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"Population models for diseases with no recovery"

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Population models for diseases with no recovery

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Abstract. An $S \to I$ epidemic model with a general shape of density-dependent mortality and incidence rate is studied. The asymptotic behaviour is global convergence to an endemic equilibrium, above a threshold, and to a disease-free equilibrium, below the threshold. The effect of vaccination is then examined.

Key words: Epidemic models — Nonlinear incidence rate — Population regulation

1. Introduction

The interplay between epidemiology and population dynamics has been studied in various models. Anderson and May [3, 4] have first considered such models, both for microparasites and macroparasites; they have analyzed how the threshold phenomena for the persistence of epidemics are modified when population size is variable; they have further discussed how a population can be regulated by an infective disease, and also compared theoretical predictions with some data. Anderson et al. [2] have applied a similar model to the analysis of the fox rabies in Europe, assuming a logistic growth for foxes in absence of the disease. They found that, when there is a latent period of the proper length, this mechanism can induce sustained oscillations. Getz and Pickering [11] have noticed the difference, so far as population regulation is concerned, between sexually transmitted diseases (where the probability of contracting the disease is proportional to the relative density of infectives in the population) and diseases transmitted by airborne agents (where that probability is proportional to the absolute density of infectives). Recently, May et al. [15] have applied similar

methods to the epidemiology of AIDS and its relevance to population growth in developing countries. Finally, Andreasen [5] has studied a model in which the age-structure of the host is explicitly considered, finding other instances of sustained oscillations.

In all these models, as usual in mathematically epidemiology, it is assumed that the rate at which new individuals become infected (the incidence rate) is proportional to number of susceptibles, S, times the contact rate $c(N)$, times the probability of encountering an infectious individuals, I/N. When N is constant, as often assumed in human epidemics, the shape of the function $c(N)$ is irrelevant. However, if N is a dynamic variable, $c(N)$ has to be specified. As described above, two extreme cases have been considered: $c(N) \equiv \beta$ (for sexual diseases), and $c(N) = \beta N$ (for airborne diseases). Andreasen [5] discusses the subject in detail, reporting also that a contact rate of the form $c(N) = \beta N^{1/2}$ seems to give the best fit to some data on rabbit myxomatosis. However, he then considers only the case $c(N) = \beta N$. Castillo-Chavez et al. [10] have incorporated in their model for AIDS the feature of a contact rate that depends non-linearly on the total population. Their model however is rather different from models used for host regulation, since it was developed for homosexual populations not reproducing themselves.

Note finally that Liu et al. [13, 14] have studied cases where incidence rates depended non-linearly on the number of infectives or susceptibles. This corresponds to a non-linear response to disease prevalence, not to a response to population density, as considered here [5].

Here I start to consider the effects of a nonlinear contact rate in host regulation models. Therefore population dynamics with density dependent mortality is coupled with an epidemics with a general shape of density-dependent transmission rate, which includes both sexually transmitted and environmentally transmitted diseases. Age structure and other delays are neglected, so that the models result in ordinary differential equations.

Recently, Brauer [6–8] has independently analyzed models similar to the one considered here.

The epidemic model itself is of the simplest kind, an $S \to I$. It is assumed that infection is permanent, but that infective individuals, although possibly subject to a higher mortality and lower fertility than susceptibles, are otherwise active in the population. The consideration of this kind of diseases originates from a discussion about brucellosis in domestic (cows) and wild (deer) populations. However the model can be applied to other diseases as well; the fox rabies model of Anderson et al. [2] is of this kind, although with a latent period; the simplest model for AIDS considered in [15] is also of this kind, interpreting the appearance of AIDS symptoms as effective removal from the population.

Also Busenberg et al. [9] have studied an $S \to I$ epidemic model, with vertical transmission and vital dynamics influenced by the epidemics. They also considered the effect of delays in population recruitment and of diffusion. However in [9] vital rates and contact rates were density-independent.

Finally, vaccination which gives either temporary or permanent immunity, is included in the model.

2. The basic model

The population (N) is divided between susceptibles (S) and infectives (I). The fertility of susceptibles is a, that of infectives is $a(1-\delta)$, $O \leqslant \delta \leqslant 1$; the newborns of infectives are susceptibles with probability p, infectives with probability $1-p$ (the possibility of vertical transmission is therefore considered in the model); non-disease related mortality is a non-decreasing function, $m(N)$, of total population size; infectives suffer also an additional mortality μ. Finally, the probability for a susceptible of getting infected is equal to $\sigma(N)I$ (note that $\sigma(N) = c(N)/N$ if $c(N)$ is the contact rate defined in the Introduction); in case of environmentally transmitted diseases one normally assumes $\sigma(N) \equiv \beta$; for sexually transmitted diseases $\sigma(N) = \beta/N$; since these are considered to be the extremes, in general one may assume $\sigma(N)$ to be a non-increasing function, while $N\sigma(N)$ is a non-decreasing function (see [10] for the same assumption; Getz and Pickering [11] consider a more general form for the input of new infectives).

The equations are, therefore,

$$\begin{aligned} \frac{dS}{dt} &= (a - m(N))S + pa(1-\delta)I - \sigma(N)SI \\ \frac{dI}{dt} &= \sigma(N)SI + (1-p)a(1-\delta)I - (m(N) + \mu)I \end{aligned} \tag{1}$$

where $N = S + I$.

Alternatively, one may use as variables N and $\phi = I/N$, giving rise to the system

$$\begin{aligned} \frac{dN}{dt} &= N(a - m(N) - (\mu + a\delta)\phi) \\ \frac{d\phi}{dt} &= \phi((1-\phi)(\sigma(N)N - \mu - a\delta) - ap(1-\delta)). \end{aligned} \tag{2}$$

In case of sexually transmitted disease ($\sigma(N) = \beta/N$), the equation for ϕ does not depend on N and can even be solved exactly, as noted in [15]; therefore the behaviour of the system is particularly easy to understand.

We will therefore consider in what follows that $N\sigma(N)$ is strictly increasing. The exact assumptions on system (1) are

(H) $a > 0$, $\mu \geqslant 0$, $0 \leqslant p, \delta \leqslant 1$, $\mu + a\delta > 0$. $N\sigma(N)$ is a strictly increasing differentiable function on $(0, \infty)$ such that $\lim_{N \to O+} N\sigma(N) = 0$. $m(N)$ is differentiable and non-decreasing on $[0, \infty)$. There exists $(N_1, N_2) \subset (0, \infty)$ such that $m(N)$ is strictly increasing on (N_1, N_2), with $m(N_1) < a < m(N_2)$. If $p(1-\delta) = 0$, assume further $m'(N) > 0$ on $[0, N_2]$.

