Hide and seek: hidden genetic variance contributing to the adaptive potential of selfing populations

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Running title: Partial self-fertilization and adaptation from standing genetic variation.

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Abstract: Standing genetic variation is considered a major contributor to the adaptive potential of species. The low heritable genetic variation observed in self-fertilising populations has led to the hypothesis that species with this particular mating system would be less likely to adapt. However, a non-negligible amount of cryptic genetic variation for polygenic traits, accumulated through negative linkage disequilibrium, could prove to be an important source of standing variation in self-fertilising species. Using a classical quantitative genetics model, we demonstrate that selfing populations are better able to store cryptic genetic variance than outcrossing populations, notably due to their lower recombination rate. Following a shift in the environment, this hidden diversity can be partially released, increasing the additive variance and adaptive potential of selfing populations. In such conditions, even though the process of adaptation itself is mating system dependant, selfers reach levels of fitness that are equal to or higher than outcrossing populations within a few generations. Outcrossing populations respond better to selection for the new optimum, but they maintain more genetic diversity resulting in a higher genetic load. In selfing populations, genetic diversity is remobilised, and new close-to-optimum genotypes are generated and quickly increase in frequency, leading to more homogenous populations. Our results bring new insights into the role of standing genetic variation for adaptation in selfing populations.

INTRODUCTION

Natural populations harbour a significant amount of genetic variation, especially at loci governing polygenic traits (Mittell *et al.* 2015; Wood *et al.* 2016; Clo *et al.* 2019). This variation, known as standing genetic variation, has been considered to be an important predictor for the adaptive potential of populations (Orr and Betancourt 2001; Hermisson and

Pennings 2005; Barrett and Schluter 2008; Pritchard *et al.* 2010; Glémin and Ronfort 2013; Matuszewski *et al.* 2015). Indeed, standing variation represents an easily accessible, hence non-negligible, source of genetic variation, available for adaptation to changing conditions (Hermisson and Pennings 2005; Barrett and Schluter 2008). Contrary to adaptation from *de novo* mutations, the probability to adapt from standing variation is higher simply because beneficial mutations already segregating in a population are expected to be present at higher frequencies (Innan and Kim 2004; Barrett and Schluter 2008). It has also been suggested that populations adapting from standing genetic variation can cope with more severe and more rapid environmental change, as they are able to cross larger distances in phenotype space (Matuszewski *et al.* 2015). The amount of heritable variance is thus expected to play a key role in adaptation, and any forces affecting it may greatly influence whether or not populations are able to survive environmental changes.

An important characteristic of populations, known to greatly affect the amount of genetic variance, is the mating system. From both theoretical (Charlesworth and Charlesworth 1995; Lande and Porcher 2015; Abu Awad and Roze 2018) and empirical works (Charlesworth and Charlesworth 1995; Geber and Griffen 2003; Clo *et al.* 2019), it is known that, compared to outcrossing populations, self-fertilization reduces, on average, the amount of additive genetic variance for polygenic or quantitative traits under stabilizing selection. This diminution is due to more efficient purifying selection under selfing and linkage disequilibria maintained between alleles at different loci: the so-called Bulmer effect (Lande and Porcher 2015; Abu Awad and Roze 2018). Because of the low genetic variance maintained in self-fertilizing populations, this mating system has been qualified as an evolutionary dead-end (Stebbins 1957; Takebayashi and Morrell 2001; Igic and Busch 2013). However, theoretical and some empirical works are now pointing towards the existence of cryptic genetic variability (see Paaby and Rockman 2014 for a review), which should, in

addition to the "visible" genetic variation, contribute to the adaptive potential of natural populations. Cryptic genetic variation has been defined as a part of a population's standing genetic variation that does not affect phenotypic variation in a stable environment, but can increase heritable variation in environmental conditions rarely experienced (Gibson and Dworkin 2004; Paaby and Rockman 2014). In other words, it defines a source of variability that is not expressed in stable conditions (due to conditional neutrality, the genetic structure of the population, etc), but which can contribute to adaptation in new conditions. Such "hidden" variability has been detected in both outcrossing (in sticklebacks (McGuigan *et al.* 2011), cavefish (Rohner *et al.* 2013), dung flies (Berger *et al.* 2011), gulls (Kim *et al.* 2013) or spadefoot toads (Ledon-Rettig *et al.* 2010)) and selfing species (*Caenorhabditis elegans*, Milloz *et al.* 2008; *Arabidopsis thaliana*, Queitsch *et al.* 2002). Two main mechanisms could explain the accumulation and the release of such variance: interactions between loci (Badano and Katsanis 2002; Carter *et al.* 2005; Shao *et al.* 2008), and phenotypic plasticity (Anderson *et al.* 2013). In this paper, we focus on interactions between loci.

