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The genetic basis of adaptation through the evolution of mating systems

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Abstract

Although adaptation can be realized through the fixation of beneficial alleles that increase viability, in many plants, populations may adapt through the evolution of self-fertilization, especially when pollination becomes inefficient. However, the genetic basis of adaptation through the latter path remains unclear. By building population genetic models, I study adaptation through the fixation of alleles that increase the selfing rate (selfing modifiers) from new mutations or/and standing variation. For adaptive alleles unrelated to selfing, we have known that selfing promotes adaptation from a new mutation only when the beneficial alleles are recessive, while for fixation from standing variation, the probability is nearly independent of the dominance, and always decreases with the selfing rate. In contrast, for adaptation through evolution of the selfing rate, when it occurs by fixation of a newly arisen mutation, we found a population that already has a higher selfing rate may be more likely to adapt than outcrossers even when the modifier is dominant if the modifier is weakly selected, for fixation from standing variation, it is more likely through recessive alleles, with the highest fixation probability found in partially selfing populations, but fixation is fastest for alleles with intermediate dominance. A further extension to multiple loci suggests that adaptation is more likely when selfing is controlled by many slight-effect modifiers rather than few large-effect modifiers. This study suggests that to understand the genetic basis of adaptation, it is necessary to determine the ecological and genetic advantages of adaptive alleles.

Introduction

Adaptation often involves fixation of alleles that increase individual fitness, which can be through new beneficial mutations, or/and through alleles that are previously present in the population before an environmental change, often called standing genetic variation (Hermisson and Pennings 2005, Barret and Schluter 2008, Orr 2010, Lai 2019). In many plant populations, adaptation may be through the evolution of their mating systems, especially when the environmental change reduces the mating success (Barret et al. 2008, Eckert et al. 2010, Pannell 2015, Cheptou 2019). Although our understanding of adaptation through mating-unrelated beneficial alleles has been greatly promoted by previous studies (Orr 2001, Hermisson and Penings 2005, Barret and Schluter 2008, Orr 2010, Ronfort and Glemin 2013, Glemin and Ronfort 2013), how the genetic properties of alleles which modify the selfing rate influence the probability of successful adaptation remains unclear.

Adaptation through the evolution of mating systems may be particularly common for today's plant populations, since an increased level of human disturbance and widespread declines in pollinator populations have intensified limitation of pollen (Larson and Barrett 2000, Knight et al. 2005) and reduced plant reproductive success (Eckert et al. 2010, Thomann et al. 2013). Compared to outcrossing, selfing depends less on extrinsic factors, and thus may offer assurance for seed reproduction when pollination service is scarce (Holsinger 2000, Eckert et al. 2006). Indeed, an increased level of self-fertilization has been widely documented in response to various environmental conditions, including human disturbances (Eckert et al. 2010), habitat fragmentation (Aguilar et al. 2006), range expansion (Levin 2012), and colonization (Barrett et al. 2008, Pannell 2015). Also, the evolution of selfingis often associated with morphological changes in several floral characters (Goodwillie et al. 2010, Sicard and Lenhard 2011), controlled by multiple loci with both large and small effects (Fishman et al 2002, 2015, Goodwillie et al. 2006), or an increased level of self-compatibility (Igic et al. 2008, Busch and Schoen 2008).

Here I build population genetic models to understand the genetic bases underlying adaptation through the fixation of alleles that modify the selfing rate, which I refer to selfing modifiers from now on.

However, adaptation through the fixation of selfing modifiers differs from that of mating-unrelated alleles in several aspects. First, the selective advantage of a modifier allele depends on both genetic and ecological factors. Regarding genetic factors, selfing enjoys a transmission advantage over outcrossing (Fisher 1941), but suffers the cost of inbreeding depression (Charlesworth and Willis 2009). In the ecological aspect, selfing imposes a cost as it may reduce opportunities for pollen export, often called pollen discounting (Harder and Wilson 1998, Porcher and Lande 2005), but is more advantageous when pollen limitation becomes severe. Second, in a finite population, a selfing modifier should have a different effective population size from a mating-unrelated locus, since the selfing rate is polymorphic at the modifier locus, and during the fixation process, the level of inbreeding is no longer constant but changes with the frequency of the modifier. Third, although previous studies show that the fixation probability of mating-unrelated alleles will often be lower in populations with higher selfing rates (Caballero and Hills 1992, Glemin and Ronfort 2013), this may not hold for modifier alleles, as the selective advantage and effective population size of a modifier may depend on the selfing rate that is already in the population The answer to this question may also help us understand the speed of the evolution of selfing rates during the transition from outcrossing to selfing, which is prevalent in plant populations (Igic and Busch 2013).

Based on the above verbal analysis, I first derive the effective selection coefficient and the effective population size for a selfing modifier. I then use the diffusion approximation to obtain the fixation probability of such a modifier from a new mutation and from standing genetic variation. I consider adaptation through fixation at a single modifier locus in three demographic situations: a constant population, a declining population, and a population after a bottleneck. In contrast to adaptive alleles unrelated to selfing, for adaptation through evolution of the selfing rate, when it is from a new mutation, the critical dominance below which selfers have higher fixation probability than outcrssers can be higher than 0.5 if the modifier allele is weakly selected, or lower than 0.5 if it is strongly selected. When adaptation is from standing variation, it is more likely through recessive modifier alleles, which is more prominent in colonizing populations after a bottleneck. Generally, partial-selfing populations will have the highest fixation probability, suggesting a nonlinear evolutionary rate from outcrossing to selfing. An

extension to multiple loci suggests that adaptation is more likely when selfing is controlled by many slight-effect modifiers rather than few large-effect modifiers.

