

## Parasite evolution and extinctions

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### Abstract

We examine the evolution of diseases that show the frequency-dependent transmission process that is commonly applied to sexually and vector-transmitted infections. As is commonly found, the basic reproductive ratio ( $R_0$ ) of the parasite is maximized by evolution. This has important implications, as it implies that for a wide range of circumstances diseases that show frequency-dependent transmission may be selected to evolve towards driving their hosts to extinction. This contrasts with the results obtained in spatially explicit models where although parasite-driven host extinction may occur, it is unlikely to evolve. We further show that an evolutionary constraint between transmission and virulence is required for evolution to lead to an endemic coexistence of both the host and the disease. Furthermore, this constraint needs to be saturating, such that transmission is 'bought' at an increasing cost in terms of virulence, to avoid evolution to extinction.

### Keywords

Extinction, frequency-dependent transmission, modelling, parasites, virulence.

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### INTRODUCTION

Pathogens have been implicated in a number of extinctions of their host including the extinction of the Thylacine, a carnivorous marsupial (McCallum & Dobson 1995), African wild dogs (Burrows *et al.* 1995) and some amphibian species (Daszak & Cunningham 1999). This possibility is clearly important to conservationists concerned with the protection of species with low population sizes as well as to researchers involved in the use of pathogens as biological control agents of pest species. The most commonly discussed mechanism by which pathogens may cause extinction is through the lowering of host population sizes to a point at which there is a high risk that stochastic events lead to extinction. Another important route to extinction is that pathogens may destabilize the host population leading to dramatic cycles in abundance that put the host population at low values for part of the cycle. Pathogens are also thought to be implicated in extinctions when two hosts share the pathogen: one of which is a large reservoir for the pathogen while the other is at a low density. In this case, a threatened population may be driven to extinction by constant seeding of the pathogen from the larger reservoir population (McCallum & Dobson 1995).

Recent work has shown that there is the possibility of deterministic pathogen-driven host extinction when we take into account the spatial structure of host populations. In this

case, the local density of susceptible individuals next to infected individuals may remain relatively high and positive even as the overall density of the host populations heads to zero (Sato *et al.* 1994; Haraguchi & Sasaki 2000). Parasite-driven host extinction can occur only when the pathogen has a significant effect on the reproduction of infected host individuals (Boots & Sasaki 2002). Classical theory on the evolution of virulence has shown that the number of secondary cases due to a single infected individual (the epidemiologically defined  $R_0$ ) is maximized in baseline models and therefore maximum transmission is selected for (Bremermann & Thieme 1989). However, once the spatial structure is included we find that  $R_0$  is no longer maximized by evolution and that we always get the evolution of a finite transmission rate (Rand *et al.* 1995; Haraguchi & Sasaki 2000). The transmission rate will usually evolve to a point just below where host extinction occurs (Boots & Sasaki 1999; Haraguchi & Sasaki 2000) and that therefore, although pathogens in spatially structured hosts may cause extinction, the evolutionarily stable (ES) transmission rate tends to be too low for this to occur.

Another established theoretical scenario in which pathogens may drive their hosts deterministically to extinction is when the transmission process depends on the frequency of infected hosts in the population rather than the density (Getz & Pickering 1983). This form of transmission is often proposed for sexually transmitted

diseases (STDs) where mating rate may be independent of density (Getz & Pickering 1983). The argument is that even at low population numbers, individuals still find each other to mate and therefore transmission of the disease is dependent on the frequency in the population. Frequency-dependent transmission has been suggested for some vector-borne diseases since a vector may efficiently search for its hosts, maintaining contacts even at low host populations. In fact, it has recently been suggested that parasites beyond just STDs and vector-borne diseases, such as cowpox virus in bank voles (Begon *et al.* 1999) and rabbit haemorrhagic disease (White *et al.* 2001), may also be transmitted in a manner more closely described by a frequency-dependent transmission term rather than a density-dependent one. As yet we know of no detailed discussion of the potential of STDs to evolve to cause extinction of their hosts. In the light of our results in spatially explicit host populations and because of the importance of frequency-transmitted diseases, we analyse a frequency-dependent host-parasite model and examine the evolutionary outcome. We show that  $R_0$  is maximized and that therefore, in contrast to parasite-driven extinction due to spatial structure, it is easy to find conditions under which evolution to host extinction occurs.

