Multi-species interactions and the evolution of biological systems

by

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Abstract

In this thesis I develop several models examining how genetic evolution can affect evolutionary processes at a broader scale.

First, I ask how evolution would proceed at a locus that governs the mutation rate between alleles mediating interactions between hosts and parasites. By relaxing several simplifying assumptions I am able to explore the affects of sex and recombination. I find that, when the modifier locus is completely linked, the mutation rate evolves toward the optimum rate. With looser linkage, however, lower mutation rates evolved. This work can potentially explain the high rates of antigenic switching observed in many asexual taxa.

Second, I investigate how ploidy levels and the genetic model underlying species interactions affect how evolution proceeds from a free-living to a parasitic life-history. I find that the transition to parasitism occurs over a broader range of parameters when the parasite is haploid. The role of host ploidy is more complicated, depending on the model governing host-parasite interactions. These results provide a first characterization of how genetic architecture affects selection on life-history in antagonistic species interactions.

Third, I develop a model of sexual selection in an environment with spatial variation in the carrying capacity, but no variation in resource type. I show that, when searching for a mate is costly, this variation can stabilize demographic fluctuations, facilitating long-term coexistence of species differing only in sexual traits. This is the first study to demonstrate the existence of conditions under which sexual selection alone can promote the long-term coexistence of ecologically equivalent species in sympatry.

Finally, I develop a model characterizing the effects of mating preferences on species interactions in hybrid zones. I find that the spatial distribution of genotypes observed in many "mosaic" hybrid zones might be better explained by species-specific differences in mating than by differences in ecology (the common explanation). In addition, I develop a statistical method that can be applied to empirical hybrid zone data to estimate how "mosaic" the hybrid zone is. I test this statistic on data from the *Mytilus edulis* and *M. galloprovincialis* hybrid zone.

Preface

I conceived and developed the model in chapter 2, with guidance and assistance from Sarah P. Otto. An undergraduate student, Jane Shen, assisted me on the project as part of her honours thesis. Sarah P. Otto helped with writing and editing the manuscript. This article has been published:

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CHAPTER 1

Introduction

To fully understand the complexities of the biological world it is necessary that we have both empirical documentation of a particular process, as well as a conceptual understanding of the mechanisms causing that process to occur. For many simple biological processes it is possible to easily intuit the outcome of a particular interaction. However, in many cases, such intuition is not possible without some aid. By providing us with additional computational power and/or methods of analysis, theoretical models can provide such an aid, and thus facilitate our understanding in these more difficult cases.

In addition to helping us understand documented biological phenomena, theoretical models can change how we understand existing data and, in some cases, lead to empirical discoveries that would not have occurred otherwise. For example, theoretical investigations of interactions between hybridizing species have led to a number of predictions about the expected spatial genetic patterns in the region where the two types overlap and form hybrid offspring (i.e., in their "hybrid zone"; Barton and Hewitt, 1985, 1989). One such prediction is that a hybrid zone should often move in space, until finally settling in a region of low population density. Several empirical studies have since found convincing evidence that such a process really does occur in nature. For example, Saitoh and Katakura (1996) found that the boundaries between three parapatric species of flightless leaf beetles mostly occur along streams or cliffs where population densities are low to non-existent. Similarly Barrowclough et al. (2005) found that the range of overlap between the northern spotted owl and the California spotted owl is restricted to a narrow band within the region of lowest documented owl density. Such empirical findings as these serve to illustrate the critical role theoretical models can play in biology.

A central focus in evolutionary biology is on understanding how processes occurring at one level of biological organization affect evolutionary dynamics at another level (e.g., how cellular processes affect organismal behaviour or how the behaviour of an individual may affect the dynamics of a population or group; Maynard Smith and Szathmary, 1997; Okasha, 2007). Because interactions between multiple levels of organization are complex and can easily be obscured by more direct interactions, many insights on this topic derive from theoretical work. At the most general level, the chapters of my thesis can be summarized as a series of theoretical models focusing on these interactions between different evolutionary levels. In chapters 2 and 3 I have examined the relationship between species-level interactions and the genetic architecture of the traits regulating those interactions, both in the context of host-parasite interactions, and in chapters 4 and 5 I have examined the relationship between population-level interactions and individual behaviour (namely female mating behaviour). I will now briefly summarize each of my chapters.

1.1 Genetics and host-parasite co-evolution

Historically host-parasite interactions have received substantial attention because of the implications any findings may have for disease control and/or pest management. Host-parasite interactions are of particular interest to evolutionary biologists, however, because they represent one of the most complex and highly-evolved relationships between separate species. In many cases, the two interacting species are locked in a perpetual evolutionary "arms race", with selection constantly favouring novel mechanisms allowing hosts to evade their parasites and parasites to invade these same hosts. Understanding how these interactions can affect selection at the most basic genetic level is critical if we hope to understand how parasite genomes evolve in response to their biotic environment.

Mutation is the fundamental source of genetic variation, without which adaptation could not occur. Models of the evolution of mutation rates in a constant environment have shown that asexual species evolve an optimal mutation rate that balances the costs and benefits of producing adaptive and deleterious mutations. In a host-parasite system, however, the fitness effect of a mutation is not constant but instead depends on the current composition of the other species. In chapter 2 I use modifier theory to ask how evolution would proceed at a locus that governs the mutation rate between alleles that mediate hostparasite interactions. In my analysis I am able to relax a number of common simplifying assumptions, and also explore the effects of sex and recombination. I find that when the modifier locus is completely linked to the locus mediating the host-parasite interaction, the mutation rate evolves toward the optimum rate. With looser linkage, however, lower mutation rates evolve.

Complementary to studies that focus on how host-parasite interactions select for changes in genetic parameters (like that above) are those that investigate how genetic parameters affect evolution of host-parasite interactions. Such studies are necessary if we hope to fully understand the origins of broad-scale macro-evolutionary patterns. In the context of hosts and parasites, such an understanding is essential as we try to characterize the traits that make a particular species more or less prone to adopting a parasitic life-style.

One assumption that is common in models of host-parasite co-evolution is that species are either completely parasitic or completely non-parasitic. While many species do fit this assumption, there are numerous examples for which this assumption is not appropriate. For example, a number of species from a range of taxonomic groups have been shown to be facultatively parasitic: ciliates (Reynolds, 1936; Thompson and Moewus, 1964), flatworms (Hooge and Tyler, 1999), fungi (Morin et al., 1993), nematodes (Benham, 1974). These species are parasitic if the opportunity arises, but are otherwise free-living and capable of reproduction without the aid of a host species. In chapter 3 I use modifier theory to investigate how evolution proceeds from a free-living to a parasitic lifehistory and, in particular, I investigate how the ploidy levels of the interacting species and the genetic model underlying species interactions affects whether selection favours a more or less parasitic life-cycle. In general, I find that the transition to parasitism occurs over a broader range of parameters when the parasite is haploid. The role of host ploidy is more complicated, depending on the model governing host-parasite interactions.

1.2 Sexual selection and co-existence

Just as genetic architecture can affect higher-level species interactions, so can the behaviour of an individual affect higher-level population dynamics. For example, the mating behaviour of females can sometimes select for particular traits in males which, under the right conditions, can split a population into multiple reproductively isolated groups (Lande, 1981; Kirkpatrick, 1982; Seger, 1985). In some situations, therefore, sexual selection (an individual-level process) seems to promote the generation of diversity (a population-level process). While appearing to be capable of generating diversity, sexual selection has not been thought to be capable of promoting the long-term co-existence of distinct types, and thus not capable of *maintaining* biodiversity. This is because changes in mating behaviour or preferences do not lead to niche divergence, which is generally considered to be a necessary precondition for co-existence when species' ranges overlap (Weissing et al., 2011).

In chapter 4 I develop a model of sexual selection in an environment with variation in resource quantity but no heterogeneity in resource type across space. I show that the resultant variation in the number of individuals can stabilize demographic fluctuations, which then allows for the stable long term co-existence of populations differing only in their mating preferences. While costs associated with searching for a mate do not enable co-existence on their own, they turn out to be critical in facilitating co-existence in this spatially explicit model.

1.3 Hybrid zones

In addition to maintaining biodiversity amongst or within populations, female mating preferences are also likely to have an impact on the spatial distribution of diverse types. The most natural place to investigate spatial interactions between distinct genotypes is in the region where their ranges meet. If reproductive isolation is not complete, then hybridization can occur. These hybrid zones are, therefore, an ideal setting for observing the forces that maintain and/or break down species boundaries (Barton and Hewitt, 1989, 1985). The majority of theoretical investigations of hybrid zones have focused on ecological differences between species, which are often assumed to exist despite mixed empirical support (Harrison and Rand, 1989; Cain et al., 1999; Bridle et al., 2001). In chapter 5 I develop and analyze a model characterizing the potential effects of mating preferences on spatial interactions between distinct mating types in hybrid zones. Interestingly, I find that the spatial distribution of genotypes observed in many "mosaic" hybrid zones (those characterized by patchy species distributions) is consistent with patterns generated by species-specific differences in mating preferences. In cases where there is little evidence for ecological differences between the interacting species, divergent mating preferences may, therefore, provide a better explanation for this mosaic pattern. In addition to the primary model, I develop a new statistical method that can be applied to empirical hybrid zone data to estimate how "mosaic" the hybrid zone is. I test this statistic on data from three loci from the hybrid zone of the marine mussels Mytilus edulis and M. galloprovincialis. The estimated "mosaicity" is significantly higher for one of these three loci, suggesting that this particular locus or a linked region may, at least partially, underlie assortative mating and/or local adaptation ..

1.4 Conclusions

In addition to providing insight into several interesting topics in biology, the chapters in this thesis also illustrate the general importance of theoretical research. Theory has enabled us to fully understand many complex processes and, additionally, revealed many interesting avenues for future theoretical and empirical work. In each of the following chapters I will discuss the empirical implications of my work, as well as any possible future directions for both theoretical and empirical research. In doing so I hope to demonstrate the importance of theoretical work to empirical biology, and vice versa. Without theory, many potentially interesting components of the natural would remain unknown to us and without empirical tests, the relevance of theoretical research (and its potential contradictions) would be greatly under-appreciated.

Mutating away from your enemies: the evolution of mutation rate in a host-parasite system

2.1 Summary

The rate at which mutations occur in nature is itself under natural selection. While a general reduction of mutation rates is advantageous for species inhabiting constant environments, higher mutation rates can be advantageous for those inhabiting fluctuating environments that impose on-going directional selection. Analogously, species involved in antagonistic co-evolutionary arms-races, such as hosts and parasites, can also benefit from higher mutation rates. We use modifier theory, combined with simulations, to investigate the evolution of mutation rate in such a host-parasite system. We derive an expression for the evolutionary stable mutation rate between two alleles, each of whose fitness depends on the current genetic composition of the other species. Recombination has been shown to weaken the strength of selection acting on mutation modifiers, and accordingly, we find that the evolutionarily attracting mutation rate is lower when recombination between the selected and the modifier locus is high. Cyclical dynamics are potentially commonplace for loci governing antagonistic species interactions. We characterize the parameter space where such cyclical dynamics occur and show that the evolution of large mutation rates tends to inhibit cycling and thus eliminates further selection on modifiers of mutation rate. We then find using computer simulations that stochastic fluctuations in finite populations can increase the size of the region where cycles occur, creating selection for higher mutation rates. We finally use simulations to investigate the model behaviour when there are more than two alleles, finding that the region where

cycling occurs becomes smaller and the evolutionarily attracting mutation rate lower when there are more alleles.

2.2 Introduction

Mutation is the fundamental source of genetic variation, without which adaptation could not occur. The rate at which mutations occur has, therefore, been of long-standing interest to evolutionary biologists (Muller, 1928; Mukai, 1964; Drake et al., 1998). The notion that mutation rates themselves are subject to natural selection has been well documented empirically (Sniegowski et al., 1997, 2000; Baer et al., 2007). It would seem at first that there should be a strong selective pressure to eliminate mutation altogether, due to the high probability that any particular mutation will have deleterious effects. This general reduction principle has been shown to hold in theoretical models pioneered by Sam Karlin and colleagues (Karlin and McGregor, 1974; Liberman and Feldman, 1986) for populations at equilibrium in non-changing environments, where there is no cost to increased replication fidelity. However, when higher replication fidelity entails a cost (due to, for example, increased energy allocation during transcription), then selection favours an intermediate mutation rate that balances the fitness cost associated with deleterious mutations and the energy savings associated with a higher mutation rate (André and Godelle, 2006).

While reducing mutation rates is evolutionarily favoured in a constant environment, were it not for costs, the same is not true in a novel environment. In a novel environment a mutator lineage (one with a higher mutation rate) still carries the burden of an increased deleterious mutation load. However, it now also has a higher probability of experiencing a beneficial mutation. When such a beneficial mutation occurs in a mutator lineage it can pull the mutator allele to a higher frequency (a mechanism referred to as genetic hitch-hiking; Maynard Smith and Haigh, 1974). The above ideas have been confirmed in a number of theoretical models (Kimura, 1967; Leigh, 1970; Johnson, 1999).

Because modifiers of mutation rate are primarily subject to indirect selection via their effects at other loci (the cost of replication fidelity being the exception to this rule), modifier dynamics are highly sensitive to their rate of recombination with the target loci that are the subject of both mutation and direct selection. Recombination has been shown to weaken the strength of indirect selection acting on mutation modifiers (Kimura, 1967; Leigh, 1970; Sniegowski et al., 1997). This can be understood as follows. Suppose a beneficial mutant arises in a mutator lineage. With a high enough recombination rate, it is probable that the beneficial allele will recombine into the non-mutator lineage during its spread. In this way the mutator lineage "shares" the benefits of the beneficial mutants it creates. Meanwhile deleterious mutations will accumulate on the mutator background more rapidly than on the non-mutator background. While recombination allows some of these mutator lineages to escape the deleterious effects of their mutations, a large number of mutator lineages will be eliminated by purifying selection before any recombination occurs. Consequently, because beneficial mutations have a longer sojourn time within a population, on average, than deleterious mutations, the benefits of producing beneficial mutations are dissipated over time by recombination, while the costs of producing deleterious mutations are more immediately felt. This intuitive argument has been considered explicitly in models of directional selection (Johnson, 1999).

A novel environment is not the only scenario that has been shown capable of selecting for higher mutation rates. For example, a number of theoretical models have shown that increased mutation rates can be advantageous in fluctuating environments, where the direction of selection periodically changes (see Leigh, 1970, 1973; Ishii et al., 1989). In this situation individuals are repeatedly under pressure to adapt. Antagonistic co-evolutionary interactions, such as those that occur between hosts and parasites, can also create selection for increased mutation rates. Because adaptive changes in one species often have detrimental effects on the other, hosts and parasites repeatedly create "novel" environments for one another (this is commonly referred to as the "Red Queen" hypothesis; Van Valen, 1973). Within host-parasite interactions, it has been shown that mean fitness is optimized by high or non-zero mutation rates, in a manner similar to that found with fluctuating abiotic environments (Nee, 1989; Sasaki, 1994; Haraguchi and Sasaki, 1996). There is also empirical evidence that host-parasite co-evolution can favour increased mutation rates. For example, Pal et al. (2007) recently found that co-evolution with viruses drove up the mutation rates in the bacterium Pseudomonas fluorescens.

Host-parasite interactions are commonly mediated through antigen molecules, which are expressed on the surface of parasite cells. For hosts, a pathogen's antigen molecule provides a useful target to aid in its detection and thus elimination. Consequently, hosts have evolved sophisticated mechanisms enabling them to detect and respond to a wide array of possible antigen types, while parasites have evolved complex mechanisms allowing them to regularly produce offspring with antigens differing from their own. This process of "antigen switching" in parasites has been well documented empirically (Brannan et al., 1994; Turner, 1997; Frank, 2002), and consequently many of the mechanisms that have evolved in order to make the process more efficient are now well understood. A good summary of many of these is available in Frank (2002).

Frank describes, for example, the process of "gene conversion," whereby some parasites can copy one of several non-expressed archival antigen alleles into a single expressed site. In this way they are able to store many variant antigen alleles in their genome, while only ever expressing a single one. Because each mutant is drawn from a pool of alleles that have been historically exposed to selection, switching in this way is more likely than random mutation to produce viable mutants. Such a strategy can be found in *Trypanosoma brucei*, which causes "sleeping sickness" in several African mammals. This particular parasite has been shown to carry hundreds of alternative loci in its genome (Pays and Nolan, 1998). For discussions of similar mechanisms see also Donelson (1995) (in *Borrelia hermsii*); Svard et al. (1998) (in *Giardia lamblia*); Kusch and Schmidt (2001) (in free-living protozoa).

In a theoretical model of host-parasite co-evolution using mean fitness arguments, Nee (1989) found that antagonistic interactions can lead to an indefinite escalation of mutation rates in both species, provided that the selection induced by these interactions is strong relative to mutation rates. Haraguchi and Sasaki (1996) later extended this model to consider the effects of deleterious mutations and found that only a small amount of unconditionally deleterious mutation was sufficient to prevent the above reported indefinite escalation of mutation rates.

Like Haraguchi and Sasaki (1996), we consider a modifier extension to the model introduced in Nee (1989). Unlike Haraguchi and Sasaki, however, we allow recombination to occur between the mutation modifier and the selected locus. We find that under certain conditions, this addition results in a qualitatively different outcome, with recombination acting to reduce the evolutionarily attracting mutation rate by distributing the benefits of advantageous mutations. We closely follow the methods of Gandon and Otto (2007), who analyzed a modifier of the rate of recombination between two loci mediating host-parasite interactions. We supplement our analytical model with computer simulations, which allow us to investigate extensions to finite populations, as well as to more alleles.

2.3 Methods and results

2.3.1 Model description

We consider two co-evolving haploid species: a host and a parasite. We follow haplotype frequencies through a life cycle consisting of a census, selection, and reproduction. Mating is random within each species, and (except where noted) population sizes are assumed constant and large enough that drift can be ignored. Antagonistic interactions between species are mediated through a single locus in hosts and a single locus in parasites, each with two alleles (A_h/a_h) in hosts and A_p/a_p in parasites). A second locus in each species determines the rate of mutation between A_i and a_i , where forward and backward mutation rates are assumed equal. Throughout *i* denotes the species type: *h* for hosts, *p* for parasites. We denote the two alleles at this mutator locus by M_i and m_i . The four haplotypes within a species are thus $\{a_im_i, a_iM_i, A_im_i, A_iM_i\}$. We let $x_{i,j}$ denote the frequency of the j^{th} genotype in species *i* (labelled in the order given above).

Fitness is determined by a matching-alleles model, introduced by Hamilton (1980). Specifically, when the host genotype matches that of the parasite (e.g., A_p parasite and A_h host, or a_p parasite and a_h host), the parasite experiences a fitness increase of $\alpha_p > 0$ and the host a fitness decrease of $\alpha_h < 0$. The fitness of the *j*th genotype in species *i* is then given by

$$w_{i,j} = 1 + \alpha_i(\zeta_j(x_{\bar{i},1} + x_{\bar{i},2}) + (1 - \zeta_j)(x_{\bar{i},3} + x_{\bar{i},4}))$$
(2.1)

where ζ_j is equal to 1 for $j \in \{1,2\}$ and o for $j \in \{3,4\}$ and where an overbar denotes the other species type ($\bar{h} = p$, $\bar{p} = h$). If $\mu_{i,M}$ ($\mu_{i,m}$) is the probability that mutation occurs at the *A*-locus in an individual of species *i* carrying the M_i (m_i) allele at the *M*-locus (with $\mu_{i,m}$ and $\mu_{i,M}$ both $\leq 1/2$), then the frequencies after selection and mutation, but before sex and recombination are given by

$$\begin{aligned} x'_{i,1} &= (1 - \mu_{i,m})(w_{i,1}/\overline{w}_i)x_{i,1} + \mu_{i,m}(w_{i,3}/\overline{w}_i)x_{i,3} \\ x'_{i,2} &= (1 - \mu_{i,M})(w_{i,2}/\overline{w}_i)x_{i,2} + \mu_{i,M}(w_{i,4}/\overline{w}_i)x_{i,4} \\ x'_{i,3} &= (1 - \mu_{i,m})(w_{i,3}/\overline{w}_i)x_{i,3} + \mu_{i,m}(w_{i,1}/\overline{w}_i)x_{i,1} \\ x'_{i,4} &= (1 - \mu_{i,M})(w_{i,4}/\overline{w}_i)x_{i,4} + \mu_{i,M}(w_{i,2}/\overline{w}_i)x_{i,2} \end{aligned}$$

$$(2.2)$$

where $\overline{w_i}$ (the mean fitness of species *i*) is given by

$$\overline{w_i} = \sum_{j=1}^4 w_{i,j} x_{i,j}$$

In the text, we assume that the modifier allele only alters the mutation rate at the *A*-locus, but in appendix A.1 we also include a cost to the modifier of producing unconditionally deleterious alleles. Letting ψ_i denote the product of the probability that a haploid individual engages in sexual reproduction and the probability of recombination between the *A* and the *M* loci in species *i*,

genotype frequencies after sex and recombination are given by

$$\begin{aligned} x_{i,1}'' &= x_{i,1}' - \psi_i D_i' \\ x_{i,2}'' &= x_{i,2}' + \psi_i D_i' \\ x_{i,3}'' &= x_{i,3}' + \psi_i D_i' \\ x_{i,4}'' &= x_{i,4}' - \psi_i D_i' \end{aligned}$$
(2.3)

where D'_i denotes the linkage disequilibrium in species *i* after mutation and selection. It can be computed as $D'_i = x'_{i,1}x'_{i,4} - x'_{i,2}x'_{i,3}$.

Denoting the frequency of *A* by $p_{i,A}$, and the frequency of *M* by $p_{i,M}$, we have

$$p_{i,A} = x_{i,3} + x_{i,4}$$

$$p_{i,M} = x_{i,2} + x_{i,4}$$
(2.4)

In the matching-alleles model, allele frequencies typically fluctuate around 1/2 over time. The key simplification that we make is that these fluctuations are relatively small, so that the allele frequencies remain near 1/2. If we define $\delta_{i,A}$ as the departure of the frequency of the *A* allele from 1/2, so that $\delta_{i,A} = (x_{i,3} + x_{i,4}) - 1/2$, we may then convert the recursion equations described in equation (2.3) into a new system of recursion equations involving $\delta_{i,A}$, $p_{i,M}$, and D_i .

Assuming that $\delta_{i,A}$ is small, specifically that it is of the order of a small term ϵ , and that the modifier also has a small effect on the mutation rate, such that $\mu_{i,M} - \mu_{i,m}$ is also of order ϵ , we find that disequilibrium rapidly evolves to a level that is of order ϵ^2 (see appendix A.2 for details). With the above assumptions it is possible to simplify the recursion for $\delta_{i,A}$. Up to order ϵ we get

$$\begin{pmatrix} \delta_{h,A}[t+1] \\ \delta_{p,A}[t+1] \end{pmatrix} = \mathbb{M} \begin{pmatrix} \delta_{h,A}[t] \\ \delta_{p,A}[t] \end{pmatrix}$$
(2.5)

where

$$\mathbb{M} = \begin{pmatrix} (1 - 2\mu_{h,M}) & \frac{\alpha_h}{(2 + \alpha_h)} (1 - 2\mu_{h,M}) \\ \frac{\alpha_p}{(2 + \alpha_p)} (1 - 2\mu_{p,M}) & (1 - 2\mu_{p,M}) \end{pmatrix}$$

While this approach requires that disequilibrium is small (order ϵ^2), it is not necessary that it remains at the steady state values predicted by the current state of the population, as is the case in a quasi-linkage equilibrium analysis (for more information on quasi-linkage equilibrium analyses see Barton, 1995). Thus equation (2.5) can be applied even when selection is large relative to the rates of sex and recombination.

The point $\delta_{h,A} = \delta_{p,A} = 0$ is an equilibrium of equation (2.5), as well as of the full recursion equations. A local stability analysis shows that this point is unstable with complex eigenvalues as long as

$$R = \sqrt{\det(\mathbb{M})} = \sqrt{(1 - 2\mu_{p,M})(1 - 2\mu_{h,M})\frac{(1 + \alpha_p/2 + \alpha_h/2)}{(1 + \alpha_p/2)(1 + \alpha_h/2)}}$$
(2.6)

is greater than one, where $det(\mathbb{M})$ is the determinant of the matrix \mathbb{M} and R is the magnitude of the leading eigenvalue of \mathbb{M} .

