The basic depression ratio of the host: the evolution of host resistance to microparasites

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The basic reproduction ratio R_0 occupies a central position in the theory of host–pathogen interactions. However, this quantity stresses the role of the pathogen. This paper proposes an additional, more host-centred characterization using the basic depression ratio D_0 . This quantity is the number of host individuals per infected by which the infected host population is depressed below its uninfected level. This paper shows that a baseline criterion for the evolution of host resistance to microparasites is that resistance evolves to minimize D_0 . This parallels the result for pathogen virulence where R_0 is maximized. The tension between these two criteria is noted. The framework established allows a discussion of trade-offs between aspects of the pathogen-free host biology and the host–pathogen interaction. For certain linear and convex trade-offs it is shown that the strain with the lowest transmission parameter β wins (despite the fact that it has the lowest intrinsic birth rate a). For corresponding concave trade-offs, either the strain with minimum β and a or the strain with maximum β and a wins. Finally, the connection with the techniques of adaptive dynamics is made. Evolutionary singular points are shown to occur at extrema of D_0 . The evolutionary attainment of the results is discussed.

Keywords: host–pathogen interaction; basic reproduction ratio; basic depression ratio; host resistance; trade-offs; adaptive dynamics

1. INTRODUCTION

The pivotal position occupied by the basic reproduction ratio R_0 in the theory of host–pathogen interactions (see, for example, MacDonald 1952; Dietz 1976; Yorke *et al.* 1979; Anderson & May 1982; Diekmann *et al.* 1990) is well known. However, this quantity, which is the expected number of secondary cases per primary in a totally susceptible population, tends to stress the role of the pathogen in the interaction. This is particularly so in the context emphasized by Anderson & May (1981) where the pathogen significantly impacts on host numbers. In this context, an additional characterization of the interaction which is more host centred might be expected. We propose that the basic depression ratio D_0 of the host fulfils this task. This dimensionless quantity is defined as the number of host individuals per infected by which the infected host population is depressed below its uninfected level. Thus,

$$D_0 = \frac{K - (X^* + I^*)}{I^*}, \quad (1)$$

where K is the carrying capacity of the host and X^* and I^* are the numbers of susceptible and infected individuals in the infected state, respectively. (It is easy to modify the numerator in order to accommodate extra categories such as latent or immune individuals.)

The basic reproduction ratio plays a central role in the baseline criterion for the evolution of pathogen virulence. In the simplest models (Bremermann & Thieme 1989) of competition between many strains of microparasite within a single host population the strain with maximum R_0 out-competes all others. Thus, pathogen virulence can be regarded as evolving so as to maximize the basic reproductive ratio. Our purpose here is to provide a

complementary picture for the evolution of host resistance. The reader will not be surprised to learn that the basic depression ratio appears in a fundamental way in the baseline criterion which emerges below.

2. THE MODEL

We consider n strains of a haploid host interacting with a directly transmitted microparasite. We denote the densities of susceptible and infected individuals of the h th strain by X_h and I_h , respectively. (For simplicity we ignore latency, immunity, etc.) We note that the baseline criterion (maximum R_0) for the evolution of pathogen virulence corresponds to the sharing of many pathogen strains by a single host population in a manner which involves only the minimum degree of interstrain interaction, namely that implied by such sharing.

Thus, in order to derive a baseline criterion for the evolution of host resistance, we use a multihost strain model in which the interactions between the strains are again as simple as possible. Accordingly, the force of infection on individuals of each host strain type is taken to be proportional to the total density $I = \sum I_h$ of infected individuals of all strains; similarly, for the force of competition, the total density of hosts $H = \sum (X_h + I_h)$ is used. (All summations are over all h from 1 to n .) To specify the dynamics it then suffices to describe the behaviour of a single strain, which we take to be the h th. Using a structure based ultimately on the host–pathogen models of Anderson & May (1981) and assuming that density dependence acts only on the birth rate and that infected individuals do not reproduce (Antonovics & Thrall 1994; Bowers *et al.* 1994), we then have

