Rate of resistance evolution and polymorphism in long- and short-lived hosts

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Recent theoretical work has shown that long-lived hosts are expected to evolve higher equilibrium levels of disease resistance than shorter-lived hosts, but questions of how longevity affects the rate of resistance evolution and the maintenance of polymorphism remain unanswered. Conventional wisdom suggests that adaptive evolution should occur more slowly in long-lived organisms than in short-lived organisms. However, the opposite may be true for the evolution of disease-resistance traits where exposure to disease, and therefore the strength of selection for resistance increases with longevity. In a single locus model of innate resistance to a frequency-dependent, sterilizing disease, longer lived hosts evolved resistance more rapidly than short-lived hosts. Moreover, resistance in long-lived hosts could only be polymorphic for more costly and more extreme resistance levels than short-lived hosts. The increased rate of evolution occurred in spite of longer generation times because longer-lived hosts had both a longer period of exposure to disease as well as higher disease prevalence. Qualitatively similar results were found when the model was extended to mortality-inducing diseases, or to density-dependent transmission modes. Our study shows that the evolutionary dynamics of host resistance is determined by more than just levels of resistance and cost, but is highly sensitive to the life-history traits of the host.

KEY WORDS: Anther smut, generation time, longevity, polymorphism, resistance, sterilizing disease.

Host longevity is widely acknowledged to be a critical factor in the evolution of pathogen virulence (May and Anderson 1983; Gandon et al. 2001; Day 2003), but only a few studies have investigated effects of longevity on the evolution of host resistance. Selection for innate or constitutive disease resistance has been hypothesized to increase with longevity because long-lived hosts potentially have a greater lifetime exposure to disease (Bell et al. 1991; Morand and Harvey 2000) and can support larger pathogen populations (Thrall et al. 1993a; Bowers et al. 1994; Kirchner and Roy 1999). Theoretical work confirms this hypothesis: Boots and Haraguchi (1999) first showed that equilibrium levels of innate resistance increase with longevity, and more recently, Carlsson-Granér and Thrall (2006) used a spatially explicit model to show that long-lived hosts evolved greater levels of resistance to sterilizing diseases than shorter-lived hosts. Miller et al. (2007) and Boots et al. (2013) used adaptive-dynamics approaches to show that long-lived hosts are predicted to invest more heavily in several types of costly resistance, including innate resistance. However, we have little understanding of how longevity affects polymorphism for resistance, or how longevity affects the rate at which such resistance evolves. In addition, longevity can vary substantially within species, due to extrinsic factors that affect survival, but we do not know how such variation affects the evolution of resistance.

Polymorphism for innate resistance has been found in a wide variety of hosts, including plants (Alexander et al. 1993; Thrall and Burdon 2003; Laine 2004; Chung et al. 2012), animals (Lively and Apanius 1995; Carius et al. 2001; Tschirren et al. 2013), and humans (Baker and Antonovics 2012). Theoretical studies have shown that polymorphisms are readily maintained depending on the degree of resistance conferred and the fitness cost in the absence of disease (Antonovics and Thrall 1994; Bowers et al. 1994; Boots and Haraguchi 1999). However, previous theoretical work on the relationship between host longevity and resistance...
evolution has largely avoided the question of polymorphism. Tellier and Brown (2009) showed that, in coevolving gene-for-gene systems, polymorphisms are more readily maintained in longer lived, perennial plants, but we lack predictions for how polymorphism evolves in systems that are not tightly coevolving. Indeed, because polymorphism complicates the analysis of adaptive dynamics models, they have been largely avoided by assuming an accelerating cost of resistance that precludes the evolution of polymorphisms (Miller et al. 2007; Boots et al. 2013), leading to a gap in our understanding that is highly relevant to the dynamics of natural systems.

Previous work on longevity has focused on equilibrium levels of resistance and not on the rate of its evolution. The rate of resistance evolution is important for understanding coevolutionary arms races, because more slowly evolving hosts may not be able to keep pace with rapidly evolving pathogens (Gandon and Michalakis 2002; Woolhouse et al. 2002). Longer life spans are associated with longer generation times (Stearns 1992; Roff 2002) and it might be expected, at least naïvely, that this will lead to a slower rate of evolution regardless of the eventual equilibrium (May and Dobson 1986). Theoretical models of pesticide insensitivity have demonstrated the opposite can occur because long-lived insects are subject to more pesticide treatments (Rosenheim and Tabashnik 1991).