When *R* from is greater than one, the frequencies in a species cycle sinusoidally outwards with time. However, when *R* is near one the cycles remain small for extended periods of time. Without loss of generality we let t = 0 denote the time at which the allele frequency in the host first passes 1/2 (equivalently $\delta_{h,A}$ first passes zero). This allows us to express the general solution to (2.5), after simplifying, as

$$\delta_{h,A}[t] = R^{t-1} (1 - 2\mu_{h,M}) \frac{\alpha_h}{(\alpha_h + 2)} \frac{\sin[\phi t]}{\sin[\phi]} \delta_{p,A}[0]$$
(2.7a)

$$\delta_{p,A}[t] = R^{t-1} \sqrt{R^2 - (1 - 2\mu_{h,M})(1 - 2\mu_{p,M})} \frac{\sin[\phi t + \sigma]}{\sin[\phi]} \delta_{p,A}[0]$$
(2.7b)

where ϕ denotes the speed of evolutionary cycles (the period is $2\pi/\phi$), and σ is the phase difference between the host and parasite cycles:

$$\phi = \cos^{-1} \left[\frac{(1 - \mu_{p,M} - \mu_{h,M})}{R} \right]$$
(2.8a)

$$\sigma = \cos^{-1} \left[\frac{\mu_{p,M} - \mu_{h,M}}{\sqrt{R^2 - (1 - 2\mu_{p,M})(1 - 2\mu_{h,M})}} \right]$$
(2.8b)

The asymmetry between (2.7a) and (2.7b) is a consequence of our starting time when $\delta_{h,A}[0] = 0$.

Recalling that $\alpha_h < 0$ and $\alpha_p > 0$ it can be shown that *R* increases with the strength of selection (magnitude of α_i). Thus, we can see from equation (2.8a) that cycle period decreases as selection becomes stronger in either species. This is illustrated in figure 2.1. Similarly the period decreases as $\mu_{i,M}$ (the mutation rate) increases in either species.

Figure 2.2 shows how the phase difference between host and parasite cycles (σ) depends on the mutation rates in the two species. Our results qualitatively confirm those of Nee (1989). When the mutation rates are equal the two species

cycle 90° out of phase, regardless of the strength of selection in either species (see equation 2.8b). When the hosts have a higher mutation rate the cycles are $> 90^{\circ}$ out of phase, and when the parasites have a higher mutation rate they are $< 90^{\circ}$ out of phase. If all else is equal, the phase difference σ is larger when selection is weak. This is because changes in one species take longer to induce a response in the other species. Interestingly, in this model only small deviations from 90° are possible in the parameter region where cycling occurs (R > 1), as indicated by the small range of the *y*-axis in figure 2.2. Nee (1989) argued that large phase shifts cannot occur, because they require that at some point in each cycle one of the two species evolves away from the currently favoured allele. For the parameters investigated here (e.g., those in figure 2.1) the phase difference from a 90° shift is always less than what would result from a single generation of evolution in the wrong direction. Thus, the phase differences from 90° that occur in this model result from slight overshooting based on allele frequencies from the previous generation.

Having described the dynamics of the selected locus, we turn now to the dynamics of the modifier locus. After selection and sexual reproduction, the change in frequency of the modifier allele is exactly given by

$$\Delta p_{i,M}[t] = p_{i,M}[t+1] - p_{i,M}[t] = \frac{4D_i[t]\alpha_i\delta_{\bar{i},A}[t]}{2 + \alpha_i(1 + 4\delta_{i,A}[t]\delta_{\bar{i},A}[t])}$$
(2.9)

This is analogous to equation (29a) in Gandon and Otto (2007). In appendix A.2, we solve for the disequilibrium in species *i*. We show that when $\delta_{i,A}$ is assumed small (of order ϵ), the effect of the mutation rate modifier is assumed weak (of order ϵ), and the disequilibrium in the previous generation (D_i) has reached order ϵ^2 , the general solution for the disequilibrium is

$$D_{i}[t] = 2(1 - \psi_{i})(\mu_{i,m} - \mu_{i,M})(1 - p_{i,M})p_{i,M}$$
$$\sum_{\tau=1}^{t} X_{i}^{\tau-1} \left(\delta_{i,A}[t - \tau] + \frac{\alpha_{i}}{(\alpha_{i} + 2)}\delta_{\overline{i},A}[t - \tau]\right) \quad (2.10)$$

where $X_i = (1 - \psi_i)(1 - 2\mu_{i,M})$ and the influence of the initial conditions is assumed to have dissipated. Substituting (2.10) into (2.9) yields

$$\Delta p_{i,M} = \frac{8\alpha_i (1 - \psi_i)(\mu_{i,m} - \mu_{i,M})(1 - p_{i,M})p_{i,M}\delta_{\bar{i},A}[t]}{2 + \alpha_i (1 + 4\delta_{i,A}[t]\delta_{\bar{i},A}[t])} \times \sum_{\tau=1}^t X_i^{\tau-1} \left(\delta_{i,A}[t - \tau] + \frac{\alpha_i}{(\alpha_i + 2)}\delta_{\bar{i},A}[t - \tau]\right) \quad (2.11)$$

which is the analog for a mutation modifier of equation (33) for the recombination modifier in Gandon and Otto (2007). Because $X_i < 1$ whenever there is some sex/recombination or mutation, the sum may be evaluated explicitly using equation (2.7). We can then average the change in modifier allele frequency over one co-evolutionary cycle, ignoring transient dynamics due to the initial conditions. We also average over all possible starting points in the host-parasite cycle. Doing so, we find that the modifier allele *M* that increases the mutation rate in species *i* spreads whenever the following is positive

$$\operatorname{sign}[\overline{\Delta p_{i,M}}] \simeq \operatorname{sign}[c_1 X_i (1 - \mu_{\bar{i},M} - \mu_{i,M})/2 - (\mu_{\bar{i},M} - \mu_{i,M})(X_i - (1 - 2\mu_{\bar{i},M}))]$$
(2.12)

where c_1 is the positive constant $-\alpha_h \alpha_p / (2 + \alpha_h + \alpha_p)$. The first term in equation (2.12) is always positive and thus always favours higher mutation rates. It is largest when sex/recombination is rare (small ψ_i and large X_i) and when selection is strong (large c_1). We may re-write equation (2.12) as

sign[
$$\overline{\Delta p_{i,M}}$$
] \simeq sign[$(R^2 - (1 - 2\mu_{i,M})(1 - \mu_{i,M} - \mu_{\bar{i},M}))X_i + R^2(\mu_{\bar{i},M} - \mu_{i,M})$]

(2.13)

in order to facilitate interpretation. Because R > 1 when there are cycles, the first term must be positive. It tends to dominate when linkage is tight (X_i large) and when the mutation rates are similar (second term small). Conditioning upon the existence of cycles (R > 1), equation (2.13) can become negative and favour lower mutation rates only when $\mu_{i,M}$ is sufficiently greater than $\mu_{\tilde{i},M}$. It follows that selection will tend to increase the mutation rate in a species, unless that mutation rate is substantially higher than the mutation rate in the other species. This creates a "ratcheting-up" effect, where an increase in the mutation rate in one species creates selection for a corresponding increase in the other species.

2.3.2 Evolutionarily attracting mutation rate

Assuming mutation rates start small we expect, based on our reasoning above, that they will increase until the second term in equation (2.13) becomes negative. Thus setting equation (2.13) (or equivalently equation 2.12) equal to zero allows us to find the evolutionarily attracting level of mutation (μ_i^*), for a given mutation rate in the other species. Defining the positive constants

$$c_{2,i} = \frac{c_1}{2 - c_1} \left(1 + \frac{1}{2(1 - \psi_i)} \right) + \frac{\psi_i}{2(1 - \psi_i)}$$

allows us to simplify μ_i^* , giving

$$\mu_i^* = \mu_{\bar{i},M} + (1/2 - \mu_{\bar{i},M}) \left(-c_{2,i} + \sqrt{c_{2,i}^2 + 2\left(\frac{c_1}{2 - c_1}\right)} \right)$$
(2.14)

As the terms in parentheses are positive, equation (2.14) shows that the evolutionarily attracting mutation rate is higher than that of the antagonistic species. Figure 2.3 plots the evolutionarily attracting mutation rate in hosts (solid line) as a function of the strength of selection in parasites (left panels) and in hosts (right panels). The shaded region indicates where cycling ceases (R < 1) and thus where selection on mutation modifiers becomes neutral. We expect populations with low initial mutation rates to evolve until they reach μ_i^* , or until mutation rates become large enough that cycles at the selected locus disappear ($R \leq 1$). In figure 2.3, therefore, we would expect population mutation rates starting at or near zero to proceed upwards until they reach the minimum of the black line or the border of the grey region.

2.3.3 Different generation times

A main assumption in our model is that host and parasite generation times are equal. We relaxed this assumption using two methods (described in more detail in appendix A.3). In both cases we varied host generation time, while assuming parasite dynamics to be governed by the same equations as in the main text. We first assumed that all hosts were subject to selection and mutation at each time step, but that only a subset of the individuals reproduced sexually. We then changed the assumption that all individuals were subject to mutation at each time step, and assumed instead that mutations only occurred when individuals reproduced sexually. In both cases we found that, when hosts lived longer, the evolutionarily attracting mutation rate in hosts was higher than it was when generation times were equal. This is because individuals who live longer undergo less recombination per unit time, and thus remain linked to the beneficial mutations they produce for more time steps (see Introduction).

2.3.4 One-species model

To help understand the effects of the speed versus the amplitude of evolutionary cycles we considered a simplified one-species model where selection fluctuated deterministically over time (see appendix A.4). We found that the speed of cycles was important in deciding whether a modifier of mutation rate was selected for or against (see equation A.4), with faster cycles selecting for higher mutation

rates. In contrast to the results of our two-species model, however, a one-species model revealed that the strength of selection at the selected locus only affected the strength of selection at the modifier locus, not the direction of selection. This qualitative difference occurs as a result of the dependence of cycle speed (ϕ) on selection strength (α_h and α_p) in the two-species model, whereas in the one-species model cycle speed is fixed. As in the two-species model we also find that higher recombination rates reduce the evolutionary attracting mutation rate in the one-species model.

2.3.5 Numerical simulations

We ran computer simulations to investigate separately the effects of two additional factors: drift in finite populations, and more than two alleles at the selected locus. We considered a Wright-Fisher model with constant population size. Each generation consisted of selection followed by recombination and then mutation. Host-parasite interactions were governed by the same fitness matrix as was used in the analytical model. Mutation rate was first allowed to evolve in only one species at a time. While it is theoretically clearer this way, it may also be biologically realistic in the case where one of the species is more constrained in its ability to modify mutation rates. All individuals in the evolving population were initialized with mutation rates equal to zero. A single novel mutator allele was introduced at the *M*-locus in a randomly drawn individual whenever fixation at that locus occurred. The mutation rate of the novel mutator was drawn from a Gaussian distribution centered at the current population mean and with a standard deviation of 0.01 (negative mutation rates were set to 0). All simulations were run for 10^7 generations.

For very large populations (10⁹ individuals in each species), where drift is negligible, simulations matched up perfectly with analytical predictions (see solid black points in figure 2.3). In smaller populations (1000 individuals in each species), however, stochastic fluctuations in allele frequency created additional opportunities that favoured the evolution of higher mutation rates (for example, by creating fluctuations when cycles would not be expected based on analytical predictions). Thus, for small populations higher mutation rates evolved (see open circles in figure 2.3)

We also used simulations to investigate the effects of higher numbers of alleles at the selected locus. With k possible alleles at the selected locus, mutation was set so that an allele of type i had a uniform probability of mutating to any of the other k - 1 types. There was a significant reduction in the size of the region in which cycling occurred with more alleles (see figure 2.4), and where cycling did occur, the period was longer. The combination of these two changes led to an overall reduction in the evolutionarily attracting mutation rate. However, the dependence on the strength of selection and recombination exhibited qualitatively similar results to those for the two-allele case. For example, in figure 2.4a high recombination causes a reduction in the evolutionarily attracting mutation rate into the region where cycles persist.

Finally, we investigated co-evolution between hosts and parasites by allowing mutation rates to evolve simultaneously in both species. As before, a single novel mutator allele was introduced into either host or parasite populations when either became monomorphic at the mutation rate locus. We focused on the two-allele case at the locus mediating species interactions. When populations were large, escalation of mutation rates in both species led to the eventual cessation of cycles, at which point evolution stopped (figure 2.5a). As before, however, when populations were small stochastic fluctuations drove mutation rates to higher values than expected, based on our analytical model (figure 2.5b). When the strength of selection differed between the species, mutation rates rose to higher levels in the species with the larger selection coefficient. In essence, the species with more at stake kept ahead in the co-evolutionary arms race (figure 2.5).

2.4 Discussion

We have used analytical and simulation models to investigate the evolution of mutation rate in a co-evolving host-parasite system. In order to maintain consistency with other similar articles we have based our models on the matching-alleles model of host-parasite interactions, where each host allele can be matched by one parasite allele (whether matching causes infection or resistance is immaterial in the haploid two-allele model because we are free to define the alleles such that A_p parasites are able to infect A_h hosts; Otto and Michalakis (1998)). We followed host and parasite populations over multiple generations, where interactions between the two species occurred at random at each time step.

We derived an expression for the evolutionary attracting mutation rate between two alleles, each of whose fitness was dependent on the current genetic composition of the other co-evolving species (see equation 2.14). We found, in accordance with previous literature for directional selection (Kimura, 1967; Leigh, 1970; Sniegowski et al., 1997), that lower mutation rates are expected to evolve with higher levels of recombination (figure 2.3).

In order to account for the higher number of deleterious mutations that often accompany increased mutation rates, several authors have imposed additional fitness costs on individuals with higher mutation rates (Sasaki, 1994; Haraguchi and Sasaki, 1996). In our model individuals with a higher mutation rate suffer a fitness cost at certain points in the cycle through their elevated probability of mutating from the more fit to the less fit allele. However, to maintain consistency with other authors, we also considered a general cost to increased mutation rates (see appendix A.1). We found, not surprisingly, that higher costs reduced the evolutionarily attracting mutation rate.

Because an imbalance in allele frequencies in one species creates selection for an imbalance in the opposite direction in the other species, cyclical fluctuations can occur at the selected locus. When these fluctuations are absent allele frequencies at the selected locus converge to a stable polymorphism, at which point selection at the mutation rate locus disappears. We characterized the parameter space in which cycling does or does not occur (see non-shaded and shaded regions in figures 2.3 and 2.4) and showed that large mutation rates can inhibit cycling (a result previously shown by both Seger 1988 and Nee 1989). We, therefore, expect that evolution will lead populations with initially small mutation rates to our predicted evolutionarily attracting mutation rate (μ_i^* from equation 2.14) or until the point where cycles disappear, should this occur first. This prediction was tested with computer simulations, which confirmed our expectations when population sizes were very large (see solid circles in figure 2.3). However, when population sizes were small, higher than expected mutation rates evolved. Drift in small populations can create stochastic fluctuations in allele frequencies (Seger and Hamilton, 1988). Such fluctuations extend the region where selection on a modifier occurs, accounting for an increased evolutionarily attracting mutation rate.

From figures 2.3 and 2.4, it is apparent that the evolutionarily attracting mutation rate predicted in our model, when interpreted as a "per site" mutation rate is extraordinarily high. When viewed as an antigenic "switching rate", or a "per trait" mutation rate, however, it is not as unrealistic and is consistent with theoretically predicted switching rates for parasites based on *within host* dynamics (Sasaki, 1994). By not including an explicit cost to high mutation rates in the text, we have implicitly assumed that the modifier has a very localized effect on the mutation rate at the locus mediating the host-parasite interaction. While mutation rates can be highly site specific (Frank, 2002), it is likely that mutation rate modification is an intricate process, and therefore probable that modifiers of mutation rate will have pleiotropic deleterious effects. Accounting for this in our model by including additional costs reduced the predicted mutation rate toward which the system evolved (see appendix A.1), as was the case in both Sasaki (1994) and Johnson (1999). It is also possible that very high mutation rates would be evolutionarily favoured at loci that mediate host-parasite interactions, but that such high rates take a long time to evolve (or may not evolve at all because of genetic constraints), so that real populations may not have reached such high levels.

A major assumption in our analytical model is that there are only two possible alleles at the selected locus. Seger (1988) has shown that dynamics can differ qualitatively with multiple alleles. We, therefore, used computer simulations to investigate more than two alleles. We found that the evolutionarily attracting mutation rate decreased, and in accordance with Seger (1988), the region where cycling occurred became smaller with more alleles (see figure 2.4). As in the case for two alleles, mutation rates did not always evolve simply to the point where cycles stopped. This can be seen by comparing points in figure 2.4a and observing that when selection is strong and recombination is high the evolutionarily attracting mutation rate lies in the region where cycling persists. Because hosts and parasites usually have a large number of potential beneficial alleles (Frank, 2002), we would predict, based on the above, that most real populations would exhibit much lower mutation rates than those predicted by a two-allele model.

Factors that led to longer cycles decreased the evolutionarily attracting mutation rate. Cycles were longer when selection was weak in either species (see figure 2.1), when the difference between host and parasite mutation rates was large (see equation (2.8a)), and when there were more alleles (results not shown). Because cycles in one species create a fluctuating selective pressure in the other species, the observed decrease in the evolutionarily attracting mutation rate with each of the above factors is consistent with previous findings that in fluctuating environments the optimal mutation rate is proportional to the inverse of the length of selective episodes (Leigh, 1970, 1973; Ishii et al., 1989).

When cycles persisted in our model, we observed that hosts and parasites were usually very close to 90° out of phase. This is consistent with the results of Nee (1989) who argued that large deviations from 90° cannot be sustained, because they would require one of the two species to regularly evolve in the "wrong" direction. While in our model, the phase shift σ can theoretically range from to 0° to 180°, we found that cycles disappear well before σ becomes too different from 90° and large deviations were, therefore, never observed (see figure 2.2). For large population sizes, cycles also never appeared drastically more or less than 90° out of phase in our simulations. However, in small populations, where cycles were largely driven by genetic drift, large phase shifts were observed (not shown), as was also noted by Gandon and Nuismer (2009) for a spatially structured population.

For a wide range of parameters, cycles were ephemeral, disappearing once mutation rates had evolved to sufficiently high levels (see figure 2.3). Furthermore, the range of parameters where cycles persist became smaller as the number of alleles increased (see figure 2.4). These findings question the legitimacy of the pervasive assumption that loci governing host-parasite interactions exhibit cyclical dynamics. A lack of empirical evidence for recurrent cycles further questions this assumption's legitimacy. To our knowledge, there is only a single empirical study that presents data supporting cyclical dynamics (i.e. changes in allele frequency which eventually return to the same value; several additional studies show change consistent with either cycles or directional selective sweeps). Stahl et al. (1999) used coalescence theory to argue that a 9.8 million year old polymorphism for disease resistance in Arabidopsis thaliana must have been maintained by frequency-dependent selection, and furthermore, showed signs of having historically differed in frequency. While consistent with cycling, their results are also consistent with an alternative explanation; a recent change in the environment could have altered the relative fitness cost of the resistance allele, resulting in a shift in allele frequencies. More long-term empirical data are, therefore, needed to determine whether true cycles occur in host-parasite systems.



FIGURE 2.1: Period of co-evolutionary cycles (in generations) as a function of the strength of selection in parasites. Other parameters were $\mu_{h,M} = \mu_{p,M} = 1 \times 10^{-3}$ per generation.



FIGURE 2.2: Phase difference (in degrees) between host and parasite cycles as a function of the difference in their per generation mutation rates. Other parameters were $\mu_{p,M} = 1 \times 10^{-3}$ and $\alpha_p = (1 + \alpha_h)^{-1} - 1$ (for each curve). Curves are only plotted where R > 1.



FIGURE 2.3: Evolutionarily attracting per generation mutation rate in hosts as a function of the strength of selection in parasites (a, c, e) and in hosts (b, d, f). The rate at which sex and recombination (ψ_i) occurs is given in each panel. Solid black lines denote the predicted mutation rate corresponding to equation (2.14) and shaded regions indicate where cycling does not occur (R < 1). $\alpha_h = -1$ in panels a, c, e, and $\alpha_p = 100$ in panels b, d, f. Filled and open circles correspond to simulations with population sizes of 10^9 and 10^3 (in both hosts and parasites), respectively. μ_p was 0.002 in all panels (results are very similar unless $\mu_p \gg 0$). Evoloved mutation rates in hosts are the mean of 50 replicate runs, each of which was averaged over the last 5×10^6 of 10^7 generations.


FIGURE 2.4: Evolutionarily attracting per generation mutation rate in hosts with multiple alleles at the selected locus. The shaded light grey regions indicate where cycling did not occur in the three (panel a) and ten (panel b) allele model, and the shaded dark grey region indicates where cycling did not occur in the two allele model and is included for reference. Shaded regions were generated using simulations; cycling was considered absent whenever the allele frequency range over the last 500 generations of the simulations fell below 0.005. With two alleles, this region corresponded well to the region where R < 1. For the large population sizes used here (10⁹ hosts and 10⁹ parasites), a clear transition from cycling to no cycling occurs. Recombination rates were set to 0.5 (filled circles) and 0 (open circles), $\alpha_h = -1$, and $\mu_p = 0.002$. Each point is the mean of 10 replicate runs, each of which was averaged over the last 5×10^6 of 10^7 generations.



FIGURE 2.5: Co-evolutionarily trajectories in simulations with differing strengths of selection in hosts and parasites. Each curve represents the mean of 100 replicate runs. Initial mutation rates were either: o in both hosts and parasites, o in hosts and 0.15 in parasites, or 0.15 in hosts and o in parasites. Points represent final values after 10^7 generations. The light shaded regions indicate where cycles are not expected in the analytical model (R < 1) for $\alpha_h = -0.9$, $\alpha_p = 9$ and the dark shaded regions indicate where cycles are not expected for both $\alpha_h = -0.9$, $\alpha_p = 99$ and $\alpha_h = -0.99$, $\alpha_p = 9$. Population sizes in both hosts and parasites were 10^9 in (a) and 10^4 in (b). When the strength of selection was stronger in the parasites we used $\alpha_h = -0.9$ and $\alpha_p = 99$; finally, when selection was stronger in the hosts we used $\alpha_h = -0.99$ and $\alpha_p = 9$. The dotted line has a slope of one and is included for reference. Recombination rates were set to o.

Ploidy and the evolution of parasitism

3.1 Summary

Levels of parasitism are continuously distributed in nature. Models of hostparasite co-evolution, however, typically assume that species can be easily characterized as either parasitic or non-parasitic. Consequently, it is poorly understood which factors influence the evolution of parasitism itself. We investigate how ploidy level and the genetic mechanisms underlying infection influence evolution along the continuum of parasitism levels. In order for parasitism to evolve, the selective benefits to successful invasion of hosts must outweigh the losses when encountering resistant hosts. However, we find that exactly where this threshold occurs depends not only on the strength of selection, but also on the genetic model of interaction, the ploidy level in each species, and the nature of the costs to virulence and resistance. With computer simulations we are able to incorporate more realistic dynamics at the loci underlying species interactions and to extend our analyses in a number of directions, including finite population sizes, multiple alleles, and different generation times.

3.2 Introduction

Understanding the complex ecological and evolutionary interactions between parasites and their hosts has long been a central focus in the biological sciences. This is largely due to the important consequences that advances in this field have had on the development of new strategies for disease and pest management. The continued need for progress has led to high levels of communication between theoreticians and empiricists, which has helped propel research in both fields (e.g., Frank, 2002; Galvani, 2003). Consequently, there are numerous theoretical models covering a wide range of topics, including: the evolution of virulence (e.g., May and Anderson, 1983; Frank, 2002; Galvani, 2003), sex (e.g., Hamilton et al., 1990; Peters and Lively, 2007), recombination and mutation rates (e.g., Gandon and Otto, 2007; M'Gonigle et al., 2009), the evolution of host resistance (e.g., Boots and Bowers, 1999; Miller et al., 2005), and local adaptation (e.g., Gandon, 2002).

One typical assumption of theoretical host-parasite models is their treatment of species as either parasitic or non-parasitic (e.g., Sasaki, 1994; Haraguchi and Sasaki, 1996; Gandon, 2002; Day and Proulx, 2004; Nuismer and Otto, 2004; Gandon and Otto, 2007). In other words, models typically operate under the assumption that a species lives strictly as a parasite. While many species do fit this assumption (e.g., those for whom the very completion of their life-cycle depends on the successful infection of a host, such as the plasmodium species that cause malaria), there are numerous examples of species for whom this assumption is not appropriate. For example, a number of species from a range of taxonomic groups have been shown to be "facultatively parasitic"; e.g., ciliates (Reynolds, 1936; Thompson and Moewus, 1964), flatworms (Hooge and Tyler, 1999), fungi (Morin et al., 1993), nematodes (Benham, 1974). These species are parasitic if the opportunity arises but are otherwise free-living and capable of reproduction without the aid of a host species. Levels of parasitism should thus be seen as distributed along a continuum in which "completely parasitic" and "completely non-parasitic" define the extreme cases. One question that then arises is, how does evolution occur along this continuum, and what are the main factors that determine whether evolution occurs toward higher or lower levels of parasitism?

