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Research article

Evolutionary implications of host–pathogen specificity: the fitness consequences of host life history traits

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Abstract. Pathogens and parasites can be strong agents of selection, and often exhibit some degree of genetic specificity for individual host strains. Here we show that this host–pathogen specificity can affect the evolution of host life history traits. All else equal, evolution should select for genes that increase individuals' reproduction rates or lifespans (and thus total reproduction per individual). Using a simple host–pathogen model, we show that when the genetic specificity of pathogen infection is low, host strains with higher reproduction rates or longer lifespans drive slower-reproducing or shorter-lived host strains to extinction, as one would expect. However, when pathogens exhibit specificity for host strains with different life history traits, the evolutionary advantages of these traits can be greatly diminished by pathogen-mediated selection. Given sufficient host–pathogen specificity, pathogen-mediated selection can maintain polymorphism in host traits that are correlated with pathogen resistance traits, despite large intrinsic fitness differences among host strains. These results have two important implications. First, selection on host life history traits will be weaker than expected, whenever host fitness is significantly affected by genotype-specific pathogen attack. Second, where polymorphism in host traits is maintained by pathogen-mediated selection, preserving the genetic diversity of host species may require preserving their pathogens as well.

Key words: disease, evolution, frequency-dependent selection, genetic diversity, life history, lifespan, polymorphism, reproduction rate, resistance, specificity, virulence

Introduction

Host–pathogen specificity

Infections typically exhibit some degree of genetic specificity, in which individual parasite strains infect some host strains more readily than others. Although genetic specificity is pervasive in host–parasite systems (Price, 1980; Crute *et al.*, 1997), little is known about its potential consequences for the evolution of host life history traits. In this paper we use a simple host–parasite model to explore

how the fitness consequences of host reproduction rate and longevity are influenced by the genetic specificity of host–parasite interactions. Because the genetics of plant–pathogen interactions are relatively well characterized, we draw our examples from this literature. However, our results should also be applicable to other host–parasite systems in which there is genetic specificity.

Host–pathogen specificity is the joint consequence of both host and pathogen characteristics. Pathogen infectiousness can be genetically determined such that particular pathogen strains can infect some host strains more readily than others; host susceptibility can also be genetically determined such that it is easier for some pathogen strains than others to become established. Thus genetic specificity is not a property of pathogens alone, or of hosts alone, but is a characteristic of the interaction between host and pathogen strains.

It is important to distinguish the genetic specificity of host–pathogen interactions from simple genetic variability in pathogen infectiousness and host susceptibility (Frank, 1996a). Different strains of pathogens may differ in their general degree of infectiousness (to all host strains), and different host strains may differ in their overall vulnerability to infection (by all pathogen strains). By contrast, host–pathogen specificity means that individual pathogen strains will be more infectious to some host strains than others, and that the infectiousness of other pathogen strains will be distributed differently among the host strains. Similarly, host–pathogen specificity implies that individual host strains will be more vulnerable to some pathogen strains than others, and that other host strains will exhibit a different pattern of susceptibility across the various pathogen strains.

Different host–pathogen systems exhibit different degrees of genetic specificity. For example, some soil-borne plant pathogens exhibit low specificity, readily infecting a wide range of host genotypes (Garrett, 1970; Weste, 1986; Borowicz and Juliano, 1991). By contrast, many plant species show quantitative differential susceptibility to wind-borne fungal pathogens (van der Plank, 1984; Roy and Bierzychudek, 1993; Clarke, 1997). Finally, there are examples of nearly absolute specificity, in which each pathogen genotype can specifically infect only the correspondingly susceptible host genotypes. Many fungal plant pathogens exhibit high degrees of genetic specificity, as do some viruses, bacteria and insects (Burdon, 1987a; Weller *et al*., 1991; Crute *et al*., 1997).

In nature, the quantitative risk of infection in any host–pathogen system is a continuous variable (rather than an all-or-nothing binary function as has been widely assumed by either gene-for-gene or matching allele models, see Parker, 1994, 1996b; Frank, 1996b). The likelihood of infection is controlled by many genetic traits in addition to the simple recognition of resistance and virulence alleles (Beynon, 1997). For example, the number of fungal pathogen spores impinging on a plant will depend on pathogen characteristics such as the number, size and ornamentation of its spores, as well as on host characteristics

such as the number, size, shape and arrangement of its leaves. The chance of each fungal spore adhering to the plant may vary with the spore ornamentation and with the orientation of the leaves, the leaf blade to leaf edge ratio, the cuticle roughness, or even the spacing between leaf hairs (Brewer and Smith, 1997). The chance of infection may then depend on factors such as the speed of spore germination, the number and placement of stomata and the presence or absence of particular plant secondary compounds. Finally, once the pathogen has invaded a cell, the interaction between resistance and virulence alleles can determine the further progress of the infection. Thus the risk and severity of infection are controlled by a wide variety of host and pathogen characteristics, and most of these are continuously variable quantitative traits. Only the resistance/virulence allele recognition mechanism can yield the binary, all-or-nothing pattern of behavior that has usually been used to characterize plant–pathogen interactions. Although the risk and severity of infection typically show quantitative variation, plant–pathogen studies have often coded infection as simply present or absent, reflecting an emphasis on major gene control of resistance (Burdon, 1987b; Clarke, 1997). This, in turn, has led to insufficient emphasis on the quantitative traits that significantly determine the risk and severity of infection.

How does specificity evolve? Parasitic attack involves many kinds of interactions with the host, and at each stage there can be genetically based variation in the hosts that influence parasite success. If there is genetic variation in the parasite, then individual parasitic strains will be more successful on some host strains than others. Host–pathogen specificity can arise as a result of evolutionary constraints, when the traits that help a parasite to exploit one set of hosts make it less able to attack other hosts, or conversely, when the traits that help a host to resist one set of pathogens make it less able to resist others. Specialization can also be favored by evolution when generalization requires plasticity, and thus carries a cost (Via, 1990; van Tienderen, 1991; Thompson, 1994; Futuyma *et al.*, 1995). Even without such costs, specialization should evolve because parasites that show host preference will be more consistently exposed to selection on a particular host, and thus can adapt to evolving host defenses faster than generalist parasites can (Kawecki, 1998). These theoretical arguments suggest that host–pathogen specificity should be widespread in nature, and observational data suggest that this is, in fact, the case (Price, 1980; Burdon, 1987a; Thompson and Burdon, 1992; Brooks and McLennan, 1993; Parker, 1996b; Crute *et al.*, 1997).

The pervasiveness of host–pathogen specificity highlights the need to understand its consequences for pathogen-mediated selection on host traits. Here we use a simple model to show how host–pathogen specificity affects the evolution of host life history traits that are correlated with resistance or susceptibility characters.

Correlation with host life history traits

Correlations between host life history traits and disease resistance can arise by pleiotropy and by genetic linkage. Recent studies have shown that life history traits are often pleiotropic with disease resistance. For example, Mestries *et al.* (1998) found that a gene that controls apical branching in sunflowers confers increased disease resistance, while also promoting earlier flowering, reducing seed number, and increasing seed oil content. Heat shock proteins provide another example of pleiotropic interactions; these multifunctional molecules affect a cell's response to acute stress, including disease, and also influence growth and longevity (Hoffmann and Parsons, 1991; Feder, 1999; Tatar, 1999). Likewise, plant secondary products, such as anthocyanins, can influence multiple traits ranging from pest resistance to cold tolerance and flower color (Fineblum and Rausher, 1997).

Pleiotropy between life history traits and disease resistance is probably based on similar genetic mechanisms to the pleiotropic interactions between life history traits and biocide resistance, which have been more extensively studied. For example, chlorsulfuron resistance in *Arabidopsis thaliana* is encoded by a single, dominant mutation in the gene encoding acetolactate synthase (Bergelson *et al.*, 1996); mutants are herbicide resistant, but produce fewer seeds. Longevity in *Arabidopsis* has also been correlated with herbicide resistance (Kurepa *et al.*, 1998). Selection experiments on longevity have also revealed correlations with biocide resistance, suggesting either pleiotropy or linkage. Arking *et al.* (1991) artificially selected for longevity in *Drosophila melanogaster*, and found that it was correlated with elevated resistance to paraquat; the correlation was so strong that paraquat resistance could be used as a bioassay for longevity phenotypes.

Correlation between life history traits and disease resistance can also arise through genetic linkage, resulting from apomixis or inbreeding. In apomictic organisms, all traits are linked, and in self-fertilizing or inbred organisms, there is also a strong degree of association (linkage disequilibrium) among traits (Hedrick, 1980). Apomixis has been recorded in about 15% of all plant families (Bierzychudek, 1987; Richards, 1997), and occurs in many animals, including trematodes, belloid rotifers, coccids, aphids and lizards (Bell, 1982). About 40% of all plant species can self-fertilize, and roughly 20% normally do so (Fryxell, 1957; Richards, 1997). Species that normally self-fertilize often have mechanisms that virtually ensure self-fertilization, such as selfing in the bud or cleistogamy. The outcrossing rate of selfing plants can be zero or very close to zero (Golenberg and Nevo, 1987; Parker, 1996a; Hamrick and Godt, 1997); thus, traits such as disease resistance and life history characters can be strongly linked.

Studies of three plant species illustrate how disease resistance can be linked to life history traits as a result of inbreeding. (1) The Mlo mildew resistance

gene is linked to a quantitative trait locus for grain number in self-fertilizing barley (Thomas *et al*., 1998); plants expressing the Mlo trait have lower yield. (2) *Amphicarpaea bracteata* self-fertilizes at least 99% of the time, leading to the development of two lineages that co-occur but rarely hybridize (Parker, 1986, 1996a). The two lineages are susceptible to different strains of the pathogen *Synchytrium decipiens*, and are also significantly different for seven morphological and life history traits (Parker, 1991). (3) *Arabidopsis thalliana* has numerous selfing lineages, with significant differences in longevity (Kurepa *et al*., 1998; Scott *et al*., 1999) and disease resistance (Crute *et al*., 1997; Buell, 1998), although to our knowledge, the correlation between these traits has not been tested.

Genetic specificity in a simple host–pathogen model

To explore the epidemiological and evolutionary implications of host–pathogen genetic specificity, we use an extension of the simple host–pathogen model presented by Kirchner and Roy (1999). The original Kirchner and Roy model described a single host strain infected by a single pathogen strain. Below, we extend this model to encompass two host strains and two pathogen strains that they share in common, and we use this model to describe how genetic specificity between hosts and pathogens can be conceptualized and quantified.

