B_1(N)$ to model laboratory fly populations. This equation has subsequently been considered by many authors, see the papers cited in Notes after Corollary 3.4 and the references therein. Velasco-Hernández (1994) uses (2.2) with $B_1(N)$ for the vector population equation in a model for Chagas disease. Mackey and Glass (1977) use (2.2) with $B(N) = B_2(N)$ to model blood cell production, where N is the concentration of cells.

Considering this maturation time in more detail, assume that the population has $m+1$ life stages. For example, a population with embryos, juveniles and adults has 3 life stages. Assuming that T_1 is the time spent in the embryo stage, and that d_1 is the death rate constant for the embryo stage, then the number of embryos at time t, $E(t)$, is given by

$$E(t) = \int_{t-T_1}^{t} B(N(s))\, N(s)\, \mathrm{e}^{-d_1(t-s)}\, ds,$$

where $N(s)$ in the integrand is the adult population size. This gives that the rate of entry into the juvenile stage is

$$B(N(t-T_1))\, N(t-T_1)\, \mathrm{e}^{-d_1 T_1}.$$

Similarly, the rate of entry into the adult stage is

$$B(N(t-T_1-T_2))\, N(t-T_1-T_2)\, \mathrm{e}^{-(d_1 T_1 + d_2 T_2)}$$

where T_2 the time spent in the juvenile stage , and d_2 is the death rate constant for the juvenile stage. For $m+1$ life stages, the rate of entry into the adult stage at time t is

$$B((N(t-T_1-\cdots-T_m))\, N(t-T_1-\cdots-T_m)\, \mathrm{e}^{-(d_1 T_1 + \cdots + d_m T_m)}$$

where d_j is the death rate constant for life stage j, and T_j is the time spent in that stage. As a special case, assume $d_j = d_1 \geqq 0$ for each life stage, and let $T = T_1 + \cdots + T_m$. Then the population equation for adults becomes

$$N'(t) = B(N(t-T))\, N(t-T)\, \mathrm{e}^{-d_1 T} - dN(t). \tag{2.3}$$

For some species, the death rate in each stage prior to the adult stage is negligible compared with the death rate of the adult stage. Then we can assume $d_1 = 0$, and (2.3) reduces to (2.2).

3. Single-species population models with delay

In this section we consider the single-species population model (2.3). To ensure the existence of a nontrivial equilibrium (though depending on T), (A3) must be replaced by (A3*)

(A3*) $B(0^+) > d\mathrm{e}^{d_1 T} > B(\infty)$.

Note that this reduces to (A3) when $d_1 = 0$ or $T = 0$. A maturation delay $T \geqslant 0$ is incorporated into the nonlinear birth term $B(N(t-T))$ that is assumed to satisfy (A1), (A2) and (A3*), whereas the linear death term is non-delayed and a death rate constant $d > 0$ is assumed.

Initially $N(t)$ is assumed to be positive, continuous and bounded on $t \in [-T, 0]$. Assume t_0 is the first time that N becomes zero. Then $N'(t_0) > 0$ by (2.3) and (A1), which is impossible. Thus, $N(t) > 0$ for all positive t for which $N(t)$ is finite. By (2.3), the assumptions on $B(N)$ and initial conditions, $N(t)$ exists and is bounded and continuous for $t \in [0, T]$. Proceeding in time steps of length T, it can be seen that $N(t)$ remains finite for all positive t. Therefore $N(t)$ is positive for all positive t.

For $T = 0$, equation (2.3) reduces to the ODE (2.1). With the above assumptions, (2.1) has a unique positive equilibrium $N_e = B^{-1}(d)$. By using the Liapunov function $V(N) = N - N_e - N_e \ln(N/N_e)$, it can be easily shown that for $N(0) > 0$, N_e is globally asymptotically stable. So the particular forms of $B(N)$ satisfying (A1)–(A3) do not affect the dynamics of (2.1). With time delay $T > 0$ incorporated, this simplicity of the dynamics is not always maintained. Indeed, the profile of $B(N)$ N also contributes to the dynamics of (2.3). We begin by making an additional assumption:

(A4) $(B(N)N)' > 0$.

The following global result is proved by monotonicity as in Smith (1995, Chapter 5). Freedman and Gopalsamy (1986, Theorem 2) use a Lyapunov function to prove the result under the additional hypothesis that $B(N)N$ is zero at $N = 0$ (which is not satisfied by $B_3(N)$).

Theorem 3.1. *Assume that* (A1), (A2), (A3*) *and* (A4) *hold. Then, for positive initial values, the unique positive equilibrium* $N_e = B^{-1}(de^{d_1 T})$ *of* (2.3) *is globally asymptotically stable for all* $T \geqq 0$.

Proof. From the assumptions, the positive steady state of (2.3) is $N_e = B^{-1}(de^{d_1 T})$. Consider (2.3) in $C([-T, 0], R^+)$. Assumption (A4) ensures that (2.3) is cooperative and irreducible and hence the solution flow of (2.3) is eventually strongly monotone; see Smith (1995, p. 89, Corollary 3.5). Under the assumptions, (2.3) satisfies a scaled version of the conditions of Smith (1995, p. 90, Proposition 4.2). This gives that all solutions of (2.3) converge to 0 or N_e. Since if 0 is an equilibrium then it is unstable, every solution with positive initial values converges to the unique positive equilibrium N_e. Finally, a linear stability analysis using the well known result for Hayes' equation $z + d - e^{-d_1 T}(B(N_e) + B'(N_e)N_e)e^{-Tz} = 0$ (see, e.g., Bellman and Cooke (1963, Theorem 13.8), or Hale and Verduyn Lunel (1993, Theorem A5)) shows that (A2) and (A4) guarantee that N_e is locally asymptotically stable. Therefore, N_e is globally asymptotically stable. □

Corollary 3.2. *For* $B(N) = B_2(N) = (p/(q + N^n))$ with $p/q > de^{d_1 T}$, $0 < n \leqq 1$, or $B(N) = B_3(N) = A/N + c$ with $c < de^{d_1 T}$, *and positive initial values, the unique positive equilibrium* $N_e = B^{-1}(de^{d_1 T})$ *of* (2.3) *is globally asymptotically stable for all* $T \geqq 0$.

