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The unavoidable costs and unexpected benefits of parasitism: population and metapopulation models of parasite-mediated competition

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Abstract

When faced with limited resources, organisms have to determine how to allocate their resources to maximize fitness. In the presence of parasites, hosts may be selected for their ability to balance between the two competing needs of reproduction and immunity. These decisions can have consequences not only for host fitness, but also for the ability of parasites to persist within the population, and for the competitive dynamics between different host species. We develop two mathematical models to investigate how resource allocation strategies evolve at both population and metapopulation levels. The evolutionarily stable strategy (ESS) at the population level is a balanced investment between reproduction and immunity that maintains parasites, even though the host has the capacity to eliminate parasites. The host exhibiting the ESS can always invade other host populations through parasite-mediated competition, effectively using the parasites as biological weapons. At the metapopulation level, the dominant strategy is sometimes different from the population-level ESS, and depends on the ratio of local extinction rate to host colonization rate. This study may help to explain why parasites are as common as they are, and can serve as a modeling framework for investigating parasite-mediated ecological invasions. Furthermore, this work highlights the possibility that the ‘introduction of enemies’ process may facilitate species invasion.

Keywords

evolutionarily stable strategy; immunity; invasion; reproduction; resource allocation; trade-off

1. Introduction

Host-parasite interactions are ubiquitous in nature and are an important force that shapes the life history strategies of both hosts and their parasites (Anderson and May, 1982; May and Anderson, 1990). In the presence of parasites, a host’s fitness will depend not only on its intrinsic rate of survival and fecundity, but also on its ability to cope with the impact of the parasite. However, these two facets of fitness may be linked to one another. Empirical and theoretical studies suggest that reproduction and immunity represent two competing needs in the host’s overall resource allocation strategy (Sheldon and Verhulst, 1996; Zerofsky et al., 2005; Zuk and Stoehr, 2002). While reproduction is obviously essential for population

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persistence, infections can greatly reduce survival or cause sterility such that resources allocated to reproduction are effectively wasted (Baudoin, 1975; Clay, 1991; Ebert et al., 2004; Lively, 1987; Roy, 1993; Roy and Bierzychudek, 1993). Because reproduction and immunity are both expensive (Kraaijeveld et al., 2002; Reznick, 1985), the way in which a host allocates resources can have a dramatic effect on the host's fitness.

Previous theoretical studies have examined the effect of host resource allocation on the ability to avoid or eliminate infection by parasites. In an optimization model, Medley (2002) demonstrated that an individual host can maximize its reproductive value by tolerating some parasite infection. Kaitala (1997) considered an evolutionary model in which parasites were able to coevolve with their hosts. In this case, the evolutionarily stable strategy (ESS) (Maynard Smith, 1982) for the host population was to maintain phenotypic polymorphisms for immunity. Similarly, van Baalen (1998) found that if parasites were not allowed to coevolve with the host, the host's ESS strategy provided some defense, but not enough to eliminate the pathogen altogether.

In these infinite population size models, a single host can eliminate any parasites it carries, but the parasite will always be present in the population, leading to a non-zero risk of infection. Thus, despite the wealth of studies on the ecological and evolutionary dynamics of host-parasite interactions, we do not know how hosts will respond over evolutionary time if fitness is density dependent, and there exists the possibility of eliminating the pathogen from the population altogether.

When we consider models that assume explicit trade-offs between reproduction and immunity, two general questions arise. First, if hosts can allocate resources to immunity that is sufficient to eliminate the parasite from the population, why are parasites so common? And second, are there potential conflicts between optimal resource allocation strategies at the level of individuals and at the level of groups? If so, how are these conflicts resolved?

Costs of immunity can be separated into two distinct classes—the standing defense cost of maintaining an immune system, and the acute cost of up-regulating the immune system once an individual is infected (Kraaijeveld et al., 2002; Lochmiller and Deerenberg, 2000; Schmid-Hempel, 2003). While many experimental studies have focused on the acute cost of up-regulating the immune system (reviewed in (Kraaijeveld et al., 2002)), artificial selection experiments have demonstrated that costs of standing immunity can lead to decreases in growth, competitive ability, and reproduction (Boots and Begon, 1993; Kraaijeveld and Godfray, 1997b; Yan et al., 1997). These results suggest that a host's optimal strategy for resource allocation will depend on the prevalence and virulence of the parasite in addition to opportunities for reproduction.

Both theoretical models and empirical studies suggest that parasites can significantly alter, and in some cases reverse, the dynamics of both direct (Greenman and Hudson, 1999; Kiesecker and Blaustein, 1999; Park, 1948; Schall, 1992) and indirect competition (Bonsall and Hassell, 1997; Holt, 1977; Holt and Pickering, 1985; Settle and Wilson, 1990; Tompkins et al., 2001). Furthermore, from an applied perspective, parasites may threaten native biodiversity by affecting the dynamics of interspecific competition and therefore facilitate ecological invasions (Bedhomme et al., 2005; Prenter et al., 2004; Torchin et al., 2002). For example, it is thought that parasite-mediated apparent competition played a role in the ecological displacement of native red squirrels by grey squirrels in England (Tompkins et al., 2003). Additionally, competition experiments conducted in laboratory demonstrated that a temperate phage could facilitate the invasion of its bacterial host in new environments occupied by other bacteria (Brown et al., 2006). The ubiquity of parasites in

nature and their potential for affecting ecological interactions warrants a close look into the mechanisms determining the outcome of parasite-mediated competition.