$$dX_h/dt = r_h X_h (1 - H/K) - \beta_h X_h I + \gamma_h I_h \quad (2)$$

and

$$dY_h/dt = \beta_h X_h Y - \Gamma_h Y_h. \quad (3)$$

Here, the strain-dependent quantities r_h , β_h and γ_h are the intrinsic growth rate, the transmission coefficient and the recovery rate, respectively. In addition, the strain-dependent loss rate is $\Gamma_h = \alpha_h + b_h + \gamma_h$, where α_h and b_h are the pathogenicity and intrinsic death rate of the h th strain, respectively. Finally, K is the carrying capacity which we take to be a strain-independent property of the host.

3. EQUILIBRIA

There are three possible types of equilibrium solution to our system of equations (see Appendix A for details). The first of these is the origin and second solutions satisfying

$$H = K, Y_h = 0 \text{ for all } h. \quad (4)$$

Solutions of this second type correspond to the host population uninfected at its carrying capacity K . Since all strains have the same carrying capacity, as expected the strain composition of equation (4) is undetermined. There are n equilibria of the final type, one for each h between 1 and n . They take the forms

$$X_h = X_h^* = H_{T,h} = \Gamma_h / \beta_h, \quad (5)$$

$$Y_h = Y_h^* = (K - H_{T,h}) / (1 + (\beta_h K / r_h)(1 - \gamma_h / \Gamma_h)) \quad (6)$$

and

$$X_k = Y_k = 0 \text{ for all } k \neq h, \quad (7)$$

and correspond to the particular host strain being alone with the pathogen provided that the threshold density $H_{T,h} < K$. (Otherwise the density at equation (6) is not feasible or the state is not distinct from equation (4).)

4. STABILITY AND INVASION BY ALTERNATIVE HOST STRAINS

We focus attention on the case where the n host strains each satisfy $H_{T,h} < K$ which means that each would support the pathogen in the absence of the other strains (see Appendix A). More complicated situations can be analysed but these only tend to add details which detract from the clarity of the overall message. So we have n possible feasible states with densities given by equations (5)–(7). The question is, which of these actually occurs in the presence of the pathogen? We answer this in the main text by establishing biologically motivated invadability criteria (Bowers & Turner 1997). A standard stability treatment using the Jacobian method is relegated to Appendix A.

Consider an attempted invasion by a strain k of a resident strain h characterized by the densities X_h^* and Y_h^* of equations (5) and (6). We need to find the average increase in the strain k population per invader. Only if this is positive will the invasion prosper. Take the invader to be uninfected and suppose it remains so for an average time T_X and becomes infected for an average time T_Y .

During the first of these periods the average rate of increase per capita is

$$\rho_X = r_k(1 - (X_h^* + Y_h^*)/K). \quad (8)$$

During the second, since infecteds do not reproduce, the rate is

$$\rho_Y = -b_k - \alpha_k. \quad (9)$$

On average the number of offspring per invader represents a population increase of

$$I_{kh} = \rho_X T_X + \rho_Y T_Y \quad (10)$$

individuals. Now the first of the times in equation (10) is determined directly by the rates of death and infection; indeed

$$T_X = 1/(b_k + \beta_k Y_h^*). \quad (11)$$

It remains to find T_Y . The probability of our invader dying while uninfected is $b_k T_X$ and the probability of such an individual dying or recovering while infected is $\Gamma_k T_Y$. Since this exhausts the possibilities, these two terms must sum to unity. Using this result and equation (11), we find

$$T_Y = \frac{\beta_k Y_h^*}{\Gamma_k(b_k + \beta_k Y_h^*)}. \quad (12)$$

Using equations (8), (9), (11) and (12) in equation (10), after a little manipulation, gives

$$I_{kh} = \frac{r_k Y_h^*}{(b_k + \beta_k Y_h^*)K} \left(\frac{(K - (X_h^* + Y_h^*))}{Y_h^*} - \frac{\beta_k K}{r_k \Gamma_k} (b_k + \alpha_k) \right). \quad (13)$$

Since, by the nature of equilibrium, $I_{hh} = 0$, it follows from equation (13) that

$$D_{0,h} = \frac{K - (X_h^* + Y_h^*)}{Y_h^*} = \frac{\beta_h K}{r_h \Gamma_h} (b_h + \alpha_h), \quad (14)$$

which, from equation (1), is the basic depression ratio of the h th strain.