**ANALYSIS**

Consider the epidemiological dynamics of a host where there is no recovery from infection (an SI model) and assume that the probability that a susceptible host is infected within a particular time interval is proportional to the frequency, rather than the density, of the infected hosts. The density of susceptibles,  $X$ , and the infecteds,  $Y$ , would then change as

$$\dot{X} = (r - bN)X - \beta X \frac{Y}{N}, \tag{1a}$$

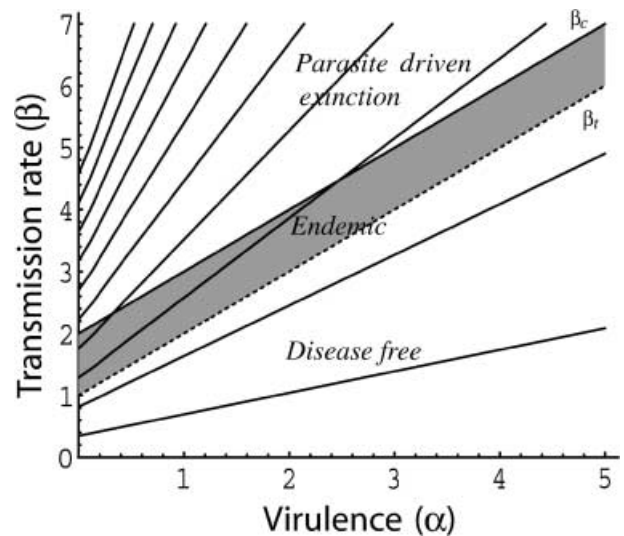
$$\dot{Y} = \beta X \frac{Y}{N} - \nu Y, \tag{1b}$$

where  $N = X + Y$  is the total host density,  $r = b - u$  is the intrinsic net growth rate of the host where  $b$  and  $u$  are, respectively, the birth rate and natural mortality of the host,  $\nu = u + \alpha$  is the mortality of an infected where  $\alpha$  is the additional mortality by infection (virulence),  $\beta$  is the infection rate and  $b$  is the coefficient of density-dependent regulation of the host (the carrying capacity in the disease-free population is therefore  $K = r/b$ ). We assume that the infection sterilizes the host, and that an infected host consumes resources at the same rate as the susceptible ones. If we plot the regions for the disease-free, the endemic, and the pathogen-driven host extinction in the parameter space of the pathogenicity  $\alpha$  and the transmission rate  $\beta$ , they are divided by two parallel lines:  $\beta = u + \alpha$  and  $\beta = b + \alpha$  (Figs 1 and 2) (see appendix for the analysis).

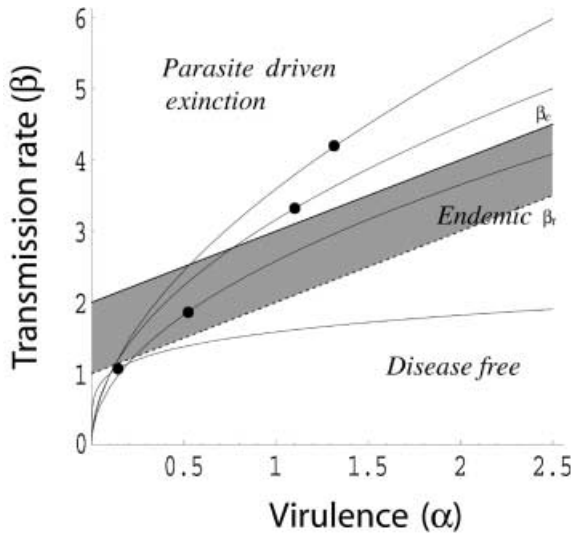
The analysis given in the appendix shows that the basic reproductive ratio of the parasite is maximized by evolution. Therefore, the relationship between the transmission rate  $\beta$  and the pathogenicity  $\alpha$  determines the course of virulence evolution and its consequence on the demography. We exemplify the effect of the trade-off by contrasting two cases:

- (i) Assume that there is no trade-off between  $\beta$  and  $\alpha$ . If the pathogenicity  $\alpha$  is fixed, the transmission rate  $\beta$  is evolutionarily escalated without limit. This evolutionary change, therefore, always leads to host extinction. Similarly, if the transmission rate is fixed at a positive value, the pathogenicity decreases without limit, and this can again lead to the host extinction if the fixed transmission rate is larger than the host birth rate  $b$  (see Fig. 1).
- (ii) Assume now that the pathogenicity  $\alpha$  and the transmission rate is constrained as  $\alpha = c\beta^n$ , where  $c$  is a positive constant and  $n > 1$ . The ES virulence under the trade-off is to maximize the basic reproductive ratio  $R_0 = \beta/(u + \alpha) = c^{-1/n}\alpha^{1/n}/(u + \alpha)$ , from which the ES virulence is obtained as

$$\alpha^* = u/(n - 1). \tag{2}$$



**Figure 1** Regions in transmission ( $\beta$ ) and virulence ( $\alpha$ ) parameter space where we have disease-free, endemic (shaded) and parasite-driven extinction (PDE). The lines represent a number of possible linear trade-offs between transmission and virulence. The ESS is always maximal  $\beta$  and  $\alpha$  and is therefore at the extreme right of each of the lines. The natural birth rate is 2 while the natural death rate is 1.



**Figure 2** Regions in transmission ( $\beta$ ) and virulence ( $\alpha$ ) parameter space where we have disease-free, endemic (shaded) and parasite-driven extinction (PDE). The lines represent a saturating trade-off function between  $\beta$  and  $\alpha$ , with the finite ESS marked as a dot. The ESS may therefore be found in each of the regions.

At the ES virulence, the transmission rate is  $\beta^* = (\alpha^*/c)^{1/n} = (u/c(n-1))^{1/n}$ . The ES virulence/transmission rate is in the region of stable endemic equilibrium if

$$b - u < \beta^* < b + \alpha^*, \tag{3}$$

but the evolution of the transmission rate and virulence leads to the host extinction if

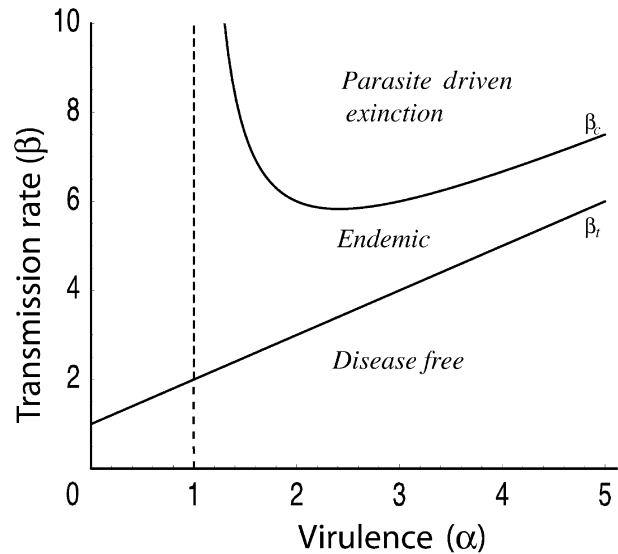
$$\beta^* > b + \alpha^*. \tag{4}$$

The latter condition can be rewritten as

$$c < \frac{1}{(n-1)u^{n-1}} \left( \frac{b}{u} + \frac{1}{n-1} \right)^{-n}. \tag{5}$$

Thus, if the pathogenicity  $\alpha$  increases slowly in a trade-off with the increase of transmission rate (i.e. for sufficiently small  $c$ ), the ES transmission rate and virulence lie in the region for the pathogen-driven extinction (Fig. 2).

