

# Evolutionary traction: the cost of adaptation and the evolution of sex

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## Abstract

The advantage of sexual reproduction remains a puzzle for evolutionary biologists. Everything else being equal, asexual populations are expected to have twice the number of offspring produced by similar sexual populations. Yet, asexual species are uncommon among higher eukaryotes. In models assuming small populations, high mutation rates, or frequent environmental changes, sexual reproduction seems to have at least a two-fold advantage over asexuality. But the advantage of sex for large populations, low mutation rates, and rare or mild environmental changes remains a conundrum. Here we show that without recombination, rare advantageous mutations can result in increased accumulation of deleterious mutations ('evolutionary traction'), which explains the long-term advantage of sex under a wide parameter range.

## Introduction

One possible advantage of sex is the relative resistance of sexual populations to the accumulation of deleterious mutations: when the population size is small (Muller, 1964), or when deleterious mutations interact synergistically and the mutation rate is high (Kondrashov, 1988), asexual populations suffer a much higher mutation load than sexual ones. However, recent studies (Keightley & Eyre-Walker, 2000) suggest that mutation rates in some sexual species are too low for mutation alone to account for the advantage of sex.

Another possible advantage of sex lies in the ability of sexual populations to adapt, i.e. to incorporate beneficial mutations (Fisher, 1958; Barton, 1995). On a background of deleterious mutations, recombination can increase the fixation probability of a beneficial mutation by freeing it from 'background trapping' (Charlesworth, 1994; Peck, 1994; Orr, 2000; Rice & Chippindale, 2001). As a result, if the environment changes frequently enough, the effect of deleterious mutations on adaptation can produce a significant advantage to sexual

reproduction (Howard & Lively, 1994; Burger, 1999; Waxman & Peck, 1999).

In the case of rare environmental changes, the advantage of sex can be explained by reversing the argument: without recombination, rare adaptation events can result in increased accumulation of deleterious mutations (Manning & Thompson, 1984; Rice, 1987). This explanation has gained much less attention, and its significance was questioned (Charlesworth & Charlesworth, 2000). Here we quantitatively study for the first time the long-term effect of adaptation on the accumulation of deleterious mutations, and compare it with other classical mechanisms. Our results suggest that this mechanism might play an important role in the advantage of sexual reproduction.

Consider a large finite asexual population in which both deleterious and beneficial mutations occur. If most deleterious mutations have small effects, almost no individual in the population is completely free of them. A rare beneficial mutation occurring in a single individual would most probably occur in an individual carrying some deleterious mutations. In such a case, there are only two possibilities. (i) The effect of the beneficial mutation is smaller than the cumulative effect of the deleterious mutations in the background. The beneficial mutation is then unlikely to spread in the population, due to background trapping (Peck, 1994; Orr, 2000).

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(ii) The effect of the beneficial mutation is larger than the cumulative effect of the deleterious mutations in the background. In that case the beneficial mutation could increase to fixation, although with a lower probability than in a similar but sexual population (Manning & Thompson, 1984; Johnson & Barton, 2002), and take the deleterious background to fixation with it. Several authors have estimated the fixation probability and fixation time of a single beneficial mutation (Manning & Thompson, 1984; Rice, 1987; Charlesworth, 1994; Peck, 1994; Johnson & Barton, 2002). Here we concentrate on the long-term implications of recurring fixations of beneficial mutations on the evolution of sex: in either case (i) or (ii), the rate of adaptation in an asexual population would be lower than in a sexually reproducing one (Charlesworth, 1994; Howard & Lively, 1994; Peck, 1994). As a result of (ii), an asexual population subject to rare beneficial mutations would also deteriorate due to the hitchhiking of deleterious mutations with each 'improvement'. We describe this reduction in fitness as 'evolutionary traction'.

### The model

When studying the long-term deterioration due to evolutionary traction, we cannot make the simplifying assumption that the population is at equilibrium when the beneficial mutation occurs. As the mutation process is bi-directional, if the intervals between beneficial mutations were long enough the population would return to the only stable equilibrium – mutation-selection balance at all loci – after each adaptation event. However, the time between the appearance of a successful beneficial mutation and the return to mutation-selection balance may be quite long. This period can be divided into two different phases: in the first, the beneficial mutation spreads to fixation, in the second, the beneficial mutation is already fixed, but the population is not yet back at equilibrium due to the overrepresentation of deleterious alleles that fixed together with the beneficial mutation. The long-term effects of the evolutionary traction are especially interesting when considering beneficial mutations that appear when the population is in this second phase. Unfortunately, this case does not easily lend itself to analysis, and we therefore study it using stochastic simulations.