Using equation (14) we can rewrite equation (13) in the particularly transparent form

$$I_{kh} = \frac{r_k Y_h^*}{(b_k + \beta_k Y_h^*)K} (D_{0,h} - D_{0,k}). \quad (15)$$

Equation (15) tells us that the strain h resists invasion by all other strains k essentially if and only if it is the strain with the minimum value of the basic depression ratio D_0 . (Since, then, $I_{kh} < 0$ for all k .) Correspondingly, any other strain k will be invadable by at least the minimizing strain h (since $I_{hk} > 0$). Thus, we expect the strain with minimum D_0 to occur stably at the densities given by equations (5) and (6) and all the other strains to be excluded. We should stress that it is proved by the standard Jacobian method that this expectation is actually true in Appendix A. The strain which has minimum D_0 and which is non-invadable but which can invade all others is indeed the winner in the community dynamics.

Two features which complicate the above invadability analysis but which do not lead to different results are, first, invasion by infecteds rather than susceptibles and, second, a non-zero rate of recovery. (We implicitly

Figure 1. The dynamics of two strains for which, although $1 < R_{0,1} < R_{0,2}$, since $D_{0,2} < D_{0,1}$ the outcome is strain 2 alone with the pathogen. X_1 , dashed line; Y_1 , dotted line; X_2 , dotted–dashed line; Y_2 , dotted–dotted–dashed line. The parameter values are $K = 10$, $r_1 = 1.0$, $\beta_1 = 0.1$, $\gamma_1 = 0.1$, $\Gamma_1 = 0.5$, $r_2 = 1.0$, $\beta_2 = 0.2$, $\gamma_2 = 0.2$ and $\Gamma_2 = 0.6$.

assumed that there was no recovery so as to avoid considering successive periods of susceptibility and infection.) We show how to handle these features in Appendix A.

5. DISCUSSION

In this section we take up three points. First, we consider the tension between the tendency to maximize R_0 (pathogen) and minimize D_0 (host). Second, we investigate the consequences for community dynamics of the existence of trade-offs between aspects of host–parasite interactions and general pathogen-free biology. The importance of such trade-offs has been emphasized in several recent papers (Antonovics & Thrall 1994; Bowers *et al.* 1994; Boots & Haraguchi 1999). Third, we develop this last point beyond community dynamics so as to make contact with the evolutionary approach of adaptive dynamics (Metz *et al.* 1996; Geritz *et al.* 1997). The first of these points was discussed in a restricted fashion in a previous paper (Bowers 1999), whereas the second and third were not. This restriction and these omissions were a consequence of two major flaws in this previous work. It failed to introduce the pivotal concept of the basic depression ratio of the host. It also failed to allow variability in the disease-free properties of the strains—the intrinsic growth rate r_h varies here—and this prevented discussion of the important trade-offs introduced above. The present paper removes both these limitations.

To begin, let us rewrite equation (14) in terms of underlying parameters by introducing the intrinsic per-capita birth rate a . This gives

$$D_{0,h} = \frac{\beta_h K (\alpha_h + b_h)}{(a_h - b_h)(\alpha_h + b_h + \gamma_h)}. \quad (16)$$