If $\mu + a\delta = 0$ then the disease has no effect on the demography, the population tends to a constant size, and the results are well known [1]; therefore I assumed $\mu + a\delta > 0$. The assumption that $\sigma(N)$ and $m(N)$ are differentiable is made in order to avoid technicalities in the use of linearizations. Finally, if $p(1-\delta) = 0$, I assumed $m'(N)$ positive to avoid degeneracies.

2.1. Well-posedness, invariant region and the trivial equilibrium

The right member of system (2) is Lipschitz in $[\varepsilon, M] \times [0, 1]$ for any $\varepsilon, M > 0$. Therefore, as long as $N(0) > 0$, there exists a unique local solution. The assumptions on $m(N)$ imply that there exists a unique $N^* > 0$ such that $m(N^*) = a$; the region $\mathscr{A} = \{(N, \phi) : 0 \leqslant N \leqslant N^*, 0 \leqslant \phi \leqslant 1\}$ is clearly positively invariant for system (2); all solutions starting in $\mathscr{A}$ stay there and cannot reach $N = 0$ in finite time, thus they can be extended globally in time. Moreover, from

$$\frac{dN}{dt} \leqslant N(a - m(N))$$

we see that if $N(t) > N^*$ for all t, then $\lim_{t \to \infty} N(t) = N^*$. Therefore only the region $\mathscr{A}$ needs be considered.

Two equilibria of system (1) are clearly $(0, 0)$ and $(N^*, 0)$.

$(0, 0)$ is always unstable. Choose in fact $\eta > 0$ such that $a - m(N) - \sigma(N)N \geqslant \varepsilon > 0$ for $0 < N < \eta$; then for any initial data (S_0, I_0) such that $S_0 + I_0 < \eta$ and $S_0 > O$, we have from (1)

$$\frac{dS}{dt} \geqslant [a - m(N) - \sigma(N)I]S \geqslant [a - m(N) - \sigma(N)N]S \geqslant \varepsilon S$$

as long as $S(t) + I(t) < \eta$. Therefore there must exist T such that $S(T) + I(T) \geqslant \eta$, so $(0, 0)$ is unstable. Note that this proof depends on the fact that $\lim_{N \to 0+} N\sigma(N) = 0$; on the other hand, diseases such that $N\sigma(N)$ is a positive constant can lead to population extinction, as noted in [15].

The linearization matrix of (1) at $(N^*, 0)$ is

$$\begin{pmatrix} -m'(N^*)N^* & ap(1-\delta) - \sigma(N^*)N^* - m'(N^*)N^* \\ 0 & \sigma(N^*)N^* + a(1-p)(1-\delta) - (m(N^*) + \mu) \end{pmatrix}$$

with eigenvalues $\lambda_1 = -m'(N^*)N^* < 0$ and $\lambda_2 = \sigma(N^*)N^* + a(1-p)(1-\delta) - (m(N^*) + \mu)$. If we define

$$R_0 = \frac{\sigma(N^*)N^* + a(1-p)(1-\delta)}{m(N^*) + \mu} \tag{3}$$

we have thus the following

Proposition 1. *If $R_0 < 1$, the equilibrium $(N^*, 0)$ of system (1) is locally asymptotically stable. If $R_0 > 1$, $(N^*, 0)$ is unstable.*

Note that $1/(m(N^*) + \mu)$ is the mean infective period, $\sigma(N^*)N^*$ is the rate of horizontal transmission from one infective in a susceptible population of size N^*, while $a(1-p)(1-\delta)$ is the rate of vertical transmission. Therefore R_0 represents the expected number of new cases produced by one infective in a susceptible equilibrium population. (3) is then the usual threshold condition.

For future use, note also that, when $(N^*, 0)$ is unstable, its stable manifold is the positive semiaxis $(S > 0, I = 0)$; in particular all trajectories with $I(t) > 0$ close to $(N^*, 0)$ are repelled from the equilibrium.

Finally, if $p(1-\delta) = 0$ there may exist an equilibrium with no susceptibles but a positive number of infectives. Precisely, if $m(0) < a(1-\delta) - \mu$, then $(0, \hat{N})$ is an equilibrium of (1) if $\hat{N}$ is the solution of $m(N) + \mu = a(1-\delta)$; clearly it will be $\hat{N} < N^*$.

The linearization matrix of (1) at $(0, \hat{N})$ is

$$\begin{pmatrix} \mu + a\delta - \sigma(\hat{N})\hat{N} & 0 \\ \sigma(\hat{N})\hat{N} - m'(\hat{N})\hat{N} & -m'(\hat{N})\hat{N} \end{pmatrix}.$$

Since in this case it is assumed $m'(N) > 0$, it turns out that if $\sigma(\hat{N})\hat{N} < \mu + a\delta$, then the equilibrium is unstable with stable manifold the positive I-semiaxis; otherwise, the equilibrium is stable. Note that the latter case may happen only if $\sigma(N^*)N^* > \mu + a\delta$, or $R_0 > 1$.

2.2. The endemic equilibrium

I now look for the existence of an equilibrium $(\bar{S}, \bar{I})$ with $\bar{I}, \bar{S} > 0$. From the first of (2) we must have

$$\bar{I}/\bar{N} = \frac{a - m(\bar{N})}{\mu + a\delta} \tag{4}$$

which gives the condition $m(\bar{N}) < a$, or $\bar{N} < N^*$.

