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The Effect of Incubation Time Distribution on the Extinction Characteristics of a Rabies Epizootic

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The continuous model of Anderson *et al*. (1981), *Nature* **289**, 765–771, is successful in describing certain characteristics of rabies epizootics, in particular, the secondary recurrences which follow the initial outbreak; however, it also predicts the occurrence of exponentially small minima in the infected population, which would realistically imply extinction of the virus. Here we show that inclusion of a more realistic distribution of incubation times in the model can explain why extinction will not occur, and we give explicit parametric estimates for the minimum infected fox density which will occur in the model, in terms of the incubation time distribution.

1. INTRODUCTION

Rabies is a virally transmitted disease which affects all mammals, and which has been recorded in various parts of the world throughout recorded history (Steele and Fernandez, 1991). In Europe, there has been an epizootic for the past sixty years. Originating in Poland in 1939, or perhaps further east, it has spread gradually westwards, and now occupies France. A similar epizootic has occurred in North America, spreading south from the area round Hudson Bay since the late 1940s (Blancou *et al*., 1991).

In Europe, the principal vector of the current epizootic is the red fox (*Vulpes vulpes*). The pathology and epidemiology of the disease has been well documented by many authors [e.g., Bacon (1985a), Toma and Andral (1977), Steck and Wandeler (1980) and Baer (1991)]. The virus is transmitted through the saliva, and the infected fox then incubates the virus for a period, which in laboratory experiments is typically about 30 days or so, but which is very variable; we discuss this further below.

During the incubation period the viral load increases, and the virus migrates to the central nervous system and subsequently to the tissues. It is at this stage where symptoms appear, and the virus is expressed in the saliva. Symptoms vary, although one form (furious rabies) causes aggressive behaviour, and may be pri-

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marily responsible for the transmission of the disease via biting. Once symptoms appear, and the animal is infective, death usually follows in a few days.

Two features of the spread of rabies command particular attention. Firstly, the disease spreads in a wave-like manner with a velocity typically of the order of 40 km y^{-1} (Steck and Wandeler, 1980), although the rate is highly variable, and the European advance seems to have stopped (British Medical Association, 1995). Secondly, the epizootic is oscillatory in character, with a typical period of several years (Toma and Andral, 1977; Macdonald and Voigt, 1985): an outbreak in a region is typically followed by subsequent outbreaks.

Anderson *et al*. (1981) introduced a continuous time population model to explain the oscillatory character of the epizootic, and Murray *et al*. (1986) showed that by allowing rabid foxes to migrate (via a diffusion term) in the model, a feature designed to represent wandering and loss of territoriality in the clinically diseased fox, travelling waves with an oscillatory tail could be predicted.

Both Anderson *et al*. (1981) and Murray *et al*. (1986) pointed to the predicted oscillation periods of their models and (in the latter case) the predicted wave speed as providing a measure of support for the use of continuous time models. However, discrete models (both spatially and temporally) are arguably more realistic: reproduction of foxes takes place annually, a rut in winter leading to the birth of litters in spring, and the offspring become independent and disperse in the autumn. The time scale of generation, 6 months, is thus much longer than that associated with the duration (and often incubation) of the disease. Apart from this, many authors [for example, see Durrett and Levin (1994), Mollison (1995) and Mollison and Levin (1995)] have emphasized the shortcomings of using continuous and homogeneous (i.e., mean field) models for ecological populations, on the basis that they cannot describe fundamental features of such populations, such as persistence (Mollison and Levin, 1995; Keeling, 1997). We discuss this further below.

Foxes live in small family groups, so that transmission of the disease by bites, for example, is likely to affect whole family units. The implicit assumption in continuous models of spatially homogeneous transmission is thus likely to be overly simplistic. Discrete models have been developed by, for example, Bacon (1985b), Ball (1985), Smith and Harris (1991) and Artois *et al*. (1997).

Despite this, continuous models can provide a very useful tool for understanding disease transmission, since they are often capable of analytic treatment, while discrete models invariably require simulation. However, Mollison (1991) has criticized the continuous models on the basis of an apparent serious failing: both Anderson *et al*. (1981) and Murray *et al*. (1986) omitted to notice that the minimum levels of infected and rabid fox populations in their models reached values which would correspond in reality to extinction of the infected population: the virus would be removed from the fox population. This is a serious issue for these models, and one which needs to be considered.

Nor is it necessarily associated with the use of a continuous model. To be sure, exponentially small but non-zero continuous populations will inevitably regenerate

and cause oscillations; but their more realistic (discrete) interpretation would allow extinction of the disease altogether: in a spatially homogeneous model, neither prospect is realistic. In reality, such 'fade-outs' are a typical feature of persistent diseases such as measles (Keeling, 1997), whose persistence is mediated by spatial transmission between different local communities. Whether such transmission can be effective in fox rabies is less clear.

In this paper we re-examine the question of oscillations in a continuous model, with a view to establishing whether realistic modifications within the confines of the model can explain the conundrum. Firstly, we give a simple analysis which predicts the minimum level of the infected population, and we show how it depends critically on the ratio of the incubation time to the regeneration time. We then re-examine the continuous model's assumption of incubation time distribution. Implicitly, this is assumed to be exponential (Mollison, 1984), but a discussion of experimental data suggests this is unlikely to be the case, and we show that an extended distribution can lead to oscillations which have less severe minima. Although this leaves the issue of discrete vs continuous models unresolved, it suggests that the continuous model may still be useful if extended incubation times are assumed. Otherwise, another reservoir for the virus may need to be assumed.

The rest of this paper proceeds as follows. In the following section, we summarize Anderson *et al.*'s (1981) continuous model for rabies epizootics. We then analyse an outbreak, and show how to predict the quiet period and minimum infected population analytically. This leads us to the incubation time distribution as the source of the extinction problem. In Section 3 we present a model which allows an arbitrary incubation time distribution, and we analyse the effect of this on the resulting epizootic dynamics. A discussion follows in Section 4.

2. A Continuous Model for Rabies Epizootics

We follow Murray *et al.* (1986) and Anderson *et al.* (1981), and divide the fox population N into three classes: S, susceptible; I, infected, but not contagious; and R, rabid. The model equations are then

$$\dot{S} = (a-b)[1-N/K]S - \beta RS, \tag{2.1a}$$

$$\dot{I} = \beta SR - \sigma I - [b + (a-b)N/K]I, \tag{2.1b}$$

$$\dot{R} = \sigma I - \alpha R - [b + (a-b)N/K]R, \tag{2.1c}$$

where

$$N = S + I + R. \tag{2.2}$$

These equations represent logistic growth of the susceptible fox population towards a carrying capacity K (for the whole population N); infection of the susceptibles by the rabid population at the usual rate βRS; development of clinical

rabies in infected foxes at a rate σ (as we shall see later, this actually represents an exponential distribution of incubation times τ_i with mean $1/\sigma$); and death of rabid foxes at a rate α. The other loss terms in the I and R equations represent the natural death rates $-bI$, $-bR$ (infected and rabid foxes are assumed not to reproduce, whereas susceptible foxes do at a rate aS); the loss terms $-[(a-b)N/K]I$, $-[(a-b)N/K]R$ represent the resource-limiting effect of N on population mortality. For a critique of this model, see Mollison (1991); in particular, the rate terms in β, σ, α are, at least, suspect.

We non-dimensionalize the populations with K, thus $S = Ks$, $I = Kq$, $R = Kr$, $N = Kn$, and choose a time scale $t \sim 1/\sigma$. The corresponding dimensionless equations are then

$$\begin{aligned} \mu \dot{s} &= \varepsilon(1-n)s - rs, \\ \mu \dot{q} &= rs - (\mu + \delta + \varepsilon n)q, \\ \mu \dot{r} &= \mu q - (d + \varepsilon n)r, \\ n &= s + q + r, \end{aligned} \tag{2.3}$$

and the parameters are given by

$$\varepsilon = \frac{(a-b)}{\beta K}, \qquad \delta = \frac{b}{\beta K}, \qquad \mu = \frac{\sigma}{\beta K}, \qquad d = \frac{(\alpha + b)}{\beta K}, \tag{2.4}$$

with typical values (based on $a = 1\ \mathrm{y}^{-1}$, $b = 0.5\ \mathrm{y}^{-1}$, $\beta = 80\ \mathrm{km}^2\ \mathrm{fox}^{-1}\ \mathrm{y}^{-1}$, $K = 2\ \mathrm{fox\ km}^{-2}$, $\sigma = 0.036\ \mathrm{d}^{-1}$, $\alpha = 0.2\ \mathrm{d}^{-1}$)

$$\varepsilon = 0.003, \qquad \delta = 0.003, \qquad \mu = 0.08, \qquad d = 0.46. \tag{2.5}$$

Figure 1 shows a numerical solution of (2.3) with the values given in (2.5).