Our single-strain model draws on the model presented by May and Anderson (1983). We denote the uninfected and infected host populations by X and Y respectively, each expressed as fractions of the carrying capacity. The pathogens cannot survive without hosts, so they need not be modeled explicitly; instead, their dynamics are represented by the infected host population. We assume that the pathogen is transmitted only horizontally, so that all hosts are born uninfected. We further assume that reproduction, infection, and death are controlled by simple Lotka–Volterra expressions. A complete list of symbols can be found in Table 1.

Host reproduction

Uninfected hosts reproduce at a rate $a(1-N)X$, or a per-capita rate of $a(1-N)$, where a is the potential per-capita reproduction rate in the absence of carrying capacity constraints, $1-N=1-(X+Y)$ is the fraction of carrying capacity that is unoccupied (and thus available for new individuals to become established), and X is the total uninfected population. We assume that infected hosts can also reproduce, but infection diminishes their fecundity by a fraction η, compared to uninfected hosts ($0 \leq \eta \leq 1$, where $\eta = 1$ indicates that infection completely sterilizes the host, and $\eta = 0$ indicates that infection has no

Table 1. Table of symbols

Symbol	Definition	Defining equation (or first use)
i	Placeholder for host strain	(3)
k	Placeholder for pathogen strain	(3)
X_i	Uninfected host population (as fraction of carrying capacity)	(1)
Y_{ik}	Infected host population (as fraction of carrying capacity)	(1)
N	Total host population	(1)
a_i	Host fecundity	(1)
τ_i	Mean lifespan of uninfected hosts	(1)
η	Sterilization factor	(1)
m	Lethality factor (ratio by which infection accelerates mortality)	(2)
s	Host–pathogen specificity coefficient	(7)
β_{ik}	Pathogen transmission coefficient	(1)
ω_i	Host fitness	(10)
L	Fitness loss under infection	(10)
r_{ik}	Lifetime risk of infection	(10)

effect on host reproduction). In other words, infected hosts produce offspring at a rate of $a(1-N)(1-\eta)Y$, and thus the total host birth rate is $a(1-N)[X+(1-\eta)Y]$. In this paper, except as noted otherwise, we use a reproduction rate of $a=10$. We assume that infection is non-sterilizing ($\eta=0$); results for partially sterilizing ($\eta=0.5$) and completely sterilizing ($\eta=1$) infections are qualitatively similar.

Host mortality

Uninfected hosts die at a rate X/τ, or a per-capita rate of $1/\tau$, where τ is the mean lifespan in the absence of infection. We assume that infection shortens lifespan, and thus accelerates mortality, by a ratio m ($m \geq 1$, where $m=1$ indicates that infection has no effect on host mortality, and $m \gg 1$ indicates that infection shortens lifespan substantially). Infected hosts therefore have a mean lifespan of τ/m, and thus their death rate is mY/τ. For the simulations shown in this paper, $m=5$. Except as noted otherwise, the host lifespan is $\tau=1$; this is equivalent to defining the model time scale in units of the uninfected host lifespan.

Infection

Hosts become infected at a rate βXY, where β reflects pathogen infectiousness and host susceptibility, X is the fraction of the carrying capacity occupied by susceptible uninfected hosts, and Y is the population of infected (and thus

infectious) hosts. For simplicity, we assume that infection is permanent; hosts do not recover and do not acquire immunity, as is typical for many plant–pathogen systems (Agrios, 1988) and some animal diseases (Baudoin, 1975). The uninfected host population will change at a rate determined by the balance between the rates of reproduction, infection, and death:

$$\frac{\mathrm{d}X}{\mathrm{d}t} = a(1-N)[X + (1-\eta)Y] - \beta XY - X/\tau \tag{1}$$

Similarly, the infected host population will change at a rate determined by the balance between infection and mortality:

$$\frac{\mathrm{d}Y}{\mathrm{d}t} = \beta XY - mY/\tau \tag{2}$$

This simple single-strain model can be straightforwardly extended to encompass two host strains and two pathogen strains. Doing so requires several conceptual elaborations, as follows.

Book-keeping issues

Dividing the host population into two separate strains requires replacing the population X with X_i, where $i = 1 \ldots\ldots 2$ designates the host strain. The hosts' characteristics, such as their reproduction rate (a) and longevity (τ), must be similarly subscripted a_i and τ_i for each host strain. Because either pathogen strain, designated by the subscript k ($k = 1 \ldots\ldots 2$), can infect either host strain, the infected host population Y must be replaced with Y_{ik}, which is the population of host strain i that is infected with pathogen strain k (for simplicity, we assume that both pathogen strains cannot simultaneously infect the same individual host; if multiple infections were allowed in the simulations presented below, their average rate of occurrence would be less than 4%). Similarly, because the rate of infection depends on the characteristics of the host and pathogen strains, the infection coefficient β must be subscripted β_{ik}, to express the capacity of pathogen strain k to infect host strain i (or, conversely, the susceptibility of host strain i to pathogen strain k). Because pathogens on either host strain can infect the other host strain, the rate that pathogen strain k infects host strain i will be $\beta_{ik} X_i \sum_i Y_{ik}$, where $\sum_i Y_{ik}$ expresses the total population of pathogen strain k. These book-keeping considerations imply that Equations (1) and (2) must be recast as:

$$\frac{\mathrm{d}X_i}{\mathrm{d}t} = a_i(1-N)\left[X_i + (1-\eta)\sum_k Y_{ik}\right] - \sum_k \left(\beta_{ik} X_i \sum_i Y_{ik}\right) - X_i/\tau_i \tag{3}$$

and

$$\frac{\mathrm{d}Y_{ik}}{\mathrm{d}t} = \beta_{ik} X_i \sum_i Y_{ik} - m Y_{ik}/\tau_i \qquad (4)$$

Genetics of interbreeding among strains

The host and pathogen populations consist of two strains (or phenotypes) that interbreed, so the dynamics of each strain will depend on the other strain, as well as on the genetics that determine the phenotype. Equations (3) and (4), above, assume haploid genetics, which implies that the proportion of offspring in each phenotype equals the proportion of parents in each phenotype times their relative fecundity. This is the simplest possible genetic system; the dynamics of more complicated genetic systems will depend on the ploidy level, the number of alleles at each locus, and the number of loci determining the phenotype. The diversity of genetic systems, particularly among plants and fungal pathogens, implies that many genetically realistic models are possible. Fortunately, the genetic details will affect only the disequilibrium rate of change of the system (Barrett, 1988); they will not affect its equilibrium states, or its direction of change when it is out of equilibrium. Therefore, for ease of comprehension we will use the relatively simple system in Equations (3) and (4) in the analysis that follows. We have also repeated the same simulations with a more complex genetic model, in which the phenotype is determined by a diploid diallelic locus with complete dominance. This diploid model has separate equations similar to Equations (3) and (4) for each of the three host and pathogen genotypes (dominant, recessive, and heterozygous), with random mating among them. The dynamics of the haploid and diploid models are almost indistinguishable, and, as expected, their equilibria are exactly identical.

Genetic specificity of host–pathogen interactions

Pathogen transmission is controlled by both host and pathogen characteristics, so the transmission coefficient β_{ik} can potentially differ for each combination of host and pathogen phenotypes. We express the individual β_{ik} values by a shared coefficient β_o (which scales the overall transmissibility of pathogens from host to host), multiplied by a specificity matrix (which quantifies how pathogen transmission is distributed among specific combinations of host and pathogen strains). We define the shared coefficient β_o such that it equals the value of β that would yield the same overall rate of infection in a single-strain model (such as Equations (1) and (2)). If pathogen transmission is non-specific (that is, if each pathogen strain is equally infectious on all host strains, and each host strain is equally vulnerable to all pathogen strains), the transmission coefficients β_{ik} are

$$\beta_{ik} = \beta_o \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} \tag{5}$$

Conversely, if the specificity of pathogen transmission is absolute (such that each pathogen strain can infect only one host strain, and each host strain is vulnerable to only one pathogen strain), the transmission coefficients β_{ik} are

$$\beta_{ik} = \beta_o \begin{pmatrix} 2 & 0 \\ 0 & 2 \end{pmatrix} \tag{6}$$

The 'generalist' matrix (Equation (5)) and the 'specialist' matrix (Equation (6)) can be viewed as end-members of a continuous spectrum of host–pathogen specificity. We can consider any particular degrees of specificity as a linear combination of 'generalist' and 'specialist' behavior. Here, we quantify the degree of host–pathogen specificity using a coefficient s, which specifies the fraction of 'specialist' behavior in the transmission matrix. Thus the β_{ik} matrix becomes s times the 'specialist' matrix, plus $(1 - s)$ times the 'generalist' matrix, yielding

$$\beta_{ik} = (1-s)\beta_o \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} + s\beta_o \begin{pmatrix} 2 & 0 \\ 0 & 2 \end{pmatrix} = \beta_o \begin{pmatrix} 1+s & 1-s \\ 1-s & 1+s \end{pmatrix} \tag{7}$$

As the specificity coefficient varies from $s = 0$ (indicating no specificity) to $s = 1$ (indicating absolute specificity), the transmission matrix (Equation (7)) varies continuously from the purely 'generalist' matrix (Equation (5)) to the purely 'specialist' matrix (Equation (6)). The specificity coefficient can also take on values down to $s = -1$, indicating increasing degrees of specificity, but with the opposite orientation (such that pathogen strain 2 can more readily infect host strain 1, and pathogen strain 1 can more readily infect host strain 2).

As the specificity parameter s changes, the overall levels of pathogen infectiousness and host vulnerability remain constant; that is, the sums across the rows and down the columns of the β_{ik} matrix do not change. Although the simple diagonal matrices defined by Equation (7) are only a subset of all conceivable transmission matrices, they have the advantage of permitting us to change the host-specificity of pathogen infection (that is, the tendency for individual pathogen strains to specialize on particular host strains), without altering the overall infectiousness of the whole pathogen population, or the overall vulnerability of the whole host population to infection. Other possible transmission matrices do not have this property. In this paper, we fix the overall level of transmissibility at $\beta_o = 15$. Because the host–pathogen specificity s is the primary object of our analysis, we vary it from $s = 0$ (no specificity) to $s = 100\%$ (absolute specificity).

The model used in this paper consists of Equations (3), (4) and (7) with the parameter values given above, except as noted otherwise. We simulate the model system's time-dependent evolution by numerical integration, and find its equilibria using multidimensional Newton–Raphson methods (Press *et al.*, 1986). Our primary focus is on the evolutionary consequences of host–pathogen specificity, rather than life history evolution per se. Therefore, we do not allow reproduction rate and longevity to change through time, but instead study how host–pathogen specificity affects the outcome of competition between two host strains with different (but fixed) reproduction rates or longevities. Thus, we are examining the selection mechanisms that drive evolution, rather than simulating their consequences through evolutionary time.