Proof. For the $B(N)$ functions given, assumptions (A1), (A2), (A3*) and (A4) are all satisfied. Thus Theorem 3.1 applies and gives the result. □

Note that the result for $B_2(N)$ with $d_1 = 0$ in Corollary 3.2 recreates by a different method Corollary 9.1 in Kuang (1993, p. 160).

If the extra condition (A4) is assumed, Theorem 3.1 shows that incorporation of maturation $T > 0$ does not make any qualitative difference to the dynamics of the model. We next consider a particular $B(N)$ satisfying (A1)–(A3*) but not (A4), and show that the dynamics of (2.3) can be quite different from that of its ODE version (2.1).

For $B_1(N) = be^{-aN}$ with $a > 0$, $b > de^{d_1 T}$, assumptions (A1)–(A3*) are all satisfied and equation (2.3) becomes

$$N'(t) = be^{-aN(t-T)} N(t-T) e^{-d_1 T} - dN(t). \tag{3.1}$$

Note that $B(N)N$ is a one-humped function (hence not monotone) with a maximum at $N = \frac{1}{a}$. For this $B(N)$, we introduce some definitions needed in the following theorem.

Let k^* be the solution with $w \in (\frac{\pi}{2}, \pi)$ of the equations

$$\begin{cases} \sin w = -\cos w[\frac{d_1}{d} w \cos w + k^* \sin w], \\ \dfrac{\sin w - w\cos w}{w - \sin w \cos w} = 2\frac{d_1}{d} w \dfrac{\cos w}{\sin w} + k^*. \end{cases} \tag{3.2}$$

For $\frac{b}{d} > e^{k^*+1}$, define T^* and T^{**} by

$$T^* = \frac{x_1}{d}, \qquad T^{**} = \frac{x_2}{d}, \tag{3.3}$$

where x_1 and $x_2 > x_1$ are the two (positive) solutions of the following equations:

$$\begin{cases} x = -\dfrac{v}{\tan v}, \\ \frac{v}{\sin v} = x(\ln \frac{b}{de} - \frac{d_1}{d} x), \end{cases} \tag{3.4}$$

for $v \in (\frac{\pi}{2}, \pi)$. Define $T' = \max\{T \geqq 0: Te^{(d-d_1)T} \leqq \frac{e}{b}\}$ and

$$T'' = \begin{cases} \infty, & \text{if } \frac{b}{d} < e^{k^*+1}, \\ T^*, & \text{if } \frac{b}{d} > e^{k^*+1}. \end{cases}$$

Theorem 3.3. *Assume* $a > 0$, $b > de^{d_1 T}$, *and* $d_1 > 0$ *in* (3.1) *with positive initial values.*

(i) If $\frac{b}{d} < e^{k^*+1}$, then the unique positive equilibrium $N_e = \frac{1}{a}\ln\frac{b}{de^{d_1 T}}$ *of* (3.1) *is locally asymptotically stable independent of* T.

(ii) If $\frac{b}{d} > e^{k^*+1}$, *then there exist* $0 < T^* < T^{**}$ *such that* N_e *loses stability when* T *increases to pass through* T^*, *and regains stability when* T *further increases to pass through* T^{**}.

(iii) *For small* $T \geqq 0$, *namely* $T < T_0$ *where*

$$T_0 = \min\left\{\frac{1}{d_1}\ln\frac{b}{d},\, T',\, T''\right\}, \tag{3.5}$$

the equilibrium N_e *is globally asymptotically stable.*

(iv) *If* $d + \frac{b}{e^2} < d_1$, *then* N_e *is globally asymptotically stable for all* $T < \min\left\{\frac{1}{d_1}\ln\frac{b}{d}, T''\right\}$.

Proof of (i) and (ii). The value of N_e is easily found as the unique positive steady state of (3.1). Linear stability of (3.1) is governed by the characteristic equation

$$zT = -(cT)e^{-zT} - dT \tag{3.6}$$

where

$$cT = (dT)\left(k - \frac{d_1}{d}(dT)\right), \quad \text{with } k = \ln\frac{b}{de}. \tag{3.7}$$

Equation (3.7) represents a parabola in the dT, cT plane (see Fig. 1). Note that $z = 0$ is not a root of (3.6). Setting $z = iy$, $y > 0$ in (3.6) gives the purely imaginary root curve parameterized as

$$cT = \frac{yT}{\sin(yT)}, \qquad dT = \frac{-yT}{\tan(yT)}. \tag{3.8}$$

Note that neither yT nor $\sin(yT)$ is zero at a root. For $yT \in (\frac{\pi}{2}, \pi)$, (3.8) gives the part of the lowest imaginary root curve with $dT > 0$. Substituting (3.8) into (3.7) gives the condition for the parabola and the lowest imaginary root curve to intersect at the critical value of k, namely $k = k^*$, as in the first equation in (3.2) with $w = yT$. These curves must also be tangential at $k = k^*$, and from the geometry there is a unique solution k^* (see Fig. 1). Differentiating to impose this condition, and simplifying leads to the second equation in (3.2). If $k = \ln\frac{b}{de} < k^*$ (i.e., $b/d < e^{k^*+1}$), such an intersection will not occur, and (i) follows. If $k > k^*$, the parabola intersects the lowest imaginary root curve in two points where $dT = dT^*$ and dT^{**}. These points of intersection given in (3.3) and (3.4) are found from (3.7) and (3.8). As T passes through T^*, stability of N_e is lost. As T passes through T^{**},

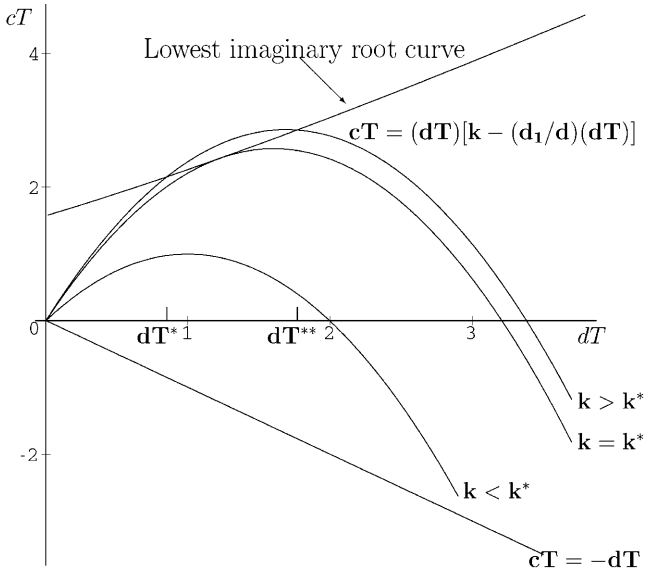


Fig. 1. Determination of T^* and T^{**} in Theorem 3.3.

stability is regained. For k sufficiently large, other imaginary root curves for $yT \in (2n\pi + \frac{\pi}{2}, 2n\pi + \pi)$ may intersect the parabola, but they do not alter the linear stability for $T < T^*$ and $T > T^{**}$. Thus (ii) is proved.