An individual-based simulation was constructed as follows. Each genome is composed of 10 000 'housekeeping loci' and 10 'adaptation loci'. At each locus there are two possible alleles: 0 and 1, and bidirectional mutation occur at rate  $m$  per genome per generation. At the housekeeping loci the good allele is always '1'. A '0' allele at a housekeeping locus  $i$  reduces the fitness by a multiplicative factor  $(1 - s_{hi})$ , where  $s_{hi}$  is drawn from a truncated exponential distribution with expectation 0.02. For the adaptation loci, the environment determines which allele combination has maximal fitness. Each

departure from this optimal combination reduces the fitness of the individual by a multiplicative factor  $(1 - s_a)$ , where  $s_a > \bar{s}_{hi}$ .

Environmental changes occur at intervals drawn from an exponential distribution with expectation  $T$  generations. At each environmental change the selection on a single randomly chosen 'adaptation' locus is changed, so that the alternative allele at that locus is advantageous. This pattern of environmental changes was chosen in order to avoid clonal interference, an alternative mechanism that can increase the advantage of sexual reproduction. We shall compare the 'adaptation fitness' (as determined by the arithmetic mean across the adaptation loci), 'housekeeping fitness' (as determined by the arithmetic mean across the housekeeping loci), and the total fitness (the product of these two components) over time in four populations:

1. Asexual with environmental changes;
2. Sexual with environmental changes;
3. Asexual without environmental changes (but with deleterious mutations);
4. Sexual without environmental changes (but with deleterious mutations).

Cases 3 and 4 are actually examples of Muller's ratchet (1) and serve as controls for the cost of adaptation in 1 and 2. Note that the version of Muller's ratchet in 3 and 4 includes both small and large deleterious mutations (in different loci), allowing the ratchet to operate more effectively (Lande, 1994; Gessler, 1995; Schultz & Lynch, 1997; Gordo & Charlesworth, 2001).

The magnitudes of mutational effects are important in this model. Evolutionary traction occurs only when the effect of a beneficial mutation is large compared with that of the deleterious mutations in its background (case ii). We concentrate here on those beneficial mutations that have relatively strong effects, a subset of the entire spectrum of mutation effects that is likely to occur in natural systems.

### Methods

In the simulations each individual is represented by two arrays: an array of the locations of the deleterious mutations ('0' alleles) in the housekeeping loci and an array of the alleles at each of the adaptation loci. In addition we keep two arrays that are chosen at random at each simulation run and used for all the individuals in the population: an array of the effects of deleterious mutations at different housekeeping loci and an array of the locations of the adaptation loci within the genome. In runs that include recombination, a single crossover event occurs at a random location in the recombining genomes. Both housekeeping loci and adaptation loci may recombine with respect to that crossover point, yielding new arrays for the recombined genome. Population size was 2000 in the results presented, and smaller scale simulations with population sizes of 500 and 5000 yielded

qualitatively similar results. Each simulation run starts with a population of individuals with allele '1' at all positions, and with an all-one environment array (so that the population is perfectly adapted), and runs for 200 000 generations. The selection against deleterious mutations in housekeeping loci,  $s_{hi}$ , was truncated so that mutations with effect  $<0.0005$ , effectively neutral in our setting, were not included. Small scale simulations without truncation obtained similar results, but the runs were far more time consuming due to the large numbers of nearly neutral mutations.

## Results

We studied the difference between sexual and asexual haploid populations in a parameter range that is considered problematic for the advantage of sex: low mutation rate (below 0.04 per genome per generation), multiplicative fitness landscape, and rare environmental changes (average time between changes  $T \geq 500$  generations). The effects of deleterious alleles at the housekeeping loci were drawn from a truncated exponential distribution with expectation 0.02, and the effect of mismatch between the adaptation loci and the environment reduces fitness by a constant factor  $s_a$ . All fitness effects are multiplicative. The difference between the sexual and asexual populations is that the sexual individuals recombine at the rate of one crossover event per genome per generation.

