

**Trematode infection and the distribution and dynamics of
parthenogenetic snail populations**

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SUMMARY

According to the Red Queen hypothesis for sex, cross-fertilization should be positively associated with the probability of exposure (*risk*) to virulent parasites. Unfortunately, risk is difficult to measure in the wild, and *prevalence* of infection is often substituted for risk. Here I suggest that prevalence of infection may not generally suffice as a surrogate for risk, since the Red Queen model can make opposite predictions depending on the distribution of risk in the wild. Specifically, the results of a matching-alleles model suggest that asexual populations should be more infected than sexual populations, when (i) the variance in risk among populations is small, and (ii) the mean risk of exposure to parasites is near the point where selection switches to favoring sex over asex. If, however, the variance in risk among populations is large, sexual reproduction should be positively associated with the prevalence of infection. In addition, the coefficient of variation for reproductive mode should increase sharply at the switch point. In light of these results, I re-evaluated data from two studies on the distribution of males in 95 populations of a freshwater snail (*Potamopyrgus antipodarum*). Populations of these snails are often mixtures of sexual and asexual individuals, and the frequency of males is correlated with the frequency of sexual females in the population. The results show a large, highly skewed variance among populations for prevalence of infection by larval trematodes. The results also show a positive, significant relationship between prevalence of infection and the frequency of males, with a sharp increase in the coefficient of variation at intermediate prevalence. In addition, experimental studies suggest that some of the necessary conditions of the Red Queen hypothesis are also met in this system. Specifically, the most common trematode infecting these snails is: (i) adapted to infecting

local host populations of the snail, and is (ii) more infective to clones that were common in the recent past. It is too early to know if the parasite theory is sufficient to explain the widespread distribution of sex. I suggest that the theory is not sufficient, but that parasites in combination with mutation accumulation in clonal lines may explain the maintenance of sex in species that occasionally produce apomictic mutants.

Key words: asexual reproduction, parasitic castration, *Potamopyrgus antipodarum*, Red Queen hypothesis, sexual reproduction, trematodes

INTRODUCTION

Ecologists and evolutionary biologists are increasingly interested in parasites. This interest stems in part from: (i) models showing that parasites can control the density of host populations (May & Anderson, 1978); (ii) models showing that host-parasite coevolution could lead to the maintenance of genetic diversity and, possibly, the maintenance of sexual reproduction (e.g., Jaenike, 1978; Bremermann, 1980; Hamilton, 1980, 1982; Bell, 1982; Judson, 1995), and (iii) phylogenetic studies showing the co-speciation of host and parasites (e.g., Brooks *et al.* 1981). In addition, parasites were suggested as influential in the choice of mates, and hence the divergence of sexually selected traits in natural populations (Hamilton & Zuk, 1982). Thus parasite-host interactions, which were almost totally ignored in the ecological and evolutionary literature 20 years ago, were suddenly suggested as potentially involved in regulating the density and genetic diversity of populations, the maintenance of sex, mate choice, and the generation of new species.

One challenge for any theory is to make unambiguous and, ideally, unique predictions. The Red Queen theory of sex is based on the idea that parasites should be under strong selection to be able to infect the most common local host genotypes (Haldane, 1949; Jaenike, 1978; Bremermann, 1980; Hamilton, 1980, 1982). Hence, as a clonal mutant spreads in a sexual population, it should be selected against in direct proportion to its frequency. If infections are sufficiently virulent to compensate for the reproductive advantage of clonal females, then sexual females should be preserved in the short term. This leads to the expectation that asexual populations, where they exist, should be associated with a low risk of infection. However, the individual hosts from

asexual populations should be easier to infect by local coevolving parasites than individuals from a sexual population. So, on one hand, sex should be associated with the relevant selection pressure (parasites); but, on the other hand, asexual populations are expected to have higher levels of infection (assuming all else equal). This kind of reasoning has led to the criticism that the parasite theory can predict any kind of association between parasites and host sex in the wild, thereby making the theory unfalsifiable (e.g., Kondrashov, 1993).

