Selective Predation and Rapid Evolution Can Jointly Dampen Effects of Virulent Parasites on *Daphnia* Populations

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ABSTRACT: Parasites are ubiquitous and often highly virulent, yet clear examples of parasite-driven changes in host density in natural populations are surprisingly scarce. Here, we illustrate an example of this phenomenon and offer a theoretically reasonable resolution. We document the effects of two parasites, the bacterium *Spirobacillus cienkowskii* and the yeast *Metschnikowia bicuspidata*, on a common freshwater invertebrate, *Daphnia dentifera*. We show that while both parasites were quite virulent to individual hosts, only bacterial epidemics were associated with significant changes in host population dynamics and density. Our theoretical results may help explain why yeast epidemics did not significantly affect population dynamics. Using a model parameterized with data we collected, we argue that two prominent features of this system, rapid evolution of host resistance to the parasite and selective predation on infected hosts, both decrease peak infection prevalence and can minimize decline in host density during epidemics. Taken together, our results show that understanding the outcomes of host-parasite interactions in this *Daphnia*-microparasite system may require consideration of ecological context and evolutionary processes and their interaction.

Keywords: pathogens, susceptibility, infectious diseases, parasite-mediated selection, evolutionary epidemiology, cryptic dynamics.

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Evidence of increasing outbreaks of infectious diseases worries ecologists and managers because parasites are frequently virulent and therefore may harm their host populations (Harvell et al. 2002; Altizer et al. 2003; Lafferty et al. 2004). Indeed, theory suggests that parasites can adversely affect host population densities, particularly when they have large effects on host mortality or reproduction (Anderson and May 1981; May and Anderson 1983). However, even though such parasites are common, clear evidence for parasite-driven reductions in host density in natural populations remains rare (Møller 2005).

The community context of host-parasite interactions may help explain why parasite-driven reductions in host density are not observed more frequently. Disease ecologists increasingly appreciate that parasitism does not operate independently of other ecological interactions (Mittelbach 2005). In particular, recent work has focused on a possible role of predators in lessening the influence of parasites on host populations. Predators harm parasites indirectly by reducing the density of susceptible hosts and directly by consuming parasites contained in infected hosts. Predator behavior can magnify this direct effect because predators often prefer infected over uninfected hosts (e.g., Hudson et al. 1992; Ives and Murray 1997; Duffy et al. 2005; Johnson et al. 2006). In fact, general theory predicts that predators that selectively cull infected hosts can greatly reduce the prevalence of infection and indirectly increase the density of hosts (Packer et al. 2003; Ostfeld and Holt 2004; Hall et al. 2005*a*).

Recent theoretical work suggests rapid evolution of host resistance can also explain the rarity of large parasite-driven reductions in host density (Duffy and Sivars-Becker 2007). There is a growing awareness that evolutionary processes can modify ecological dynamics (Hairston et al. 2005; Johnson and Stinchcombe 2007), including in host-parasite systems. In such systems, parasites can rapidly select for increased host resistance (e.g., Duncan et al. 2006; Lohse et al. 2006; Koskella and Lively 2007). This directional selection can lead to smaller and shorter epidemics with smaller parasite-driven decreases in host density, and it ultimately can terminate the disease outbreak

(Duffy and Sivars-Becker 2007). Furthermore, epidemics should be less severe in genetically diverse populations because the rate of evolution of host resistance increases with genetic variation for susceptibility to the parasite (Fisher 1958).

If directional selection is common and genetic diversity is high, rapid evolution of host resistance may prevent large effects of parasites on host densities. Thus, the outcomes of host-parasite interactions may be affected by both the community context in which they are embedded and the interplay of ecological and evolutionary processes. We illustrate this point by quantifying the high virulence of two parasites, the yeast *Metschnikowia bicuspidata* and the bacterium *Spirobacillus cienkowskii*, on individuals of the host *Daphnia dentifera*. We then documented population-level implications of this virulence on host dynamics and density in four lakes. The dynamic data revealed a surprising result: while *Spirobacillus* epidemics were associated with significant changes in host population density and dynamics, *Metschnikowia* epidemics were not. We offer a potential resolution using a parameterized evolutionary epidemiological model that explored the joint roles of selective predation and rapid evolution of resistance in host-parasite dynamics. The model predicted that the combination of very high selectivity of predation by bluegill on *Metschnikowia*-infected *D. dentifera* (measured here) and rapid evolution of host resistance in response to selection by *Metschnikowia* (documented previously by Duffy and Sivars-Becker [2007]), may both operate to temper the virulent yeast parasite's influence on host dynamics.

Empirical Methods

Study System

We studied individual and/or population-level effects of parasites on *Daphnia dentifera* Forbes populations in seven lakes in southwestern Michigan: Baker, Bassett, Bristol, Cloverdale, Pine, and Warner lakes (Barry County) and Three Lakes Two (3L2; Kalamazoo County); see table A1 in the online edition of the *American Naturalist* for a summary of the studies done in different lakes. *Daphnia dentifera* is a widespread grazer in the plankton of lakes in temperate North America (Hebert 1995) and reaches high abundance in our study systems. The generation time of *Daphnia* depends on water temperature, ranging from ~1 week during warm summer temperatures to ~3 weeks during cool autumn temperatures. In these study lakes, numerous internal parasites infect *D. dentifera* (Hall et al. 2005*b*). We focus here on two of the most common ones: *Metschnikowia bicuspidata*, a yeast, and *Spirobacillus cienkowskii*, a bacterium. Epidemics of these two parasites generally occur in autumn (Duffy et al. 2005; Cáceres et al. 2006).

Both *Metschnikowia* and *Spirobacillus* are horizontally transmitted; transmission occurs when spores are released from dead *Daphnia* and consumed by uninfected *Daphnia* (Ebert 2005). *Metschnikowia* and *Spirobacillus* both infect multiple species of *Daphnia* (Green 1974; Ebert 2005). *Metschnikowia* infections are primarily seen in adults (Hall et al. 2005*b*, 2007), whereas *Spirobacillus* infections are commonly seen in both juveniles and adults (M. A. Duffy and S. R. Hall, unpublished data). Like many parasites of *Daphnia* (Green 1974), these two are visibly detectable to the human eye. Ordinarily transparent bodies of *Daphnia* become less transparent when filled with ascospores of *Metschnikowia* and become red and opaque when infected with *Spirobacillus*. Because of this increased opacity, infected hosts become more visible (and vulnerable) to visually oriented fish predators (Duffy et al. 2005; this study). While both parasites were present (albeit frequently at very low prevalences) in all study lakes, we did not observe any *D. dentifera* individuals coinfected with both *Spirobacillus* and *Metschnikowia* during this study (M. A. Duffy and S. R. Hall, unpublished data).

