

Continued hope for a general explanation of sex

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Some natural phenomena may defy explanations in terms of single causes. The genetic basis for Haldane's Rule, for example, depends in part on whether the rule manifests itself in terms of hybrid inviability or sterility and varies among taxa (Orr, 1997). West *et al.* (1999) suggest that the widespread occurrence of sexual reproduction similarly requires multiple explanations. Currently, neither models of mutation accumulation nor those of changing environments, notably the Red Queen, can on their own fully account for the maintenance of sexual reproduction given the two-fold advantage of asexuality. The motivation for West *et al.*'s argument makes sense: creatures typically suffer from parasites as well as from deleterious mutations, and sexual reproduction may be the best way to fight their combined attack. This may be especially true, they argue, because both processes can complement each other and act synergistically. Encouraged by successful simulations of a number of specific cases (e.g. Howard & Lively, 1998), the authors invite further work in this area.

We agree with West *et al.* in that an integrated approach is required to explain why sex abounds. After decades of thorough exploration, all potentially contributing factors have probably been identified. The discovery of yet another mechanism that could instantly solve the riddle seems doubtful. However, we are sceptical that the way forward lies in the analysis of pairwise or multiple interactions of potential causes as proposed by the authors.

Imagine for the moment that specific interactions of deleterious mutation loads and parasite–host dynamics can account for the maintenance of sexual reproduction. The parameter space that covers these dynamics will not be easily defined but is extremely large. The list of factors that need to be specified includes the rate of mutation and the distribution of mutational effects, the genetic basis of the parasite–host interaction, as well as the resulting multivariate fitness functions. The Red Queen dynamics alone have been modelled in a variety of different ways (Otto & Michalakis, 1998), some or all of which may be fair representations of some natural systems. The crucial point is that any one of the resulting

models is necessarily specific, and its analysis is complex. A thorough exploration of a general phenomenon via a collection of specific models seems a daunting task. If the widespread occurrence of sexual reproduction indeed required such a compartmentalized analysis, then we would be a long way from understanding the problem. This would quite simply be sad.

However, the situation may not be quite so bleak. The need for a collection of distinct models would arise if the region of the parameter space in which sex is favoured had a complicated shape and was possibly even disjunct. We find this hard to imagine. Why should the vast majority of taxa exist in exactly these specific pockets and branches of the parameter space and why should they restrict their movements to these regions as they diversify and speciate? It appears much more likely that the relevant region is large and continuous, in which case there should be a general explanation for the maintenance of sexual reproduction.

This argument does not deny the usefulness of specific models to explain the recurring yet isolated emergence of asexual lineages. West *et al.* call for detailed case studies aimed at parameter estimation. We agree that such studies would be extremely useful in order to understand just what sets the balance of forces in favour of asexuality in these cases. While the yardstick of a two-fold advantage for asexuals is a useful shorthand, it does not apply universally even in anisogamous species. The benefit of paternal care in some breeding systems is only one example. Depending on the genetic mechanisms that bring about the transition to parthenogenesis, the relative fitness of asexuals may be either smaller or larger than two. For example, a new parthenogen that arises through the duplication of one haploid genome of its sexual parent would be entirely homozygous. Aside from the obvious case of recessive lethals, there should be a fitness loss due to the large class of mutants that are slightly deleterious and partially recessive. The number of such mutations in the new parthenogen need not be large to melt away the two-fold advantage. A better understanding of the genetic mechanisms of asexuality seems therefore necessary. We believe that the explanations for particular cases of asexuality may well be varied. As a consequence, they differ from the reason why the vast majority of taxa reproduces sexually. We remain hopeful that an explanation for the maintenance of

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sexual reproduction can be found that matches the phenomenon in its generality.

In agreement with the authors, we believe that varying selection in heterogeneous environments plays a key role in this general mechanism. To take a stab at it, we would like to propose a slight modification of one of the existing theories. The most robust mechanism so far proposed and one which provides a generous and immediate advantage to sexual reproduction is the interaction between stabilizing and directional selection (Charlesworth, 1993). Stabilizing selection on a quantitative trait predictably builds up negative linkage disequilibria, which can impede the response to directional selection in asexual lines. In contrast, recombination breaks down these genetic associations, increases the genetic variance and thus facilitates adaptation to a moving phenotypic optimum.