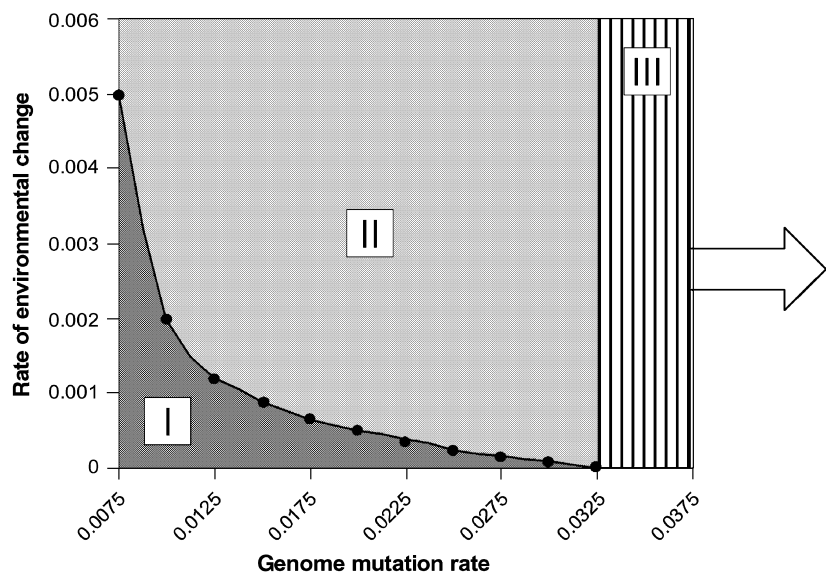
Figure 1 demonstrates that rare environmental changes can significantly extend the parameter range where sex is advantageous. In the parameter range studied, Muller's ratchet (where there is no environmental change) is insufficient to account for the two-fold advantage for genomic mutation rates below 0.03. A similar figure is obtained when only the 'housekeeping

fitness' is considered instead of the overall fitness, indicating that background trapping is insufficient to account for the two-fold advantage in that parameter range. Each environmental change affects only a single locus of the 'adaptation loci', so beneficial mutations usually appear separately and clonal interference is likely to be weak. Most of the advantage of sexuals in area II of Fig. 1 can thus be attributed to evolutionary traction – the accumulation of deleterious mutations in asexuals during adaptation events.

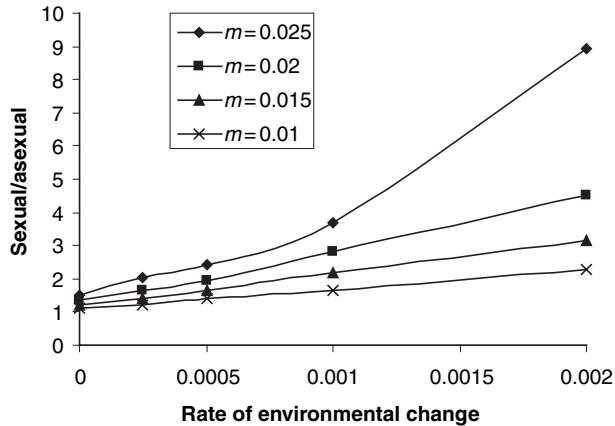
Figure 2 shows that the resulting advantage of sex in terms of the average fitness of the 10 000 housekeeping loci increases as a function of both genomic mutation rate and rate of environmental change.

Figure 3 shows the results of a single run with genomic mutation rate  $m = 0.02$ . In the constant environment (Fig. 3a) the asexual population suffers a small load of deleterious mutations in comparison with the similar sexual one, probably as a result of Muller's ratchet. The asexual population also manages to adapt to the changing environment ( $T = 1000$ ), in the sense of incorporating the 'right' adaptation allele after most environmental change, so that mismatch with the environment does not accumulate (Fig. 3b). However, during many of the adaptation events the increase in 'adaptation fitness' due to the spread of a beneficial allele is accompanied by a decrease in 'housekeeping fitness' due to the hitchhiking of deleterious alleles at other loci (Fig. 3c). The asexual population accumulates a loss of 'housekeeping fitness', whereas the sexual population does not: during the spread of a beneficial allele, there is plenty of time for recombination to separate it from its deleterious neighbours.