Empirical work on a number of different host-parasite systems has uncovered a variety of genetic mechanisms employed by hosts and parasites to generate the phenotypic variation needed to defend against and invade one another (Frank, 2002). For example, a single allele in flax (*Linum usitatissimum*) causes resistance to the fungal pathogen *Melampsora lini*, and a single virulent allele in the pathogen allows infection of both non-resistant and resistant strains of flax (a "gene-for-gene" interaction (Flor, 1942, 1955, 1956)). Host-parasite interactions have also been shown to exert strong selection on the underlying genes that modulate species interactions (e.g., favouring changes in expression level (Nuismer and Otto, 2005) or ploidy level (Nuismer and Otto, 2004)). That there are many ways species can interact on a genetic level, and that these interactions have been shown to be under selection, suggests that the nature of the genetic interactions between species also exerts a selective force on the degree of parasitism. Here we ask how ploidy level, an important component of such genetic interactions, influences evolutionary transitions along the continuum from free-living to parasitic life-histories.

Using a combination of analytical models and simulations, we examine evolution at a locus that modifies the amount of time a facultatively parasitic species spends parasitizing its host species. This is done in the context of each of the three models of host-parasite interactions that are thought to describe a large number of host-parasite systems (Nuismer and Otto, 2004).

3.3 Model summary

We consider two interacting species, denoted H and P for hosts and parasites, respectively. The term "parasite" is used loosely here, as the species in question can spend anywhere from o to 100% of its time as a parasite. Species interactions are governed by a single locus (from here on referred to as the A-locus) with two alleles in each species (A_H and a_H in hosts, and A_P and a_P in parasites). We suppose that parasites spend a proportion of their life cycle parasitizing hosts, and the remaining proportion as free-living organisms. A second locus (from here on referred to as the M-locus or the "modifier" locus) determines how a parasitic individual partitions its time between these two strategies; individuals of genotype i spend a proportion f_i of their life cycle as parasites (see table C.1 for a complete list of parameters and their descriptions).

We consider here three models of host-parasite interactions. The matchingalleles model (abbreviated MAM) is based on a system of self/non-self recognition (Hamilton, 1980; Frank, 1994; Peters and Lively, 1999; Grosberg and Hart, 2000), as typically occurs in immune systems that develop via the elimination of self-compatible MHC molecules. In this model hosts are susceptible to parasites carrying only alleles that mimic or "match" their own cell signals and are resistant to parasites possessing any non-matching alleles. The inverse-matchingalleles model (abbreviated IMAM) is essentially the opposite of the MAM; hosts can *defend* against parasites carrying any matching alleles and are susceptible to parasites carrying only non-matching alleles (Frank, 1994). This model describes components of the vertebrate MHC system, where host alleles influence the array of antigen molecules that can be detected. Hosts can only defend against parasites whose antigens they can detect. In the gene-for-gene model (abbreviated GFG), avirulent parasite alleles produce signal molecules that bind to cell surface receptors on resistant host cells, triggering an immune response and thus unsuccessful invasion (Albersheim and Anderson-Prouty, 1975; Gabriel and Rolfe, 1990). Virulent pathogens, however, are able to suppress the production of these elicitors and are, therefore, able to invade both resistant and non-resistant hosts. These systems are typically characterized by dominant resistance alleles and recessive virulence alleles (Frank, 2002); we shall assume these dominance interactions throughout. Gene-for-gene interactions were first discovered and have since been shown to be quite common in plant-pathogen interactions (Gabriel and Rolfe, 1990).

Because we are interested in the effects of ploidy on species interactions, we will consider all combinations of haploid and diploid hosts and parasites. We let $\{x_{H,1}[t], ..., x_{H,k}[t]\}$ and $\{x_{P,1}[t], ..., x_{P,l}[t]\}$ denote the frequencies of the *k* host and *l* parasite genotypes at time *t*. As a free-living organism, each individual has some basal fitness, which we arbitrarily set to 1. Selection coefficients for other life stages are then measured relative to this fitness. Parasitic individuals that successfully infect hosts experience a fitness gain of α_P , while those that encounter resistant hosts experience a fitness loss of β_P . If a parasite attempts to find a host, but fails, and if it can no longer reproduce as a free-living organism, then fitness would be lower in both cases. Infection by a parasite is assumed to lower host fitness by α_H .

We define the indicator variable $\eta_{i,j}$ to equal 1 if parasites of genotype *i* can infect hosts of genotype *j*, and o otherwise. Table 3.2 summarizes the infection patterns for each of the models considered here. The fitness of a genotype *i* parasite at time *t* is then given by

$$w_{P,i}[t] = (1 - f_i) + f_i \sum_{j=1}^k (1 + \alpha_P^{\eta_{i,j}} \cdot (-\beta_P)^{(1 - \eta_{i,j})}) x_{H,j}[t],$$
(3.1)

and the fitness of a genotype *i* host is given by

$$w_{H,i}[t] = 1 - \alpha_H \sum_{j=1}^{l} \eta_{j,i} f_j x_{P,j}[t].$$
(3.2)

The above ignores demographic fluctuations and assumes that each individual engages in at most one host-parasite interaction per time-step.

Costs of resistance and virulence have been demonstrated in some GFG systems (Tian et al., 2003; Thrall and Burdon, 2003). Without such costs, we would expect the resistant host alleles and/or virulent parasite alleles to spread to fixation. We, therefore, assume that both the virulent parasite allele and the resistant host allele are costly. In hosts we assume that the resistant allele (A_H) reduces the fitness of its carriers by an amount c_H . In parasites, we consider two types of costs: a conditional cost ($c_{P,c}$) that only impacts individuals involved in host-parasite interactions (e.g., reduces growth within a host), and an un-

conditional cost $(c_{P,u})$ that impacts all virulent individuals (e.g., reduces growth within and outside of hosts). The effects of these costs act additively, so that the fitness of a virulent individual of genotype *i* is reduced by $(f_i c_{P,c} + c_{P,u})$. The frequency of genotype *i* in species *j* (*j* = *H* or *j* = *P*) after selection may then be computed as

$$x'_{j,i} = \frac{x_{j,i}[t]w_{j,i}[t]}{\bar{w}_j[t]},$$
(3.3)

where $\bar{w}_j[t] = \sum_i x_{j,i}[t] w_{j,i}[t]$ is the mean fitness of species *j* (the sum is taken over all genotypes).

While we largely focus on the effects of ploidy and the model of genetic interaction, it is worth mentioning that the above model also captures possible ecological changes in the opportunity for parasitism; if the environment clearly favours one life-history strategy over another (as may occur, for example, when a new host species becomes available), then parasitism would be expected to evolve, regardless of the genetic architecture underlying species interactions. This possibility would be captured by high values of α_P (large advantages of successful invasion) and potentially low values of β_P (weak host defenses against the parasite). In cases where the environmental forces favouring parasitism are not absolute, however, our analysis will help predict how the underlying genetics shapes the course of evolution.

We let ψ_H and ψ_P denote the proportion of hosts and parasites, respectively, that undergo sexual reproduction at each time step, and we assume that the remaining individuals consist of surviving parents or asexual offspring. We let $x''_{H,i}$ and $x''_{P,i}$ denote the frequency of genotype *i* individuals in hosts and parasites, respectively, formed through random mating within the parental generation after selection. In both hosts and parasites all sexual individuals contribute their gametes to a general gamete pool, out of which offspring are selected at random. Recombination between the modifier and the *A*-locus occurs during meiosis in parasites at rate *r*. After reproduction, genotype frequencies in species *j* are then given by

$$x_{j,i}[t+1] = (1-\psi_j)x'_{j,i} + \psi_j x''_{j,i} .$$
(3.4)

3.4 Analytical results

We make the assumption that selection is weak (α_H , α_P , and β_P are all on the same order as some small term ϵ), and that most individuals are sexual in both species (ψ_H and ψ_P are on the order of 1- ϵ ; this assumption is relaxed in the Appendix). We also assume that the modifier has a small effect (i.e. we set

 $f_M = f_m + \Delta_M$ or $f_{Mm} = f_{mm} + \Delta_{Mm}$ and $f_{MM} = f_{mm} + \Delta_{MM}$ and then assume that the Δ 's are also of order ϵ). Performing a change of variables allows us to describe the system in terms of the departure from a frequency of 0.5 at the A locus in each species ($\delta_H[t]$ in hosts and $\delta_P[t]$ in parasites), the frequency of the modifier in parasites ($p_M[t]$), and several higher order association measures, such as the departure from Hardy-Weinberg equilibrium and linkage disequilibrium (as defined in Barton and Turelli, 1991).

A quasi-linkage equilibrium analysis (Barton and Turelli, 1991) showed that all genetic associations are of order ϵ^2 or higher, and that changes in allele frequency at the *M*-locus are governed largely by terms of order ϵ , which describe differences in fitnesses of the different genotypes. Specifically, a modifier *M* of parasitism level will spread only if the difference between the marginal fitnesses of alleles *M* and *m*, which we denote by $\bar{w}_{\text{diff}} = \bar{w}_M - \bar{w}_m$, is positive. The expressions for \bar{w}_{diff} for an allele that increases parasitism for the four combinations of host/parasite ploidy levels are given in table 3.3.

As is typical in models of host-parasite co-evolution, dynamics at the *A*-locus are characterized by cyclical fluctuations (figure 3.1). In the matchingalleles and the inverse-matching-alleles models, these cycles are symmetric about an allele frequency of 0.5 (equivalently, about $\delta_H = 0$ and $\delta_P = 0$). By assuming (for these cases) that these cycles are small (e.g., that both δ_H and δ_P are also on the order of the small term ϵ), we are able to find simple conditions under which selection favours increased levels of parasitism (table 3.4).

It is clear from the expressions in table 3.4 that the fitness effects of matching versus not matching the genotype of the host, α_P/β_P , must be sufficiently beneficial for parasites to adopt a less free-living life-cycle in both MAM and IMAM. However, where this threshold occurs depends on both the model of genetic interactions and the ploidy level of each species (figure 3.2). In general, the matching-alleles model tends to favour parasitism more strongly than the inverse-matching-alleles model (compare figure 3.2A to figure 3.2B), mainly because it is easier for a parasite to mimic hosts that are heterozygous diploid (MAM) than to evade detection by them (IMAM). In both MAM and IMAM, the transition to parasitism occurs over a broader range of parameters when the parasite is haploid, because such parasites express only one antigen allele (compare solid to dashed lines in figure 3.2). The role of host ploidy is more complicated, however. Diploidy allows for the appearance of heterozygous hosts that are infected by any type of parasite in MAM, but resistant to every type of parasite in IMAM. Thus host diploidy favours (disfavors) the evolution of parasitism in MAM (IMAM) (compare thick to thin lines in figure 3.2).

Because cycles in the gene-for-gene model are not typically centered around

o.5 we take a slightly different approach in this case. We first solve for the equilibrium δ_H and δ_P , and then substitute these into the expressions for \bar{w}_{diff} . Assuming weak selection, we are again able to simplify the expressions for \bar{w}_{diff} . For all ploidy combinations, we find

$$\bar{w}_{\text{diff}} = \frac{(\alpha_P - c_{P,c})f^2 \alpha_H - c_H c_{P,u}}{f^2 \alpha_H},\tag{3.5}$$

where f denotes the resident parasitism level ($f = f_m$ for haploid parasites and f_{mm} for diploid parasites). Unlike for MAM and IMAM models, there are no major effects of ploidy on the evolution of parasitism in the GFG. While qualitative dynamics at the *A*-locus differ between cases, parasitism is favoured for the same combinations of selection and cost parameters across all ploidy levels. This contrasting result for GFG is a consequence of our empirically motivated assumption of complete dominance. With both the resistant allele in hosts and the virulent allele in parasites completely dominant, the two species are essentially composed of only two types, and thus effectively interact as haploids.

In contrast to ploidy, the nature of costs of virulence are critically important to the evolution of parasitism in the GFG (figure 3.3). Consider setting $c_{P,u}$ equal to zero. With just conditional costs ($c_{P,c}$), we find,

$$\bar{w}_{\rm diff} = \alpha_P - c_{P,c} , \qquad (3.6)$$

and thus parasitism should evolve whenever the benefits to successful invasion, α_P , are greater than the conditional cost of the virulent allele $c_{P,c}$. In contrast, when $c_{P,c}$ equals zero,

$$\bar{w}_{\rm diff} = \left(\alpha_P - c_{P,u} \frac{c_H}{f^2 \alpha_H}\right). \tag{3.7}$$

Here the cost term is weighted by $1/f^2$. With lower resident parasitism levels (smaller *f* values), a larger selective benefit to parasitism (α_P) is required in order for selection to favour further increases in parasitism. This makes it exceedingly difficult for parasitism to evolve from initially low levels when costs are unconditional. Intuitively, because the unconditional cost is paid by all virulent individuals, it is unlikely that any fitness gains acquired through parasitism will sufficiently compensate for the costs of virulence when the chance of infecting a host is low.

3.5 Simulation model summary

We ran computer simulations to investigate the robustness of our model to violations of its assumptions, such as small cycles (figures B.1, B.2), weak selection (figure B.3), infinite population sizes (figure B.4), and high rates of sexual reproduction (figure B.5). We also investigated the effect of differences in generation times (figure B.6) and of multiple alleles (figure B.7) on the evolution of parasitism. In each case we employed a Wright-Fisher model with constant and finite population size. Each time step consisted of selection followed by sex and recombination (with r=0.5). Because population sizes were finite, mutation between alleles at the *A*-locus was necessary to ensure that allelic variation at this locus was not permanently lost. Mutation between alternative alleles at the *A*-locus occurred in both species at rate μ per generation.

In order to investigate the evolution of parasitism we initialized populations with low levels of parasitism (f = 0.1), and tracked evolution at the modifier locus. We also ran simulations initialized with high levels of parasitism (f = 0.9), but because the final level of parasitism attained was typically similar, these results are not presented. Where this change did affect the final outcome, we provide a more detailed discussion. All individuals were initially identical at the modifier locus, and whenever fixation occurred, a novel modifier allele was introduced at low frequency (we used 0.01), and in linkage equilibrium with the A-locus. The parasitism level (f) corresponding to the novel modifier was drawn from a Gaussian distribution centered on the current level of parasitism with a standard deviation of 0.1 (parasitism levels were re-drawn if they fell outside the range [0,1]). While introducing a mutant allele into the population at linkage equilibrium is not biologically realistic, it eliminates unwanted artifacts that may result from biased initial associations between the modifier and the A-locus. It is also worth mentioning that the initial frequency of the new modifier and the standard deviation used to draw new mutants did not qualitatively affect results, but they did affect the speed of the simulations.

We examined a number of extensions to our model (see Appendix). Most extensions had little effect on our results. Here we focus on only the simplest and most informative extensions. Unless specified otherwise, simulations were run for 10^6 generations and initial frequencies at the *A*-locus in each species were drawn independently from a uniform distribution.

3.5.1 MAM/IMAM simulation results

Small cycles

We begin by examining the simpler case when cycles at the *A*-locus are small in amplitude. To constrain cycle size in the simulations we increased the mutation rate, which pushes allele frequencies toward intermediate values and thus dampens cycles (exposure to multiple parasites per time step has also been shown to dampen cycles (Lively, 2010)). With intermediate to high mutation rates, cycles were characterized by smooth sinusoidal curves (figure 3.1C, 3.1D; note that for very high mutation rates cycles were absent altogether, as in figure 3.1A, 3.1B). When cycles were absent or small, increased levels of parasitism evolved as predicted in table 3.4 (columns 1 and 2 in figure B.1).

Large cycles

Large amplitude cycles are observed with lower mutation rates (figure 3.1E, 3.1F). Mutation to other serotypes in *Borrelia hermsii* has been estimated to occur at a rate somewhere between 10^{-3} and 10^{-4} per generation (Stoenner et al., 1982), and new variant surface glycoproteins arise in trypanosomes at a rate somewhere between 10^{-2} and 10^{-6} , per cell doubling time (Turner and Barry, 1989). We thus set $\mu = 10^{-5}$ to investigate realistic mutation rates. With large amplitude cycles a few cases did not match the small-cycle analytical approximations in table 3.4 (figure 3.4), although the large-cycle conditions in table 3.3 continued to hold, given the observed dynamics for δ_H and δ_P (results available upon request). We will describe these cases in turn.

When parasites were diploid and hosts were haploid, large cycles led to a reduction in the size of the region where parasitism evolved (figure 3.4C and 3.4D). Because in MAM and IMAM heterozygous parasites could not invade either haploid host, parasites responded slowly to changes in allele frequency in the hosts. Consequently, the proportion of time parasites spent "losing" the host-parasite arms race grew as cycle size increased (left column in figure 3.1), and thus the region where parasitism was favoured shrunk.

When parasites were haploid and hosts were diploid, the opposite scenario occurred. Here it was the diploid hosts that were slow to respond to allele frequency changes in the haploid parasites. Furthermore, because heterozygous hosts in IMAM are more resistant than homozygous hosts, cycles tended to dampen (remaining near $\delta_i = 0$), whereas a slow coevolutionary response in hosts was observed in MAM (right column, figure 3.1). The region where parasitism was favoured thus grew slightly with MAM (figure 3.4E).

When both species were diploid, general conclusions could not be drawn about which species would lag behind in the arms race. Unlike the previous comparisons, whether the region where parasitism was favoured slightly grew or shrunk depended more sensitively on the strength of selection in hosts (α_H , see figures B.2 and B.3).

3.5.2 GFG simulation results

Because high mutation rates drive allele frequencies to 1/2, which is not generally the equilibrium in the gene-for-gene model, we only consider low mutation rates and thus large cycles in this case. With conditional costs our simulations exactly matched our predictions, and parasitism evolved whenever the fitness benefit of successfully invading a host, α_P , was greater than the cost of the virulent allele, c_{P,c} (figures 3.3A, B.8). As predicted for unconditional costs, the initial level of parasitism present in the population strongly affected which parameter combinations favoured further evolution of parasitism (figures 3.3B, B.9). In large populations ($N = 10^6$ individuals) and initially low levels of parasitism (f = 0.1), increased parasitism never evolved, as expected. With high initial levels of parasitism, however, evolution of a more parasitic life history was possible. In other words, the system exhibited bistability. Interestingly, in regions where the evolution of a free-living life cycle was expected, the GFG system would often converge to an M/m polymorphism fixed for allele *a*. That is, the initial mA/ma polymorphism involving a costly virulent allele and a sensitive allele was replaced with an Ma/ma polymorphism involving sensitive alleles with higher and lower levels of parasitism (explaining why the regions in figures B.8 and B.9 were grey rather than white). With unconditional costs the effect of initial conditions described above disappeared altogether in small populations (figure B.10). Stochastic fluctuations in allele frequency at the interaction locus, combined with drift at the modifier locus, allowed occasional excursions into the parameter space in which further evolution of parasitism became advantageous.

3.6 Discussion

We have used analytical and simulation methods to investigate the evolution of parasitism in a pair of co-evolving species. Our results provide an initial characterization of how genetic architecture affects selection on life-history in antagonistic species interactions.

By and large, the evolution of parasitism depends on the mean fitness of

allelic variants at a locus governing how much time a species spends as a parasite and is not strongly influenced by genetic associations. By comparing mean fitness of these allelic variants we were able to characterize the conditions under which high levels of parasitism were expected to evolve. While the fitness effects of matching or not matching the genotype of the host had to be sufficiently beneficial in order for parasites to adopt a more parasitic life-cycle, the exact threshold depended on both the model of genetic interactions and, in most situations, the ploidy level of each species. In situations where hosts are only able to defend against parasites for which they have the correct allele, as with IMAM, hosts that carry a larger suite of alleles (diploids) or parasites that carry few alleles (haploids) tend to thrive. Thus lower ploidy levels in either species tend to increase the benefits to parasitism. In contrast, in situations where parasites must match host genotypes in order to invade (e.g., MAM), diploid hosts can be infected by a greater number of parasite types, and thus diploidy in hosts tends to favour parasitism, while haploidy in parasites is again most conducive to further evolution of parasitism. With GFG interactions ploidy had little impact on the evolution of parasitism because of the complete dominance assumed.

The above predictions were derived under a number of assumptions, the most significant being intermediate allele frequencies at the locus governing host-parasite interactions (i.e., small cycles). Using simulations we were able to investigate our model's behaviour when no such constraints were imposed on allele frequencies. The predictions based on small cycles were altered slightly under some conditions (panels C-E, G, H in figure 3.4), although the main qualitative results continued to hold under all conditions. The differences from our predictions occurred mostly when host and parasite fluctuations were not 90° out of phase with one another (figure 3.1). Typically this occurred when heterozygotes of one species had low fitness (e.g., hosts in MAM and parasites in IMAM). These low fitness heterozygotes reduced the efficacy of selection in this species, as beneficial alleles, when rare, were found almost exclusively in the heterozygous form. As a result this species responded slowly to changes in allele frequency in the other species. This meant that more time was spent in a population configuration that favoured the faster responding species, and thus the region of parameter space where parasitism evolved was shifted in favour of that species. Violations of our other main assumptions (infinite population sizes, weak selection, and primarily sexual populations) were also tested using simulations and shown to have only minor effects (see Appendix).

In nature, parasites typically have much shorter generation times than their hosts, and furthermore, many host-parasite interactions are governed by more than two alleles (e.g., trypanosomes are known to possess hundreds of allelic antigen variants (Van Der Ploeg et al., 1982)). Using simulations we investigated how these extensions changed our general conclusions. While neither led to any qualitative changes across ploidy combinations, more alleles at the interaction locus had significant and opposite effects in the matching-alleles and inversematching-alleles models. Because higher genetic diversity among hosts with more alleles makes them resistant to a larger number of parasites in MAM, more alleles were less conducive to the evolution of parasitism. Similarly, with MAM, high diversity in parasites tends to help hosts recognize their parasites as genetically distinct. The opposite held true in the IMAM, where greater genetic diversity in hosts allows parasites to invade a greater proportion of host genotypes and greater genetic diversity in parasites allows them to remain undetected by more host genotypes. Thus, the more alleles segregating at the genes mediating host-parasite interactions, the more conducive IMAM systems are to the evolution of parasitism.

Another factor found to have a large influence on the evolution of parasitism was the nature of the costs to virulence in the GFG models. Interestingly, conditional costs were much more conducive to the evolution of parasitism. When parasitism is rare, unconditional costs of virulence typically outweigh the benefits of being parasitic and result in the spread of sensitive parasites and resistant hosts, which prevents the evolution of further parasitism. Had unconditional costs been weak enough to allow parasitism to increase when low, then they would have been too weak to prevent the fixation of virulent alleles once parasitism levels were high. In the absence of factors such as strong genetic drift, which may stochastically shift parasitism levels upward, a predominantly free-living life history is thus expected with substantial unconditional costs of virulence.

Previous theoretical work has shown that transitions between haploidy and diploidy are expected as a consequence of host-parasite interactions (Nuismer and Otto, 2004). In particular, haploidy is most favoured in parasites because of the advantage of reducing antigenic expression to a single allele, while diploidy is more often favoured in hosts because of the advantage (in many cases) of heterozygous hosts being able to recognize multiple parasites. In accordance with the above theoretical predictions, a survey of empirical data revealed an association between ploidy and life history (Nuismer and Otto, 2004); parasitic protists are three to four times as likely as non-parasitic protists to be haploid. This pattern would, however, be consistent with either parasites evolving more haploid life-cycles (Nuismer and Otto, 2004), or haploids evolving more parasitic life cycles (herein). Indeed, if transitions in parasitism occur more frequently

than transitions in ploidy, transitions in parasitism may be more important in explaining the association between parasitism and haploidy.

Some groups of species today are almost wholly parasitic (e.g., Apicomplexa), while others contain a mixture of both free-living and parasitic individuals (e.g., dinoflagellates) (Als et al., 2004; Moran and Wernegreen, 2000), and many are wholly non-parasitic. In groups such as dinoflagellates, the ability to photosynthesize and thus produce ones own food may make the switch between parasitic and free-living life-styles relatively easy, whereas in other groups it appears that the ability to regain a free-living lifestyle has been altogether lost (e.g., no *Borrelia* sp. proliferating in an environment outside of a vertebrate or invertebrate host has been observed (Barbour and Hayes, 1986)). A comparative phylogenetic analysis of closely related groups of species, which differ in their proportions of parasitic species, would provide additional insight into exactly what sorts of traits facilitate acquisition or loss of parasitism, and furthermore, just how common such transitions have been.

There are a number of worthwhile extensions to our model. Ample empirical evidence suggests that many, if not most, host-parasite interactions are governed by more than a single locus (May and Anderson, 1983). For example, the brown planthopper (Nilaparvata lugens), a pest on rice in South East Asia, was originally assumed to be engaged in a GFG interaction, but it has since been shown to contain several biotypes, each determined by different coadapted gene complexes (Thompson and Burdon, 1992). Extending our model to include multiple interaction genes would allow us to consider the buildup of the co-adapted gene complexes that facilitate life-history transitions. Furthermore, the model presented here assumes that some level of parasitism is already present or that at least the genetic architecture is already in place for proper parasitic invasion of hosts. *De novo* evolution of parasitism realistically requires more than a single mutational event, perhaps mediated by intermediate stages involving mutualistic or trophic interactions. More detailed models on these early stages could provide insight into how parasitic life styles have evolved out of non-parasitic ones.

