Condition-Dependent Sex and the Rate of Adaptation

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ABSTRACT: Recent modeling has shown that condition-dependent sex can evolve much more readily than sex that occurs at a uniform rate, even in the face of substantial costs of sex. Specifically, evolution favors genes that cause organisms to allocate more resources to sexual reproduction when they are in poor condition and to asexual reproduction—including increased life span—when they are in good condition. This form of fitness-associated sex (FAS) evolves because modifier genes that promote their own escape from low-fitness genetic backgrounds and that remain longer in high-fitness genetic backgrounds rise in frequency alongside the spread of high-fitness genotypes due to selection. Importantly, FAS does not evolve because it is good for the individual or good for the species but because it is in the selfish interest of modifier genes that promote FAS to move from low- to high-fitness genetic backgrounds. Even though FAS does not evolve for the good of its descendants, we show here that FAS often hastens the rate of adaptation. Ironically, the rate of adaptation is most likely to be accelerated by FAS when sex is costly, because FAS makes it more likely that individuals in poor condition will suffer the costs of sex, improving the efficiency with which less fit alleles are eliminated.

Keywords: cost of sex, abandon-ship mechanism, facultative sex, rate of adaptation.

Introduction

In many facultative sexual organisms, the probability of sexual reproduction is not uniform under all circumstances (Bell 1982). Rather, individuals under stress are more likely to reproduce sexually than ones that are functioning well. In particular, starvation induces a shift from asexual to sexual reproduction in various organisms (bacteria: Dubnau 1991; Redfield 1993; Jarmer et al. 2002; Foster 2005; yeast: Kassir et al. 1988; Mai and Breeden 2000; *Chlamydomonas*: Harris 1989; and daphnia: Kleiven et al. 1992). Stressful environments involving drought or high salinity result in a higher frequency of sex among soil microfungi and in increased recruitment from seeds in the clonal plant *Hieracium pilosella* (Bruun et al. 2007). In addition, antagonistic species interactions have the potential to induce stress (and sex) in both hosts and parasites. For example, during an epidemic in daphnia, host genotypes that were more susceptible to infection showed an increased tendency to engage in sex (Mitchell et al. 2004), whereas in the nematode *Strongyloides ratti*, sex is induced in response to a host immune response (Gemmill et al. 1997; West et al. 2001). The last example is of particular interest, as sex in this organism does not involve a switch to a more resistant stage in the life cycle, such as spores or seeds. Last, competitive stress has been shown to increase allocation to sexual reproduction in several plant species (van Kleunen et al. 2001; Rautiainen et al. 2004); similarly, marginal reproductive allocation is negatively correlated with plant size in spring wheat under competition (Liu et al. 2008). These data indicate that a variety of stress-related cues can induce the switch to sexual reproduction in a fitness-associated way, although more research is needed to assess how often and why this phenomenon has evolved. Regardless of how it evolved, our focus in this article is to explore the impact of fitness-associated sex (FAS) on the speed of adaptation.

To begin, we review the theoretical work on FAS, which so far has focused on the conditions under which FAS evolves and its consequences for populations subject to recurrent deleterious mutations. Redfield (1988) was the first to explore FAS, using computer simulations with recurrent deleterious mutations to demonstrate that bacteria evolve a higher average fitness if they preferentially undergo genetic transformation when carrying a heavy load of mutations. Later, Gessler and Xu (2000) used simulations to demonstrate that a gene promoting recombination when fitness is low can spread throughout a population. Hadany and Beker (2003) subsequently investigated this process analytically, using a haploid model where fitness was determined by a single locus. In that model, a modifier that induces a higher probability of recombination when associated with the less fit allele at the fitness locus (fitness-associated recombination [FAR]) always spreads within the population, even when an individual's assessment of its condition is subject to substantial noise. With a single fitness locus in a haploid model, recombination—and hence FAR—has no effect on the dynamics of the selected

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locus and so no effect on the average fitness of a population. Rather, the success of a FAR allele is entirely explained by a "selfish" advantage: the FAR allele breaks away from the less fit allele at the selected locus, remains linked to the more fit allele, and can increase to fixation together with the selected allele. This process has thus come to be known as the "abandon-ship" mechanism for the evolution of recombination because of the advantage to modifier alleles that are able to escape from low-fitness genetic backgrounds (metaphorically, sinking ships).