Individual-Level Studies

To measure survivorship of field-collected individuals infected with *Metschnikowia*, 50 *Metschnikowia*-infected and 50 uninfected individuals were randomly collected from Warner Lake during an epidemic in October 2002. Infected animals were kept at an intermediate temperature (18°C) in beakers containing filtered lake water and were fed algae (*Ankistrodesmus falcatus*; Tessier and Consolatti 1991) daily. For *Spirobacillus*, survivorship of 40 infected and 40 uninfected animals, collected from two lakes (Bassett and Pine) and maintained using similar methods, was measured at two temperatures: 15°C, an intermediate temperature, and 25°C, the temperature in surface waters during summer. Survivorship was checked daily until >95% of the infected *D. dentifera* had died. For both parasites, we used the number of days until death of the last animal at intermediate temperature (15° or 18°C) to produce a conservative estimate of the mortality component of virulence (as a rate, 1/days). We tested for significant differences in time until death for each lake-parasite-temperature combination using Kolmogorov-Smirnov two-sample tests, since data were nonnormally distributed.

We measured the effect of the parasites on fecundity (number of eggs) using randomly selected infected and uninfected adult females during the peak of *Spirobacillus* or *Metschnikowia* epidemics. One of these high infection periods for *Metschnikowia* occurred in Baker Lake in 2003. The *Metschnikowia* epidemic in Bassett Lake in 2003

started after the population had ceased reproducing asexually. Since we could not collect fecundity information from this epidemic, we instead took advantage of two *Metschnikowia* epidemics that occurred in 2004 to examine *Metschnikowia*-induced fecundity effects in Bassett and Warner lakes. For *Spirobacillus*, these peaks in infection occurred in Bassett, Pine, and 3L2 in 2003 (see app. A in the online edition of the *American Naturalist* for details). We used ANOVAs (in SAS 9.1; SAS Institute, Cary, NC) to test for differences in fecundity of infected and uninfected adult females; data for each lake were analyzed separately.

We measured the selectivity of fish predation on infected individuals following the methods in Duffy et al. (2005; also see app. A). Selectivity was calculated using Chesson's α (Chesson 1983), which compares the proportions of infected and uninfected prey items (*D. dentifera*) in the environment with those consumed by predators (bluegill *Lepomis macrochirus*). When there are two prey types, an α of 0.5 indicates neutral selectivity; an α greater than 0.5 indicates a preferred prey item. The sum of the Chesson's α for both prey types is 1 (Chesson 1983). These two proportions (environmental and predator-consumed prey) were measured in two lakes with *Metschnikowia* epidemics: Baker (September 19 and 23, 2002) and Bristol (September 14, 2003). For comparison, we also show similar data for *Spirobacillus*-infected *D. dentifera* (Duffy et al. 2005).

Population Dynamics

We measured parasite prevalence and population dynamics in Baker, Bassett, Pine, and 3L2 lake populations between July and November 2003. These lakes were chosen because they contain large *D. dentifera* populations and are located near the W. K. Kellogg Biological Station. The frequency of sampling varied with the prevalence of infections and water temperature, with an average of 4 days between samples. The lakes were sampled more frequently once epidemics began, in order to increase our ability to detect parasite-driven changes in the host populations. Beginning in mid-October, the frequency of sampling decreased again as the surface temperature in the lakes dropped, since this greatly reduces vital rates of *Daphnia*, the parasites, and their predators (Hall et al. 2006). Four zooplankton samples were collected on each date using a 153-μm mesh Wisconsin bucket net. Each of these four samples combined four whole-water-column vertical net tows taken at four different sites within the deep basin of each lake (a number based on extensive spatial sampling by Hall et al. [2005*b*]). Three samples were counted to determine *Daphnia* density (after preservation in ethanol). We used the remaining sample to estimate per capita fecundity (no. eggs per individual) of live animals. We combined per capita fecundity with temperature-dependent egg development time to calculate per capita birth rate for each lake date (Rigler and Downing 1984). With this fourth sample, we also determined prevalence of infection (infected/total density), but we lacked some early data for *Spirobacillus* prevalence due to misclassification of hemoglobin production as infection. We defined epidemics as starting once prevalence surpassed 1% (Duffy et al. 2005).

With these data on population dynamics, we then examined relationships between infection prevalence, population density, and vital rates. Instantaneous population growth rate (r) between sampling days was calculated as $r_{ij} = (\ln N_j - \ln N_i)/(j - i)$, where $\ln N_i$ and $\ln N_j$ are the natural logs of the densities on days i and j. We calculated the instantaneous per capita death rate (d_i) of the population by subtracting growth rate (r_{ij}) from the per capita birth rate (b_i). Before these calculations were made, vital rates and natural log of densities were LOWESS smoothed (SAS 8; SAS Institute). We then calculated (cross) correlation coefficients between infection prevalence and population density and vital rates. Data were first binned into 5-day intervals to facilitate time-series analysis (Legendre and Legendre 1998). Because a priori simulation results suggested maximal effects on r should occur before the peak in infection prevalence (Duffy 2006), we calculated correlations between infection prevalence and r at a 5-day (1 sample) lag.

Empirical Results

Both *Metschnikowia* and *Spirobacillus* are highly virulent, greatly reducing host survivorship (fig. 1*A*, 1*B*). Animals infected with *Metschnikowia* all died within 20 days (yielding an estimate of virulence mortality, v, of 0.05 day^{-1} for the evo-epidemiological model; see "Evo-epidemiological Modeling: Methods" and table 2); only 25% of the control animals died during this time. Animals infected with *Spirobacillus* died within two (25°C) to four (15°C) days (yielding a conservative estimate of $v = 0.25$ day^{-1}); meanwhile, over 90% of control animals survived during this same time span. The differences in survivorship of infected and uninfected *Daphnia dentifera* were all significant (Kolmogorov-Smirnov $D_{\max} > 0.75$, $P < .001$). Furthermore, both parasites significantly reduced *Daphnia* fecundity of adult females (fig. 1*C*, 1*D*; $P < .002$ in all cases; table A2 in the online edition of the *American Naturalist*). The fecundity of *Metschnikowia*-infected adult females was 66%–80% of the fecundity of uninfected adult females, yielding an estimate of the effect on fecundity (f) of 0.75. *Spirobacillus* virtually sterilized its hosts (i.e., $f = 0$): only 2% of adult females infected with *Spirobacillus* carried any eggs.