Models and results

I consider a selfing rate modifier locus with two alleles A and a in a hermaphroditic, diploid population with non-overlapping generations. asexual reproduction, that is, apomixis (Asker and Jerling 1992), which only happens in less than 1% of the species (Mogie 1992), is not considered and thus seeds will be produced from either selfing or outcrossing. The population already has a background selfing rate r_0, and the selfing rate of the three genotypes AA, Aa and aa are $r_0 + r$, $r_0 + hr$ and r_0, where h is the dominance coefficient. The inbreeding depression in the population is d and the level of pollen discounting is c, which means for an individual with a selfing rate r_i, a proportion $r_i c$ of its pollen will not be disseminated compared to a completely outcrossing individual. After the population suffers from pollen limitation with a strength m, and a proportion m of its ovules which should have been outcrossed will not be fertilized. Since the number of viable offspring from selfing relative to outcrossing is $(1-d)/(1-m)$,I can define an effective inbreeding depression, which incorporates the effect of pollen limitation as

$$d_e = 1 - \frac{1-d}{1-m}. \tag{1}$$

The evolution towards a higher selfing rate will increase the average fitness only when $1 - m < 1 - d$, so that $d_e < 0$, but $d_e > 0$ will also be considered for a thorough analysis. Moreover, it is assumed that the genetic properties of the selfing modifier locus are independent of the environment, so r and h are the same before and after pollen limitation.

To model the drift at a modifier locus, the key is to get the effective selective coefficient and the effective population size, based on which the fixation probability of alleles starting from any frequency can be calculated. This is done by first considering the frequency change and its variance after one discrete generation (see section 1 in File S1), and then using the diffusion approximation by considering an infinitesimal time interval $dt \to 0$. The overall allele frequency change is obtained by a weighted average of changes among selfed and outcrossed seeds. For outcrossed seeds, the allele frequency is the average of those in the pollen and ovule pool. The overall variance is the sum of two components:

variance in selfed and outcrossed offspring given that the proportion of selfed seeds is fixed, and variation of the actual proportion of selfed offspring. The first component is calculated by assuming the number of selfed and outcrossed offspring per individual is subject to a Poisson distribution. After that, the fixation probability of a modifier allele starting from any frequency can be easily obtained. The expected fixation probability from standing variation is integrated over the initial frequency distribution under the selection-drift-mutation equilibrium before pollen limitation. For declining populations, the fixation probability is modified to account for the reduction of effective population size caused by demographic decline, and the population goes extinction when all pre-existing alleles and all mutations that appears before the population size declines to 0 will not go fixation.

In the Appendix (section 2 in File S1), we show that the effective selection coefficient R the effective population size of the selfing enhancer allele A are

$$R = \frac{1 - 2d_e - c(1 - 2d_e r_0)}{2(1 - d_e r_0)(1 - c r_0)} r, \tag{2a}$$

$$N_e = \frac{2(1 - d_e r_0)}{2 + [1 - 3d_e + F(1 - d_e)] r_0} N. \tag{2b}$$

F is the inbreeding coefficient, which measures the deviation from the Hardy-Weinberg equilibrium. Although F will change with time, it approaches the equilibrium much quickly than the allele frequency changes (Hartfield and Glemin 2016). Therefore, F is first approximated with its equilibrium value, which depends on the allele frequency. However, it is shown that a secondary approximation of F as a frequency-independent constant works well (Table S1)given by

$$F \approx \frac{(1 - d_e) r_0}{2 - (1 + d_e) r_0} + \left(2 - \frac{1 - c}{1 - c r_0}\right) \frac{(1 - d_e) r_0 + h(1 - r_0)}{(2 - (1 + d_e) r_0)^2} r, \tag{3}$$

Equation (2a) shows the selective advantage depends on the background selfing rate, and unlike mating-unrelated loci, equation (2b) and (3) shows that the effective population size depends on the effect of the modifier r. N_e is also regulated by ecological factors and decreases with d_e and c (see Appendix (File S1)). In contrast, the effective population size of mating-unrelated alleles should increase with d_e since d_e lowers the level of inbreeding in the population (Caballero and Hill 1992).

Adaptation in a constant population

When fixation is from a single new modifier mutant, equation (7) shows that fixation is more likely through dominant modifiers. However, whether a higher background selfing rate will promote or inhibit fixation depends on the dominance coefficient.For a selfing modifier, the critical dominance coefficient h_c below which selfing increases the fixation probability is

$$h_c \approx \frac{1-2d_e}{2(1-d_e)(1-c-2d_e)}. \tag{4}$$

As shown in Fig. 1, h_c is higher than 0.5 when the pollen limitation is slight and pollen discounting is stronger (larger d_e and c). In this case, the critical dominance above which adaptation is less likely in selfers than outcrossers becomes more restricted compared to mating-unrelated alleles. On the contrary, when the modifier is strongly favored (d_e and c small), h_c is often smaller than 0.5. Therefore, when the evolution of selfing will increase the average fitness (i.e., $d_e < 0$), outcrossers may be much more likely to adapt than selfers. In contrast, h_c is always 0.5 for mating-unrelated alleles. This difference is mainly because the selective advantage of a selfing modifier depends on the background selfing rate (see equations (2) and (8)).

When fixation is through standing variation, for mating-unrelated alleles, the fixation probability is nearly independent of the dominance (Orr and Betancourt 2001), which holds for both outcrossing and selfing populations (Glemin and Ronfort 2013). However, for modifier alleles, fixation from standing variation is more likely through recessive alleles, as shown in Fig. 2. This pattern is more prominent when the background selfing rate r_0 is intermediate, and when the modifier is more strongly selected against before the environmental change and population size is larger(see Fig. S1). Also, for mating-unrelated alleles, fixation probability from standing variation decreases with the selfing rate (Glemin and Ronfort), suggesting adaptation is less likely in selfing population than in outcrossing populations (Hartfield et al. 2017). For selfing modifiers, this result usually holds when it is not very recessive ($h = 0.5, 0.9$ in Fig. 2). Contrary to that, when the modifier allele is recessive enough, fixation probability will be the highest when the background selfing rate is at an intermediate level ($h = 0.1$ in Fig. 2). However, when the modifier allele is weakly selected and pollen discounting is strong (Fig. 2(c)), for all level of dominance, fixation

probabilities increase almost monotonically with the background selfing rate. The above findings are robust to the effect of the selfing modifier r, as the fixation probability is nearly independent of r (Fig. S2).

Despite a higher fixation probability for recessive modifier alleles when adaptation is from standing variation, generally, fixation is fastest when the allele is intermediate dominant, while slowest for dominant alleles (Fig. S3), although when the allele is under weak selection fixation is quickest for recessive alleles (Fig. S3(c)). The above findings are robust to r (Fig. S4). As a contrast, for mating-unrelated alleles, more dominant alleles will go to fixation more quickly (Glemin and Ronfort 2013).