From the second of (1) it must be

$$\sigma(\bar{N})\bar{S} = m(\bar{N}) + \mu - a(1-p)(1-\delta). \tag{5}$$

Since $\bar{S} = \bar{N} - \bar{I}$, we finally have

$$\sigma(\bar{N})\bar{N}\left(1 - \frac{a - m(\bar{N})}{\mu + a\delta}\right) = m(\bar{N}) + \mu - a(1-p)(1-\delta)$$

or

$$\sigma(\bar{N})\bar{N} = F(m(\bar{N})) \tag{6}$$

where

$$F(x) = \frac{[x + \mu - a(1-p)(1-\delta)](\mu + a\delta)}{x + \mu - a(1-\delta)}.$$

Now the two cases $p(1-\delta) > 0$ and $p(1-\delta) = 0$ must be treated separately. First assume $p(1-\delta) > 0$. Then $F(x)$ is a positive, decreasing function on $(a(1-\delta) - \mu, +\infty)$. If $m(0) \geqslant a(1-\delta) - \mu$, $F(m(N))$ is thus a non-increasing function on $(0, +\infty)$ with $\lim_{N \to 0+} F(m(N)) > 0 = \lim_{N \to 0+} N\sigma(N)$. If $m(0) < a(1-\delta) - \mu$, $F(m(N))$ is a non-increasing function on $(\hat{N}, +\infty)$, where $\hat{N}$ is defined, as in the previous subsection, by $m(\hat{N}) = a(1-\delta) - \mu$; further we note that $\lim_{N \to \hat{N}+} F(m(N)) = +\infty > \hat{N}\sigma(\hat{N})$. Since $N\sigma(N)$ is an increasing function, and $F(m(N))$ is negative for $N < \hat{N}$, in either case there exists a (unique) solution

$\bar{N}$ of (4), with $0 < \bar{N} < N^*$ if and only if

$$\sigma(N^*)N^* > F(m(N^*)). \tag{7}$$

Noting that $m(N^*) = a$, we see that $F(m(N^*)) = a + \mu - a(1-p)(1-\delta)$ and therefore condition (7) is equivalent to $R_0 > 1$.

Now consider the case $p(1-\delta) = 0$. $F(x)$ is a positive constant; therefore a unique solution of (6) with $\bar{N} < N^*$ exists if and only if (7) holds. However, it may well be that $\bar{N} < \hat{N}$ (when the latter exists); such a solution is not acceptable, since, because of (4) and (5), it would correspond to $\bar{I} > \bar{N}$ and $\bar{S} < 0$.

Therefore we have

Proposition 2. *If $R_0 > 1$, and either of the following conditions holds:*
(i) $p(1-\delta) > 0$;
(ii) $p(1-\delta) = 0$ *and* $m(0) + \mu \geqslant a(1-\delta)$;
(iii) $p(1-\delta) = 0$ *and* $\hat{N}$ *satisfies* $\sigma(\hat{N})\hat{N} < F(\hat{N}) = \mu + a\delta$;
then there exists a unique positive equilibrium $(\bar{S}, \bar{I})$. Moreover, $\bar{N} = \bar{S} + \bar{I}$ is the unique positive solution of (6); it satisfies the inequalities $\bar{N} < N^*$ and, when $m(0) < a(1-\delta) - \mu$, $\bar{N} > \hat{N}$. Therefore, the following relations for $m(\bar{N})$ hold

$$a(1-\delta) - \mu < m(\bar{N}) < a. \tag{8}$$

On the other hand, if $R_0 \leqslant 1$, or if $R_0 > 1$, $p(1-\delta) = 0$, and $\sigma(\hat{N})\hat{N} \geqslant \mu + a\delta$, there are no equilibria $(\bar{S}, \bar{I})$ of (1) with $\bar{S}, \bar{I} > 0$.

As for the stability of $(\bar{S}, \bar{I})$, its linearization matrix is

$$A = \begin{pmatrix} a - m(\bar{N}) - \sigma(\bar{N})\bar{I} - m'(\bar{N})\bar{S} - \sigma'(\bar{N})\bar{S}\bar{I} & ap(1-\delta) - \sigma(\bar{N})\bar{S} - m'(\bar{N})\bar{S} - \sigma'(\bar{N})\bar{S}\bar{I} \\ \sigma(\bar{N})\bar{I} - m'(\bar{N})\bar{I} + \sigma'(\bar{N})\bar{S}\bar{I} & -m'(\bar{N})\bar{I} + \sigma'(\bar{N})\bar{S}\bar{I} \end{pmatrix}. \tag{9}$$

After some computations, we have

$$\operatorname{tr} A = -\frac{(a - m(\bar{N}))ap(1-\delta)}{m(\bar{N}) + \mu - a(1-\delta)} - m'(\bar{N})\bar{N} < 0$$

and

$$\det A = \sigma(\bar{N})\bar{I}B + m'(\bar{N})\bar{I}C + \sigma'(\bar{N})\bar{S}\bar{I}[B + a - m(\bar{N})]$$

where

$$B = \sigma(\bar{N})\bar{S} - ap(1-\delta) > 0, \quad C = \sigma(\bar{N})\bar{I} - (a - m(\bar{N})) + ap(1-\delta) > 0.$$

Since $\sigma'(N) > -\sigma(N)/N$ by assumption, we have

$$\det A > \sigma(\bar{N})\bar{I}B + m'(\bar{N})\bar{I}C - \sigma(\bar{N})\bar{I}\frac{\bar{S}}{\bar{N}}[B + a - m(\bar{N})] = m'(\bar{N})\bar{I}C \geqslant 0.$$

We have therefore established

Proposition 3. *If $R_0 > 1$, the equilibrium $(\bar{S}, \bar{I})$ is asymptotically stable.*

2.3. Global stability

Here I show that the asymptotic stability of the trivial equilibrium (below the threshold), or of the endemic equilibrium (above the threshold), is indeed global; precisely

Theorem 4. *When $R_0 \leqslant 1$, for any $(S_0, I_0) \in \mathbb{R}^{2+}\backslash\{(0,0)\}$ if $p(1-\delta) > 0$, or for any (S_0, I_0) such that $S_0 > 0$, $I_0 \geqslant 0$ if $p(1-\delta) = 0$, we have*

$$\lim_{t\to\infty} S(t) = N^*, \qquad \lim_{t\to\infty} I(t) = 0.$$

Proof. As discussed above, it is clear that $\limsup_{t\to\infty} N(t) \leqslant N^*$, and that the region $\mathscr{A} = \{(N, \phi) : 0 \leqslant N \leqslant N^*, 0 \leqslant \phi \leqslant 1\}$ is positively invariant. Using (2), we see that in $\mathscr{A}$

$$\text{If } \sigma(N)N - \mu - a\delta \geqslant 0, \qquad \frac{d\phi}{dt} \leqslant \phi[\sigma(N)N - \mu - a\delta - ap(1-\delta)]$$

$$\text{If } \sigma(N)N - \mu - a\delta \leqslant 0, \qquad \frac{d\phi}{dt} \leqslant \phi[-ap(1-\delta)] \tag{10}$$

and so

$$\frac{d\phi}{dt} \leqslant \phi[\max\{\sigma(N)N - \mu - a\delta - ap(1-\delta), -ap(1-\delta)\}]. \tag{11}$$

Since

$$\sigma(N)N - \mu - a\delta - ap(1-\delta) \leqslant \sigma(N^*)N^* - \mu - a\delta - ap(1-\delta) = (R_0 - 1)(\mu + a)$$

(11) yields

$$\frac{d\phi}{dt} \leqslant \phi[\max\{(R_0 - 1)(\mu + a), -ap(1-\delta)\}].$$

If $R_0 < 1$ and $p(1-\delta) > 0$, then $\lim_{t\to\infty} \phi(t) = 0$, and therefore $\lim_{t\to\infty} N(t) = N^*$.