Proof of (*iii*) *and* (*iv*). We prove (iii) by using a global convergence theorem for strongly order preserving (SOP) dynamical systems. But since (A4) is not satisfied for $B_1(N)$, SOP under the standard ordering for (3.1) does not hold. In what follows, we use the exponential ordering for monotone dynamical systems as initiated by Smith and Thieme (1990), see Smith (1995, p. 102).

Let $C_+ = ([-T, 0], R^+)$. For $\mu \geqq 0$, define

$$K_\mu = \{\phi \in C_+ : \phi \geqq 0 \text{ and } \phi(\theta)\mathrm{e}^{\mu\theta} \text{ is non decreasing on } [-T, 0]\}.$$

Then, K_μ is a closed cone in C_+, and thus it induces a partial ordering on C_+, defined by $\phi_1 \leqq_\mu \phi_2$ if and only if $\phi_2 - \phi_1 \in K_\mu$. Denote the right hand side of (3.1) by $f(N_t)$, i.e., f: $C_+ \to R$ is defined by

$$f(\phi) = b\phi(-T)\mathrm{e}^{-a\phi(-T)}\mathrm{e}^{-d_1 T} - d\phi(0).$$

It is known (see Smith (1995, p. 108)) that if

$$\begin{cases} f(\phi_2) - f(\phi_1) + \mu(\phi_2(0) - \phi_1(0)) > 0, \\ \text{for } \phi_i \in C_+, i = 1, 2, \quad \text{satisfying } \phi_1 <_\mu \phi_2, \end{cases} \tag{3.9}$$

then, the solution flow is SOP with respect to the ordering $\leqq_\mu$. Using the mean value theorem, there exists $\mu \geqq 0$ such that (3.9) holds for $f(N_t)$ defined above provided

$$\mu + \min_{\phi \geqq 0} \frac{\partial f(\phi)}{\partial \phi(0)} + e^{\mu T} \min_{\phi \geqq 0} \frac{\partial f(\phi)}{\partial \phi(-T)} \geqq 0,$$

that is

$$F(\mu) = \mu - d - be^{-2} e^{(\mu - d_1)T} \geqq 0. \tag{3.10}$$

Since $F(\mu)$ is concave down with $F(0) < 0$, (3.10) is true iff $F(\mu)$ has a nonnegative maximum, which is equivalent to $Te^{(d-d_1)T} \leqq \frac{e}{b}$, hence the definition of T' above. The precompactness of the solution flow is shown by integrating (2.3) with $B_1(N)$, giving

$$N(t) = N(0)e^{-dt} + e^{-dt}e^{-d_1 T} \int_0^t B_1(N(s-T))N(s-T)e^{ds}\,ds.$$

Thus

$$\begin{aligned} N(t) &\leqq N(0)e^{-dt} + \frac{b}{ae} e^{-dt}e^{-d_1 T} \int_0^t e^{ds}\,ds \\ &= \frac{be^{-d_1 T}}{aed} + \left(N(0) - \frac{be^{-d_1 T}}{aed}\right)e^{-dt} \\ &\leqq \frac{be^{-d_1 T}}{aed} + \left|N(0) - \frac{be^{-d_1 T}}{aed}\right|. \end{aligned}$$

By the global convergence theorem for SOP semiflows (see Smith (1995, p. 18)), every solution of (3.1) with positive initial values converges to N_e. Combining this with (i) and (ii), and noting that N_e depends on T, we conclude that N_e is globally asymptotically stable for $T < T_0$ as in (3.5), thus proving (iii). Taking $\mu = d_1$ in (3.10) gives the result of (iv). □

Note that in the special case that $d_1 = d$, T' is given explicitly as $T' = \frac{e}{b}$. In the special case that $d_1 = 0$, from (3.2) $w = \pi$ and $k^* = 1$, and (3.4) has a unique positive solution $\bar{T}^*$. The definitions of T' and T'' precede the statement of Theorem 3.3 (with $d_1 = 0$, $k^* = 1$).

Corollary 3.4. *Assume $a > 0$, $b > d$, and $d_1 = 0$ in* (3.1) *with positive initial values.*

(i) *If $\frac{b}{d} \leqq e^2$, then $N_e = \frac{1}{a}\ln\frac{b}{d}$ is locally asymptotically stable, independent of T.*
(ii) *If $\frac{b}{d} > e^2$, then there exists a $\bar{T}^* > 0$ such that Hopf bifurcation occurs when T increases through $\bar{T}^*$.*

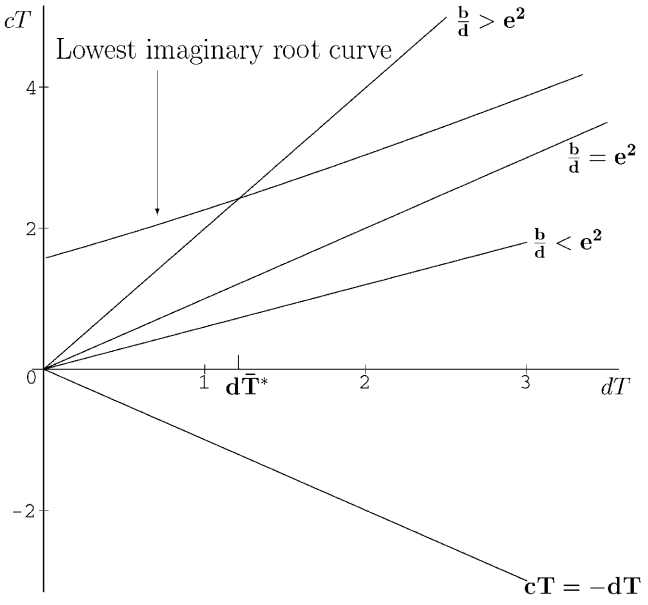


Fig. 2. Determination of $\bar{T}^*$ in Corollary 3.4.