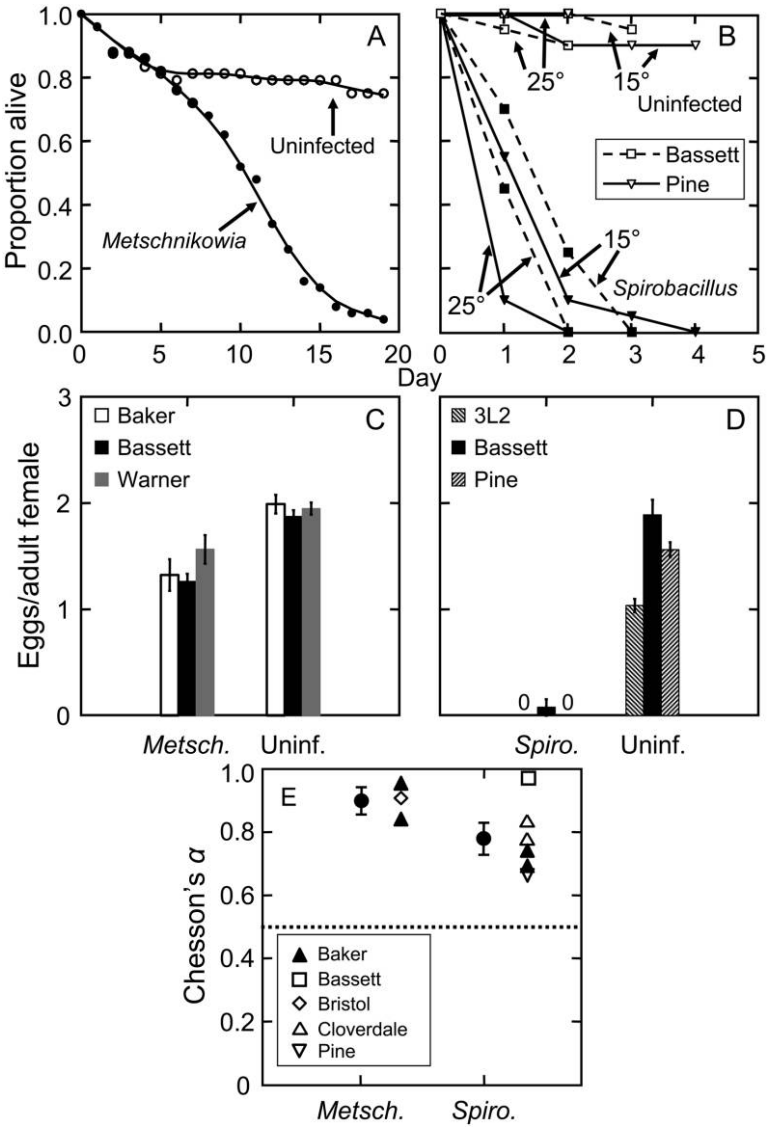

Figure 1: Individual-level effects of *Metschnikowia* (*Metsch.*) and *Spirobacillus* (*Spiro.*) infections on field-collected *Daphnia dentifera*. *A*, Survivorship of uninfected (*open circles*) and *Metschnikowia*-infected (*closed circles*) *D. dentifera* collected from Warner Lake. Data are fitted with LOWESS smoothing lines. *B*, Survivorship of uninfected (*open symbols*) and *Spirobacillus*-infected (*closed symbols*) *D. dentifera* from Pine Lake (*solid lines*, *inverted triangles*) and Bassett Lake (*dashed lines*, *squares*). Temperature treatments are labeled in the figure. *C*, Fecundity of field-collected *Metschnikowia*-infected and uninfected *D. dentifera* adult females. Error bars represent ±1 SE. *D*, Fecundity of field-collected *Spirobacillus*-infected and uninfected *D. dentifera* adult females. Error bars represent ±1 SE. Note that none of the *Spirobacillus*-infected adults in Pine Lake and 3L2 carried any eggs; therefore, the means for these lakes are 0. *E*, Selectivity of fish predation on *D. dentifera* infected with *Metschnikowia* and with *Spirobacillus* (from Duffy et al. 2005); the circles represent the overall mean Chesson's α for *Metschnikowia*-infected (*left*) and *Spirobacillus*-infected (*right*) *D. dentifera*, and the error bars represent ±1 SE. Symbols to the right of the circles indicate mean Chesson's α for that parasite for each lake-day. For two prey items (infected or uninfected *D. dentifera*), Chesson's α greater than 0.5 indicates preference for infected prey. In each case, the comparison is between predation on infected and uninfected *D. dentifera*.

We found very high selectivity of bluegill predation on *Metschnikowia*-infected *D. dentifera* (fig. 1*E*). The mean value of Chesson's α for bluegill feeding on *Metschnikowia*-infected *D. dentifera* was 0.90 (95% confidence interval [CI]: 0.76–1.0). Such a selectivity value means that in an environment with equal numbers of infected and uninfected *D. dentifera*, bluegill will eat nine *Metschnikowia*-infected *D. dentifera* for every one uninfected *D. dentifera*. This estimate is much higher than measures of selectivity of bluegill predation on *Spirobacillus* (mean Chesson's α:

0.75; 95% CI: 0.67–0.85; Duffy et al. 2005) and another *Daphnia* parasite, *Polycaryum* (mean Chesson's α: 0.63, Johnson et al. 2006*b*). For those two parasites, in an environment with equal numbers of infected and uninfected *Daphnia*, bluegill would eat only two to three infected *Daphnia* for every uninfected *Daphnia*.

In lake populations, *Spirobacillus* epidemics were associated with negative changes in host population density and dynamics while *Metschnikowia* epidemics were not (table 1). For both diseases, epidemics reach a single peak, then crash; neither becomes endemic (i.e., persists throughout autumn; fig. 2). While we were unable to fully track the termination of the Bassett *Metschnikowia* epidemic in this study (due to the beginning of deer hunting season), no *Metschnikowia* infections were observed when sampling resumed the following spring and summer (M. A. Duffy and S. R. Hall, unpublished data). *Metschnikowia* epidemics occurred in Baker and Bassett lakes, with 8%–11% peak infection prevalence (fig. 2*A*, 2*B*). Epidemics of *Spirobacillus* occurred in Bassett, Pine, and 3L2 and ranged from 6%–12% peak infection prevalence (fig. 2*B*–2*D*). *Spirobacillus* epidemics appear to reduce *Daphnia* population density (fig. 2*B*–2*D*; table 1). While this effect was only significant in Bassett Lake, the magnitude of the correlation was large and negative in all three lakes (table 1). Instantaneous population growth rate (r) showed a strong and significant negative correlation with *Spirobacillus* prevalence in all three lakes (fig. 2*E*–2*H*; table 1). *Spirobacillus* prevalence was significantly and positively correlated with host population death rate (d) in Bassett Lake (fig. 2*E*–2*H*; table 1). In contrast, *Metschnikowia* epidemics did not correlate with host density or r (fig. 2*A*, 2*B*, 2*E*, 2*F*; table 1) and its prevalence was negatively (rather than positively) correlated with d in Bassett Lake (fig. 2*F*; table 1).