Selection for faster host reproduction under host–pathogen genetic specificity

Reproduction rates (number of offspring per individual per unit time) are a major component of evolutionary fitness – so much so, that in many empirical studies an individual's fitness is measured by its reproduction rate (although its reproductive lifespan is also relevant). One would therefore expect that evolution should favor hosts with higher reproduction rates, and if slower-reproducing hosts are otherwise identical to their faster-reproducing competitors, competitive exclusion should drive them to extinction. Here we test this proposition in our model host–pathogen system, under different levels of host–pathogen specificity.

Dynamics of fixation and polymorphism

Figure 1 shows the behavior of our host–pathogen model under two different levels of genetic specificity, assuming that both strains of hosts and pathogens are otherwise identical, except host strain 2 has a reproduction rate 10% greater than host strain 1 ($a_1 = 10$ and $a_2 = 11$ in Equation (3)). As the left-hand column of Figure 1 shows, when host–pathogen genetic specificity is as low as 10%, the model behaves as one would intuitively expect: host strain 2 rapidly dominates the gene pool and strain 1 is rapidly driven to extinction (Fig. 1a). This creates a disadvantage for pathogen strain 1, which is slightly less infectious than pathogen strain 2 against host strain 2. Thus the extinction of host strain 1 also entails the extinction of pathogen strain 1 (Fig. 1b, c), and polymorphism is rapidly lost from both the host and pathogen populations.

At slightly higher levels of specificity, however, the model system's behavior is strikingly different. Raising host–pathogen specificity from 10 to 20% transforms the competitive exclusion process in Figure 1a–c to an asymmetrical oscillation that slowly converges to a polymorphic equilibrium in both the host and the pathogen (Fig. 1d–f). Although host strain 1 has a clear reproductive

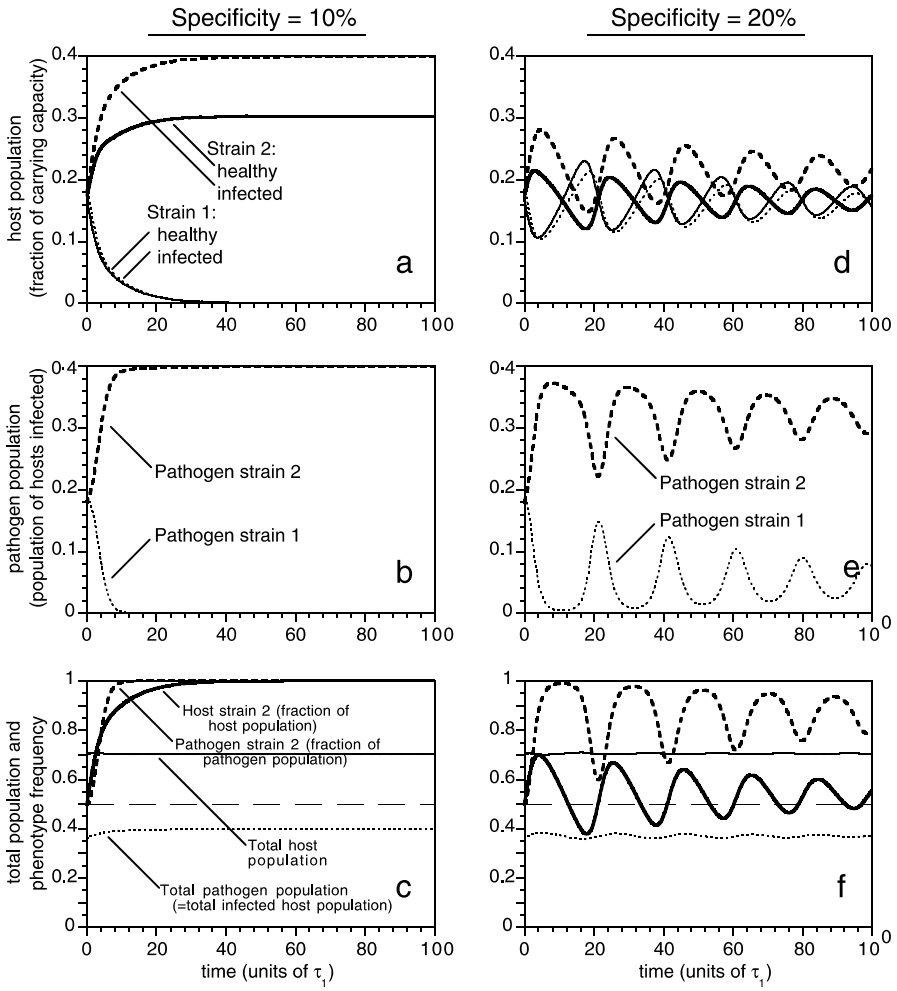


Figure 1. Selection for increased fecundity, illustrated by host and pathogen population trajectories through time at two different levels of host–pathogen specificity; in both cases, host strain 2's reproduction rate is 10% greater than host strain 1's ($a_1 = 10,\ a_2 = 11$). Each of the three rows of panels depicts the behavior of a different group of variables. The first row shows healthy and infected populations (solid and dotted lines, respectively) of host strains 1 and 2 (thin and thick lines, respectively). The second row shows the populations of pathogen strain 1 (thin dotted line) and pathogen strain 2 (thick dotted line). Note that these are not the same as the populations of the infected host strains, because as long as host–pathogen specificity is not absolute, pathogen strain 1 can infect host strain 2 and vice versa. The third row shows the total populations of the hosts and pathogens (thin solid and thin dotted lines, respectively), the frequency of host strain 2 (thick solid line), and the frequency of pathogen strain 2 (thick dotted line); the horizontal dashed line indicates equal frequencies of strain 1 and strain 2. Model parameters are $a_1 = 10$, $a_2 = 11$, $\tau_1 = \tau_2 = 1$, $\eta = 0$, $\beta_o = 15$, and $m = 5$.

disadvantage compared to host strain 2, both strains persist in the population, at nearly equal frequencies.

Closer examination of Figure 1 shows how this can happen. When both pathogen strains are equally prevalent, host strain 2's higher reproduction rate gives it a competitive advantage over host strain 1. As host strain 2 becomes more prevalent, pathogen strain 2 gains a competitive advantage over pathogen strain 1, because it can more efficiently exploit host strain 2. As pathogen strain 2 increases in frequency, host strain 2 loses its advantage over host strain 1, because of its greater susceptibility to infection by pathogen strain 2. Because the pathogen strain frequencies adjust to more heavily exploit the more successful host strain, the intrinsic fitness advantage of the faster-reproducing host strain will tend to be offset by a greater burden of infection. The strength of this pathogen-mediated negative feedback mechanism will depend on the fitness consequences of infection and the degrees of host–pathogen specificity. If these are high enough, pathogen-mediated feedback can outweigh the intrinsic advantage that one host strain has over the other, and both strains will persist.

As the specificity parameter s is increased further, the oscillation in the host and pathogen populations becomes more symmetrical, decreases in amplitude, and increases in frequency. The frequency of oscillation increases because at higher host–pathogen specificity, changes in host frequencies have bigger effects on pathogen fitness, leading to faster changes in pathogen frequencies (and vice versa). The oscillations become more symmetrical and sinusoidal, in part, because pathogen strain 1 is not driven as close to extinction at higher levels of specificity.

It has long been understood that pathogen-mediated frequency-dependent selection can maintain polymorphism in host resistance genotypes (Gillespie, 1975; Hamilton, 1980; May and Anderson, 1983b; Barrett, 1988; Hamilton *et al.*, 1990). Our results show that host–pathogen specificity can also ensure the coexistence of unequal competitors – including host strains with large intrinsic fitness differences. Note that our more fecund host strain's reproductive advantage is not offset by greater intrinsic susceptibility to infection; the symmetry in the transmission matrix β_{ik} implies that both host strains have equal susceptibility, but their susceptibility is partitioned differently between the two pathogen strains. Thus the more successful host strain gives an advantage to the pathogen strain that can more efficiently attack it; it is this ecological feedback, rather than an intrinsic fitness trade-off within the host itself, that maintains polymorphism despite large fitness differences between the host strains.

Equilibria

To explore our model system more comprehensively, we mapped its equilibrium host and pathogen strain frequencies across the entire possible range of host–

pathogen specificity (Fig. 2), by solving Equations (3) and (4) for the host and pathogen populations at which all the time derivatives are zero. Figure 2 shows the central tendency in the system's behavior at the two specificity values featured in Figure 1 (shown as small open circles in Fig. 2), as well as all other values of host–pathogen specificity. Figure 2 illustrates the continuum of behavior linking the two particular examples shown in Figure 1 and thus lets us assess their generality. One can readily see that the two distinct modes of behavior (fixation and polymorphism) that were observed in Figure 1 are separated by a discontinuous shift in the equilibrium frequency of the two host strains (Fig. 2a). Below this threshold (which varies according to the difference between the two host strains' reproduction rates), host–pathogen specificity is too low (and thus frequency-dependent selection by the pathogens is too weak) to maintain polymorphism in the face of host strain 2's reproductive advantage.

General model dynamics

The short-term dynamics of our model system can be visualized with the aid of vector-field diagrams, as shown in Figure 3. The arrows in Figure 3 show how any combination of host and pathogen frequencies will change over a fixed interval of time; thus longer arrows indicate faster changes in strain frequencies. These diagrams are useful because they depict the system's dynamics under any initial conditions, not just an individual trajectory from a particular initial condition (as in the trajectories in Figure 1, which are shown in Figure 3 as continuous lines). These vector-field diagrams also help in putting the individual simulations into context. For example, at higher specificity values the equilibrium point (shown by the large black dot) moves farther from the edge of the diagram (Fig. 3b and c). The vector field becomes increasingly convergent and its average velocity of rotation increases.

Specificity threshold for maintenance of polymorphism

The reversal of the vector field along the upper boundary between Fig. 3a and b provides another way to visualize the specificity threshold. Below the threshold, host strain 2's higher reproduction rate more than offsets its greater vulnerability to pathogen strain 2, even when pathogen strain 2 comprises the entire pathogen population (that is, the vector field flows from left to right everywhere in Fig. 3a). Above the threshold, high frequencies of pathogen strain 2 are sufficient to offset host strain 2's higher reproduction rate, producing a net fitness disadvantage (that is, the vector field flows from right to left along the top boundary of Figure 3b and c). The reversal of the vector field along this boundary is necessary for the onset of cycling and thus is characteristic of the specificity threshold.