I suspect that part of the solution to this apparent paradox may lie in clearly discriminating between *risk* of infection and *prevalence* of infection. I use "risk" here to mean the probability of exposure to infective parasite propagules, and "prevalence" to mean the frequency of infected individuals in a population. A simple model is first presented to estimate risk and prevalence in sexual and asexual populations. I then compare the results of the model to results gained from a freshwater snail (*Potamopyrgus antipodarum*), which has populations that are either completely asexual or contain mixtures of sexual and asexual individuals.

A MODEL

In what follows, I present a simple model to generate the expected relationship between risk and prevalence of infection in sexual and asexual populations. Two haploid loci are assumed, each with two alleles. Contact between host and parasite genotypes occurs at random, and infection takes place if the parasite matches the host at both loci. The parasite is killed if it does not match the host at both loci. This is the matching-alleles model of host-parasite coevolution (see Otto & Michalakis, 1998), which is based on the

idea that hosts possess self/non-self recognition systems for the detection and elimination of parasites.

The recursion equation for the frequency of the ij^{th} host type (H_{ij}) in the next generation is given by

$$H'_{ij} = (1 - r) \frac{H_{ij}(1 - TVP_{ij})}{\bar{W}_H} + rh_i h_j,$$

where i and j give the alleles at the first and second locus respectively (e.g., H_{11} has allele 1 at both loci); T gives the probability of host contact with a parasite propagule (i.e., risk); V gives the reduction in fitness for infected hosts (i.e., infected hosts have a fitness of $1 - V$); and \bar{W}_H gives the mean fitness of hosts after selection. In addition, h_i gives the normalized frequency of the i^{th} allele at the first locus, and h_j gives the normalized frequency of the j^{th} allele at the second locus. Finally, r is the frequency of recombination between loci (see Gillespie, 1998 for a derivation of r).

Similarly, the recursion equation for the frequency of the ij^{th} parasite genotype (P_{ij}) in the next generation is given by

$$P'_{ij} = (1 - r) \frac{TP_{ij}H_{ij}}{\bar{W}_P} + rp_i p_j,$$

where i and j give the alleles at the first and second parasite locus respectively (e.g., P_{11} has allele 1 at both loci), and \bar{W}_P gives the mean fitness of parasites after selection. p_i gives the normalized frequency of the i^{th} allele at the first parasite locus, and p_j gives the normalized frequency of the j^{th} allele at the second parasite locus. These last two variables were modified in the simulation to incorporate a mutation rate of 0.003. The high mutation rate is a proxy for both mutation and migration, and is set above zero to

prevent parasite genotypes from going to fixation, especially under the high virulence that leads to high amplitude oscillations (e.g., Lively, 1999).

The simulations were initiated in linkage equilibria for both host and parasite, and allowed to run for 900 generations; this period was enough to allow the cycles to reach stable values for their periods and amplitudes. I then calculated the prevalence of infection as:

$$Prev = \sum_{i=1}^2 \sum_{j=1}^2 TP_{ij} H_{ij}.$$

I also calculated the mean of this value for generations 901-1000 for both sexual and asexual hosts.

For sexual host populations, I set the recombination rate (r) to 0.5 to simulate the situation where the interaction loci are on different chromosomes for both host and parasite. To simulate asexual host populations, I fixed the host for a single genotype; parasites remained sexual in these runs with a recombination rate of one half ($r = 0.5$). In all simulations, I set virulence (V) to 0.8, to mimic the situation for the highly virulent larvae of castrating trematodes. These simulations assume that, even if the entire host population is infected, the fitness of individuals is sufficient to replace the population in the next generation (in other words, uninfected intermediate hosts are producing greater than 5 offspring each).

RESULTS

The results show that (all else equal) an asexual population should have a higher prevalence of infection for any given risk of infection (Fig. 1A). For example, if each individual from a single asexual clone were exposed to one propagule from a population

of coevolving parasites, we would expect all of them to become infected under this model. However, the same rate of exposure in a sexual population would produce only about one third of this number of infected individuals. The genetic diversity of the sexual population has reduced the prevalence of infection by about two thirds.