Table 1: Summary of population-level effects of epidemics of *Metschnikowia* and *Spirobacillus* during 2003

		Density (no. $M^{-2} \times 10^3$)		Population growth rate (day^{-1})		Death rate (day^{-1})	
Lake	Parasite	r	P	r	P	r	P
Baker	*Metschnikowia*	.08	.7	.14	.6	.39	.09
Bassett	*Metschnikowia*	.55	.06	.54	.09	**−.66**	**.03**
Bassett	*Spirobacillus*	**−.85**	**<.001**	**−.90**	**.04**	**.83**	**.001**
Pine	*Spirobacillus*	−.62	.10	**−.80**	**.003**	.63	.09
3L2	*Spirobacillus*	−.76	.08	**−.82**	**.03**	.15	.8

Note: Coefficients (r) and significance values (P) describe each cross-correlation between infection prevalence and host population density, instantaneous population growth rate, and population death rate. The binned time series, binned at 5-day intervals, was used for this analysis. The correlation between infection prevalence and population growth rate was calculated at a lag of one sampling interval (5 days). Correlations significant at the .05 level are bold.

Evo-epidemiological Modeling: Methods

We found that both *Spirobacillus* and *Metschnikowia* strongly reduced fecundity and life span and increased predation mortality. However, *Metschnikowia* epidemics were not associated with significant changes in host population dynamics. This was surprising, given that *Metschnikowia* is quite virulent (fig. 1). While *Metschnikowia* had smaller effects on fecundity and mortality (in the absence of fish) than *Spirobacillus*, it is still one of the most virulent *Daphnia* parasites (Ebert et al. 2000), and it drove large reductions in host density in lab microcosm and field mesocosm experiments (Ebert et al. 2000; Duffy 2007).

Two mechanisms may help explain why *Metschnikowia* did not significantly affect host population dynamics in these lake populations: the extremely high selectivity of fish predation on *Metschnikowia*-infected hosts (fig. 1*D*) and rapid evolution of resistance of the host populations (Duffy and Sivars-Becker 2007). We explored the combined effects of selective predation and evolution of host resistance on *Daphnia*-microparasite interactions using a previously developed susceptible-infected (*SI*) model (Duffy and Sivars-Becker 2007). While our primary interest is in understanding the factors that may have reduced the effects of *Metschnikowia* epidemics on host populations, we also use the model to study the *Daphnia*-*Spirobacillus* system as a comparison.

The dynamics of this model can be described using the following set of equations:

$$\frac{dS}{dt} = b_{\max}(S + fI)[1 - c(S + I)] - nS - mS - \beta SI, \quad (1a)$$

$$\frac{dI}{dt} = \beta SI - nI - vI - m_I I, \quad (1b)$$

$$\frac{d\beta}{dt} = -V_c I \quad (1c)$$

(see table 2 for a summary of symbols used in the model). Change in density of susceptible hosts (eq. [1a]) represents gains from production and losses to a variety of sources. Per capita production reflects maximal birth rate of susceptible hosts ($b_{\max}$), reduction in maximal fecundity of infected hosts ($0 \le f < 1$) as estimated using methods presented above (see "Individual-Level Studies"), and density dependence via parameter c. This strength-of-density dependence term c assumes that both susceptible and infected hosts consume resources equally. It was approximated as the inverse of a reasonable carrying capacity for these lakes (Tessier and Woodruff 2002). Susceptible hosts

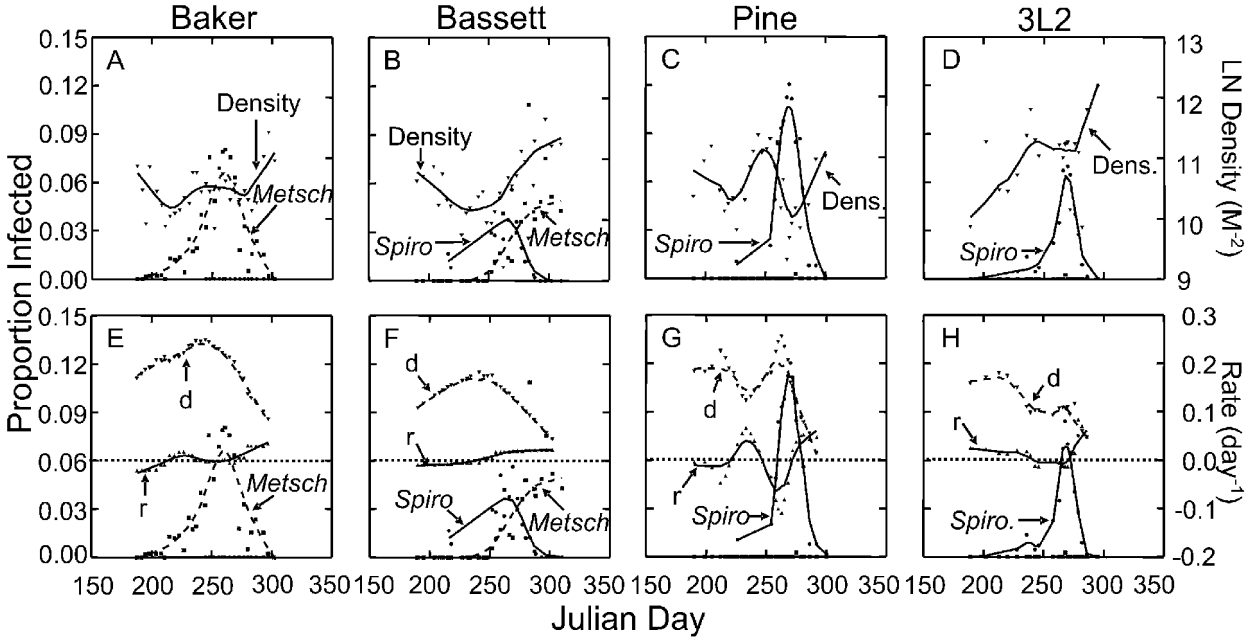

Figure 2: Population dynamics and infection prevalence in four lake populations. Infection prevalence is shown on the left axis in all panels; *Spirobacillus* prevalence is shown with solid lines and circle symbols and *Metschnikowia* prevalence with dashed lines and square symbols. *A–D*, *Daphnia dentifera* density (*right axis*, *solid line*, *inverted triangles*). *E–H*, *Daphnia dentifera* population death rate (*d*; *right axis*, *dashed line*, *inverted triangles*) and population growth rate (*r*; *right axis*, *solid line*, *triangles*). Dotted lines indicate 0 population growth rate. Lines indicate LOWESS smoothed curves.