Here, we extend the analytical model of resistance polymorphism developed by Antonovics and Thrall (1994) to investigate the factors that contribute to the relationship between host longevity and resistance evolution. Our primary focus was on resistance to sterilizing diseases with frequency-dependent transmission, likely to be typical for many sexually transmitted and vector transmitted diseases. We first ask whether longevity affects the range of conditions over which a polymorphism is maintained. Next, we use simulations to determine how longevity affects the rate of resistance evolution, extending the study by including resistance to diseases that vary in transmission mode (frequency or density-dependence) and form of virulence (sterilizing or mortality-inducing). Finally, we use data from the anther-smut disease system to examine the likely outcomes for resistance evolution when there is life-span variation among and within host species.

The Model
We initially use the model of Antonovics and Thrall (1994) for frequency-dependent, sterilizing disease where resistance is controlled by a single locus with two alleles, and the host is haploid. Throughout, we assume the pathogen is genetically uniform. The model additionally assumes that the disease is completely sterilizing, that there is no disease-induced mortality or recovery, and that all infected hosts transmit the disease at the same rate. A cost of resistance, $c$, is incorporated as a reduction in the birth rate, $b_R$, of the resistant host relative to the birth rate of the susceptible host, $b_S = b - c$. Costs have been demonstrated for many systems (Webster and Woolhouse 1999; Tian et al. 2003; Karasov et al. 2014), and are as high as 20% for resistance to anther-smut disease in Silene latifolia (Biere and Antonovics 1996). Disease-independent population regulation is included by making birth rates a negative function of host density, $-kN$; density regulation is a prerequisite for stable host–pathogen coexistence in diseases with frequency-dependent transmission (Getz and Pickering 1983; Thrall et al. 1993a). The death rate, $\mu$, is kept constant for susceptible, resistant, and infected hosts. The infection rate of susceptible and resistant hosts is determined by the transmission coefficient $\beta_S$ and $\beta_R$, respectively, and by the frequency of infected individuals in the population ($I/N$). We assume that $\beta_S > \beta_R$.

The dynamics of the model can be represented by the following equations:

\[
\frac{dS}{dt} = S(b - \mu - kN) - S\beta_S \frac{I}{N} \quad (1)
\]

\[
\frac{dR}{dt} = R(b - c - \mu - kN) - R\beta_R \frac{I}{N} \quad (2)
\]

\[
\frac{dI}{dt} = S\beta_S \frac{I}{N} + R\beta_R \frac{I}{N} - \mu I. \quad (3)
\]

where $S$ is the number of healthy susceptible hosts, $R$ the number of healthy resistant hosts, $I$ the number of infected hosts, and $N$ is the total population size.

To address the generality of our results, we created three additional models: (1) density-dependence, sterilizing; (2) frequency-dependent, mortality-inducing; and (3) density-dependent, mortality-inducing. To model density-dependent transmission, we changed the force of infection term from $\beta S(I/N)$ to $\beta SI$. To model mortality-inducing diseases, we assumed that infected individuals reproduced at the same rate as healthy individuals, but suffered additional mortality, $\alpha$:

\[
\frac{dS}{dt} = (S + I_s)(b - kN) - \mu S - \beta_S S(I_s + I_R) \quad (4)
\]

\[
\frac{dR}{dt} = (R + I_R)(b - c - kN) - \mu R - \beta_R R(I_s + I_R) \quad (5)
\]

\[
\frac{dI_s}{dt} = \beta_S S(I_s + I_R) - I_s(\mu + \alpha) \quad (6)
\]

\[
\frac{dI_R}{dt} = \beta_R R(I_s + I_R) - I_R(\mu + \alpha). \quad (7)
\]

where $I_s$ is the number of infected susceptible hosts and $I_R$ is the number of infected resistant hosts.
To test the prediction that resistance evolves more rapidly in long-lived hosts, we ran simulations for all four models by introducing the resistant genotype at low frequency (0.1) to susceptible populations at equilibrium prevalence and calculating the time to near fixation of the resistant genotype (frequency \( \geq 0.99 \)). The results were not qualitatively affected by a lower (0.01) starting frequency of the resistant genotype (data not shown). We ran additional simulations on the focal model of a frequency-dependent, sterilizing disease to further explore how factors that are commonly correlated with longevity, such as birth rate and generation time (defined as the time until first reproduction), affected the time to fixation.