The above several differences mainly result from the characteristic that the evolution at a selfing modifier locus will change the level of inbreeding at the locus itself. At the selection-mutation-drift equilibrium before the environmental change, because selfing enhancer alleles is exposed more in homozygotes, it will be kept at an even lower frequency than mating-unrelated alleles of the same selective disadvantage. Moreover, a higher dominance will strengthen the selection at two aspects. First, it directly increases the selfing rate of the heterozygote. Second, an enhanced selfing rate of the heterozygotes further increases the homozygosity, which indirectly increases the strength of selection. As a result, compared to mating-unrelated alleles, dominant alleles will be more strongly selected against before the environmental change, but are more favored after that. The above results indicate that in terms of both the fixation probability and time to fixation, the latter advantage is usually not able to compensate for the former disadvantage.

Adaptation in a declining population

The previous section considers populations that are still able to persist itself and maintain a constant size after pollen limitation. However, some populations may not produce sufficient offspring and thus will suffer a demographic decline and go extinct. To investigate adaptation in declining populations, I consider a population which has an expected offspring number $1-\lambda$ after pollen limitation, and will be successfully rescued when the selfing enhancer allele A goes to fixation.

. For rescue from new mutations, equation (16) shows that the critical dominance at which selfers and outcrossers have the same rescue probability is higher than that in a constant population. Therefore, demographic decline favors selfers to be more likely to adapt than outcrossers.

For rescue from standing variation, demographic decline favors adaptation through dominant alleles compared to that that in a constant population , which can be seen, for example, by comparing $r_0 = 0$ in Figs. 3(a) and 2(a), and is more prominent when r is small (Fig. S5). Moreover, for all levels of dominance (Fig. 3(b)), the proportion that rescue from standing variation is lower for dominant alleles, and decreases with the background selfing rate, suggesting an increased relative contribution from new mutations in selfing populations. However, how dominance influences the overall rescue probability from both sources should depend on the relative contribution from standing variation. Rescue will be more likely through recessive alleles when the contribution from standing variation is larger, which happens under a smaller effect r (Fig. S5), a larger initial population size and a faster decline rate (Glemin and Ronfort 2013).

Adaptation after a bottleneck

In the previous sections, we consider that the environmental change happens in the original habitat. However, the evolution of self-fertilization is often associated with bottleneck effects to some degree (Eckert et al. 2010, Aguilar et al. 2006, Levin 2012, Barrett et al. 2008, Pannell 2015). We consider a population of an ancestral size N_0 and suffers from a bottleneck effect of N_c individuals in the new environment. Equation (7) indicates that the bottleneck effect will have little effect on the fixation probability of a new mutant. For adaptation from standing variation, compared to a constant population, the bottleneck effect lowers the fixation probability (compare the y axis in Figs. 3(c) and 2(a)). Fixation is even more biased for recessive alleles, especially when the background selfing is low, which can be easily seen by comparing Fig. 3(c) with Fig. 2(a) at $r_0 = 0$. In contrast, fixation probability is usually insensitive to dominance for mating-unrelated alleles (Fig. S6). Moreover, for all levels of dominance, fixation probability always decreases with the background selfing rate. It is often considered that self-compatible populations are more likely to establish after long-distance dispersal, known as Baker's law (Baker 1951, Cheptou 2012). However, it is often misinterpreted as an association between higher selfing rates with successful colonization. Our result indicates that establishment of the colony through the

genetic evolution of selfing is actually more probable for outcrossing populations. This result supports the viewof Pannell et al. (2015) that Baker's law should be interpreted in terms of an enhanced capacity of selfing associated with colonization.

Genetic architectures under adaptation

Previous results consider fixation at a single modifier locus. However, as selfing rate is often controlled by multiple modifier loci, it is critical to ask whether adaptation is more likely when the selfing rate is controlled by many slight-effect modifier loci or few large effect loci, given the mutation rate is the same at each locus. For adaptation from standing variation, as the fixation probability at a single locus is insensitive to r (Fig. S2), the genetic architecture of many slight-effect loci should have more advantages. However, the answer is not clear for adaptation from new mutations. Although genetic architecture of many slight-effect loci has a higher overall mutation rate, the fixation probability at a single locus is lower. Here we assume modifier loci act additively on the selfing rate, as selfing rates sometimes have an approximately linear relationship with phenotypic values of several quantitative characters (Karron et al. 1997, Strand et al. 2017, Fishman et al. 2002, 2015). In this case, we show in equation (19) that in a constant population, the effect of genetic architecture on fixation can be assessed by the value of $r^{-1}P_{fix}^{new}(r)$, which generally decreases with r (Fig. S7), so adaptation is more likely from many small-effect modifier loci. This may explain why QTL analysis found little evidence for large-effect loci underlie floral traits associated with mating system divergence in some species like *Mimulus* (Fishman et al. 2002, 2015). However, in a declining population, the genetic architecture of few large-effect loci may have more advantages (see discussion below equation (19)).

Incorporating the genetic basis of inbreeding depression

Up to now, we have treated inbreeding depression as a constant parameter. However, as inbreeding depression is caused by deleterious mutations, it will evolve with the mating system, and previous models and empirical evidence have shown that a higher selfing rate will lower the inbreeding depression (Lande and Schemske 1985, Roze 2015). Moreover, selection against deleterious mutations may also inhibit fixation of a linked beneficial mutation, known as background selection (Charlesworth et al. 1993,

Charlesworth 2012), and is more severe in selfing populations due to a reduced effective recombination rate. By incorporating the genetic basis of inbreeding depression, Fig. 4 shows that both from new mutations and standing variation, the fixation probability is highest at an intermediate selfing rate, suggesting the trade-off between the benefit of a lower inbreeding depression and the cost of a higher background selection. More specifically, the selfing rate corresponding to the highest fixation probability is higher for recessive alleles when fixation from a new mutation (Fig. 4(a)), but lower when from standing variation (Fig. 4(b)). Although the rate of the transition from outcrossing to selfing has been estimated at the phylogenetic scale (Igic and Busch 2013), the above result implies that at a smaller scale during this transition, the evolution of self-fertilization accelerates when the population initially starts from a predominantly outcrossing, while slows down later when it approaches predominantly selfing.