In this paper, we develop two models to study the evolution of host resource allocation strategy. The first model includes an explicit trade-off function between reproduction and immunity and is used to determine resource allocation strategies that maximize fitness in a population, as well as that which is an evolutionarily stable strategy (ESS), bearing in mind that fitness maximizing strategies and the ESS are not necessarily the same. While certain resource allocation strategy may allow the hosts to maximize their population density in the presence of parasites, such a strategy may not be an ESS because it leads to a lower competitive ability. Under this scenario, a host population that has a density maximizing strategy may be invaded by other host genotype and being competitively excluded. In contrast to previous models that focus on the cost of mounting an immune response once an individual is infected (e.g., Day and Burns, 2003), here we focus on the standing costs that are paid by all individuals, regardless of the state of infection. We use evolutionary invasion analysis (Otto and Day, 2007) to determine whether a particular genotype can resist being invaded by all other possible genotypes in a population. We also extend this approach to ask whether being parasitized can affect one's competitive ability relative to a non-parasitized population. Both of our models are constructed based on the interaction between invertebrate hosts and their microbial pathogen. We choose this system for our modeling effort because a large number of empirical studies have greatly improved our understanding of host-parasite interactions (Carton et al., 2005; Hoffmann, 2003; Leavy, 2007) and its increasing importance in evolutionary biology and ecology (Rolff and Siva-Jothy, 2003).

We assume in our model that parasites cannot co-evolve in response to changes in the host. Changes in parasite physiology would enhance the ability of the parasite to persist in the population through Red Queen dynamics (Jokela et al., 2000). By eliminating the possibility of parasite response, we create a conservative test of the ability of hosts to eliminate pathogens from the population.

Previous models of host-parasite interaction have shown that the evolutionary outcome in a single large population may be quite different from the outcome in a subdivided metapopulation (Boots and Sasaki, 1999; Gandon et al., 1996; Kirchner and Roy, 1999; Thrall and Burdon, 1997; Thrall and Burdon, 2002). For example, Kirchner and Roy (1999) found that in a metapopulation model of host-parasite interaction, selection favored hosts with reduced investment in survival, because in demes where individuals had lower survival, the parasite was less able to persist. Thus, migration rates out of demes where individuals had relatively low survival rates were actually higher. In a model with explicit trade-offs between allocation to immunity and reproduction, we might expect the optimal allocation strategy to shift under the conditions of a subdivided metapopulation. In the second part of this study, we explore whether a metapopulation structure alters the patterns that we observe in the within-population model. While the models presented here are relatively simple, they offer an important step towards forwarding our understanding of the trade-offs that hosts face in deciding how best to cope with the ever-present risk of parasitism.

2. Model I. Resource allocation strategies — A single-population model

2.1. Model description

This model is modified from one developed by Kirchner and Roy (1999) which explores the role of parasites in the evolution of host lifespan. To investigate the evolutionary dynamics of resource allocation strategies, we have changed their original susceptible-infected (*SI*) model into a susceptible-infected-susceptible (*SIS*) model (Figure 1), which allows infected individuals to recover. We introduce a resource-dependent trade-off between recovery and

reproduction, and then determine how hosts allocate resources to these two traits. We assume a linear trade-off function between the amount of resources available to reproduction versus immunity, as in the classic Y-model for resource allocation (de Jong and van Noordwijk, 1992). The host-parasite interaction model that we discuss here focuses on the population dynamics of the host rather than the parasite, as we are interested in the evolution of the host's resource allocation strategy. All hosts are in the susceptible class (S) at birth, and become infected via horizontal transfer from already infected hosts. Hosts recover from the infection at a rate that is positively correlated with the host's investment in immunity. However, a host genotype that maintains a high immunity level will have a low reproductive rate, and hence, low fitness.

We limit our analysis to trade-offs between reproduction and immunity that are due to the evolutionary cost of maintaining a high immunity level, rather than the cost of mounting an immune response after infection (Schmid-Hempel, 2003). Such maintenance costs are apparent in the cellular defense response in insects. Insects with a relatively high concentration of circulating hemocytes are more effective at clearing invading parasites at the onset of an infection (Eslin and Prevost, 1998). However, this immune capability may come at the cost of diverting resources from other fitness components. For example, in a selection experiment carried out with a population of *Drosophila melanogaster* and its natural parasitoid, *Asobara tabida*, parasitoid-resistant lines doubled the number of circulating haemocytes but had a low larval competitive ability (Kraaijeveld and Godfray, 1997b; Kraaijeveld et al., 2001).

In our model, recovered hosts move from the infectious class (I) back to the susceptible class and are not immune to future infections. This model is appropriate for invertebrate systems in which the hosts have innate immunity but not acquired immunity (but see (Little and Kraaijeveld, 2004)). We express the model as a pair of ordinary differential equations as follows:

$$\frac{dS}{dt} = rx(1-S-I)S - \beta SI + r(1-x)I - \mu S \quad (1)$$

$$\frac{dI}{dt} = \beta SI - r(1-x)I - m\mu I \quad (2)$$

where the density of $S + I = 1$. As in standard SIS models, β is the parasite transmission rate, infection occurs at a rate βSI , μ is the mortality rate of the host, and m is the ratio by which infection increases host mortality rate ($m > 1$) and can be viewed as a measurement of parasite virulence. Thus, susceptible hosts die at a rate μS and infectious hosts die at a rate $m\mu I$. We chose to use a multiplicative form of infection mortality instead of the more standard additive form to account for the possible interactions between different mortality sources (Williams and Day, 2001). A more general model that partitioned the mortality rate into extrinsic and intrinsic components and linked the intrinsic mortality rate to the resource allocation term did not produce qualitatively different predictions (results not shown).