Chapter 3

Parameter	Description			
f_i	proportion of time spent as a parasite by genotype i			
$x_{i,j}$	frequency of genotype j in species of type i ($i = H$ or P)			
α_P	fitness gained by a parasite that successfully infects a host			
β_P	fitness lost by a parasite that attempts but fails to infect a resistant host			
α_H	fitness lost by hosts when they are infected			
$\eta_{i,j}$	indicator variable defined to equal 1 if parasites of genotype i can			
	infect hosts of genotype <i>j</i> , and o otherwise			
$w_{i,j}$	fitness of genotype j in species of type i			
c_H	cost of the resistant allele in hosts (GFG only)			
$C_{P,C}$	conditional cost of the virulent allele in parasites (GFG only)			
$C_{P,u}$	unconditional cost of the virulent allele in parasites (GFG only)			
ψ_i	proportion of species of type <i>i</i> that reproduce sexually			
r	recombination rate in parasites			
Δ_M	effect size of the modifier (haploid parasites)			
Δ_{Mm}	effect size of the modifier when present in heterozygotes (diploid parasites)			
Δ_{MM}	effect size of the modifier when present in homozygotes (diploid parasites)			
δ_i	deviation from a frequency of 0.5 at the A -locus in species i			
p_M	frequency of the modifier in parasites			
\bar{w}_M, \bar{w}_m	marginal fitnesses of alleles M and m			
$\bar{w}_{ m diff}$	difference between marginal fitnesses (i.e., $\bar{w}_M - \bar{w}_m$)			
μ	mutation rate at the A-locus in both species (simulations only)			

 TABLE 3.1: Description of parameters.

TABLE 3.2: Invasion matrices. Each entry represents the outcome of interactions in the three models in the following order {matching-alleles, inverse-matching-alleles, gene-for-gene}. I is used to denote infection ($\eta_{i,j} = 1$ in equations (3.1) and (3.2)) and R resistance ($\eta_{i,j} = 0$). Both haploid and diploid hosts and parasites are included in the table.

			Host	
		A_H or $A_H A_H$	Анан	ан or анан
			()	
Parasite	A_P or $A_P A_P$	{I,R,I}	{I,R,I}	{ R , I , I }
	$A_P a_P$	$\{R,R,R\}$	$\{I,R,R\}$	$\{R,R,I\}$
	a_P or $a_P a_P$	{R,I,R}	$\{I,R,R\}$	$\{I,R,I\}$

Model	Host ploidv	Parasite ploidy	$ar{w}_{ m diff}$
	1	1	$\frac{(\alpha_{\rm P} - \beta_{\rm P})/2 + (\alpha_{\rm P} + \beta_{\rm P})(2\delta_{\rm H}\delta_{\rm P})}{(2\delta_{\rm H}\delta_{\rm P})}$
MAM	1	2	$\frac{(\alpha_F - \beta_F)}{(\alpha_P - 3\beta_P)/4 + (\alpha_P + \beta_P)(2\delta_H\delta_P + \delta_P^2)}$
	2	1	$(3\alpha_P - \beta_P)/4 + (\alpha_P + \beta_P)(2\delta_H\delta_P - \delta_H^2)$
	2	2	$(5\alpha_P - 3\beta_P)/8 + (\alpha_P + \beta_P)(4\delta_H\delta_P(1 + \delta_H\delta_P) - 3\delta_H^2 + \delta_P^2)/2$
IMAM	1	1	$(\alpha_P - \beta_P)/2 - (\alpha_P + \beta_P)(2\delta_H\delta_P)$
	1	2	$(lpha_P-3eta_P)/4-(lpha_P+eta_P)(2\delta_H\delta_P-\delta_P^2)$
	2	1	$(lpha_P - 3eta_P)/4 - (lpha_P + eta_P)(2\delta_H\delta_P - \delta_H^2)$
	2	2	$(lpha_P-7eta_P)/8-(lpha_P+eta_P)(4\delta_H\delta_P(1-\delta_H\delta_P)-\delta_H^2-\delta_P^2)/2$
GFG	1	1	$(3\alpha_P - \beta_P)/4 + (\alpha_P + \beta_P)(\delta_P - \delta_H(1 - 2\delta_P))/2 - c_{P,c}(1 + 2\delta_P)/2$
	1	2	$(7lpha_P-eta_P)/8+(lpha_P+eta_P)(2(1+2\delta_H)(1-\delta_P)\delta_P-\delta_H)/4-$
			$c_{P,c}(3/4+(1-\delta_P)\delta_P)$
	2	1	$(5\alpha_P - 3\beta_P)/8 + (\alpha_P + \beta_P)(3\delta_P + 2(1 - 2\delta_P)(\delta_H^2 - \delta_H))/4 - c_{P,c}(1 + 2\delta_P)/2$
	2	2	$(13\alpha_P - 3\beta_P)/16 + (\alpha_P + \beta_P)(\delta_H^2(1 - 2\delta_P)^2 - \delta_H(1 - 2\delta_P)^2 + 3(1 - \delta_P)\delta_P)/4 - \delta_H(1 - 2\delta_P)^2 + 3(1 - \delta_P)\delta_P/4 - \delta_H(1 - 2\delta_P)^2 + \delta_H(1 - 2\delta_$
			$c_{P,c}(3/4 + (1-\delta_P)\delta_P)$

TABLE 3.3: The fitness advantage of the modifier allele, $\bar{w}_{diff} = \bar{w}_M - \bar{w}_m$, when genetic associations are weak. We have dropped a factor Δ_M from the haploid parasite cases and $(p_M(\Delta_{MM} - \Delta_{Mm}) + (1 - p_M)\Delta_{Mm})$ from the diploid parasite cases; these terms can be interpreted as the average effect size of the modifier.

TABLE 3.4: Invasion condition for a modifier that increases the level of parasitism in MAM and IMAM, assuming small cycles around allele frequencies of 1/2 (or $\delta_H = \delta_P = 0$).

Model	Host ploidy	Parasite ploidy	Invasion condition
	1	1	$\alpha_P > \beta_P$
лала	1	2	$\alpha_P > 3\beta_P$
MAN	2	1	$\alpha_P > \beta_P/3$
	2	2	$\alpha_P > 3\beta_P/5$
	1	1	$\alpha_P > \beta_P$
τλαλα	1	2	$\alpha_P > 3\beta_P$
110174101	2	1	$\alpha_P > 3\beta_P$
	2	2	$\alpha_P > 7\beta_P$



FIGURE 3.1: Sample trajectories from simulations (after a burn-in period) in the matching-alleles model with complete parasitism (f = 1). Column labels indicate ploidy levels and row labels mutation rates. The background is coloured grey to indicate when the parasite is "losing" the arms race with the host, and white when it is "winning". Other parameters were $\alpha_P = 0.05$, $\beta_P = 0.05$, $\alpha_H = 0.05$, $\psi_H = \psi_P = 1$, r = 0.5, and population sizes were 10^6 in both species.



FIGURE 3.2: Invasion conditions in the matching-alleles (A) and inversematching-alleles model (B). Solid (dashed) lines correspond to haploid (diploid) parasites, and thick (thin) lines to haploid (diploid) hosts. For a given case, parasitism is expected to evolve when selection is such that the point (α_P , β_P) lies below the corresponding line. The slopes of these lines can be inferred from the invasion conditions in table 3.4. Note that there are two lines with the same slope in panel (B).



FIGURE 3.3: Invasion conditions in the gene-for-gene model with conditional (A) and unconditional costs (B). For a given case, parasitism is expected to evolve for all ploidy combinations when α_P lies to the right of the plotted line. The three curves for each unconditional cost in panel (B), from left to right, correspond to different initial parasitism levels of f = 0.9, 0.7, and 0.5. $\alpha_H = 0.05$ and $c_H = 0.01$.



FIGURE 3.4: Evolutionary convergent level of parasitism (f) as a function of the strength of selection in parasites under the matching-alleles model (column 1) and the inverse-matching-alleles model (column 2). The mutation rate was ($\mu = 10^{-5}$), and thus large cycles occurred in all cases except in panel F. Dashed lines denote the analytical invasion condition assuming small cycles (table 3.4). Cells are shaded based on the mean level of parasitism present in the population after 10^6 generations of evolution in a single simulation (darker = higher, see grayscale in panel H). Initial frequencies at the *A*-locus were randomly drawn for each cell. Different ploidy combinations are indicated on the right hand side. Other parameters were as in figure 3.1.

Sexual selection enables long-term coexistence despite ecological equivalence

4.1 Summary

Empirical data indicate that sexual preferences are critical for maintaining species boundaries (Eberhard, 1985; Seehausen and Van Alphen, 1999; Gray and Cade, 2000; Wilson et al., 2000; Irwin et al., 2001; Huber, 2003), yet theoretical work has suggested they can play only a minimal role in maintaining biodiversity on their own (Turner and Burrows, 1995; Panhuis et al., 2001; Van Doorn et al., 2004; Johansson and Ripa, 2006; Weissing et al., 2011). This is because long-term coexistence within overlapping ranges is thought to be unlikely in the absence of ecological differentiation Weissing et al. (2011). Here we challenge this widely held view by generalizing a standard model of sexual selection to include two ubiquitous features of populations with sexual selection: spatial variation in local carrying capacity and mate-search costs in females. We show that, when these two features are combined, sexual preferences can single-handedly maintain coexistence. Remarkably, coexistence can occur for spatial variation in local carrying capacity that is so slight that it might go unnoticed empirically. This is the first study to demonstrate that sexual selection alone can promote the long-term coexistence of ecologically equivalent species with overlapping ranges, thus providing a novel explanation for the maintenance of biodiversity.

CHAPTER 4

4.2 Introduction

A central objective of evolutionary ecology is to understand the mechanisms that allow species to coexist. One such mechanism is ecological differentiation. By occupying different niches, species in overlapping ranges are able to reduce direct competition among one another (Schluter, 2000). While there are numerous examples of closely related species occupying different ecological niches, many recently diverged and coexisting taxa are known to differ most dramatically in their secondary sexual characters, exhibiting few, if any, ecological differences (Eberhard, 1985; Seehausen and Van Alphen, 1999; Gray and Cade, 2000; Wilson et al., 2000; Irwin et al., 2001; Huber, 2003). It seems, therefore, that sexual selection is an important mechanism for maintaining coexistence. Indeed, models of sexual selection have shown that populations of choosy females and their preferred males can arise and, under various conditions, form reproductively isolated mating groups (Fisher, 1930; Lande, 1981, 1982; Kirkpatrick, 1982; Seger, 1985). However, because sexual selection does not lead to ecological differentiation, species differing only in their mating preferences compete for the same ecological niche. This has traditionally led to the conclusion that, if their ranges overlap, one of these species will eventually displace the other (Turner and Burrows, 1995; Panhuis et al., 2001; Van Doorn et al., 2004; Johansson and Ripa, 2006; Weissing et al., 2011).

Coexistence can become less difficult when species are able to reduce their range overlap. Sexual selection provides a natural mechanism whereby they may accomplish this. Any process that creates spatial variation in female preferences indirectly also creates selection on male display traits, locally favouring those males that are most preferred by the local females. As a consequence, spatially segregated mating domains, characterized by the co-occurrence of matching display and preference traits, can emerge from populations with an initially random spatial distribution. Once segregated, interactions between different mating types are limited to individuals at the peripheries of these domains. In finite populations, however, the mating domains may shrink or grow, and the interface between them may drift randomly in space. Such fluctuations eventually lead to one mating domain replacing all others (Fig. 4.1A, C). In a pioneering study, Payne and Krakauer (Payne and Krakauer, 1997) argued that lower dispersal in males with better mating prospects facilitates spatial segregation and maintains coexistence. In finite populations, however, such mating-dependent dispersal fails to stabilize coexistence (Fig. C.3). Given these difficulties associated with sexual selection, a recent review concluded that sexually divergent, but ecologically equivalent, species cannot coexist for significant lengths of time

(Weissing et al., 2011).

4.3 Model summary

Here we report model results that suggest the contrary and demonstrate that sexual selection can promote long-term coexistence, even without any ecological differentiation. Building on a standard model of sexual selection (Kirkpatrick, 1982), we develop an individual-based model, which naturally allows us to consider finite populations and to examine the long-term fate of species differing only in their secondary sexual characters in an ecologically neutral context. We assume a simple genetic structure with individuals characterized by two unlinked haploid loci: the first locus (with alleles Q and q) governs a display trait that is expressed only in males, while the second (with alleles P and p) governs a preference trait that is expressed only in females (we later generalize this to more than two alleles and quantitative mating traits; see Supplementary Information (SI) and Fig. 4.4D–E). Because we are interested in coexistence, and not speciation, we assume that the genetic variation at both loci is already present, for example, due to recent migration from allopatric ranges. All else being equal, females bearing a P(p) allele prefer (Kirkpatrick, 1982; Seger, 1985; Payne and Krakauer, 1997) to mate with males carrying a Q(q) allele by a factor α , and a female's preference for a given male attenuates with increasing distance between them. Likewise, competition decreases as the distance between individuals increases. Competition is assumed to reduce an individual's probability of surviving until it reaches reproductive maturity. Importantly, hybrids suffer no intrinsic fitness costs, other than potentially carrying mismatched preference and trait alleles. Further model details are provided in the SI.

Mating domains can be lost either through movement of the interface between them (as described above), or when individuals of one mating type colonize the domain of another mating type. In particular, because selection at the preference locus disappears when there is no variation at the display locus, foreign preference alleles may drift into regions with low variation in male display alleles, eventually leading one mating type to displace the other. Loss of mating domains can, however, be prevented by the inclusion of two features ubiquitous in populations experiencing sexual selection: spatial variation in local carrying capacity and mate-search costs in females. Spatial variation in carrying capacity is present in most, if not all, biological systems (see Figs. 4.1 and 4.4 and the SI for model details). Mate-search costs occur if a female spends time and energy looking for a suitable mate and rejecting non-preferred males, thereby reducing her ability to invest in offspring. To account for such costs we assume that the fecundity of a particular female increases from 0 to a maximum level with the local density of available males, weighted according to her preference (SI).

4.4 Results and discussion

Our model confirms the longstanding view that sexual selection in homogeneous spatial models, without mate-search costs, does not facilitate coexistence and can, in fact, hasten the demise of species (compare Fig. 4.2A to 4.2B). Spatial variation in local carrying capacity, on its own, also has little, if any, effect in stabilizing populations (compare Fig. 4.2B to 4.2C). Sexual selection with matesearch costs slightly prolongs coexistence in a spatially homogeneous environment by helping to prevent mixing of the mating domains, but this effect is weak (Fig. 4.2D). However, in an environment with spatial variation in local carrying capacity, sexual selection with mate-search costs dramatically increases coexistence times (compare Fig. 4.2E to Fig. 4.2B and also Fig. 4.1A, C to Fig. 4.1B, D). In this case, mate-search costs curb the neutral drift of preference alleles, thus preventing the dilution of mating domains, while areas of high local carrying capacity provide spatial "anchors", stabilizing the mating domains at a relatively constant size and location (Fig. 4.1B, D). This anchoring is a consequence of the net flow of migrants that occurs each generation from the high-density regions into the low-density regions.

While neither spatial variation in local carrying capacity nor mate-search costs suffice on their own to stabilize populations, surprisingly little of both can be enough to ensure the long-term persistence of divergent mating types (Fig. 4.3). When mate-search costs in females are high, coexistence can be main-tained with less than 20% spatial variation in local carrying capacity. When mate-search costs are low, 50% spatial variation in local carrying capacity is sufficient to stabilize mating domains. Throughout our analyses, we have kept population sizes relatively small, so as to exacerbate the challenge of coexistence owing to drift in finite populations. When population sizes are larger, we find that less than 10% variation in local carrying capacity is needed to stabilize mating domains (Fig. C.4D). Because movement and demographic stochasticity obscure spatial variation in local carrying capacity across space, levels of variation in this range would be virtually undetectable in nature.

The stabilizing effect of spatial variation in local carrying capacity and matesearch costs readily extends to more realistic and natural landscapes (Fig. 4.4) and also to multiple genotypes (Fig. 4.4D–E) . While the spatial distribution of mating types becomes less predictable in complex environments, coexistence is again greatly facilitated. As long as spatial variation in local carrying capacity does not become so insignificant that it hardly affects the landscape, or so asymmetric that a single local population dominates, different mating domains are maintained in mosaic sympatry Mallet (2008); Mallet et al. (2009) (Fig. C.7). Our findings are also robust to changes in female preference strength, matesearch distance, movement distance, and competition distance (Figs. C.4A, C.5), to changes in the relative importance of ecological competition versus sexual selection (Fig. C.4B–C), to changes in the genetic architecture of the display and preference traits (Fig. C.8), and to the inclusion of fitness differences caused by the male display trait (Fig. C.9). Generally, coexistence will be maintained if female preferences are sufficiently strong to prevent extensive interbreeding, and if individuals move and interact on a spatial scale such that they are affected by spatial variation in local carrying capacity. This phenomenon can be interpreted in terms of a more general mechanism: whenever positive frequency dependence creates multiple possible stable states, global coexistence of these states can become possible in a spatially structured environment if this structure allows the states to become anchored in space. Our results in Fig. 4.4 also extend a previous finding from theoretical work on hybrid zones, predicting that the spatial interface between species moves in space until settling in a region of low population density (Barton and Hewitt, 1985, 1989). Similarly, earlier theoretical work (Dieckmann, 2004) using reflective boundaries for such anchoring, has shown that ecologically equivalent types can coexist when fecundity drops, or mortality or mobility rise, in the company of heterospecifics.

Because both spatial variation in local carrying capacity and costs associated with mate search are ubiquitous in nature, our model may provide an explanation for the coexistence of many species whose reproductive barriers are primarily sexual. For example, local habitat availability and quality vary around the shoreline of Lake Victoria. It is, therefore, possible that the mechanism reported here could explain how ecologically similar cichlid species can coexist in such vast diversity. That sexual differences have been the primary force maintaining species boundaries in this group is supported by the increasing frequency of hybridization that is occurring as a consequence of high turbidity levels, which reduce a female's ability to discern different male phenotypes (Seehausen et al., 1997). Similar explanations could plausibly be applied to other species pairs that seem to be largely maintained by sexual selection (e.g., species of fruit flies (Hollocher et al., 1997), weakly electric fish (Feulner et al., 2008), frogs (Ryan and Wilczynski, 1988), crickets (Gray and Cade, 2000), and grasshoppers (Tregenza et al., 2000), among others). To test this hypothesis, one could analyse spatial associations between mating domains and local carrying capacity: Fig. 4.4 suggests that boundaries of mating domains should often align with troughs of

low local carrying capacity (occasionally mating domains span such troughs, and very rarely they abut where ridges of high local carrying capacity are narrow).

Our work demonstrates that under reasonable conditions, with variation in local carrying capacity over space and costs to females that encounter few preferred mates, sexual selection can maintain species that are not ecologically differentiated. This is in stark contrast to the widespread opinion that sexual selection, on its own, is unable to maintain ecologically equivalent species that overlap in space. Throughout, we have deliberately avoided making any claims about the emergence of diversity and speciation, choosing instead to focus on the coexistence of mating types. Further theoretical work is, therefore, needed to determine which conditions are most conducive to the initial appearance of variation in mating preferences, as well as to the maintenance of these variants.



FIGURE 4.1: Sexual selection enables long-term coexistence of ecologically equivalent species. We consider a population distributed across a continuous habitat in one dimension (columns A, B) or two dimensions (columns C, D) with a local carrying capacity that is either spatially uniform (A, C: top panels) or that exhibits two peaks (**B**, **D**: top panels). Each peak is of Gaussian shape with standard deviation σ_k . The level v of spatial variation may be altered by changing the height of these peaks relative to the base. A value of v = 0.25, as shown in **B** and **D**, means that local carrying capacity is elevated by 25% at the peaks. The four lower rows show model runs through time. Each generation, individuals survive after a round of local competition and reproduce after a round of local mating, followed by offspring movement and the death of all parents. Competition between individuals decreases with their distance according to a Gaussian function with standard deviation σ_s . Coloured curves in **A** and **B** show the effective local density of competitors of each type (weighted by their competitive effect, SI, Eq. C.4), across the one-dimensional arena, while dots in C and D show surviving adults. Individuals are coloured according to their genotype at the display locus (similar patterns are observed at the preference locus; Fig. C.2). Females are α times more likely to mate with a preferred male, when encountered. Males are encountered with a probability that decreases with the distance between male and female according to a Gaussian function with standard deviation $\sigma_{\rm f}$. Female fecundity declines with the strength of mate-search costs m (SI). Movement distances are drawn from a Gaussian function with standard deviation σ_m , centered at 0, with wrap-around boundaries. The total carrying capacity is K = 500, supporting the survival of approximately half of the N = 1000 offspring produced each generation; other parameters: $\sigma_{\rm k} = 0.1$, $\sigma_{\rm s} = 0.05$, $\alpha = 5$, $\sigma_{\rm f} = 0.05$, $\sigma_{\rm m} = 0.05$, and m/K = 1 (roughly halving fecundity, Fig. C.1).



FIGURE 4.2: Conditions for long-term coexistence. Panels show distributions of allele frequencies at the display locus through time across 1000 model runs in a two-dimensional landscape; coexistence occurs only while these frequencies remain intermediate. Inset panels depict the spatial variation in local carrying capacity as viewed along transects at y = 0.25. A. Homogeneous environment with no sexual selection ($\alpha = 1$). **B.** Same as A, except that females are choosy $(\alpha = 5)$. C. Same as B, except with variation in local carrying capacity (v = 0.25). **D.** Same as B, except with mate-search costs in females (m/K = 1). **E.** Same as B, except with spatial variation in local carrying capacity (v = 0.25) and matesearch costs in females (m/K = 1); only when both features are combined is long-term coexistence observed. To focus on the maintenance of coexistence, we begin with two equally sized and spatially segregated populations of PQ and pq genotypes (all individuals on the left half of the arena initially have the PQgenotype, while all individuals on the right initially have the *pq* genotype). This mimics a scenario in which types that previously arose in allopatry come back into contact, revealing the conditions under which they can persist in sympatry. All other parameters are as in Fig. 4.1.



FIGURE 4.3: Conditions for long-term coexistence. Shading indicates the number of generations that polymorphism at the display locus persists when females are choosy ($\alpha = 5$) in a two-dimensional landscape (darker = longer). Each cell represents the mean time to loss of polymorphism for 10 replicate model runs. Letters indicate parameter combinations used to generate the lower four panels in Fig. 4.2. Side panels illustrate the extent of spatial variation in local carrying capacity for the three parameter values shown along the vertical axis. Model runs are initialized as in Fig. 4.2. All other parameters are as in Fig. 4.1.



FIGURE 4.4: Mosaic sympatry. Four representative model runs in a patchy twodimensional landscape with random variation in local carrying capacity. Panel **A** depicts the underlying spatial variation in local carrying capacity, while panels **B**–**E** show results from independent model runs after 10,000 generations overlaid on the local carrying capacity. Panels **B** and **C** are initialized with two types, whereas panels **D** and **E** are initialized with ten display alleles and ten corresponding preference alleles, all at equal frequencies and distributed randomly across the arena (SI, Section C.2.2). Some of these alleles are then lost during the colonization phase. As in Fig. 4.1, individuals are coloured according to their genotype at the display locus. The spatial arena is eight times larger than in Fig. 4.1 and the total carrying capacity is K = 4000, supporting the survival of approximately half of the N = 8000 offspring produced each generation. All other parameters are as in Fig. 4.1.

Assortative mating and spatial structure in hybrid zones

5.1 Summary

The spatial genetic composition of hybrid zones exhibits a range of possible patterns, with many characterized by patchy distributions. While several hypothetical explanations exist for the maintenance of these "mosaic" hybrid zones, they remain virtually unexplored theoretically. Using computer simulations we investigate the roles of dispersal and assortative mating in the formation and persistence of hybrid zone structure. To quantify mosaic structure we develop a likelihood method, which we apply to simulation and empirical data. We find that long distance dispersal can lead to a patchy distribution that assortative mating can then reinforce, ultimately producing a mosaic capable of persisting over evolutionarily significant periods of time. By reducing the mating success of rare males, assortative mating creates a positive within-patch frequency-dependent selective pressure. Selection against heterozygotes can similarly create a rare-type disadvantage and we show that it can also preserve structure. We find that mosaic structure is maintained across a range of assumptions regarding the form and strength of assortative mating. Interestingly, we find that higher levels of mosaic structure are sometimes observed for intermediate assortment strengths. The high incidence of assortment documented in hybrid zones suggests that it may play a key role in stabilizing their form and structure.

5.2 Introduction

Hybrid zones provide a natural setting in which to study the effects of selection and gene flow on alleles or combinations of alleles (Barton and Hewitt, 1985, 1989). Theoretical studies have provided methods to infer important quantities such as the strength of selection against hybrids and dispersal distance from empirical measurements of the spatial distribution of genotypes within a hybrid zone. Consequently, genetic spatial structure can be an informative property of a hybrid zone (Barton, 1979; Barton and Hewitt, 1985, 1989). To date the majority of theory has assumed that a monotonic change in genetic composition will be observed along a transect through a hybrid zone; that is, the hybrid zone will be "clinal" (Bazykin, 1969; Barton and Hewitt, 1985, 1989). However, a number of hybrid zones exhibit significant departures from a cline, with patches alternating in species composition (e.g., Howard, 1986; Harrison and Rand, 1989; Bierne et al., 2003). These "mosaic" hybrid zones are a spatial patchwork of populations, each fixed (or nearly fixed) for only one of the parental species' types.