The mechanism works well when the optimum for a trait moves steadily in one direction. The phenotypic mean then follows with some delay which is smaller in sexuals than in asexuals (Charlesworth, 1993). Reversals of the optimum and cyclically fluctuating environments make the conditions for sex more stringent, in part because large genetic loads are built up and in part because reversals imply that the optimum moves occasionally through the populations mean, thus weakening the advantage of sex at those times (Charlesworth, 1993). The steady one-directional movement of the optimum, however, appears implausible, because it predicts, for example, gradual changes in the fossil record, which are typically not observed (Charlesworth, 1993).

This problem might be alleviated if one allows for selection on more than one trait. For example, steadily moving selection might be distributed over a number of traits (Crow, 1992; Charlesworth, 1993). Under conditions that favour sexual reproduction, this would lead to a reduction in the rate of phenotypic change per trait, which should nevertheless accumulate with time. Kondrashov & Yampolsky (1996) consider a model of fluctuating selection in which the trait optima cycle with offset periods. This regime appears to generate unacceptably high lag loads. Alternatively, one could imagine that selection alternates through time among traits or sets of traits. For a given trait, intervals of selection in one direction would be interspersed with those of stabilizing selection. During the latter phases, the phenotypic mean for that trait could 'catch up' with the optimum and thus reduce the overall directional load. A persistent advantage to sexual reproduction would be assured as long as there is at all times a sufficient directional component to selection on at least one trait.

A number of conditions are critical for this explanation to apply. While the increase in genetic variance due to recombination aids adaptation to a moving optimum, it causes a segregation load for those traits currently under stabilizing selection. The net advantage of recombination across both of these processes would have to be high

enough for sex to be maintained. Of course, this requirement applies similarly to the case of directional selection on a single trait, as long as one allows for some sort of organismal complexity. As in the single-character model, our scheme of intermittent directional selection per trait avoids the problems of sigmoidal reversals in the phenotypic optimum. Pleiotropy naturally sets an upper limit to the number of independent axes on which selection can act. Yet partial genetic correlations could possibly aid the proposed mechanism, in the sense that antagonistic selection could maintain the directional momentum when selection on one trait is relaxed. There should be some critical level of genetic correlation between a pair of traits above which the system reverts to the case of fluctuating selection on a single character. We realize that both analysis and critical test of this scheme would be extremely challenging and in this sense hardly preferable to the approach of West *et al.* Yet it might hold the promise of a step towards a general explanation.

The time-scale on which selection alternates between traits could be such that most of the response to selection would not manifest itself in measurable phenotypic change. This view of 'frustrated adaptation' may well be a typical feature of selection in heterogeneous environments. The target traits involved would range from morphology to metabolism and life history. Imagine a natural population that is in principle subject to abiotic stresses such as drought or cold, predators, competing species and, of course, parasites. All these selective agents operate on the existing genetic variance, but one of them may be the dominant factor at any one time. For example, predator density may be on the increase for some time, or temperatures may be cooling, or food levels may be lower in some years than others. As a consequence, the population permanently responds to selection in some direction. And yet sustained selection that leads to measurable phenotypic change in a given trait happens only rarely.

The proposed mechanism is very general in that all creatures have several to many phenotypic traits, and some of these should be sufficiently uncorrelated to serve as independent axes among which selection can alternate. Selection per trait need not be strong. Some minimal length of a given selection time interval may be required, but no further assumption seems necessary in this regard. Nor does one need to specify particular genetic interactions, as in host-parasite models. As long as there is a component of stabilizing selection, negative linkage disequilibria are built up as necessary and sufficient genetic prerequisites. The mechanism also explains recombination across all of the genome, rather than subsets of it where, for example, resistance genes might be clustered.

A basic tenet of ecological theory is the existence of limiting factors. If one of them is temporarily absent, another one will take its place. To the extent that there is

relevant genetic variance, these factors constitute selective agents. Viewed this way, populations constantly chase the Red Queen in n dimensions on a tortuous route and without reversals.

We believe that this idea deserves further study.

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