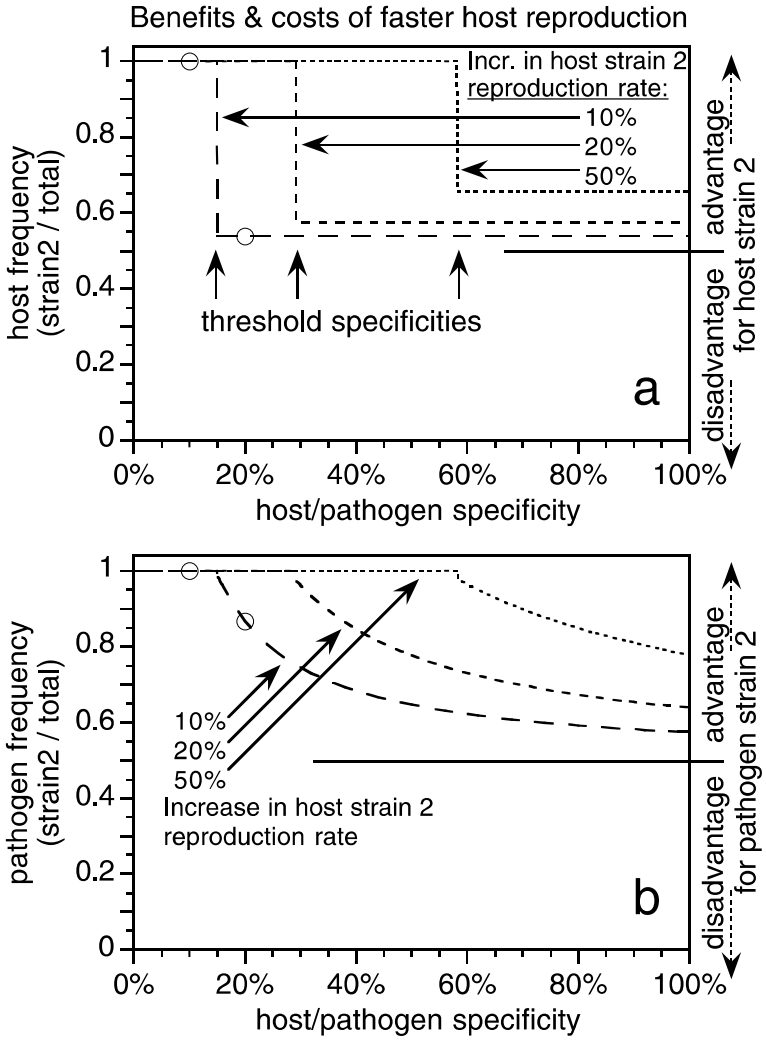
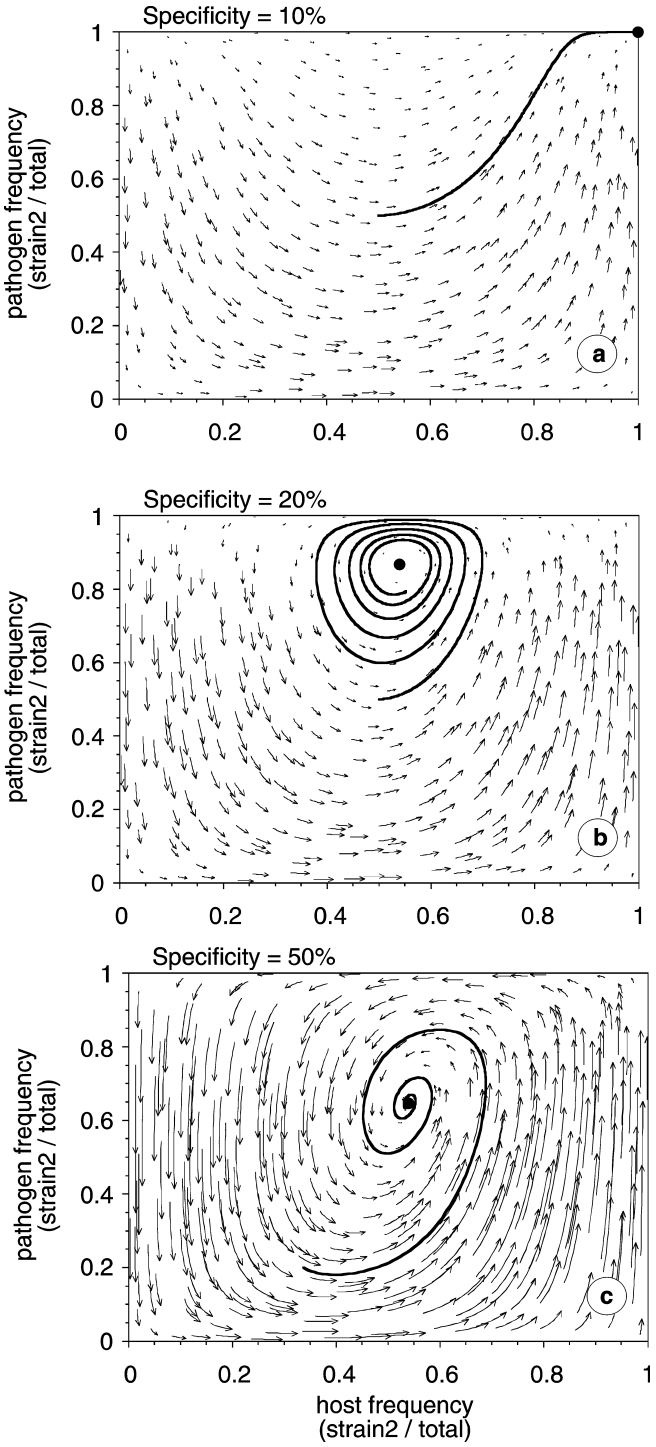


Figure 2. Equilibrium frequencies in host and pathogen populations (expressed as the fraction of each population that strain 2 represents), as a function of host–pathogen specificity. Curves are shown for three different rates of reproduction in host strain 2: 10, 20 and 50% greater than strain 1 (dashed line, small dashes and dotted line, respectively, corresponding to values of $a_2 = 11$, 12, and 15 in Equation (3)). Small circles mark conditions corresponding to the two simulations shown in Figure 1. (a) Frequency of strain 2 in the uninfected host population. Note the abrupt transition in host strain frequency, corresponding to the shift in dynamic behavior shown in Figure 1. (b) Frequency of pathogen strain 2. Note that the abrupt transition in host strain frequencies does not correspond to an abrupt change in pathogen strain frequencies.

These vector-field diagrams also help to reveal global system properties. From Figure 3a, one can see that below the specificity threshold, all possible initial conditions lead to loss of polymorphism, through the extinction of host


Specificity = 10%
pathogen frequency
(strain2 / total)
a
Specificity = 20%
pathogen frequency
(strain2 / total)
b
Specificity = 50%
pathogen frequency
(strain2 / total)
c
host frequency
(strain2 / total)
0
0.2
0.4
0.6
0.8
1

strain 1 and pathogen strain 1. By contrast, Figure 3b and c show that above the specificity threshold, all possible trajectories preserve polymorphism; none of the flow lines intersect the system boundaries (which represent fixation). However, at specificity values near the specificity threshold (Fig. 3b), many cycling trajectories pass very close to the system boundary for long periods of time, increasing the risk of stochastic extinction (which is not included in the model equations).

Dynamics of extinction and reintroduction

Figure 3 also helps one to visualize the consequences of extinction and reintroduction in our model system. Above the specificity threshold, stochastically induced extinction of either host strain would lead to extinction of one of the pathogen strains; likewise, extinction of either pathogen strain would lead to extinction of one of the host strains. That is, if the system is driven onto one of the boundaries of Figure 3b and c, the vector field will carry it into one of the corners representing fixation of one of the host strains and one of the pathogen strains.

Persistent polymorphism can be restored after any of these dual-extinction events (that is, from any corner of the diagram), but this requires reintroducing both the missing host and the missing pathogen. After a single host or pathogen strain is lost, its reintroduction can restore polymorphism if it occurs before its counterpart host or pathogen strain is lost (that is, while the system is still traveling along one of the boundaries, before it becomes fixed in a corner). The likelihood of such reintroduction events will depend on how frequently individuals migrate into the system, compared to the time required for the disadvantaged host or pathogen strain to be driven to extinction (that is, the time required for the system to be carried into the next corner). Recognizing these extinction/reintroduction boundary dynamics may be important for understanding the loss of genetic diversity in fragmented natural populations,

Figure 3. Vector-field diagram of host and pathogen strain frequencies for model parameters corresponding to the simulations shown in Figure 1 (10% higher reproduction rate in host strain 2) under host–pathogen specificity of 10, 20 and 50% (panels a–c, respectively). The arrows depict changes in strain frequencies during equal intervals of time (here, 0.2 time units). Thus, longer arrows indicate more rapid changes in frequencies. The solid dots show the equilibrium strain frequencies (corresponding to the open circles in Fig. 2). The solid lines show the trajectories of the simulations in Figure 1. The angular velocity of the system around the equilibrium point indicates the frequency of oscillation through time, which increases systematically with increasing specificity. The numbers of arrows, their starting positions, and the length of time they represent are the same in all panels; their apparent increase in density from (a) to (c) is an artifact of their increasing length, reflecting the system's increasing frequency of oscillation.

and for managing natural systems to preserve genetic diversity. Where frequency-dependent selection by pathogens helps to maintain genetic diversity in the host population, loss of genetic diversity in the pathogens will ultimately entail the loss of genetic diversity in the host as well.

Selection for greater host longevity under host–pathogen genetic specificity

One would expect longer-lived individuals to have an inherent fitness advantage, all else equal. This makes aging paradoxical; if longevity is advantageous, why are lifespans typically so much shorter than what would seem to be physiologically possible? Aging has been interpreted as an unstoppable process of cellular degeneration (Finch, 1990; Rose, 1991), or as the result of weaker selection against any mutations that become harmful after individuals have already reproduced and passed their genetic liabilities on to their offspring (Haldane, 1941; Partridge and Barton, 1993). There may also be trade-offs between lifespan and reproduction rate, such that intermediate lifespans optimize fitness (Stearns, 1992). Life history theory also suggests that in an unpredictable environment, this optimum should shift toward early and rapid reproduction, even at the cost of premature death (Williams, 1957; Stearns, 1992). The fitness consequences of longevity make it natural to ask how host–pathogen interactions would affect selection on lifespan traits. Here we extend our earlier work (Kirchner and Roy, 1999) by exploring how the genetic specificity of host–pathogen interactions affects selection on lifespan traits.