This result, by itself, would suggest that we should see populations composed of a single clone associated with higher rates of infection. But the argument under the Red Queen hypothesis is that parasites are selecting for the mode of reproduction, not simply responding to it. Thus at some risk of infection, the selection imposed by parasites selects for sexual reproduction in the host population. In a recent simulation study, we asked: what is the probability of infection that would shift the selection on hosts to reproduce sexually versus asexually (Howard & Lively, 1994)? The results of that model suggest that for highly virulent parasites, such as castrating species of trematodes ($V \geq 0.8$), a 30% chance of exposure to miracidia would shift selection on the host to cross-fertilization, even for a two-fold cost of sex (Details given in legend to Fig. 1).

Fig. 1B gives the expected results for infection in sexual and asexual populations given that a risk of exposure of 0.3, or greater, shifts the population to sexual reproduction. The results show that, if the risk of exposures is great enough, the most infected populations should also be sexual. But the figure also shows that there should be a large overlap in prevalence in sexual and asexual populations, especially in the segment of risk parameter space in which the shift in host reproductive modes occurs (here at 0.3).

This overlap in prevalence in sexual and asexual populations is more clearly illustrated in Fig. 2, which gives the expected frequency of sexual individuals in the simple model against risk of exposure (Fig. 2A) and parasite prevalence (Fig. 2B). It is

especially obvious here that risk does not translate directly into prevalence, and that there is a large overlap zone for expected prevalence in sexual and asexual populations.

Nonetheless, if there is a wide distribution of risk and prevalence in the wild, we should expect, if the Red Queen hypothesis is correct, that the frequency of sexual individuals should be positively correlated with the prevalence of infection (Fig. 2B). But we should also expect the data to show substantial scatter at intermediate levels of prevalence.

If, however, the variance in risk is small, and the mean risk is positioned very near the transition point, then sexual and asexual populations would not be expected to differ in prevalence of infection in the wild, or sexuals may be even less infected than asexuals. Hence, the general criticism of the Red Queen hypothesis appears to be correct, because the existence and direction of any significant correlation depends on the position of the mean and the variance in risk. However, it is possible to reformulate the predictions for the biogeographic distribution of sexual host populations: sexual host populations should be positively associated with the prevalence of infection by virulent parasites, but only if the range of prevalences is high and includes populations with very low and high prevalences. In addition, the variance in reproductive mode should increase dramatically with the prevalence of infection.

THE DISTRIBUTION OF ASEXUAL SNAIL POPULATIONS

Based on these predictions, I reanalyzed data for the frequency of males and the prevalence of castrating digeneans for a common freshwater snail (*Potamopyrgus antipodarum*) in New Zealand lakes and streams (Lively, 1987, 1992). The frequency of males in this gonochoric gastropod is significantly correlated with the frequency of sexual females in populations that contain both diploid sexual individuals and triploid

asexual individuals (Fox *et al.* 1996), and it serves as a measure of the frequency of sexual individuals in the population. The frequency of males is highly variable among populations, and many populations that contain no males appear to be composed completely of asexual females. The data set includes 65 lakes that were sampled between 1985 and 1991, and 30 streams that were sampled between 1985 and 1986. The snails (usually about 100) from all 95 locations were dissected to determine their gender and the presence/absence of trematode larvae; these larvae from about a dozen different species invariably destroy the reproductive organs of both males and females. Most of the lakes were sampled in multiple locations and/or multiple years; means were calculated from these sample to provide a single datum for each location.

The distribution of prevalences is given in Fig. 3. It is apparent from this distribution that there is a large variance in prevalence, and that the distribution is highly skewed. Specifically, there are many populations with low prevalence, and a few populations with high prevalence.