If $R_0 = 1$ and $p(1-\delta) > 0$, $\phi(t)$ monotonically decreases to a limit $\tilde{\phi}$. If $\tilde{\phi} > 0$ then $N(t)$ converges to a limit $\tilde{N} < N^*$; then, for t large enough, $N(t) \leqslant \tilde{N} + \varepsilon < N^*$, and from (11)

$$\frac{d\phi}{dt} \leqslant \phi[\max\{\sigma(\tilde{N} + \varepsilon)(\tilde{N} + \varepsilon) - \sigma(N^*)N^*, -ap(1-\delta)\}];$$

this implies $\lim_{t\to\infty} \phi(t) = 0$, which as above implies $N(t) = N^*$.

If $p(1-\delta) = 0$, the semiaxis $\{\phi = 1, N > 0\}$ is invariant for system (2). However, if $\phi(0) = 1 - \varepsilon < 1$, then we have $1 - \phi(t) \geqslant \varepsilon$ and, since in this case

$$\sigma(N)N - \mu - a\delta \leqslant \sigma(N^*)N^* - \mu - a\delta = (R_0 - 1)(a + \mu) \leqslant 0$$

we have

$$\frac{d\phi}{dt} \leqslant \phi[\varepsilon(R_0 - 1)(a + \mu)].$$

If $R_0 < 1$, this yields $\lim_{t\to\infty} \phi(t) = 0$, and then $\lim_{t\to\infty} N(t) = N^*$. If $R_0 = 1$, one proceeds as in the previous case.

Theorem 5. *When $R_0 > 1$ then:*

(i) *If $p(1-\delta) > 0$, for any $S_0 \geq 0$, $I_0 > 0$, we have*

$$\lim_{t\to\infty} S(t) = \bar{S}, \qquad \lim_{t\to\infty} I(t) = \bar{I}.$$

(ii) *If $p(1-\delta) = 0$ and $\hat{N}$ does not exist or satisfies $\sigma(\hat{N})\hat{N} < \mu + a\delta$, for any $S_0 > 0$, $I_0 > 0$, we have*

$$\lim_{t\to\infty} S(t) = \bar{S}, \qquad \lim_{t\to\infty} I(t) = \bar{I}.$$

(iii) *If $p(1-\delta) = 0$ and $\hat{N}$ satisfies $\sigma(\hat{N})\hat{N} \geq \mu + a\delta$, for any $S_0 \geq 0$, $I_0 > 0$, we have*

$$\lim_{t\to\infty} S(t) = 0, \qquad \lim_{t\to\infty} I(t) = \hat{N}.$$

Proof. Because of Poincaré–Bendixson theory, the ω-limit set must consist either of equilibria or of limit cycles. Using DuLac's criterion [16] with $g(S, I) = (IS)^{-1}$, it follows that there cannot be limit cycles. In fact,

$$\frac{\partial}{\partial S}\left(\frac{S'}{IS}\right) + \frac{\partial}{\partial I}\left(\frac{I'}{IS}\right) = -\frac{m'(N)}{I} - ap(1-\delta)\frac{1}{S^2} - \frac{m'(N)}{S} < 0.$$

Since there are no limit cycles, all trajectories converge to an equilibrium, $(0, 0)$ and $(N^*, 0)$ are both repellent when approached with positive S (the former) and with positive I (the latter), as seen through the local analysis.

In the case (i) the only equilibrium left is $(\bar{S}, \bar{I})$. In case (ii) there may exist also $(0, \hat{N})$, but that is unstable when approached from positive S. In case (iii) the only equilibrium left is $(0, \hat{N})$.

Note that when $p(1-\delta) = 0$, (1) is similar to a prey-predator model; indeed if $\sigma(N)$ and $m(N)$ are both constant, then (1) is the classical Lotka–Volterra model which exhibits the well-known cycles. In order to avoid this case, I added the assumption of $m'(N)$ strictly positive when $p(1-\delta) = 0$. For more information on global stability in two-species population models see for instance [12].

3. The model with vaccination

I consider here the effect of vaccination on the dynamics of the model. For brucellosis a vaccine is available which results in temporary immunity; it is also possible that animals die because of vaccination. In the model I disregard the latter effect, since the computations become more involved, without qualitative differences.

The class of vaccinated individuals, $V(t)$, is therefore added to system (1), together with the vaccination rate ν, and the rate γ at which vaccinated individuals lose the immunization ($\gamma = 0$ if the vaccination is permanent).

The resulting system is

$$\begin{aligned} \dot{S} &= a(S+V) + ap(1-\delta)I - m(N)S - \sigma(N)SI - \nu S + \gamma V, \\ \dot{I} &= \sigma(N)SI + a(1-p)(1-\delta)I - (m(N)+\mu)I, \\ \dot{V} &= \nu S - \gamma V - m(N)V. \end{aligned} \tag{12}$$

Summing up the equations, we obtain

$$\dot{N} = (a - m(N))N - (\mu + a\delta)I. \tag{13}$$

Reasoning as in Sect. 2, it is clear that system (2) is well posed, and that the region $\{(S, I, V) : 0 \leq S, I, V; S + I + V \leq N^*\}$ is positively invariant and globally attractive from the positive orthant. Therefore this region only needs to be analyzed.

An equilibrium of (12) is $(0, 0, 0)$; as in Sect. 2, it can be shown to be unstable.