In Figures 4 and 5, host strain 2 has a longer lifespan than host strain 1, but both strains have equal reproduction rates. Thus we are varying lifespan without changing reproductive rate, allowing us to assess the evolutionary implications of lifespan alone, without the reproductive tradeoffs that have been the hallmark of previous studies (Gadgil and Bossert, 1970; Law, 1979; Jokela and Lively, 1995). In our simulations, pathogens affect host lifespan in two different ways, and it is important to distinguish between them. First, infection accelerates mortality and thus decreases lifespan by a factor m (Equation (4)); this extrinsic effect on longevity is the same for all infected hosts in our model. Second, pathogens may mediate selection on hosts' intrinsic longevity (τ in Equations (3) and (4)), that is, their genetically determined lifespan in the absence of disease and other stress factors. Our investigation focuses on how host longevity affects pathogen attack, and thus host fitness.

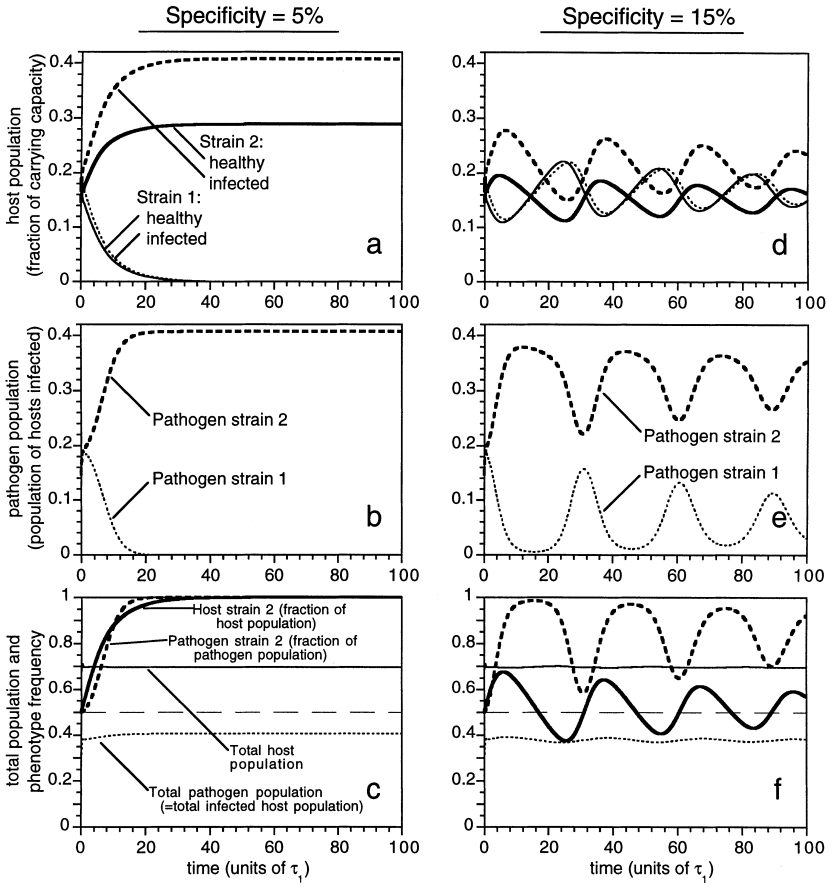
Host–pathogen specificity's effects on selection for host longevity (Figs. 4 and 5) are generally similar its effects on selection for host reproduction rates (Figs. 1 and 2), and we summarize them as follows. (1) When host–pathogen

Evolutionary Ecology **15:** 155, 2001.

Erratum

J.W. Kirchner and B.A. Roy (2000), Evolutionary implications of host-pathogenspecificity: the fitness consequences of host life history traits. *Evolutionary Ecology* **14** (8): 665–692.

In issue 14:8 of *Evolutionary Ecology*, Figure 4 published on page 682 was a duplicate of Figure 5. Please find below the correct Figure 4



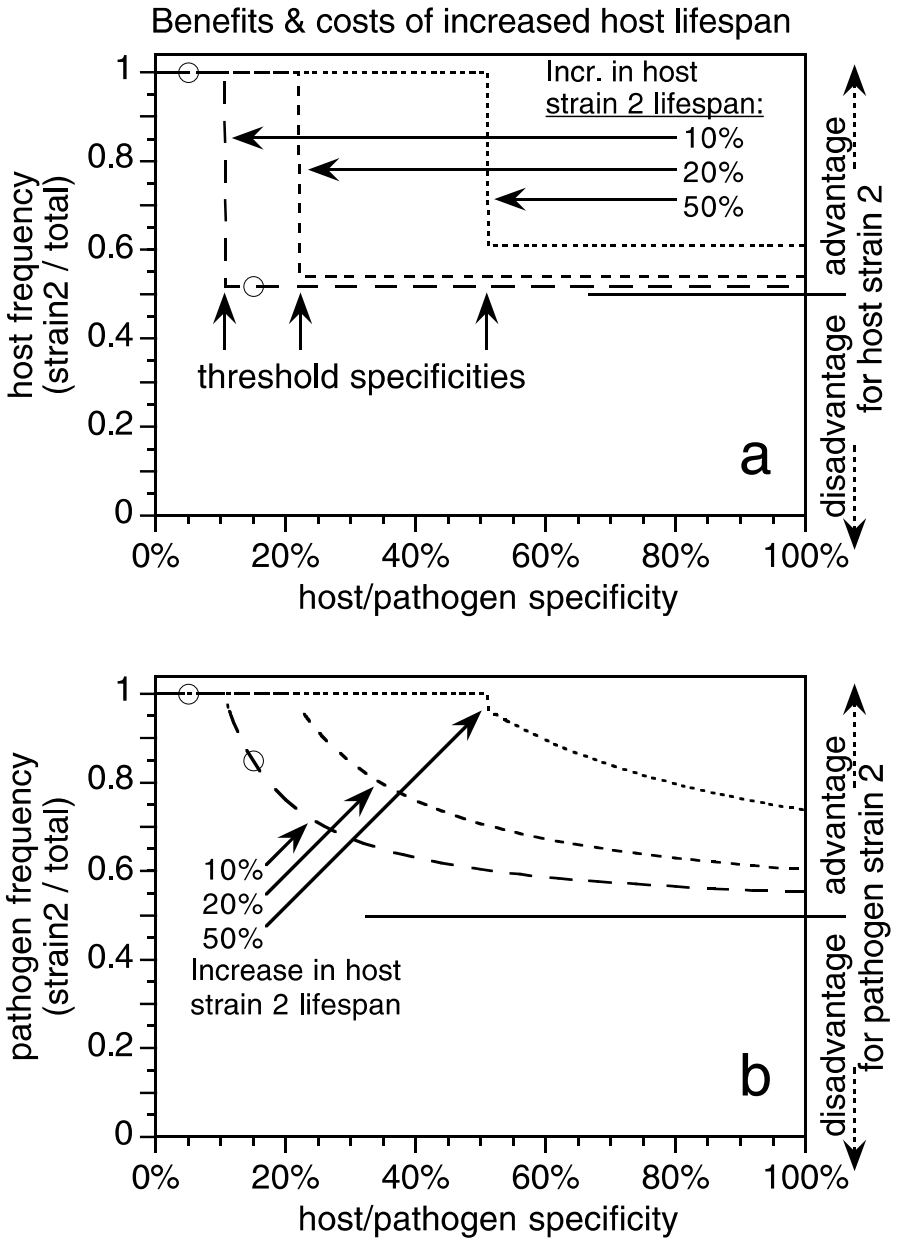


Figure 4. Selection for longevity, illustrated by host and pathogen population trajectories through time at two different levels of host–pathogen specificity; in each case, host strain 2's lifespan is 10% greater than host strain 1's ($\tau_1 = 1, \tau_2 = 1.1$). For a guide to the layout and symbols see the caption for Figure 1.

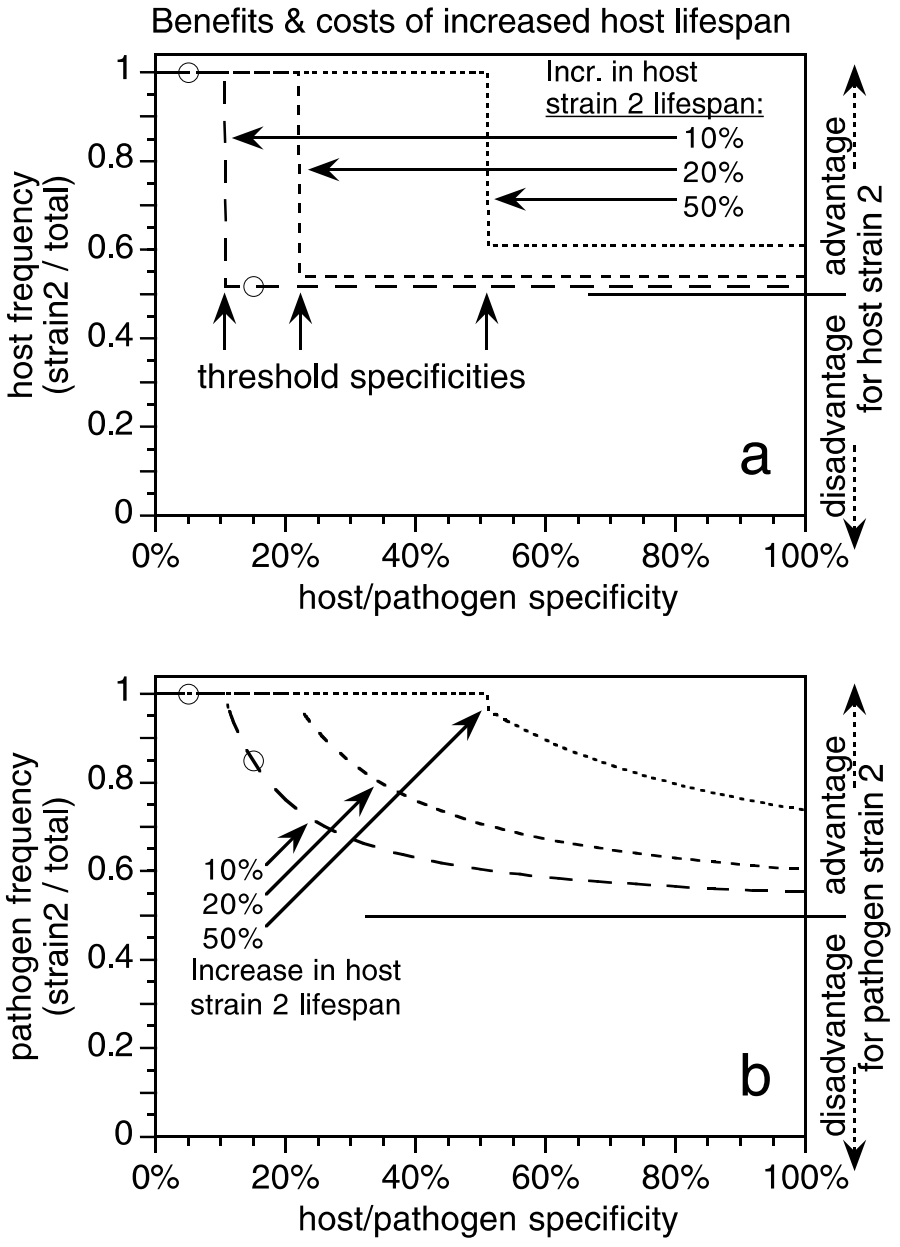


Figure 5. Equilibrium frequencies in host and pathogen populations (expressed as the fraction of each population that strain 2 represents), as a function of host–pathogen specificity. Curves are shown for three different increases in lifespan for host strain 2: 10, 20 and 50% longer than strain 1 (dashed line, small dashes and dotted line, respectively, corresponding to values of $\tau_2 = 1.1$, 1.2, and 1.5). Small circles mark conditions corresponding to the two columns of Figure 4. (a) Host strain frequency, (b) Pathogen strain frequency.