Conclusion

While the genetic basis of adaptation through fixation of mating-unrelated adaptive alleles has been well studied (Haldane 193, Orr 2001, Hermisson and Pennings 2005, Glemin and Ronfort 2013), it is not clear whether these results can apply to the case when adaptation is through the evolution of mating systems. In this study, we investigate fixation of selfing modifier alleles from new mutations and standing variation in populations under different demographic situations. While the critical dominance h_c below which a selfing population has a higher fixation probability than an outcrossing population is always $h_c = 0.5$ for mating-unrelated alleles, for selfing modifiers, h_c can be either larger or smaller than 0.5, depending on the genetic and ecological advantages (Fig. 1). On the other hand, adaptation from standing variation is more likely through recessive modifier alleles (Fig. 1), which seems to be supported by previous genetic analysis for the quick evolution of selfing rates in *Mimulus guttatus* (Roels and Kelly 2011), but fixation is quickest for intermediate dominant modifier alleles (Fig. 2). Generally, compared to a constant population, adaptation is more likely through dominant alleles under a demographic decline, while a bottleneck effect favors recessive alleles.

These characteristics of adaptation through the evolution of mating systems result from two factors. First, a modifier allele has a different inbreeding coefficient from mating-unrelated alleles, as it directly

influences the level of inbreeding at the locus itself. Second, dominance has two-fold effects, as it directly increases the selfing rate of the heterozygote, which further increases the homozygosity. Although the dominance coefficient distribution of mating-unrelated alleles is generally unknown (Orr 2010), for modifier alleles, it may be possible to estimate dominance by combining QTL analyses of selfing-related characters (Fishman et al. 2002, 2014) with studies on the association between selfing rate and phenotypic values. This work also provides insights on how the selfing rate of the population affects adaptation through evolution towards a higher selfing rate. Generally, a higher selfing rate limits the further increase of self-fertilization, but this may be counterbalanced by the coevolution of deleterious mutations in the genome (Fig.5).

Although we contrast adaptation through the evolution of mating system with that through increase of viability or fertility, adaptation may involve both paths through fixation of alleles that simultaneously influence several aspects of individual fitness. For example, an allele that reduces the flower display may not only allow more resources to be allocated for fertility (Sargent et al. 2007), but also increase the selfing rate (Sicard and Lenhard 2011). On the other hand, alleles that increase the selfing may impose a fitness cost. For example, reduction of the flower size may be caused by deleterious mutations that inhibit the development (Kelly and Willis 2001). This pleiotropy may make genetic basis underlying adaptation more complicated. All in all, this work suggests the importance of a mechanistic understanding of the source of selective advantage of adaptive alleles.

Methods

Adaptation in a constant population size

The fixation probability of a selfing modifier allele with an initial frequency x is given by (Kimura 1962)

$$\pi(x) = \frac{\int_0^x G(p)\,dp}{\int_0^1 G(p)dp}, \tag{5}$$

where

$$G(p) = \exp\left[-\int \frac{2M(p)}{V(p)}dp\right], \tag{6a}$$

$$M = Rp(1-p)[h + F - hF + (1-F)(1-2h)\,p], \tag{6b}$$

$$V = \frac{p(1-p)}{2N_e}. \tag{6c}$$

M and V is the expected change of the allele frequency and its variance under the limit of an infinitesimal time interval. When $N_e(h + F - hF)R \gg 1$, the fixation probability can be approximated as

$$P_{fix}^{new} \approx \frac{(2h(1-r_0) + (1-d_e)r_0)\big(1 - 2d_e - c(1-2d_e r_0)\big)}{2(1-cr_0)(1-d_e r_0)^2} r + o(r) \tag{7}$$

The fixation probability of a selfing modifier mutant in a completely outcrossing ($r_0 = 0$) and a nearly completely selfing ($r_0 = 1 - r$) population can be approximated as

$$P_{fix}^{new}(r_0 = 0) \approx (1 - c - 2d_e)hr + o(r), \tag{8a}$$

$$P_{fix}^{new}(r_0 = 1 - r) \approx \frac{1 - 2d_e}{2(1-d_e)} r + o(r). \tag{8b}$$

When the above two equations are equal, we can solve for the critical dominance h_c at which the fixation probability is the same for outcrossers and selfers, given in equation (4).

For adaptation from standing variation, denote the mutation rate from allele a to A as ν_1, and the backward mutation rate as ν_2. Before pollen limitation happens, allele A is selected against, and in a finite population under selection-drift-mutation balance, the stationary distribution of frequency of allele A is (Ewens 2012)

$$\Psi(x) = \frac{C_1}{V(x)} \exp\left[2\int_0^x \frac{M_d(p)}{V(p)} dp\right] \tag{9}$$

where C_1 is a constant which normalizes the integral as $\int_0^1 \Psi(x)dx = 1$, and $M_d(p) = M(p) + (1-p)\nu_1 - p\nu_2$, with d_e replaced by d. Therefore, the expected fixation probability from standing genetic variation is (Orr 2001)

$$P_{fix}^{sv} = \int_0^1 \pi(x)\Psi(x)dx \tag{10}$$

Adaptation in a declining population

Suppose the maximum number of offspring an individual can produce is W_0, the absolute fitness of aa individuals after pollen limitation happens is

$$W = W_0\big((1-d)r_0 + (1-r_0)(1-m)\big) = W_0\big((1-m) + (m-d)r_0\big) \tag{11}$$

The absolute fitness of AA individuals is

$$W' = W_0\big((1-d)(r_0+r) + (1-r_0-r)(1-m)\big) = W\left(1 - \frac{d_e}{1-d_e r_0} r\right) \tag{12}$$

Therefore, for the evolution of selfing to rescue the population ($W' > 1$), it requires $r > (1-d_e r_0)(1-W^{-1})/d_e$. Denote the rate of demographic decline as $\lambda = 1 - W$, the fixation probability from a single mutant is reduced to (Glemin and Ronfort 2013)

$$P_{fix}^{new*} \approx 2\frac{N_e}{N}\big((h + F - hF)R - \lambda\big) \tag{13}$$