When the infected host can reproduce with the same birth rate as the susceptibles, the phase diagram is changed as illustrated in Fig. 3 (see appendix). There are two threshold transmission rates,  $\beta_r$  and  $\beta_c$ , that divide the equilibrium state of the dynamics in the parameter space of the transmission rate  $\beta$  and the pathogenicity  $\alpha$  into three regions. The disease-free and the endemic regions are divided by the first threshold,  $\beta_r = u + \alpha$  such that  $\beta > \beta_r$  is required for the invasion of the pathogen. Host extinction due to a non-sterilizing parasite occurs when the parasite is both very harmful and transmissible, i.e. when  $\alpha > r$  and



**Figure 3** Regions in transmission ( $\beta$ ) and virulence ( $\alpha$ ) parameter space where the infected individuals are able to reproduce. The PDE region is more restricted. The trade-off functions in Figs 1 and 2 can be mapped onto this different set of predicted outcomes.

$\beta > \beta_c = \alpha(u + \alpha)/(\alpha - r)$ . The invasibility criteria of a mutant pathogen are the same as in the previous section: the mutant can invade if and only if it has a large basic reproductive ratio. Therefore, the effect of pathogen evolution on the demography (particularly on the host extinction) is completely analogous to the one discussed in the previous section – only the phase diagram for the demographic equilibrium is replaced from Figs 1 and 2 to Fig. 3.

**DISCUSSION**

With frequency-dependent transmission, when there is no constraint between transmission and virulence, we would expect the evolution of maximal transmission and minimum virulence. Our results suggest that if a parasite can increase transmissibility without increasing the host mortality (or even if this dependence is weak), it would wipe its host and therefore itself out. When the transmission of the parasite is density dependent, the evolution of maximal transmission will tend to cause instability in the host population dynamics, increasing the risk of stochastic extinction. However, such population instability will often lead to the stochastic fade-out of the pathogen, leaving the disease-free host population. Virulence is often thought to be a by-product of transmission as an increased production of infective stages may damage host tissues (see Lipsitch & Moxon 1997; Mackinnon & Read 1999) and therefore in reality transmission may not be bought without a substantial

cost in terms of virulence. However, we only find a finite virulence and transmission when there is a saturating relationship between the two (as shown in Fig. 2). Without this relationship – where higher transmission becomes increasingly costly in terms of increased virulence – we will again tend to get the evolution to parasite-driven host extinction and it may therefore follow that the persisting STDs seen in nature will tend to show this form of constraint (Mackinnon & Read 1999) and it may therefore follow that the persisting STDs seen in nature will tend to show this form of constraint. Even when we do have this saturating relationship there is still the possibility of the evolution to extinction (see Fig. 2) as the finite ES transmission rate lies within the extinction region. Therefore, independently of the form of the relationship between transmission and virulence, there is always the possibility of evolution to extinction when transmission is frequency dependent.

There is an important contrast between the results presented here and those found with the host population spatial structure. In both cases there is the possibility of pathogen-driven host extinction, but they do not come about due to the same process. In the case of spatial models, there is a need for the parasite to substantially reduce the host's reproduction (Boots & Sasaki 2002), whereas in frequency-dependent parasites, extinction may still occur even if the infected individuals reproduce at exactly the same rate as the susceptible individuals (Fig. 3). The other important contrast is in the evolution of the parasite. In the spatial case, evolution can head to the boundary between endemic coexistence and parasite-driven extinction (Haraguchi & Sasaki 2000). In contrast to the frequency-dependent case, we have shown that evolution may easily lead to extinction. This again makes it clear that there are distinct processes involved in the spatial models and the frequency-dependent models.