All simulations were deterministic and run using the Runge–Kutta function to approximate the differential equations (R version 2.12.0, The R Foundation for Statistical Computing; deSolve package; Soetaert et al. 2010).

**Analysis and Results**

**EFFECT OF LONGEVITY ON THE STRENGTH OF SELECTION**

For a frequency-dependent, sterilizing disease model and assuming no cost of resistance \( (c = 0) \), the relative fitness of the resistant genotype (i.e., the per capita growth rate of the resistant genotype over the susceptible genotype) can be expressed as:

\[
\frac{W_R}{W_S} = \frac{X - (\beta_R \frac{I}{N} + \mu)}{X - (\beta_S \frac{I}{N} + \mu)},
\]

where \( X = b - kN \). Because both the numerator and denominator of equation (4) must be positive, and \( \beta_R < \beta_S \), it can be seen that the relative fitness of the resistant genotype, \( W_R/W_S \), will increase as \( \mu \) decreases; selection for resistance therefore increases as longevity increases. If \( \mu \) is small compared to the infection rate of the resistant host, \( \beta_R \frac{I}{N} \), then the relative fitness of the resistant genotype should increase approximately as a function of the transmission ratio \( \beta_R/\beta_S \). However, if \( \mu \) is large compared to the infection rate, then the relative fitness will not be strongly affected by \( \beta_R/\beta_S \). If \( c > 0 \), then selection for resistance will also depend on the ratio of cost and relative benefit of resistance (Antonovics and Thrall 1994), as we discuss below.

**CONDITIONS FOR RESISTANCE POLYMORPHISM IN STERILIZING PATHOGENS**

Antonovics and Thrall (1994) demonstrated that the ability of a resistant genotype to invade a susceptible population depends on \( \theta \), the magnitude of its cost relative to its benefit in reducing disease transmission:

\[
\theta = c/(\beta_S - \beta_R),
\]

and that polymorphism in resistance is maintained if:

\[
\frac{\beta_R - \mu}{\beta_R} < \theta < \frac{\beta_S - \mu}{\beta_S}.
\]

To examine the effect of longevity on the parameter space for resistance evolution, we held \( b \) and \( \beta_S \) constant at 1, and varied \( c \) and \( \beta_R \) across a range of mortality rates (\( \mu = 0.01\)–0.5), representing host longevities from 50 to 2 years. With \( \beta_S = 1 \), the above inequality can be rewritten in terms of \( c \) such that resistance polymorphism is maintained if:

\[
\frac{(1 - \beta_R)(\beta_R - \mu)}{\beta_R} < c < (1 - \mu) + \beta_R(\mu - 1).
\]

Above the upper threshold of \( c \), resistance is lost from the population, whereas below the lower threshold, the resistance goes to fixation.

Analysis of inequality 11 shows that longer lived hosts can evolve resistance over a broader range of resistance costs and that populations of longer lived hosts are more likely to go to fixation for resistance than to maintain polymorphism (Fig. 1). In the longest lived hosts (Fig. 1D), stable polymorphism can only be maintained with a very high resistance and high cost.

**RATE OF RESISTANCE EVOLUTION**

Where resistance evolved to fixation, longevity increased both equilibrium disease prevalence as well as the rate of resistance fixation (Fig. 2). The time to resistance fixation declined nonlinearly with increasing host longevity. A greater level of resistance also accelerated the rate of fixation. The negative relationship between longevity and time to fixation was not significantly altered when we assumed a trade-off between longevity and birth rate (Fig. S1) or between longevity and generation time (Fig. S2).