We assume the level of pollen limitation is independent of the population size, so the probability for a population starting from an initial size N_0 to be rescued by new mutations is approximately (Orr and Unckless 2008)

$$P_{res}^{new} = 1 - \exp\left[-\frac{2N_0 \nu_1 P_{fix}^{new*}}{\lambda}\right] \tag{14}$$

To obtain the critical dominance at which the fixation probability is the same for outcrossers and selfers, note that the rescue probability from new mutations in a completely outcrossing ($r_0 = 0$) and a nearly completely selfing ($r_0 = 1 - r$) population are

$$P_{res}^{new}(r_0 = 0) \approx 1 - \exp\left[2N_0\nu_1\left(2 - \frac{(1-c-2d_e)hr}{\lambda}\right)\right], \tag{15a}$$

$$P_{res}^{new}(r_0 = 1-r) \approx 1 - \exp\left[2N_0\nu_1\left(1 - \frac{(2(1-2d_e) - 3\lambda)r}{4(1-d_e)\lambda}\right)\right]. \tag{15b}$$

Therefore, the critical dominance is

$$h_{c2} = h_c + \frac{\lambda}{1-c-2d_e}\left(\frac{1}{r} - \frac{3}{4(1-d_e)}\right) \tag{16}$$

Since r is assumed to be small and $d_e < 0.5$, the second term is usually positive, and thus $h_{c2} > h_c$. The probability for the population to be rescued by standing variation is approximately

$$P_{res}^{sv} = \int_0^1 \left(1 - P_{fix}^{new*}\right)^{2N_0 x} \Psi(x)dx \tag{17}$$

The population will go extinction when alleles from both standing variation and new mutations cannot fix, so the overall rescue probability is $P_{res} = 1 - (1 - P_{res}^{sv})(1 - P_{res}^{new})$, and the relative contribution to rescue from standing variation is $\Pi_{sv} = P_{res}^{sv}/P_{res}$.

Adaptation after a bottleneck

When the population with an initial size N_0 suffers a bottleneck effect with an initial population size N_c, suppose the allele frequency in the ancestral population is x, given that $N_0 \gg N_c$, the probability that the allele frequency after the bottleneck is x' is approximately a binomial distribution. Therefore, the expected fixation probability from standing variation is approximately

$$P_{fix}^{sv*} = \int_0^{2N_c} \pi(k/2N_c)\binom{2N_c}{k} dk \int_0^1 x^2(1-x)^2\psi(x)dx \tag{18}$$

Adaptation from multiple loci

To figure out whether adaptation is more likely when the selfing rate is controlled by many slight effect modifier loci or few large effect loci, we suppose there are n identical modifier loci, and we assume fixation of a selfing enhancer allele at one of the loci is enough for successful adaptation. Given a certain time interval Δt, and assume the mutation events happen as a Poisson process, the number of mutations arising in the whole genome is subject to a Poisson distribution with a mean $\lambda = 2Nnu\Delta t$. Therefore, the probability of adaptation is

$$P_{fix(multi)}^{new} = 1 - \sum_{j=0}^{\infty} \frac{\lambda^j e^{-\lambda}}{j!}\left(1 - P_{fix}^{new}\right)^j = 1 - \exp\left[-2NnuP_{fix}^{new}\Delta t\right]. \tag{19}$$

Note that P_{fix}^{new} depends on the effect r. Equation (11) suggests that we can directly assess the effect of genetic architecture by examining the value nP_{fix}^{new}. When modifier loci act additively, $n \propto r^{-1}$. For adaptation in a declining population, equation (14) still holds, with ν_1 replaced by $n\nu_1$. Therefore, the genetic architecture can be assessed through $r^{-1}P_{fix}^{new*}$, which increases with r.

Incorporating the genetic basis of inbreeding depression

It has been firmly established that inbreeding depression is mainly contributed by two categories of deleterious mutations (Charlesworth and Willis 2009): slightly deleterious, partially dominant mutations, and large-effect, highly recessive lethal and sublethal mutations. Slightly deleterious, partially dominant mutations also causes background selection (Charlesworth 2012). We assume there is a fixed level of background inbreeding depression d_0 for populations with different levels of selfing rate. This highly recessive large-effect mutations, as inbreeding depression contributed by mutation of this category is

nearly independent of the selfing rate (Lande et al. 1994). Therefore, here we only consider the influences of the selfing rate on the inbreeding depression contributed by slightly deleterious mutations. Assume the haploid genomic mutation rate is U, and all deleterious mutations are identical with selection coefficient s and dominance h_d. For a population at the equilibrium state, so that the inbreeding depression can be approximated by (Roze 2015)

$$d = 1 - (1 - d_0)\left(1 + \frac{I_2}{4}\right)\exp\left[-U\frac{1 - 2h_d}{2h_d + r_0(1 - 2h_d)}(1 + I_1) + \frac{r_0}{2 - r_0}I_2\right], \tag{20}$$

where

$$I_1 = 2U(1 - h)(1 - 2h)\frac{2 + r_0}{2 - r_0}\,T, \tag{21a}$$

$$I_2 = U^2(1 - 2h_d)^2 T, \tag{21b}$$

$$T = \frac{2r_0(1 - r_0)}{(4 - r_0)[2h_d + r_0(1 - 2h_d)]^2}. \tag{21c}$$

The effect of the background selection on reducing the effective population (Nordborg et al. 1996) is

$$\alpha \approx \exp\left[-\frac{2U}{(h_d + F_d - h_d F_d)s + L(1 - F_d)}\right], \tag{22}$$

where L is the number of crossovers along the chromosomes and $F_d = r_0/(2 - r_0)$. The fixation probability can be calculated by replacing N_e with αN_e in equations (5) and (10).

Simulations

Simulations are written in R 4.0.2 and the code is archived on Dryad [filed upon acceptance]. Every generation, reproduction occurs first based on the individual selfing rate, and then selection. The expected genotype frequencies are calculated, based on which the next generation is drawn from a multinomial distribution. For adaptation from standing variation, we run $6N_0$ generations to reach the selection-drift-mutation equilibrium (Hermisson and Penngings 2005), with forward and backward mutations are introduced, and after pollen limitation happens, the input of mutations stops. For adaptation in a declining population, the population size in the next generation is drawn from a Poisson distribution with the mean being the product of the current population size and the average fitness. The population is considered as extinction when $N = 0$, and is considered as rescued when the modifier allele goes to fixation or the population size exceeds $10N_0$.