If the simple model given above can be generalized to the more complicated situation for the snails, then we would expect to find that prevalence is positively associated with sex, and that there are very few highly sexual populations having low prevalences. The results are consistent with these expectations (Fig. 4). The product-moment correlation between prevalence of infection and male frequency is highly significant ($r = 0.363$; $df = 94$; $P < 0.001$ for log transformed data; identical results were obtained for the Spearman rank correlation). In addition, there are very few highly sexual populations (>10% males) where the prevalence of parasites is low (<5%). Finally, the

coefficient of variation for male frequency increases sharply at intermediate values of prevalence (Fig. 5), as predicted by the model.

Although these results are consistent with expectation under the Red Queen, there are alternative explanations that might also fit the data. One sensible alternative is that males are simply more susceptible to infection than females. Such a gender asymmetry would produce a positive relationship between parasite prevalence and male frequency without any underlying coevolution. In laboratory infection experiments, however, males were not more susceptible than females (Lively, 1989). This set of experiments involved fully reciprocal cross-exposure treatments between one set of two lakes, and another set of three lakes. Hence, I could estimate relative susceptibility of males and females to both local and foreign sources of parasites. There were no significant differences between males and females in experimental infections for any of the five comparisons using the local parasite source, or any of the eight comparisons involving remote sources of parasites. There is therefore no indication that males are more susceptible to parasites from either potentially coevolving sources (the local sources) or non-coevolving sources (the remote sources). To determine whether there might have been a small, difficult-to-detect bias towards greater male susceptibility, I collapsed all thirteen comparisons into a single 2-by-2 matrix (infected females: 286; infected males 225; uninfected females: 871; uninfected males: 338). The difference in infection in this more powerful test was also non-significant ($c^2 = 0.01$; $df = 1$; $P = 0.916$). Note added 12Dec03: the 286 above should be 586.

These latter results suggest that the observed correlation between male frequency and parasite prevalence (Fig. 4) is not likely to be an artifact of greater male

susceptibility. I nonetheless reexamined the data by calculating the correlation between male frequency and the prevalence of infection in females. Thus, any bias in male susceptibility under field conditions could not affect the relationship between male frequency and prevalence of infection. I am less confident in these estimates for prevalence, because all data were excluded for which gender and infection were not determined for the same set of individuals (Note: I often dissected many extra snails in an effort to detect rare parasites where gender was not examined). The results of this reanalysis, however, were virtually identical to those gained from the fuller data set ($r = 0.393$; $df = 94$; $P < 0.001$). Thus there is a positive, significant relationship between male frequency and prevalence of trematode infection in the wild, independent of whether males are included in the estimates of prevalence. Thus the parasite theory of sex cannot be rejected by these data.

I wish to emphasize that male *P. antipodarum* are not environmentally induced by cues that might be associated with risk of infection, but rather are genetically determined (chromosomal sex determination). Hence the above results suggest the possibility that the sexual females (which produce the males) have not been replaced by asexual females in those populations where parasites are abundant enough to generate strong, frequency-dependent selection against asexual lineages; but there is no indication that either sex or gender is a facultative response to the presence of parasites.

DISCUSSION

Here I have considered expectations for the biogeography of sex if parasites are responsible for the persistence of sex in species that occasionally produce ameiotic

mutants. Based on the results of a simulation model, I argue that sexual populations may be either more infected or less infected than asexual host populations, depending on the distribution of risk of infection and parasite prevalence in natural populations. However, the model predicts that a negative association should only be observed between host sex and parasite prevalence under very narrow conditions, which can be specified. Hence, the parasite model of sex is subject to test based on biogeographic data.

Specifically, assuming that parasites contribute to selection for sex in local host populations, a negative association between host sex and parasite prevalence would require that the variance in risk is small, and that the mean risk of infection is positioned very near the "switch point." (The switch point is the minimum risk of infection that selects for sexual reproduction.) For the model present above, this combination should show asexual populations to have higher prevalences of infection than sexual populations. It should also show a narrow range for the distribution of prevalences among populations, with few populations that have low prevalences.