It is instructive to rewrite the basic depression ratio of the host (equation (16)) in a fashion which reveals its relationship with the basic reproduction ratio of the pathogen $R_0 = \beta K / (\alpha + b + \gamma)$. We find dropping subscripts that

$$D_0 = \frac{R_0(\alpha + b)}{(a - b)}. \quad (17)$$

This expression displays the tension between the two criteria of maximizing R_0 (pathogen) and minimizing D_0 (host). In the special case where α , a and b do not vary with strain, the winning host strain is that in which the fixed pathogen has the minimum basic reproduction ratio. Thus, in this case, the evolution of resistance in a variable host faced with a fixed microparasite leads to completely the opposite baseline criterion to that which characterizes the evolution of virulence in a variable microparasite faced with a fixed host. In the general case, the winning strain is that which minimizes $R_0(\alpha + b)/(a - b)$ not just R_0 . (Figure 1 provides an illustration of a two-strain case in which, although $R_{0,1} < R_{0,2}$ strain 2 wins since $R_{0,2}(\alpha_2 + b_2)/(a_2 - b_2) < R_{0,1}(\alpha_1 + b_1)/(a_1 - b_1)$.) However, even in this general case there is a broad tension between the two conditions for host and parasite which should inform our thinking about coevolution.

We now leave this tension aside and discuss our results in their own right. If one assumes the parameters in equation (16) can be varied independently (subject of

Figure 2. The dynamics of five strains subject to a linear trade-off $a = \beta + 2$. X_1 , dashed line; Y_1 , dotted line. The parameter values are $K = 10$, $b = 1.0$, $\gamma = 0.1$, $\alpha = 4.0$, $r_2 = 1.0$, $\beta_1 = 2.0$, $\beta_2 = 4.0$, $\beta_3 = 5.0$, $\beta_4 = 6.0$ and $\beta_5 = 7.0$. Strain 1, having minimum β and a , survives infected and excludes all others.

course to the constraint $H_{T,b} < K$ which ensures each strain can support the pathogen), then the minimizing principle suggests that winning host strains will tend to have low transmission β , high birth rate a , high recovery γ , low pathogenicity α and low intrinsic death rate b . All these results are not unexpected but it is nice to have quantified theoretical justification for them. What is much more important is the behaviour that results when there is a trade-off such as

$$a = f(\beta) \text{ with } f'(\beta) > 0, \quad (18)$$

particularly between a pathogen-free demographic parameter (a) and a parameter (β) modelling some aspect of the host-pathogen interaction. Clearly, this can only be investigated when a formula such as equation (16) is available. (The condition on the derivative in equation (18) is necessary to make the relationship a trade-off: as transmission increases so does the intrinsic birth rate.)

From equations (16) and (18) we see that winning host strains minimize

$$D(\beta) = \frac{L\beta}{(f(\beta) - b)}, \quad (19)$$

where $L = K(\alpha + b)/(\alpha + b + \gamma)$ is a positive constant. Now

$$D'(\beta) = \frac{(f(\beta) - b)L - L\beta f'(\beta)}{(f(\beta) - b)^2}. \quad (20)$$

If f is linear, say as in equation (21) below with $C = 0$, it then follows that $D'(\beta)$ is positive (we assume that r is always positive so that, in particular, $a_0 - b > 0$, where a_0 is the infection-free birth rate). Thus, in this case, as illustrated in figure 2, the lowest value of β wins (and a is now also forced to its lowest value). If f is nonlinear, for simplicity (this captures this essence of more general results) a quadratic of the form

$$f(\beta) = a_0 + B\beta + C\beta^2, \quad (21)$$

then equation (20) is zero at the feasible value

$$\beta = \beta^* = \sqrt{(a_0 - b)/C}. \quad (22)$$

This happens for C positive in which case f is concave up (C negative ensures equation (20) is positive with results as for the linear case). One can directly derive the result

$$D''(\beta^*) = L \frac{\{-\beta^* f''(\beta^*)\}}{(f(\beta^*) - b)^2} \quad (23)$$

Thus, given the concavity of f , we see that the extremum at β^* is a maximum. The winning host strain can now be either at the lowest value of β and lowest value of a or the highest value of β and highest value of a , the outcome depending only on the particular distribution of strains. (See figure 3*a,b* for a dynamical illustration.)