Very low rates of sexual reproduction (one recombination event in 100 generations, results not shown) were significantly better than asexuality, but not as good as



**Fig. 1** The advantage of sex due to different mechanisms, as a function of genome mutation rate and the rate of environmental change ( $1/T$ ). The advantage of sex is measured as the average population fitness in the sexual population after 200 000 generations divided by that value in the asexual population. In area I sex does not have the required two-fold advantage. In area III (and for all higher mutation rates) Muller's ratchet can account for the advantage of sex even without environmental changes. In area II the cost of adaptation (in terms of accumulating deleterious mutations) results in at least a two-fold advantage to the sexual population.



**Fig. 2** The advantage of sex as a function of the rate of environmental change, for four genomic mutation rates. The vertical axis is the ratio of average 'housekeeping fitness' (defined by the 10 000 housekeeping loci only) in the sexual population after 200 000 generations to that in the asexual population. The horizontal axis is the rate of environmental changes per generation ( $1/T$ ). The ratio increases as a function of both mutation rate and environmental change, and exceeds the value 2 for much of the parameter space. Population size = 2000.

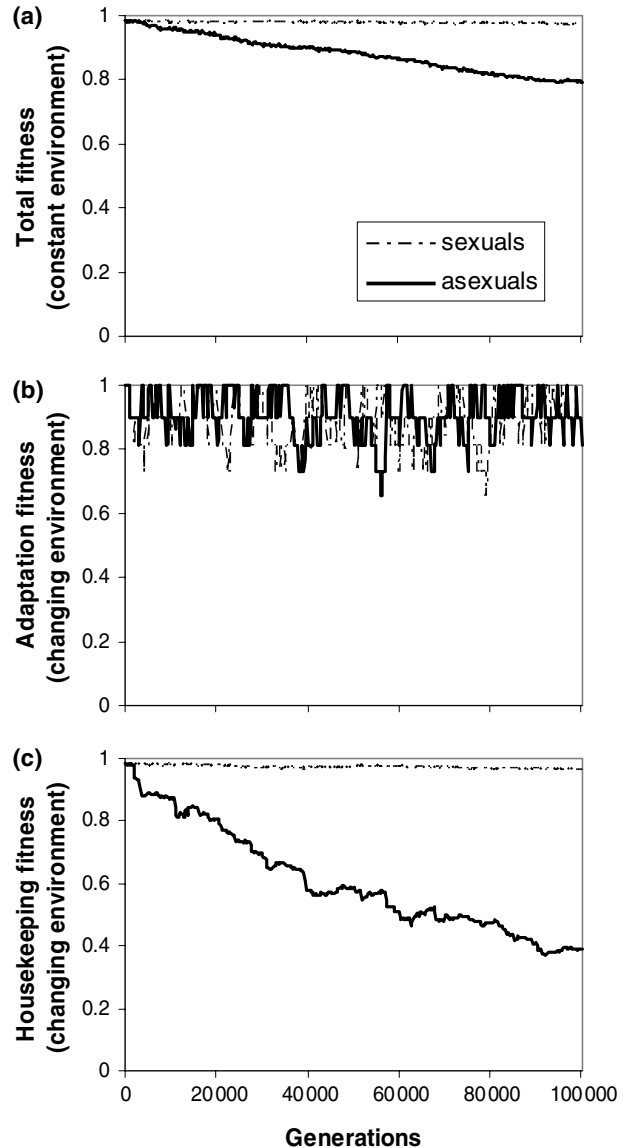
obligatory sex in terms of average fitness. However, our results do not account for the evolution of obligatory sex: if the cost of sex is proportional to the amount of sex, lower frequencies of sexual reproduction are still usually preferred.

## Discussion

Several processes determine the accumulation of deleterious mutations in finite populations. Muller's ratchet and evolutionary traction facilitate the accumulation of deleterious mutations, while back mutations counter their effect. In all these processes recombination acts against the deterioration: it reduces the stochastic loss of advantageous alleles by drift (Muller, 1964), increases the fixation probability of beneficial mutations (Charlesworth, 1994), and decreases the probability of fixation of deleterious alleles because of traction. In this paper, we demonstrated that under rare environmental changes evolutionary traction might be a crucial factor in the long-term advantage of sex and recombination. This process does not require a very small population, as an adaptation event acts as a bottleneck in an asexual population, whereby the first individuals that acquire the beneficial mutation become the parents of the entire subsequent population.