To model resource allocation, we include a term r , which is the resource acquisition rate of the host, and x , which is the proportion of resource allocated to reproduction ($0 < x < 1$) (with $1 - x$ equal to the proportion allocated to recovery from infection). The potential per capita reproduction rate in the absence of carrying capacity constraints is given by rx and the per capita recovery rate from infection is simply $r(1-x)$. We assume that host population growth is under density-dependent regulation, with the term $(1 - S - I)$ representing the unoccupied fraction of carrying capacity that is available for new individuals. The host population can never reach a density of one in this model due to its own mortality. To

simplify the model, we assume that infected individuals are sterile, but regain full fertility once they have recovered.

Anderson and May (1991) define the basic reproductive ratio of the parasite (R_0) as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible. We can calculate R_0 by multiplying the transmission rate by the duration of the infection period and host density:

$$R_0 = \frac{\beta}{(r(1-x) + m\mu)} \left(1 - \frac{\mu}{rx}\right) \quad (3)$$

Three equilibria (host extinction, parasite extinction, and host-parasite coexistence) exist in this system. The trivial equilibrium occurs when the host reproduction rate is less than the host mortality rate:

$$S^* = 0 \text{ and } I^* = 0 \text{ if } rx < \mu \quad (4)$$

The host population can persist and eliminate parasites when two conditions are met. First, the host reproduction rate is higher than the host mortality rate. Second, the basic reproductive ratio of the parasite is less than one. In other words, the parasite cannot persist if each infected host recovers or dies from an infection before spreading the parasite to at least one susceptible host:

$$S^* = 1 - \frac{\mu}{rx} \text{ and } I^* = 0 \text{ if } rx > \mu \text{ and } R_0 < 1 \quad (5)$$

When parasites are absent, the equilibrium host density increases with investment in reproduction (x), as shown in figure 2A. When reproductive rates of hosts and parasites are sufficiently high, stable coexistence of hosts and parasites can occur, with equilibrium values of infected and uninfected individual given by:

$$S^* = \frac{m\mu + r(1-x)}{\beta} \text{ and } I^* = \frac{(m\mu + r - rx)[\beta(rx - \mu) - rx(m\mu + r - rx)]}{\beta[m\mu + rx(m\mu + r - rx)]} \quad (6)$$

if $rx > \mu$ and $R_0 > 1$

In the presence of parasites, the equilibrium density of susceptible hosts increases with the host recovery rate $r(1-x)$. When the host recovery rate is sufficiently high, an infected host either recovers or dies before infecting another host and eventually drives the parasite to extinction (figure 2B).

2.2. The density maximizing strategy and the evolutionarily stable strategy

We define the fitness of a host genotype as the population density at equilibrium (i.e., S^* in the absence of parasites or $S^* + I^*$ in the presence of parasites). The rationale behind this definition is that the total density of hosts at equilibrium can be used as an indicator of relative colonization rate of a genotype in a metapopulation context, assuming a small proportion of hosts migrate into other patches in each generation. This definition of fitness is relevant in our second model concerning resource allocation strategy evolution at the metapopulation level.

In the absence of parasites, the density of hosts increases with investment in reproduction (eq [5], see Figure 2A for an example). The resource allocation strategy that maximizes the host density is simply to invest fully in reproduction (i.e., $x = 1$).

Based on our model assumption that the hosts can increase recovery rate through heavier investment in immunity, a strategy that eliminates the parasites and confers resistance to future epidemics exists in most of the parameter space (see the peak of S^* in Figure 2B for an example). Under this condition, an infected host always recovers or dies before spreading the parasite to another susceptible host such that the parasite can never spread (i.e., $I^* = 0$). This immunizing strategy (x_{imu}) is derived by solving for the stability boundary that separates the equilibria for parasite extinction (eq [5]) and host-parasite coexistence (eq [6]), and is given by:

$$x_{imu} = \frac{(r+m\mu-\beta) + \sqrt{(r+m\mu-\beta)^2 + 4\beta\mu}}{2r} \quad (7)$$

The immunizing strategy (x_{imu}) may or may not be a strategy that maximizes the total density of hosts at equilibrium. When conditions favor the coexistence of hosts and parasites, the strategy that maximizes the total density of hosts is derived by solving for the maximum of $(S^* + I^*)$ in eq (6). This density maximizing strategy, x_{max} , and its condition boundary are given by:

$$x_{max} = \frac{-\beta m + (m-1)(r+m\mu) + \sqrt{\beta m(\beta m - (m-1)(r-\mu+2m\mu))}}{r(m-1)} \quad (8)$$

if $\beta m - (m-1)(r-\mu+2m\mu) \geq 0$

When conditions favor the extinction of parasites, the density maximizing strategy is equivalent to the strategy that eliminates the parasites (i.e., $x_{max} = x_{imu}$).

In the context of within-population evolution, we are interested in identifying the evolutionarily stable strategy (ESS) that prevents the invasion of other genotypes. The ESS is a strategy that ensures the persistence of a particular genotype, and may or may not be a strategy that eliminates the parasites or maximizes host density. This distinction is important because when the strategy that maximizes host density is not evolutionarily stable (i.e., the x_{max} genotype can be invaded by other genotypes) it is generally considered irrelevant from an evolutionary perspective. The ESS for resource allocation (x_{ESS}) is analytically derived by expanding the model to include multiple host genotypes and examining the Jacobian matrix (see Appendix). The resulting ESS is:

$$x_{ESS} = \frac{1}{2(-1+2m)r} \times \left((-2+3m)r - 2m(\beta+\mu) + 3m^2\mu + \sqrt{m} \sqrt{4\beta(r-\mu) + 2m^2(r-2\beta)\mu + m^3\mu^2 + m[r^2 + 4\beta(\beta+3\mu-r)]} \right)$$

To better understand the implications of these analytical solutions, we numerically compare x_{imu} , x_{max} and x_{ESS} under a range of parameter settings. Figure 3 illustrates how each of the four model parameters (i.e., r , μ , β , and m) affects the values of x_{imu} , x_{max} and x_{ESS} . Under all conditions, the ESS requires the same or a higher investment in reproduction than the other strategies (i.e., $x_{ESS} \geq x_{max} \geq x_{imu}$).