2.1. ***Small incubation time asymptotics.*** We see that $\varepsilon, \delta \ll \mu \ll 1$, and this forms a basis for a direct solution to the model. We put

$$r = \mu\rho, \tag{2.6}$$

and then

$$\dot{s} = \nu(1-n)s - \rho s, \tag{2.7a}$$

$$\dot{q} = \rho s - (1 + \delta' + \nu n)q, \tag{2.7b}$$

$$\mu\dot{\rho} = q - (d + \varepsilon n)\rho, \tag{2.7c}$$

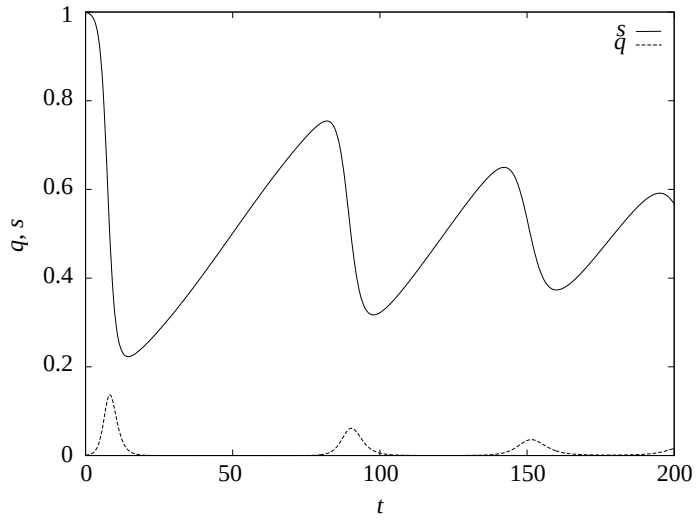

Figure 1. Numerical solution of (2.3) using the values given in (2.5). The plots show the evolution of q and s as functions of t.

where

$$n = s + q + \mu\rho, \tag{2.8}$$

and

$$\nu = \frac{\varepsilon}{\mu} = \frac{a-b}{\sigma}, \qquad \delta' = \frac{\delta}{\mu} = \frac{b}{\sigma}. \tag{2.9}$$

Since $\mu \ll 1$, (2.7c) implies that, after a rapid transient in a time of $O(\mu)$, (and with $\varepsilon \ll 1$)

$$\rho \approx q/d. \tag{2.10}$$

Neglecting relatively small terms in (2.7a,b), we then derive

$$\begin{aligned} \dot{s} &\approx \nu(1-s)s - \frac{sq}{d}, \\ \dot{q} &\approx q\left(\frac{s}{d} - 1\right), \end{aligned} \tag{2.11}$$

and this is easily solved using the fact that $\nu \ll 1$. One might query the provenance of the term in ν. When sq/d is $O(1)$, this term is negligible in any case, and its form is unimportant at leading order. However, it *is* important if q is small, as we shall see, and in that case we have $n \approx s$, and we have the term as written.

The procedure is similar to the relaxation oscillation analysis developed by Fowler and McGuinness (1982) for the Lorenz equations; see also Grasman *et al*. (1984). There is a fast (outbreak) phase when $s, q = O(1)$. Neglecting $O(\nu)$ in (2.11) gives a first integral

$$q = d\ln s - s - [d\ln s_- - s_-]. \tag{2.12}$$

Here, s_- is the value of s at the beginning of the outbreak when $q \approx 0$. During the outbreak, s decreases from s_- to a value s_+ given by the root of

$$d \ln s_+ - s_+ = d \ln s_- - s_-, \tag{2.13}$$

with $s_+ < s_-$, since $q \to 0$ at the end of the outbreak.

Following the fast phase, s tends to s_+, and thus q decreases exponentially towards zero. There follows a slow phase in which q is exponentially small (but crucially non-zero) and s recovers over a time of $O(1/\nu)$, and hence we put

$$t = \tau/\nu, \tag{2.14}$$

and anticipate that q is exponentially small. Then

$$\frac{ds}{d\tau} = s' \approx s(1-s), \tag{2.15}$$

whence

$$s \approx \frac{s_+}{s_+ + (1-s_+)e^{-\tau}}, \tag{2.16}$$

and

$$q \approx \exp\left[\frac{1}{\nu}\int_0^\tau \left(\frac{s}{d} - 1\right) d\tau\right], \tag{2.17}$$

since $q = O(1)$ as $\tau \to 0$. Note that the correction to the exponent is expected to be of $O(1)$, resulting in a numerical factor of $O(1)$ in (2.17).

The minimum value of q thus occurs when $s = d$, and is

$$q_{\min} \approx \exp\left[\frac{1}{\nu}\int_{s_+}^d \left(\frac{s}{d} - 1\right)\frac{ds}{s(1-s)}\right]; \tag{2.18}$$

hence

$$q_{\min} \approx \left(\frac{s_+}{d}\right)^{\frac{1}{\nu}} \left(\frac{1-s_+}{1-d}\right)^{\frac{1}{\nu}(\frac{1}{d}-1)}. \tag{2.19}$$

Since $\nu \ll 1$, we see [most easily from (2.18), since $s < d$] that $q_{\min}$ is very small, of order $\exp[-O(1/\nu)]$. If we take an initially healthy population $s_- = 1$, and then determine s_+ from (2.13) using $d = 0.46$, we obtain $s_+ \approx 0.16$. From (2.19), we then have

$$q_{\min} \approx \exp\left[-\frac{0.53}{\nu}\right], \tag{2.20}$$

and if $\nu = 0.038$, then $q_{\min} \approx 6 \times 10^{-7}$. Since the carrying capacity is $K \sim 1$ fox km^{-2}, this corresponds to an infected minimum of ~ 1 fox $(10^3$ km$)^{-2}$, e.g., one

in England. As Mollison (1991) pointed out, such values are untenable, and point towards extinction of the virus in the fox.

Other features of the oscillatory response are easily characterized. The next outbreak occurs at $\tau = \tau^*$, where q grows to be (suddenly) $O(1)$ again, and

$$s = s^* = \frac{s_+}{s_+ + (1 - s_+)e^{-\tau^*}}, \tag{2.21}$$

and τ^* is given by [since $q = O(1)$ there]

$$\int_{s_+}^{s^*} \left(\frac{s}{d} - 1\right) \frac{ds}{s(1-s)} = 0. \tag{2.22}$$

With s_+ given in terms of s_- by (2.13), (2.22) and (2.13) give a Poincaré map to determine s^* from s_-, and the duration of the quiet period between is given by τ^* from (2.21). We do not pursue further details here.

3. INCUBATION TIME DISTRIBUTION

Mollison (1991) criticized the continuous model on several counts, and we only aim to consider one of these here. As we see below, the decay term $-\sigma I$ in (2.1b) represents incubation with a mean time of $1/\sigma$. Anderson *et al.* (1981) use a value $1/\sigma = 28$ days and $\frac{1}{a-b} = 2$ years, and we see from the definition of $\nu = (1/\sigma)/[1/(a-b)]$, that the exponentially small minimum of q is precisely associated with the small ratio of incubation time to population growth time.

Now, incubation time estimates are entirely based on laboratory experiments, where fixed quantities of virus are injected directly, for example intra-muscularly. These experiments show a diversity in incubation times, depending on the site of injection. More importantly, experiments reviewed by Steck and Wandeler (1980) indicate that incubation times in about 10% of inoculated foxes are systematically large, >100 days. The data of Parker and Wilsnack (1966) is typical: 23 of 28 foxes injected with varying viral loads had incubation times in the range 14–57 days, while the other five died of other causes after incubating the virus for between 116 and 176 days. Whether death was due to viral debilitation or not, this points to the fact that incubation time is variable, and can reach high values. If we also consider the likely fact that naturally transmitted viral loads are likely to be less effective than those in the laboratory, it suggests (particularly in view of the crucial importance of the parameter ν) that we should consider the effect in the model of a more realistic distribution of incubation times, i.e., one with a longer tail, as we expect this to allow for less dramatic fade-outs in the infected population.