## Host-parasite coevolution

Evolutionary traction might bear special importance for the effect of host-parasite coevolution on the evolution



**Fig. 3** Results of a single run. The 'housekeeping fitness' and 'adaptation fitness' of sexual and asexual populations, with or without environmental changes, as a function of time. (a) In the absence of environmental changes some mutational load accumulates in the asexual population as a result of Muller's ratchet, but the effect does not generate a two-fold advantage for the sexual population even after 200 000 generations. (b) When the environment does change, the average 'adaptation fitness' of both sexual and asexual populations fluctuates, but neither population deteriorates significantly. (c) Due to the adaptation events, many deleterious mutations in the 'housekeeping loci' accumulate in the asexual population, but not in the sexual one. This effect is much stronger than the ratchet in the current setting. Mutation rate = 0.02 per genome per generation, environment change rate ( $1/T$ ) is 0.001 in the run with environmental changes, population size = 2000,  $s_{hi}$  are drawn from a truncated exponential distribution with expectation 0.02, and  $s_a = 0.1$ .

of sex. It has been shown that host–parasite interactions can account for the evolution of sex under strong specificity of the parasite to a certain host genotype ('matching alleles' model) and strong negative effects of infection on host fitness, leading to frequency-dependent selection and intensive cycling (Hamilton, 1980; Hamilton *et al.*, 1990; Howard & Lively, 1994). These conditions are thought not to be widely satisfied (Parker, 1994). In the current model, much more general interactions between host and parasite are sufficient to account for the advantage of sex. Specifically, even a gene-for-gene model of co-evolution (Flor, 1956), without dramatic effects of parasite infection on host fitness, could satisfy the conditions of the model. The result is not limited to that context – many kinds of environmental changes carry the potential for a relatively large and rare beneficial mutation, especially at the beginning of an adaptation process (Orr, 1998). Recent studies (Fay *et al.*, 2002; Smith & Eyre-Walker, 2002; Sawyer *et al.*, 2003) found that the rate of advantageous substitutions in the genome is considerably higher than previously thought. Those advantageous substitutions that have significant fitness effects can result in evolutionary traction.

### Predictions

Evolutionary traction, Muller's ratchet, and background trapping have different predictions in a changing environment. Part of the difference might be demonstrated when comparing sexual and asexual populations moving from a 'good' environment (A) to a new environment (B) where there is selection on an additional factor, adapting to it, and then returning to A. Such a scenario was studied by Zeyl & Bell (1997). Background trapping predicts that the advantage of sex would appear mainly in the adaptation to the new environment (B). Evolutionary traction predicts, in agreement with the experimental result, that the sexual population would have a significant advantage when returning to environment A.

The different mechanisms would also have different effects on the level of polymorphism in the population, especially in a changing environment. While under Muller's ratchet different deleterious alleles would accumulate in different lineages and fixations would occur at a relatively constant rate, evolutionary traction would lead to fixation of the same deleterious alleles in the entire population during adaptation, and to a highly nonuniform distribution of fixation events. Our results suggest that the decrease in genetic variation during adaptation would be much more significant in an asexual population than in a sexual one. Variation is expected to decrease both in loci affecting fitness, where it would result in an increase in inbreeding depression (the decrease in fitness of individuals having parents from the same population, in comparison with individuals of mixed heritage), and in neutral loci (Barton, 2000; Kim & Stephan, 2003).

The strength of the evolutionary traction depends on the parameters in various ways. First, if the rate of beneficial mutations is high enough, so that few independent beneficial mutations occur during the spread of the first beneficial mutation, each bottleneck would include a few individuals and its effect would be weaker, but bottlenecks might occur more frequently. Secondly, if population size is very large, the time to fixation of the beneficial mutation would be very long, while the rate of appearance of such mutations would be higher. Thirdly, if either the effect of beneficial mutations is small or the rate of environmental change is high, background trapping might be a more important factor than the traction, at least in the short run.

Background trapping and evolutionary traction complement each other in the case of strong beneficial mutations: the traction leads to fixation of deleterious mutations of small effect during adaptation events in asexual populations. Background trapping makes the reversal of this process, by beneficial back mutations of small effect, very slow. Together, these two forces may account for the long-term advantage of sex and recombination under a very wide parameter range.

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