are lost due to background, nonconsumptive mortality (at rate n), mortality from fish predation (at rate m), and transmission of the parasite. Infected *Daphnia dentifera* transmit infections to susceptible hosts at rate β according to a density-dependent interaction (βSI; de Jong et al. 1995; Regoes et al. 2003). We varied m along a range that resulted in overall population death rates, d, that matched those in natural lake populations (see below). Change in density of infected hosts (eq. [1b]) reflects gains from infection and losses due to background sources (n), additional mortality due to virulence effects (at rate v, determined using the survivorship data), and predation (at rate m_I).

This model incorporates evolution of resistance of the host population. Rapid (within-season) evolution of increased resistance has been found for *D. dentifera*-*Metschnikowia* interactions and another *Daphnia*-microparasite pairing (Duncan et al. 2006; Duffy and Sivars-Becker 2007; Duncan and Little 2007). Further, our results from the *Daphnia*-*Metschnikowia* system indicate that the host populations contain much higher genetic diversity and potential for evolution than the parasite (Duffy and Sivars-Becker 2007). This observation justifies a model that allows hosts to evolve but does not include coevolution of host and parasite. Mean transmission rate (e.g., mean susceptibility, β) of the host population decreases proportionally to genetic variation (e.g., clonal variance in susceptibility, V_c) and the density of infected hosts (I). However, we constrain this parameter to 0 or positive values (i.e., $\beta \geq 0$). Thus, higher I and/or V_c leads to faster evolution of host resistance and hence faster termination of epidemics. We note that this model assumes that genetic variation for host susceptibility does not change through time. While selection by the parasite would change the variance in addition to the mean (Duffy and Sivars-Becker 2007), quantitative genetic models frequently make this simplifying assumption of constant genetic variation for mathematical tractability.

We used this model to explore the effects of selective predation and rapid evolution of resistance on host-parasite dynamics. To do so, we simulated this model as parameterized for the two parasites *Metschnikowia* and *Spirobacillus* (see table 2). To incorporate the selectivity of predation, we assumed that $m_I = m\alpha/(1 - \alpha)$, where m is predation rate on susceptible hosts and α is Chesson's selectivity coefficient for infected hosts as measured in natural populations (fig. 1*D*). We contrasted scenarios in which predators do not feed selectively ($\alpha = 0.5$, $m = m_I$; "neutral selectivity" or "nonselective") to those in which they prefer infected prey (for *Metschnikowia*, $\alpha =$

Table 2: Model parameters, variables, and parameter values for the *Daphnia-Metschnikowia* and *Daphnia-Spirobacillus* systems

Parameter/variable	Units	Definition	Value
α	…	Selectivity of predators on infected *Daphnia dentifera*	.50, .75, .90[a]
b_{max}	Day^{-1}	Maximum birth rate	.4[b]
β	$(No.\ M^{-2})^{-1}\ day^{-1}$	Mean transmission rate	Eq. (1c)
β_0	$(No.\ M^{-2})^{-1}\ day^{-1}$	Initial transmission rate	6.1×10^{-6}[c]
c	$(No.\ M^{-2})^{-1}$	Density dependent reduction in host fecundity	1×10^{-5}[d]
f	…	Fecundity modifier for infected *D. dentifera*	0, .75[e]
I	$No.\ M^{-2}$	Density of infected *D. dentifera*	Eq. (1b)
m	Day^{-1}	Fish predation mortality on susceptible hosts	0–.05[f]
m_I	Day^{-1}	Fish predation mortality on infected hosts	$m\alpha/(1-\alpha)$
n	Day^{-1}	Nonselective mortality	.05[g]
S	$No.\ M^{-2}$	Density of susceptible *D. dentifera*	Eq. (1a)
t	Day	Time unit	…
v	Day^{-1}	Death rate due to parasite (virulence)	.05, .25[h]
V_c	$(No.\ M^{-2})^{-2}$	Clonal variance in transmission rate	$0–6 \times 10^{-11}$[c]

[a] This study (fig. 1*E*); α is 0.5 for nonselective predation; in scenarios with selective predators, $\alpha = 0.75$ for *Spirobacillus* epidemics and $\alpha = 0.9$ for *Metschnikowia* epidemics.

[b] Maximum birth rate at summer temperatures was based on laboratory life-table studies using food collected from local lakes (Tessier and Woodruff 2002).

[c] Duffy and Sivars-Becker (2007)

[d] Tessier and Woodruff (2002)

[e] This study (fig. 1); $f = 0$ for *Spirobacillus* epidemics; $f = 0.75$ for *Metschnikowia* epidemics.

[f] This range yielded death rates (d) matching those seen in field populations (figs. 2, B1, B2).

[g] Duffy (2006); González and Tessier (1997).

[h] This study (fig. 1*A*, 1*B*); $v = 0.05$ for *Metschnikowia*, $v = 0.25$ for *Spirobacillus* epidemics.

0.9, yielding $m_I = 9m$; for *Spirobacillus*, $\alpha = 0.75$, $m_I = 3m$; "selective"). In these simulations, we varied predation mortality on susceptible hosts (m) over a range (0–0.05 day^{-1}) that yielded overall population death rates (d) that approximate death rates seen in field populations (fig. 2). We also contrasted cases where the transmission rate could and could not evolve. The transmission rate can evolve if genetic variation exceeds 0 ($V_c > 0$) but cannot when hosts lack genetic variation in susceptibility ($V_c = 0$; therefore, $\beta = \beta_0$). This latter situation simplifies to a standard *SI* model. Initial transmission rate (β_0) was set to 6.1×10^{-6} $(no.\ M^{-2})^{-1}\ day^{-1}$ (Duffy and Sivars-Becker 2007). Additionally, initial density of susceptible hosts was set to 100,000 M^{-2}, and initial density of infected hosts was assumed to be low (1 M^{-2}); however, the results of this model are not sensitive to these initial density conditions.