specificity is very low, the longer-lived strain (strain 2) grows to dominate the gene pool because it ultimately produces more offspring than the shorter-lived strain (Fig. 4a–c); the shorter-lived host strain (strain 1) and its associated pathogen are rapidly driven to extinction. (2) Above the specificity threshold, host and pathogen frequencies oscillate, converging toward polymorphic equilibrium (Fig. 4d–f); as one host strain becomes more successful, its advantage is offset by selection for the pathogen strain that can more easily exploit it. (3) The threshold between the fixation and polymorphic regimes is abrupt (Fig. 5). (4) Above the specificity threshold, large differences in longevity between the two host strains produce only small differences in their equilibrium frequencies (Fig. 5a), because greater host longevity reduces the mortality rate of infected hosts, and thus creates a larger and more persistent reservoir of disease, from which infection can spread to the healthy population. Greater host longevity can even be disadvantageous if infections are sterilizing and host–pathogen specificity is high (Kirchner and Roy, 1999). (5) The pathogen on the longer-lived host is always at a selective advantage over the pathogen on the shorter-lived host (Fig. 5b), but this advantage becomes smaller and smaller with increasing specificity, so that at high specificity levels, the two pathogen strains are cycling in nearly even proportions.

Discussion

Our model assumes that life history traits can be genetically linked to, or are pleiotropic with, resistance traits. This is a reasonable assumption given the pervasiveness of self-fertilization, mating with close relatives, and apomixis in plants (Hamrick and Godt, 1997; Richards, 1997), and given that recent studies have shown that resistance and life history traits are often linked (Parker, 1996a; Mestries *et al*., 1998; Thomas *et al*., 1998; Zhu *et al*., 1999).

Our results show that frequency-dependent selection can act to maintain polymorphism in host life history traits and not just host resistance traits. It has long been understood that frequency-dependent selection can maintain polymorphism in resistance alleles, because as particular resistance alleles become more common in the host population, they strengthen selection for pathogens that can evade them and infect the host (Haldane, 1949; Jaenike, 1978; Hamilton, 1982; Tooby, 1982; May and Anderson, 1983a; Barrett, 1988; Seger and Hamilton, 1988; Hamilton *et al*., 1990; Lively, 1996). Our analysis shows that a similar mechanism can maintain polymorphism in other host characteristics as well, because more successful (and thus more common) host strains create a larger evolutionary advantage for the pathogen strains that can exploit them.

For pathogen-mediated selection to maintain polymorphism in host life history traits, the degree of host–pathogen specificity must be sufficiently high and the fitness consequences of infection must be sufficiently severe, compared to the intrinsic fitness differences between the host strains (Fig. 6). These qualitative observations have also been made by others (Burdon, 1974; May and Anderson, 1983a; Barrett, 1988; Parker, 1992), but our analysis provides a quantitative framework for analyzing how pathogen-mediated selection can maintain polymorphism. We can also derive an approximate mathematical expression for the specificity threshold (see Appendix), which shows that the greater the fitness impact of disease and the average risk of infection, the smaller the degree of host–pathogen specificity that is required for polymorphism to persist, and the larger the fitness differences between hosts that can co-exist at any given level of specificity (Fig. 6). Conversely, the larger the intrinsic fitness difference between the host strains, the greater the host–pathogen specificity that is required to overcome it and thus maintain polymorphism (Fig. 6).

Many evolutionary explanations for polymorphism in life history traits assume antagonistic pleiotropy, or equivalently, assume that beneficial traits are accompanied by costs or tradeoffs (Roff, 1992; Stearns, 1992). Models have also examined how costs of resistance influence polymorphism in resistance traits (see for example Gillespie, 1975; Leonard and Czochor, 1980; May and Anderson, 1983b; van Baalen, 1998; Boots and Haraguchi, 1999). However, in our analysis, increased host longevity or fecundity comes at no direct cost (both host strains are equally susceptible to infection and both pathogen strains are equally infectious). Instead, polymorphism is maintained because changes in pathogen strain frequencies (which shift to exploit the more successful host) can eliminate the successful host's advantage. Thus the polymorphism is not maintained by tradeoffs among characteristics of either the hosts or the pathogens; it is instead maintained by stabilizing feedback between the strain frequencies in the host population and the strain frequencies in the pathogen population. This feedback, and thus the maintenance of polymorphism, does not require delicate balancing of parameters in the host–pathogen system.

The evolutionary consequences of host–pathogen relationships depend critically on the genetic specificity of the host–pathogen interaction. Previous analyses have generally assumed either that parasites are generalists (e.g., Holt and Pickering, 1985; Holt and Lawton, 1994) or that they are absolute specialists (e.g., Barrett, 1988; Frank, 1993; Hochberg and Holt, 1995; Hochberg and van Baalen, 1998). Our analysis shows that different levels of host–pathogen specificity lead to qualitatively different patterns of selection for host life history traits. Above the specificity threshold, pathogen-mediated selection greatly diminishes the fitness advantages conferred by host life history traits (Figs. 2 and 5). Selection is directional below the specificity threshold, systematically

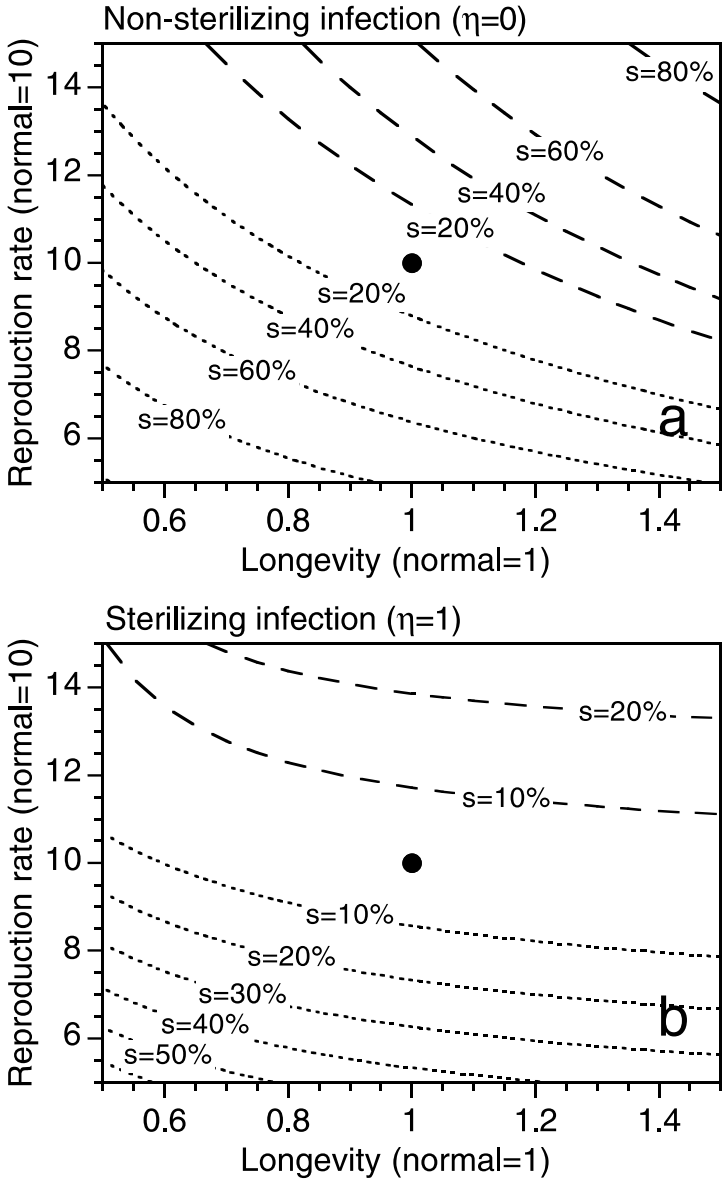


Figure 6. Characteristics of host strains that can invade a model system dominated by a 'normal' host strain ($a_1 = 10,\ \tau_1 = 1$) and its associated pathogen strain, and characteristics of hosts that can drive the 'normal' strain to extinction (see Appendix). For a given degree of host–pathogen specificity, hosts below the dotted line cannot invade against the 'normal' host strain (indicated by the solid dot in the center of each panel). Hosts above the dashed line will drive the 'normal' strain to extinction, and hosts between the dotted and dashed lines can co-exist with the 'normal' strain. The domain of co-existence grows with the degree of host–pathogen specificity, and with the fitness consequences of infection; the domain of co-existence is larger for sterilizing infections ($\eta = 1$, panel b) than non-sterilizing infections ($\eta = 0$, panel a).

increasing the frequency of advantageous host traits, whereas above the threshold, despite the advantages these traits confer, their frequencies converge toward polymorphic equilibria under stabilizing selection. Real-world host–pathogen systems are likely to fluctuate between these two domains, and thus fluctuate between directional and stabilizing selection. Even if the level of host–pathogen specificity remains constant (because it is genetically determined), the specificity threshold may fluctuate above and below that level (as, for example, the overall incidence of infection fluctuates). The net selection on host traits will integrate over these fluctuations between directional and stabilizing selection. The more time that the system spends above the specificity threshold (and thus under stabilizing selection), the smaller the net effect of selection on host traits will be.

Our analysis shows that some degree of host–pathogen specificity is required for pathogen-mediated selection to maintain polymorphism in host life history traits. That is, maintaining polymorphism by pathogen-mediated selection requires that the epidemiological consequences of host characteristics are borne to a larger extent by the hosts that carry those traits than by those that lack them. In this paper, we have shown that this condition may be met when individual host strains are more tightly coupled to some pathogen strains than to others. In other work, we have shown that even when different host strains are attacked by a single common pathogen, geographical isolation of host subpopulations can – under certain conditions – localize the epidemiological consequences of host traits strongly enough that polymorphism can be maintained (Kirchner and Roy, 1999). It remains to be seen whether similar results can be achieved through mechanisms other than geographical isolation and genetic specificity.