References

Aguilar, R., Ashworth, L., Galetto, L., & Aizen, M. A. (2006). Plant reproductive susceptibility to habitat fragmentation: review and synthesis through a meta-analysis. Ecology letters, 9(8), 968-980.

Asker, S., & Jerling, L. (1992). Apomixis in plants. CRC press.

Baker, H. G. (1955). Self-compatibility and establishment after 'long-distance' dispersal. Evolution, 9(3), 347-349.

Barrett, S. C., Colautti, R. I., & Eckert, C. G. (2008). Plant reproductive systems and evolution during biological invasion. Molecular ecology, 17(1), 373-383.

Barrett, R. D., & Schluter, D. (2008). Adaptation from standing genetic variation. Trends in ecology & evolution, 23(1), 38-44.

Bell, G. (2017). Evolutionary rescue. Annual Review of Ecology, Evolution, and Systematics, 48, 605-627.

Bodbyl Roels, S. A., & Kelly, J. K. (2011). Rapid evolution caused by pollinator loss in Mimulus guttatus. Evolution: International Journal of Organic Evolution, 65(9), 2541-2552.

Busch, J. W., & Schoen, D. J. (2008). The evolution of self-incompatibility when mates are limiting. Trends in plant science, 13(3), 128-136.

Caballero, A., & Hill, W. G. (1992). Effective size of nonrandom mating populations. Genetics, 130(4), 909-916.

Charlesworth, B., M. T. Morgan, and D. Charlesworth. 1993a. The effect of deleterious mutations on neutral molecular variation. Genetics.134:1289–1303.

Charlesworth, D., & Willis, J. H. (2009). The genetics of inbreeding depression. Nature reviews genetics, 10(11), 783-796.

Cheptou, P. O. (2012). Clarifying Baker's law. Annals of botany, 109(3), 633-641.

Cheptou, P. O. (2019). Does the evolution of self-fertilization rescue populations or increase the risk of extinction?. Annals of Botany, 123(2), 337-345.

Eckert, C. G., Kalisz, S., Geber, M. A., Sargent, R., Elle, E., Cheptou, P. O., ... & Porcher, E. (2010). Plant mating systems in a changing world. Trends in Ecology & Evolution, 25(1), 35-43.

Eckert, C. G., Samis, K. E., & Dart, S. (2006). Reproductive assurance and the evolution of uniparental reproduction in flowering plants. Ecology and evolution of flowers, 183, 203.

Ewens, W. J. (2012). Mathematical population genetics 1: theoretical introduction (Vol. 27). Springer Science & Business Media.

Fisher, R. A. (1941). Average excess and average effect of a gene substitution. Annals of Eugenics, 11(1), 53-63.

Fishman, L., Beardsley, P. M., Stathos, A., Williams, C. F., & Hill, J. P. (2015). The genetic architecture of traits associated with the evolution of self-pollination in Mimulus. New Phytologist, 205(2), 907-917.

Fishman, L., Kelly, A. J., & Willis, J. H. (2002). Minor quantitative trait loci underlie floral traits associated with mating system divergence in Mimulus. Evolution, 56(11), 2138-2155.

Glémin, S., & Ronfort, J. (2013). Adaptation and maladaptation in selfing and outcrossing species: new mutations versus standing variation. Evolution: International Journal of Organic Evolution, 67(1), 225-240.

Goodwillie, C., Ritland, C., & Ritland, K. (2006). The genetic basis of floral traits associated with mating system evolution in Leptosiphon (Polemoniaceae): an analysis of quantitative trait loci. Evolution, 60(3), 491-504.

Goodwillie, C., Sargent, R. D., Eckert, C. G., Elle, E., Geber, M. A., Johnston, M. O., ... & Winn, A. A. (2010). Correlated evolution of mating system and floral display traits in flowering plants and its implications for the distribution of mating system variation. New Phytologist, 185(1), 311-321.

Haldane, J. B. S. (1927). A mathematical theory of natural and artificial selection, part V: selection and mutation. In Mathematical Proceedings of the Cambridge Philosophical Society (Vol. 23, No. 7, pp. 838-844). Cambridge University Press.

Harder, L. D., & Wilson, W. G. (1998). A clarification of pollen discounting and its joint effects with inbreeding depression on mating system evolution. The American Naturalist, 152(5), 684-695.

Hermisson, J., & Pennings, P. S. (2005). Soft sweeps: molecular population genetics of adaptation from standing genetic variation. Genetics, 169(4), 2335-2352.

Holsinger, K. E. (2000). Reproductive systems and evolution in vascular plants. Proceedings of the National Academy of Sciences, 97(13), 7037-7042.

Igic, B., Lande, R., & Kohn, J. R. (2008). Loss of self-incompatibility and its evolutionary consequences. International Journal of Plant Sciences, 169(1), 93-104.

Igic, B., & Busch, J. W. (2013). Is self-fertilization an evolutionary dead end?. New Phytologist, 198(2), 386-397.

Karron, J. D., Jackson, R. T., Thumser, N. N., & Schlicht, S. L. (1997). Outcrossing rates of individual Mimulus ringens genets are correlated with anther–stigma separation. Heredity, 79(4), 365-370.

Kelly, J. K., & Willis, J. H. (2001). Deleterious mutations and genetic variation for flower size in Mimulus guttatus. Evolution, 55(5), 937-942.

Kimura, M. (1962). On the probability of fixation of mutant genes in a population. Genetics, 47(6), 713.

Knight, T. M., Steets, J. A., Vamosi, J. C., Mazer, S. J., Burd, M., Campbell, D. R., ... & Ashman, T. L. (2005). Pollen limitation of plant reproduction: pattern and process. Annu. Rev. Ecol. Evol. Syst., 36, 467-497.

Lai, Y. T., Yeung, C. K., Omland, K. E., Pang, E. L., Hao, Y., Liao, B. Y., ... & Hung, H. Y. (2019). Standing genetic variation as the predominant source for adaptation of a songbird. *Proceedings of the National Academy of Sciences*, *116*(6), 2152-2157.

Lande, R., & Schemske, D. W. (1985). The evolution of self-fertilization and inbreeding depression in plants. I. Genetic models. Evolution, 39(1), 24-40.