Faster resistance fixation in longer-lived hosts was not specific to sterilizing diseases with frequency-dependent transmission, but also occurred in simulations that assumed density-dependent transmission (Fig. 2B and D) or classic mortality-inducing virulence (Fig. 2C and D). Increased longevity also led to higher disease prevalence (Fig. 2C) or disease density (Fig. 2B and D), thereby increasing the risk of infection. In density-dependent sterilizing diseases, resistance level had a larger effect on the disease density for short life spans, which may explain why resistance-level had a larger effect on time to fixation in density than in frequency-dependent, sterilizing diseases. In mortality-inducing diseases, the relationship between longevity and the time to fixation depended on the level pathogen-induced mortality (virulence). At high levels of virulence, the rate of resistance evolution increased with longevity similar to that seen in sterilizing diseases, although the prevalence remained low. However, at low levels of virulence, the time to fixation increased with longevity (Fig. S4), likely because the fitness cost of infection was not strong enough to counteract the longer generation time.
EFFECT OF LONGEVITY ON THE PROBABILITY OF INFECTION

To understand the mechanism driving the relationship between host longevity and infection risk, we calculated the probability of infection as a function of host life span for the case of a frequency-dependent, sterilizing disease. At equilibrium, the probability that an individual will survive to time $t$, $P(A_t)$, and be infected $P(A_t \cap I_t)$ can be expressed as the probability of surviving minus the probability of surviving and remaining healthy:

$$P(A_t \cap I_t) = (1 - \mu)^t - \left[(1 - \mu) \left(1 - \frac{I^*}{N^*}\right)^t\right]. \quad (12)$$

If we assume that the average life span of a host is $1/\mu$, then the probability that an individual will survive to its expected life span, $P(A_{1/\mu})$, and be infected, $P(I_{1/\mu})$, can be expressed as:

$$P(A_{1/\mu} \cap I_{1/\mu}) = (1 - \mu)^{1/\mu} - \left[(1 - \mu) \left(1 - \frac{I^*}{N^*}\right)^{1/\mu}\right]. \quad (13)$$

Further, the probability that an individual will be diseased, given that it survives to its expected life span, $P(I_{1/\mu} | A_{1/\mu})$, can be expressed as probability of surviving and being infected divided by the probability of surviving:

$$P(I_{1/\mu} | A_{1/\mu}) = \frac{P(A_{1/\mu} \cap I_{1/\mu})}{P(A_{1/\mu})}. \quad (14)$$

Results of simulations from equation (14) show that the probability of infection given survival increases nonlinearly with longevity (Fig. 3). When we held equilibrium prevalence ($I^* / N^*$ in 13) constant, the probability of infection given survival increased with longevity due to longer exposure time (dashed line, Fig. 3). However, prevalence is known to increase as a function of transmission and mortality rate, such that $\frac{I^*}{N^*} = \frac{\beta - \mu}{\beta}$ (Thrall et al. 1993a). When we allowed prevalence to increase with longevity, the probability of infection increased at a much steeper rate (solid line, Fig. 3). Indeed, this strong increase in infection probability closely mirrors the rapid decrease in the time to fixation observed in our simulations (Fig. 2A), suggesting the increased risk of...
Figure 2. Effect of host longevity on the time to resistance fixation. *Solid lines*—time to resistance fixation, *Dashed lines*—disease prevalence (A, C) or disease density (B, C) at equilibrium. Each simulation was run twice with $\beta_R$ 25% and 50% lower than $\beta_S$. (A) Frequency-dependent, sterilizing disease: $\beta_S = 0.5$, $b = 1$, $c = 0.05$, $k = 0.001$. (B) Density-dependent sterilizing disease: $\beta_S = 0.0005$, $b = 1$, $c = 0.05$, $k = 0.001$. (C) Frequency-dependent mortality-inducing disease: $\beta_S = 1$, $b = 1$, $c = 0.02$, $k = 0.001$, $\alpha = 0.4$. The cost of resistance was lower for this simulation, because resistance did not evolve when $c = 0.05$. (D) Density-dependent mortality-inducing disease: $\beta_S = 0.01$, $b = 1$, $c = 0.1$, $k = 0.001$, $\alpha = 1.5$.

Longevity and Resistance to Anther-Smut Disease

**VARIATION IN LONGEVITY WITHIN SPECIES**

To determine the likely sensitivity of disease resistance evolution to variation in longevity as found within a field situation, we ran simulations using mortality and transmission rates estimated from demographic studies of anther-smut disease on two host species: *Dianthus pavonius* and *Silene caroliniana*. Anther smut is a sterilizing disease of plants in the carnation family (Caryophyllaceae) caused by species of fungi in genus *Microbotryum*. Individual *Microbotryum* species are highly host specific (Le Gac et al. 2007), but the basic biology of the disease is similar across all hosts. The anthers of infected plants produce spores in place of pollen and these are transmitted to new hosts via pollinators. The disease does not affect mortality, but seed production is also prevented, and recovery is rare (Alexander et al. 1996).

