NEWS AND COMMENTARY

Evolutionary genetics

No sex please we're at QLE (quasi-linkage equilibrium)

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Bill Hamilton had a great influence over many areas of evolutionary biology. One of his most inspiring ideas was that sex and recombination serve to protect hosts from parasites (Hamilton *et al.*, 1990). This 'Red Queen' view is widely accepted as an explanation of pervasive sexual reproduction in higher organisms, largely because species interactions are likely to generate the cyclic and continual changes in allele frequency required to maintain sexuality. Models of the Red Queen have supported Hamilton's view, showing that sexual reproduction and higher recombination rates can be favoured in hosts evading coevolving parasites (Bell and Maynard Smith, 1987; Nee, 1989). But how general is this interpretation – do biotic interactions commonly favour higher rates of recombination, or are specific conditions required? Can the Red Queen alone provide enough selective benefit to account for the ubiquity of sex in higher organisms?

Otto and Nuismer (2004) set out to provide a broad-scale assessment of ecological and genetic interactions that could underpin the Red Queen process. Their stark conclusion is that interactions between species are an unlikely explanation of the prevalence of sex. If anything, species interactions select against higher levels of recombination. On the surface, this looks like the death-knell of the Red Queen.

Otto and Nuismer (2004) initially studied a two species model with two interacting loci, each with two alleles. This model was then extended to include more loci and more interactions between species. A large, unstructured population was assumed, to avoid considering drift and spatial effects. The fitness consequences of species interactions were taken to follow some well-known patterns of epistasis (matching genotype, gene for gene, quantitative trait). In all cases, the Red Queen favoured modifier alleles that reduced the rate of recombination, or the frequency of sex, within a population. Increasing the number of loci or the number of interacting species made

this gloomy outcome for the Red Queen even worse. Even allowing for different generation times between the interacting species did not rescue the Red Queen.

To derive general results, an assumption was made that the populations studied were at quasi-linkage equilibrium (QLE). This assumption follows from Barton's (1995) genome-wide model for studying the evolution of recombination, which Otto and Nuismer extend to several interacting species. The QLE approach makes the analysis feasible (otherwise linkage disequilibrium would have to be calculated independently between each pair of alleles). It assumes that selection per locus is weak, so only species interactions with minor fitness consequences can be modelled. QLE further assumes that the recombination rates between loci are much stronger than the selection generating associations between alleles at those loci.

It is perhaps not surprising that recombination is not favoured by the Red Queen under these assumptions. Although sex generates beneficial allele combinations, it also causes the break-up of currently favoured combinations. The balance of these two forces determines whether modifiers that increase recombination are favoured. As QLE means that host and parasite populations are essentially able to track changes in the genotypic composition of one another's populations, the negative effect of increased recombination predominates. There is therefore little advantage to modifiers that increase the rate of recombination. Even if the modifier becomes associated with rare favoured combinations, this advantage is weak when recombination is frequent and is swamped by the cost of producing unfit combinations of alleles. The QLE assumptions also explain why the Red Queen is not boosted by an increase in the number of loci or parasite species, and differences in generation time. These extra factors simply dilute selection per locus, as QLE already is constrained to weak selection.

The particular types of biological interaction and ecological reality that the Red Queen hypothesis was devised to include are arguably quite different to a system that would generate QLE. The idea of Red Queen that Hamilton had in mind, as well as other more favourable models (eg Bell and Maynard Smith, 1987), was of sudden switches in the direction of selection that generate adaptive lags between the host and parasite populations. Such switches effectively generate strong per locus selection. Recombination then allows hosts (or parasites) to evolve more quickly in response to the emergence of antagonistic genotypes in parasites (or hosts). Otto and Nuismer (2004) carried out a range of simulations that allowed strong selection, low rates of recombination and deviations of disequilibria from QLE. Not surprisingly, under these conditions, the Red Queen could favour increases in sex and recombination, especially in models with the strongest selection per locus and the lowest rates of recombination.

Perhaps, the best way of seeing the QLE assumption is as a null model of species interactions. Investigation of this null model points to a serious restriction in the generality of the Red Queen. For the Red Queen to be effective, species interactions need to generate strong selection on particular genotypes and recombination between interacting loci needs to be rare relative to selection. Otto and Nuismer (2004) discuss some data from plant disease-resistance loci, which they suggest are unlikely to fulfil these requirements. However, this is little more than an armchair assessment. A more wide ranging evaluation of the genetics of host-parasite interactions is needed, but empirical data are currently thin on the ground. In addition, we also need to wait for an analysis of Red Queen models in combination with other forces (eg drift, spatial structure) that may show species interactions in a more favourable light.

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