We should like to finish by mentioning an intriguing connection between our present work and the theory of adaptive dynamics as applied to the evolution of host resistance (Boots & Haraguchi 1999). In the above, we

Figure 3. The dynamics of five strains subject to a nonlinear trade-off $a = \beta + 2 + 1/16\beta^2$. X_1 , dashed line; Y_1 , dotted line; X_5 , dotted-dashed line; Y_5 , dotted-dotted-dashed line. The parameter values are $K = 10$, $b = 1.0$, $\gamma = 0.1$, $\alpha = 4.0$, $r_2 = 1.0$, $\beta_1 = 2.0$, $\beta_2 = 3.0$, $\beta_3 = 4.0$ and $\beta_4 = 5.0$. (a) $\beta_5 = 7.0$ and strain 1, having minimum β and minimum a , survives infected and excludes all others. (b) $\beta_5 = 9.0$ and strain 5, having maximum β and maximum a , survives infected and excludes all others.

have considered community dynamics, invoked only one time-scale and regarded the set of all possible strains as fixed. In adaptive dynamics, evolution is pictured as occurring via small mutations of resident strains. Thus,

another, much slower time-scale, that of mutation, is also considered. On this time-scale possible new strains arise. Invadability criteria such as that in equation (15) determine whether a mutant strain prospers or not and it is

Figure 4. Pairwise invasibility plot for a linear trade-off $a=f(\beta)$. Any resident strain β_1 will be replaced by a nearby mutant with lower transmission parameter β_2 . Evolution is in the direction of $\beta_{\min}$.

assumed that a single resident strain is replaced by a mutant which can invade the resident but cannot be invaded by it. (It is the truth of this assumption in our community dynamics which we have proved in Appendix A.) The outcomes are displayed in pairwise invasibility plots (PIPs) which, assuming the resident and mutant differ in only one parameter, display the zero contours and the sign structure of I_{kh} with the resident value on the x -axis and the mutant on the y -axis. Of particular interest are singular points (Metz *et al.* 1996; Geritz *et al.* 1997) where another branch of the zero contour crosses the obvious branch $y=x$ (on which the resident and mutant are identical). The classification of the behaviour in the neighbourhood of such singularities is basic to an understanding of the evolutionary dynamics. Such points are distinguished by finding the gradient of I_{kh} with respect to the mutant parameter, evaluating this with mutant and resident parameter values equal and setting the result equal to zero. When we apply this recipe to equation (15) in the circumstances where equation (18) applies, we find that evolutionarily singular points occur precisely where $D'(\beta) = 0$, that is at extrema of the basic depression ratio. Thus, for a linear trade-off there are no such singularities and the PIP is as in figure 4 showing evolution towards the lowest β . For a trade-off of the form in equation (21), there is a singularity at equation (22) and the PIP (see figure 5) shows that this is an evolutionary repeller.

The investigation of such connections between pure community dynamics and the evolutionary perspective provided by adaptive dynamics may provide fertile ground in the future.

APPENDIX A

(a) *Single-strain model*

It is useful to deal with the single-strain model first. Here the equilibria satisfy just one pair ($n=1$) of the multistrain equations given below in equations (A7) and (A8) and, if our single strain is the h th, we have explicitly that $H=X_h+Y_h$ and $Y=Y_h$. This quickly leads to three equilibria, i.e. one at the origin, an uninfected one $X_h=K$, $Y_h=0$ and an infected one

Figure 5. Pairwise invasibility plot for a concave up, quadratic trade-off $a=f(\beta)$. Any resident strain β_1 below the singular point will be replaced by a nearby mutant with lower transmission parameter β_2 . In this case, evolution is in the direction of $\beta_{\min}$. Similarly, for residents above the singular point, evolution is in the direction of $\beta_{\max}$.

$$X_h = X_h^* = H_{T,h} = \Gamma_h / \beta_h \quad (\text{A1})$$

and

$$Y_h = Y_h^* = (K - H_{T,h}) / (1 + (\beta_h K / r_h)(1 - \gamma_h / \Gamma_h)). \quad (\text{A2})$$

The first two of the above equilibria are necessarily feasible (in the sense of having non-negative densities), while the third is feasible (and distinct) if and only if $H_{T,h} < K$.