Of the factors capable of generating mosaic patterns, habitat heterogeneity has received the most attention (Harrison and Rand, 1989; Cain et al., 1999; Bridle et al., 2001; Bridle and Butlin, 2002). This hypothesis assumes that the hybrid zone consists of alternating patches of different habitats and that the individuals preferentially occupy their own parent's habitat. The patchy species distribution then reflects the patchy environmental distribution. This hypothesis has been tested in a number of empirical studies (e.g., Howard and Harrison, 1984b,a; Howard et al., 1993; Harrison and Bogdanowicz, 1997; Bridle et al., 2001; Bridle and Butlin, 2002). However, where ecological patterns reflecting the patchiness of the hybrid zone have been found, they often explain only a small proportion of the deviations from a clinal distribution (e.g., Bridle et al., 2001; Bridle and Butlin, 2002; Bierne et al., 2002b).

Long distance dispersal during colonization has also been shown to be capable of creating patchy population structures (see Nichols and Hewitt, 1994; Ibrahim et al., 1996; Le Corre et al., 1997; Bialozyt et al., 2006). However, without any reinforcing mechanism, the spatial structure created by this process will tend to be transient, reverting to a cline over many generations. The pattern of dispersal on its own is not, therefore, sufficient to explain the persistence of structure observed in many hybrid zones. Several authors (e.g., Cruzan and Arnold, 1993; Jiggins and Mallet, 2000; Bridle and Butlin, 2002; Bailey et al., 2004) have suggested that assortative mating may also contribute to stabilizing the observed mosaic distribution in hybrid zones, but this idea has yet to be theoretically tested.

In this paper we develop a simulation model to investigate the role of assortative mating and colonization patterns in the formation and maintenance of mosaic spatial structure within a hybrid zone without habitat heterogeneity. We also develop a likelihood method to quantify the level of "mosaicity" within a hybrid zone. We find that when dispersal during colonization contains sufficiently many long distance dispersers, assortative mating can reinforce the initial spatial distribution of colonists to enhance the mosaic pattern. This mosaic structure is then able to persist for prolonged periods of time, even in the face of high levels of dispersal.

5.3 Model description

We consider the population dynamics of a one-dimensional hybrid zone using a computer simulation to investigate the role of migration and assortative mating in generating mosaic structure. Our simulation proceeds with discrete generations, tracking genotypes at two loci for diploid individuals along 30 ecologically identical patches, flanked on the left and right by pure patches of two different species. Individuals at the left boundary were assumed fixed for allele a at the first locus and allele b at the second, while those at the right were assumed fixed for alleles A and B. The A-locus is always assumed to affect assortative mating, while the role of the *B*-locus changes depending on our analyses. Recombination occurs between the loci at rate ρ . Each generation, individuals reproduce sexually within their patch to create the next generation and then die. The offspring then may migrate to a different patch, and new individuals migrate in from the pure edge populations. Hybrids are assumed to be completely viable and fertile for the majority of our analyses, but we also consider viability selection against hybrids through under-dominance at the Blocus. All interior patches were initially empty, and initial colonization occurred via dispersal from the edge populations.

5.3.1 *Reproduction and population growth*

We assume that population growth within each patch is logistic, with growth rate r and carrying capacity K (we used r = 1.25 and K = 1000 for the majority of our simulations). Each individual has a Poisson distributed number of offspring with mean

$$1+r(K-n)/K$$

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where n is the current patch population size. When viability selection acts, individuals heterozygous at the *B*-locus survive to reproduce with probability 1 + s(s being the strength of selection for or against hybrids). Assortative mating occurs through female preference. Females mate assortatively using the "best of N'' scheme presented in Seger (1985). In this model a female surveys N males and then chooses a mate. For brevity we will often use the term "lek" to refer to the group of N males sampled by a female, even though this is not the precise meaning of the term. We chose the best of N mating scheme for its generality. Where N = 1, this model reduces to random mating for all female preference strengths, whereas at the other extreme where N is the whole patch, the model becomes equivalent to the "fixed relative-preference" scheme of Kirkpatrick (1982). We will use N = frp to denote this case. Assortment usually occurs with respect to the A-locus, however, when we consider two-locus assortment (see below), then both loci are assumed to affect female preferences. We let $\psi_{i,i}$ denote the probability that a female of genotype *i* mates with a male of genotype *j* from among the males in her lek, and *c* denote the strength of a female's preference, ranging from one (random mating) to infinity (mating only with preferred males, if present). $\psi_{i,j}$ can be interpreted as a combination of all pre-zygotic isolating factors, including both pre-mating (e.g., female choosiness) and post-mating, pre-zygotic factors (e.g., conspecific sperm precedence). We consider the following three models of assortative mating.

Linear-preference (k loci)

While we investigate assortative mating based on at most two loci, we will describe a general version of this preference model for k loci. In this model preferences of parental species towards hybrids are intermediate between their preferences towards the pure types. If a female of type i and a male of type j share a total of t alleles across the k bi-allelic loci that underlie assortative mating (that is, both have t alleles from the same source population), then the probability that female i mates with male j in her lek is

$$\psi_{i,j} = \left(1 + \frac{t}{2k}(c-1)\right)f_j \tag{5.1}$$

where f_j denotes the frequency of genotype *j* males in the female's sample of *N*, and the $\psi_{i,j}$'s are standardized across all males. For example, in the one-locus case, if c = 2, then, if there were equal genotype frequencies, a homozygous female is twice as likely to mate with a conspecific than a heterospecific and 1.5 times as likely to mate with a heterozygous individual. A heterozygous female

in this case would be 1.5 times as likely to mate with another heterozygote than with either con-specific.

Self-preference

In this model a female prefers males of her own genotype by an equal factor (*c*) over all other males in her lek, discriminating equally against any other genotype. The probability that a female of genotype i mates with a male of genotype j is then given by

$$\psi_{i,j} = c^{o_{i,j}} f_j \tag{5.2}$$

where f_j again denotes the frequency of genotype j males in the female's sample of N, and $\delta_{i,j}$ is Kronecker's Delta, which is equal to one when i = j and zero otherwise. Again the $\psi_{i,j}$'s are standardized across all males.

Dominant-preference

In this model we assume that heterozygous males and females are indistinguishable from homozygous individuals characteristic of the source populations on the right side of the hybrid zone. Equation (5.2) then applies where $\delta_{i,j}$ is one if the phenotypes of *i* and *j* are the same.

5.3.2 Dispersal

There are two types of dispersal in our model: internal dispersal among the 30 patches and dispersal of new immigrants from the pure edge patches. In the internal patches, after reproduction each individual disperses with probability *m*. Individual dispersal distances were drawn randomly from a mixture of two exponential distributions, generating a leptokurtic (fat-tailed) dispersal kernel (Clark, 1998):

$$pE(\mu_s) + (1-p)E(\mu_l)$$
 (5.3)

where $E(\mu)$ is an exponential distribution with mean μ . We assumed that $\mu_s < \mu_l$, so that p represents the proportion of short-distance dispersers. Dispersal distance was measured as the number of patches away from the focal patch, with an equal probability of being in either direction. Individuals that dispersed beyond the edge patches and into the pure source populations were assumed to have a negligible impact, and thus were removed from the system. In addition to local migration between patches, a fixed number *I* of individuals arrived each generation from each of the pure patches. These migrated according to the same dispersal kernel as above, relative to the edge of the pure patches.
5.3.3 Analyzing simulation results

To analyze the results of our simulation we developed a likelihood method to quantify the degree of "mosaicity" of a hybrid zone (i.e., deviation from a monotonic cline). We fit a series of horizontal steps to allele frequency data along a transect through the hybrid zone (figure 5.1). In order to compute the allele frequency within a patch we sampled every individual. A model with k steps is defined by k step locations $s = \{s_1, s_2, \dots, s_k\}$ and k - 1 step heights $h = \{h_1, h_2, \dots, h_{k-1}\}$, where h_i is the height between steps s_i and s_{i+1} . Because we assumed that the edge patches were fixed for each parental type, we added an initial step of height 0 and a final step of height 1 (figure 5.1). In appendix D.1 we show how the likelihood of the observed allele frequency data given this model can be computed. For a set of data and given number of steps, we found the set of step locations and heights that maximize this likelihood and then used likelihood ratio tests to find the number of statistically significant steps required to best explain the data (see appendix D.1 for details). A similar approach to ours was used by Macholán et al. (2008) in order to fit step models through data collected from the Mus musculus musculus/M. m. domesticus hybrid zone. However, Macholán et al. constrained their step heights to change monotonically through the hybrid zone, and thus their approach cannot be used to make inferences as to the level of mosaic structure a hybrid zone displays.

Once the step-wise model is fit to the allele frequencies, any measure of mosaicity may be investigated. Here, we focus on the sum of the magnitudes of the downward step sizes as a measure of the "mosaicity" of a data set, given by:

$$M = \sum_{i=1}^{k-2} \max(0, h_i - h_{i+1})$$
(5.4)

(figure 5.1). This quantity has a minimum of zero for a clinal model (monotonically increasing steps), regardless of the steepness of the cline, and grows as the number and size of reversals in step height increases, attaining its maximum possible value when the hybrid zone consists of patches alternating between fixation on one or the other allele. For such cases (where each patch is fixed for either the *a* or the *A* allele), *M* is equal to the number of times the frequency of the *A* allele changes in frequency from 1 to 0 and back to 1 again.

Because wider hybrid zones (e.g., those with more patches) have a greater number of possible locations where reversals in allele frequency may occur, Mmay be inflated in hybrid zones with finer levels of sampling. Accounting for the number of samples when computing M, however, would lead to the same hybrid zone having different mosaicity scores when sampled at different scales (an undesireable outcome). Thus we have assumed that the scale of sampling has been chosen so that it appropriately captures the spatial distribution of alleles across the hybrid zone, that is, no patches are missed during sampling. We have not, therefore, included the number of patches in our measure of mosaicity. Four sample best fit models with associated *M* values are shown in figure 5.2.

Other measures of structure

Two additional measures that are commonly applied to quantify other aspects of genetic structure within a hybrid zone are linkage disequilibrium and bimodality. Linkage disequilibrium measures the association between alleles at different loci, and bimodality measures the lack of heterozygotes at a single locus, compared with the expectation under Hardy-Weinberg equilibrium (Jiggins and Mallet, 2000). We also assess these measures in our simulations.

To compute linkage disequilibrium we use Lewontin's D', which is linkage disequilibrium standardized by its maximum possible value given the observed allele frequencies (see Lewontin, 1988, for details). This statistic varies from -1 to 1, with -1 representing a population composed entirely of A/b and a/B genotypes, 1 representing a population composed entirely of A/B and a/bgenotypes, and 0 representing a population with no associations between loci. To measure bimodality we use F_{IS} , as presented in Jiggins and Mallet (2000), which is computed as

$$F_{IS} = 1 - \frac{p_{Aa}}{2p_A p_a} \tag{5.5}$$

where p_{Aa} is the frequency of heterozygotes and p_A and p_a denote the frequencies of the two alleles. This statistic lies between -1 and 1, with 0 implying that a population is at Hardy-Weinberg equilibrium, and 1 (-1) representing a complete lack of heterozygotes (homozygotes).

To compute both F_{IS} and D' for a given population we pooled individuals from all patches. Alternatively, we could have computed a patch average of each statistic. Because many patches were often fixed or nearly fixed for a single genotype, however, we found that such an approach did not provide meaningful results. In particular a mosaic hybrid zone consisting of patches alternating in state, from fixation on one allele to fixation on the other, would have a maximum mosaicity score, but in each patch both F_{IS} and D' would be undefined. At the other extreme, if hybrids never survive, F_{IS} and D' would be maximal within each patch, regardless of whether the mosaicity score were low or high. Thus, we see that the mosaicity score provides a distinct measure of the "patchiness" of the hybrid zone.

5.4 Results

Because our findings are largely insensitive to which model of assortative mating was used, we primarily present results from the one-locus linear-preference model, and will only explicitly state when this is not the case. We compute mosaicity for the one-locus linear model at the *A*-locus, which governs assortative mating (figure 5.2).

We found that a combination of long distance dispersal and assortative mating allow mosaic population structure to form (figures 5.2, 5.3) and persist for long periods of time (figure 5.4A). The initial mosaic structure is generated by individuals leap-frogging over heterospecific populations during colonization to found new populations. These processes have been discussed in detail elsewhere (e.g., Nichols and Hewitt, 1994; Ibrahim et al., 1996). In contrast with these previous studies, which assumed random mating, we found that once a mosaic population structure establishes, female preference acts to preserve the mosaic patterns (figure 5.4A). This is a consequence of a within-patch mating advantage to males of the more abundant female type, leading to within-patch fixation (or near fixation) on whichever mating type attains a higher frequency during the early stages of colonization. Once patches have reached carrying capacity, invasion by the other mating type becomes unlikely, and thus the final mosaic pattern persists, even with relatively high levels of between-patch dispersal ($m = 0.01, Nm \approx 10$).

The strength of assortative mating strongly affected the final level of mosaic structure observed in any particular hybrid zone (figure 5.2). Where mating was random, the constant arrival of foreign migrants biases patches on the left toward one allele and patches on the right toward the other, creating a gradual, roughly monotonic cline (figure 5.2A). With weak female preference mosaic structure was not stable over time. While sexual selection was a sufficiently strong force to reduce the extent of within patch co-existence of the two mating types, it was not strong enough to prevent the occasional invasion by the rare mating type. The constant arrival of different migrant types from each end of the zone, combined with migration among patches eventually removes any traces of the founding population structure, producing a cline that was both steeper and more monotonic than when mating was random (figure 5.2B). Weak female preference thus resulted in slightly lower final mosaicity values than those obtained in the neutral case (figure 5.4A). For stronger assortative mating the hybrid zone became a mosaic of alternating patches of each genotype (figure 5.2C, 5.2D). Due to the near fixation of each patch on one allele type or the other, the mosaicity scores in these cases can be interpreted as approximately counting the number of complete reversals in patch genotype frequency (e.g., figure 5.2D has three nearly complete down-steps and a mosaicity score of 2.91).

The effects of assortative mating extended to other loci in the genome. Linkage disequilibrium between the assortative mating locus and an unlinked neutral locus persisted at higher levels with stronger female preference (figure 5.4B). Tighter linkage further increases the level of disequilibrium (figure 5.4B). Bimodality at both loci was also higher with stronger female preferences (figure 5.4C), achieving nearly the maximum possible value at the assortative mating locus when c = 10.

When migration distances were short, dispersal did not create a sufficient level of genetic patchiness for assortative mating of any level to reinforce, and thus no mosaics were observed. Increasing the mean of the long distance dispersal component (μ_l) led to a roughly linear increase in the observed level of mosaicity, when assortative mating was sufficiently strong enough to maintain a mosaic pattern (figure 5.3). To account for changes in mean dispersal distance that occur when increasing μ_l we ran a separate set of simulations where we decreased μ_s whenever we increased μ_l , in order to maintain a constant mean dispersal distance. Results remained qualitatively identical and thus have not been included. Similarly, increasing the proportion of individuals within a patch that disperse each generation (m), or the number of foreign migrants arriving each generation (I), sped up the rate at which colonization occurred, but did not qualitatively change results. Varying either population growth rate (r) or carrying capacity (K) also had little effect, and thus further exploration of these parameters has not been included.

The level of mosaic structure not only depended on the strength of female preference, but also on her lek size (figure 5.5A). Whenever mating was nonrandom (e.g., for lek sizes greater than 1), the level of mosaicity increased with female mate preferences from $c \approx 1.5$. For small leks mosaicity scores remained high throughout the entire range of strong female preferences (e.g., N = 2,5 in figure 5.5A). Surprisingly, however, large leks displayed a decline in mosaicity with very strong female preferences (e.g., N = 20, *frp* in figure 5.5A). This implies that when a female samples only a small number of individuals from the population before mating, mosaic structure is more stable than when she has access to many males. This occurs because, when females only sample a few males, there is a high chance that the lek of a rare female will not contain any males of her preferred type and she will, therefore, mate with a more common male, which further reduces the expected mating success of the rare males. Conversely, when females sample many males, the lek of a rare female will often contain at least one male of her preferred type. A few males and females may, in this case, be sufficient to colonize a patch occupied by heterospecifics. At very strong mate preferences and large lek sizes the population structure reduces to a noisy cline, with different alleles often co-existing in the same patch. However, the mosaicity level is approximately 2-3 times that for random mating (figure 5.5A). The higher mosaicity score is due to a complete lack of heterozygotes, whose presence in the random mating case acts to reduce differences in allele frequencies between adjacent patches and thus the average step size. A drop in mosaicity values below those of the random mating case can be observed for intermediate mating preferences in the limiting case where a female samples the entire patch of males before mating (see figure 5.5 and the c = 1000 curve in figure 5.3). With intermediate *c* values, rare types are selected against, but not so strongly that they do not occasionally fix. The constant arrival of migrants from the boundaries thus eventually overwhelms any traces of the founding population structure, eventually creating a steep monotonic cline.

Changing the model of female preference did not qualitatively affect results (see figure 5.5B). However, with both the dominant and self-preference models the strength of female preferences required to overwhelm the mosaic structure was weaker than in the one-locus linear model (compare the $c \approx 10^2$ region in the dominant and self-preference models to the $c \approx 10^3$ region in the one-locus linear model). This occurs because the weak discrimination against hybrids combined with the reduced preference strength of hybrids in the linear model effectively reduces the efficacy of assortative mating for a given preference strength, compared to the other two models. Mean mosaicity scores were lower with the dominant-preference model, due to there being a slight bias toward patches fixing the dominant allele. In the two-locus linear model results were qualitatively unchanged when female preferences were weak. When preferences were stronger, however, curves appeared qualitatively more similar to those from the one-locus model with a smaller lek size than used in the simulations. This shift is likely a consequence of recombination breaking down genotypes of rare individuals, making co-existence and thus invasion more difficult for that species.

So far we have treated hybrids as having equal fitness as parentals. In a similar manner to assortative mating, an intrinsic reduction in hybrid viability or fertility can create a frequency-dependent selective pressure against the rarer of the two parental species within a patch (figure 5.6). This is because each hybridization event represents a larger fraction of the rare species' matings, and thus each hybrid death reduces the fitness of the rare species by a proportionally larger amount. Barton and Whitlock (1997) showed that stabilizing selection on

polygenic traits can similarly induce frequency-dependent selection against rare genotypes and thus, through an analagous process to that described above, can also lead to the maintenance of different allelic combinations between populations, provided migration rates are low enough. As expected, we found that as the strength of selection against heterozygotes increased a tighter correlation emerged between mosaicity scores at the assortative mating locus and the viability locus. When hybrids were lethal, recombination never occured and the two loci were in essence completely linked. With strong assortative mating there was higher concordance between mosaicity scores at both loci, even when viability selection was relatively weak (figure 5.6C). The marginal decline in mosaicity observed for strong viability selection arises due to a slight reduction in the initial establishment of highly mosaic populations and does not represent a reduction in the stability of mosaics, once established.

In the simulation results presented, we assumed that allele frequencies were determined from the entire patch (K = 1000 individuals). The majority of empirical hybrid zone data most certainly contain many fewer samples. In order to investigate this sampling effect we sampled 100 individuals from each patch (without replacement) and then fit the best model to the sampled data. Results remained largely unchanged, with sampled data usually producing a model missing a few small steps but having a nearly identical mosaicity score.

Although we have only presented models consisting of 30 patches here, it is worth mentioning that the width of the cline or mosaic for any particular run often fluctuated well within the limits of these 30 patches, typically settling down to a much narrower final width than is possible with 30 patches. The resultant clines or mosaics were thus flanked on either side by large regions consisting of pure parental genotypes (e.g. figure 5.2). To assess whether the width of the hybrid zones would differ noticeably with more patches, we ran simulations with twice the number of patches (60). Indeed the hybrid zones in these cases settled into a comparable width as with 30 patches, but with larger flanking regions of pure parental species on either side. Thus our results are not likely to be affected by the number of patches in the hybrid zone.

5.4.1 Application to Mytilus edulis and M. galloprovincialis hybrid zone data

The smooth-shelled mussels *Mytilus edulis* and *M. galloprovincialis* form a mosaic hybrid zone that stretches around the coast of western Europe. While differences in temperature, salinity, and wave exposure affect species composition within the hybrid zone (Gardner, 1994; Bierne et al., 2002b), Bierne et al. (2002b) argued that local adaptation was not sufficient on its own to explain the observed pattern in this hybrid zone. In a separate study Bierne et al. (2002a) suggested that the presence of assortative fertilization has likely contributed in maintaining the current population structure. To test our methods we fit models to three separate loci from this hybrid zone, using data presented in Bierne et al. (2003) (figure 5.7). Mosaicity scores and 95% bootstrap confidence intervals were 3.66 (3.08, 3.85) for Glu-5′, 2.43 (1.88, 2.70) for mac-1′, and 2.72 (2.14, 2.97) for *Efbis*. The mosaicity score for Glu-5′ is significantly higher than that for both mac-1′ and *Efbis*, despite similar sample sizes, suggesting that Glu-5′ is possibly more closely linked to a locus influencing assortative mating or experiencing under-dominant selection. Furthermore, this difference between mosaicity scores demonstrates our method's ability to detect differences among loci from the same species with realistic levels of empirical sampling.

5.5 Discussion

Our results show that assortative mating, when coupled with long-distance dispersal during colonization, can lead to the stable persistence of mosaic patterns, even in the absence of ecological differences between incipient species. Furthermore, these results are robust to changes in a variety of assumptions about migration, female mating behaviour, and the fitness of hybrids. It has been previously demonstrated that founder effects caused by long distance dispersal into vacant habitats during colonization can create spatially mosaic populations (Nichols and Hewitt, 1994; Ibrahim et al., 1996), and it is this process that drives the initial mosaic patterns observed in our simulations. However, this process alone can not explain the long-term persistence of spatial structure in these populations (figure 5.4). Rather, assortative mating and/or hybrid inviability are essential to stabilize the mosaic structure in the absence of environmental heterogeneity.

We have further shown that the effects of assortative mating will likely carry over to other regions of the genome, even with high levels of recombination. The combination of continued immigration of pure AB and ab genotypes into the hybrid zone, and the slow decay of linkage disequilibrium which has been shown to characterize stepping-stone models (De and Durret, 2007), led to a non-zero final value of D', even when mating was random (figure 5.4). These equilibrium values of linkage disequilibrium were noticeably higher when female preference was stronger and/or when linkage to the assortative mating locus was tighter (figure 5.4B). Furthermore, higher levels of bimodality can be maintained at neutral loci with stronger female preferences (figure 5.4C). Sampling at a neutral locus will, therefore, not tend to reveal just how mosaic the

hybrid zone may be at loci directly involved in assortative mating. However, such data can still potentially provide insight into whether a hybrid zone does have an underlying mosaic structure.

While our results indicate that assortative mating can stabilize mosaic hybrid zones for extensive periods of time, it is likely that other factors work in concert with this process. For example, habitat heterogeneity could strengthen the mosaic effect observed here. The combination of ecological differences between incipient species and a patchy environment could create a small degree of initial spatial segregation within a population. Assortative mating could then help push sub-populations towards fixation on one or the other type, whichever is locally more abundant. Similarly, in some cases the combined effects of viability selection against hybrids (which we have shown can also preserve mosaic structure) and assortative mating may allow for the preservation of a highly mosaic structure, where each force in isolation would not be sufficient to do so.

We have also presented a method that can be used to fit step-wise models through one-dimensional empirical hybrid zone data in order to objectively estimate their level of mosaicity. Our mosaicity statistic measures the number of reversals in allele frequency. It is not proposed as an alternative to the types of cline fitting that have been traditionally used in mosaic hybrid zones (e.g., see Bridle et al., 2001), but instead provides a complementary measure. To test our method we applied it to data from the *Mytilus edulis/M. galloprovincialis* hybrid zone (Bierne et al., 2003). Our best fit models exhibited high mosaicity scores at all three loci, demonstrating that it is informative when applied to empirical data sets. Interestingly, we found a statistically higher mosaicity score at *Glu-5'*, suggesting linkage to a locus involved in assortment, hybrid inviability, or ecological adaptation.

How common is assortment likely to be in hybrid zones? Assortative mating is thought to evolve as a consequence of divergence, with recently diverged species being more likely to hybridize (Felsenstein, 1981; Coyne and Orr, 1997). Bailey et al. (2004) documented strong assortative mating between the field grasshoppers *Chorthippus brunneus* and *C. jacobsi*, which form a mosaic hybrid zone in northern Spain. The reported "isolation index" of I = 0.59 between these species corresponds to a *c* of 3.9 in our model. Bridle et al. (2006) have also recently argued that this assortative mating, through preferences for male song, likely plays an important role in maintaining the observed structure in this hybrid zone. Howard and Gregory (1993) conducted sperm competition experiments between the ground crickets *Allonemobius fasciatus* and *A. socius*, which form a mosaic hybrid zone in northeastern United States (Britch et al., 2001). When mated to both types of males *A. socius* females exhibited a conspecific sperm precedence of at least 95%, and *A. fasciatus* females of at least 98%. These translate into *c* values of approximately 42.5 and 49 respectively. The strength of assortative mating documented in both of these hybrid zones is sufficiently strong to lead to a high level of mosaicity in our model, provided that patchiness was initially present.