If however there is a wide variance for risk, the variance in prevalence should also be high, and sexual populations should show a tendency to have higher prevalences of infection than asexual populations. This association is largely driven by selection in low-risk, low-prevalence populations to favor asexual reproduction. But, because of the expected overlap in prevalence between sexual and asexual populations around the "switch point," the data should be very messy. In particular, the variance in sex should increase dramatically in the region of the switch point (which would have the side effect of making any positive association more difficult to detect).

Data for the frequency of snails (*P. antipodarum*) infected by castrating trematode larvae show a large range (0-50%) and highly skewed distribution for 95 populations in New Zealand (Fig. 3). Many populations show a very low prevalence and a few populations show a high prevalence. If the arguments given above are correct, this is the kind of situation where sexual reproduction in hosts should be associated with higher levels of infection than asexual host populations. Such an association is in fact observed (Fig. 4). In addition, the coefficient of variation spikes at an intermediate level of prevalence, as expected under the model (Fig. 5).

These results are interesting in their own right, but I have a few reservations about the model. Firstly, the model is much simpler than the complicated situation observed in the snails. Most pressing is that the genetics underlying resistance in the snails (and in general) will be much more complicated and interesting than the two-locus, two-allele haploid model presented here. Secondly, the snails seem to have either asexual populations or mixed populations (sexuals and asexuals together), instead of either sexual or asexual populations as assumed by the model. It nonetheless seems that the basic conclusions of the model are likely to hold, provided mixed populations have greater genetic diversity for resistance and that this diversity reduces, but does not eliminate, infection at the switch point.

Another way to attack the ecological hypotheses for sex is to determine if the necessary conditions of the theories are met. One of these conditions for the Red Queen hypothesis is that the most common host genotypes become disproportionately infected by parasites, and driven down in frequency. If this is not the case in the wild, then the Red Queen theory is surely incorrect. We have found both to be true for the New

Zealand snail system. Specifically, we have shown that among lakes, the most common clone is sometime significantly overinfected and sometimes significantly underinfected (Dybdahl & Lively, 1995). This result is expected if parasites are responding to common host genotypes with a time lag (Dybdahl & Lively, 1995; Morand *et al.* 1996; Gandon *et al.* 1996). In addition, we have found that change in the frequency of host clones is correlated with the lagged change in infection of these same clones, which meets a clear prediction of the Red Queen model (Dybdahl & Lively, 1998). Finally, we have found in two separate experiments that recently common clones are more susceptible to infection by local parasites than clonal genotypes that were rare during the same period of time (Dybdahl & Lively, 1998; Lively & Dybdahl, 2000a). In the second of these experiments, we also found that the recently common clones were not more susceptible than rare clones to a remote source of parasites (Lively & Dybdahl, 2000a). This later finding suggests that local coevolutionary interactions with parasites accounts for the advantage of possessing a rare genotype, rather than greater resistance *per se* (see also Lively & Dybdahl, 2000b); and it explains previous experimental results showing strong local adaptation by parasites in this system (Lively, 1989). None of these experimental studies confirm that sex in the snails is maintained by parasites; but the data could have put the Red Queen in an extremely embarrassing position.

The Red Queen theory is, in fact, put into a rather embarrassing position by a recent study of parasitoids. Kraaijeveld & Godfray (2001) exposed individuals from 20 populations of *Drosophila melanogaster* to both sympatric parasitoids and to a reference strain of parasitoids (the braconid wasp, *Asobara tabida*). In addition, they exposed a reference strain of hosts to each of the 20 populations of parasitoids. The idea is that if

local coevolution is working in this interaction, the parasitoids should generally be best able to infect hosts drawn from the same population (or vice versa, depending on the genetic basis for resistance). Instead they found that success of parasitoids was significantly and positively correlated with success on the host reference strain, and that the residuals were significantly and negatively correlated with host resistance to the parasitoid reference strain. They conclude that directional selection for resistance to attack by the parasitoid, and not any kind of rare advantage, is responsible for their results. In addition, in experimental studies, they found that replicate host lines selected for resistance to one strain of parasitoid in the lab were also more resistant to other strains of the parasitoid (Kraaijeveld & Godfray, 1999). Hence, a general resistance, and not one depending on a specific genetic match, was observed. These results are contrary to expectation under the Red Queen theory.