When the resource acquisition rate is extremely low ($r < 0.6$ in Figure 3A), investment in reproduction is fundamental for survival and x_{ESS} is equal to one. As resource availability increases, the ESS becomes a balance between reproduction and immunity but is never a

strategy that eliminates the parasite. Compared to the ESS, the density maximizing strategy requires a higher investment in immunity and the immunizing strategy requires the highest investment in immunity. When the resource availability becomes extremely high, the host only needs to invest a small fraction of resource acquired in immunity to eliminate the parasite and maximize population density. Under this condition, x_{max} and x_{imu} becomes equivalent and converge toward x_{ESS} . Both x_{ESS} and x_{imu} monotonically increase with the extrinsic mortality rate as reproduction becomes more important under a higher mortality rate (Figure 3B). Parasite extinction occurs when the host mortality rate is sufficiently high (eq[5]) and all three strategies lead to full investment in reproduction (i.e., $x_{ESS} = x_{max} = x_{imu} = 1$). Because the infection prevalence increases with the parasite transmission rate, a high investment in immunity (i.e., a lower x) would be required for the host to eliminate the parasite (Figure 3C). In contrast, the immunity investment required to eliminate the parasite decreases as virulence increases (Figure 3D). When the virulence becomes too high, the parasite kills the host before it can spread to another susceptible individual and the infection cannot sustain itself in the host population. All three strategies become full investment in reproduction under this situation.

Pairwise invasibility plots (Geritz et al., 1998) are useful tools for visualizing the evolutionary trajectory of the resource allocation strategy in a population. In the absence of the parasite, the host evolves toward full investment in reproduction (i.e., $x_{ESS} = 1$, see Figure 4A). With few exceptions (see discussion of Figure 3, above), the ESS in the presence of the parasite is a strategy that balances reproduction and immunity (Figure 4B). The host genotype with this evolutionarily stable resource allocation strategy is resistant to invasions and can invade populations of all other genotypes when parasites are present. Intriguingly, evolutionary stability is maintained by parasite-mediated competition and density-dependent regulation. When the resident host has a high level of investment in reproduction and low immunity (i.e., $x_{ESS} < x_R$, see the right hand part of Figure 4B), infection is prevalent in the population (see the right hand part of Figure 2B). Under this scenario, the resources invested in reproduction are mostly wasted because the host cannot reproduce during the infection period. A mutant can invade the population if it can recover faster from infection and reproduce, provided that its investment in reproduction is sufficiently high. The result is that the host evolves toward a lower investment in reproduction (i.e., a smaller x) until it reaches the ESS. In contrast, when the resident host has a low level of investment in reproduction and high immunity ($x_R < x_{ESS}$, see the left hand side of Figure 4B), parasites are rare and the risk of infection is low. A successful mutant would require a higher investment in reproduction than the resident genotype while maintaining a sufficiently high recovery rate. Under this scenario, the host evolves toward a higher investment in reproduction (i.e., a larger x) until it reaches the ESS. Thus, regardless of the initial condition, the host always evolves toward a single ESS under this model.

The predictions from our population model have several implications. First, in most of the parameter space, the host actually has the potential to eliminate the parasite through high investment in immunity (i.e., by adapting x_{imu}), assuming that the parasite does not evolve some counter-adaptation. However, such a strategy is not evolutionarily attainable because natural selection acts at the individual level, rather than the population level. Instead of eliminating parasites, the stable equilibrium state is host-parasite coexistence. Second, in the presence of parasites, a single ESS exists and the host evolves toward this ESS regardless of the initial condition. Furthermore, the host with the x_{ESS} genotype can invade populations of any other genotype and is resistant to counter-invasion.

3. Model II. Resource allocation strategies —A metapopulation model

In our second model, we extend our earlier results to determine the evolutionary dynamics in a metapopulation using the framework developed by Nee and May (1992). The metapopulation consists of three types of demes, including those in which the parasite is absent (H , for “host-only”, occupied by hosts with genotype $x_H = 1$), those in which the parasite is present (P , for “parasite-present”, occupied by hosts with genotype $x_P = x_{ESS}$), and extinct demes in which there is no host (V , for “vacant”).