Looking for positive equilibria of (12), setting $\dot{V} = 0$, we obtain

$$V = \frac{\nu}{\gamma + m(N)} S. \tag{14}$$

Looking at (13) and (14) we see that a disease-free equilibrium is obtained for

$$N = N^*, \quad I = 0, \quad S = S^* = \frac{m(N^*) + \gamma}{m(N^*) + \gamma + \nu} N^*, \quad V = V^* = \frac{\nu}{m(N^*) + \gamma + \nu} N^*.$$

The linearization matrix of (12) at $(S^*, 0, V^*)$, is, using $m(N^*) = a$,

$$A = \begin{pmatrix} -\nu - m'(N^*)S^* & ap(1-\delta) - \sigma(N^*)S^* - m'(N^*)S^* & a + \gamma - m'(N^*)S^* \\ 0 & \sigma(N^*)S^* + a(1-p)(1-\delta) - (m(N^*)+\mu) & 0 \\ \nu - m'(N^*)V^* & -m'(N^*)V^* & -\gamma - a - m'(N^*)V^* \end{pmatrix}.$$

The eigenvalues of A are

$$\lambda_1 = \sigma(N^*)S^* + a(1-p)(1-\delta) - (m(N^*)+\mu) \tag{15}$$

and the eigenvalues of

$$B = \begin{pmatrix} -(\nu + m'(N^*)S^*) & a + \gamma - m'(N^*)S^* \\ \nu - m'(N^*)V^* & -(a + \gamma + m'(N^*)V^*) \end{pmatrix}.$$

The trace of B is clearly negative, while

$$\det B = m'(N^*)N^*(a + \gamma + \nu) > 0.$$

$(S^*, 0, V^*)$ is thus linearly asymptotically stable or unstable, according to whether λ_1 is negative or positive.

Setting

$$R_\nu = \frac{\sigma(\bar{N})\bar{N}\dfrac{a+\gamma}{a+\gamma+\nu} + a(1-p)(1-\delta)}{a+\mu} \tag{16}$$

we obtain

Proposition 6. *If $R_\nu < 1$, the equilibrium $(S^*, 0, V^*)$ is asymptotically stable. If $R_\nu > 1$, $(S^*, 0, V^*)$ is unstable.*

Note that R_ν can be interpreted as the expected number of new cases produced by one infective into a population vaccinated at rate ν. In fact, the first addendum represents the horizontal transmission (the rate is decreased, with respect to (3), by a factor $(a+\gamma)/(a+\gamma+\nu)$, since this is the fraction of susceptible individuals in an equilibrium disease-free population), the second addendum represents the vertical transmission, which is not influenced by vaccination. The following relation holds between R_ν and R_0:

$$R_\nu = \left(1 - \frac{\nu}{a+\gamma+\nu}\right) R_0 + \frac{\nu}{a+\gamma+\nu} \frac{a(1-p)(1-\delta)}{a+\mu}.$$

The condition $R_\nu < 1$ can then be read as

$$\nu > \frac{(a+\gamma)(R_0 - 1)}{1 - \dfrac{a(1-p)(1-\delta)}{a+\mu}}. \tag{17}$$

As in Sect. 2, if $p(1-\delta) = 0$, there may exist an equilibrium on the positive I-semiaxis. Precisely, if $m(0) < a(1-\delta) - \mu$, then $(0, \hat{N}, 0)$ is an equilibrium of (12). The linearization matrix of (12) at $(0, \hat{N}, 0)$ is

$$A = \begin{pmatrix} a - m(\hat{N}) - \sigma(\hat{N})\hat{N} - \nu & 0 & a+\gamma \\ \sigma(\hat{N})\hat{N} - m'(\hat{N})\hat{N} & -m'(\hat{N})\hat{N} & 0 \\ \nu & 0 & -m(\hat{N}) - \gamma \end{pmatrix}$$

whose eigenvalues are $-m'(\hat{N})\hat{N} < 0$ and the eigenvalues of

$$B = \begin{pmatrix} a - m(\hat{N}) - \sigma(\hat{N})\hat{N} - \nu & a+\gamma \\ \nu & -m(\hat{N}) - \gamma \end{pmatrix}.$$

$$\det B = -(a - m(\hat{N}))(m(\hat{N}) + \gamma + \nu) + \sigma(\hat{N})\hat{N}(m(\hat{N}) + \gamma).$$

Therefore $\det B$ is positive if

$$\sigma(\hat{N})\hat{N} > (a - m(\hat{N})) \frac{m(\hat{N}) + \gamma + \nu}{m(\hat{N}) + \gamma} = (\mu + a\delta) \frac{m(\hat{N}) + \gamma + \nu}{m(\hat{N}) + \gamma} \tag{18}$$

and negative if the reverse inequality holds. It is also clear that $\det B > 0$ implies $\operatorname{tr} B < 0$.

Therefore we have that $(0, \hat{N}, 0)$ is locally asymptotically stable if (18) holds; unstable if the reverse inequality holds.

3.1. The endemic equilibrium

Looking for an equilibrium $(\bar{S}, \bar{I}, \bar{V})$ with $\bar{S}, \bar{I} > 0$, we see that (4) and (5) hold and

$$(a+\gamma)\bar{N} - (m(\bar{N}) + \mu + a\delta + \gamma)\bar{I} = (m(\bar{N}) + \nu + \gamma)\bar{S}. \tag{19}$$

Using (4) and (5) in (19) gives

$$\sigma(\bar{N})\bar{N}\left[a + \gamma - \frac{(m(\bar{N}) + \mu + a\delta + \gamma)(a - m(\bar{N}))}{\mu + a\delta}\right]$$
$$= (m(\bar{N}) + \nu + \gamma)(m(\bar{N}) + \mu - a(1-p)(1-\delta))$$

and then

$$\sigma(\bar{N})\bar{N} = F_\nu(m(\bar{N})) \tag{20}$$

with

$$F_\nu(x) = \frac{(x + \nu + \gamma)(x + \mu - a(1-p)(1-\delta))(\mu + a\delta)}{(x+\gamma)(x + \mu - a(1-\delta))}.$$

Because of (4), we only look for solutions of (20) with $a > m(\bar{N})$, or $\bar{N} < N^*$.

$F_\nu(x)$ is negative in $\{x > 0: -\mu + a(1-p)(1-\delta) < x < -\mu + a(1-\delta)\}$ (this set may well be empty); moreover solutions of (20) with $m(\bar{N}) < -\mu + a(1-p)(1-\delta)$ are not acceptable because of (5). Therefore we need only consider $F_\nu(x)$ in $\{x > 0: x > -\mu + a(1-\delta)\}$; in this interval $F_\nu(x)$ is a positive and decreasing function of x.