These results points to the most frustrating aspect of the Red Queen theory of sex. One could rightly ask: "Is there another parasite of these flies that attacks in a frequency-dependent way? Perhaps they simply got the wrong biological antagonist." The problem with this kind of reasoning is that it could render the Red Queen model unfalsifiable. It also leads to the question of which parasites are the most likely to generate a rare advantage that is sufficient to overcome the reproductive advantages of asexuals when common. The trematode parasites of molluscs seem to be a likely choice, because of sterilizing effect they have on their hosts, and the evidence for local adaptation to host populations (Lively, 1989; Lively & Dybdahl, 2000a). But what of other invertebrate groups, which also have the capacity to produce asexual mutants? Do they also have

parasites that have such debilitating effects? Do these parasites attack in a frequency-dependent manner?

A final way to attack the Red Queen involves theory. In simulation studies, we challenged a sexual population of haploid hosts with competition from one or more clones (Lively & Howard, 1994). The sexual population had two segregating alleles at each of three loci, making for eight possible genotypes. We found that the introduction of two clones with different genotypes was sufficient to drive the sexual host population extinct, even when the effects of infection were severe. Thus, in these simulations at least, parasites were selecting for clonal diversity, and not sex per se (see also Judson, 1997; Lythgoe, 2000). This result makes sense, because, under the Red Queen hypothesis, parasites are a source of frequency-dependent selection. They can not respond to reproductive mode of their hosts per se.

If this result is generally true then, strictly speaking, the Red Queen theory for genetic diversity is correct; but the extension of the theory to the maintenance of sex does not hold. We also found, however, that if we allowed mildly deleterious mutations to accumulate in the clones, that parasites aided in the stochastic accumulation of these mutations by periodically driving clones through bottlenecks (Howard & Lively, 1994, 1998; Lively & Howard, 1994). In other words, parasites facilitated the action of Muller's ratchet, and the ratchet drove the clones to extinction. The combination of mutation accumulation and parasites then could favor sexual reproduction even when clones were periodically sampled from the sexual population, since clones were driven to extinction as fast as they were generated in the simulation. More generally, any process that keeps clones from fixing in the short term, and also aids the accumulation of

mutations, would accomplish the same thing (Lively & Howard, 1994). The advantage of antagonistic coevolution over other forms of selection is that the clonal bottlenecks may be more predictable.

Finally, it may be premature to conclude that highly virulent parasites are required to protect sexual populations from replacement by asexual females. In our simulations that included spontaneous deleterious mutations, we found that parasites that reduce host fitness by as little as 30% could be sufficient to select for sex. In addition, the models of Hamilton *et al.* (1990) show that sexual reproduction is favored if there are synergistic effects of combining different species of parasites. So, even if each parasite has a low virulence, the combination of many different parasite species in the same host may reduce the ability of that host to successfully compete for limited resources. We have found support for this idea in an annual plant infected by rust (Lively *et al.* 1995).

Unfortunately, the combinations of ideas (e.g., parasites and mutations, or parasites and resource competition) make tests of models even more difficult. The effort, nonetheless, seems worthwhile. And, fortuitously, the consideration of combinations of models does not preclude the finding that sex has one simple and elegant solution (West *et al.* 1999).