Our metapopulation model rests on four assumptions. First, the dynamics at the population level occur at a much faster time scale compared to the metapopulation dynamics, such that host population density is at equilibrium in all local patches immediately following colonization or invasion. Based on our analysis of within population dynamics (see Figure 5 for an example), the density of hosts reach equilibrium in few generations after a colonization or invasion event. Assuming that local extinction is a relatively rare event (i.e., the expected time to local extinction is longer than the time for a host population to reach equilibrium density), this approximation using the separation of time scales greatly simplifies the model and allows us to track the dynamics analytically. Second, we assume that all local patches are identical (i.e., r , μ , β , and m are the same in all demes). Under certain conditions (e.g., low resource availability, high extrinsic mortality, or high parasite virulence, see Figure 3), x_{ESS} is equal to one (i.e., $x_P = x_H = 1$) regardless of whether the parasite is present in the local patch, such that all hosts have the same genotype. To obtain biologically meaningful results, we focus only on the condition where the x_{ESS} is less than one in the presence of parasite (i.e., $x_P < x_H = 1$). Third, the colonization rate of a genotype is a monotonically increasing function of its population density. And fourth, parasites can only disperse with their hosts and always accompany the x_P host in a colonization event. In other words, we assume all the susceptible x_P hosts carry dormant parasites and the infection status has no effect on dispersal. Examples of dormant parasites that can be transmitted by susceptible hosts include several bacterial and fungal pathogens of insects (Butt, 2002; Orlova et al., 1998).

Based on our findings in Model I, the three patches in this model can be described as: (1) patches that are occupied by hosts but not parasites, in which the hosts evolve to become inferior competitors but good colonizers. These patches occur with a frequency F_H , (2) patches occurring with frequency F_P that are occupied by hosts and parasites, where the hosts evolve to become superior competitors but poor colonizers; and (3) vacant patches with frequency F_V that are a result of a local extinction event and are available for colonization immediately. This model does not consider the spatial structure of metapopulations, but could be extended to investigate spatial dynamics using cellular automata techniques.

Figure 6 is a schematic representation of this metapopulation model, which can be expressed as a system of ordinary differential equations:

$$\frac{dF_H}{dt} = c_H F_H F_V - c_P F_H F_P - e F_H \quad (10)$$

$$\frac{dF_P}{dt} = c_P F_P F_V + c_P F_H F_P - e F_P \quad (11)$$

$$\frac{dF_V}{dt} = eF_H + eF_P - c_H F_H F_V - c_P F_P F_V \quad (12)$$

where c is the colonization rate of each host genotype, e is the local extinction rate and $F_H + F_P + F_V = 1$. Based on our second and third assumptions, we assume that $c_P < c_H$.

The equilibrium frequencies for the three patch types are affected by the ratio of local extinction rate to the host colonization rate (Figure 7). Global extinction occurs when the local extinction rate is higher than the colonization rate of the x_H genotype:

$$F_H^* = 0, F_P^* = 0, \text{ and } F_V^* = 1 \text{ if } c_P < c_H < e \quad (13)$$

Host persistence and parasite extinction occur when the local extinction rate takes a value between the colonization rates of the two genotypes:

$$F_H^* = 1 - \frac{e}{c_H}, F_P^* = 0, \text{ and } F_V^* = \frac{e}{c_H} \text{ if } c_P < e < c_H \quad (14)$$

The two host genotypes can coexist when the local extinction rate is lower than the colonization rate of the x_P genotype and is higher than the ratio of the colonization rate of the x_H genotype to that of the x_P genotype. Under this condition, parasites coexist with their host in some local patches (F_P^*) but not others (F_H^*); a higher local extinction rate reduces the parasite prevalence at the metapopulation level (i.e., F_P^* decreases when e increases):

$$F_H^* = \frac{e}{c_P} - \frac{c_P}{c_H}, F_P^* = 1 - \frac{e}{c_P}, \text{ and } F_V^* = \frac{c_P}{c_H} \text{ if } \frac{c_P}{c_H} < \frac{e}{c_P} < 1 \quad (15)$$

When the local extinction rate is too low, parasites can spread to all non-vacant patches and eliminate the host with the x_H genotype:

$$F_H^* = 0, F_P^* = 1 - \frac{e}{c_P}, \text{ and } F_V^* = \frac{e}{c_P} \text{ if } \frac{e}{c_P} < \frac{c_P}{c_H} \quad (16)$$

Figure 8 shows the domain of feasibility of this metapopulation model.

4. Discussion

Ever since the groundbreaking work of Anderson and May (1978), a quarter century of theoretical and empirical work on host-parasite interactions has taught us much about host population dynamics when faced with parasites. However, until recently, few models have considered that the resources that a host uses to fight off parasites may come at the expense of investment in other fitness-related traits. We have used several approaches here to explore the consequences of these trade-offs, both in terms of the fitness of the host, and of the ability of the parasite to persist in the population.

Two important points are illustrated by our results. First, while sufficient investment in immune function may enable a population to eliminate a parasite altogether, selection at the individual level makes this an evolutionarily unstable strategy. Second, an infected genotype with an ESS level of investment can always invade an uninfected population. This suggests

that carriers of a parasite can use the parasite as a Trojan horse, allowing it to invade a healthy population. We discuss both of these issues in greater detail below.

4.1. Within-population models of host-parasite dynamics

In a relatively simple model with trade-offs between host reproductive rate and the rate of recovery from infection, we found that it was possible for the host population to eliminate the parasites in certain parameter space by evolving a high recovery rate. This assumes, of course, that the parasite has not evolved a counter-measure to overcome the strong defenses of the host. Nonetheless, our results indicate that the ESS for the host is to maintain a certain level of infection within the population even when it is theoretically possible to eliminate the parasites. This ESS is an evolutionary trap and does not depend on the initial condition of the host population.

The results of our model rest on four particular assumptions. First, as with many previous models (e.g., Boots and Bowers, 1999; Bowers, 2001; Bowers et al., 1994; van Boven and Weissing, 2004), we assumed that the population size was regulated by density-dependent reproduction. Day and Burns (2003) showed that density-dependent regulation results in an intermediate ESS for immunity, whereas the population evolves either toward maximal or minimal immunity when there is no density-dependent regulation. If no single ESS exists or the direction of evolution depends on the initial condition of the population, the evolutionary dynamics at the metapopulation level can be substantially more complex.