As in Sect. 2, we therefore see that, if $p(1-\delta) > 0$, there exists a feasible solution of (20) if and only if

$$\sigma(N)N^* > F_\nu(m(N^*)) = \frac{(m(N^*) + \nu + \gamma)(m(N^*) + \mu - a(1-p)(1-\delta))}{(m(N^*) + \gamma)}. \tag{21}$$

If $p(1-\delta) = 0$, we have to add to (21) the condition

$$\sigma(\hat{N})\hat{N} < F_\nu(m(\hat{N})) = \frac{(m(\hat{N}) + \nu + \gamma)(\mu + a\delta)}{(m(\hat{N}) + \gamma)}. \tag{22}$$

Note that (22) is just the condition for the instability of $(0, \hat{N}, 0)$: see (18).

Through some algebraic manipulation we obtain

Proposition 7. *If $R_\nu > 1$ and, if $p(1-\delta) = 0$, (22) holds, there exists an endemic equilibrium $(\bar{S}, \bar{I}, \bar{V})$, where $\bar{N} = \bar{S} + \bar{I} + \bar{V}$ is the unique solution in $(0, N^*) \cap (\hat{N}, N^*)$ of (20).*

If the previous condition does not hold, there are no equilibria of (12) in the positive orthant.

To study the stability of $(\bar{S}, \bar{I}, \bar{V})$ it is more convenient to use as variables $N(t)$, $S(t)$ and $I(t)$. The linearization matrix of the resulting system in $(\bar{N}, \bar{S}, \bar{I})$ is

$$A = \begin{pmatrix} a - m(\bar{N}) - m'(\bar{N})\bar{N} & 0 & -(\mu + a\delta) \\ a + \gamma - m'(\bar{N})\bar{S} - \sigma'(\bar{N})\bar{S}\bar{I} & -(m(\bar{N}) + \nu + \gamma + \sigma(\bar{N})\bar{I}) & -(a + \gamma - ap(1-\delta) + \sigma(\bar{N})\bar{S}) \\ \sigma'(\bar{N})\bar{S}\bar{I} - m'(\bar{N})\bar{I} & \sigma(\bar{N})\bar{I} & 0 \end{pmatrix}.$$

The characteristic polynomial of A (after a change of sign) is

$$z^3 + a_1 z^2 + a_2 z + a_3. \tag{23}$$

Routh–Hurwitz criterion states that all solutions of (23) have negative real part if and only if $a_1, a_2, a_3 > 0$ and $a_1 a_2 > a_3$.

After some computations we see that

$$a_1 = m'(\bar{N})\bar{N} + C + B\frac{DG + \nu F}{DF},$$

$$a_2 = m'(\bar{N})\bar{N}B\frac{DG + \nu F}{DF} + \frac{BC}{DF}(EF + DG) + \sigma'(\bar{N})\bar{S}\bar{I}H,$$

$$a_3 = m'(\bar{N})\bar{N}B\left(\frac{\nu E}{D} + \frac{CG}{F}\right) + BCE + \sigma'(\bar{N})\bar{S}\bar{I}CH.$$

where

$$B = a - m(\bar{N}),$$

$$C = m(\bar{N}) + \gamma + \nu,$$

$$D = m(\bar{N}) + \gamma,$$

$$E = m(\bar{N}) + \mu - a(1-p)(1-\delta),$$

$$F = m(\bar{N}) + \mu - a(1-\delta),$$

$$G = ap(1-\delta),$$

$$H = \mu + a\delta.$$

Using the fact that

$$\sigma'(\bar{N})\bar{S}\bar{I} = \sigma'(\bar{N})\bar{N}\bar{S}B/H > -\sigma(\bar{N})\bar{S}B/H = -BE/H$$

through long computations, one sees that the Routh–Hurwitz conditions are satisfied.

Therefore we have

Proposition 8. *When an equilibrium* $(\bar{S}, \bar{I}, \bar{V})$ *of system* (12) *with positive* $\bar{S}$ *and* $\bar{I}$ *exists, it is asymptotically stable.*

3.2. *A global result*

Assuming that $\sigma(N)$ is non-increasing, it is possible to prove that, when $R_v \leqslant 1$, the stability of the disease-free equilibrium is global. Namely

Theorem 9. *If* $\sigma(N)$ *is non-increasing, and* $R_v \leqslant 1$, *for any nonnegative* $(S_0, I_0, V_0) \neq (0,0,0)$ *if* $p(1-\delta) > 0$, *or for any* (S_0, I_0, V_0) *such that* $S_0 + V_0 > 0$, $I_0 \geqslant 0$ *if* $p(1-\delta) = 0$, *we have*

$$\lim_{t\to\infty} S(t) = S^* \quad \lim_{t\to\infty} I(t) = 0 \quad \lim_{t\to\infty} V(t) = V^*.$$

For its proof, I need

Lemma 10. *Set* $z(t) = (a+\gamma)V(t) - \nu S(t)$. *If* $\sigma(N)$ *is non-increasing, either* $z(t)$ *is definitely nonnegative, or is definitely nonpositive.*

Proof. We have

$$\dot{z} = -(m(N(t)) + \gamma + \nu)z + \nu I(t)w(t)$$

where $w(t) = \sigma(N(t))S(t) - ap(1-\delta)$.

If $p(1-\delta) = 0$, $w(t)$ is positive and the thesis is obvious.

Otherwise, look at the phase plane (w, z). We have

$$\dot{w} = f(t) + \sigma(N)z - \sigma(N)Iw$$

where

$$f(t) = (\sigma'(N)N + \sigma(N))(a - m(N))S - \sigma'(N)I(\mu + a\delta)S > 0.$$

The quadrant $(w > 0, z > 0)$ is positively invariant; in fact, when $z = 0$ and $w > 0$, $\dot{z} > 0$; when $z > 0$ and $w = 0$, $\dot{w} > 0$. Furthermore, when $z = 0$ and $w < 0$, $\dot{z} < 0$; when $z = w = 0$, $\dot{z} = 0 < \dot{w}$. This implies that a trajectory can leave the half-plane $\{z \leqslant 0\}$ only by entering the positive quadrant; since this is positively invariant, it is then trapped there.