The above studies focused on haploid populations, but fitness-associated recombination does not evolve so readily in diploid populations (Agrawal et al. 2005). The reason is that recombination shuffles a modifier allele between the two haplotypes carried by a diploid individual, but the fitness of a diploid individual provides no information about which of the two haplotypes is more fit and which is less fit. The abandon-ship mechanism does work in diploids, however, as long as a modifier alters the tendency of an individual to engage in sex (fitness-associated sex [FAS]) rather than recombination. That is, modifiers that promote sexual reproduction in low-fitness individuals while promoting asexual reproduction (or increased longevity) in high-fitness individuals spread rapidly within a population (Hadany and Otto 2007).

Another major difference between recombination and sexual reproduction is the cost of sex. Sexual reproduction entails a variety of substantial costs: the "twofold cost" of producing males (Maynard Smith 1978), the energy and time costs of searching for a suitable mate and courting it, and the risks of predation, disease, and injury while courting and mating (Partridge and Hurst 1998).

In a previous model investigating the evolution of fitness-associated sex, we incorporated costs of sex and found that FAS can evolve even in the face of substantial costs in both haploid and diploid species (Hadany and Otto 2007). The reason that FAS evolves even though sex is costly can be seen most easily in the simplest haploid model (see appendix of Hadany and Otto 2007). First, if a modifier allele happened to be associated with the fittest genotype, then it would gain no benefit from moving to a different background, especially if doing so involves costly sex. Thus, any mutation resulting in a decreased level of sex in the fittest individuals spreads within the population. Once the fittest individuals rarely undergo sex, alleles inducing increased levels of sex (even costly sex) in less fit genotypes can spread. Because deleterious alleles are eventually eliminated by selection, a modifier allele is essentially doomed unless it recombines away from deleterious alleles at the selected locus; thus, the benefits to the modifier of moving out of a bad genetic background outweigh whatever costs that sexual reproduction might impose. Similar results were obtained in a diploid model, illustrating that FAS is generally favored when less fit individuals reproduce sexually more often than more fit individuals (Hadany and Otto 2007). The above results showed that the abandon-ship mechanism can favor the evolution of FAS. In addition, FAS would gain a further evolutionary advantage if, during times of stress, sexual reproduction results in a more resistant or more dispersive life-history stage. Relative to a strategy of engaging in sex uniformly over time, FAS might also be favored by concentrating sexual reproduction during periods of time where resources are limiting and the scope for fast asexual growth is lower, reducing the costs of sex.

When sexual reproduction is costly, FAS influences the dynamics at selected loci, because the costs of sex are imposed most heavily on the less fit individuals in the population, thus enhancing the effectiveness of natural selection. As a result, we have shown that the average fitness of a population at equilibrium between deleterious mutations and selection can be increased by FAS, compared with populations that are asexual or that engage in a uniform level of sex across all individuals (Hadany and Otto 2007). Here, we explore the extent to which FAS alters the rate of adaptation in a novel environment. Various theoretical (Fisher 1930; Hamilton et al. 1990; Waxman and Peck 1999) and experimental (Rice and Chippindale 2001; Colegrave 2002; Goddard et al. 2005) studies have found that sex and recombination can facilitate adaptation, under the right circumstances. However, these studies have assumed that sex occurs at a uniform rate across fitness classes. Instead, we study the effect of FAS on adaptation and show that FAS can often accelerate adaptation, particularly when sex is costly because the costs of sex are disproportionately born by individuals carrying the less fit allele.

Model

Haploid Model with One Selected Locus

To begin, we start with a one-locus haploid model, which illustrates the role that costly sex can play on adaptation with FAS. We ignore mutations, assume that mating is random among the sexually produced gametes, and consider a hermaphroditic population with nonoverlapping generations. At the selected locus **A**, carriers of allele a have low viability $(1 - s)$ relative to carriers of the alternate allele A, with a viability of 1. (Our choice of notation is made for consistency with Hadany and Otto [2007], who focused on mutation-selection balance.) Letting x_1 and x_2 represent the frequencies of the A and a alleles, respectively, among the juveniles, these frequencies after selection become

$$x_1^s = x_1\frac{1}{\overline{W}} = \text{frequency } (A) \text{ after selection},$$

$$x_2^s = x_2\frac{1-s}{\overline{W}} = \text{frequency } (a) \text{ after selection}, \quad (1)$$

where $\overline{W} = 1 - sx_2$ is the mean viability due to selection at the **A** locus.