In some systems, however, assortative mating will likely play only a small role, if one at all. In the *Bombina bombina – B. variegata* (fire-bellied toad) hybrid zone, MacCallum et al. (1998) found that *B. bombina*-like hybrids were most often associated with pond habitats, whereas *B. variegata*-like hybrids were most often found in puddles. This strong habitat specialization explains most of the observed spatial variation, leaving little need for additional processes.

Mosaic hybrid zones may be more common than has been reported. The pattern observed in any particular hybrid zone may reflect the scale at which individuals are sampled (Schilthuizen, 2000; Ross and Harrison, 2002). When sampling is too coarse a mosaic pattern can appear clinal. Harrison and Bogdanowicz (1997) provided a simple characterization of hybrid zones, based on the shape of the genotypic distribution at the cline center. Mosaic hybrid zones tend to exhibit an overabundance of parental types, relative to hybrids and thus have a bimodal genotypic distribution. Resampling our mosaic hybrid zones on a coarser spatial scale would, on average, lead to a clinal pattern with a bimodal distribution of genotypes. This suggests that many bimodal hybrid zones may be mosaic at a finer spatial scale than measured. Jiggins and Mallet (2000) found a strong positive correlation between the measured strength of assortative mating and the level of bimodality in a survey of several empirical hybrid zones. While bimodality does not necessarily imply that a hybrid zones is mosaic (Cruzan and Arnold, 1993; Emms and Arnold, 1997), the study by Jiggins and Mallet (2000) suggests that an underlying correlation between mosaicity and assortativity may exist.

Understanding the mechanisms by which assortative mating occurs in hybrid zones would provide insight into the applicability of our model, as well as possibly reveal interesting theoretical extensions to other models of sexual selection. Our findings depend on sexual selection inducing positive frequency-dependent selection; rare males are always at a disadvantage in the best of *N* mating scheme. This is not necessarily the case with other models of assortative mating. In a "grouping-based" model, females mate within some group of individuals with a fixed probability and otherwise mate with a male drawn randomly from the population (Felsenstein, 1981; Otto et al., 2008). Because group membership may be frequency independent (e.g., groups could be chosen based on spatial or temporal proximity), this model does not necessarily induce a rare-

type disadvantage, and thus we would expect it to yield a qualitatively different outcome.

Our model assumes an underlying demic system. Consideration of a similar model in continuous space may provide an interesting avenue for future research. In a homogeneous environment, where there are no patch boundaries stabilizing the sizes of pure (or nearly pure) populations, we would expect fluctuations in population size to lead to the eventual loss of mosaic structure. This may not be the case, however, in heterogenous environments. Ecologically heterogeneous environments that favour some degree of local adaptation, or environments where the carrying capacity and thus the density of individuals varies in space, may stabilize population sizes of the different mating types, and thus allow for the preservation of mosaic structure. Temporal fluctuations in populations size, or regularly occuring local extinctions followed by re-colonization via long distance dispersal may also allow for the long term persistence of mosaic structure, although, in this case it would vary spatially in time.

Despite having received significant empirical attention, mosaic hybrid zones have remained largely unexplored in the theoretical literature, and the majority of models so far have assumed an underlying clinal structure. Both theoretical and empirical work have demonstrated, however, that clinal models do not always make accurate predictions about evolutionary processes occurring in a mosaic hybrid zone. For example, Cain et al. (1999) found that reinforcement evolved under a much wider set of circumstances for a mosaic hybrid zone than for a clinal one, and the empirical hybrid zones described in Bridle and Butlin (2002) and Cruzan and Arnold (1993) did not conform well to the clinal model expectations. Given that our current estimate of the prevalence of mosaic hybrid zones in nature is probably underestimated (because their detection is sensitive to the scale of sampling) and that predictions based on clinal models may not apply to mosaic hybrid zones, it is important that theory be developed to help understand the forces creating and maintaining mosaic hybrid zones and the effects that these mosaic hybrid zones have on evolutionary processes.



FIGURE 5.1: An example model fitted to hypothetical allele frequency data along a transect through a hybrid zone. This model has five fitted steps. The height between step s_i and step s_{i+1} is h_i . Because there is only a single down-step the mosaicity score, M, is simply the magnitude of this step (i.e., $h_2 - h_3$, see equation 5.4).



FIGURE 5.2: Example simulated hybrid zones with varying strengths of assortative mating (increasing across panels A to D), after 1000 generations. The most likely stepwise model is indicated by the line through the data. Assortative mating was based on the one-locus linear-preference model. Parameters were $\mu_s = 1$, $\mu_l = 15$, m = 0.01, p = 0.75, r = 1.25, K = 1000, I = 50, and N = 5.



Mean of long distance dispersal (μ_l)

FIGURE 5.3: Mosaicity as a function of long distance dispersal distance (μ_l) in the one-locus linear-preference model. Each point is the mean of 100 replicate simulations. Different curves correspond to different female preference strengths (indicated by labels). Error bars denote \pm one standard error. Other parameters were as in figure 5.2 with N = frp. Curves were plotted after 1000 generations.



FIGURE 5.4: Mosaicity at the assortative mating locus (panel A), linkage disequilibrium between the assortative mating locus and a freely recombining neutral second locus (panel B) and bimodality at each locus (panel C) plotted over time. Each curve is the mean of 100 replicate simulations. Different curves correspond to different female preference strengths in the one-locus linear-preference model (the key in C applies to all panels). Recombination rates were set to $\rho = 0.5$ (free recombination) for all curves except the topmost curve in panel B, which corresponds to $\rho = 0.1$. In panel C, under random mating (c = 1) both loci display nearly identical trajectories, and thus the *A*-locus has been omitted for clarity. Error bars denote \pm one standard error and are only shown at generation 25000 for clarity. Other parameters were as in figure 5.2 with N = frp.



FIGURE 5.5: Mosaicity as a function of mate preference for different female lek sizes in the linear-preference model (A) and under different preference models with N = frp (B). Each point is the mean of 100 replicate simulations. Error bars denote the standard error and are only plotted for the rightmost points. Other parameters were as in figure 5.2 with N = frp and $\rho = 0.5$. Simulations were run for 1000 generations.



Strength of selection against hybrids (s)

FIGURE 5.6: Mosaicity at each locus as a function of the strength of selection against hybrids in the one-locus preference model. Each curve is the mean of 250 replicate simulations. Different panels correspond to different female preference strengths (indicated by labels). Error bars denote the standard error. Other parameters were as in figure 5.2 with N = frp and free recombination ($\rho = 0.5$).



FIGURE 5.7: Best fit models for three diagnostic loci in the *Mytilus edulis/M.* galloprovincialis hybrid zone (data from Bierne et al., 2003). Mosaicity scores and 95% bootstrap confidence intervals were 3.66 (3.08, 3.85) for *Glu-5'*, 2.43 (1.88, 2.70) for *mac-1'*, and 2.72 (2.14, 2.97) for *Efbis*.

Chapter 6

Conclusions

Overall, the above models illustrate how mathematics can be a useful tool in guiding our understanding when interactions between populations or species lead to complex dynamics.

In chapter 2 I used modifier theory to investigate the evolution of mutation rate at a locus regulating host-parasite interactions. I found that lower mutation rates evolved when recombination occurred between those loci and the loci regulating mutation rate. This finding can potentially help to explain the high rates of antigenic switching that have evolved in many asexual taxa, where linkage is complete. In this model, higher mutation rates tended to dampen the cycles in allele frequency characteristic of host-parasite interactions. When mutation rates evolved to be sufficiently high, cycles disappeared altogether, effectively eliminating selection at the modifier locus. In small populations, however, stochastic fluctuations in allele frequency still occurred and thus led to higher mutation rates than expected from the deterministic theory.

In chapter 3 I developed a model to investigate how ploidy and the architecture of the genetic interactions between hosts and their parasites might affect the evolution of parasitism itself. Because parasites who possess only a single allele are often able to better evade detection by hosts (i.e., homozygotes or haploids often outperform heterozygotes), I found that the transition to parasitism occurred over a broader range of parameters when the parasite was haploid. The role of host ploidy was more complicated and depended on the model governing host-parasite interactions. These results provide a first characterization of how genetic architecture affects selection on life-history strategies in antagonistic species interactions.

In chapter 4 I investigated the implications of mating interactions for longterm co-existence of biological diversity. I found that, when two criteria were met (spatial variation in the carrying capacity and search costs associated with rarity in females), sexual selection dramatically prolonged co-existence times. Essentially, these criteria together ensure that rare males and rare females arriving into a high density area of another type have low fitness and that such areas are relatively fixed in space and time. This is the first study to demonstrate the existence of conditions under which sexual selection alone can promote the long-term co-existence of ecologically equivalent populations with overlapping ranges even in the face of drift. This work thus marks an important contribution to our understanding of the role played by sexual selection in the maintenance of biodiversity.

In chapter 5 I considered the effects of mating preferences on the spatial distribution of genotypes observed in hybrid zones. I found that the distribution of genotypes observed in many so-called "mosaic" hybrid zones might be better explained by species-specific differences in mating preferences rather than by differences in ecology, the more commonly invoked cause. In analyzing the model I also developed a statistic to quantify the level of "mosaicity" of a particular hybrid zone. I tested this statistic on empirical data from the coastal hybrid zone between the mussel species *Mytilus edulis* and *M. galloprovincialis* (Bierne et al., 2003). I found that "mosaicity" was significantly higher for one of the three loci analyzed. This suggests that that locus or a linked locus, at least partially, underlies assortative mating and/or local adaptation. Interestingly, previous observations indicate that assortative mating does occur in this hybrid zone, consistent with the potential role of mating preferences in shaping the mosaic nature of the zone (Bierne et al., 2002a).

6.1 Future directions

Because the natural world is vastly complex, models are necessarily simplifications of the actual processes occurring in real ecosystems. For this reason, mismatches between models and the systems they are meant to represent are to be expected. Mismatches should not, however, be viewed as "failures" of the theoretical models, but instead, as opportunities for future insights (e.g., understanding why there was a discrepancy). Only through direct empirical tests can we identify when and where such mismatches occur. Such empirical tests are, therefore, indispensable as we seek to develop models that better map onto the world around us.

Many theoretical models address questions that are currently beyond the realm of empirically testable hypotheses. For example, there is little, if any, empirical support for or against the ubiquitous theoretical assumption that allele frequencies at loci regulating host-parasite interactions display cyclical dynamics. Thus, there is still a need for experimental tests of many of the most basic assumptions and/or findings of some of the earliest and simplest theoretical models. With this caveat, however, I will discuss some of the most promising empirically testable hypotheses that emerge from the models discussed above.

The primary finding in chapter 2 that lower mutation rates evolve with a higher recombination rate between the loci regulating host-parasite interactions and the loci regulating mutation rate could possibly be tested experimentally. For example, comparing mutation assays for antibiotic resistance in closely related species of microbes that differ in their level of sexuality would allow one to evaluate whether a correlation between sexuality and mutation rate exists in nature. The secondary finding that higher mutation rates evolved in small populations could also be experimentally tested by, for example, controlling population size in a microbial host-parasite system, and then measuring the rate of accumulation of mutations allowing hosts or parasites to invade and/or evade one another.

In chapter 4, the primary finding that sexually divergent, but ecologically equivalent, species can co-exist depended critically on two assumptions. The first of these (that there exists spatial variation in the carrying capacity) is surely met in most, if not all habitats. However, the same is not necessarily true for the second assumption, namely that rare mating types suffer a fitness cost. It is well known that female preferences can create frequency-dependent selection against males possessing non-preferred traits. While an analogous cost to rarity in females is often assumed to exist, to my knowledge, there is little empirical support for or against such an assumption. Such a cost seems plausible (e.g., females who rarely encounter their preferred male phenotypes may have to spend longer searching for a mate), however, an empirical justification for such an assumption would be valuable. Once the more basic assumptions regarding costs to rarity have been experimentally verified, it seems realistic that an experiment could directly test the main result presented in this paper (e.g., using a spatially structured grid of connected vials with varying resources and Drosophila strains with divergent preferences).

In addition to mismatches with empirical work, the simplicity of theoretical models should not be viewed as necessarily limiting their potential power. Often, it is this simplicity that can lead to general wide-ranging hypotheses and findings. For example, because the models I have developed above are not based on any particular species (or pairs of species in the case of hosts and parasites), the main findings should apply to any species (or pairs of species) that satisfy the central assumptions. This creates opportunities for potentially interesting comparative analyses testing whether species that fit the assumptions of a model confirm its predictions better than less relevant species. Furthermore, those cases where the models do not seem to apply provide avenues for future theoretical exploration. There are a number of comparative analyses and theoretical studies that would provide interesting avenues for future research as follow-ups to the models presented here.

In chapter 3 I investigated how the genetic architecture regulating hostparasite interactions might select for increases or decreases in the level of parasitism of the parasitic species. I found that, in general, parasitism should more easily evolve in haploids than in diploids. This is similar to a finding by Nuismer and Otto (2004), who used a theoretical model to show that, in order to better evade detection by hosts, parasites should more often evolve toward haploid genomes than diploid ones. A survey of protists confirmed their prediction (i.e., there was a correlation between parasitism and haploidy). Such a finding is, however, also consistent with my model (i.e., haploids more readily evolve parasitism). Comparative analyses, such as those presented in Pagel (1994), could be used to evaluate whether parasites more often evolve haploidy or haploids more often evolve parasitism.

In addition to the above comparative study, there is a challenging, but potentially interesting theoretical follow-up. In the model, as presented, evolution of parasitism from a non-parasitic life-style can occur in a single evolutionary step. This is because we assumed from the outset that all of the machinery was in place for parasitism to evolve (e.g., only a mutation at a modifier locus was necessary in order for parasitism to initially appear; all the alleles necessary for successful invasion and resistance were already present in both species). As a result, this model does not fully address the initial stages in the evolution of parasitism. Such a model is needed in order for us to appreciate why some species might be more likely to undergo large shifts in life-history strategies. It is possible that parasitism could evolve through a number of complex evolutionary pathways (e.g., degradation of a mutualistic relationships or a gradual exploitation of a newly encountered species are two such possibilities). In addition to helping understand the origins of parasitism and life-history shifts, such a model may also provide insight into how adaptation proceeds when many complex genetic changes are required.

In chapter 4 I investigated how sexual selection might enable long-term co-existence of ecologically equivalent species. In doing so, however, I assumed that genetic variation in mating preferences and trait displays was already present in the population. How the most basic assumptions of my model inhibit or facilitate the process of speciation and the generation of this variation is, therefore, necessary if we hope to gain a full appreciation of the model's generality. If it turns out that costs to rarity in females and variation in the local carrying capacity prevent sympatric speciation by sexual selection, then my model is most applicable in cases of secondary contact between sexually divergent mating types, but it cannot help explain origins of diversity. If, on the other hand, the parameter space in which long-term co-existence occurs in my model overlaps with that where speciation can occur by sexual selection, then my model may provide a general mechanism whereby sympatric speciation can produce species capable of stable co-existence, without any disruptive ecological selection or allopatry. Additionally, generalizing the model (e.g., to quantitative or multi-dimensional preference and display traits) would provide insight into the broader applicability and robustness of these results.

In chapter 5 I suggested that variation in mating preferences between species might provide a better explanation for the spatial structure observed in some mosaic hybrid zones. In order to assess whether such mating preferences really do provide a better explanation it would be worthwhile to conduct a metaanalysis of hybrid zone data, quantifying the level of "mosaicity" within each hybrid zone, and testing for a correlation between that trait and the documented level of assortative mating, versus ecologically relevant attributes. In some species, it might also be possible to conduct reciprocal transplants among patches in a mosaic hybrid zone. If individuals survive to reproduction equally well in the different patches, but suffer reduced mating success, that would indicate that the explanation provided here may be the more appropriate one.

In most complex biological systems, intuitively understanding the outcome of a particular process can be difficult, if not impossible. In my thesis I have developed models demonstrating how the use of additional theoretical tools can aid in our pursuit of a fuller understanding. Often these models can provide unexpected insights and, additionally, exciting directions for future research, both empirical and theoretical.

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Mutating away from your enemies (Chapter 2)

A.1 Cost of deleterious mutations

Here we modify the model by including an explicit cost to modifiers that increase the mutation rate. This cost reflects the assumption that mutators will suffer from a higher load of unconditionally deleterious mutations at sites other than the *A*-locus. Rather than model these other sites explicitly, we incorporate a cost $C_i\mu_i$ of having a mutation rate of μ_i . Technically this is equivalent if the unconditionally deleterious mutations are lethal. To incorporate costs of producing unconditionally deleterious mutations we add the following step between mutation/selection (equation 2.2) and sex/recombination (equation 2.3).

$$\begin{aligned} x_{i,1}'' &= (1 - C_i \mu_{i,m}) / \bar{C}_i \ x_{i,1}' \\ x_{i,2}'' &= (1 - C_i \mu_{i,M}) / \bar{C}_i \ x_{i,2}' \\ x_{i,3}'' &= (1 - C_i \mu_{i,m}) / \bar{C}_i \ x_{i,3}' \\ x_{i,4}'' &= (1 - C_i \mu_{i,M}) / \bar{C}_i \ x_{i,4}' \\ \bar{C}_i &= 1 - C_i \mu_{i,m} (x_{i,1}' + x_{i,3}') - C_i \mu_{i,M} (x_{i,2}' + x_{i,4}') \end{aligned}$$
(A.1)

A mutation modifier *M* that increases the mutation rate by $(\mu_{i,M} - \mu_{i,m})$ will experience a reduction in frequency each time step that is proportional to $C_i(\mu_{i,M} - \mu_{i,m})$. In order that costs do not dominate dynamics at the modifier locus (i.e., they are not so large as to drive all mutation rates to o) we must assume that the C_i are of order ϵ^2 , where ϵ is a small term, as discussed prior to equation (2.10). An analysis similar to that in the main text shows that a modifier that increases

the mutation rate invades whenever the following is positive

$$\overline{\Delta p_{i,M}} = c_3 [c_1 X_i (1 - \mu_{\bar{i},M} - \mu_{i,M})/2 - (\mu_{\bar{i},M} - \mu_{i,M}) (X_i - (1 - 2\mu_{\bar{i},M}))] - C_i (1 - p_{i,M}) p_{i,M} (\mu_{i,M} - \mu_{i,m})$$
(A.2)

where c_3 is the positive constant

$$c_{3} = \frac{(R^{\frac{4\pi}{\phi}} - 1)\phi \csc^{2}[\phi]\alpha_{h}^{2}(1 - \psi_{i})(1 - p_{i,M})p_{i,M}(\mu_{i,M} - \mu_{i,m})(\delta_{p,A}[0])^{2}}{\pi \log[R](R^{2} - 2\cos[\phi]X_{i}R + X_{i}^{2})(\alpha_{i} + 2)^{2}(1 - 2\mu_{\tilde{i},M})}$$
(A.3)

Costs always select against higher mutation rates, but as long as the costs are sufficiently weak that equation (A.2) is positive when the mutation rate in a species is zero, then evolution will lead the system toward a non-zero level of mutation. The evolutionarily attracting mutation rate can be determined by setting $\overline{\Delta p_{i,M}}$ equal to 0 using equation (A.2) and numerically solving for μ_i .

We used simulations to investigate model behaviour when costs differed between hosts and parasites (see main text for simulation methods). In accordance with Haraguchi and Sasaki (1996), we found that when mutation rates were allowed to co-evolve from low initial values (zero in each species), populations experienced an initial phase of selection for high mutation rates followed by a subsequent phase of selection for decreased rates in the species bearing the higher costs (see trajectories beginning at the origin in figure A.1). In contrast to Haraguchi and Sasaki (1996), however, mutation rates in our model remained at non-zero values in both species (convergence toward equilibrium values occurred from both directions; figure A.1). Furthermore, unlike Haraguchi and Sasaki (1996), we did not observe any asymmetries between hosts and parasites. This is because parasite populations did not require hosts for their survival in our model, whereas in the model of Haraguchi and Sasaki (1996), parasite survival was dependent on their ability to find a host. Consequently, Haraguchi and Sasaki (1996) find that it is more often the hosts that tend to retreat towards a zero mutation rate, due to their having less at stake.

Interestingly, we did not observe a large effect of population size when costs were included (compare left and right panels of figure A.1). Because sufficiently large costs can outweigh any indirect benefits to mutation rate modifiers, selection for higher mutation rates is likely to disappear while rates are still low enough to permit co-evolutionary cycling (as was the case for the parameters presented in figure A.1). When this happens, the added indirect benefits created by stochastic allele frequency fluctuations in small populations have only a small effect and thus do not significantly change the final outcome of co-evolution.

A.2 Solving the recursion equations for the disequilibrium

Here we derive recursion equations for the disequilibrium in species *i*. By definition

$$D_i'' = x_{i,1}'' x_{i,4}'' - x_{i,2}'' x_{i,3}''$$

We can then use equations (2.2) and (2.3) to write D_i'' in terms of genotype frequencies from the previous generation. Making the following substitutions

$$x_{i,1} = 1/2 (1 - p_{i,M})(1 - 2\delta_{i,A}) + D_i$$

$$x_{i,2} = 1/2 p_{i,M}(1 - 2\delta_{i,A}) - D_i$$

$$x_{i,3} = 1/2 (1 - p_{i,M})(1 + 2\delta_{i,A}) - D_i$$

$$x_{i,4} = 1/2 p_{i,M}(1 + 2\delta_{i,A}) + D_i$$

gives us a recursion equation for D_i .

We next assume that $\delta_{i,A}$ is small (specifically on the order of a small term ϵ) and that the mutation rate modifier has a small effect (i.e. $\mu_{i,M} - \mu_{i,m}$ is also of order ϵ). A simple analysis of the first three terms in the Taylor series of D_i (taken with respect to ϵ) shows that the $\mathcal{O}(\epsilon^2)$ term is the first that could possibly grow in a single generation (both the $\mathcal{O}(1)$ and $\mathcal{O}(\epsilon)$ terms only decay by a factor proportional to $X_i = (1 - \psi_i)(1 - 2\mu_{i,M})$). It follows that any initial disequilibrium in the system will rapidly evolve to a level that is at most of order ϵ^2 . We, therefore, make the assumption that disequilibrium is already of this order in order to avoid any transient effects of initial conditions. Our recursion equation for D_i can then be simplified to

$$D_{i}[t] = (1 - \psi_{i}) \left[(1 - 2\mu_{i,M}) D_{i}[t - 1] + 2p_{i,M}(1 - p_{i,M}) (\mu_{i,m} - \mu_{i,M}) \left(\delta_{i,A}[t - 1] + \frac{\alpha_{i}}{(\alpha_{i} + 2)} \delta_{\overline{i},A}[t - 1] \right) \right] + O(\epsilon^{3}).$$

We assume that enough time has passed that the initial disequilibrium $D_i[0]$ exerts negligible influence. With this assumption we can solve the above recursion equation to get

$$D_{i}[t] = 2(1 - \psi_{i})(\mu_{i,m} - \mu_{i,M})(1 - p_{i,M})p_{i,M}$$

$$\sum_{\tau=1}^{t} ((1 - \psi_{i})(1 - 2\mu_{i,M}))^{\tau-1} \left(\delta_{i,A}[t - \tau] + \frac{\alpha_{i}}{(\alpha_{i} + 2)}\delta_{\overline{i},A}[t - \tau]\right) + O(\epsilon^{3}).$$

A.3 Different generation times

Here we relax the assumption made in the main text that host and parasite generation times are equal. We assume that parasite dynamics remain exactly as they are in the main text, and then vary the generation times in hosts in two ways.

In the first model we assume that all hosts are subject to mutation and selection at every time step, but that only a proportion g take part in sexual reproduction. This is incorporated by replacing equation (2.3) in the main text (for hosts only), with

$$\begin{aligned} x_{h,1}'' &= (1-g)x_{h,1}' + g(x_{h,1}' - \psi_h D_h') = x_{h,1}' - g\psi_h D_h' \\ x_{h,2}'' &= (1-g)x_{h,2}' + g(x_{h,2}' + \psi_h D_h') = x_{h,2}' + g\psi_h D_h' \\ x_{h,3}'' &= (1-g)x_{h,3}' + g(x_{h,3}' + \psi_h D_h') = x_{h,3}' + g\psi_h D_h' \\ x_{h,4}'' &= (1-g)x_{h,4}' + g(x_{h,4}' - \psi_h D_h') = x_{h,4}' - g\psi_h D_h' \end{aligned}$$
(A.1)

It is clear from equation (A.1) that when g = 1 the model reduces to that presented in the main text. It is also clear that this modification effectively scales recombination rates in hosts by the factor g. This has the net effect of reducing the recombination rate in hosts (by a factor g), which will ultimately increase the evolutionarily attracting mutation rate, provided it is predicted to lie within a region where cycles occur (see figure 2.3). Thus, increasing host generation time (smaller g) results in hosts evolving a higher mutation rate.