The simple characterization of diseases into those with density-dependent transmission, on the one hand, and frequency-dependent transmission, on the other hand, is perhaps unrealistic. At very low densities, the pure frequency dependence may sometimes break down since individuals may have difficulty in finding mates. However, in many of these cases, this process will not stop the population becoming extinct as the low population sizes that cause the frequency dependence to break down also lead to a high risk of stochastic extinction. Indeed, it seems likely that frequency-dependent and density-dependent transmissions are at two ends of a continuum of transmission types (Antonovics *et al.* 1995; McCallum 2000). Furthermore, the pattern of transmission is likely to shift along this continuum according to the combination of densities studied and the scale of the observation (Fromont *et al.* 1998). Specific formalizations of the transmission

process will lead to different chances of parasite-driven extinction and therefore different risks of the evolution to extinction. This work emphasizes, however, that since  $R_0$  is maximized in both the density- and frequency-dependent cases, when PDE regions exist, there is the possibility of evolution to extinction independently of the relationship of the constraint between transmission and virulence.

## REFERENCES

- Antonovics, J., Iwasa, Y. & Hassell, M.P. (1995). A generalized model of parasitoid, venereal, and vector-based transmission processes. *Am. Nat.*, 145, 661–675.
- Begon, M., Hazel, S.M., Baxby, D., Bown, K., Cavanagh, R., Chantrey, J. *et al.* (1999). Transmission dynamics of a zoonotic pathogen within and between wildlife host species. *Proc. R. Soc. Lond. B*, 266, 1939–1945.
- Boots, M. & Sasaki, A. (1999). 'Small worlds' and the evolution of virulence: infection occurs locally and at a distance. *Proc. R. Soc. Lond. B*, 266, 1933–1938.
- Boots, M. & Sasaki, A. (2002). Parasite-driven extinction in spatially explicit host–parasite systems. *Am. Nat.*, 159, 706–713.
- Bremermann, H.J. & Thieme, H.R. (1989). A competitive-exclusion principle for pathogen virulence. *J. Math. Biol.*, 27, 179–190.
- Burrows, R., Hofer, H. & East, M.L. (1995). Population-dynamics, intervention and survival in African wild dogs (*Lycaon-Pictus*). *Proc. R. Soc. Lond. B*, 262, 235–245.
- Daszak, P. & Cunningham, A.A. (1999). Extinction by infection. *Trends Ecol. Evol.*, 14, 279.
- Fromont, E., Pontier, D. & Langlais, M. (1998). Dynamics of a feline retrovirus (FeLV) in host populations with variable spatial structure. *Proc. R. Soc. Lond. B*, 265, 1097–1104.
- Getz, W.M. & Pickering, J. (1983). Epidemic models – thresholds and population regulation. *Am. Nat.*, 121, 892–898.
- Haraguchi, Y. & Sasaki, A. (2000). The evolution of parasite virulence and transmission rate in a spatially structured population. *J. Theor. Biol.*, 203, 85–96.
- Lipsitch, M. & Moxon, E.R. (1997). Virulence and transmissibility of pathogens: what is the relationship? *Trends Microbiol.*, 5, 31–37.
- Lipsitch, M., Siller, S. & Nowak, M.A. (1996). The evolution of virulence in pathogens with vertical and horizontal transmission. *Evolution*, 50, 1729–1741.
- Mackinnon, M.J. & Read, A.F. (1999). Genetic relationships between parasite virulence and transmission in the rodent malaria *Plasmodium chabaudi*. *Evolution*, 53, 689–703.
- McCallum, H. (2000). Achievement and challenge. *Trends Ecol. Evol.*, 15, 352–353.
- McCallum, H. & Dobson, A. (1995). Detecting disease and parasite threats to endangered species and ecosystems. *Trends Ecol. Evol.*, 10, 190–194.
- Rand, D.A., Keeling, M. & Wilson, H.B. (1995). Invasion, stability and evolution to criticality in spatially extended, artificial host–pathogen ecologies. *Proc. R. Soc. Lond. B*, 259, 55–63.
- Sato, K., Matsuda, H. & Sasaki, A. (1994). Pathogen invasion and host extinction in lattice structured populations. *J. Math. Biol.*, 32, 251–268.