The population engages in FAS, with sex occurring at rate σ_1 among the most fit A individuals and at rate σ_2 among the least fit a individuals. For FAS to occur, it is not necessary that an individual be able to detect which allele it carries or be able to assess the fitness of other individuals within the population. Rather, we assume that the species has previously evolved an internal gauge of whether it is currently in high condition (unstressed) or low condition (stressed). This internal gauge might be neuronally based or hormonally based (involving such signals as glucagon, epinephrine, and norepinephrine), or in unicellular organisms, it might simply be based on molecular signals of stress and/or starvation (e.g., cAMP). Previous work has shown that evolution eventually leads to the reduction of sex among fit individuals, σ_1, and an increase in the frequency of sex among less fit individuals, σ_2 (Hadany and Otto 2007). We thus assume that individuals that are relatively less fit allocate more to sexual reproduction ($\sigma_1 < \sigma_2$).

With probability σ_i, adult haploids of genotype i reproduce sexually, producing haploid gametes that unite at random with other gametes. Consequently, the fraction of gametes that are A or a is $y_1 = \sigma_1 x_1^s/\bar{\sigma}$ or $y_2 = \sigma_2 x_2^s/\bar{\sigma}$, respectively, where $\bar{\sigma} = \sigma_1 x_1^s + \sigma_2 x_2^s$ is the average allocation to sexual reproduction. With probability $1 - \sigma_i$, an adult haploid reproduces asexually, including the possibility that the individual survives to the next generation (without senescence). A cost of sex, c, is incorporated, such that the overall contribution to the juveniles of the next generation through sexual reproduction is equal to the average level of investment in sex, $\bar{\sigma}$, multiplied by a factor $(1 - c)$. Consequently, the allele frequencies in the next generation become

$$x_1' = \frac{(1-\sigma_1)x_1^s + (1-c)\bar{\sigma}\,(y_1)}{1 - c\bar{\sigma}},$$

$$x_2' = \frac{(1-\sigma_2)x_2^s + (1-c)\bar{\sigma}\,(y_2)}{1 - c\bar{\sigma}}, \quad (2)$$

where the first and second terms in the numerator correspond to offspring produced asexually and sexually, respectively.

Equation (2) can be iterated to show that at any time t,

$$\left(\frac{x_1}{x_2}\right)_{\text{time } t} = \left(\frac{x_1}{x_2}\right)_{\text{time } 0}\left(\frac{1}{1-s}\right)^t\left(\frac{1-c\sigma_1}{1-c\sigma_2}\right)^t. \quad (3)$$

There are two main qualitative results that can be gleaned from equation (3). First, in the absence of a cost of sex ($c = 0$), FAS has no effect on the dynamics of selection, and equation (3) reduces to the standard solution describing allele frequency change in the haploid model of selection. This is true even though modifier genes that strengthen FAS—reducing σ_1 and/or increasing σ_2—are able to spread (Hadany and Otto 2007). The fact that FAS can evolve without having any effect on adaptation or the mean fitness of a population emphasizes that what drives the spread of FAS modifiers is the advantage of escaping low-fitness genetic backgrounds, not improving fitness. Second, costs of sex hasten the spread of the beneficial allele in FAS populations whenever individuals in poor condition undergo sex at higher rates than individuals in good condition ($\sigma_1 < \sigma_2$). This is because disadvantageous alleles are eliminated both by natural selection and because their carriers are more likely to engage in sex and so suffer from the various costs of sex.

Diploid Model with One Selected Locus

We next consider a diploid model with one selected locus where FAS has an additional effect on adaptation by altering the departure from Hardy-Weinberg proportions. The model is entirely analogous to the haploid model considered above, except that the viabilities are now $W_{11} = 1$, $W_{12} = (1 - hs)$, and $W_{22} = (1 - s)$, and the allocations to sexual reproduction are σ_{11}, σ_{12}, and σ_{22} among AA, Aa, and aa individuals, respectively. The recursion equations for the frequencies of the AA, Aa, and aa juveniles become

$$x_{11}' = \frac{(1-\sigma_{11})x_{11}^s + (1-c)\bar{\sigma}\,y_1^2}{1 - c\bar{\sigma}},$$