A related idea has been presented in models of persistence in measles (Keeling and Grenfell, 1997, 1998); allowing for an essentially constant incubation period, as opposed to the more common assumption of an exponential density,

causes persistence to occur in smaller communities. This question of persistence is also bound up with the issue of spatial variation in models (Tilman and Kareiva, 1997). Local 'fade-outs' or extinctions lead to increased susceptibility, and later re-infection can occur through long-range spatial transfer (Mollison and Levin, 1995). In this context, it is of interest to note that, although we do not analyse Murray *et al.*'s (1986) reaction diffusion model here, it also exhibits the same pathological minima in the infectives' density; this can be understood as being associated with the short-range dispersion kernel associated with diffusion [see the articles by Levin and Pacala and by Lewis in the book edited by Tilman and Kareiva (1997)], whereas the 'great leaps' associated with a dispersion kernel with a long tail can cause effective disease re-emergence. There is a natural affinity between the two ideas.

3.1. ***Variable incubation time model.*** We build the model using the ideas of age-structured populations (Hoppensteadt, 1975). Let $u(a, t)$ be the population density of those infected foxes at time t who have been infected for a period a (the 'age' of infection). The total infective population is then

$$I = \int_0^\infty u(a, t)\, da, \tag{3.1}$$

and by analogy with (2.1b), u satisfies

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = -[\lambda(a) + \{b + (a + b)N/K\}]u, \tag{3.2}$$

where $\lambda(a)$ is the incubation time specific removal rate. The initial condition for (3.2) is the 'birth' rate

$$u(0, t) = \beta SR. \tag{3.3}$$

The equation for S is the same as before, while that for R is modified to

$$\dot{R} = \int_0^\infty \lambda(a)u(a, t)\, da - \alpha R - [b + (a - b)N/K]R. \tag{3.4}$$

We now introduce the incubation time density $\phi(\tau)$: $\phi(\tau)\, d\tau$ is the fraction of foxes with an incubation time in the range $(\tau, \tau + d\tau)$. We have

$$\int_0^\infty \phi(a)\, da = 1, \tag{3.5}$$

and of a cohort of infected individuals of incubation time a, a fraction $\phi(a)\, da / \int_a^\infty \phi(\eta)\, d\eta$ will die in time da, thus λ in (3.2) is given by

$$\lambda(a) = \frac{\phi(a)}{\int_a^\infty \phi(\eta)\, d\eta}, \tag{3.6}$$

and thus

$$\phi(a) = \lambda(a) \exp\left[-\int_0^a \lambda(\xi)\, d\xi\right]. \tag{3.7}$$

For example, suppose λ is constant. Integration of (3.2) using (3.3) regains (2.1b), with $\lambda = \sigma =$ constant. We therefore see that the assumption of constant $\lambda = \sigma$ in (2.1) is equivalent to the choice of an exponential density $\phi = \lambda e^{-\lambda a}$, as mentioned earlier.

We non-dimensionalize the equations as before, but now also choosing

$$\phi = \frac{1}{\tau_i} f\left(\frac{\tau}{\tau_i}\right), \qquad a \sim \tau_i, \qquad u \sim K/\tau_i, \qquad \lambda = \frac{\Lambda}{\tau_i}, \tag{3.8}$$

where τ_i is a typical incubation time (so $\tau_i = 1/\sigma$ in the previous model).

As before, we obtain

$$\begin{aligned} \dot{s} &= \nu(1-n)s - \rho s, \\ \mu\dot{\rho} &= \int_0^\infty \Lambda(a)u(a,t)da - (d+\varepsilon n)\rho, \\ u_t + u_a &= -[\Lambda(a) + (\delta' + \nu n)]u, \\ u(0,t) &= \rho s, \end{aligned} \tag{3.9}$$

where

$$n = s + \mu\rho + \int_0^\infty u\, da. \tag{3.10}$$

3.2. ***Small incubation time analysis.*** If we now follow the procedure described in Section 2 for $\mu \ll 1$, we have, approximately,

$$\rho \approx \frac{1}{d}\int_0^\infty \Lambda(a)u(a,t)\, da, \tag{3.11}$$

and

$$\dot{s} \approx \left[\nu(1-s) - \frac{1}{d}\int_0^\infty \Lambda(a)u(a,t)\, da\right]s. \tag{3.12}$$

As before, we replace n by s in the ν term on the basis that this term is only significant when u is small. We solve for u (ignoring δ' and ν) using the method of characteristics, which yields

$$u(a,t) = \frac{s(t-a)}{d}\int_0^\infty \Lambda(\xi)u[\xi, t-a]\, d\xi \exp\left[-\int_0^a \Lambda(\omega)\, d\omega\right] \tag{3.13}$$

for $t > a$. (The neglect of δ' and ν is relaxed in Section 4.)

Although we have been coy about initial conditions, it needs to be recognized that s, ρ and u (in particular) satisfy initial conditions. That for ρ is lost by the singular approximation (3.11). If we suppose $u = u_0(a)$ when $t = 0$, $a > 0$, then (3.13) applies for $t > a$; while for $t < a$, we have

$$u = u_0(a-t)\exp\left[-\int_{a-t}^{a}\Lambda(\omega)\,d\omega\right], \qquad t < a. \tag{3.14}$$

The dimensionless incubation time density is defined by

$$f(\xi) = \Lambda(\xi)\exp\left[-\int_0^{\xi}\Lambda(\omega)\,d\omega\right]. \tag{3.15}$$

Now we define [by inspection of (3.13)]

$$u(a,t) = \frac{f(a)V(t-a)}{\Lambda(a)}, \tag{3.16}$$

at least for $t > a$; then (3.13) implies

$$V(t) = \frac{s(t)}{d}\int_0^{\infty} f(\xi)V(t-\xi)\,d\xi, \tag{3.17}$$

and this is valid for $t > 0$. Substituting this into (3.12), we gain the companion equation

$$\dot{s} = \nu(1-s)s - V(t); \tag{3.18}$$

this pair now forms the incubation distribution analogue to (2.11). Note that (3.16) still has meaning for $t < a$, and (3.14) then implies $V(t) = V_0(-t)$ for $t < 0$, where

$$V_0(\xi) = u_0(\xi)\exp\left[\int_0^{\xi}\Lambda(\omega)\,d\omega\right], \qquad \xi > 0, \tag{3.19}$$

is a prescribed function.

3.3. ***Asymptotic solution.*** We now analyse (3.17) and (3.18) when $\nu \ll 1$. There is a fast (outbreak) phase when we neglect $O(\nu)$, thus

$$\dot{s} = -V, \tag{3.20a}$$

$$V(t) = \frac{s}{d}\int_0^{\infty} f(\xi)V(t-\xi)d\xi. \tag{3.20b}$$

These equations have a first integral,

$$d\ln s - \int_0^{\infty} f(\xi)s(t-\xi)\,d\xi = \text{constant}, \tag{3.21}$$

which is the analogue of (2.12). Suppose a fast pulse occurs at $t \approx t_0$. Then we need to solve (3.21) to relate the values of $s_\pm$ as $t - t_0 \to \pm\infty$. The equation is a nonlinear singular Volterra integral equation, but for the present purposes we require only the relation between s_- and s_+, the values of s before and after the outbreak. Since the density f satisfies

$$\int_0^\infty f(\xi)\, d\xi = 1, \tag{3.22}$$

it follows that [from (3.21) as $t \to \pm\infty$]

$$d \ln s_+ - s_+ = d \ln s_- - s_-, \tag{3.23}$$

just as in (2.13).

In the succeeding slow phase (just as before), $t - t_0 = \tau/\nu$, V is small, and we assume specifically that $V \ll \nu$; then $s = s(\tau)$ is given by (2.16), and V is determined by (3.20b). This is a Volterra equation for V, as can be seen by writing it as

$$\begin{aligned} V(t) &= \frac{s}{d} \int_{-\infty}^{t} f(t-\omega) V(\omega)\, d\omega \\ &= \frac{s}{d} \left[\int_{t_-}^{t} f(t-\omega) V(\omega)\, d\omega + h(t) \right], \end{aligned} \tag{3.24}$$

where

$$h(t) = \int_{-\infty}^{t_-} f(t-\xi) V(\xi)\, d\xi, \tag{3.25}$$

and t_- is chosen in the matching region between fast and slow phases, i.e., $1 \ll t_- - t_0 \ll 1/\nu$. Equation (3.24) is of the typical form of the renewal equation in age-structured population models (Frauenthal, 1986). For convenience, we now put $t_- = 0$. Since this value of t is located in the matching region between fast and slow phases, we can at leading order take V in the integral for h to be the solution for the preceding fast pulse, and h is essentially a weighted integral of V over the preceding fast pulse.