White, P.J., Norman, R.A., Trout, R.C., Gould, E.A. & Hudson, P.J. (2001). The emergence of rabbit haemorrhagic disease: will a non-pathogenic strain protect the UK? *Phil. Trans. R. Soc. Lond. B*, 356, 1087–1095.

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**APPENDIX**

To analyse the dynamics of eqn 5, it is convenient to transform variables to the total host density  $N = X + Y$  and the fraction of infected host in the population,  $p = Y/N$ . System 5 is then rewritten as

$$\dot{N} = [(r - bN)(1 - p) - vp]N, \tag{A1a}$$

$$\dot{p} = p(1 - p)[\beta - v - r + bN]. \tag{A1b}$$

There are four equilibria:

$$E_0 : (N, p) = (0, 0), \text{ trivial solution} \tag{A2a}$$

$$E_1 : (N, p) = (0, 1), \text{ parasite-driven extinction} \tag{A2b}$$

$$E_2 : (N, p) = (K, 0), \text{ disease-free equilibrium} \tag{A2c}$$

$$E_3 : (N, p) = ((r + v - \beta)/b, 1 - v/\beta), \tag{A2d}$$

endemic equilibrium

By assuming a positive intrinsic growth rate of host ( $r > 0$ ), the trivial solution is always unstable. We here examine the local stability of the four equilibria (defined in eqn A2) of the dynamics (3). We assume that  $r = b - u > 0$  in the following:

- (i) The Jacobian at the trivial equilibrium  $E_0 : (N, p) = (0, 0)$  is

$$J = \begin{pmatrix} r & 0 \\ 0 & \beta - (v + r) \end{pmatrix}, \tag{A3}$$

and hence  $E_0$  is always unstable because  $r > 0$ .

- (ii) The Jacobian at the pathogen-driven extinction equilibrium  $E_1 : (N, p) = (0, 1)$  is

$$J = \begin{pmatrix} -v & 0 \\ 0 & (v + r) - \beta \end{pmatrix}, \tag{A4}$$

thus  $E_1$  is locally stable if and only if  $\beta > r + v = b + \alpha$ .

- (iii) The Jacobian at the disease-free equilibrium  $E_2 : (N, p) = (K, 0)$  is

$$J = \begin{pmatrix} -bK & -vK \\ 0 & \beta - v \end{pmatrix}, \tag{A5}$$

thus  $E_2$  is locally stable if  $\beta < v = u + \alpha$ .

- (iv) Finally, we examine the local stability of the endemic equilibrium  $E_3 : (N, p) = (\hat{N}, \hat{p})$  with  $\hat{N} = (r + v - \beta)/b$  and  $\hat{p} = (1 - v)/\beta$ . We first see that the endemic equilibrium exists in the feasible region  $\hat{N} > 0$  and  $0 < \hat{p} < 1$ , if and only if

$$u + \alpha < \beta < b + \alpha. \tag{A6}$$

The Jacobian at the endemic equilibrium  $E_3$  is

$$J = \begin{pmatrix} -b\hat{N}(1 - \hat{p}) & -\beta\hat{N} \\ b\hat{p}(1 - \hat{p}) & 0 \end{pmatrix}, \tag{A7}$$

Because the trace is always negative,  $\text{tr}(J) = -b\hat{N}(1 - \hat{p}) < 0$ , and the determinant is positive,  $\det(J) = \beta b\hat{N}\hat{p}(1 - \hat{p}) > 0$ , we conclude that the endemic equilibrium  $E_3$  is always locally stable when the internal equilibrium exists (whose condition is given by eqn A6).

We can summarize the results for the local stabilities of the four equilibria as the transmission rate varies as

1. If the transmission rate is lower than the mortality of an infected,  $\beta < v$ , the disease-free equilibrium is locally stable.
2. If the transmission rate is intermediate,  $v < \beta < r + v$ , the endemic equilibrium is locally stable.
3. If the transmission rate is larger than the second threshold,  $\beta > r + v$ , the pathogen-driven extinction equilibrium is locally stable.