(iii) *For small* $T \geqq 0$, *namely* $T < T_0 = \min\{T', T''\}$, *the equilibrium* N_e *is globally asymptotically stable.*

Proof. Set $d_1 = 0$ in the proof of Theorem 3.3. Now (3.7) represents a straight line in the dT, cT plane (see Fig. 2). Classical results on Hayes' equation show that N_e is asymptotically stable for all $T \geqq 0$ if $\ln \frac{b}{de}$ (i.e., $\frac{b}{d} \leqq e^2$). If $\ln \frac{b}{de} > 1$ (i.e., $\frac{b}{d} > e^2$), then N_e loses stability at some $\bar{T}^*$. From (3.6), it can be seen that iy is a simple root and no integral multiple of iy is a root. When $d_1 = 0$, $\frac{dRe(z)}{dt} = \frac{y^2}{(1+dT)^2+(yT)^2} > 0$ at $z = iy$, $T = \bar{T}^*$. Thus, Hopf bifurcation occurs at $\bar{T}^*$. □

Notes. For case (i) in the above corollary, N_e is actually globally asymptotically stable if the inequality is strict, i.e., $\frac{b}{d} < e^2$, see Kuang (1992, Corollary 4.3). The result of case (ii) is established in Brauer (1987, Theorem 5) as a special case of a delayed nonlinear renewal equation result. When the delay is normalized to 1, Smith (1995, Theorem 5.3, p. 114) gives conditions for global attractivity of N_e. So and Yu (1994, Theorem 4.1) also have results on global attractivity of N_e for small values of the delay T.

From Theorem 3.3 and Corollary 3.4, it is possible that for fixed values of the parameters, as T increases the equilibrium N_e of (3.1) switches from being stable to unstable. As it loses stability, stable

periodic solutions with period $\in (2T, 4T)$ may arise by Hopf bifurcation. Stability of the bifurcating periodic solutions has not been proved, but the numerical simulations in the next paragraph support this conclusion. This model with $d_1 = 0$ is the one proposed by Nisbet and Gurney (1982, Section 8.3) to explain oscillations in blowfly data. When $d_1 > 0$ in (3.1), it is possible that for a further increase in T, N_e regains stability. This phenomenon does not occur in the model with $d_1 = 0$ that has been considered previously in the literature.

These stability switches are illustrated in Figs. 3(a)–(d) by numerical simulations using XPPAUT (Ermentraut, 1996). These figures show numerical solutions of (3.1) for $t \in [0, 25]$ with $a = 1$, $d = 1$, $b \in \{20, 80\}$, $d_1 \in \{0, 1\}$ and $T \in \{0.2, 1.0, 2.4\}$ with initially $N(t) = 3.5$ on $[-T, 0]$. In Fig. 3(a), with $b = 20$, $d_1 = 1$, $k = \ln b/d - 1 < k^* \approx 3.21$ when $d_1 = d$. Thus, in agreement with Theorem 3.3(i), N tends to N_e (depending on T) for all values of T. Numerically this convergence to equilibrium appears to be global, although Theorem 3.3(i) only assures local stability and T_0 in (3.5) ≈ 0.14 for these parameter values. Figure 3(b), with $d_1 = 1$ and $b = 80$, gives $k > k^*$. As predicted by Theorem 3.3(ii), N tends to N_e for $T = 0.2 < T^* \approx 0.85$, whereas N oscillates about N_e for $T = 1.0$ (i.e., $T^* < T < T^{**}$). For a large value of T, namely $T = 2.4 > T^{**} \approx 1.77$, N again tends to N_e. Figures 3(c) and 3(d) have $d_1 = 0$, thus the results of Corollary 3.4 are illustrated. In Fig. 3(c), $b = 20$ so $b/d > e^2$, and for $T = 0.2$ and $T = 1.0$ (both are less than $\bar{T}^* \approx 1.21$), N tends to N_e. But for $T = 2.4 > \bar{T}^*$, N oscillates about N_e. Such oscillatory behavior does not occur for these same values of a, d, b, T but with $d_1 = 1$ (Fig. 3(a)). When b is increased to 80, oscillation now occurs for $T = 1.0$ and $T = 2.4$ since $\bar{T}^* \approx 0.58$ for these parameter values. The oscillation for $T = 2.4$, $d_1 = 0$ should be compared with the convergence to equilibrium for $T = 2.4$, $d_1 = 1$ (Fig. 3(b)). Note the different scale for N on Fig. 3(d) compared with other figures, and that in all figures behavior of $N(t)$ for small time depends on the initial values taken.

When $B(N) = B_2(N) = \frac{p}{q + N^n}$ with $n > 1$, assumption (A4) is also not satisfied. Assuming that $p, q > 0$, $n > 1$ and $\frac{p}{q} > de^{d_1 T}$, results qualitatively like Theorem 3.3 and Corollary 3.4 can be derived for equations (2.3) and (2.2) with this $B(N)$. For the parameters estimated from blood cell date and used by Mackey and Glass (1977), namely $d = 0.1$, $\frac{p}{q} = 0.2$ (giving $\frac{qd}{p} = 0.5$), $n = 10$ and $T = 6$, periodic solutions of (2.2) occur. However, for $d_1 = 0.1$, $\frac{qd}{p} = 0.5$ and large enough values of $n \geqq 21$, stability switches as found in Theorem 3.3 occur as T increases. This value of n is found by MAPLE from the characteristic equation with $B_2(N)$.