Lande, R., Schemske, D. W., & Schultz, S. T. (1994). High inbreeding depression, selective interference among loci, and the threshold selfing rate for purging recessive lethal mutations. Evolution, 48(4), 965-978.

Larson, B. M., & Barrett, S. C. (2000). A comparative analysis of pollen limitation in flowering plants. Biological journal of the Linnean Society, 69(4), 503-520.

Levin, D. A. (2012). Mating system shifts on the trailing edge. Annals of Botany, 109(3), 613-620.

Miller, J. S., Blank, C. M., & Levin, R. A. (2019). Colonization, Baker's law, and the evolution of gynodioecy in Hawaii: implications from a study of Lycium carolinianum. American journal of botany, 106(5), 733-743.

Mogie, M. 1992. The Evolution of Asexual Reproduction in Plants. Chapman & Hall, London.

Nordborg, M., Charlesworth, B., & Charlesworth, D. (1996). The effect of recombination on background selection. Genetics Research, 67(2), 159-174.

Orr, H. A. (2005). The genetic theory of adaptation: a brief history. Nature Reviews Genetics, 6(2), 119-127.

Orr, H. A. (2010). The population genetics of beneficial mutations. Philosophical Transactions of the Royal Society B: Biological Sciences, 365(1544), 1195-1201.

Orr, H. A., & Betancourt, A. J. (2001). Haldane's sieve and adaptation from the standing genetic variation. Genetics, 157(2), 875-884.

Orr, H. A., & Unckless, R. L. (2008). Population extinction and the genetics of adaptation. The American Naturalist, 172(2), 160-169.

Pannell, J. R. (2015). Evolution of the mating system in colonizing plants. Molecular Ecology, 24(9), 2018-2037.

Pannell, J. R., Auld, J. R., Brandvain, Y., Burd, M., Busch, J. W., Cheptou, P. O., ... & Hovick, S. M. (2015). The scope of Baker's law. New Phytologist, 208(3), 656-667.

Porcher, E., & Lande, R. (2005). The evolution of self-fertilization and inbreeding depression under pollen discounting and pollen limitation. Journal of evolutionary biology, 18(3), 497-508.

Ronfort, J., & Glemin, S. (2013). Mating system, Haldane's sieve, and the domestication process. Evolution, 67(5), 1518-1526.

Roze, D. (2015). Effects of interference between selected loci on the mutation load, inbreeding depression, and heterosis. Genetics, 201(2), 745-757.

Sargent, R. D., Goodwillie, C., Kalisz, S., & Ree, R. H. (2007). Phylogenetic evidence for a flower size and number trade-off. American Journal of Botany, 94(12), 2059-2062.

Sicard, A., & Lenhard, M. (2011). The selfing syndrome: a model for studying the genetic and evolutionary basis of morphological adaptation in plants. Annals of botany, 107(9), 1433-1443.

Spigler, R. B., & Ashman, T. L. (2012). Gynodioecy to dioecy: are we there yet?. Annals of Botany, 109(3), 531-543.

Strandh, M., Jönsson, J., Madjidian, J. A., Hansson, B., & Lankinen, Å. (2017). Natural selection acts on floral traits associated with selfing rate among populations of mixed-mating Collinsia heterophylla (Plantaginaceae). International Journal of Plant Sciences, 178(8), 594-606.

Thomann, M., Imbert, E., Devaux, C., & Cheptou, P. O. (2013). Flowering plants under global pollinator decline. Trends in plant science, 18(7), 353-359.

	Mating-unrelated allele	Selfing modifier allele
Adaptation from new mutations in a constant population	Fixation probability is higher for dominant alleles; selfers have a higher fixation probability when $h < 0.5$.	Fixation probability is higher for dominant alleles; selfers have a higher fixation probability for for all h, but strongly selected
Adaptation from standing variation in a constant population	Fixation probability is nearly independent of dominance; fixation probability decreases with the selfing rate; fixation is quickest for dominant alleles	Fixation probability is higher for recessive alleles; fixation is quickest when alleles are intermediate dominant, while slowest for dominant alleles; fixation probability is highest at an intermediate selfing rate
Adaptation in declining populations	h_c increases; rescue is more likely through dominant alleles; rescue probability from standing variation is lower in selfers	h_c increases; favors rescue through dominant alleles; rescue probability from standing variation is lower in selfers.
Adaptation in populations after bottleneck	Fixation probability is usually insensitive to dominance; adaptation is less likely in selfers.	Recessive alleles have a much higher fixation probability; adaptation is less likely in selfers.
Genetic architecture of adaptation	N/A	Many small-effect loci rather than few large-effect loci,
Under the coevolution of inbreeding depression	N/A	The fixation probability from both new mutations and standing variation is highest at an intermediate selfing rate

Table 1. Comparison of the genetics of adaptation for mating-unrelated alleles with selfing modifier alleles. h_c is the critical dominance above which fixation probability is lower in selfers than outcrossers.

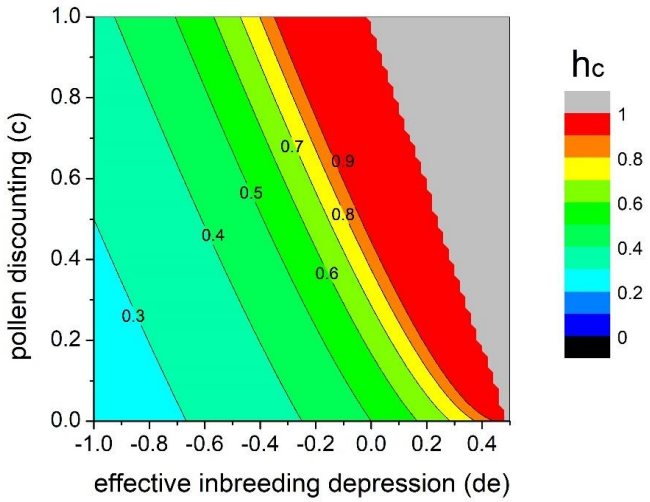

Figure 1. Effects of pollen discounting c and effective inbreeding depression d_e on the value of critical dominance h_c. Results are calculated based on equation (4), but the value is set to be 1 if $h_c > 1$,. The grey area is where for all level of dominance, the selfing modifier is selected against in a completely outcrossing population and thus cannot fix, but favored in a highly selfing population (see equation (8)).