The integral equation for V is thus

$$DV(t) = \int_0^t f(t-\xi) V(\xi)\, d\xi + h(t), \tag{3.26}$$

where we write

$$D = \frac{d}{s}. \tag{3.27}$$

Suppose first that s/d is constant. Then a Laplace transform of (3.26) gives the transform as

$$\hat{V} = \frac{\hat{h}}{D - \hat{f}}. \tag{3.28}$$

In practice we are interested in the large time behaviour of V. Consider first the case where $f(\xi)$ is exponentially small as $\xi \to \infty$; i.e., $f = \exp[-O(\xi)]$; this includes the exponential distribution time of Anderson *et al.* (1981), and essentially corresponds to the case where $\Lambda \to$ constant at large ξ. Then also $h = \exp[-O(t)]$ as $t \to \infty$, so $\hat{h}(p)$ and $\hat{f}(p)$ tend to zero algebraically as $p \to \infty$. The large time behaviour is then determined by the zeros of $D - \hat{f}$. If $\hat{f}(p_i) = D$, then the large time dependence of (3.28) is (assuming simple poles)

$$V \sim \sum_i \left(-\frac{\hat{h}(p_i)}{\hat{f}'(p_i)} \right) \exp(p_i t). \tag{3.29}$$

Following an outbreak, $s\ (= s_+) < d$, and evolution of V is determined by the zeros of

$$\int_0^\infty f(\omega) e^{-p\omega}\, d\omega = \frac{d}{s} > 1. \tag{3.30}$$

Since $f \geq 0$ and $\int_0^\infty f(\omega)\, d\omega = 1$, we see that there is a unique real root of this equation, *providing* f is $\exp[-O(\omega)]$ at ∞, and that $p < 0$ if $s < d$, $p > 0$ if $s > d$. Moreover, it is easy to see that any other complex root has a lower real part, and thus the real exponent gives the required asymptotic behaviour.

More generally, if $s(\tau)$ is now slowly varying, we suggest in the Appendix (which is available on the electronic version) that the leading order solution of (3.26) is [cf. (2.17)]

$$V \sim \exp\left[\frac{1}{\nu} \int_0^\tau p(\xi)\, d\xi \right], \tag{3.31}$$

where $p(\tau)$ is determined by

$$\int_0^\infty f(\xi) e^{-\xi p}\, d\xi = \frac{d}{s}, \tag{3.32}$$

with s given by (2.16), and the quiet interval P between outbreaks is given by

$$P = T/\nu, \qquad \int_0^T p(\xi)\, d\xi = 0. \tag{3.33}$$

The minimum value of V is (since $p = 0$ when $s = d$)

$$V_{\min} \sim \exp\left[\frac{1}{\nu} \int_{s_+}^d p(s) \frac{ds}{s(1-s)} \right], \tag{3.34}$$

where we write $p(s)$ to denote the solution of (3.32) as a function of s. From (3.15) and (3.16), we have that the infection rate is

$$u(0, t) \approx V(t), \tag{3.35}$$

and also $\rho \approx V/s$, so that $V_{\min}$ provides a measure of how small the rabid fox population becomes.

3.4. ***Some examples.*** The preceding case ($\Lambda = 1$, $f = e^{-\xi}$) is reclaimed in (3.32) since then $1/(1 + p) = d/s$, i.e., $p = (s/d) - 1$, as previously found.

If the incubation time were a fixed value ($= 1$), then $f(\xi) = \delta(\xi - 1)$ and (3.32) is

$$p = \ln\left(\frac{s}{d}\right), \tag{3.36}$$

and (3.34) still gives $V_{\min} = \exp[-O(1/\nu)]$. Note that the minimum here is *less* than that of the exponential distribution, indicating greater eradication, in contrast to what happens in measles (Keeling and Grenfell, 1998).

However, suppose we put $f(\xi) = (1 - \psi)\delta(\xi - 1) + \psi\delta(\xi - L)$, where L represents the longevity experienced by a small but significant fraction ψ of the foxes in (for example) Parker and Wilsnack's (1966) experiments. Then (3.32) is

$$(1 - \psi)e^{-p} + \psi e^{-pL} = \frac{d}{s}. \tag{3.37}$$

If ψ is relatively small and L is relatively large (for example, if 10% of foxes can incubate the virus for 150 days as opposed to the normal 30 days, we would take $\psi = 0.1$, $L = 5$), then, since the ratio of the two exponential terms is $[(1 - \psi)/\psi]e^{(L-1)p}$, and equals one when

$$p = p^* = -\frac{1}{(L - 1)} \ln\left(\frac{1 - \psi}{\psi}\right) \approx -\frac{1}{L} \ln\left(\frac{1}{\psi}\right), \tag{3.38}$$

we have, roughly, that

$$\begin{aligned} p &\approx \ln\left[\frac{(1 - \psi)s}{d}\right], \qquad p > p^*, \\ p &\approx -\frac{1}{L} \ln\left[\frac{d}{s\psi}\right], \qquad p < p^*, \end{aligned} \tag{3.39}$$

and that the second relation applies when $s < d$. The implication of this is that decay of V is much slower because of the small pool of long incubation time foxes. Adoption of the second relation in the approximate form $p \approx -\frac{1}{L} \ln\left(\frac{1}{\psi}\right)$ leads to the expression, using (3.39),

$$V_{\min} \approx \exp\left[-\frac{1}{\nu L}\ln\left(\frac{1}{\psi}\right)\ln\left\{\frac{d(1-s_+)}{s_+(1-d)}\right\}\right]. \tag{3.40}$$

The minimum now scales as $\exp\left[-O\left[\frac{1}{\nu L}\ln\left(\frac{1}{\psi}\right)\right]\right]$ and is typically much larger than $\exp\left[-O\left(\frac{1}{\nu}\right)\right]$. With $\nu = 0.038$, $L = 5$, $\psi = 0.1$, then $\exp[-1/\nu] \sim 10^{-12}$, while $\exp\left[-\frac{1}{\nu L}\ln\frac{1}{\psi}\right] \sim 10^{-5}$, still small but much less dramatic than the 30 day distribution. If we suppose 1% of foxes can incubate the virus for 500 days, then $V_{\min} \sim 10^{-3}$. In fact the critical quantity is the fraction ψ_g which can incubate the virus for the fox population regeneration time, since then $\nu L \approx 1$, and $V_{\min} \sim \psi_g^{\alpha}$ with α being $O(1)$. In this view, the critical issue is whether a small but significant percentage of foxes can incubate the virus for a long time.

3.5. ***Algebraic distributions.*** This discussion naturally leads towards the idea that the tail of the distribution is long, and a natural extension is to consider the case where $f(\xi) = O(\xi^{-\lambda})$ as $\xi \to \infty$, with $\lambda > 1$. In this case, we immediately see from (3.30) that exponential solutions will still exist for $s > d$, when $p > 0$ and V is growing, but for $s < d$, there are *no exponentially decaying solutions*.

We can conveniently illustrate what happens by choosing

$$f(\xi) = \frac{\lambda - 1}{(1+\xi)^{\lambda}}, \tag{3.41}$$

with $\lambda > 1$. The Laplace transform of $f(\xi)$ is

$$\hat{f}(p) = (\lambda - 1)\, p^{\lambda - 1} e^{p} \int_p^{\infty} \xi^{-\lambda} e^{-\xi} d\xi, \tag{3.42}$$

where the integral is $\Gamma[-(\lambda-1), p]$, and the integral definition $\hat{f} = \int_0^{\infty} e^{-p\xi} f(\xi)\, d\xi$ exists for Re $p \geq 0$ but not Re $p < 0$, while $\hat{f}$ provides the analytic continuation for all values of p, with $\hat{f}$ having a singularity at $p = 0$. This singularity is a branch point.