Our results highlight the role of disease in maintaining the genetic diversity of host populations. Pathogen-mediated selection can maintain polymorphism in host traits, including traits with substantial fitness consequences; in the absence of pathogen-mediated selection or similar stabilizing mechanisms, fitness differences among host strains inevitably lead to competitive exclusion. This implies that in some cases, preserving the genetic diversity of host organisms may require preserving the pathogens that afflict them. Disease and parasitism are often regarded as threats to conservation efforts (Gilbert and Hubbell, 1996; Hess, 1996; Real, 1996; Hiers and Evans, 1997; Jorgenson *et al.*, 1997), but our results suggest that they can sometimes be essential for preserving biological diversity. Here it is important to distinguish between two classes of pathogens. Introduced non-native pathogens can decimate host populations, because those hosts have had no chance to evolve resistance or tolerance to them (Gilbert and Hubbell, 1996; Real, 1996). By contrast, native pathogens that have coevolved with their hosts may pose little threat to the survival of host species, and may instead help to preserve their diversity.

Summary

Pathogens and parasites commonly exhibit genetic specificity, infecting some host strains more readily than others. We used a simple host–pathogen model to explore how host–pathogen specificity affects pathogen-mediated selection on two host life history traits, reproduction rate and longevity. When host–pathogen specificity is low, a host strain with greater intrinsic fitness will out-compete a less fit strain, driving it to extinction (Figs. 1a–c, 3a and 4a–c). However, at higher levels of host–pathogen specificity, pathogen-mediated frequency-dependent selection will permit both host strains to persist in the population, despite large intrinsic fitness differences between them (Figs. 1d–f, 3b, c and 4d–f). An abrupt specificity threshold separates the competitive exclusion domain from the polymorphic domain (Figs. 2 and 5). Above this threshold, pathogen-mediated selection regulates the two host strains at comparable equilibrium frequencies, even if their intrinsic fitnesses differ substantially (Figs. 1, 2, 4 and 5). The threshold value of specificity (that is, the degrees of specificity required to maintain polymorphism) increases with increasing fitness differences between the host strains, and decreases with increasing risks and fitness consequences of infection (see Appendix). Above the specificity threshold, maintaining polymorphism in the host requires maintaining polymorphism in the pathogen as well; elimination of either pathogen strain results in the extinction of one of the host strains, and vice versa (Fig. 3). Because pathogen-mediated selection can maintain polymorphism in host traits, preserving the genetic diversity of host organisms may require preserving the pathogens that afflict them.

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Appendix

Threshold conditions for invasion of host strains

Here we derive the conditions under which systems dominated by a single host strain (and its associated pathogen strain) can be invaded by another host strain with different longevity and/or fecundity.

Figure 3 shows that under host–pathogen specificity, model systems with only one host strain will normally have only one pathogen strain; the less efficient pathogen on that host will be competitively excluded. The equilibrium healthy and infected populations in the single-host, single-pathogen system can be found by solving the single-strain versions of Equations (3) and (4):

$$\frac{dX_1}{dt} = a_1(1 - X_1 - Y_{11})[X_1 + (1-\eta)Y_{11}] - \beta_{11}X_1Y_{11} - X_1/\tau_1 = 0 \quad (8)$$

$$\frac{dY_{11}}{dt} = \beta_{11}X_1Y_{11} - mY_{11}/\tau_1 = 0 \quad (9)$$

We denote these equilibrium populations as X_1^* and Y_{11}^*. Another host strain (here denoted as strain 2) can invade this equilibrium if its fitness is greater than strain 1's. While the population of host strain 2 remains small, the fitness of each host strain is

$$\begin{aligned}\omega_i &= a_i(1 - X_1^* - Y_{11}^*)\tau_i\left[1 - \frac{\beta_{i1}Y_{11}^*}{\beta_{i1}Y_{11}^* + 1/\tau_i}\left(1 - \frac{1-\eta}{m}\right)\right] \\ &= a_i(1 - X_1^* - Y_{11}^*)\tau_i[1 - r_{i1}L] \end{aligned} \quad (10)$$

where $a_i(1 - X_1^* - Y_{11}^*)\tau_i$ is the average reproductive potential of an uninfected host, $r_{i1} = \beta_{i1}Y_{11}^*/(\beta_{i1}Y_{11}^* + 1/\tau_i)$ is the lifetime risk of infection of host strain i by pathogen strain 1 (i.e., the ratio between the rate of infection and the total rate of loss of uninfected individuals to both infection and death), and $L = 1 - (1-\eta)/m$ is the fractional reduction in fitness when individuals become infected. Note that strain 2 does not appear in either the carrying capacity factor $1 - X_1^* - Y_{11}^*$ or the per-capita infection rate $\beta_{i1}Y_{11}^*$, because its initial population will be too small to affect these terms materially. The invasion criterion can be simplified to

$$a_2\tau_2[1 - r_{21}L] > a_1\tau_1[1 - r_{11}L] \quad (11)$$

Even if it has a nominal fitness disadvantage ($a_2\tau_2 < a_1\tau_1$), strain 2 can nonetheless invade if the fitness consequences of infection (L), the overall risk of infection, and/or the degree of specificity are sufficiently high. The difference between the risks of infection for the two host strains (r_{11} and r_{21}) will depend on the degree of host–pathogen specificity (because $\beta_{11} = \beta_o(1+s)$ and $\beta_{21} = \beta_o(1-s)$) and the longevity of each host strain.

A similar line of argument can be used to derive the conditions under which strain 2 can drive strain 1 to extinction. For strain 1 to become extinct, it must have a fitness disadvantage when strain 2, and its associated pathogen strain, dominate the model system. That is, strain 2 can drive strain 1 to extinction if

$$a_2\tau_2[1 - r_{22}L] > a_1\tau_1[1 - r_{12}L] \quad (12)$$

where $r_{i2} = \beta_{i2}Y_{22}^*/(\beta_{i2}Y_{22}^* + 1/\tau_i)$ is the risk of infection for each host strain when host strain 1 is ignorably small, and thus the risk of infection is controlled by pathogen strain 2.

Between these invasion and extinction thresholds, both host strains can co-exist, provided that pathogen strains can migrate into the system (because maintaining polymorphism in the host population requires the presence of both pathogen strains – see Figure 3b and c).

Figure 6 shows the domains of co-existence and exclusion under different degrees of host–pathogen specificity, for both sterilizing and non-sterilizing infections. As one would expect from Equations (11) and (12), higher degrees of host–pathogen specificity correspond to larger domains of co-existence (Fig. 6a). The domains of co-existence are also larger when the fitness consequences of infection are more severe, such as when infection sterilizes the host (Fig. 6b).

References

Agrios, G.N. (1988) *Plant Pathology*. Academic Press, San Diego, CA.

Arking, R., Buck, S., Berrios, A., Dwyer, S. and Baker, G.T. (1991) Elevated paraquat resistance can be used as a bioassay for longevity in a genetically based long-lived strain of *Drosophila*. *Develop. Genet.* **12**, 362–370.

Barrett, J.A. (1988) Frequency-dependent selection in plant–fungal interactions. *Philos. Trans. Royal Soc. B* **319**, 473–482.

Baudoin, M. (1975) Host castration as a parasitic strategy. *Evolution* **29**, 335–352.

Bell, G. (1982) *The Masterpiece of Nature: The Evolution and Genetics of Sexuality*. University of California Press, Berkeley.

Bergelson, J., Purrington, C.B., Palm, C.J. and López-Gutiérrez, J.-C. (1996) Costs of resistance: a test using transgenic *Arabidopsis thaliana*. *Proc. Royal Soc. London B* **263**, 1659–1663.

Beynon, J.L. (1997) Molecular genetics of disease resistance: an end to the 'gene-for-gene' concept. In I.R. Crute and J.J. Burdon (eds) *The Gene-For-Gene Relationship*. CAB International, Wallingford, UK, pp. 359–377.

Bierzychudek, P. (1987) Patterns in plant parthenogenesis. In S.C. Stearns (ed) *The Evolution of Sex and its Consequences*. Birkhauser-Verlag, Basel, pp. 197–217.

Boots, M. and Haraguchi, Y. (1999) The evolution of costly resistance in host–parasitoid systems. *Amer. Natur.* **153**, 359–370.

Borowicz, V.A. and Juliano, S.A. (1991) Specificity in host–fungus associations: do mutualists differ from antagonists? *Evol. Ecol.* **5**, 385–392.

Brewer, C.A. and Smith, W.K. (1997) Patterns of leaf surface wetness for montane and subalpine plants. *Plant Cell Environ. Cell Environ* **20**, 1–11.

Brooks, D.R. and McLennan, D.A. (1993) *Parascript*. Smithsonian Institution Press, Washington.

Buell, C.R. (1998) A weed leading the field of plant-pathogen interactions. *Plant Physiol. Biochem.* **36**, 177–186.

Burdon, J.J. (1974) Fungal and insect parasites contributing to niche differentiation in mixed species stands of eucalypt saplings. *Aust. J. Bot.* **22**, 103–114.

Burdon, J.J. (1987a) *Diseases and Plant Population Biology*. Cambridge University Press, Cambridge.

Burdon, J.J. (1987b) Phenotypic and genetic patterns of resistance to the pathogen *Phakopora pachyrhizi* in populations of *Glycine canescens*. *Oecologia* **73**, 257–267.

Clarke, D.D. (1997) The genetic structure of natural pathosystems. In I.R. Crute, E.B. Holub and J.J. Burdon (eds) *The Gene-for-Gene Relationship in Plant-parasite Interactions*. C. A. B. International, Oxon, United Kingdom, pp. 231–243.

Crute, I.R., Holub, E.B. and Burdon, J.J. (eds) (1997) *The Gene-for-Gene Relationship in Plant-Parasite Interactions*. CAB International, Oxon, UK.

Feder, M.E. (1999) Engineering candidate genes in studies of adaptation: the heat-shock protein Hsp70 in *Drosophila melanogaster*. *Amer. Natur.* **154**(suppl), S55–S66.

Finch, C.E. (1990) *Longevity, Senescence and the Genome*. University of Chicago Press, Chicago.

Fineblum, W.L. and Rausher, M.D. (1997) Do floral pigmentation genes also influence resistance to enemies? The W locus in *Ipomoea purpurea*. *Ecology* **78**, 1646–1654.

Frank, S.A. (1993) Specificity versus detectable polymorphism in host–parasite genetics. *Proc. Royal Soc. London B* **254**, 191–197.

Frank, S.A. (1996a) Problems inferring the specificity of plant–pathogen genetics. *Evol. Ecol.* **10**, 323–325.