Using simulations, we calculated the effects of selectivity and evolution of host resistance on peak infection prevalence, length of the epidemic, and maximal decline in host density during the epidemic (see fig. 3 and figs. B1, B2 in the online edition of the *American Naturalist* for sample simulations). Peak infection prevalence is the maximal value of the density of infected hosts (I) over total host density ($S + I$), or $I/(S + I)$. Following precedent, we defined epidemics as occurring when infection prevalence surpasses 1% (Duffy et al. 2005; Cáceres et al. 2006; Duffy 2007). Given that definition, epidemic length denotes the number of days during which infection prevalence exceeded 1%. The parasite-induced drop in host density during epidemics was calculated by subtracting the parasite-free equilibrial host density from a minimal host density that inevitably occurred during the epidemic.

Evo-epidemiological Modeling: Results

Our model highlights that high selectivity of predation, when combined with rapid evolution of resistance, may reduce repercussions of *Metschnikowia* epidemics on host populations. Without evolution of resistance, both parasites should persist in the host populations indefinitely, regardless of whether predation is selective (fig. 3*A*, 3*B*; fig. B1*A*, B1*B*; fig. B2*A*, B2*B*). Therefore, rapid evolution of host resistance provides a strong candidate mechanism for the termination of epidemics (fig. 4*C*, 4*D*). Furthermore, selective predation keeps peak infection prevalence lower: maximal prevalence of infection decreases dramatically with increasing predation mortality rate (m; fig. 4*A*, 4*B*). This selectivity component is stronger for simulated epidemics of *Metschnikowia* than of *Spirobacillus* (fig. 4*A*) and reflects underlying biology: bluegill predation on *Metschnikowia*-infected hosts is extremely selective (fig. 1*E*). In fact, neither parasite can withstand too much mortality from selective predators, regardless of genetic diver-

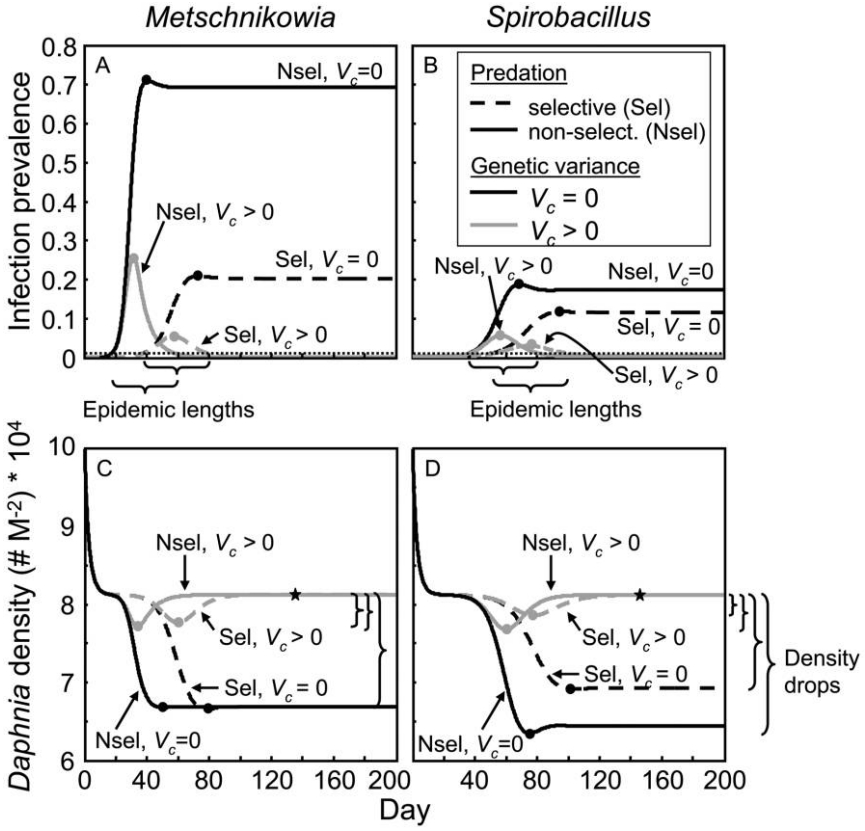

Figure 3: Sample simulation results for the evo-epidemiological model (see also figs. B1, B2 in the online edition of the *American Naturalist*). *A*, *C*, simulation of *Metschnikowia* epidemics; *B*, *D*, simulations of *Spirobacillus* epidemics. *A*, *B*, Infection prevalence. Peak infection prevalence for each simulation is indicated by the circle. Epidemic length is the number of days above 1% infection prevalence (*dotted line*), as indicated by the brackets below *A* and *B*. Note that the epidemics do not end without evolution (e.g., when there is no genetic variation, $V_c = 0$). In this case, the disease does not crash but instead persists indefinitely. *C*, *D*, *Daphnia dentifera* density. The minimal density reached during the epidemic is indicated by the circles, while the stars indicate equilibrial density of hosts without parasites. The difference between these two values determined the parasite-induced drop in host density during an epidemic, shown in figure 4*E*, 4*F*; this density drop is indicated by the brackets on the panels. For these simulations, $m = 0.025$ day^{-1}.

sity of the host. Thus, selective predation places upper limits (~0.04 day^{-1}) on the predation mortality rates over which epidemics can occur. However, despite lower selectivity of fish predation, *Spirobacillus* epidemics are always expected to be smaller than those of *Metschnikowia* (fig. 4*B*). This result emerges due to highly virulent effects of *Spirobacillus* on fecundity and mortality of hosts (fig. 1*B*, 1*D*).

Rapid evolution of resistance, driven by high genetic diversity, also prevents epidemics from reaching high prevalence. This effect is also particularly strong for *Metschnikowia* epidemics: with high genetic variation (V_c), rapid evolution of resistance keeps prevalence below 20%, while without genetic variation (i.e., when there is no evolution, $V_c = 0$), peak infection prevalence can reach nearly 80% (fig. 4*A*). Thus, when both evolution of host resistance and selective predation are included in the model, overall epidemic dynamics match those observed in natural populations (figs. 2, 3; fig. B1, B2).