In our second model we assume that all hosts are subject to selection every time step, but only a proportion g take part in sexual reproduction, at which point mutation and recombination occur. This can be incorporated by replacing our recurrence equation (2.3) in the main text (for hosts only) with

$$\begin{aligned} x_{h,1}^{\prime\prime\prime} &= (1-g)x_{h,1}^{\prime} + g(x_{h,1}^{\prime\prime} - \psi_h D_h^{\prime\prime}) \\ x_{h,2}^{\prime\prime\prime} &= (1-g)x_{h,2}^{\prime} + g(x_{h,2}^{\prime\prime} + \psi_h D_h^{\prime\prime}) \\ x_{h,3}^{\prime\prime\prime} &= (1-g)x_{h,3}^{\prime} + g(x_{h,3}^{\prime\prime} + \psi_h D_h^{\prime\prime}) \\ x_{h,4}^{\prime\prime\prime} &= (1-g)x_{h,4}^{\prime} + g(x_{h,4}^{\prime\prime} - \psi_h D_h^{\prime\prime}) \end{aligned}$$
(A.2)

where $x'_{h,j}$ denotes the frequency of genotype *j* after selection and $x''_{h,j}$ denotes the frequency of genotype *j* after selection *and* mutation. Again it is clear that when g = 1 our model reduces to that in the main text. A similar analysis to

that in the main text then yields

$$\delta_{h,A}[t] = R^{t-1} (1 - 2g\mu_{h,M}) \frac{\alpha_h}{(\alpha_h + 2)} \frac{\sin[\phi t]}{\sin[\phi]} \delta_{p,A}[0]$$

$$\delta_{p,A}[t] = R^{t-1} \sqrt{R^2 - (1 - 2g\mu_{h,M})(1 - 2\mu_{p,M})} \frac{\sin[\phi t + \sigma]}{\sin[\phi]} \delta_{p,A}[0]$$

where *R*, ϕ and σ are:

$$R = \sqrt{(1 - 2\mu_{p,M})(1 - 2g\mu_{h,M})\frac{(1 + \alpha_p/2 + \alpha_h/2)}{(1 + \alpha_p/2)(1 + \alpha_h/2)}}$$
$$\phi = \cos^{-1}\left[\frac{(1 - \mu_{p,M} - g\mu_{h,M})}{R}\right]$$
$$\sigma = \cos^{-1}\left[\frac{\mu_{p,M} - g\mu_{h,M}}{\sqrt{R^2 - (1 - 2\mu_{p,M})(1 - 2g\mu_{h,M})}}\right]$$

The recursion equation for $D_h[t]$ (equation 2.10) also changes becoming:

$$D_{h}[t] = 2(1 - \psi_{h})g(\mu_{h,m} - \mu_{h,M})(1 - p_{h,M})p_{h,M}$$
$$\sum_{\tau=1}^{t} X_{i}^{\tau-1} \left(\delta_{h,A}[t - \tau] + \frac{\alpha_{h}}{(\alpha_{h} + 2)}\delta_{p,A}[t - \tau]\right)$$

where $X_h = 1 - g\psi_h - 2g\mu_{h,M} + 2g\mu_{h,M}\psi_h$.

An analysis following that in the main text shows that a modifier of mutation rate in hosts can invade whenever the following is positive

$$sign[\overline{\Delta p_{h,M}}] \simeq sign[c_1 X_h (1 - \mu_{p,M} - g\mu_{h,M})/2 + (g\mu_{h,M} - \mu_{p,M})(X_h - (1 - 2\mu_{p,M}))]$$
(A.3)

and in parasites

$$sign[\overline{\Delta p_{p,M}}] \simeq sign[c_1 X_p (1 - g\mu_{h,M} - \mu_{p,M})/2 + (\mu_{p,M} - g\mu_{h,M})(X_p - (1 - 2g\mu_{h,M}))]$$
(A.4)

From the first of these equations, it can be seen that lengthening the generation time in hosts (reducing g) increases the relative importance of the first term in equation (A.3), which will tend to increase the evolutionarily attracting mutation rate in the host. The reverse is true in the parasite, where all else being equal a longer host generation time effectively reduces the host's mutation rate per unit time, which reduces selection for increased mutation rates in the parasite.
A.4 One-species model

Here we consider a simplified version of the model above where instead of two interacting species there is only a single species under a fluctuating selection regime. As before we consider two loci, each with two alleles. The four possible haplotypes are then *am*, *aM*, *Am* and *AM*. We let x_j denote the frequency of the j^{th} genotype (labelled in the order just given).

The *A*-locus is assumed to be under a fluctuating selection regime. That is, the fitness of genotype j in the t^{th} generation is given by

$$w_j[t] = \begin{cases} 1 + \alpha \sin[\beta t] & \text{if } j = 1,2\\ 1 - \alpha \sin[\beta t] & \text{if } j = 3,4 \end{cases}$$
(A.1)

As in the two-species model we construct recursion equations, beginning with selection, then mutation, and finally sex and recombination. Performing a change of variables allows us to describe the system with recursions for the linkage disequilibrium (D[t]), the departure from a frequency of 0.5 at the *A* locus $(\delta[t])$, and the frequency of the modifier $(p_M[t])$. In addition to the order assumptions made in the two-species model (see the main text preceding equation 2.5), we must assume here that selection is also weak (α is on the order of ϵ ; this assumption wasn't necessary in the two-species model, but there we assumed $\delta_{h,A}$ and $\delta_{p,A}$ were both small). It can then be shown in a similar manner to that in appendix A.2 that, transient initial effects aside, the disequilibrium will remain of order at most ϵ^2 . With these assumptions we can find a general solution for $\delta[t]$ which, after simplification, is given by

$$\delta[t+1] = \frac{\alpha(1-2\mu_M)((1-2\mu_M)\sin[\beta t] - \sin(\beta[t-1]))}{4(2\mu_M^2 + (1-\cos[\beta](1-2\mu_M)))}.$$
 (A.2)

As in the two species model we next find a general solution for the linkage disequilibrium (D[t]), again ignoring transient effects of initial conditions. This can be simplified to

$$D[t] = (1 - \psi)(1 - p_M)p_M(\mu_m - \mu_M)\sum_{\tau=1}^t ((1 - \psi)(1 - 2\mu_M))^{\tau-1}(2\delta[t - \tau] - \alpha \sin[\beta(t - \tau)])$$
(A.3)

Finally we consider the change in frequency of a mutation rate modifier, averaged over a complete selective cycle. The expected change per generation is then

$$E[\Delta p_M[t]] \approx (1-\psi)(\mu_m - \mu_M)p_M(1-p_M)\frac{\alpha^2(\cos[\beta](1+X\theta) - X - \theta)}{(1+X^2 - 2X\cos[\beta])(1+\theta^2 - 2\theta\cos[\beta])}$$
(A.4)

where $\theta = (1 - 2\mu_M)$. It is apparent from equation (A.4) that the direction of selection on a modifier depends on the speed of evolutionary cycles (β), with faster cycles (larger β) selecting for higher mutation rates. In contrast to the two-species model, where the direction of selection was also dependent on the strength of selection (because the speed of evolutionary cycles ϕ contained both α_h and α_p), we find that the strength of selection, α , in the one-species model does not affect the sign of selection on a modifier, although it does affect the strength of indirect selection.



FIGURE A.1: Co-evolutionarily trajectories in simulations with differing costs associated with mutation rate modifiers. Each curve represents the mean of 100 replicate runs. Solid points represent final values after 10⁷ generations for trajectories initialized with both host and parasite mutation rates set to 0 and + symbols represent final values for populations initialized with mutation rates of 0 in hosts and 0.165 in parasites, or 0.165 in hosts and 0 in parasites. The shaded region indicates where cycles are not expected in the analytical model (R < 1). Population sizes were 10⁹ (left panel) and 10³ (right panel) in both hosts and parasites. When costs were equal we used $C_h = C_p = 0.5$ and when they differed we used $C_h = 0.25$, $C_p = 0.5$ and $C_h = 0.5$, $C_p = 0.25$. The dotted line has a slope of one and is included for reference. Recombination rates were set to 0, α_h to -0.9, and α_p to $1/(1 + \alpha_h) - 1$ (so that the strength of selection was the same in both species). The parameters in this figure are identical to figure 2.5 with $\alpha_h = -0.9$ and $\alpha_p = 9$, except for the addition of costs of mutation.

Ploidy and the evolution of parasitism (Chapter 3)

B.1 Additional analyses

Quasi-linkage equilibrium analyses were also performed relaxing the assumption that ψ_H and ψ_P were near one. The main difference is that the departure from Hardy-Weinberg at the *A* locus (denoted $F_{A,H}$ in hosts and $F_{A,P}$ in parasites) then becomes substantial (see table B.1 for the full expressions for $F_{A,H}$ and $F_{A,P}$). Full expressions for $\overline{w}_{\text{diff}}$ are given in table B.2. Because $F_{A,H}$ and $F_{A,P}$ are still on the same order as the strength of selection, however, these terms again drop out when we assume selection is weak and focus on the leading order terms.

B.2 Simulations

We summarize here a number of extensions to our model that were examined using simulations. Simulations matched our analytical predictions when mutation rates were high and cycles were small in every case, except when we considered more alleles at the interaction locus (discussed below). Where discrepancies were observed, they could be explained by accounting for the allele frequency dynamics (i.e., calculating δ_H and δ_P in every generation and using these in table 3.3). Also note that in each case, any shifts that did occur did not affect our main conclusions that parasitism is more likely to evolve under MAM than IMAM (but see results with three alleles) and that haploid parasites are more likely to evolve higher parasitism levels than diploids.

Figure B.1: simulations of MAM/IMAM comparing low and high mutation rates (μ = 10⁻¹ versus μ = 10⁻⁵).

- Figure B.2: same as figure B.1, except with selection in hosts reduced ($\alpha_H = 0.01$).
- Figure B.3: same as figure B.1, except with stronger selection in hosts ($\alpha_H = 0.5$) and in parasites ($0 < \alpha_P < 1$).
- Figure B.4: same as figure B.1, except with population sizes of 10³ in both species.
- Figure B.5: same as figure B.1, except with some hosts reproducing asexually ($\psi_H = 0.2$). Mutations were introduced at the same rate during sexual and asexual reproduction.
- Figure B.6: same as figure B.1, except with different generation times in hosts and parasites. Only 20% of hosts reproduced at each time step, and thus had, on average, a generation time five times that of parasites. Mutations were introduced only during reproduction, so that hosts had 20% the rate of mutations per unit times as parasites.
- Figure B.7: same as figure B.1, except with three alleles at the *A*-locus in each species. See below for a more detailed description of this case.
- Figure B.8: evolutionary convergent level of parasitism in the GFG with conditional costs to virulence.
- Figure B.9: evolutionary convergent level of parasitism in the GFG with unconditional costs to virulence.
- Figure B.10: same as figure B.9, except with population sizes of 10³ in both species.

B.2.1 Three alleles at the interaction locus

Qualitative shifts occurred in all cases when there were three alleles at the *A*-locus. These shifts could be described analytically by developing the model explicitly for multiple alleles. With MAM, the region where parasitism evolved shrunk with more alleles, whereas with IMAM it grew (figure B.7). This is because with MAM the heterozygous parasites can infect a lower proportion of the genotypes when there are more alleles present, whereas the opposite is true in the IMAM. For example, with three or more alleles, a host homozygous for an allele not present in a heterozygous parasite cannot be invaded by that parasite in the matching-alleles model, whereas when there are only two alleles

a heterozygous parasite can invade all possible host genotypes. In the inversematching-alleles model the opposite is true, with new host genotypes providing additional targets for heterozygous parasites (in the case of two alleles, heterozygous parasites cannot invade any host genotypes, but with three they can invade hosts homozygous for the allele that the parasite does not carry). Large cycles had the same effect with three alleles as they did with two, reducing and enlarging the same regions (figure B.7).

Model	Host ploidy	Parasite ploidy	$ar{w}_{ m diff}$
MAM/IMAM	1 2	2	$F_{A,P} = (1/4 - \delta_P^2)^2 f_{mm} (\alpha_P + \beta_P) (1 - \psi_P) / \psi_P$ $F_{A,P} = (1/4 - \delta_P^2)^2 f_{-\alpha_H} (1 - \psi_P) / \psi_P$
	2	2	$F_{A,H} = (1/4 - \delta_H^2) f_{m} \alpha_H (1 - \psi_H) / \psi_H$ $F_{A,H} = (1/4 - \delta_H^2)^2 (3/4 - \delta_P^2) 2 f_{mm} \alpha_H (1 - \psi_H) / \psi_H,$ $F_{A,B} = (1/4 - \delta_R^2)^2 (1/4 + \delta_R^2 + F_{A,H}) 2 f_{mm} (\alpha_B + \beta_B) (1 - \psi_B) / \psi_B$
GFG	1 2 2	2 1 2	$\frac{F_{A,P} = (1/4 - \delta_P^2)^2 (c_{P,u} + f_{mm} c_{P,c} - f_{mm} (\alpha_P + \beta_P) (1 - \psi_P) / \psi_P}{F_{A,H} = (1/4 - \delta_H^2)^2 (c_H - f_m \alpha_H (1/2 - \delta_P)) (1 - \psi_H) / \psi_H}$ $F_{A,H} = (1/4 - \delta_H^2)^2 (c_H - f_m \alpha_H (1/2 - \delta_P)) (1 - \psi_H) / \psi_H$
			$F_{A,P} = (1/4 - \delta_P^2)^2 (c_{P,u} + f_{mm} c_{P,c} + f_{mm} (\alpha_P + \beta_P) (\delta_H^2 - \delta_H - 3/4))(1 - \psi_P)/\psi_P$

TABLE B.1: Equations for $F_{A,H}$ and $F_{A,P}$ when ψ_H and ψ_P are not assumed to be near 1.

Model	Host ploidy	Parasite ploidy	$ar{w}_{ m diff}$
MAM	1	1	$(\alpha_P - \beta_P)/2 + (\alpha_P + \beta_P)(2\delta_H\delta_P)$
	1	2	$(\alpha_P - 3\beta_P)/4 + (\alpha_P + \beta_P)(2\delta_H\delta_P + \delta_P^2 + F_{A,P})$
	2	1	$(3lpha_P-eta_P)/4+(lpha_P+eta_P)(2\delta_H\delta_P-\delta_H^2-F_{A,H})$
	2	2	$(5lpha_P-3eta_P)/8+(lpha_P+eta_P)[4\delta_H\delta_P(1+\delta_H\delta_P)-3\delta_H^2+\delta_P^2+$
			$(1+4\delta_H^2)F_{A,P} - (3-4\delta_P^2)F_{A,H} + 4F_{A,P}F_{A,H}]/2$
IMAM	1	1	$(lpha_P-eta_P)/2-(lpha_P+eta_P)(2\delta_H\delta_P)$
	1	2	$(lpha_P - 3eta_P)/4 - (lpha_P + eta_P)(2\delta_H\delta_P - \delta_P^2 - F_{A,P})$
	2	1	$(lpha_P-3eta_P)/4-(lpha_P+eta_P)(2\delta_H\delta_P-\delta_H^2-F_{A,H})$
	2	2	$(lpha_P-7eta_P)/8-(lpha_P+eta_P)[4\delta_H\delta_P(1-\delta_H\delta_P)-\delta_H^2-\delta_P^2-$
			$(1+4\delta_H^2)F_{A,P} - (1+4\delta_P^2)F_{A,H} - 4F_{A,H}F_{A,P}/]2$
	1	1	$(3\alpha_P - \beta_P)/4 + (\alpha_P + \beta_P)(\delta_P - \delta_H(1 - 2\delta_P))/2 - c_{P,c}(1 + 2\delta_P)$
GFG	1	2	$(7\alpha_P - \beta_P)/8 + (\alpha_P + \beta_P)(2(1 + 2\delta_H)(1 - \delta_P)\delta_P - \delta_H - 2(2\delta_H + 1)F_{A,P})/4 - c_{P,c}(3/4 + (1 - \delta_P)\delta_P - F_{A,P})$
	2	1	$(5\alpha_P - 3\beta_P)/8 + (\alpha_P + \beta_P)(3\delta_P + 2(1 - 2\delta_P)(\delta_H^2 - \delta_H + F_{A,H}))/4 - c_{P,c}(1 + 2\delta_P)$
	2	2	$\frac{(13\alpha_P - 3\beta_P)}{(1 - 2\delta_P)^2 F_{A,H} + (4\delta_H^2 - 4\delta_H - 3)F_{A,P} + 4F_{A,H}F_{A,P}]} - 3(\delta_P - 1)\delta_P + (1 - 2\delta_P)^2 F_{A,H} + (4\delta_H^2 - 4\delta_H - 3)F_{A,P} + 4F_{A,H}F_{A,P}]/4 - \delta_P$
			$c_{P,c}(3/4 + (1-\delta_P)\delta_P + F_{A,P})$

TABLE B.2: Full equations for $\bar{w}_{\text{diff}} = \bar{w}_M - \bar{w}_m$, without assuming high levels of sexual reproduction in either species (e.g., without assuming ψ_H and ψ_P are on the order of $1 - \epsilon$).



FIGURE B.1: Evolutionary convergent level of parasitism (f) in MAM and IMAM. Right two columns are identical to figure 3.4. Left two columns report simulations with $\mu = 10^{-1}$ for comparison. Dashed red lines denote the analytical invasion condition assuming small cycles (table 3.4). Cells are shaded based on the mean level of parasitism present in the population after 10^6 generations of evolution in a single simulation (darker = higher, see grayscale in panel P). Parameters were $\alpha_H = 0.05$, $\psi_H = \psi_P = 1$, r = 0.5 and population sizes of 10^6 in both species.



Figure B.2: Same as figure B.1, except with $\alpha_H = 0.01$.



FIGURE B.3: Same as figure B.1, except with stronger selection in hosts ($\alpha_H = 0.5$) and in parasites (note change in axes ranges).



FIGURE B.4: Same as figure B.1, except with population sizes of 10^3 in both species.



FIGURE B.5: Same as figure B.1, except with some hosts reproducing as exually ($\psi_H = 0.2$). Mutations were introduced at the same rate during sexual and a sexual reproduction.



FIGURE B.6: Same as figure B.1, except with different generation times in hosts and parasites. Only 20% of hosts reproduced at each time step, and thus had, on average, a generation time five times that of parasites. Mutations were introduced only during reproduction, so that hosts had 20% the rate of mutations per unit times as parasites.



FIGURE B.7: Same as figure B.1, except with three alleles at the *A*-locus in each species. Dashed red lines denote the analytical invasion condition for the two-allele case, as given in table 3.4, and are included for comparison.



FIGURE B.8: Evolutionary convergent level of parasitism (*f*) in the GFG with conditional costs to virulence, as indicated by column headings. Dashed red lines denote the value of α_P for which \bar{w}_{diff} in eq. (3.6) is zero. Other parameters were as in figure B.1, along with $\mu = 10^{-5}$ and $c_H = 0.01$.



FIGURE B.9: Evolutionary convergent level of parasitism (f) in the GFG with unconditional costs to virulence and differing initial levels of parasitism, as indicated by column headings. Dashed red lines denote the value of α_P for which \bar{w}_{diff} in eq. (3.7) is zero. The poor fit for small β_P (grey triangular regions to the right of the dashed red lines) is a consequence of selection being insufficiently strong to maintain the costly virulent allele, thereby reducing the advantage of being parasitic. Thus cycles do not occur and parasitism does not evolve. Other parameters were as in figure B.1, along with $\mu = 10^{-5}$ and $c_H = 0.01$.



FIGURE B.10: Evolutionary convergent level of parasitism (f) in the GFG with unconditional costs to virulence, differing initial levels of parasitism, and small populations. All parameters are as in figure B.9, except population sizes were 10^3 .

Sexual selection enables co-existence (Chapter 4)

C.1 Model description

We consider an individual-based model with discrete non-overlapping generations in one- or two-dimensional continuous space with wrap-around boundaries. Below, we describe the two-dimensional model, from which the corresponding one-dimensional model is readily generated by removing the spatial y-dimension. Each individual has a spatial location and is characterized by a display trait (expressed only in males) and a preference trait (expressed only in females). In our main set of model runs, these traits are assumed to be governed by separate unlinked haploid loci, each with two alleles (display alleles are denoted by Q/q and preference alleles by P/p). Each generation, N individuals are produced and compete for resources, with those experiencing stronger competition being more likely to die before reaching reproductive maturity. Resources in our model may be interpreted in the broadest possible sense, describing the biotic and abiotic factors that are subject to local ecological competition. Among the individuals surviving ecological competition, females choose mates, with the probability of a specific male being chosen depending on her mating preference and the spatial distance separating them. Females produce offspring in proportion to their fecundities. Offspring then disperse from their natal location and the parents die. Below we detail these steps in the order in which they occur. The names and descriptions of all parameters and variables are listed in Table C.1.

C.1.1 Competition for resources

The habitat at each location (x, y) is characterized by the local density k(x, y) of available resources. The total amount of resources over the spatial arena is given by $K = \iint k(x, y) \, dx \, dy$. The function relating resource gain to survival is chosen such that if every individual received an equal share of these resources, the expected number of survivors would be *K*. Consequently, we refer to k(x, y) as the local carrying capacity and to *K* as the total carrying capacity. Except for Figs. 4.4 and C.7, we investigate a local carrying capacity that is bimodal, with peaks located at (x, y) = (0.25, 0.25) and (0.75, 0.25). To do so, we combine two Gaussian functions according to

$$k(x,y) = \left(\exp\left(-\frac{(x-0.25)^2 + (y-0.25)^2}{2\sigma_k^2}\right) + \exp\left(-\frac{(x-0.75)^2 + (y-0.25)^2}{2\sigma_k^2}\right) + b\right) k_0,$$
(C.1)

where σ_k denotes the width of the two Gaussian peaks. The parameters *b* and k_0 allow us to adjust the average height and degree of variation in k(x, y). Specifically, the height is adjusted such that the total carrying capacity equals *K*, and the degree of variation is adjusted to give the desired relation between peaks and troughs. Specifically, we measure the degree of spatial variation in local carrying capacity as

$$v = \frac{\max k(x,y) - \min k(x,y)}{\min k(x,y)}.$$
(C.2)

A value of v = 0.25 therefore means that the local carrying capacity is 25% higher at the peaks than at the troughs. For Fig. C.7, landscapes are generated in a similar way, except that the heights and widths of the two peaks differ. For Fig. 4.4, the landscape is generated by adding white noise to the baseline level, filtered to have a reasonable amount of spatial autocorrelation, with the highest peak set to twice the height of the lowest trough.

Through competition, each individual obtains a share of the local carrying capacity, which we refer to as its resource share,

$$\rho_i = \frac{k(x_i, y_i)}{\sum_j n_{ij}}, \qquad (C.3)$$

where n_{ij} is the contribution of individual *j* to the effective density of competitors at the location of individual *i*, and the sum extends over all *N* individuals. The competitive impact of individual *j* on individual *i* decreases with the distance d_{ij} separating them, according to a Gaussian function with standard

deviation $\sigma_{\rm s}$,

$$n_{ij} = \exp(-d_{ij}^2/(2\sigma_s^2))/(2\pi\sigma_s^2);$$
 (C.4)

in the one-dimensional model, the divisor is $\sqrt{2\pi\sigma_s}$. Note that the effect n_{ii} of an individual *i* on itself declines as σ_s increases, because the individual then competes for resources over larger distances and thus has less of a negative impact on its available resources.

As defined, the resource share of an individual *i* is approximately K/N. This can be seen by assuming that the *N* individuals in the population are distributed over the arena according to the local carrying capacity, so that their expected density is N k(x, y)/K. Replacing the sum over individuals in Eq. C.3 with an integral over space, we obtain

$$\rho_i = \frac{k(x_i, y_i)}{\iint \frac{N k(x, y)}{K} \frac{\exp(-d_{ij}^2/(2\sigma_s^2))}{2\pi \sigma_s^2} \,\mathrm{d}x \,\mathrm{d}y}$$

$$\approx K/N + O(v) ,$$
(C.5)

where the second line assumes that spatial variation in the local carrying capacity is low. In our individual-based model runs, departures from the above occur due to clumping, fecundity variation over space (Section C.1.4), as well as discrepancies due to replacing the sum in Eq. C.3 with the integral in Eq. C.5 (especially when σ_s is very small or large relative to the arena). That said, the mean resource share is typically close to K/N in our model runs.