$$2x_{12}' = \frac{(1-\sigma_{12})2x_{12}^s + (1-c)\bar{\sigma}\,(2y_1y_2)}{1 - c\bar{\sigma}}, \quad (4)$$

$$x_{22}' = \frac{(1-\sigma_{22})x_{22}^s + (1-c)\bar{\sigma}\,(y_2^2)}{1 - c\bar{\sigma}},$$

where the frequency of Aa and aA heterozygotes are merged and counted as $2x_{12}$. In equation (4), the gametic frequencies are given by $y_1 = (\sigma_{11}x_{11}^s + \sigma_{12}x_{12}^s)/\bar{\sigma}$ and $y_2 = (\sigma_{12}x_{12}^s + \sigma_{22}x_{22}^s)/\bar{\sigma}$, with an average allocation to sexual reproduction of $\bar{\sigma} = \sigma_{11}x_{11}^s + 2\sigma_{12}x_{12}^s + \sigma_{22}x_{22}^s$, which are functions of the postselection frequencies:

$$x_{11}^{s} = x_{11}\frac{1}{\overline{W}},$$

$$2x_{12}^{s} = 2x_{12}\frac{1 - h\,s}{\overline{W}}, \tag{5}$$

$$x_{22}^{s} = x_{22}\frac{1 - s}{\overline{W}}.$$

The mean viability in this diploid model equals $\overline{W} = 1 - 2hsx_{12} - sx_{22}$.

To assess the rate of adaptation with FAS, we first rewrite these dynamics in terms of the frequency of allele *A*, given by *p*, and Wright's measure of the departure from Hardy-Weinberg, given by $f = 1 - [x_{12}/(pq)]$, where $q = 1 - p$. As these equations are fairly complicated, we then assume that selection is weak, so that both *s* and *c* are of the order of some small term, ξ. This does not necessarily require that the total cost of sex be small, because *c* can be considered as the marginal cost experienced by the **A** locus after all other loci in the genome have accounted for their share of the total cost of sex. The impact of assuming weak selection and costs is explored through simulations (below). As long as each genotype engages in some sex, the departure from Hardy-Weinberg approaches a steady state value on a timescale that depends on the degree of sex, which we assume is frequent relative to the strength of selection ($\sigma_i \gg \xi$). This steady state value, otherwise known as a quasi-linkage equilibrium (QLE) value, is, to leading order,

$$\tilde{f} = \frac{2\,pq\,(X - 1) + 1 - \sqrt{4\,pq\,(X - 1) + 1}}{2\,pq\,(X - 1)} + O(\xi), \tag{6}$$

where $X = \sigma_{12}^2/(\sigma_{11}\sigma_{22})$ measures how often *Aa* heterozygotes engage in sex, relative to the multiplicative expectation based on the sexual allocation of the two homozygotes. When the fitness alleles affect sex multiplicatively ($X = 1$), the departure from Hardy-Weinberg, $\tilde{f}$, is 0 to constant order. More generally, $\tilde{f}$ has the same sign as $(X - 1)$. That is, when heterozygotes engage in sex more than the multiplicative expectation ($X > 1$), heterozygosity is eliminated more rapidly than it is created, and excess homozygosity develops ($\tilde{f} > 0$). Conversely, when heterozygotes engage in less sex than the multiplicative expectation ($X < 1$), heterozygosity is preserved to a greater degree, and excess heterozygosity develops ($\tilde{f} < 0$).

As a technical aside, if FAS is very weak and all individuals engage in nearly the same amount of sex, then $\tilde{f}$ must be calculated to the next order, and selection contributes to equation (6) by an amount equal to $-pq\,(Y - 1)(1 - \bar{\sigma})/\bar{\sigma} + O(\xi^2)$, where $Y = W_{12}^2/(W_{11}W_{22})$. Thus, selection itself causes an additional departure from Hardy-Weinberg, leading to excess heterozygosity ($-\tilde{f}$) when heterozygotes are more fit than expected based on the geometric average fitness of the homozygotes ($Y > 1$), as found by Chasnov (2000; see also eq. [8] in Otto 2003). If the degree of asexual reproduction were roughly proportional to fitness, having relatively more fit heterozygotes ($Y > 1$) would mean that heterozygotes engage in less sex than expected ($X < 1$), in which case natural selection and FAS would both drive *f* to become negative. Similarly, both natural selection and FAS would drive *f* to become positive, with excess homozygosity, when heterozygotes are relatively low in fitness.