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REFERENCES

- BELL, G. (1982). *The Masterpiece of Nature: The Evolution and Genetics of Sexuality*. University of California Press, Berkeley.
- BREMERMANN, H. J. (1980). Sex and polymorphism as strategies in host-pathogen interactions. *Journal of Theoretical Biology* **87**, 671–702.
- BROOKS, D. R., THORSON, T. B. & MAYES, M. A. (1981). Freshwater stingrays (Potamotrygonidae) and their helminth parasites: testing hypotheses of evolution and coevolution. In *Advances in cladistics: proceedings of the first meeting of the Willi Hennig society* (ed. Funk, V. A. & Brooks, D. R.), pp 147-175. New York Botanical Gardens, New York.
- DYBDAHL, M. F. & LIVELY, C. M. (1995). Host-parasite interactions: infection of common clones in natural populations of a freshwater snail (*Potamopyrgus antipodarum*). *Proceedings of the Royal Society of London, B* **260**, 99–103.
- DYBDAHL, M. F. & LIVELY, C. M. (1998). Host-parasite coevolution: evidence for rare advantage and time-lagged selection in a natural population. *Evolution* **52**, 1057–1066.
- FOX, J. A., DYBDAHL, M. F., JOKELA, J. & LIVELY, C. M. (1996). Genetic structure of coexisting sexual and clonal subpopulations in a freshwater snail (*Potamopyrgus antipodarum*). *Evolution* **50**, 1541–1548.
- GANDON, S., CAPOWIEZ, Y., DUBOIS, Y., MICHALAKIS, Y. & OLIVIERI, I. (1996). Local adaptation and gene-for-gene coevolution in a metapopulation model. *Proceedings of the Royal Society of London, B* **263**, 1003–1009.
- GILLESPIE, J. H. (1998). *Population Genetics: A Concise Guide*. Johns Hopkins

- University Press, Baltimore.
- HALDANE, J. B. S. (1949). Disease and evolution. *La Ricerca Scientifica* (Suppl.) **19**, 68–76.
- HAMILTON, W. D. (1980). Sex versus non-sex versus parasite. *Oikos* 35:282–290.
- HAMILTON, W. D. (1982). Pathogens as causes of genetic diversity in their host populations. In *Population Biology of Infectious Diseases* (ed. Anderson, R. M. & May, R. M), pp 269–296. Springer-Verlag, New York.
- HAMILTON, W. D., AXELROD, R. & TANESE, R. (1990). Sexual reproduction as an adaptation to resist parasites (A review). *Proceedings of the National Academy of Sciences, USA* **87**, 3566–3573.
- HAMILTON, W. D. & ZUK, M. (1981). Heritable true fitness and bright birds: a role for parasites? *Science* **218**, 384–387.
- HOWARD, R. S. & LIVELY, C. M. (1994). Parasitism, mutation accumulation and the maintenance of sex. *Nature* 367, 554–557. Reprinted figures in *Nature* **368**, 358.
- JAENIKE, J. (1978). An hypothesis to account for the maintenance of sex within populations. *Evolutionary Theory* **3**, 191–194.
- JUDSON, O. P. (1995). Preserving genes: a model of the maintenance of genetic variation in a metapopulation under frequency-dependent selection. *Genetical Research, Cambridge* **65**, 175–191.
- JUDSON, O. P. (1997). A model of asexuality and clonal diversity: cloning the Red Queen. *Journal of Theoretical Biology* **186**, 33–40.
- KONDRASHOV, A. S. (1993). Classification of hypotheses on the advantage of amphimixis. *Journal of Heredity* **84**, 372–387.

- KRAAIJEVELD, A. R. & GODFRAY, H. C. J. (1999). Geographic patterns in the evolution of resistance and virulence in *Drosophila* and its parasitoids. *American Naturalist* **153**, S61-S74.
- KRAAIJEVELD, A. R. & GODFRAY, H. C. J. (2001). Is there local adaptation in *Drosophila*-parasitoid interactions? *Evolutionary Ecology Research* **3**, 107-116.
- LIVELY, C. M. (1987). Evidence from a New Zealand snail for the maintenance of sex by parasitism. *Nature* **328**, 519-521.
- LIVELY, C. M. (1989). Adaptation by a parasitic trematode to local populations of its snail host. *Evolution* **43**, 1663-1671.
- LIVELY, C. M. (1992). Parthenogenesis in a freshwater snail: reproductive assurance versus parasitic release. *Evolution* **46**, 907-913.
- LIVELY, C. M. (1999). Migration, virulence, and the geographic mosaic of adaptation by parasites. *American Naturalist* **153**, S34-S47.
- LIVELY, C. M. & DYBDAHL, M. F. (2000a). Parasite adaptation to locally common host genotypes. *Nature* **405**, 679-681.
- LIVELY, C. M. & DYBDAHL, M. F. (2000b). In Search of the Red Queen: A response. *Parasitology Today* **16**, 508.
- LIVELY, C. M. & HOWARD, R. S. (1994). Selection by parasites for clonal diversity and mixed mating. *Philosophical Transactions of the Royal Society of London, B* **346**, 271-281.
- LIVELY, C. M., JOHNSON, S. G., DELPH, L. F. & CLAY, K. (1995). Thinning reduces the effect of rust infection on jewelweed (*Impatiens capensis*). *Ecology* **76**, 1851-1854.