*Dianthus pavonius* is an alpine perennial endemic to the Maritime Alps region of Italy and France. Annual mortality and transmission rates were estimated for a population of *D. pavonius* in the Parco Marguareis in the Piemonte province of Italy. From 2009 to 2013, we monitored survival and disease status of 382 individually tagged plants. We used these data to calculate annual mortality and transmission rates. *Silene caroliniana* is a perennial species native to Eastern North America. From 1999 to 2004, we monitored two populations ($N = 272$ and 162) on the Blue Ridge Parkway in Nelson County, Virginia, and calculated mortality and transmission rates of individually tagged plants.

We used the minimum and maximum mortality rates observed in each population to estimate the potential range in life span, and the transitions from healthy to diseased state of individual plants plus disease prevalence in the previous year to
estimate transmission rates. Then, we ran simulations to evaluate the fate of an allele that conferred 50% higher resistance using maximum and minimum annual mortality rates, and the average, minimum, and maximum transmission rates. Because no information is available on costs of resistance for these species, we ran all simulations using a first relatively low cost, $c = 0.05$, and then a higher cost, $c = 0.2$, comparable to that observed in *S. latifolia* (Biere and Antonovics 1996). We used a discrete version of the basic frequency-dependent, sterilizing model that allowed reproduction to occur prior to infection (eqs. 15–17), since in both species the flowering season is only a few weeks long and plants that become infected during flowering reproduce normally and only express the smutted anthers in the following year. Density-dependent regulation was represented by $b' = b/(1 + kN)$.

$$S_{t+1} = S_t (1 - \mu) \left[ 1 + b' - \left( \beta_S \frac{I_t}{N_t} \right) \right]$$  \hspace{0.5cm} (15)$$

$$R_{t+1} = R_t (1 - \mu) \left[ 1 + (b' - c) - \left( \beta_R \frac{I_t}{N_t} \right) \right]$$  \hspace{0.5cm} (16)$$

$$I_{t+1} = I_t (1 - \mu) + S_t (1 - \mu) \left( \beta_S \frac{I_t}{N_t} \right) + R_t (1 - \mu) \left( \beta_R \frac{I_t}{N_t} \right).$$  \hspace{0.5cm} (17)$$

In *D. pavonius*, mortality ranged from 13.9% in 2009 to 27.7% in 2013, giving a longevity range of 3.6–7.2 years (Table S1). Transmission rates ranged from 0.041 in 2010 to 0.291 in 2013, with an average of 0.145. When the transmission rate was at or below the average observed rate of $\beta = 0.145$, the pathogen could not persist at any level of host longevity within the estimated range. However, when the transmission rate was at the upper end of the observed range ($\beta = 0.291$), pathogen persistence and the fate of an introduced resistance gene strongly depended on longevity (Fig. 4A). At longevities less than 4.3 years, local extinction of the pathogen was predicted for all estimates of transmission rate and cost, and resistance did not evolve. However, at longevities greater than 4.3 years, the disease was predicted to persist at equilibrium, with resistance evolving to a stable polymorphism.

In *S. caroliniana* Population 1, mortality ranged from 5 to 23%, giving an estimated longevity of 4.3–18 years (Table S1). Transmission rate ranged from 0 to 0.027. In simulations, disease was unable to persist and resistance did not evolve. In *S. caroliniana* Population 2, mortality ranged from 2.1 to 15.2%, giving an estimated longevity range of 6.6–47 years. The average transmission rate was much higher ($\beta = 0.23$) and extremely variable, ranging from 0 to 0.65. At the average transmission rate, disease persisted at a high prevalence and resistance was predicted to evolve to fixation at all, but the very lowest estimate of longevity (Fig. 4B). At the upper transmission rate, the population was driven to near extinction when resistance was not allowed to evolve (prevalence > 95%, data not shown).

**VARIATION IN LONGEVITY AMONG HOST SPECIES**

Marr and Delph (2005) reviewed studies from five different species infected by *Microbotryum* and found a highly significant negative correlation between longevity and per year disease transmission rates. This finding was corroborated in a subsequent review (Carlsson-Granér and Thrall 2006) and remains when we add our own data on disease transmission in two additional species, *D. pavonius* and *S. caroliniana* (Fig. S4).