Using the steady state value of $\tilde{f}$ from equation (6), we can track the change in allele frequency at the selected locus. The total change, Δp^{T}, can be decomposed into a part due solely to natural selection from equations (5), Δp^{S}, and a part due to reproduction, Δp^{R}, where $\Delta p^{\mathrm{T}} = \Delta p^{\mathrm{S}} + \Delta p^{\mathrm{R}}$. To leading order, a single round of natural selection changes the beneficial allele frequency by

$$\Delta p^{\mathrm{S}} = spq(1 - \tilde{f})[ph + q(1 - h)] + spq\tilde{f} + O(\xi^2). \tag{7}$$

This has the familiar form for the change in allele frequency due to weak selection in populations out of Hardy-Weinberg proportions. Assuming intermediate dominance ($0 \le h \le 1$), the beneficial allele frequency always rises faster when there is excess homozygosity, because the effects of the alleles are fully revealed in homozygotes. Thus, FAS will hasten adaptation if heterozygotes tend to engage in a high degree of sex, $\sigma_{12}^2 > \sigma_{11}\sigma_{22}$. If the beneficial allele tends to be dominant ($h < 1/2$), the heterozygote will be relatively fit, and we might expect heterozygotes to allocate more to asexual reproduction (like the fittest *AA* individuals), preserving heterozygosity; in this case, FAS would slow adaptation. Conversely, if the beneficial allele tends to be recessive ($h > 1/2$), the heterozygote will be relatively unfit and more likely to reproduce sexually in populations exhibiting FAS (converting heterozygotes into homozygotes); in this case, FAS would hasten adaptation.

In addition, reproduction changes the allele frequency, because the costs of sex will generally be paid by the less fit individuals in populations engaging in FAS. Again, to leading order, this change is

$$\Delta p^{\mathrm{R}} = cpq(1 - \tilde{f})[p(\sigma_{12} - \sigma_{11}) + q(\sigma_{22} - \sigma_{12})] + cpq\tilde{f}(\sigma_{22} - \sigma_{11}) + O(\xi^2). \tag{8a}$$

The sign of equation (8*a*) is more easily seen when the equation is written as

$$\Delta p^{R} = c[(p - \tilde{x}_{12})q(\sigma_{12} - \sigma_{11}) + (q - \tilde{x}_{12})p(\sigma_{22} - \sigma_{12})] + O(\xi^2). \quad (8b)$$

Because x_{12} represents half the total frequency of heterozygotes, it must be less than or equal to the frequency of the rarer allele ($x_{12} \leq \min[p, q]$), ensuring that the sign of equation (8b) is determined by the form of FAS (the σ_{ij} terms). As long as less fit individuals engage in sex more often ($\sigma_{22} \geq \sigma_{12} \geq \sigma_{11}$, with at least one of the inequalities being a strict inequality), FAS will hasten adaptation because bearers of the less fit *a* allele will be more likely to pay the costs of sex, as observed in the haploid model.

Overall, FAS hastens adaptation under any of the following conditions: (1) Heterozygotes engage in sex more than the multiplicative expectation ($\sigma_{12}^2 > \sigma_{11}\sigma_{22}$), in which case FAS hastens adaptation with or without a cost of sex. (2) Individuals engage in sex at or near the multiplicative expectation ($\sigma_{12}^2 \approx \sigma_{11}\sigma_{22}$ leading to $\tilde{f} \approx 0$). In this case, FAS has little effect on the change due to selection (Δp^{S}; eq. [7]), and the main effect of FAS is to promote the elimination of less fit alleles, which more often pay the costs of sex (Δp^{R}; eqq. [8]). (3) The marginal cost of sex experienced by the **A** locus, *c*, is high relative to the strength of selection, *s*, so that Δp^{R} becomes larger than Δp^{S}. (4) The degree of FAS is substantial ($\sigma_{22} \gg \sigma_{11}$), amplifying the extent to which the costs of sex eliminate the less fit allele, again causing Δp^{R} to become larger than Δp^{S}. The only situation where FAS does not accelerate adaptation is when both $\sigma_{12}^2 < \sigma_{11}\sigma_{22}$ and the cost of sex is very close to 0.