Second, we also assumed that the trade-off between investment in reproduction and investment in immune function was linear. An obvious benefit of this assumption is that it makes the model analytically tractable. However, other shapes for the trade-off (e.g., concave, convex, sigmoidal) have been shown previously to alter the ESS for susceptibility (Boots and Haraguchi, 1999; Bowers, 2001). For example, in an SIS model with a trade-off between rates of resource acquisition (r) and parasite transmission (β), Boots and Haraguchi (1999) found that if the trade-off function were linear or convex, the parasite strain with the minimum β would always win. In contrast, with a concave trade-off function, strains with either a minimum or maximum β could win.

Third, we assume that organisms trade off reproductive capacity for recovery rate, and that the cost is paid independent of whether or not a host is infected (i.e., hosts incur a constitutive standing cost of immunity, as opposed to a facultative response cost). This assumption is consistent with recent studies showing that fitness consequences of exposure to parasites may be due in part to the cost of immunity rather than the cost of infection (Graham et al., 2005; Zerofsky et al., 2005). Recent models have shown that the evolutionary dynamics of host-parasite models may differ depending on whether hosts try to fight off parasites through lower transmission rates, higher recovery rates, or higher tolerance (Boots and Bowers, 1999; van Boven and Weissing, 2004). Models have also explored the cost of maintaining the baseline level of immunity, versus the cost that is incurred when genes are up-regulated in response to a parasite (Kraaijeveld et al., 2002; Lochmiller and Deerenberg, 2000; Schmid-Hempel, 2003). The costs of up-regulating defense machinery are only incurred by the infected individuals, whereas the standing costs for maintaining the immune system are incurred by both susceptible and infected individuals. Here, too, the evolutionary dynamics of host-parasite interactions depend on the specific cost scenario and immunity component involved (i.e., enhanced recovery, reduced virulence, and reduced susceptibility) (van Boven and Weissing, 2004).

Under the simplifying assumptions inherent in our model, we found that the host ESS did not eliminate the pathogen from the population. Future studies should consider whether a

similar strategy would evolve under different types of defense against parasites, and for standing versus facultative costs.

Finally, we have focused on the way in which hosts evolve in the presence of parasites, assuming that parasite transmission rate and virulence remain constant for the time scale concerned in this model. Our original rationale for doing so was to create a conservative test of the hypothesis that hosts would not evolve to eliminate parasites from a population, even when it was biologically possible. By preventing parasites from co-evolving in response to host change, it should be easier for hosts to drive the parasite to extinction. As shown in Figure 3, an immunizing strategy exists for the host in all parameter space examined. However, the immunizing strategy for eliminating the parasites always requires more investment in immunity than the ESS and thus is not attainable by the host from an evolutionary perspective.

There may be some biological justification for the assumption of constant parasite transmission rate and virulence as well. First, parasites with little or no host-specificity may not have a strong response to the life history evolution of one particular host species. Second, parasite may evolve in response to the change of host strategy but the coevolutionary dynamic keeps these two parameters relatively stable. Artificial selection experiments demonstrate that the evolution of host resource allocation strategy can occur very quickly, reaching a maximal response in as little as five generations (Kraaijeveld and Godfray, 1997a). This empirical result provides justification for our simplifying assumption that transmission rate and virulence do not change in response to host evolution. In the more complex situation in which parasite transmission rate and virulence evolve in response to changes in host resource strategy, more than one evolutionarily stable outcome may be possible. A coevolution model by van Baalen (1998) found that the ESS for the hosts is to have a limited investment in recovery rate when parasites do not coevolve. However, two possible outcomes exist when the parasites coevolve to adapt to their hosts. In the first scenario, parasites become relatively avirulent and the host invests little in recovery ability. The second scenario corresponds to an escalated arms race in which the host invests heavily in recovery ability to defend against rare but virulent parasites (van Baalen, 1998).

4.2. Invasion analysis

Our invasion analysis demonstrated that the ESS genotype could displace all other genotypes in the presence of the parasites, even when the resident genotype has a high level of investment in immunity that is sufficient to eliminate the parasites in isolation. Under this scenario, the invading hosts act as reservoirs such that the parasites are always present in the population. Even though the resident hosts can recover from an infection at a faster rate than the invaders, the invaders are superior competitors because of their higher reproduction rate. This result may inform our understanding of the role that parasites play in the process of invasion.

The conventional 'escape from enemies' hypothesis has provided a popular explanation for the success of invading species. The idea is that an invading species that leaves its costly parasites behind can out-compete local species, which must reserve some of their resources for immunity. This model predicts that invaders should suffer lower levels of damage from parasites relative to the local species, should evolve greater investment in reproduction relative to the populations from which they originate, and should be less able to fight off parasites when reintroduced to their native habitat. Some studies have found strong support for this hypothesis (Blair and Wolfe, 2004; Cappuccino and Carpenter, 2005; Wolfe et al., 2004).

But one might equally turn this idea on its head, arguing that invaders could succeed by introducing enemies to which resident populations are not adapted. While few explicit models of this idea exist (Brown et al., 2006; Tompkins et al., 2003), one can trace the genesis of the idea to early work on apparent competition. In the first model of apparent competition in a host-microparasite system, Holt and Pickering (1985) found that in the presence of a parasite that infects two distinct populations, the population with relatively low resistance would be displaced by the more resistant population. In the model we present here, we show the more general result that any non-parasitized population can be displaced, even if it has higher resistance than invading parasitized population. This result has direct applications to understanding the causes and dynamics of ecological invasions. Our result is similar to an idea developed by Wodarz and Sasaki (2004), who suggest that a parasite can be used as a biological weapon in inter-specific competition, leading to the evolution of suboptimal immunity in the host. We note, however, that their results are based on the assumption that cross-specific infection is always lethal, which is not likely to be generally true.