The Jacobian takes the form

$$\begin{pmatrix} -r_h X_h / K + r_h(1 - (X_h + Y_h) / K) - \beta_h Y_h - r_h X_h / K - \beta_h X_h + \gamma_h \\ \beta_h Y_h & \beta_h X_h - \Gamma_h \end{pmatrix}. \quad (\text{A3})$$

It follows very directly that the origin is always unstable and the uninfected state is stable when $K < H_{T,h}$ (so that the infected state is not feasible) and is not if this inequality is reversed. At the infected state the Jacobian is

$$\begin{pmatrix} -r_h X_h^* / K + r_h(1 - (X_h^* + Y_h^*) / K) - \beta_h Y_h^* - r_h X_h^* / K - \beta_h X_h^* + \gamma_h \\ \beta_h Y_h^* & 0 \end{pmatrix}. \quad (\text{A4})$$

Using equilibrium conditions the standard trace and determinant conditions then reduce to

$$-r_h X_h^* / K - \beta_h Y_h^* \gamma_h / \Gamma_h < 0 \quad (\text{A5})$$

and

$$\beta_h Y_h^* (r_h X_h^* / K + \alpha_h + b_h) > 0, \quad (\text{A6})$$

which are satisfied essentially if and only if the uninfected state is feasible, that is $H_{T,h} < K$.

(b) *Multistrain model*

We begin our analysis of the multistrain model by establishing the equilibria corresponding to equations (2) and (3). A small amount of manipulation shows that these satisfy

$$\{r_h(1 - H/K) - \beta_h Y(1 - \gamma_h / \Gamma_h)\} X_h = 0 \quad (\text{A7})$$

and

$$\beta_h X_h Y - \Gamma_h Y_h = 0. \quad (\text{A8})$$

The origin is clearly a solution and it follows immediately that there is another solution

$$H = K, Y_h = 0 \text{ for all } h. \quad (\text{A9})$$

This corresponds to the host population being uninfected at its carrying capacity K . The strain composition of this solution is not determined, which is not surprising given that all strains have the same carrying capacity. The systematic solution of equations (A7) and (A8) proceeds as follows. If X_h is non-zero, then the other factor in equation (A7) must be zero. Suppose this occurs for two or more distinct strains. Then, if we choose any two of these h and k , we must have

$$\beta_h Y(1 - \gamma_h/\Gamma_h)/r_h = \beta_k Y(1 - \gamma_k/\Gamma_k)/r_k. \quad (\text{A10})$$

Thus, either $Y=0$, which leads to equation (A9) or equation (A10) cannot be satisfied (except by a ‘conspiracy of parameters’, which we reject). It follows that, if there are solutions other than equation (A9), they must have at most one non-zero X_h . From equation (A8) we see that, if any X_h is zero, then so is the corresponding Y_h .

Thus, if all the X_h are zero, we obtain the equilibrium at the origin. It remains to discuss the case where exactly one X_h is non-zero. We know that, not only are all the other susceptible strain densities zero, but also all the other infected ones. Hence, it follows that $H=X_h+Y_h$ and $Y=Y_h$ and equations (A7) and (A8) reduce to the single-strain equations solved above. Since X_h is non-zero, it follows that either $Y_h=0$ and $X_h=K$ (which can be subsumed in equation (A9)) or

$$X_h = X_h^*, Y_h = Y_h^* \quad (\text{A11})$$

and

$$X_k = Y_k = 0 \text{ for all } k \neq h, \quad (\text{A12})$$

where the quantities in equation (A11) are as in equations (A1) and (A2). There are n equilibria of this last type and they correspond to each host strain alone with the pathogen and complete the possibilities.

The origin and the uninfected state in equation (A9) are feasible whatever values the parameters take. The state of equations (A11) and (A12) is feasible—we include it being distinct from that of equation (A9)—if and only if $H_{T,h} < K$.