Proof of Theorem 9. Suppose $z(t) \leqslant 0$ for $t > t_0$, i.e. $\nu S(t) \geqslant (a+\gamma)V(t)$. Then $\dot{V} \geqslant (a - m(N))V \geqslant 0$; therefore $V(t)$ tends to a limit $\bar{V} > 0$. The ω-limit set must then be contained in the plane $\{V = \bar{V}\}$. Since the ω-limit set is invariant for system (12), the points belonging to ω-limit set must satisfy $\nu S = (m(N) + \gamma)\bar{V}$; this, together with $z(t) \leqslant 0$ and $N(t) \leqslant N^*$ yields

$$\nu S = (m(N) + \gamma)\bar{V} \leqslant (a+\gamma)\bar{V} \leqslant \nu S.$$

The only possibility is that both inequalities are equalities; i.e. $m(N) = a$, or $N = N^*$, and $\nu S = (a+\gamma)\bar{V}$. Therefore the ω-limit set consists of a single point, which then has to be an equilibrium of (12); the only one satisfying $N = N^*$ is $(S^*, 0, V^*)$.

Next suppose $z(t) \geqslant 0$ for $t > t_0$, i.e. $\nu S(t) \leqslant (a+\gamma)V(t)$, or

$$S(t) \leqslant \left(\frac{a+\gamma}{a+\gamma+\nu}\right)(N(t) - I(t)). \tag{24}$$

Then, if $\phi = I/N$,

$$\dot{\phi} = \phi[\sigma(N)S - (\mu + a\delta)(1-\phi) - ap(1-\delta)]$$

$$\leqslant \phi\left[(1-\phi)\left(\sigma(N)N\left(\frac{a+\gamma}{a+\gamma+\nu}\right) - (\mu + a\delta)\right) - ap(1-\delta)\right]$$

using (24). Then, proceeding as in the proof of Theorem 4, one has that, if $p(1-\delta) > 0$,

$$\dot{\phi} \leqslant \phi\left[\max\left\{\sigma(N)N\left(\frac{a+\gamma}{a+\gamma+\nu}\right) - (\mu + a\delta) - ap(1-\delta), -ap(1-\delta)\right\}\right]$$

$$\leqslant \phi[\max\{(R_v - 1)(a+\mu), -ap(1-\delta)\}]$$

From this it follows that $\lim_{t\to\infty}\phi(t)=0$. Then from (13) $\lim_{t\to\infty}N(t)=N^*$ and then from (12) $\lim_{t\to\infty}S(t)=S^*$, $\lim_{t\to\infty}V(t)=V^*$.

The case $p(1-\delta)=0$ can be handled as in the proof of Theorem 4.

4. Discussion and examples

The results obtained here for this $S\to I$ model with vital rates depending on epidemic state are standard results for most epidemic models: there exists a threshold below which the disease goes to extinction and above which there exists one endemic equilibrium which is globally stable. This has been obtained for a general shape of density-dependent mortality and of density-dependent infectivity.

Similar models have been discussed by May and Anderson [4], and, in greater detail by Busenberg et al. [9]. Their models do not include density dependence of mortality; justification for that is that often the diseases that regulate a host (and are therefore interesting to be studied in this context) keep the host population at a level at which density-dependent factors are hardly operating [4]. Although this may be true (assuming $m(N)$ to be constant for low N, the equilibrium population $\bar N$ of model (1) may be regulated by disease only), the inclusion of density-dependence makes the general picture much clearer. When vital rates (and hence population density) depend on epidemic state, the usual concept of threshold population size loses any meaning [5]; however, if density-dependence is taken into account, the threshold condition is a threshold in disease transmissibility at the disease-free equilibrium population level N^*; this even when the population level at which the population is regulated by the disease, is very far from N^*.

The effects of vaccination can be adequately described only when density-dependence is explicitly considered. Note that, when vaccination is included in the model, the endemic equilibrium $\bar N$ (if it exists) is always an increasing function of v; in fact $\bar N$ is found through (20) and $F_v(x)$ is an increasing function of v. Further note that $\bar I/\bar N$ is given by (17); if $m(N)$ is constant around $\bar N$, an increase of vaccination rate leads to an increase of $\bar N(v)$ and to a proportional increase of $\bar I(v)$. $\bar I(v)$ decreases only when v approaches $(R_0-1)(a+\mu)/[a+\mu-a(1-p)(1-\delta)]$, and density-dependent factors start to operate. A graph of $\bar N$ and $\bar I$ as functions of v is presented in Fig. 1.

When vaccination was included in the model, below the threshold the disease-free equilibrium was proved to be globally stable. Above the threshold, on the other hand, it was possible only to prove the local stability of the endemic equilibrium. The technique used for the $S\to I$ model was essentially two-dimensional and could not be extended to system (12). The results of the numerical solutions I computed seem to indicate that the endemic equilibrium is indeed globally stable.

The presence of vertical transmission ($p<1$) contributes to the strength of an epidemic. If $q=1-p$ (the probability of vertical transmission), note that the endemic equilibrium $\bar N$ decreases with increasing q. The prevalence rate $\bar I/\bar N$ may also increase with increasing q, if mortality is density-dependent around $\bar N$.

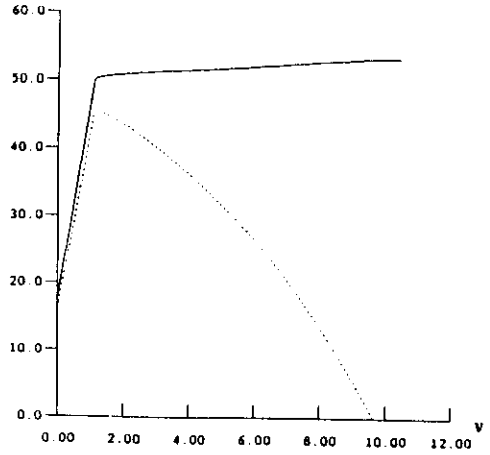

Fig. 1. The *solid line* represents $\bar N$, solution of (23); the *dashed line* $\bar I$, while v varies from 0 to above the threshold given by (17); parameter values are $a=0.2$, $\mu=0.05$, $\delta=0.3$, $p=0.5$, $\gamma=0.5$, $\sigma(N)\equiv 0.05$, $m(N)=0.1+0.001[(N-50)_+]^2$

However, even in the extreme case $q=1$ an effective horizontal transmission is always necessary for persistence of the disease; for instance when the equilibrium $(0,\bar N)$ (a totally infected population) exists, it is stable only if $\sigma(\bar N)\bar N>\mu+a\delta$.

The presence of vertical transmission also increases the level of vaccination necessary for elimination of a disease: it increases R_0 and, at fixed R_0, it increases R_v: see (17).