4.3. Metapopulation models of host-parasite dynamics

It is now well-established that solutions for evolutionarily stable strategies within populations do not necessarily predict the outcome of selection acting on a metapopulation (Hanski, 1999; Hanski and Gilpin, 1997). For example, metapopulation models have demonstrated that in subdivided populations, life history traits can evolve not simply due to their direct correlation with fitness, but also because of their effect on rates of extinction and colonization (Hanski, 1999). Of relevance to the models discussed here, a metapopulation structure can increase the ability of competitors to coexist (Hanski, 1999).

We showed that for a single panmictic population, parasites create an evolutionary trap, in which a strategy that eliminates the parasite is never favored by selection. This is not necessarily the case, however, in a metapopulation model, in which the ESS at the population level may or may not be the dominant strategy at the metapopulation level. Because the competitive advantage of the ESS genotype over the full reproduction genotype stems from parasite-mediated competition, the parasite prevalence at the metapopulation level determines the success of the ESS genotype. When local extinction rate is high compared to host colonization rate, parasites are restricted to a small fraction of local patches and the dominant strategy is to fully invest in reproduction. These results are in a similar vein to work by Kirchner and Roy (1999), who found that in a metapopulation, parasites could favor the evolution of reduced lifespan of hosts. If hosts died before they had a chance to transmit the parasite to other individuals within a population, migration rates to other populations would increase.

The metapopulation model that we present here makes no assumptions about underlying spatial structure. However, especially in the context of parasite transmission, spatial structure may have important consequences for host-parasite dynamics (Haraguchi and Sasaki, 2000; Keeling, 1999; Lively and Dybdahl, 2000; Rand et al., 1995). In particular, the structure of the host contact network within which the parasite is transmitted can affect the dynamics of epidemics (Jones and Handcock, 2003; Pastor-Satorras and Vespignani, 2001a; Pastor-Satorras and Vespignani, 2001b; Pastor-Satorras and Vespignani, 2002; Verdasca et al., 2005; Zekri and Clerc, 2001). In addition to studies of the effect of network structure on host infection rates, others have studied how network structure can affect the evolution of parasite virulence (Read and Keeling, 2003). However, the effects of host contact network structure on the coevolutionary dynamics of both host and parasites have yet to be investigated.

5. Conclusion

The ecology and evolution of invertebrate immunity has attracted much research attention in recent years (Rolff and Siva-Jothy, 2003). In addition to studies that have focused on the underlying physiological and genetic mechanisms of invertebrate immune system (Carton et al., 2005; Hoffmann, 2003; Leavy, 2007), mathematical models have proved indispensable in developing explicit hypotheses for empirical studies. Through the use of relatively simple SIS and metapopulation models, here we shown that tradeoffs between reproduction and immunity may be able to explain why certain populations or species are able to invade others, and why parasites remain as common as they do, despite the evolution of elaborate host defenses to ward them off. While these simple models have allowed us to draw some rather general conclusions, we are now in need of more detailed models to determine the validity of our simplifying assumptions, and of further empirical studies to test the claims about host-parasite coevolution and host invasions that have been put forward here and elsewhere.

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Appendix: Evolutionarily stable strategy analysis

To investigate the evolutionarily stable strategy of resource allocation (i.e., x_{ESS}) at the population level, we expand our basic model to include two host genotypes. The resident genotype is denoted by the subscript ‘R’ and the mutant is denoted by the subscript ‘M’. We assume that the two host genotypes have the same resource acquisition rate (r) and mortality rate (μ). Parasites can cross-infect the two host genotypes with the same transmission rate (β) and exhibit identical virulence (m) in each host. In other words, the two host genotypes only differ in their resource allocation strategy (i.e., $x_R \neq x_M$). We begin the model with the assumption that the population is at equilibrium with only resident hosts and introduce the mutant at a very low density. The model can be expressed as the following set of differential equations:

$$\frac{dS_R}{dt} = rx_R(1-S_R-S_M-I_R-I_M)S_R - \beta S_R(I_R+I_M) + r(1-x_R)I_R - \mu S_R \quad (\text{A1})$$

$$\frac{dI_R}{dt} = \beta S_R(I_R+I_M) - r(1-x_R)I_R - m\mu I_R \quad (\text{A2})$$

$$\frac{dS_M}{dt} = rx_M(1-S_R-S_M-I_R-I_M)S_M - \beta S_M(I_R+I_M) + r(1-x_M)I_M - \mu S_M \quad (\text{A3})$$

$$\frac{dI_M}{dt} = \beta S_M(I_R+I_M) - r(1-x_M)I_M - m\mu I_M \quad (\text{A4})$$