The above results are obtained by assuming that the departure from Hardy-Weinberg proportions reaches a steady state faster than the allele frequencies change. This assumption requires that all individuals engage in sex frequently in comparison with the strength of selection and the cost of sex. We are, however, also interested in cases where selection is strong (e.g., in the face of dramatic environmental change). In addition, we are interested in species that rarely engage in sex, especially when individuals are in good condition, as this is a FAS strategy that

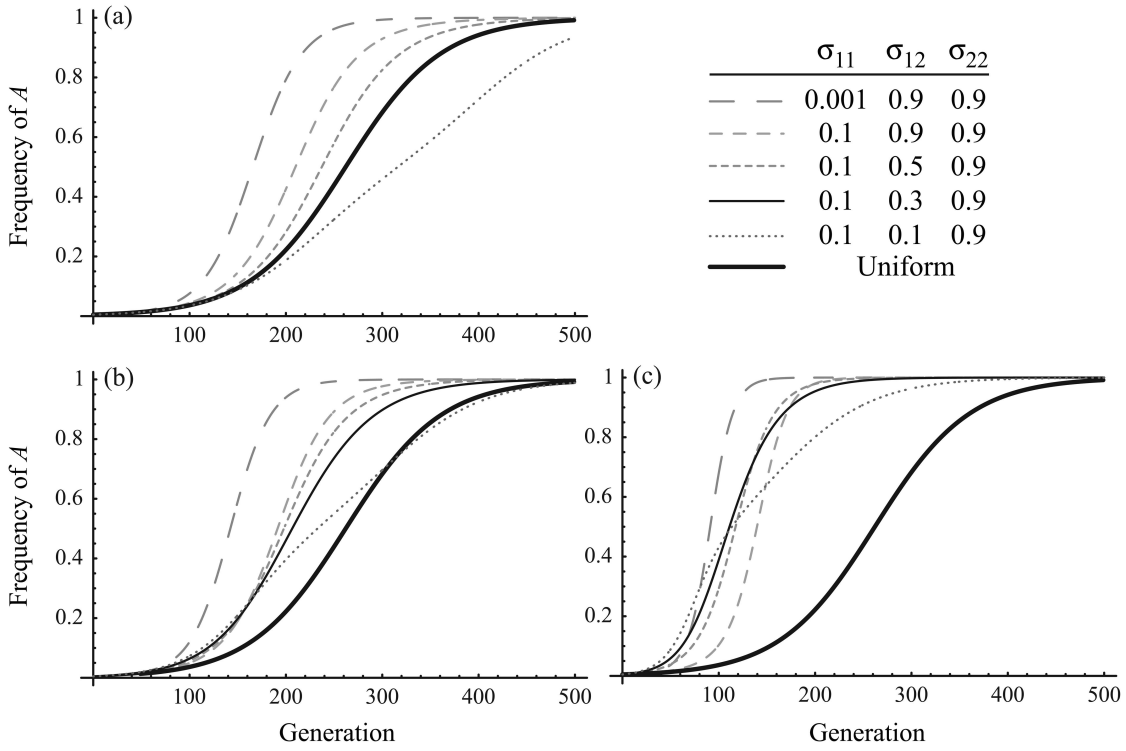

Figure 1: Rate of adaptation in a diploid population exhibiting fitness-associated sex (FAS). *a*, In the absence of a cost of sex ($c = 0$), the rate of adaptation is determined primarily by the form of FAS, with adaptation proceeding faster when heterozygotes engage in more sex than expected based on the extent of sex among homozygotes ($\sigma_{12}^2 > \sigma_{11}\sigma_{22}$; the thin solid curve with $\sigma_{12}^2 = \sigma_{11}\sigma_{22}$ is identical to the thick solid curve for uniform levels of sex). Adding a cost of sex, with $c = 0.01$ in *b* and 0.05 in *c*, causes selection to proceed more rapidly with FAS because both natural selection and the costs of sex act to eliminate deleterious alleles and preserve beneficial alleles. Additional parameters: $W_{12} = (W_{22})^{1/2} = 0.98$; the initial frequency of allele *A* was set to 0.005; mutation was assumed negligible.