Frank, S.A. (1996b) Statistical properties of polymorphism in host–parasite genetics. *Evol. Ecol.* **10**, 307–317.

Fryxell, P.A. (1957) Mode of reproduction in higher plants. *Bot. Rev.* **23**, 135–233.

Futuyma, D.J., Keese, M.C. and Funk, D.J. (1995) Genetic constraints on macroevolution: the evolution of host affiliation in the leaf beetle genus *Ophraella*. *Evolution* **49**, 797–809.

Gadgil, M. and Bossert, W.H. (1970) Life historical consequences of natural selection. *Amer. Natur.* **104**, 1–24.

Garrett, S.D. (1970) *Pathogenic Root-infecting Fungi*. Cambridge University Press, London.

Gilbert, G.S. and Hubbell, S.P. (1996) Plant diseases and the conservation of tropical forests. *BioScience* **46**, 98–106.

Gillespie, J.H. (1975) Natural selection for resistance to epidemics. *Ecology* **56**, 493–495.

Golenberg, E. and Nevo, E. (1987) Multilocus differentiation and population structure in a selfer, wild emmer wheat, *Triticum dicoccoides*. *Heredity* **58**, 451–456.

Haldane, J.B.S. (1941) *New Paths in Genetics*. Allen and Unwin, London.

Haldane, J.B.S. (1949) Disease and evolution. *La Ricerca Scientifica* **19**(suppl), 68–76.
Hamilton, W.D. (1980) Sex versus non-sex versus parasite. *Oikos* **35**, 282–290.
Hamilton, W.D. (1982) Pathogens as causes of genetic diversity in their host populations. In R.M. Anderson and R.M. May (eds) *Population Biology of Infectious Diseases*. Springer-Verlag, New York.
Hamilton, W.D., Axelrod, R. and Tanese, R. (1990) Sexual reproduction as an adaptation to resist parasites (a review). *Proc. Natl. Acad. Sci USA* **87**, 3566–3573.
Hamrick, J.L. and Godt, M.J. (1997) Effects of life history traits on genetic diversity in plant species. In J. Slivertown, M. Franco and J.L. Harper (eds) *Plant Life Histories*. Cambridge University Press, Cambridge, pp. 102–118.
Hedrick, P.W. (1980) Hitchhiking: a comparison of linkage and partial selfing. *Genetics* **94**, 791–808.
Hess, G. (1996) Disease in metapopulation models: implications for conservation. *Ecology* **77**, 1617–1632.
Hiers, J.K. and Evans, J.P. (1997) Effects of anthracnose on dogwood mortality and forest composition of the Cumberland plateau (USA). *Conser. Biol.* **11**, 1430–1435.
Hochberg, M.E. and Holt, R.D. (1995) Refuge evolution and the population dynamics of coupled host-parasitoid associations. *Evol. Ecol.* **9**, 633–661.
Hochberg, M.E. and van Baalen, M. (1998) Antagonistic coevolution over productivity gradients. *Amer. Natur.* **152**, 629–634.
Hoffmann, A.A. and Parsons, P.A. (1991) *Evolutionary Genetics and Environmental Stress*. Oxford University Press, New York.
Holt, R.D. and Lawton, J.H. (1994) The ecological consequences of shared natural enemies. *Annu. Rev. Ecol. Syst.* **25**, 495–520.
Holt, R.D. and Pickering, J. (1985) Infectious disease and species coexistence: a model of Lotka–Volterra form. *Amer. Natur.* **126**, 196–211.
Jaenike, J. (1978) An hypothesis to account for the maintenance of sex within populations. *Evol. Theory* **3**, 191–194.
Jokela, J. and Lively, C.M. (1995) Parasites, sex, and early reproduction in a mixed population of freshwater snails. *Evolution* **49**, 1268–1271.
Jorgenson, J.T., Festa-Blanchet, M., Gaillard, J.-M. and Wishart, W.D. (1997) Effects of age, sex, disease, and density on survival of bighorn sheep. *Ecology* **78**, 1019–1032.
Kawecki, T.J. (1998) Red queen meets Santa Rosalia: arms races and the evolution of host specialization in organisms with parasitic lifestyles. *Amer. Natur.* **152**, 635–651.
Kirchner, J.W. and Roy, B.A. (1999) The evolutionary advantages of dying young: epidemiological implications of longevity in metapopulations. *Amer. Natur.* **154**, 140–159.
Kurepa, J., Smalle, J., Van Montagu, M., Inze, D. (1998) Oxidative stress tolerance and longevity in *Arabidopsis*: the late-flowering mutant gigantea is tolerant to paraquat. *Plant J.* **14**, 759–764.
Law, R. (1979) Optimal life histories under age-specific predation. *Amer. Natur.* **114**, 399–417.
Leonard, K.J. and Czochor, R.J. (1980) Theory of genetic interactions among populations of plants and their pathogens. *Annu. Rev. Phytopathol.* **18**, 237–258.
Lively, C.M. (1996) Host–parasite coevolution and sex. *BioScience* **46**, 107–114.
May, R.M. and Anderson, R.M. (1983a) Epidemiology and genetics in the coevolution of parasites and hosts. *Proc. Royal Soc. London B* **219**, 281–313.
May, R.M. and Anderson, R.M. (1983b) Parasite–host coevolution. In D.J. Futuyma and M. Slatkin (eds) *Coevolution*. Sinauer Associates, Inc., Sunderland, MA, pp. 186–206.
Mestries, E., Gentzbittel, L., de Labrouhe, D.T., Nicolas, P. and Vear, F. (1998) Analyses of quantitative trait loci associated with resistance to *Sclerotinia sclerotiorum* in sunflowers (*Helianthus* annuus L.) using molecular markers. *Molecular Breeding* **4**, 215–226.
Parker, M.A. (1986) Individual variation in pathogen attack and differential reproductive success in the annual legume, *Amphicarpaea bracteata*. *Oecologia* **69**, 253–259.
Parker, M.A. (1991) Nonadaptive evolution of disease resistance in an annual legume. *Evolution* **45**, 1209–1217.

Parker, M.A. (1992) Disease and plant population genetic structure. In R.S. Fritz and E.L. Simms (eds) *Plant Resistance to Herbivores and Pathogens: Ecology, Evolution, and Genetics*. University of Chicago Press, Chicago, pp. 345–362.

Parker, M.A. (1994) Pathogens and sex in plants. *Evol. Ecol.* **8**, 560–584.

Parker, M.A. (1996a) Cryptic species within *Amphicarpaea bracteata* (Leguminosae): evidence from isozymes, morphology, and pathogen specificity. *Can. J. Bot.* **74**, 1640–1650.

Parker, M.A. (1996b) The nature of plant–parasite specificity. *Evol. Ecol.* **10**, 319–322.

Partridge, L. and Barton, N.N. (1993) Optimality, mutation and the evolution of ageing. *Nature* **362**, 305–311.

Press, W.H., Flannery, B.P., Teukolsky, S.A. and Vetterling, W.T. (1986) *Numerical Recipes: the Art of Scientific Computing*. Cambridge University Press, New York.

Price, P.W. (1980) *Evolutionary Biology of Parasites*. Princeton University Press, Princeton, NJ.

Real, L.A. (1996) Sustainability and the ecology of infectious disease. *BioScience* **46**, 88–97.

Richards, A.J. (1997) *Plant Breeding Systems*. Chapman & Hall, London.

Roff, D.A. (1992) *The Evolution of Life Histories: Theory and Analysis*. Chapman and Hall, New York, NY.

Rose, M.R. (1991) *The Evolutionary Biology of Aging*. Oxford University Press, Oxford.

Roy, B.A. and Bierzychudek, P. (1993) The potential for rust infection to cause natural selection in apomictic *Arabis holboellii* (Brassicaceae). *Oecologia* **95**, 533–541.

Scott, D.B., Jin, W., Ledford, H.K., Jung, H.S. and Honma, M.A. (1999) EAF1 regulates vegetative change and flowering time in *Arabidopsis*. *Plant Physiol.* **120**, 675–684.

Seger, J. and Hamilton, W.D. (1988) Parasites and sex. In R.E. Michod and B.R. Levin (eds) *The Evolution of Sex*. Sinauer, Sunderland, MA, pp. 176–193.

Stearns, S.C. (1992) *The Evolution of Life Histories*. Oxford University Press, Oxford.

Tatar, M. (1999) Transgenes in the analysis of life span and fitness. *Amer. Natur.* **154**(suppl), s67–s81.

Thomas, W.T.B., Baird, E., Fuller, J.D., Lawrence, P., Young, G.R., Russell, J., Ramsay, L., Waugh, R. and Powell, W. (1998) Identification of a QTL decreasing yield in barley linked to Mlo powdery mildew resistance. *Molecular Breeding* **4**, 381–393.

Thompson, J.N. (1994) *The Coevolutionary Process*. University of Chicago Press, Chicago.

Thompson, J.N. and Burdon, J.J. (1992) Gene-for gene coevolution between plants and parasites. *Nature* **360**, 121–125.

Tooby, J. (1982) Pathogens, polymorphism and the evolution of sex. *J. Theor. Biol.* **97**, 557–576.

van Baalen, M. (1998) Coevolution of recovery ability and virulence. *Proc. Royal Soc. London B* **265**, 317–325.

van der Plank, J.E. (1984) *Disease Resistance in Plants*. Academic Press, Orlando.

van Tienderen, P.H. (1991) Evolution of generalists and specialists in spatially heterogeneous environments. *Evolution* **45**, 1317–1331.

Via, S. (1990) Ecological genetics and host adaptation in herbivorous insects: the experimental study of evolution in natural and agricultural systems. *Annu. Rev. Entomol.* **35**, 421–446.

Weller, S.J., Ohm, H.W., Petterson, F.L., Foster, J.E. and Taylor, P.L. (1991) Genetics of resistance of CI 15160 durum wheat to biotype D of Hessian fly. *Crop Sci.* **31**, 1163–1168.

Weste, G. (1986) Vegetation changes associated with invasion by *Phytophthora cinnamoni* of defined plots in the Brisbane Ranges, Victoria, (Australia), 1975–1985. *Aust. J. Bot.* **34**, 633–648.

Williams, G.C. (1957) Pleiotropy, natural selection, and the evolution of senescence. *Evolution* **11**, 398–441.

Zhu, H., Gilchrist, L., Hayes, P., Kleinhofs, A., Kudrna, D., Liu, Z., Prom, L., Steffson, B., Toojinda, T. and Vivar, H. (1999) Does function follow form? Principal QTLs for *Fusarium* head blight (FHB9 resistance are concident with QTLs for inflorescenes traits and plant height in a doubled-haploid population of barley. *Theoret. Appl. Gen.* **99**, 1221–1232.