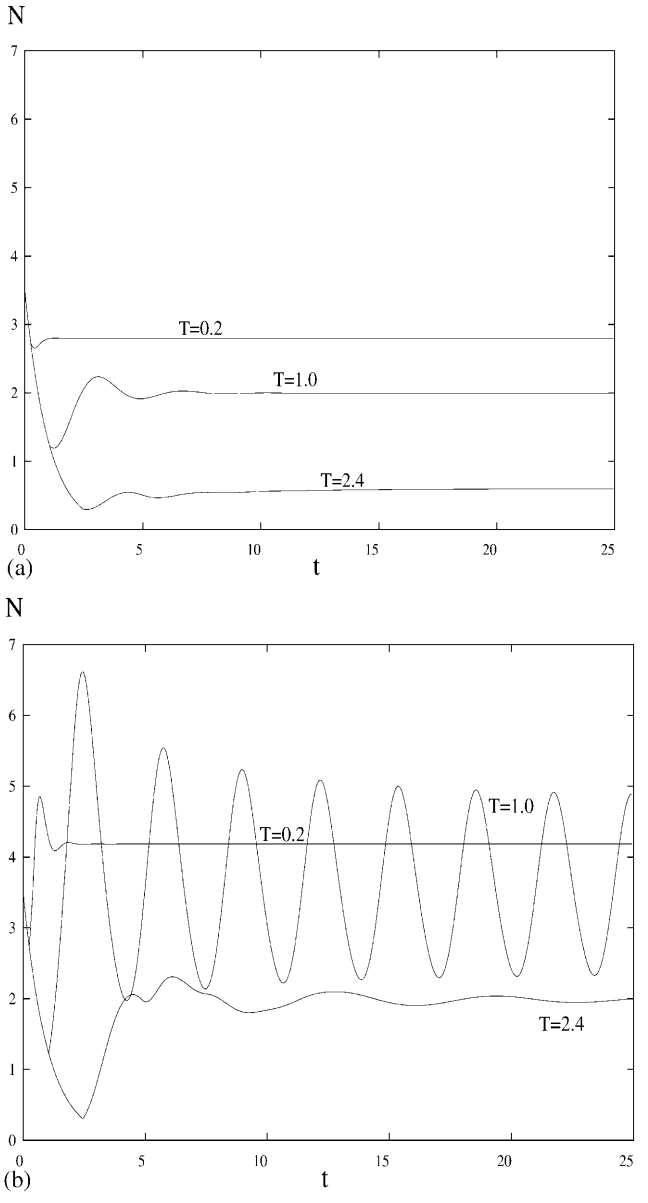
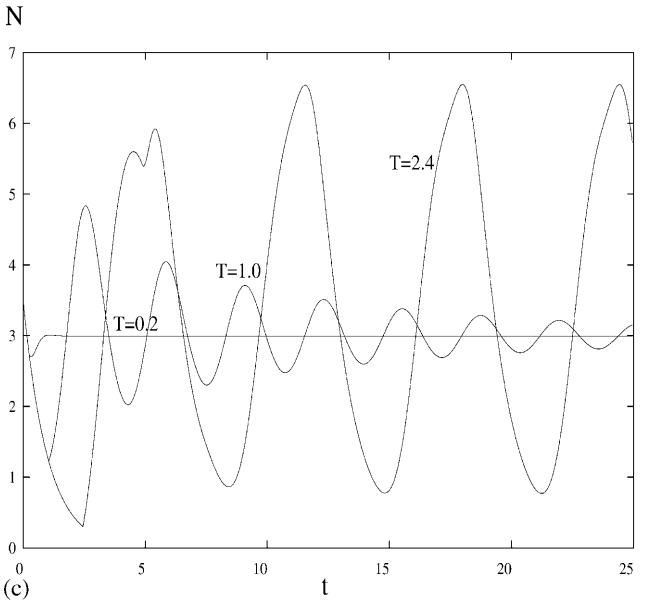


Fig. 3. Numerical simulations for (3.1) with $a = d = 1$: **(a)** $d_1 = 1$, $b = 20$; **(b)** $d_1 = 1$, $b = 80$; **(c)** $d_1 = 0$, $b = 20$; **(d)** $d_1 = 0$, $b = 80$.

Another quantity of some interest when $B(N)N$ is zero at $N = 0$ (*e.g.*, $B_1(N)$ and $B_2(N)$) is the growth rate at low density (initial growth rate), denoted by r. By linearization of (2.3) at $N = 0$, $r = B(0)\,\mathrm{e}^{-T(d_1 + r)} - d$. When $T = 0$, $r = B(0) - d$. Thus time delay decreases the initial growth rate.



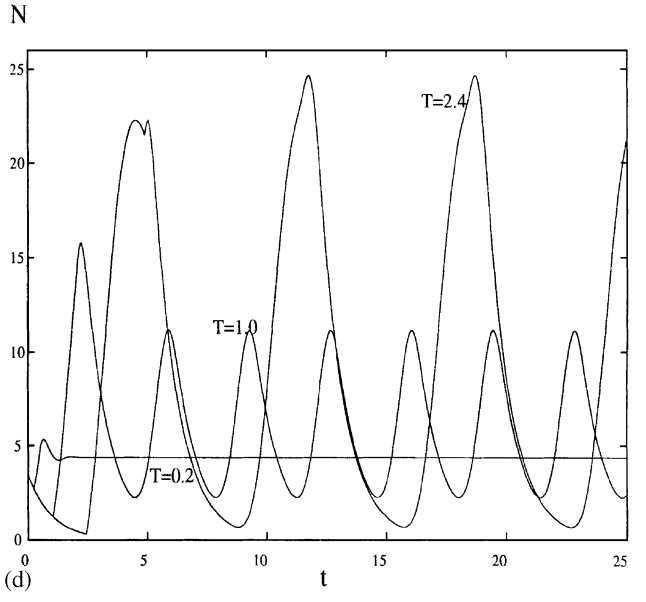


Fig. 3. Continued.

4. SIS epidemic model

We assume now that disease has entered the population, and that the population is divided into susceptible and infective classes, with the size of each class given by $S(t)$ and $I(t)$, respectively, so that

$N(t) = S(t) + I(t)$. Transmission of disease is assumed to occur due to contact between susceptibles and infectives; vertical transmission is ignored. The disease is assumed to confer no immunity, 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. In the absense of maturation delay, disease transmission is modeled by the equations

$$\begin{aligned} S'(t) &= B(N)\,N - dS - \frac{\lambda SI}{N} + \gamma I \\ I'(t) &= \frac{\lambda SI}{N} - (d + \varepsilon + \gamma)\,I. \end{aligned} \tag{4.1}$$

Here $\varepsilon \geqq 0$ is the disease induced death rate constant, $\gamma \geqq 0$ 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 (1992), de Jong et al. (1995) and references therein. Adding the equations in (4.1) gives $N' = B(N)\,N - dN - \varepsilon I$, which reduces to (2.1) in case there are no disease induced deaths or in the absence of disease ($\varepsilon = 0$ or $I = 0$). For $B_3(N)$ with $c = 0$, model (4.1) reduces to the SIS model with recruitment-death demographics analyzed by Zhou and Hethcote (1994, Sect. 2). They also analyze (4.1) with generalized logistic demographics (see Zhou and Hethcote (1994, Sect. 3)); see also Allen and Cormier (1996, Sect. 2). Bremermann and Thieme (1989) consider a more general epidemic model that has some similarities with (4.1), but their model uses mass action incidence, and has multiple classes of infective individuals who, on recovery, are permanently immune. For a model of a vertically transmitted disease with maturation delay see Busenberg and Cooke (1993, Sect. 4.2), and for models with delay on recruitment into a core group see Brauer (1999).