To determine whether either increased resistance evolution or disease-driven extinction of long-lived hosts could account for this negative correlation, we ran pair-wise simulations using transmission rates and longevities reported in the literature and from our own field studies for anther smut on five different species that varied substantially in life span: *S. latifolia* (2.6–3 years), *S. virginica* (1.6–4.1 years), *D. pavonius* (3.7–7.5 years), *S. caroliniana* (7.7–16.7 years), and *S. acaulis* (100+ years). We used equations (15) and (17) to simulate epidemics in the absence of resistance evolution using the estimated transmission rate for the pathogen and the range of longevities reported for each host, and we determined whether the diseased was lost, maintained, or drove the host population extinct.

The high transmission rates (as found in anther smut on *S. latifolia* and *S. virginica*) enabled persistence of the disease on all host species, except in the longest lived host *S. acaulis*, where the host and pathogen were driven to extinction (Table S2). In contrast, lower transmission rates (as found in anther smut on *D. pavonius*, *S. caroliniana*, and *S. acaulis*) could not maintain persistent infections on shorter lived host populations (*S. latifolia* and *S. viriginica*). In several cases, simulations predicted loss of
the pathogen from its own host population, at least at the lower ranges of longevity (S. virginica, D. pavonius, S. caroliniana). Because host extinction was observed in only one instance (S. acaulis), these results suggest that the pattern of decreasing transmission rate with increasing longevity could well be driven by increased resistance evolution of longer lived hosts rather than the result of local extinction of hosts, leading to selection favoring reduced infectiousness of the pathogen.

Resistance evolution occurred more rapidly in longer lived hosts despite their longer generation times, and this result was quite general for different transmission modes and virulence effects. This accelerated deterministic rate of allele fixation was driven by both the increased risk of disease as well as greater pathogen prevalence associated with a longer life span.

Applying this theory to real-world populations, variation in longevity on the order of that observed within two different species, resulted in widely different predicted outcomes ranging from loss of the resistant allele to polymorphism or to fixation. Consequently, spatial variation in environmental factors, such as precipitation, temperature, and grazing, which result in site variation in host mortality could lead to strongly different fates of introduced resistance genes among populations of the same host species, even without changes in transmission rate. In addition, species inhabiting alpine regions, such as D. pavonius, are widely considered to be more vulnerable to habitat loss through climate change (Dirnböck et al. 2011; Pauli et al. 2012). Current climate models predict increased summer temperatures and decreased

Discussion

Our study confirms that host life-history traits, especially longevity, play an important role in determining the evolution of disease resistance. We found that long-lived hosts evolve resistance more rapidly and under a wider range of conditions than short-lived hosts, and are much less likely to maintain polymorphisms for resistance genes. Standing genetic variation in disease-related traits, an important ingredient for coevolution, may therefore be strongly influenced by host longevity.

Figure 4. Predicted fate of an allele that confers 50% greater resistance in (A) Dianthus pavonius and (B) Silene caroliniana over a range of longevities observed in the field. Solid and wide dashed lines show the predicted frequency of the resistant genotype at equilibrium, assuming two different levels of cost. Dotted lines show the equilibrium prevalence of disease when resistance is not allowed to evolve. Shading represents the range of observed longevity values. (A) Dianthus pavonius: results are only for simulations that used the upper estimate of transmission rate, $\beta_S = 0.294$, because lower rates $\beta_S$ resulted in local extinction of the pathogen. (C) Silene caroliniana (population 2): results are for the average transmission rate, $\beta_S = 0.23$. 
precipitation across the Western Alps (Engler et al. 2011), which could affect host mortality rates and lead to systemic changes in disease prevalence and resistance evolution over time, including local extinction of either the pathogen or the host.