Increasing genetic diversity (V_c), and, therefore, increasing the rate of evolution of resistance, decreases epidemic length (fig. 4*C*, 4*D*). This result makes intuitive sense because epidemics should shorten if the transmission rate degrades faster with higher genetic variance (i.e., eq. [1c]). However, for *Metschnikowia*, selectivity of predation adds nuance to this prediction. In general, at low predation mortality rates (m), selectivity of predation shortens epidemics (fig. 4*C*). However, at low to moderate levels of genetic diversity and moderate predation rates, selective predation actually lengthens epidemics. This result arises because the very high selectivity of predation greatly decreases infected host densities (relative to the nonselective

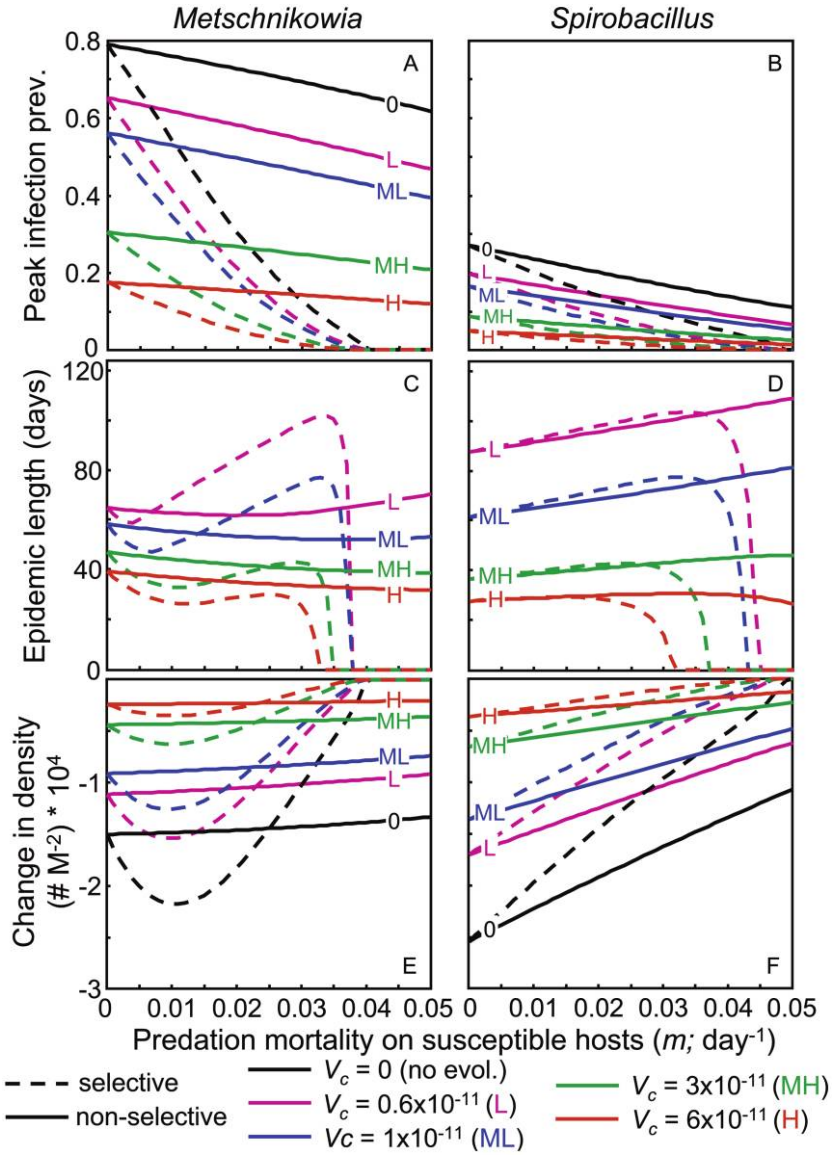

Figure 4: Effects of selective predation and rapid evolution of host resistance on (*A*, *B*) peak infection prevalence, (*C*, *D*) length of epidemic, and (*E*, *F*) maximal drop in host density over a range of predation mortality rates on susceptible hosts, *m*. *A*, *C*, *E*, Simulations of *Metschnikowia* epidemics. *B*, *D*, *F*, Simulations of *Spirobacillus* epidemics. All results are based on transient dynamics for *Daphnia*-microparasite interactions as illustrated in figure 3 and figures B1, B2 in the online edition of the *American Naturalist*. Without genetic variation (i.e., $V_c = 0$), there is no potential for evolution of host resistance. In this case, the disease persists indefinitely instead of dying out (see fig. 3); therefore, epidemic length is infinite and is not plotted in *C* or *D*. Increasing genetic variance (V_c) corresponds to increasingly rapid evolution of host resistance. Different levels of genetic variance (V_c) are shown with different colors and labels (see key). To reduce clutter, only lines for nonselective predation simulations (*solid lines*) are labeled; the selective predation simulations (*dashed lines*) for each level of genetic variance begin at the same point along the *Y*-axis (i.e., at $m = 0$ day^{-1}) as the nonselective predation simulations.

case). This food-web effect, in turn, indirectly slows the evolution of transmission rates (which is proportional to *I*; see eq. [1c]) and hence the end of epidemics (fig. B1). Thus, the length of epidemics here depends on the interplay between evolution of resistance and selective predation. When parameterized for the bacterial parasite (*Spirobacillus*), we do not see these counterintuitive increases in epidemic length when predation is selective. Instead, in most cases, selective predation has only a minor effect on epidemic length (fig. 4*D*).

Such an evolution-predation interaction also appears when examining the drop in host density during epidemics. Interestingly, while increasingly rapid evolution of resistance always minimizes this drop (fig. 4*C*, 4*D*), selective predation does not always reduce it. For *Metschnikowia* epidemics, at low to moderate predation mortality rates, selective predation actually enhances this decrease in host density (as compared with a nonselective predator). This result emerged because lower predation mortality rate allows larger prevalence of infection (fig. B1*A*), and these abundant, infected hosts have very high per capita death rates due to the high selectivity of predation. This density-selectivity combination leads to high per capita death rates and increased drops in densities in these situations (fig. B1, *left panels*). However, for a given peak infection prevalence, the drop in host density expected for *Spirobacillus* epidemics consistently exceeded that anticipated for *Metschnikowia* epidemics (fig. 4*E*, 4*F*; fig. B3 in the online edition of the *American Naturalist*). These simulation-based results are important because they mirrored our otherwise perplexing field results; those findings indicated significant effects of *Spirobacillus* but not *Metschnikowia* epidemics on host densities.