In order to incorporate maturation delay into the epidemic model (4.1), we assume that there is no horizontal transmission to individuals who are not yet adults, all newly matured adults are susceptible and the rate of entry into the adult stage is $B(N(t-T))\,N(t-T)\,\mathrm{e}^{-d_1 T}$. Setting $S = N - I$ gives the system

$$\begin{aligned} I'(t) &= \lambda(N - I)\frac{I}{N} - (d + \varepsilon + \gamma)I \\ N'(t) &= B(N(t-T))\,N(t-T)\,\mathrm{e}^{-d_1 T} - dN - \varepsilon I. \end{aligned} \tag{4.2}$$

Throughout this section, $B(N)$ is assumed to satisfy (A1), (A2) and another strengthened version of (A3), namely

(A3′) $B(0^+) > (d+\varepsilon)\mathrm{e}^{d_1 T}$ and $d\mathrm{e}^{d_1 T} > B(\infty)$.

With nonnegative initial values, namely $N(t) > 0$, $N(t) \geqq I(t) \geqq 0$ on $[-T, 0]$, solutions exist and remain for all $t > 0$ in the nonnegative quadrant with $N(t) \geqq I(t)$. If $B(N)N$ is zero at $N = 0$, then the trivial equilibrium $N = 0$, $I = 0$ (with $\lim_{(I,N)\to(0,0)} \frac{SI}{N} = 0$, since $0 \leqq S \leqq N$) exists, and is always unstable since $(I, N) = (0, N(t))$ where $N(t)$ is a solution to (2.3) remains away from (0, 0).

For this epidemic model, the basic reproduction number

$$R_0 = \frac{\lambda}{d+\varepsilon+\gamma}, \tag{4.3}$$

gives the average number of new infectives produced by one infective during the mean death adjusted infective period. When there is no delay, R_0 acts as a sharp threshold, as shown by the following result.

Theorem 4.1. *Consider the model system* (4.2) *with nonnegative initial values*, $T = 0$, $B(N)$ *satisfying* (A1), (A2) *and* (A3′) *and* R_0 *given by* (4.3). *If* $R_0 < 1$, *then the disease dies out with* $I(t) \to 0$ *and* $N(t) \to N_e = B^{-1}(d)$ *as* $t \to \infty$. *If* $R_0 > 1$ *and* $I(0) > 0$, *then the disease remains endemic with* $I(t) \to I^* = (1 - \frac{1}{R_0})N^*$ *and* $N(t) \to N^* = B^{-1}(d + \varepsilon(1 - 1/R_0))$ *as* $t \to \infty$.

Proof. The disease-free equilibrium with $I = 0$ and the unique endemic equilibrium with $I^* > 0$ are found easily from the steady states of (4.2) using the assumptions on $B(N)$.

For the disease-free equilibrium, consider $V = \frac{1}{2}I^2$. Then along trajectories of (4.2), $V' \leqq 0$ provided $R_0 < 1$, and $V' = 0$ iff $I = 0$. Thus $I \to 0$ as $t \to \infty$. The N' equation of (4.2) is then asymptotically autonomous, and the limit equation is the ODE (2.1). By the results of Sect. 3, and theory of asymptotically autonomous systems (see, Castillo-Chavez and Thieme (1995, Theorem 2.5)), $N(t) \to B^{-1}(d)$ as $t \to \infty$.

For local stability of the endemic equilibrium, the Jacobian matrix evaluated at this equilibrium is

$$J = \begin{pmatrix} -\lambda(1 - \frac{1}{R_0}) & \lambda(1 - \frac{1}{R_0})^2 \\ -\varepsilon & \varepsilon(1 - \frac{1}{R_0}) + B'(N^*)N^* \end{pmatrix}.$$

By (A2), $B'(N^*) < 0$, so $\det J > 0$, and trace $J < 0$ provided $\lambda > \varepsilon$, which is certainly true if $R_0 > 1$. Periodic solutions can be eliminated

by using the Bendixson-Dulac theorem (see, for example, Hale and Kocak (1991, Theorem 12.9)) since (4.2) gives

$$\frac{\partial}{\partial I}\left(\frac{I'}{NI}\right)+\frac{\partial}{\partial N}\left(\frac{N'}{NI}\right)<0$$

for $N>0$ and $I>0$ provided $\lambda>\varepsilon$. As the ODE system is 2-dimensional, the endemic equilibrium is globally asymptotically stable provided $R_0>1$ and $I(0)>0$. □

For $B(N)N=A$ (i.e., $B_3(N)$ with $c=0$), this sharp threshold result is proved for a contact rate depending on N (i.e., $\lambda(N)$) by Zhou and Hethcote (1994, Sect. 2).

Incorporating maturation delay $T>0$ in the model, R_0 still acts as the threshold for the existence of the endemic equilibrium. The steady states of (4.2) and the behavior when $R_0<1$ are given in the following results.

Theorem 4.2. *Consider* (4.2) *with* $B(N)$ *satisfying* (A1), (A2) *and* (A3′), *and* R_0 *given by* (4.3). *If* $R_0\leqq 1$, *then the disease free equilibrium, namely*

$$I=0,\qquad N_e=B^{-1}(d\mathrm{e}^{d_1T})$$

is the only nontrivial equilibrium. If $R_0>1$, *then there is also the endemic equilibrium, namely*

$$I^*=\left(1-\frac{1}{R_0}\right)N^*,\qquad N^*=B^{-1}\left(\left(d+\varepsilon\left(1-\frac{1}{R_0}\right)\right)\mathrm{e}^{d_1T}\right). \tag{4.4}$$

Theorem 4.3. *Consider* (4.2) *with* $R_0<1$, $B(N)$ *satisfying* (A1), (A2) *and* (A3′) *and positive initial values with* $N(t)\geqq I(t)$ *on* $[-T,0]$. *Then* $I(t)$ *tends to zero. If in addition either the hypotheses of Theorem* 3.1, *or Theorem* 3.3 (*iii*) *or* (*iv*) *hold, then* N_e *is globally asymptotically stable.*

Proof. Using $V=\frac{1}{2}I^2$ as in the proof of Theorem 4.1, the result for $I(t)$ follows. From results of Castillo-Chavez and Thieme (1995, Theorem 2.5), the N' limit equation is (2.3), and the globally asymptotic results for that equation in Sect. 3 apply. □

In the case of no disease related death ($\varepsilon=0$), $N^*=N_e$ and the following result holds.