Anderson et al. [2] have discussed this model (allowing also for a latent period of the disease) assuming that mortality depends linearly on population density (logistic growth) and that $\sigma(N)N=\beta N$. Here I let $m(N)$ and $\sigma(N)$ be general increasing functions; the main result here is that the asymptotic behaviour does not depend on the exact shape of these functions.

The effect of the shape of $\sigma(N)$ can be seen on the presence of (damped) oscillations and on the speed of convergence to the endemic equilibrium. These quantities depend on the linearization matrix A (see (9)). Precisely, if

$$\Delta=\frac{(\operatorname{tr}A)^2}{4}-\det A,$$

(damped) oscillations will appear only if $\Delta<0$. The period of the oscillations will be approximately $2\pi/\sqrt{-\Delta}$. Finally the rate of convergence to $(\bar S,\bar I)$ is given by

$$\lambda_{\max}=\begin{cases}\dfrac{\operatorname{tr}A}{2}+\sqrt{\Delta} & \text{if } \Delta>0\\[2ex] \dfrac{\operatorname{tr}A}{2} & \text{otherwise}\end{cases}\tag{25}$$

If we let $\lambda=-\sigma'(\bar N)\bar N/\sigma(N)$, we see that $\operatorname{tr}A$ does not depend on λ, while

$$\det A=(1-\lambda)(a-m(\bar N))(m(\bar N)+\mu-a(1-p)(1-\delta))+m'(\bar N)\bar I C.$$

Therefore the lower is λ, the greater is possibility that there are oscillations. In this notation, $\lambda = 0$ corresponds to a constant $\sigma(N)$, while the limiting case of $\lambda = 1$ corresponds to $\sigma(N) = \beta/N$; in the latter case the system can be reduced to a single autonomous equation (see (2)), and therefore oscillations can never occur. Note, however, that if tr A is relatively large, oscillations will hardly be visible, even when they occur; if tr A is small, then oscillation tend to occur for λ at least up to 1/2.

In Figs. 2 and 3 I compare the numerical solutions of system (1) obtained for two different functions $\sigma(N)$, scaled so as to have the same endemic equilibrium. In Fig. 2 I present an example in which there is monotonic convergence to the equilibrium for both functions; if there are no oscillations, the rate of convergence is faster when λ is smaller (see (25)). In Fig. 3 I present an example of (damped) oscillations; the solid line corresponds to $\lambda = 1/2$, the dashed line to $\lambda = 0$; the parameter values were chosen so as to amplify the oscillations and the difference between the two curves.

Brauer [6, 7] has studied a model similar to (1), which differs in that infective individuals do not contribute to demography: their birth rate is 0, and the vital rates of susceptibles depend only on susceptible density. This may be a reasonable approximation for quickly fatal diseases, such as rabies. In his

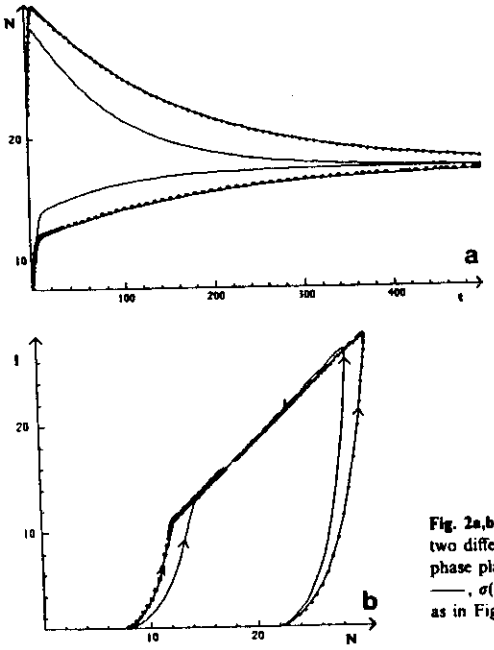

Fig. 2a,b. Numerical solutions of (1) for two different initial values. **a** $N(t)$ vs. t; **b** phase plane (N, I). —•—, $\sigma(N) = 0.21N^{-1/2}$; ——, $\sigma(N) = 0.025$. Other parameter values as in Fig. 1

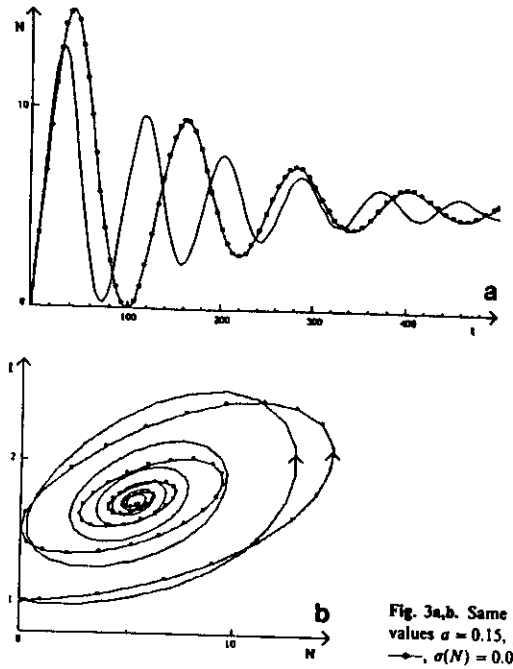

Fig. 3a,b. Same as in Fig. 2 with parameter values $\alpha = 0.15$, $\mu = 0.1$, $\delta = 0.4$, $p = 0.6$, —•—, $\sigma(N) = 0.075N^{-1/2}$; ——, $\sigma(N) = 0.025$

models, he allows for any distribution of the times from infection to death; when the distribution is exponential, as in (1), his results are that, above a threshold, the endemic equilibrium is always stable. Other distributions, for instance a fixed time τ between infection and death, may give rise to sustained oscillations.

Anderson et al. [2] have found that the introduction of a latent period in system (1) may change the qualitative behaviour; namely, even assuming constant $\sigma(N)$ and logistic growth without the disease, sustained oscillations could arise for appropriate values of the latent period. When a latent period is present, the shape of $m(N)$ and $\sigma(N)$ can actually change the qualitative behaviour, giving rise, for instance, to multiple endemic steady states (Pugliese, in preparation).

This paper was mainly designed to study systematically the effects of a disease on population dynamics, with general density dependent mortality and infectivity. The model for the rest was kept as simple as possible. It would be only a first step for applications. For instance, in a model of brucellosis, it would probably be important to consider the interaction of various animal populations, with different epidemiological features.

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