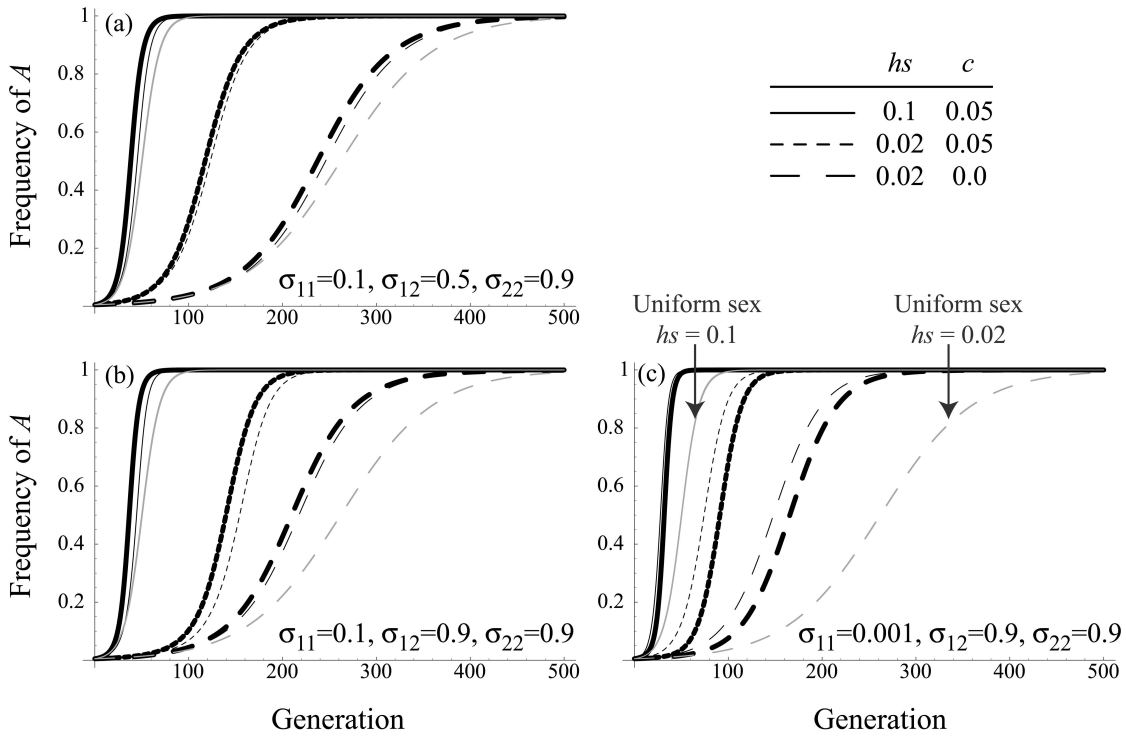

Figure 2: Comparison of quasi-linkage equilibrium (QLE) approximations with exact recursions. The QLE approximation (*thin black curves*) from equations (6)–(8b) is compared to the rate of adaptation from the exact recursions (*thick black curves*) using equation (4). For comparison, the gray curves show the rate of adaptation when sex occurs at a uniform rate (*solid*: $hs = 0.1$, *dashed*: $hs = 0.02$; unaffected by the cost of sex). *a*, The approximation is accurate when all individuals reproduce sexually at modestly high rates and heterozygotes engage in an intermediate level of sex ($\sigma_{11} = 0.1$, $\sigma_{12} = 0.5$, $\sigma_{22} = 0.9$), even with stronger selection and costs of sex. *b*, The QLE approximation begins to break down when costs are substantial, fitness-associated sex (FAS) is strong, and heterozygotes do not engage in an intermediate level of sex ($\sigma_{11} = 0.1$, $\sigma_{12} = 0.9$, $\sigma_{22} = 0.9$), because FAS and the costs of sex interact to alter the departure from Hardy-Weinberg (eq. [6]). *c*, The QLE approximation also breaks down if there is a class of individuals that rarely engages in sex ($\sigma_{11} = 0.001$, $\sigma_{12} = 0.9$, $\sigma_{22} = 0.9$). Nevertheless, increasing either s or c with FAS significantly increased the rate of adaptation in each of these cases, as predicted. Fitness is multiplicative, with $W_{12} = (W_{22})^{1/2} = 1 - sh$; the initial frequency of allele A was set to 0.005; and mutation was assumed negligible.