As in §4, in discussing stability we restrict attention to the states of equations (A11) and (A12). Let the surviving strain be h . The rows of the Jacobian corresponding to this strain are

$$\begin{pmatrix} -q_h X_h^* & -(q_h + \beta_h) X_h^* & \dots & \dots \\ 0 & \beta_h Y_h^* & \dots & \dots \\ -q_h X_h^* + r_h - q_h(X_h^* + Y_h^*) - \beta_h Y_h^* & -(q_h + \beta_h) X_h^* + \gamma_h & & \\ \dots & \dots & -q_h X_h^* & -(q_h + \beta_h) X_h^* \\ \dots & \dots & 0 & \beta_h Y_h^* \end{pmatrix}, \quad (\text{A13})$$

where we have written $q_h=r_h/K$ to save space. The rows of the Jacobian corresponding to the $n-1$ strains k with $X_k=Y_k=0$ take the form

$$\begin{pmatrix} 0 & 0 & \dots & r_k(1 - (X_h^* + Y_h^*)/K) - \beta_k Y_h^* & \gamma_k & \dots & 0 & 0 \\ 0 & 0 & \dots & \beta_k Y_h^* & -\Gamma_k & \dots & 0 & 0 \end{pmatrix}. \quad (\text{A14})$$

The largely block diagonal structure means that, from equation (A13), this state is stable if, first, it is intrinsically stable (that is stable in a single-strain model, which means that $H_{T,h} < K$) and if, second, all the diagonal blocks in equation (A14) satisfy the usual trace and determinant conditions. These are that, for the fixed h and for all k ,

$$r_k(1 - (X_h^* + Y_h^*)/K) - \beta_k Y_h^* - \Gamma_k < 0 \quad (\text{A15})$$

and

$$(r_k(1 - (X_h^* + Y_h^*)/K) - \beta_k Y_h^*)(-\Gamma_k) - \gamma_k \beta_k Y_h^* > 0. \quad (\text{A16})$$

If the second of these applies, then so does the first, which is therefore redundant. Thus, we require that, for all k ,

$$r_k(1 - (X_h^* + Y_h^*)/K) < \beta_k Y_h^*(1 - \gamma_k/\Gamma_k). \quad (\text{A17})$$

Using the intrinsic stability shown to be necessary above, we have that Y_h^* is positive. This allows us to recast equation (A17) as

$$\frac{K - (X_h^* + Y_h^*)}{Y_h^*} < \frac{\beta_k K(1 - \gamma_k/\Gamma_k)}{r_k}. \quad (\text{A18})$$

Next, equations (A1) and (A2) allow this to be rewritten as

$$\frac{K - (X_h^* + Y_h^*)}{Y_h^*} < \frac{K - (X_k^* + Y_k^*)}{Y_k^*}. \quad (\text{A19})$$

In the light of the definition in equation (1) this verifies our principal result, which was presented following equation (15) in §4. The strain with the minimum basic depression ratio wins.

(c) *Invasibility criteria*

There are two points to consider. We first turn our attention to invasion by an infected. Before any recovery, this yields a negative contribution

$$1/\Gamma_k(-b_k - \alpha_k), \quad (\text{A20})$$

to the increase I_{kh} in §4. Hence, as is obvious biologically, infecteds cannot prosper unless susceptibles do. For these reasons attention can be restricted to susceptibles.

The second point we need to consider is the inclusion of recovery in calculations based on an attempted invasion of a resident strain h by a strain k . Following any period of susceptibility $T_{X,n}$ (initial or after one or more recoveries), we find that the subsequent period of susceptibility is

$$T_{X,n+1} = \left(\frac{\gamma_k}{b_k + \beta_k Y_h^*} \right) \left(\frac{\beta_k Y_h^*}{\Gamma_k} \right) T_{X,n}. \quad (\text{A21})$$

(The calculation, which applies on average, is a small extension of those in §4) The scaling factor in equation (A21), which is less than 1, also applies to successive periods of infection. The overall effect of recovery is thus to multiply equation (13) in §4 by a convergent geometric series with the above scaling factor as a common ratio and a positive sum. This leaves the conclusion following equation (15) in §4 unchanged.

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As this paper exceeds the maximum length normally permitted, the author has agreed to contribute to production costs.