To determine if the mutant genotype can invade the resident population, we linearize the system at equilibrium in the absence of mutant (i.e., $S_R = S^*$ and $I_R = I^*$ in eq[6], $S_M = I_M = 0$). This results in an upper triangular Jacobian matrix (**J**):

$$\mathbf{J} = \begin{bmatrix} \mathbf{R} & \mathbf{A} \\ \mathbf{0} & \mathbf{M} \end{bmatrix} \quad (\text{A5})$$

where **0** is a 2×2 matrix of zeros and **R**, **A** and **M** are defined by the following:

$$\mathbf{R} = \begin{bmatrix} rx_R - 2rx_RS_R - rx_RI_R - \beta I_R - \mu & -rx_RS_R - \beta S_R + r - rx_R \\ \beta I_R & \beta S_R - r + rx_R - m\mu \end{bmatrix} \quad (\text{A6})$$

$$\mathbf{A} = \begin{bmatrix} -rx_RS_R & -rx_RS_R - \beta S_R \\ 0 & \beta S_R \end{bmatrix} \quad (\text{A7})$$

$$\mathbf{M} = \begin{bmatrix} rx_M - rx_MS_R - rx_MI_R - \beta I_R - \mu & r - rx_M \\ \beta I_R & -r + rx_M - m\mu \end{bmatrix} \quad (\text{A8})$$

The eigenvalues of the Jacobian matrix are those of submatrices **R** and **M**. Because the resident reaches equilibrium in the absence of the mutant, both eigenvalues of submatrix **R** have negative real part. Thus, the invasion success of the mutant is determined by the eigenvalues of submatrix **M**. If both eigenvalues of submatrix **M** have negative real parts then the system is stable in the absence of mutant. In other words, x_R is an ESS when both eigenvalues of submatrix **M** have negative real parts for any x_M given that $x_R = x_M$. Based on this definition, we obtained an analytical solution of the ESS for host strategy (i.e., x_{ESS}) by solving for the x_R that satisfies the condition

$$\frac{\partial \lambda}{\partial x_R} = 0 \quad (\text{A9})$$

where λ is the dominant eigenvalue of submatrix **M**. The resulting solution is given in eq (9) of the main text.

Figure 1.

Schematic representation of the susceptible-infected-susceptible (*SIS*) model, where r is the resource acquisition rate of the host, x is the proportion of resource allocated to reproduction ($0 < x < 1$), β is the parasite transmission rate, μ is the mortality rate of the host, and m is the ratio by which infection increases host mortality.

Figure 2.

Equilibrium host density. (A) In the absence of the parasite, equilibrium host density increases monotonically with investment in reproduction (x). Host population cannot persist if the potential per capita reproduction rate is equal to or lower than the mortality rate ($rx \leq \mu$). (B) When the parasite is present in the environment, the density of susceptible hosts is maximized when the investment in immunity is sufficiently high to eradicate epidemics. Parameter values are: $r = 10$, $\mu = 0.2$, $\beta = 10$, and $m = 2$.

Figure 3.

Effect of model parameters on host strategies. Dashed lines: the immunizing strategy (x_{imm}); dotted lines: the density maximizing strategy (x_{max}); solid lines: the evolutionarily stable strategy (x_{ESS}). In some part of the parameter space, the immunizing strategy and the density maximizing strategy are equivalent. (A) Host strategies as a function of resource acquisition rate (r). (B) Host strategies as a function of host mortality rate (μ). (C) Host strategies as a function of parasite transmission rate (β). (D) Host strategies as a function of parasite virulence (m). For each comparison, the other parameters are held constant with $r = 10$, $\mu = 0.2$, $\beta = 10$, and $m = 2$.

Figure 4.

Pairwise invasibility plots. The x-axis shows the investment strategy of the resident (x_R) and the y-axis is the strategy of the mutant (x_M). Black regions show the parameter space where the mutant can invade the resident population whereas white regions show the parameter space where the resident is resistant to invasion. Arrows indicate potential evolutionary trajectories of resource allocation strategy in a population. (A) Parasite absent in the population. (B) Parasite present in the population. Parameter values are the same as in Figure 2.

Figure 5.

Within population dynamics. Dashed lines: density of S_H (susceptible hosts with genotype x_H); solid lines: density of S_P (susceptible hosts with genotype x_P); dotted lines: combined density of I_H and I_P (total density of infected hosts). (A) Colonization of a vacant patch by hosts with genotype x_H . (B) Colonization of a vacant patch by hosts with genotype x_P . (C) Failed invasion of x_H hosts into a patch occupied by x_P hosts. (D) Successful invasion of x_P hosts into a patch occupied by x_H hosts. For invasion events (panels C and D), the resident hosts occupy the patch at equilibrium density. Hosts with genotype x_H are initiated with a density of $S_H = 0.001$ and $I_H = 0$ at time 0 because they are originated from a host-only patch. Hosts with genotype x_P are initiated with a density of $S_H = 0$ and $I_H = 0.001$ at time 0 based on the assumption that parasites always accompany x_P hosts in a colonization or invasion event (see text). Parameter values are the same as in Figure 2. Under this condition, the generation time of the host is equivalent to five time units.

Figure 6.

Schematic representation of the metapopulation model. The parasite is present in the "P" patches (denoted by a subscript P) but not the "H" patches (denoted by a subscript H for "host-only"). "V" patches are vacant patches that are available for colonization. c_H and c_P are the colonization rates of the two host genotypes and e is the local extinction rate.

Figure 7.

Fractions of three patch types at equilibrium in the metapopulation model, as a function of the ratio of local extinction rate to colonization rate of genotype x_H (denoted by e/c_H).

Parameter value: $c_P = 0.1 c_H$

Figure 8.

Domains of feasibility for the metapopulation model. I. (white region): global extinction ($F_H = 0$ and $F_P = 0$, eq [13]), II. (light gray region): parasite extinction ($F_H > 0$ and $F_P = 0$, eq [14]), III. (dark gray region): parasites present in some local patches ($F_H > 0$ and $F_P > 0$, eq [15]), and IV. (black region): parasites coexist with hosts in all non-vacant patches ($F_H = 0$ and $F_P > 0$, eq [16]).