Recall that $D = d/s$, and again initially assume D is constant. From (3.25), note that the primary contribution to h comes from the fast oscillation of V in the preceding fast pulse in $t < 0$. For large $t > 0$, we have for the algebraic f given by (3.41) that $f(t - \xi) \approx f(t)$ for $\xi \sim O(1)$, and thus

$$h \approx \Delta s f(t), \tag{3.43}$$

where

$$\Delta s = s_- - s_+, \tag{3.44}$$

since $\int_{-\infty}^{\infty} V(\xi)\,d\xi \approx \Delta s$, using $\dot{s} \approx -V$ in the fast phase. The Laplace transform $\hat{V}$ is given in this case by

$$\hat{V} = \frac{\Delta s\,\hat{f}(p)}{[D - \hat{f}(p)]}, \tag{3.45}$$

and

$$V = \frac{1}{2\pi i}\int_{c-i\infty}^{c+i\infty} \hat{V}(p)e^{pt}\,dp, \tag{3.46}$$

where $c > 0$.

We are interested in the long time behaviour of V and this is determined by the singularities of $\hat{V}$. Since $\hat{f} = O(1/p)$ as $p \to \infty$, we can complete the contour in (3.46) by a large semi-circle in Re $p < 0$, together with a keyhole contour indented round the branch point at $p = 0$, and contributions from any poles of $\hat{V}$. Since $\hat{f}$ is holomorphic for Re $p > 0$ and bounded for Re $p = 0$ (and $D - \hat{f} \neq 0$ when $D > 1$ for Re $p \geq 0$), any poles p_i of $\hat{V}$ have Re $p_i < 0$, and their contribution $\exp(p_i t)$ to V is negligible as $t \to \infty$ compared with the contribution from the keyhole contour round $p = 0$. It follows that

$$V \sim \frac{1}{2\pi i}\int_0^{\infty} \left\{\hat{V}_-[-x] - \hat{V}_+[-x]\right\} e^{-xt}dx, \tag{3.47}$$

where $\hat{V}_\pm$ represent the values of $\hat{V}$ above $(+)$ and below $(-)$ the branch cut on Re $p < 0$ [there is no contribution from the indentation $|p| = \varepsilon$, $\varepsilon \to 0$, as $\hat{f}$ (and thus $\hat{V}$) is bounded near zero, as we now show].

To determine $\hat{V}_\pm$, we require $\hat{f}_\pm$, which we can obtain by writing $\hat{f}$ as (Abramowitz and Stegun, 1964)

$$\begin{aligned}\hat{f}(p) &= (\lambda - 1)p^{\lambda-1}e^p\Gamma(1-\lambda, p)\\ &= (\lambda - 1)p^{\lambda-1}e^p\Gamma(1-\lambda) - (\lambda-1)\Gamma(1-\lambda)e^p\gamma^*(1-\lambda, p)\\ &= (\lambda - 1)p^{\lambda-1}e^p\Gamma(1-\lambda) - (\lambda-1)\Gamma(1-\lambda)\sum_0^{\infty}\frac{p^n}{\Gamma(n+2-\lambda)}.\end{aligned} \tag{3.48}$$

We assume temporarily that λ is not an integer here. Note that $\hat{f}(0) = 1$ and is bounded. The second expression is entire, and thus we have

$$\begin{aligned}\hat{f}_+(-x) &= -(\lambda-1)\Gamma(1-\lambda)[e^{i\lambda\pi}x^{\lambda-1}e^{-x} + e^{-x}\gamma^*(1-\lambda, -x)],\\ \hat{f}_-(-x) &= -(\lambda-1)\Gamma(1-\lambda)[e^{-i\lambda\pi}x^{\lambda-1}e^{-x} + e^{-x}\gamma^*(1-\lambda, -x)].\end{aligned} \tag{3.49}$$

From (3.45), we have

$$\hat{V}_- - \hat{V}_+ = \frac{\Delta s(\hat{f}_- - \hat{f}_+)D}{(D - \hat{f}_+)(D - \hat{f}_-)}, \tag{3.50}$$

the arguments of $\hat{V}_\pm$ and $\hat{f}_\pm$ being $-x$; hence, near $x = 0$,

$$\hat{V}_-(-x) - \hat{V}(-x) = (\lambda - 1)\Gamma(1 - \lambda)(2i \sin \lambda\pi)x^{\lambda-1}e^{-x} \times \left[\frac{\Delta s D}{(D-1)^2} + O(x, x^{\lambda-1})\right], \tag{3.51}$$

and application of Laplace's method to (3.47) then implies

$$V \sim \left\{\frac{(\lambda - 1)\Gamma(1 - \lambda)\Gamma(\lambda)\Delta s D \sin \lambda\pi}{\pi(D-1)^2}\right\} \frac{1}{(1+t)^\lambda}[1 + O(t^{-1}, t^{-(\lambda-1)})]. \tag{3.52}$$

The crucial result is that the algebraic tail of the incubation distribution time causes an algebraic decline of V: it is the tail of the distribution that is critical in determining the minimum of V. Using the reflection formula $\Gamma(\lambda)\Gamma(1 - \lambda) = \pi \operatorname{cosec} \pi\lambda$, (3.52) is simply

$$V \sim \left[\frac{\Delta s D}{(D-1)^2}\right] \frac{(\lambda - 1)}{(1+t)^\lambda} \qquad \text{as } t \to \infty, \tag{3.53}$$

and this formula applies equally if λ is an integer.

In the Appendix (which is available on the electronic version), we show that when D is a slowly varying function of t, the appropriate generalization of (3.53) is

$$V \sim \left[\frac{D_0 \Delta s}{(D_0 - 1)(D - 1)}\right] f(t), \tag{3.54}$$

where $D_0 = D(0)$. Thus V is positive ($s < d$, i.e., $D > 1$, $\lambda > 1$) and declining until a value τ^* (where $s < d$) by which point

$$V_{\min} \sim \nu^\lambda. \tag{3.55}$$

For $\nu = 0.038$, we have $V_{\min} \sim 0.7 \times 10^{-2}$ if $\lambda = 1.5$ and $V_{\min} \sim 0.5 \times 10^{-4}$ if $\lambda = 3$. Practically, therefore, the effect of an algebraic decay on the minimum infective fox density is only significant if $\lambda < 3$.

4. DISCUSSION

In this paper we have shown firstly that the minimum in the infected fox population between rabies outbreaks is small, in the continuous model of Anderson *et al.* (1981). Explicitly, the minimum following the initial outbreak (when $s_- = 1$) is given by (2.19) and (2.13):

$$q_{\min} \approx \left[\left(\frac{s_+}{d} \right) \left(\frac{1 - s_+}{1 - d} \right)^{\left(\frac{1}{d} - 1 \right)} \right]^{\frac{1}{\nu}},$$

$$s_+ e^{-s_+/d} = e^{-1/d}, \qquad (s_+ < 1,\ d < 1). \tag{4.1}$$

This gives a numerical value relative to the carrying capacity of the environment, $K \approx 1$ fox km^{-2}.

The value of $q_{\min}$ is determined by two quantities d and ν, with typical values of $d = 0.46$ and $\nu = 0.038$. The value is thus exponentially small, principally because the value of ν is very small. The parameters ν and d represent the ratios of various time scales. If t_{inc} is the mean incubation time, t_{gr} is the fox population growth time, t_{con} is the mean time between effective (transmissive) contacts, and t_{dis} is the mean duration of clinical disease, then in fact the definitions of ν and d imply

$$\nu = \frac{t_{\text{inc}}}{t_{\text{gr}}}, \qquad d = \frac{t_{\text{con}}}{t_{\text{dis}}}. \tag{4.2}$$

For the epizootic to be viable, we thus require t_{con} to be less than t_{dis}—but not too much smaller, since as $d \to 0$, $s_+ \approx \exp(-1/d)$. More germanely, we see that exponentially small minima are associated with values of incubation time $t_{\text{inc}} \ll t_{\text{gr}}$.

Secondly, an examination of the data on which the estimate of $t_{\text{inc}} = 28$ days is based indicates that in fact this estimate does not apply to a small but significant fraction of foxes which under laboratory conditions can incubate the disease for periods of 150 days or more. In order to incorporate this type of extended incubation distribution time into the continuous model, we have adapted the equations to allow for a distribution of incubation times, and have shown that the same type of relaxation oscillation analysis gives us explicit recipes for the minimum rabid or infective population.