Theorem 4.4. *Consider* (4.2) *with* $\varepsilon=0$, $R_0=\frac{\lambda}{d+\gamma}$, $B(N)$ *satisfying* (A1), (A2) *and* (A3′), *and positive initial values with* $N(t)\geqq I(t)$ *on* $[-T,0]$. *If in addition either* (A4) *holds or conditions of Theorem* 3.3 *hold such that* N_e *is globally asymptotically stable, then* I^* *is globally asymptotically stable if* $R_0>1$.

Proof. When $\varepsilon = 0$, the total population equation is the same as equation (2.3). If (A4) also holds, then N_e is globally asymptotically stable for all $T \geqq 0$ (by Theorem 3.1). If $N \to N_e$, then using results of Castillo-Chavez and Thieme (1995, Theorem 2.5), the behavior of I is governed by the logistic equation

$$I'(t) = \lambda\left(1 - \frac{I}{N_e}\right)I - (d + \gamma)I.$$

If $R_0 > 1$, then $I = 0$ is unstable and I^* becomes globally asymptotically stable. □

By contrast for $B(N) = B_1(N)$, if conditions of Theorem 3.3 hold such that N oscillates about N_e, then numerical simulations of (4.2) with $\varepsilon = 0$ indicate that $I(t)$ oscillates about I^* if $R_0 > 1$. Both N and I oscillate with the same period $\in (2T, 4T)$, with the amplitude of I increasing as R_0 increases. As predicted by Theorem 3.3(ii), if these parameter assumptions are satisfied, then stability of the endemic state is lost at $T = T^*$ but regained for large $T > T^{**}$ with I approaching I^*. Parameter R_0 again acts as a threshold, determining whether the disease dies out, or remains in the population (either tending to an endemic value or oscillating).

We conclude with some preliminary results on model (4.2) with disease related death when $R_0 > 1$. For $\varepsilon > 0$, linear stability of the endemic equilibrium (4.4) is governed by the determinantal equation

$$0 = \begin{vmatrix} -\lambda(1 - \frac{1}{R_0}) - z & \lambda(1 - \frac{1}{R_0})^2 \\ -\varepsilon & C(N^*)\mathrm{e}^{-d_1 T}\mathrm{e}^{-Tz} - d - z \end{vmatrix} \tag{4.5}$$

where $C(N) = (B(N)N)'$. Since this no longer decouples, the analysis of (4.5) is quite hard. However, for $B(N) = B_2(N)$ with $n = 1$, or $B(N) = B_3(N)$, the following is true.

Theorem 4.5. *Consider* (4.2) *with* $\varepsilon > 0$, $B(N) = \frac{p}{q+N}$ *with* $\frac{p}{q} > (d + \varepsilon)\mathrm{e}^{d_1 T}$ *or* $B(N) = \frac{A}{N} + c$ *with* $d\mathrm{e}^{d_1 T} > c$, *and positive initial values* $N(t) \geqq I(t)$ *on* $[-T, 0]$. *If* $R_0 > 1$, *then* (I^*, N^*) *given by* (4.4) *is locally asymptotically stable.*

Proof. Equation (4.5) can be written as

$$z^2 + \left(\lambda\left(1 - \frac{1}{R_0}\right) + d\right)z + \lambda\left(1 - \frac{1}{R_0}\right)d + \varepsilon\lambda\left(1 - \frac{1}{R_0}\right)^2$$
$$= \left(\lambda\left(1 - \frac{1}{R_0}\right) + z\right)C(N^*)\mathrm{e}^{-d_1 T}\mathrm{e}^{-Tz}. \tag{4.6}$$

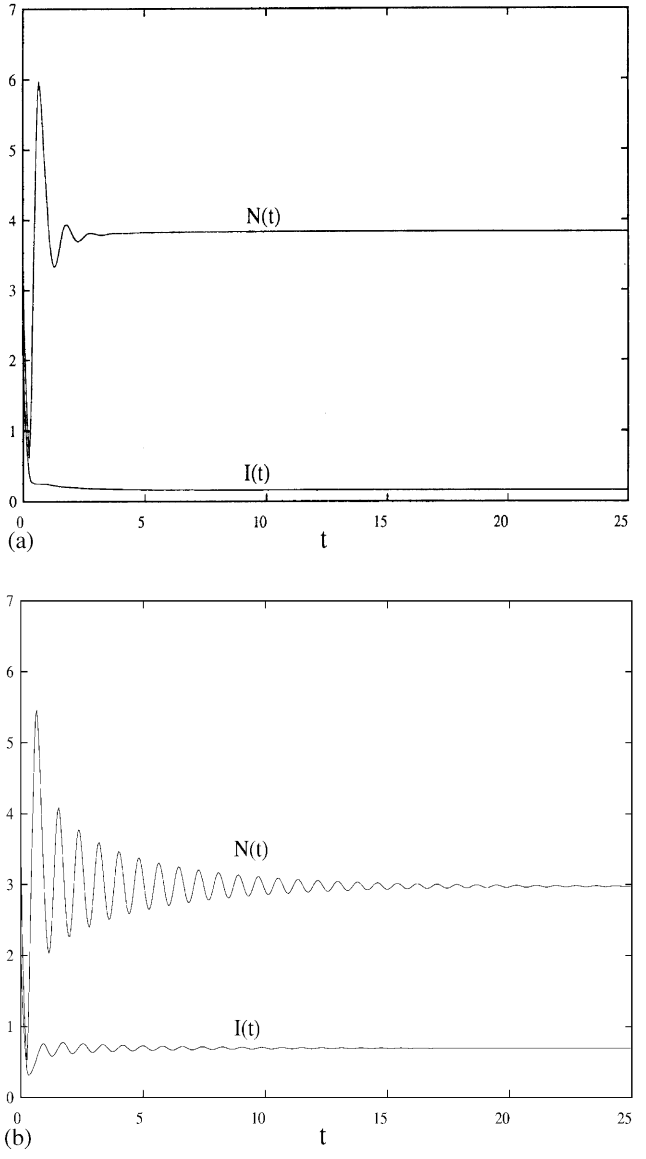
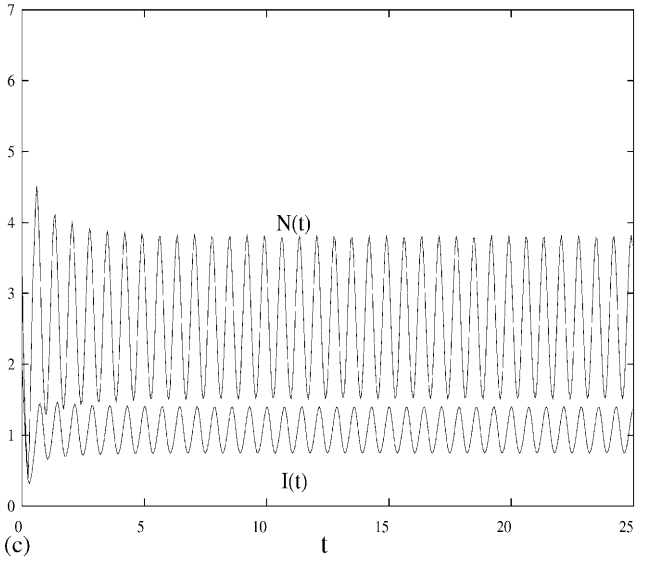