In Fig. C.1 we show the effect of spatial variation in local carrying capacity $k(x_i, y_i)$ on various components of fitness, including the resource share, ρ_i . Interestingly, ecological competition is weaker (ρ_i is higher) in regions of low carrying capacity (Fig. C.1A), increasing the survival probability of individuals in these regions (s_i , Fig. C.1B). This occurs because females are less likely to encounter preferred males wherever the carrying capacity is low, causing their fecundity to be lower due to increased mate-search costs (c_i ; Section C.1.4 and Fig. C.1C). Consequently, fewer offspring are produced than expected based on the low local carrying capacity, resulting in weaker competition among those offspring. The net result of lower ecological competition and higher search costs in regions with low local carrying capacity is that females have roughly equal fitness across space.

C.1.2 Survival

We assume that individuals that gain more resources are more likely to survive to reproductive maturity. The probability s_i of such survival is assumed to

be zero when an individual fails to gain any resources, to rise approximately linearly with its resource share ρ_i when that share is small, and to taper off at a maximal survival probability of s_{max} (ranging between 0 and 1). Specifically, we use a hyperbolic (or Holling type-2) function (Coulson et al., 2011) to relate resource share to the probability of survival,

$$s_i = \frac{s_{\max}}{1 + r/\rho_i},\tag{C.6}$$

where *r* is the resource share that must be obtained for an individual to survive with a probability equal to half the maximal survival probability. Unless stated otherwise, we assume that the maximum probability s_{max} of surviving to reproductive maturity equals 1.

The value of *r* is chosen to ensure that, on average, *K* individuals survive to reproduce if all individuals obtain an equal share of resources ($\rho_i = K/N$). By setting the expected survival probability s_i to K/N in Eq. C.6 and substituting $\rho_i = K/N$, we obtain $r = s_{max} - K/N$. With this choice of *r*, approximately *K* individuals survive each generation (with a variance that is typically small). For example, in Fig. C.1, the average survival probability was 0.484, close to the expected value of K/N = 1/2. While competition for resources causes substantial mortality, survival probabilities across the arena differ only slightly (Fig. C.1B). Importantly, the survival of an individual does not depend on whether or not it is a hybrid.

C.1.3 Mating

Of the individuals that survive to mate, the probability that female *i* chooses male *j* as a mate depends on whether his display trait matches her preference trait and on the spatial distance separating them. Females bearing a *P* (*p*) allele prefer males bearing a *Q* (*q*) allele by a factor α . We assume that females encounter males in the vicinity of their home location. Specifically, each female spends a proportion of time at distance d_{ij} from her home that is described by a Gaussian distribution with standard deviation σ_f , so that her encounter probability e_{ij} with a male at distance d_{ij} is proportional to

$$e_{ij} = \exp(-d_{ij}^2/(2\sigma_{\rm f}^2))/(2\pi\sigma_{\rm f}^2);$$
 (C.7)

in the one-dimensional model, the divisor is $\sqrt{2\pi}\sigma_{\rm f}$. In our main model, we assume that females encounter resources and males over the same spatial scales (i.e., $\sigma_{\rm f} = \sigma_{\rm s}$); we relax this assumption in Fig. C.5. The probability that female *i*

chooses male *j* as a mate is proportional to

$$p_{ij} = \alpha^{\delta_{ij}-1} e_{ij} , \qquad (C.8)$$

where δ_{ij} equals 1 when the display trait of male *j* matches the preference trait of female *i*, and 0 otherwise. Once a female chooses a mate, we assume that all her offspring are sired by that male (monogamy).

C.1.4 Reproduction

The fecundity of a female *i* is given by:

$$f_i = f_{\max}(1 - c_i)$$
, (C.9)

where f_{max} is the maximum fecundity and c_i (ranging from 0 to 1) measures the cost associated with finding a preferred mate for female *i*. The factor $1 - c_i$ is assumed to be zero when there are no preferred males locally, to rise approximately linearly with the local density of preferred males,

$$\mu_i = \sum_{\text{males } j} p_{ij} , \qquad (C.10)$$

and to taper off at 1 when preferred mates are readily encountered, resulting in maximal fecundity. Specifically, we use a hyperbolic (or Holling type-2) function (Doebeli and Dieckmann, 2003),

$$1 - c_i = \frac{1}{1 + m/\mu_i},$$
 (C.11)

where *m* is the value of μ_i at which a female's fecundity is halved by mate-search costs. Because μ_i is obtained by summing over the entire male population, its value can be large, on the order of the number of surviving males, so values of *m* on the order of the surviving population's size *K* are needed for costs to be appreciable. This is why we express *m* relative to *K*, specifying the ratio *m*/*K* in the figures. We refer to c_i as the mate-search cost of female *i* and to *m* as the strength of mate-search costs.

Unless noted otherwise, we use m = 500. In our main simulations (with m/K = 1), mate-search costs reduce female fecundity by about 50%, on average, from the maximum fecundity (Fig. C.1C), with relatively minor differences in fecundity among females over space. Other values for m are explored in Fig. 4.3. For m = 0, all females have equal and maximal fecundity. As m is raised, fecundity declines, on average, and becomes more variable, with females in low-

density regions or surrounded by non-preferred males having lower fecundity (Fig. C.2).

After mating, offspring are produced. Inheritance at both loci is Mendelian, and we assume no linkage between the display and preference loci, except where noted (Section C.2.6). To allow us to explore various parameters relating to competition and mate-search costs independently, we hold the total number of offspring constant at *N*. For each offspring, a mother is chosen in proportion to the females' fecundities. Consequently, the maximum fecundity f_{max} only matters insofar as it is high enough to result in at least *N* offspring being produced across the population. Similar patterns are observed when f_{max} is fixed and offspring numbers are given by a Poisson distribution with a mean of f_i for each female (data not shown). We consider *N* to be the total number of offspring surviving the phase during which resources are largely provided by the parents, after which the offspring migrate and begin the next phase of competition for resources.

C.1.5 Movement

Each offspring moves from its mother's location according to a distance drawn from a Gaussian function with mean 0 and standard deviation σ_m . Movements occur in all directions with equal probability.

C.2 Model extensions

To assess the robustness of our results, we consider several extensions and/or modifications to our main model described above.

C.2.1 Incorporating mating-dependent dispersal

To compare our results with those of Payne and Krakauer (1997), we consider mating-dependent dispersal. In their model, male movement distances are lower for males with better mating prospects, and we thus assume that the movement distance of male j is drawn from a Gaussian function with mean 0 and standard deviation

$$\sigma_{\mathrm{m},j} = \sigma_{\mathrm{m}} \exp\left(-l \frac{\sum_{i} p_{ij}}{\sum_{ik} p_{ik}}\right) , \qquad (C.12)$$

where *l* determines how quickly movement distances decrease with increasing mating prospects and p_{ij} is given by Eq. C.8 in Section C.1.3. For l = 0, the above reduces to our main model. We find that the addition of mating-dependent

dispersal in males extends coexistence times only marginally, if at all (compare Fig. C.3A to C.3B). We also examine the related case in which males with low mating prospects move farther, but again, coexistence times are not appreciably prolonged in our individual-based model.

C.2.2 Introducing multiple allelic types

To examine whether coexistence of more than two types is possible, we extend our main model so that one of n alleles p_1, \ldots, p_n can occur at the preference locus and one of n alleles q_1, \ldots, q_n can occur at the display locus. Specifically, in Fig. 4.4, we consider n = 10 preference and display types. A female with preference allele p_i prefers males with display allele q_i to all other males by the factor α . All other components of mate choice remain the same as for our main model with n = 2 mating types.

C.2.3 Allowing competition to impact fecundity

In our main model, competitive interactions reduce the survival probability of an individual. Alternatively, individuals that gain fewer resources might survive, but have lower fecundity. To explore this possibility, we allow all *N* offspring to survive, while reducing their reproductive success according to the impact of competition, as measured by s_i . Specifically, for males, the probability of being chosen as a mate is set to $p_{ij} = \alpha^{\delta_{ij}-1}e_{ij}s_i$. Likewise for females, fecundity is set to $f_i = f_{\max}(1 - c_i)s_i$. Such competition-dependent fecundity generates less demographic stochasticity, because all individuals reach reproductive maturity and can mate, albeit with reduced probability when their resource share ρ_i is low. Indeed, all else being equal, incorporating competitive effects on fecundity, rather than survival, enables long-term coexistence over a wider range of parameters (compare Fig. C.6 to Fig. 4.3).

C.2.4 Altering the strength of density-dependent competition

To measure the strength of density dependence on survival, we may define $\lambda = r/(1 - K/N)$, with $r = s_{max} - K/N$ (Section C.1.2). In our main model, the maximum survival rate s_{max} is set to 1 so that $\lambda = 1$, indicating that survival is strongly density-dependent. At the other extreme, if s_{max} is set to K/N, all individuals survive with probability $s_{max} = K/N$, regardless of their resource share, so there is no density-dependent effect on survival ($\lambda = 0$). As shown in Fig. C.4B, coexistence does not occur in the absence of density dependence ($\lambda = 0$); spatial variation in local carrying capacity then becomes irrelevant and

cannot stabilize mating domains in space. As the importance of competition increases (larger λ , or equivalently, larger s_{max}), coexistence can occur over a broader parameter space. Once about half of the mortality is due to density-dependent competition ($\lambda > 0.5$), results become similar to those for $\lambda = 1$ (Fig. C.4B).

We also explored the effects of density-dependent competition by varying the total carrying capacity K (Fig. C.4C), while holding the total number of offspring constant. Because we are interested in the effects of population size per se, we also keep constant the relative strength of mate-search costs (m/K = 1), so the ease with which females encounter preferred mates remains unaffected by variation in K. Again, when density-dependent competition is weak (K near N), coexistence requires much higher levels of spatial variation in local carrying capacity. Conversely, when K is very small, stochasticity in survival becomes so great that coexistence is not maintained without high levels of spatial variation in local carrying capacity. Thus, intermediate values of K, relative to N, best facilitate co-existence.

The effects of demographic stochasticity can also be seen in Fig. C.4D, where the strength of density dependence and the expected survival probability K/N are held constant ($\lambda = 1$ and K/N = 1/2), while the total number N of offspring is varied, as is the time point at which co-existence is evaluated (at generation 5N). Again, we also keep constant the relative strength of mate-search costs (m/K = 1). All else being equal, larger population sizes facilitate the maintenance of coexisting types, as expected given the reduced stochasticity.

C.2.5 Altering the spatial scale of competition, mate-search, and migration

In the main model, we specified the spatial scale of several phenomena, including the breadth of the competition function ($\sigma_s = 0.05$), the breadth of the mate-search function ($\sigma_f = 0.05$), and movement distances ($\sigma_m = 0.05$). Fig. C.5 illustrates the minimum level of variation, v, in local carrying capacity required for coexistence to occur in our simulations for at least 5*N* generations. Coexistence is easier to maintain when females search in smaller regions for males (small σ_f) and when movement is localized (small σ_m) because mating types that predominate in different spatial locations remain more isolated. By contrast, coexistence is easier to maintain when competition occurs across a broad spatial range (large σ_s) because individuals near the resource peaks compete more strongly for resources available in the troughs, reducing the population size in the troughs and promoting isolation of the mating types near each peak.

C.2.6 Incorporating alternative genetic architectures

Our main model assumes free recombination between the trait and preference loci. Fig. C.8 explores the effect of linkage, finding no substantive differences between complete linkage and free recombination between the trait and preference loci.

To test whether our findings are robust to changes in the number of loci, we consider a quantitative genetic model in which an individual's preference and display trait are determined by two quantitative characters. This model can be interpreted as assuming that a large (infinite) number of additive loci code for each of the two traits. Complementing our main model, which features a finite number of alleles, this extension allows for arbitrarily many mating types. In this quantitative genetic model, the probability that female i mates with male j is proportional to

$$p_{ij} = \exp(-(p_i - q_j)^2 / (2\sigma_p^2))e_{ij}$$
, (C.13)

where $p_i - q_j$ is the difference between the preference trait of female *i* and the display trait of male *j*, σ_p denotes the strength of female preference (smaller σ_p means females are choosier), and e_{ij} is proportional to the encounter probability between female *i* and male *j*, as defined in Eq. C.7. Offspring trait values are drawn from a Gaussian function centred at the mean of the parental phenotypes for each trait, with a standard deviation σ_0 that measures the variation among offspring due to segregation, recombination, and mutation. All other details of the quantitative genetic model are the same as for our main model.

Despite the different genetic assumptions, the behaviour of the quantitative genetic model closely resembles that of the allelic model (Fig. C.8). Coexistence of mating domains is again possible over a wide range of parameters, provided female preferences are sufficiently strong (small σ_p). As in the allelic model, loss of mating domains in the quantitative model, when it happens, tends to occur through the replacement of one type by the other. Compared with the allelic model, the quantitative genetic model exhibits two additional mechanisms through which mating domains may be lost. First, when female preference is weak (large σ_p), interbreeding between adjacent mating domains may become so common that the resultant offspring form their own mating domains, facilitating the merging of the original domains. Second, the random drift of matched trait and preference values in one mating domain may cause them to coincide by chance with the values in an adjacent mating domain, so the two originally separate domains may merge due only to the random genetic drift of quantitative mating traits that results from segregation, recombination, and mutation in finite populations.

We note that our results bear some connection to those of Day (2000), who analyzed a spatial model of costly sexual preferences and male traits using a quantitative genetic model. A key difference is that Day (2000) incorporated ecological differences across space, with natural selection favoring different optimal male traits as a function of position (essentially incorporating niche differences across space). In parallel to our results, costly female preferences evolved and could maintain more diversity in male traits than expected based on the variation in the optimum trait across space.

C.2.7 Incorporating asymmetric display costs

Display traits can incur fitness costs in males. Our main model assumes that such costs, if present, affect all individuals equally. It may often be the case, however, that display traits differ in their effects on fitness. We therefore examine what happens when the Q allele causes males to have a reduced survival probability relative to those carrying the q allele (i.e., for Q-bearing individuals, the survival probability s_i is reduced by a factor 1 - a, with a ranging between 0 and 1). Provided that the resultant cost is not so strong that the stabilizing effect of spatial variation in local carrying capacity is overwhelmed by selection against Q-bearing males, our main findings remain largely unchanged (Fig. C.9).

Symbol	Eq.	Description
Model parameters		
a		Strength of selection against <i>Q</i> -bearing males (only C.2.7)
k(x,y)	C.1	Local carrying capacity at location (x, y)
1	C.12	Strength of mating-dependence in male dispersal (only C.2.1)
т	C.11	Strength of mate-search costs
s _{max}	C.6	Maximum survival probability
υ	C.2	Spatial variation in local carrying capacity
Κ		Total carrying capacity
Ν		Number of offspring
α	C.8	Strength of female preference
f_{\max}	C.9	Maximum female fecundity
λ		Strength of density-dependent competition
$\sigma_{ m f}$	C.8	Width of mate-search distribution
$\sigma_{\rm k}$	C.1	Width of peaks in local carrying capacity
$\sigma_{ m m}$		Width of movement distribution
$\sigma_{ m o}$		Width of offspring distribution (only C.2.6)
$\sigma_{ m p}$	C.13	Width of female preference (only C.2.6)
$\sigma_{ m s}$	C.4	Width of competition distribution
Model variables		
Ci	C.11	Mate-search costs of female <i>i</i>
d_{ij}	C.4	Spatial distance between individuals i and j
e _{ij}	C.7	Propensity for female i to encounter male j
f_i	C.9	Fecundity of female <i>i</i>
n _{ij}	C.4	Competitive effect of individual <i>j</i> on individual <i>i</i>
p_{ij}	C.8	Propensity for female i to choose male j as a mate
Si	C.6	Survival probability of individual <i>i</i>
μ_i	C.10	Local density of preferred males as seen by female i
$ ho_i$	C.3	Resource share of individual <i>i</i>

TABLE C.1: Model parameters and model variables.



FIGURE C.1: Variation in three components of fitness as a function of the local carrying capacity experienced by each individual at t = 1000 for the model run in Fig. 4.1D. Individuals are coloured according to their genotype at the display locus. **A.** Resource share ρ_i in males and females. **B.** Survival probability s_i of males and females. **C.** Mate-search costs c_i of females. Lines show least-squares regression lines.



FIGURE C.2: Mate-search costs for the model run in Fig. 4.1D. Panels in column **A** are identical to those in Fig. 4.1D, except that only females are shown and they are coloured according to their preference allele. Panels in column **B** show the costs associated with searching for a mate and rejecting non-preferred males for each female (Eq. C.9), as a function of her location *y*. For m/K = 1, female fecundity is typically only halved by mate-search costs.



FIGURE C.3: Effects of mating-dependent dispersal in males. Panels show distributions of allele frequencies at the display locus through time across 1000 replicate model runs in a two-dimensional homogeneous landscape; coexistence occurs only while these frequencies remain intermediate. Darker shading indicates a higher probability of observing a given frequency of the *Q* allele. Panel **A** is identical to Fig. 4.2B. Panel **B** is the same as **A**, except with mating-dependent dispersal in males (l = 100). Results for other values of *l* are qualitatively identical. Model runs are initialized as in Fig. 4.2. All other parameters are as in Fig. 4.1B.



FIGURE C.4: Minimum level of spatial variation v in local carrying capacity needed to ensure long-term coexistence (grey regions) in a two-dimensional bimodal landscape. v was increased until the average persistence time of 20 replicate runs exceeded 5N generations (vertical lines indicate standard errors). **A.** Effect of the strength α of female preference. Coexistence becomes more likely as female preferences become stronger (larger α), although once preference exceeds $\alpha \approx 5$, its impact is small. **B.** Effect of the strength λ of density-dependent competition (varying s_{max} while holding K = 500 and N = 1000). The limit $\lambda = 0$ corresponds to completely density-independent survival, while the limit $\lambda = 1$ corresponds to completely density-dependent survival. **C.** Effect of the expected survival probability K/N (N = 1000, $\lambda = 1$, and m/K = 1 are held constant). Values near K/N = 0 correspond to very small mating populations, while the limit K/N = 1 corresponds to the absence of ecological competition. **D.** Effect of population size N (holding constant K/N = 0.5, $\lambda = 1$, and m/K = 1). All other parameters are as in Fig. 4.1D.



FIGURE C.5: Minimum level of spatial variation v in local carrying capacity needed to ensure long-term coexistence (grey regions) in a two-dimensional bimodal landscape. v was increased until the average persistence time of 20 replicate runs exceeded 5N generations (vertical lines indicate standard errors). The three curves show the effects of the competition width σ_s (red), the width of the mate-search distribution σ_f (green), and the width of the movement distribution σ_m (blue), while holding all other parameters constant at their values in Fig. 4.1D.



Strength of mate-search costs in females, m/K

FIGURE C.6: Conditions for long-term coexistence with competition-dependent fecundity (Section C.2.3) in a two-dimensional bimodal landscape. All parameters are as in Fig. 4.3.



FIGURE C.7: Effects of altering the shape of the local carrying capacity (Eq. C.1) in a two-dimensional bimodal landscape. Shading indicates how long polymorphism persists at the display locus (darker = longer). Each cell represents the mean time to loss of polymorphism for 10 replicate model runs. Side panels indicate the extent of spatial variation in local carrying capacity along transects at y = 0.25 for nine parameter combinations indicated by the closest black circle. The inset at the bottom center corresponds to the parameter combination used in Fig. 4.3. Spatial variation in local carrying capacity is relatively weak throughout this figure, with v ranging from 0.28 for $\sigma_k = 0.01$ (far left) to 0.038 for $\sigma_k = 0.2$ (far right). All other parameters are as in Fig. 4.1D.



Spatial variation in local carrying capacity, v

FIGURE C.8: Effects of changes in genetic architecture in a two-dimensional bimodal landscape. Variance in display trait after 5,000 (**A**) and 25,000 (**B**) generations for a variety of genetic architectures, averaged over 20 replicate model runs (vertical lines indicate standard errors). The dashed line indicates the maximum possible variance in the allelic model (0.25). For determining variances in the allelic model, alleles Q and q are assigned trait values 0 and 1, respectively. In the quantitative genetic model, the initial preference/display trait values are set to 0/0 or 1/1 (corresponding to P/Q or p/q in the allelic model) with equal probability, yielding an initial variance of 0.25. Over time, the variance of 0.25 can be exceeded due to random genetic drift. For comparison, the red curve shows results of our main model. Model runs are initialized as in Fig. 4.2. All other parameters are as in Fig. 4.1; in the quantitative model, $\sigma_0 = 0.01$.



Spatial variation in local carrying capacity, v

FIGURE C.9: Effects of asymmetric fitness costs of display traits in the allelic model in a two-dimensional bimodal landscape. Variance in display trait after 5,000 (**A**) and 25,000 (**B**) generations when males bearing the Q allele have their survival lowered by a factor 1 - a relative to males bearing the q allele, averaged over 20 replicate model runs (vertical lines indicate standard errors). The dashed line indicates the maximum possible variance in this allelic model (0.25). For comparison, the red curve (identical to that in Fig. C.8) shows results of our main model, corresponding to the limit a = 0. Model runs are initialized as in Fig. 4.2. All other parameters are as in Fig. 4.1.
Appendix D

Hybrid zones (Chapter 5)

D.1 Hybrid zone structure likelihood method

Here we describe a likelihood method for fitting a series of steps to allele frequency data, as in figure 5.1. We consider a one-dimensional transect through a hybrid zone, with *m* "patches". We assume an initial step height at zero, before the first patch, and a final step height at one, after the last patch. A stepwise model through the hybrid zone will consist of *k* step locations s = $\{s_1, s_2, \dots, s_k\}$ and k - 1 step heights (in addition to the first and last step heights fixed at zero and one), $h = \{h_1, h_2, \dots, h_{k-1}\}$, where h_i is the height between steps s_i and s_{i+1} . The stepwise model "partitions" the patches, and we will refer to a particular partition as the set of patches between two adjacent model steps. The step heights correspond to the estimated allele-frequency for each partition. Our method aims to quantify both the number and placement of these steps using a maximum likelihood approach.

Suppose that the expected genotype frequencies within the *i*th patch are $E_i[AA]$, $E_i[Aa]$, and $E_i[aa]$, and the *i*th patch has observed genotype counts of $x_{i,AA}$, $x_{i,Aa}$, and $x_{i,aa}$ for the genotypes AA, Aa and aa. The likelihood of sampling (with replacement) from the underlying frequencies is given by the multinomial probability

$$\binom{n_i}{x_{i,AA} \quad x_{i,Aa} \quad x_{i,aa}} E_i [AA]^{x_{i,AA}} E_i [Aa]^{x_{i,Aa}} E_i [aa]^{x_{i,aa}}$$

where $n_i = x_{i,AA} + x_{i,Aa} + x_{i,aa}$ is the number of individuals in the *i*th patch and $\binom{n}{x_1 x_2 x_3}$ is the multinomial coefficient defined as $n!/(x_1!x_2!x_3!)$.

The expected genotypic frequencies are a function of the allele frequencies given by the partition allele frequency and the inbreeding coefficient for the patch, f_i . Since f_i is not directly of interest we set it to its most likely value,

given the local genotypic values; that is, we define f_i as

$$f_i = 1 - \frac{x_{i,Aa}}{2p_i(1-p_i)n_i}$$

where p_i is the observed allele frequency in the *i*th patch. If the *i*th patch is within the *j*th partition, it shares that partition's step height, h_j , and its expected frequencies are

$$E_i[AA] = h_j^2 + f_i h_j (1 - h_j)$$

$$E_i[Aa] = 2h_j (1 - h_j)(1 - f_i)$$

$$E_i[aa] = (1 - h_j)^2 + f_i h_j (1 - h_j)$$

In cases where an expected frequency was negative, that frequency was set to zero and the other expectations were standardized appropriately.

The likelihood of observing the data across all m patches can then be calculated as

$$\Pr(x|s,h) = \prod_{i=1}^{m} \binom{n_i}{x_{i,AA}, x_{i,Aa}, x_{i,aa}} E_i[AA]^{x_{i,AA}} E_i[Aa]^{x_{i,Aa}} E_i[aa]^{x_{i,aa}}$$
(D.1)

where the product is taken over all m patches. For a given set of step locations s we find the heights h that maximize equation (D.1) using univariate optimization in R (R Development Core Team, 2008).

For a given number of steps, k, equation (D.1) must be maximized with respect to step locations. For large data sets it is not feasible to exhaustively search for the best model, as the number of possible models is on the order of m! for m patches. Instead, we used a genetic algorithm to identify the best model for a given number of steps. The algorithm begins with a randomly generated initial pool of k-step models. It then runs through multiple generations of mutation, recombination and selection. Mutation randomly replaces one or more steps within a model with other possible steps, recombination switches steps between different models (while maintaining step number), and selection samples the best models, weighted by their log-likelihood, to initiate the next generation.

To find the number of statistically significantly steps required to best explain the data, we started with the best single step model (k = 1) and added steps until the difference between the best k step model and k + 1 step model was not statistically significant following a likelihood ratio test. Each step requires two additional parameters (a step location and a step height), so we compared the likelihood ratio with a Chi-squared distribution with two degrees of freedom. Simulations revealed that our use of two degrees of freedom was in fact a conservative assumption, while one degree of freedom was not. This method to fit mosaic hybrid zone data is available as an R package at http://www.zoology.ubc.ca/prog/mosaic/