The quantity $V_{\min}$ is the density of newly infected foxes, and represents the minimum infective population. (In the exponential case, $V_{\min} = q_{\min}$.) The general distributional recipe for $V_{\min}$ then follows from (3.34), (3.32) and (2.13) (with $s_- = 1$):

$$V_{\min} \approx \exp\left[\frac{1}{\nu} \int_{s_+}^{d} \frac{p(s)ds}{s(1-s)} \right],$$

$$\int_0^\infty f(\xi)e^{-p\xi}\,d\xi = \frac{d}{s},$$

$$s_+ e^{-s_+/d} = e^{-1/d}, \tag{4.3}$$

where f is the distribution, which is here assumed to decay exponentially at infinity. [Note that $f = e^{-\xi}$ corresponds to the case studied in Section 2, and gives $p = (s/d) - 1$, agreeing with (2.18) (since also $q_{\min} = dV_{\min}/s$, and $s = d$ at $q_{\min}$).]

We chose two particular types of distribution to illustrate the dramatic effect of extended incubation times. If a fraction $1 - \psi$ have $t_{\text{inc}} = 1$ (dimensionlessly, corresponding to 28 days) and a fraction ψ have $t_{\text{inc}} = L$, then p is given by

$$(1-\psi)e^{-p} + \psi e^{-pL} = d/s \tag{4.4}$$

and if $L \gg 1$, $\psi \ll 1$, (3.40) gives

$$V_{\min} \approx \exp\left[-\frac{1}{\nu L}\ln\left(\frac{1}{\psi}\right)\ln\left\{\frac{d(1-s_+)}{s_+(1-d)}\right\}\right], \tag{4.5}$$

and the minimum can be significantly increased. In fact $V_{\min} \sim \psi^{1/\tilde{\nu}}$, where, since $L = t_{\text{res}}/t_{\text{inc}}$ is the ratio of incubation times of resistant foxes and normal foxes, $\tilde{\nu}$ is defined by $t_{\text{res}}/t_{\text{gr}}$. The mean incubation time is in fact irrelevant in this case. If a fraction ψ_g can incubate the virus for the growth time t_{gr}, then $V_{\min} \sim \psi_g$. A value of 10^{-2} or even 10^{-3} for this fraction corresponds practically to the sort of epizootic minima which are observed.

A different perspective on this result arises if we consider different values of L and corresponding values of ψ. If as L increases, $\psi = \exp[-O(L)]$, then the minimum remains exponentially small. This suggests our other particular type of distribution, in which $f(\xi)$ decays more slowly than exponentially, and (4.3) does not apply. In the Appendix (available on the electronic version), we show quite generally that for algebraically decaying f

$$V \sim \left[\frac{D_0 \Delta s}{(D_0-1)(D-1)}\right] f(t), \tag{4.6}$$

where $\Delta s = s_- - s_+$ and $D_0 = d/s_+$. The minimum of this occurs when $D > 1$, i.e., $s < d$, and in fact when

$$\tau = \frac{\lambda(D-1)}{D-d} = \ln\left(\frac{D_0 - d}{D-d}\right). \tag{4.7}$$

Thus $V_{\min} \sim \nu^\lambda$ and the exponential minimum of the exponential distribution is alleviated by the algebraic one.

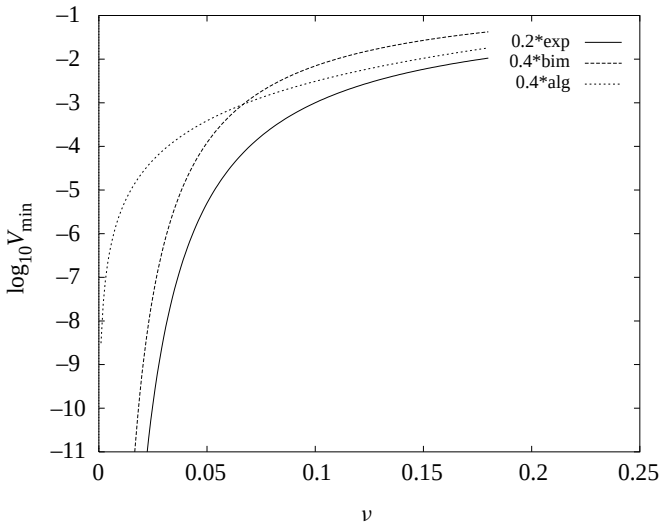

Figure 2. The dependence of $V_{\min}$ on ν for three different incubation delay distributions: (i) the exponential distribution $f = e^{-\xi}$ in (4.3); (ii) the two-delay distribution with $L = 5$ and $\psi = 0.1$, using (4.3) and (4.4); and (iii) the algebraically decaying distribution, using (4.6) and (4.7), with a decay exponent $\lambda = 3$. We have arbitrarily multiplied the theoretical results by the factors 0.2, 0.4 and 0.4, respectively, which appears (see Fig. 3) to be more consistent with direct numerical results.

We term the three typical densities we have considered the exponential, the bimodal, and the algebraic. Figure 2 plots the theoretical dependence of $V_{\min}$ as a function of ν for these three distributions, and this shows that the bimodal distribution causes an order of magnitude rise in the minimum, but the algebraic density has a much more dramatic effect.

In Fig. 3 we compare the theoretical results for the exponential and algebraic densities with the results of a direct numerical simulation of the model (3.9). The introduction of multiplicative factors (here 0.2 and 0.4) of $O(1)$ is consistent with the nature of the approximations (geometric optics and not physical optics) we have introduced, and we can see that the theoretical results mimic the numerical results. There is, however, a noticeable deviatoric trend away from the asymptotic result as ν becomes smaller (i.e., to the right of the figure). The numerical results for the Volterra integral equation which we show in the Appendix (available on the electronic version) suggest that the large time approximate solutions derived there are quite accurate, and we consider that the deviations in Fig. 3 are due to the neglect of one of the terms in (3.9). It is in fact possible to obtain a good fit to the curves by modulating each with the $O(1)$ factor $\exp(0.04/\nu)$. This suggests that the correction is effective over the slow phase, and consideration of various possibilities leads to reconsideration of the neglect of the term

$$k(t) = \delta' + \nu n \approx \delta' + \nu s \tag{4.8}$$

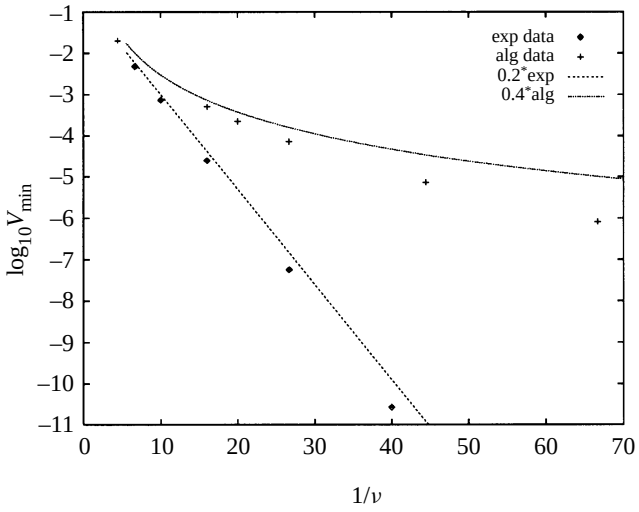

Figure 3. $\log_{10}[\min u(0,t)]$ plotted against $1/\nu$. The points indicate the results of direct numerical computation of (3.9) using standard parameters given in (2.5), except that ν is varied by altering ε (only). Arbitrary multiplication of the theoretical results for $\log_{10} V_{\min}$ by factors of 0.2 (exponential) and 0.4 (algebraic) are indicated.

in (3.9). It is straightforward to repeat the solution for u with the same neglect of $O(\mu)$ as before, and we find that

$$u(0,t) = V(t) \exp\left[-\int_0^t k(t')\,dt'\right], \tag{4.9}$$

where V satisfies the same equation as before. Since the numerical computations give $\min u(0,t)$, we can obtain an improved estimate of the minimum by using (4.9). Using s given by (2.15), (4.9) leads to the improved estimate

$$\min u(0,t) = V_{\min} \exp\left[-\left(1+\frac{\delta'}{\nu}\right)\tau_{\min}\right], \tag{4.10}$$

where we take $\tau_{\min}$ as the value where V is predicted to be minimum. The result of this improved estimate is shown for the exponential and algebraic cases in Fig. 4, and clearly gives good agreement.