Note that the two threshold transmission rates,  $v$  and  $r + v$ , can be expressed in terms of the host birth rate  $b$ , the natural death rate  $u$ , and the pathogenicity  $\alpha$  as  $v = u + \alpha$  and  $r + v = b + \alpha$ .

Next, we analyse the invasibility of a mutant pathogen in the population where the resident pathogen strain is at an endemic equilibrium. Let  $\beta'$  and  $v'$  be the transmission rate and the mortality of an infected mutant-strain, respectively. The densities of susceptibles,  $X$ , the resident strain infecteds,  $Y$ , and the mutant-strain infecteds,  $Z$ , change as

$$\dot{X} = (r - bN)X - \beta XY/N - \beta' XZ/N, \tag{A8a}$$

$$\dot{Y} = \beta XY/N - vY, \tag{A8b}$$

$$\dot{Z} = \beta' XZ/N - v'Z, \tag{A8c}$$

where  $N = X + Y + Z$ . If the initial density of mutant strain is sufficiently small, we can linearize the dynamics for  $Z$  as

$$\dot{Z} = [\beta' \hat{X} / \hat{N} - v']Z, \tag{A9}$$

where  $\hat{X} = \hat{N}(1 - \hat{p}) = \hat{N}v/\beta$  is the equilibrium density of the susceptible host in the population endemic with the resident strain, and  $\hat{N} = (u + \alpha - \beta)/b$  is the equilibrium total host density in the same population. Therefore, the mutant can increase when rare if and only if

$\beta'v/\beta - v' > 0$ , or

$$\frac{\beta'}{v'} > \frac{\beta}{v}. \quad (\text{A10})$$

This implies that the basic reproductive ratio  $R_0 = \beta/(u + \alpha)$  is maximized through evolution.

We have assumed above that the infection sterilizes the host, but here we examine the case where the infected host can reproduce just as efficiently as a susceptible. The density of susceptibles,  $X$ , and the infecteds,  $Y$ , would then change as

$$\dot{X} = (b - bN)N - uX - \beta X \frac{Y}{N}, \quad (\text{A11a})$$

$$\dot{Y} = \beta X \frac{Y}{N} - (u + \alpha)Y, \quad (\text{A11b})$$

where  $N = X + Y$  is the total host density,  $b$  and  $u$  are the birth rate and the natural mortality of the host, respectively,  $\alpha$  is the additional mortality by infection (virulence),  $\beta$  is the infection rate, and  $b$  is the coefficient of density-dependent regulation in the host.

As in the case examined in the text, we transform variables to the total host density  $N = X + Y$  and the fraction of infected host in the population,  $p = Y/N$ . The system (A11) is then rewritten as

$$\dot{N} = [(r - bN) - \alpha p]N, \quad (\text{A12a})$$

$$\dot{p} = p[(\beta - \alpha)(1 - p) - (b - bN)], \quad (\text{A12b})$$

where we define  $r = b - u$  be the intrinsic net growth rate of the host and  $K = r/b$  be the carrying capacity in the disease-free population, as described in the text. There are four equilibria in the dynamics (A12):

$E_0 : (N, p) = (0, 0)$ , trivial solution

$E_1 : (N, p) = (0, 1 - b/(\beta - \alpha))$ , parasite-driven extinction

$E_2 : (N, p) = (K, 0)$ , disease-free equilibrium

$E_3 : (N, p) = \left( \frac{\alpha}{b} \left[ \left( \frac{r}{\alpha} - 1 \right) + \frac{u + \alpha}{\beta} \right], 1 - \frac{u + \alpha}{\beta} \right)$ , endemic equilibrium

The derivatives of the flow (A12) at a point  $(N, p)$  is, by setting  $\dot{N} = F(N, p)$ ,  $\dot{p} = G(N, p)$ :

$$\frac{\partial F}{\partial N} = [(r - bN) - \alpha p] - bN, \quad \frac{\partial F}{\partial p} = -\alpha N,$$

$$\frac{\partial G}{\partial N} = bp, \quad \frac{\partial G}{\partial p} = [(\beta - \alpha)(1 - p) - (b - bN)] - (\beta - \alpha)p.$$

In the following, we assume that  $b > u$ :

- (i) The Jacobian at the trivial equilibrium  $E_0 : (N, p) = (0, 0)$  is

$$J = \begin{pmatrix} r & 0 \\ 0 & \beta - \alpha - b \end{pmatrix}. \quad (\text{A13})$$

Because we assume that  $r = b - u > 0$ , the trivial equilibrium  $E_0$  is always unstable.