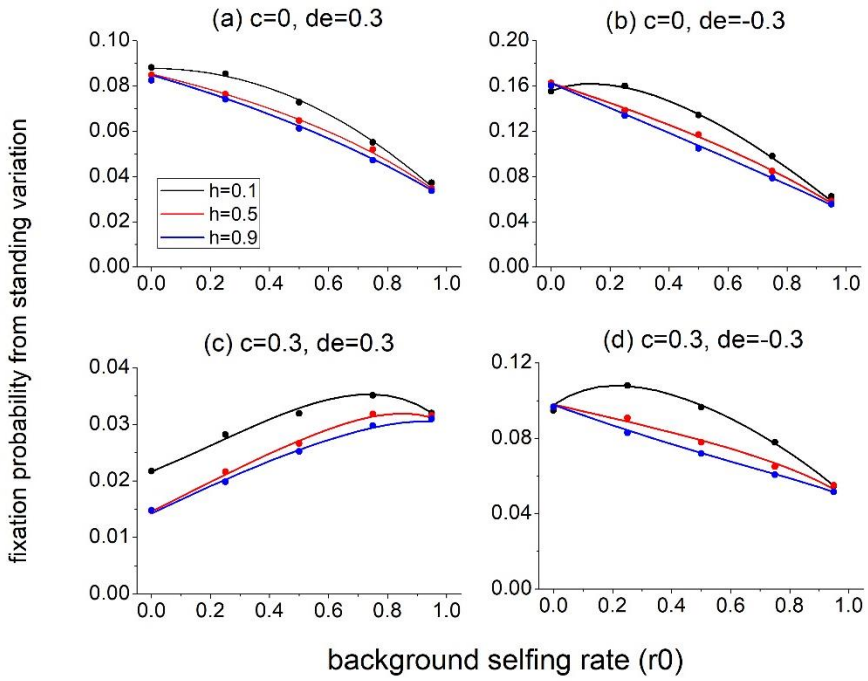

Figure 2. Effects of background selfing rate on fixation probability from standing variation in a constant population. Lines are model predictions from equation (10), and dots are simulation results. For all panels, $r = 0.01, d = 0.6, N = 20000, \nu_1 = \nu_2 = 10^{-6}$.

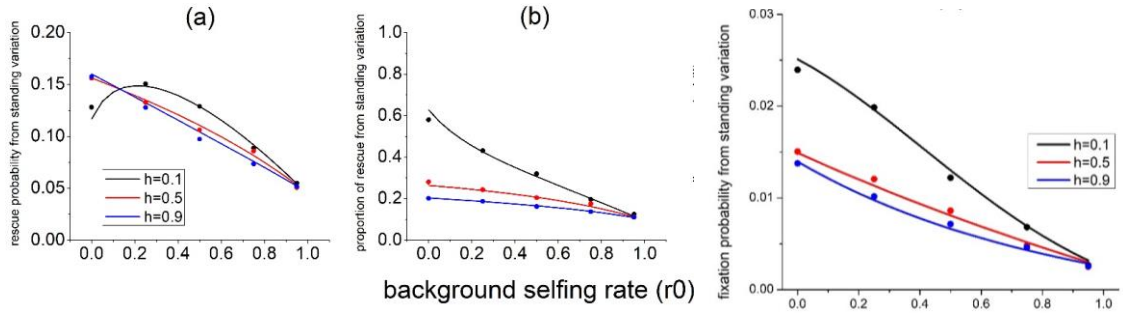

Figure 3. Effects of the background selfing rate on the rescue probability in declining populations(panels (a), (b)) and populations suffering a bottleneck (panel (c)). Lines in panels (a), (b) and (c) are model predictions from equation (14), (17) and (18), respectively, and dots are simulation results. For panel (a) and (b), $r = 0.05, d = 0.6, d_e = -0.3, c = 0, N_0 = 20000, \lambda = 0.002, \nu_1 = \nu_2 = 10^{-6}$. For panel (c), $r = 0.01, d = 0.6, d_e = -0.3, N_0 = 20000, N_c = 500, \nu_1 = \nu_2 = 10^{-6}$.

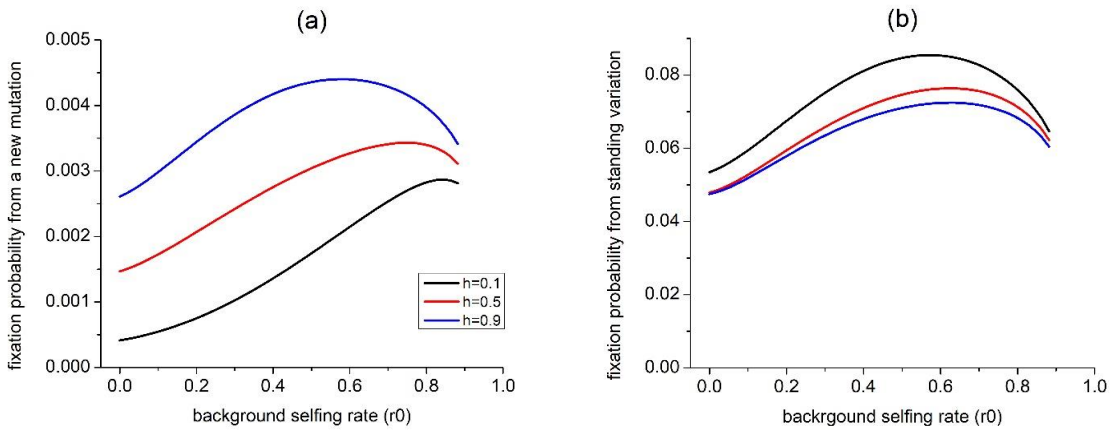

Figure 4. Effects of the background selfing rate on the population survival probability from a new mutation (panel (a)) and standing variations (panel (b)) when incorporating the genetic basis of inbreeding depression and background selection. Parameters related to deleterious mutations are $U = 0.4, h_d = 0.2, s = 0.1, d_0 = 0.4, L = 10$; and other parameters are $r = 0.01, c = 0, m = 0.5, N = 20000, \nu_1 = \nu_2 = 10^{-6}$.