Although the use of continuous and spatially homogeneous models is clearly problematic in ecological models (Mollison and Levin, 1995), we have developed an apparently novel method whereby the low infection minima in such models can be quantitatively understood. In more realistic models, similar concepts may yet apply. There is a clear analogy between the necessity of long-tailed dispersion kernels in order to explain the persistence of infectious diseases (Mollison and Levin, 1995) and the corresponding effect of long incubation time densities here. Figure 5 shows the difference between algebraic and exponential distributions of survival times; it is clear that if Parker and Wilsnack's (1966) data is typical, whereby

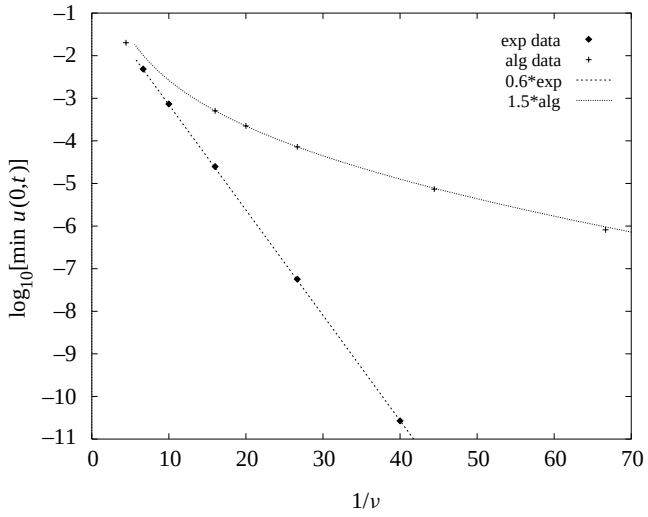

Figure 4. The same data as used in Fig. 3, but compared with the improved theoretical estimates in (4.10). The multiplication factors are 0.6 and 1.5.

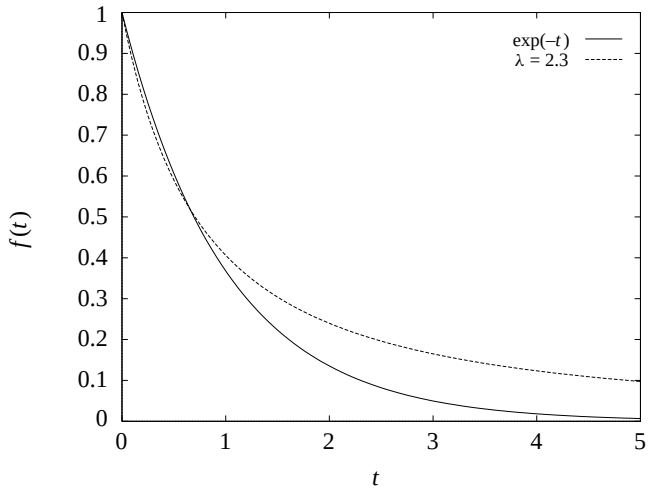

Figure 5. A comparison of the survival distributions for the algebraic density $f(t) = (\lambda - 1)/(1 + t)^{\lambda}$ and the exponential density $f(t) = \exp(-t)$, using a value of $\lambda = 2.3$. The functions plotted are the fraction surviving to time t, given by $\int_t^{\infty} f(t)\,dt$.

(more than) 10% of foxes can survive for five times the typical incubation time, then an algebraic density is more relevant; and the predicted minimum of $u(0, t)$ for the value $\lambda = 2.3$ in Fig. 5 is, from (4.10), 0.4×10^{-3}. Nor is the spatial dispersion concept likely to be as effective for fox rabies as for human diseases such as measles, unless some other vector is involved: foxes cannot catch trains, and if they only wander in the short period of furious rabies, it seems unlikely that an appropriate dispersion kernel will be other than localized.

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APPENDIX

We wish to solve the integral equation [cf. (3.24)]

$$DV = \int_0^t f(\xi)V(t-\xi)d\xi + \int_0^\infty f(t+\xi)V_0(\xi)d\xi, \tag{A1}$$

where $D = D(\tau)$ is a slowly varying function of $\tau = \nu t$, $\nu \ll 1$, and f is a density function satisfying $f(\infty) = 0$, $\int_0^\infty f(\xi)\,d\xi = 1$, and is related to the function $\Lambda(\xi)$ by

$$f(\xi) = \Lambda(\xi)\exp\left[-\int_0^\xi \Lambda(u)\,du\right],$$

$$\Lambda(\xi) = \frac{f(\xi)}{\int_\xi^\infty f(u)\,du}. \tag{A2}$$

Typical forms for consideration are the exponential $f = e^{-\xi}$, and the algebraic $f = (\lambda - 1)/(1 + \xi)^{\lambda}$, with $\lambda > 1$. In the main text, the solutions for constant D are found by the Laplace transform, and these solutions are given, for large t, by

$$V \sim -\frac{\hat{h}(p)}{\hat{f}'(p)} \exp(pt), \tag{A3}$$

where p is the (unique) real root of

$$\int_0^{\infty} f(\xi) e^{-p\xi}\, d\xi = D, \tag{A4}$$

if f decays exponentially at infinity.

If f decays algebraically at infinity, then (A4) has no solution for $p < 0$, i.e., if $D > 1$, and the long time solution (when D is constant) is given for the specific algebraic case $f = (\lambda - 1)/(1 + \xi)^{\lambda}$ by (3.53), which can be written in the more general form

$$V \sim \frac{f}{D-1}\left[\int_0^{\infty} V_0(\xi) d\xi - \frac{\int_0^{\infty} f'(\xi) V_0(\xi)\, d\xi}{D-1}\right]. \tag{A5}$$

We wish to find ways to generalize (A3) and (A5) to the case of slowly varying D.

1. Exponential case. Analysis is facilitated by the observation that, when $f = e^{-\xi}$, the exact solution of (A1) is

$$V = \frac{h_0}{D(\tau)} \exp\left[\frac{P(\tau)}{\nu}\right], \tag{A6}$$

where

$$h_0 = \int_0^{\infty} f(\xi) V_0(\xi)\, d\xi \tag{A7}$$

and

$$P(\tau) = \int_0^{\tau} \left(\frac{1}{D(X)} - 1\right) dX. \tag{A8}$$

The generalization of (A3) to (A6) is reminiscent of WKB theory, and suggests that we try the ansatz

$$V \sim P_1(\tau) \exp[P_0(\tau)/\nu] \tag{A9}$$

directly in (A1). Substituting this in, we find

$$\left[D - \int_0^{\infty} f(\xi) e^{-\xi P_0'}\, d\xi + O(\nu)\right] P_1 \sim \exp\left[-\frac{(\tau + P_0)}{\nu}\right] \int_0^{\infty} k e^{-\xi} V_0(\xi)\, d\xi, \tag{A10}$$

if $f \sim ke^{-\xi}$ as $\xi \to \infty$. Note that in order for the integral on the left to exist, we need $P_0' > -1$, so that $P_0 + \tau > 0$ and the right-hand side appears exponentially small. At leading order, this appears to vindicate (3.31) and (3.32), and in the particular case where $f = e^{-\xi}$, we regain at leading order the exact solution (A6), since $D = \int_0^\infty \exp[-(1+P_0')\xi]\,d\xi$ implies $D = 1/(1+P_0')$, i.e., $P_0' = (1/D) - 1$, as in (A8). It is not clear in this procedure how to extend the method to find higher order terms, however.

2. Algebraic case. Now we consider the case when $f = O(\xi^{-\lambda})$ as $\xi \to \infty$, when evidently the preceding method fails. The approximation is quite different in this case. We write

$$V = f(t)W(t), \tag{A11}$$

so that W is asymptotically constant if D is constant. It seems reasonable to imagine that W varies slowly if D does. We have, exactly,

$$DW = \int_0^{t/2} \frac{f(\xi)\,f(t-\xi)}{f(t)}\,\{W(\xi) + W(t-\xi)\}\,d\xi + \int_0^\infty \frac{f(t+\xi)}{f(t)} V_0(\xi)\,d\xi, \tag{A12}$$

and also, after interchanging the order of double integration,

$$\int_0^\infty DV\,d\xi = \int_0^\infty V\,d\xi - \int_0^\infty f' V_0\,d\xi. \tag{A13}$$

The distinction between the algebraic and exponential cases lies in the following. When $f = e^{-\xi}$, then the kernel function $f(\xi)\,f(t-\xi)/f(t) = 1$, and all parts of the range $(0, t/2)$ appear to contribute to the integral. However, if f decays algebraically, then for large t, $f(t-\xi)/f(t) \approx 1$ for $\xi = O(1)$, but the kernel decreases away from $\xi = 0$. Specifically, with $t = \tau/\nu$ and $f(\xi) \sim (\lambda-1)/(1+\xi)^\lambda$ as $\xi \to \infty$,

$$\begin{aligned} DW = &\int_0^{\tau/2\nu} f(\xi)\left[1 + \frac{\nu\lambda\xi}{\tau+\nu}\cdots\right]\{W(\xi) + W(t-\xi)\}\,d\xi \\ &+ \int_0^\infty V_0(\xi)\left[1 - \frac{\nu\xi\lambda}{\tau+\nu}\cdots\right]d\xi, \end{aligned} \tag{A14}$$

(we assume $V_0 \to 0$ as $\xi \to \infty$). It seems reasonable to expect that W will be slowly varying when $\tau = O(1)$, but that W will vary more rapidly when $t = O(1)$. We can thus approximate (A14) by (since $\int_0^\infty f\,d\xi = 1$)

$$DW(\tau) \sim \int_0^\infty V\,d\xi + O(\nu) + W(\tau) - \nu\left\{\int_0^\infty \xi f(\xi)\,d\xi\right\} W' + \int_0^\infty V_0(\xi)\,d\xi, \tag{A15}$$

where we retain the term in W' in anticipation of W becoming large.