- (ii) The Jacobian at the pathogen-driven extinction equilibrium  $E_1 : (N, p) = (0, \hat{p}_e)$  where  $\hat{p}_e = 1 - b/(\beta - \alpha)$  is

$$J = \begin{pmatrix} r - \alpha \hat{p}_e & 0 \\ b \hat{p}_e & -(\beta - \alpha) \hat{p}_e \end{pmatrix}, \quad (\text{A14})$$

The pathogen-driven extinction equilibrium  $E_1$  exists if  $\beta > b + \alpha$  (by which  $0 < \hat{p}_e < 1$  holds). Under this condition, the stability of equilibrium  $E_1$  is determined by the sign of the eigenvalue:  $r - \alpha \hat{p}_e < 0$ , or

$$\beta > \frac{\alpha(u + \alpha)}{\alpha - r} \equiv \beta_l. \quad (\text{A15})$$

- (iii) The Jacobian at the disease-free equilibrium  $E_2 : (N, p) = (K, 0)$ , where  $K = r/b$ , is

$$J = \begin{pmatrix} -r & -\alpha r/b \\ 0 & \beta - (u + \alpha) \end{pmatrix}. \quad (\text{A16})$$

Thus, the disease-free equilibrium is stable if and only if

$$\beta < u + \alpha \equiv \beta_c. \quad (\text{A17})$$

- (iv) Finally, we examine the stability of the endemic equilibrium  $E_3 : (N, p) = (\hat{N}, \hat{p})$ , where  $\hat{N} = (\alpha/b)[(r/\alpha - 1) + (u + \alpha)/\beta]$  and  $\hat{p} = 1 - (u + \alpha)/\beta$ . We first see that such an endemic equilibrium exists in the feasible region (i.e.  $\hat{N} > 0$  and  $0 < \hat{p} < 1$ ) if the transmission rate lies in between the two thresholds defined above (eqns A15 and A17):

$$\beta_l < \beta < \beta_c. \quad (\text{A18})$$

The Jacobian at the endemic equilibrium  $E_3$  is expressed as

$$J = \begin{pmatrix} -b\hat{N} & -\alpha\hat{N} \\ b\hat{p} & -(\beta - \alpha)\hat{p} \end{pmatrix}. \quad (\text{A19})$$

Because the trace is always negative,  $\text{tr}(J) = -b\hat{N} - (\beta - \alpha)\hat{p} < 0$ , and the determinant is positive,  $\det(J) = \beta b \hat{N} \hat{p} > 0$ , if  $\hat{N}$  and  $\hat{p}$  exist in the feasible region (i.e. if eqn A18 is satisfied), the endemic equilibrium is locally stable. Thus, the local stability condition for the endemic equilibrium is given by eqn A18.

Therefore, we have shown that:

1. If the transmission rate is smaller than  $\beta_s$ , the pathogen cannot invade the susceptible population (disease-free region).
2. If the transmission rate is in between two thresholds,  $\beta_l < \beta < \beta_s$ , the pathogen is maintained in the locally stable endemic equilibrium (endemic region).
3. If the transmission rate is larger than  $\beta_s$ , the host population is driven to extinction by the spread of pathogen (pathogen-driven extinction region).

When the parameters are in the pathogen-driven extinction region, the fraction  $p$  of infected host approaches a positive constant,  $\hat{p}_e = 1 - b/(\beta - \alpha)$ , while the total host density  $N$  converges to zero.