The negative correlation between life span and transmission rate in the anther-smut system (Marr and Delph 2005; Carlsson-Granér and Thrall 2006) was confirmed by additional data from two species, and suggests that long-lived hosts have indeed evolved greater resistance than shorter lived hosts. A counter hypothesis is that there has been evolution of lower infectiousness in the pathogen, as a result of local population extinction. O’Keefe and Antonovics (2002) demonstrated that evolution of decreased infectiousness is possible for sterilizing pathogens in spatially structured populations because local extinction of the host also results in decreased fitness of pathogens. Such spatial structuring is to be expected in these perennial species as they have no specialized means of long-distance seed dispersal and pollinator movements are also quite local (Alexander 1990; Carlsson-Granér 2006; Carlsson-Granér et al. 2014). However, our simulations show that in all but the most extreme cases, pathogens with observed high transmission rates can persist on hosts with longer life spans than those they currently occupy, and at higher prevalence. This result argues that the low transmission rates observed in long-lived hosts are a result of resistance evolution in the host rather than evolution of lower infectiousness in the pathogen. Moreover, in the anther-smut system, there appears to be low within-population variation in infectivity (Alexander et al. 1993; Kaltz and Shykoff 2002) and local maladaptation of the pathogen (Kaltz et al. 1999), suggesting that the pathogen’s evolutionary potential is low compared with that of the host’s. However, this issue deserves further investigation: our model does not account for spatial structure within these species, nor the consequences of year-to-year variation in their longevity and transmission as there was insufficient data to estimate the distributional properties of such variation with any confidence.

Our results also cast light on the broader debate about the relationship between longevity and pathogen abundance observed in comparative studies. Although some authors have argued that a positive relationship is expected because longer-lived organisms have a greater likelihood of encountering parasites (Bell et al. 1991; Poulin and Morand 2000), others have argued that a negative relationship is expected if longer-lived organisms “invest” more heavily in immunity (Zuk and Stoehr 2002; Miller et al. 2007; Arriero and Möller 2008; Cooper et al. 2012; Boots et al. 2013). Comparative studies in mammals and birds have shown contrasting patterns: a positive correlation between longevity and pathogen species richness has been found in primates (Nunn et al. 2003), but a negative correlations between longevity and parasite species richness have been found in ungulates (Morand and Harvey 2000; Ezenwa et al. 2006; Cooper et al. 2012) and birds (Arriero and Möller 2008). Our findings demonstrate conflicting forces: while longer lived organisms do indeed have a much greater likelihood of encountering disease, they are also more likely to evolve resistance, and to do so more rapidly. Direct predictions of disease prevalence from host longevity will be further complicated by polymorphism within populations, which we show is a more likely outcome in shorter-lived species. Additionally, induced host defenses, such as acquired immunity will also reduce disease prevalence (Miller et al. 2007), and if present, can reduce selection on innate resistance (Boots et al. 2013).

Evolution of a “live fast, die young” life-history strategy has been suggested as a potentially important alternative to the evolution of costly resistance (Minchella 1985; Hochberg et al. 1992; Agnew et al. 2000; Ebert et al. 2004). Life-history trade-off theory predicts that such a shift in resources toward early reproduction will result in reduced life span (Roff 2002). Our results suggest that for relatively short-lived hosts, small reductions in life span have the potential to greatly reduce the probability of infection at the individual and population level, further alleviating the need for costly resistance. Of course, pathogens that target juvenile hosts, such as seedling damping-off diseases, should still generate strong selection for resistance, regardless of life history. In addition, long-term maintenance of costly resistance alleles in the annual Arabidopsis thaliana (Tian et al. 2003; Karasov et al. 2014) suggests that short life histories do not necessarily negate the need for disease resistance. Importantly, we have shown that, in very long-lived hosts, small reductions in life span have a negligible effect on disease risk. Thus, while earlier reproduction may still be favored in long-lived hosts, selection for such life-history evolution will be weak and it is unlikely to supplant the relatively rapid progression of selection for resistance.

Diseases that rely on a living host to persist across years and whose propagules cannot persist in the environment or on an alternate host species, represent a special case: if host generations are not overlapping, and disease transmission is seasonal, then the disease cannot persist. Correspondingly, it has been shown that anther-smut disease is absent from annual Silene species (Thrall et al. 1993b; Hood et al. 2010), even though many such species have been shown to be physiologically susceptible to anther-smut disease (Gibson et al. 2013).

Understanding the conditions that facilitate resistance evolution is important because variation in host resistance can strongly affect transmission rates and disease dynamics (Antonovics 1994; Thrall and Burdon 2000; Duffy and Sivars-Becker 2007; Boots et al. 2009). This study demonstrates that resistance evolution is determined by much more than just the level of resistance and its corresponding fitness cost. To understand this evolution, we need to consider the effects of host life history in the same way as has been commonly done for the evolution of pathogen virulence.
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LITERATURE CITED