- LYTHGOE, K. A. (2000). The coevolution of parasites with host-acquired immunity and the evolution of sex. *Evolution* **54**, 1142–1156.
- MAY, R. M. & ANDERSON, R. M. (1978). Regulation of stability of host-parasite population interactions. II Destabilizing processes. *Journal of Animal Ecology* **47**, 249–267.
- MORAND, S., MANNING, S. D. & WOOLHOUSE, M. E. J. (1996). Parasite-host coevolution and geographic patterns of parasite infectivity and host susceptibility. *Proceedings of the Royal Society of London, B* **263**, 119–128.
- OTTO, S. P. & MICHALAKIS, Y. (1998). The evolution of recombination in changing environments. *Trends in Ecology and Evolution* **13**, 145–151.
- SAMARTINS, J. S. (2000). Simulated coevolution in a mutating ecology. *Physical Review E* **61**, R2212–R2215.
- WEST, S. A., LIVELY, C. M. & READ, A. F. (1999). A pluralist approach to sex and recombination. *Journal of Evolutionary Biology* **12**, 1003–1012.

FIGURE LEGENDS

Fig. 1. The relationship between probability of exposure to a single parasite propagule, and the prevalence of infection in sexual and asexual hosts. A) The results for sexual and asexual populations assuming that parasites are responding to reproductive mode, but not selecting for it. B) The results for sexual and asexual populations assuming that sexuals are favored by selection if the probability of exposure is greater than 0.3. I refer to this value as the "switch point." Here the switch point was determined from computer simulations that considered host-parasite coevolution in concert with the accumulation of deleterious mutations (Howard & Lively 1994). The mutation rate (U) per genome per generation was 0.5 in a population of 1000 hosts, and selection against individual mutations was 0.025; the mutations were assumed to have independent effects. Parasite virulence (V) was 0.8. The switch point is sensitive to the parameter values chosen, but the main ideas of the figure should hold as long as sexuals show prevalences greater than zero at the switch point.

Fig 2. The expected relationship between A) risk of infection and the frequency of sexual individuals in the host population (see also Sá Martins, 2000), and B) prevalence of infection and the frequency of sexual individuals in the host population. Note the overlap for prevalences in B. This overlap is due to a drop in prevalence in sexual populations at the switch point (see Fig. 1B).

Fig. 3. Distribution of prevalence for infection by digenetic trematodes in *P. antipodarum*.

Fig. 4. Relationship between prevalence of infection by trematodes and the frequency of males for 95 populations of the freshwater snail, *P. antipodarum*. Squares represent lake populations (from Lively 1992); circles represent stream populations (from Lively 1987).

Fig. 5. Relationship between the running mean for prevalence of infection and the running mean for the coefficient of variation (CV) for male frequency. Each circle indicates a “sliding window” of 20 data points taken from data ranked from lowest to highest with respect to prevalence of infection. For example, the first circle gives the mean prevalence and CV for male frequency calculated for the 20 sites with the lowest prevalence of infection; the second circle gives the same calculations for the next 20 sites; and the last circle gives the calculations for the 20 sites having the highest prevalence of infection. Note the steep increase in the CV, which is associated with the inclusion of the first highly sexual populations in the running mean. The solid horizontal line is the mean CV from randomization runs. In these runs, male frequencies were randomized 20 times and the CV calculated as above. The dashed horizontal lines are one standard deviation on either side of this mean.