is expected to be strongly favored (Hadany and Otto 2007). To assess the robustness of our results, diploid simulations were conducted using the exact recursion equations (fig. 1). In the absence of costs of sex, the relative tendency of heterozygotes to engage in sex determines whether adaptation proceeds more rapidly (fig. 1*a*). The more often heterozygotes engage in sex, the faster adaptation proceeds. In the special case where the level of sex in heterozygotes is the geometric mean of the level in the two homozygotes ($\sigma_{11} = 0.1$, $\sigma_{12} = 0.3$, $\sigma_{22} = 0.9$) and costs of sex are absent, the rate of adaptation is unaffected by FAS, as expected from equation (7). With costs of sex, adaptation is accelerated by FAS when more fit individuals are less likely to engage in sex (fig. 1*b*, 1*c*). Indeed, the cost of sex rapidly becomes the most important factor determining the impact of FAS on the speed of adaptation. Figure 2 shows that the QLE results provide a good guide to the behavior of the system unless selection is strong, costs of sex are substantial, or sex is rare among fit individuals.

Discussion

A wide array of evidence supports the basic tenet of this article, that sexual reproduction in facultative sexuals is often condition dependent, with individuals in poorer condition being more likely to reproduce sexually (Bell 1982; see references in "Introduction"). We have explored the effect of such fitness-associated sex on the ability of a population to respond to environmental change, in both haploid and diploid species. When sex has no cost, FAS has no effect at all on the rate of adaptation in haploids, while the effect of FAS in diploids depends on the form of condition dependence. Specifically, the effect of FAS in diploids depends on the relative allocation to sexual re-

production of heterozygotes compared to the geometric average allocation to sex of the two homozygotes. Whenever heterozygotes engage in more sex than expected based on this geometric average, FAS facilitates adaptation. The opposite occurs when heterozygotes engage in less sex than expected. Thus, in the absence of costs of sex, whether adaptation would be hastened or not depends on the specifics of the case and the form that FAS takes. A clearer result emerges, however, when sex entails a cost, as is likely to be common in nature. In both haploid and diploid species with costly sex, FAS causes less fit individuals in the current environment to pay the costs of sex more often than more fit individuals. Thus, the cost of sex helps to eliminate maladapted alleles—alongside natural selection—and adaptation is significantly hastened.

Our previous results demonstrated that an association between low fitness and sex is likely to evolve due to the "selfish" interest of a gene that benefits by moving out of poor genetic backgrounds (Hadany and Otto 2007). As we show here, such an association can also benefit the population as a whole by increasing the rate of adaptation, especially when the costs of sex are significant, because the costs of sex amplify the effects of natural selection. That FAS can hasten adaptation is consistent with the modeling work of Leontiev et al. (2008), who demonstrated that the evolution of drug resistance in a viral population is hastened if drug-sensitive viruses are more likely to allow coinfection of the same cell by an additional virus, especially when coinfection has a cost.

This study is the first to show that the cost of sex can have a positive effect on the evolutionary success of sexual reproduction. Indeed, FAS can generate a long-term advantage for populations exhibiting some sexual reproduction over entirely asexual populations. Similarly, in the context of dispersal, Hadany et al. (2004) found that stress-induced dispersal can facilitate adaptation on a rugged fitness landscape, and again, this effect is stronger when dispersal is costly. These results might seem to contradict the results of Hadany and Beker (2003), who found very weak effects of fitness-associated recombination on the rate of adaptation, but that study investigated fitness-associated recombination (FAR, not FAS), and recombination was assumed to have no cost.

Finally, our results help to explain why at least some individuals should reproduce sexually (i.e., those in poor conditions). At the same time, our results make it even harder to explain the evolution of obligatory sex: none of the advantages of sex presented here would apply if the whole population were reproducing sexually. Thus, we not only need to explain how obligatory sex evolves within facultatively sexual species, but we also need to explain how obligatory sex evolves in species that engage in FAS. Our results imply that adaptation to new environments, one of the classical scenarios under which sex is advantageous, might favor FAS more strongly than obligatory sex. The explanation for the evolution of obligatory sex must thus involve additional factors not considered in this study, such as drift and selective interference among loci (see Otto 2009, in this issue), spatially varying selection (see Agrawal 2009, in this issue), or the effects of sexual selection (Agrawal 2001; Siller 2001; Hadany and Beker 2007).

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