The evolutionary epidemiological model, then, helps us to interpret the underwhelming influence of the highly virulent yeast parasite. Three main ingredients highlighted by the model were present. First, fish predation on infected *Metschnikowia* was highly selective (fig. 1*D*). Second, these host populations contained significant genetic variation for susceptibility to *Metschnikowia* and underwent rapid evolution of resistance during these epidemics (Duffy and Sivars-Becker 2007). Finally, overall death rates in these populations indicated moderate-to-high predation mortality rates (fig. 2; fig. B1*J*). Together, these three components suggest that rapid evolution of resistance, selective predation, and moderate predation mortality rates may have decreased peak infection prevalence and minimized the effects of epidemics on host population density and death rate.

Discussion

Both the bacterial and the yeast parasites lowered fecundity and shortened life span of infected *Daphnia dentifera*. Epidemiological theory says that such virulent parasites should have strong, adverse effects on host populations (Anderson and May 1981; May and Anderson 1983). However, in nature, only epidemics of the bacterium *Spirobacillus* were associated with significant changes in host population density and vital rates. To resolve this apparent paradox, we turned to a theory that embraced two other vital components of this system's natural history: high selectivity of predators for infected hosts and high genetic variation for susceptibility within host populations. The combination of very highly selective predation (measured here) and rapid evolution of resistance, driven by high genetic variance (measured previously; Duffy and Sivars-Becker 2007), may have jointly moderated the influence of the yeast *Metschnikowia* on these host populations. More specifically, this selective predation-evolution combination should have reduced peak infection prevalence of *Metschnikowia* and may have minimized its effects on *Daphnia* population densities.

Epidemics of the virulent bacterium *Spirobacillus* harmed host populations, a result that was expected based on general theory (Anderson and May 1981; May and Anderson 1983). Our individual-level studies indicated that *Spirobacillus* is particularly virulent: infected hosts almost never carry any eggs and die very quickly (fig. 1). Thus, it was not surprising that we found significant changes in host density and population dynamics during *Spirobacillus* epidemics (fig. 2; table 1). Our evo-epidemiological model, parameterized with these individual-level data, supports that even small *Spirobacillus* epidemics should have large effects on host populations (fig. 4). Moreover, it predicts that these epidemics should have more potent repercussions for host populations than *Metschnikowia* epidemics (fig. B3). However, we must qualify this prediction with a caveat: it assumes that host populations contain similar levels of genetic diversity in resistance to both parasites. Unfortunately, it is difficult to transmit *Spirobacillus* experimentally, and this limitation prevents estimation of genetic diversity for resistance to it.

In contrast, the modest influence of *Metschnikowia* on host dynamics was initially perplexing. This parasite also substantially decreases host life span and fecundity in natural populations (fig. 1) and therefore should also harm host populations. The virulent effects we measured in natural populations support previous laboratory studies on *Metschnikowia*-infected *Daphnia* (Ebert et al. 2000; Hall et al. 2006; Duffy and Sivars-Becker 2007). Further, previous studies have documented dramatic effects of *Metschnikowia* epidemics in laboratory microcosm and lake mesocosm experiments (Ebert et al. 2000; Duffy 2007). Thus, at first we found this discrepancy between high virulence on individuals and undetectable population-level effects of *Metschnikowia* surprising.

Our theoretical results suggest this discrepancy may be resolved by considering both community context and rapid evolution. First, previous empirical work demonstrated evolution of high resistance of the Baker and Bassett *D. dentifera* populations in response to these epidemics (Duffy and Sivars-Becker 2007). It is interesting to note, then, that for these two epidemics, *Metschnikowia* had no detectable effect on host population dynamics, yet it had

a dramatic effect on genetic composition; similar "cryptic dynamics" have recently been reported from rotifer-algae and bacteria-phage interactions in the laboratory (Yoshida et al. 2007). Second, in this study, we found remarkably high selectivity of fish predation on *Metschnikowia*-infected *D. dentifera* (fig. 1*E*). Previous theoretical work has suggested that either selective predation (Packer et al. 2003; Ostfeld and Holt 2004; Hall et al. 2005*a*) or rapid evolution of host resistance (Duffy and Sivars-Becker 2007) can reduce infection prevalence and consequently minimize the effects of parasites on host populations. Here, we show that they can combine to greatly reduce peak infection prevalence and, in some cases, shorten epidemic length and minimize parasite-driven declines in host density.

Interestingly, though, our theoretical results offered some more nuanced conclusions. In general, simulations of the model suggest very important effects of genetic diversity of hosts: populations with large variation in susceptibility have high potential for rapid evolution of host resistance. Therefore, they generally have the shortest and smallest epidemics and only small changes in host density. However, for *Metschnikowia* epidemics, selective predation can actually increase both the length of the epidemics and parasite-driven declines in host density at low predation rates. These results reflected the combination of the density of infected hosts (which can still reach fairly high levels with low predation intensity) and very high per capita mortality rate of those infected hosts due to the very high selectivity of fish predation. Ultimately, the net result of that density-mortality rate combination sets the host population up for a large (if only temporary) decline. Furthermore, selective predation increases epidemic length at some predation rates because it reduces the density of infected hosts. Since transmission rate declines proportionately to density of infected hosts, predators indirectly slow evolution of transmission rate when "keeping the herd healthy" and therefore prolong epidemics. This initially counterintuitive effect should arise when predation rate is relatively high and genetic diversity for susceptibility is low.

In this study, we hypothesize that rapid evolution of host resistance contributes to the termination of epidemics, based in part on evidence for evolution in these populations (Duffy and Sivars-Becker 2007). However, any mechanism that decreases transmission rates could produce the same pattern. In particular, seasonal decreases in water temperature may be important. Temperature significantly affects transmission rates, as well as vital rates of hosts and predators (Hall et al. 2006), so declining water temperatures in autumn may also contribute to the termination of epidemics. We are currently studying the joint roles of temperature and evolution of resistance in driving the termination of epidemics (M. A. Duffy, S. R. Hall, and A. R. Ives, unpublished manuscript).

Overall, the results emerging from these *Daphnia*-microparasite systems indicate strong interactions between host, parasite, and food web as well as between ecological and evolutionary processes. Both parasites reduced fecundity and life span and increased predation risk, yet only *Spirobacillus* had significant effects on host population dynamics. Our theoretical results suggest a possible explanation for why *Metschnikowia*'s high virulence did not translate into major population-level effects: the rapid evolution of resistance combined with very highly selective fish predation may have reduced peak infection prevalence and dampened parasite-driven declines in host density. Thus, our results highlight that parasitism must be understood in light of both community context and the interplay of ecological and evolutionary processes.

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