Fig. 4. Numerical simulations for (4.2) with $B(N) = B_1(N)$, $a = d = d_1 = 1$, $b = 80$, $\gamma = 0.5$, $T = 0.2$ and $\varepsilon = 10$: **(a)** $\lambda = 12$; **(b)** $\lambda = 15$; **(c)** $\lambda = 20$; **(d)** $\lambda = 28$.

By Theorem 4.1, the endemic equilibrium is locally stable when $T = 0$. For $T > 0$, note that zero is not a root and look for nonzero purely imaginary roots by setting $z = iv, v > 0$, in (4.6). Taking the modulus of each side gives a quadratic in $w = v^2$. For the given $B(N)$, $C(N^*) > 0$, and it is easy to see that the constant term in the quadratic is positive.



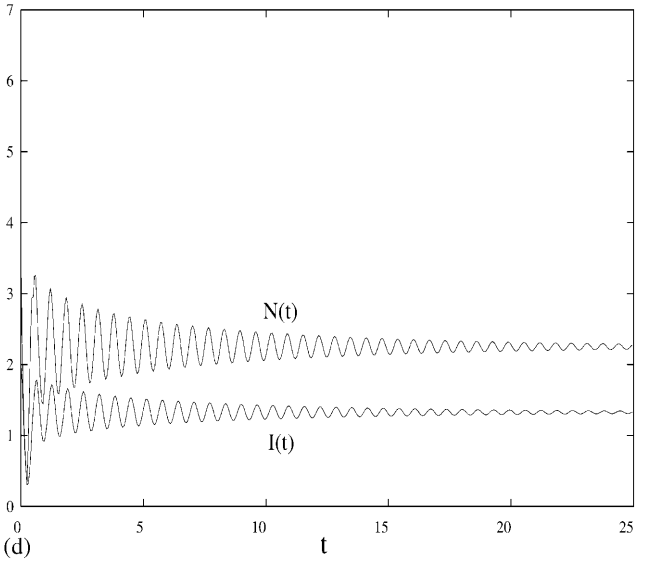


Fig. 4. Continued.

For $R_0 > 1$, with algebraic manipulation, it can be seen that the quadratic has no positive root, thus no purely imaginary root is possible for (4.6). By the results of Theorem A.1 in Cooke and van den Driessche (1996), all roots have negative real parts for $T \geqq 0$, and so the endemic equilibrium (I^*, N^*) is locally asymptotically stable. □

Numerical simulations of (4.2) using XPPAUT with $\varepsilon > 0$ and $B(N) = B_2(N)$ with $n = 1$ or $B(N) = B_3(N)$ (so that (A4) is true) show that when $R_0 > 1$, $(I, N) \to (I^*, N^*)$. Numerical solutions of (4.2) with $B(N) = B_1(N)$ indicate that the effect of disease transmission with disease related death ($\varepsilon > 0$) can be very complicated. Figure 4 shows the results of some numerical simulations of (4.2) with $B(N) = B_1(N)$, $a = d = d_1 = 1$, $b = 80$, $T = 0.2$, $\gamma = 0.5$ and $\varepsilon = 10$ with $N(t) = 3.5$ and $I(t) = 2$ on $[-T, 0]$. The contact rate constant λ takes the values 12, 15, 20 and 28 in Fig. 4(a), (b), (c) and (d) respectively, thus $R_0 = \frac{\lambda}{11.5} > 1$. In Fig. 4(a) with $\lambda = 12$, $(I, N) \to (I^*, N^*)$ in a non-oscillatory way (similar to the behavior when $\varepsilon = 0$, see Figure 3(b) with $T = 0.2$). For $\lambda = 15$, (I, N) still approaches (I^*, N^*) but now in an oscillatory way, see Fig. 4(b). When λ is increased to 20, sustained oscillations (periodic solutions) of (I, N) about (I^*, N^*) occur, see Fig. 4(c). Comparing this with Fig. 3(b) for $T = 0.2$, such sustained oscillations are caused by disease transmission and disease related death. If λ is further increased to 28, (I, N) regains convergence to (I^*, N^*), again in an oscillatory way, see Fig. 4(d). Note that in Fig. 4, N^* decreases but I^* increases as $R_0 > 1$ increases. Qualitatively, similar results are observed for the same parameter values except that $d_1 = 0$ (no death in pre-adult stages), or $\gamma = 0$ (SI model). According to the model given by (4.2) with $\varepsilon > 0$, the maturation delay and contact rate constant of the disease determine (for $R_0 > 1$) whether the disease approaches an endemic value or whether solutions oscillate. This latter phenomenon is left for further study.

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