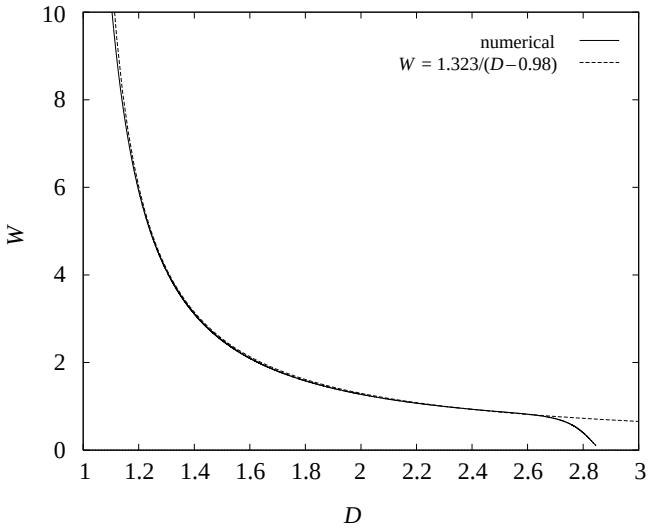

Figure 6. Numerical solution of the integral equation (A1), plotted as W vs D, with $\nu = 0.01$, and the functions D, V_0, and f are as described in the text. Comparison is made with the theoretical estimate $W \approx R/(D - 0.98)$, where $r = 1.323$.

Next, (A13) implies

$$\int_0^\infty V\,d\xi \sim -\frac{\int_0^\infty f'V_0\,d\xi}{D_0 - 1}, \tag{A16}$$

where $D_0 = D(0)$. Using the fact that $\int_0^\infty \xi f\,d\xi = f(0) \equiv f_0$, we have, for $\tau = O(1)$,

$$W \sim \frac{R - \nu f_0 W'}{D - 1}, \tag{A17}$$

where

$$R = \int_0^\infty V_0\,d\xi - \frac{\int_0^\infty f'V_0\,d\xi}{D_0 - 1}. \tag{A18}$$

In Fig. 6 we show a comparison of the leading order approximation $W \sim R/(D-1)$ to the numerically computed solution of (A1), using the algebraic density $f = (\lambda - 1)/(1 + \xi)^\lambda$ with $\lambda = 3$, and $\nu = 0.01$, $D = d + (D_0 - d)e^{-\tau}$, $d = 0.46$, $D_0 = d/s_+ = 2.846436$, $V_0 = e^{-\xi}$, whence we compute $R = 1.322972$.

Clearly, the leading order approximation is singular at $D = 1$, and higher order terms are worse. This is a typical strained coordinate problem, and in Fig. 6 we have arbitrarily shifted the location of the singularity by $O(\nu)$ to improve the fit—this is a slight sham, since the improvement worsens at larger W.

An improved approximation results from using matched asymptotic expansions near $D = 1$, and the result of this is that a uniformly accurately leading order

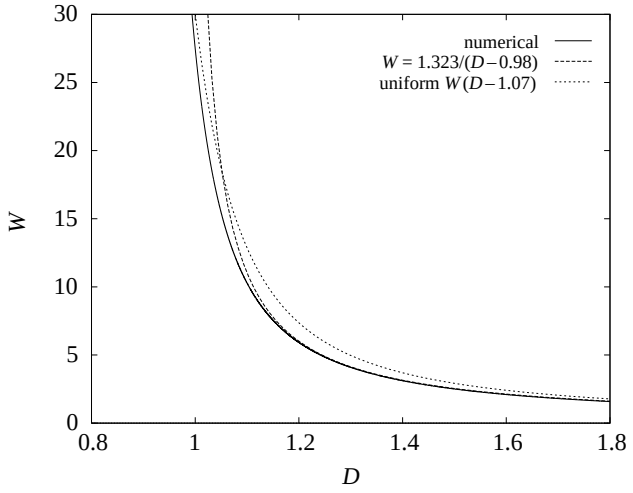

Figure 7. The same graphs as in Fig. 6, but in addition, the uniform approximation $W(D)$ based on (A19) but with an origin shift of 0.07 is shown. Note the different horizontal and vertical scales.

approximation is given by [for $D = d + (D_0 - d)e^{-\tau}$]

$$W \sim R\left[\frac{\pi}{2\nu f_0(1-d)}\right]^{1/2} \exp\left[\frac{(D-1)^2}{2f_0\nu(1-d)}\right] \operatorname{erfc}\left[\frac{D-1}{\{2f_0\nu(1-d)\}^{1/2}}\right]. \quad \text{(A19)}$$

In the singular region near $D = 1$, $W \sim 1/\nu^{1/2}$ and $\nu W' = O(1)$, so that $\nu W' \ll W$ and the basis of retaining only the $\nu f_0 W'$ term in (A17) is still valid. However, this basis is lost for higher values, when $\nu W' \sim W$. Figure 7 shows that the uniform approximation (A19) [arbitrarily shifted as $W(D - 1.07)$ rather than $W(D - 1)$] is an improvement over the $O(1)$ solution, but its error is $O(\nu^{1/2})$ [note the origin shift $0.07 = O(\nu^{1/2})$ here]. However, we believe these two figures indicate that the approximation is consistent with the numerical solution.

3. Approximations for $V_{\min}$. We use $V_{\min} = \min V(t)$ as a measure of the minimum in the infective population. In fact, (3.16) implies that $V(t) = u(0, t)$, i.e., the recruitment rate. When $\Lambda = 1$ (i.e., the exponential density $f = e^{-\xi}$), then (3.13) implies $u(0, t) \approx (s/d)\int_0^\infty u(\xi, t)\, d\xi = sq/d$, and since $V = V_{\min}$ when $s = d$, we see that $q_{\min} \approx V_{\min}$ in this case. Therefore $V_{\min}$ is a suitable quantity to study in the more general case.

When f has an exponential tail, (A7) indicates that $V \approx V_{\min}$ when $P' = 0$, and this is when $D = 1$. For the particular choice $f = e^{-\xi}$, we have

$$V_{\min} = c_1 \exp\left[\frac{1}{\nu}\left\{\left(\frac{1}{d} - 1\right)\ln\left(\frac{D_0 - d}{1-d}\right) - \frac{1}{d}\ln D_0\right\}\right], \quad \text{(A20)}$$

where the exact solution (A6) would suggest $c_1 = h_0$.

If f has an algebraic tail, $f \sim (\lambda - 1)/(1 + \xi)^{\lambda}$ as $\xi \to \infty$, we have

$$V \sim \frac{Rf(t)}{D - 1} \tag{A21}$$

for $D > 1$. This has a minimum when $D > 1$ (thus the approximation is valid), and we find

$$V_{\min} \approx \frac{c_3(\lambda - 1)R\nu^{\lambda}}{(D - 1)\tau^{\lambda}}, \tag{A22}$$

where, if $D = d + (D_0 - d)e^{-\tau}$, then R is given by (A18), and $\tau = \ln x$, where $x > 1$ is the unique positive root of

$$\ln x = \lambda(1 - \beta x), \tag{A23}$$

and $\beta = (1 - d)/(D_0 - d) < 1$, since $D_0 > 1 > d$. We allow a constant c_3 on the same basis that c_1 is included in (A20).

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