To maintain the population as close as possible to the phenotypic optimum, stabilizing selection disfavors apparent genetic and phenotypic diversity (Lande and Porcher 2015; Abu Awad and Roze 2018). However, the structuration of the additive variance also strongly depends on the trait mutation rate and the prevalence of pleiotropy (Lande and Porcher 2015; Abu Awad and Roze 2018). When the per-trait mutation rate is weak, associations between loci are negligible, but when the rate increases, the creation and maintenance of co-adapted gene complexes structure the additive variance into positive within-loci components and negative among-loci components, reducing the observed additive variance (Abu Awad and Roze 2018). The remobilization of alleles contributing to this last component of variance could boost the evolvability of populations forced to undergo directional selection after a change in the phenotypic optimum (Le Rouzic and Carlborg 2008). Indeed, if associations

between loci are broken, segregating alleles could express some or all of their additive effects in new-genetic backgrounds. Classical models analyzing the effect of selfing on adaptation from standing genetic variation have considered a single locus (Glémin and Ronfort 2013), thus neglecting interactions among loci that could result in other forms of standing genetic variation. As self-fertilization reduces the effective recombination rate (Nordborg 2000), allowing the maintenance of co-adapted gene complexes, the storage of hidden genetic diversity should be stronger in selfing populations (as suggested in Lande and Porcher 2015; Abu Awad and Roze 2018), potentially increasing their probability to adapt to an environmental change beyond that expected from single-locus models.

In this paper, we explore this hypothesis, using a quantitative genetics framework. We describe and quantify how, to what degree, and under which conditions populations accumulate hidden genetic variation in this theoretical framework of polygenic traits. Though these polygenic trait models are based on simple hypotheses, they have so far proven to be surprisingly accurate in predicting the distribution of epistatic coefficients (Martin *et al.* 2007) andI inferring the mean dominance coefficient of mutations (Manna *et al.* 2011). We show that, in models allowing for hidden genetic diversity and when adaptation is only possible from pre-existing standing genetic variation, selfing populations are able to perform just as well as their mixed-mating and outcrossing counterparts.

MATERIAL AND METHODS

General assumptions

We consider the evolution of a quantitative trait Z in a population of size N, made of diploid individuals reproducing through partial self-fertilization, with a constant selfing rate σ. The phenotypic value z of an individual is determined by the additive action of L loci each with an infinite possible number of alleles and is given by

$$z = g + e, \quad (1)$$

where g is the genetic component of the individual's phenotype, and is given by $g = \sum_j^L g_j^M + g_j^P$, with $g^{\mathrm{M}}{}_j$ (respectively $g^{\mathrm{P}}{}_j$) the additive allelic effect at locus j inherited from the maternal (respectively paternal) gamete. The random environmental effect, e, is drawn from a Gaussian distribution of mean 0 and variance V_{E}, and is considered to be independent from the genetic components of fitness. The trait initially undergoes stabilizing selection around an optimal phenotypic value (set arbitrarily at 0). The fitness value W_{Z} of an individual with phenotype z is thus described by the Gaussian function:

$$W_Z = e^{-d^2/2\omega^2}, \quad (2)$$

where d is the distance between the individual's phenotype z and the optimum trait value and ω^2 is the width of the fitness function, and represents the strength of selection.

Simulation model

We implement the model described above into an individual based simulation model written in C++, a modified version of the "continuum of alleles" program provided in Abu Awad and Roze (2018). The simulation program is available in File S1 and online (https://github.com/dialaAbAw/SelfingAdaptation). The life cycle can be summarized by five

159 successive events: (1) phenotype-dependent choice of the maternal parent (selection), (2)
160 mating-type choice (selfing versus outcrossing), (3) phenotype-dependent choice of the
161 paternal parent in the case of outcrossing, (4) production of gametes (recombination) and (5)
162 mutation. We simulate two phases. In the first one, the population evolves in a stable
163 environment (for a fixed trait optimum value $Z_{OPT} = 0$) until mutation-selection-drift
164 equilibrium (M-S-D) and we explore the effect of the mating system on the genetic
165 components and structure of a quantitative trait under stabilizing selection. In the second
166 phase, we consider the rate of adaptation following a brutal shift in the optimum (Z_{OPT} shift
167 from 0 to 2.5, the shift being of order $L \cdot a^2$).

168 Each generation before equilibrium, the number of new mutations per chromosome
169 per generation is sampled from a Poisson distribution with parameter U, the per-trait haploid
170 genomic mutation rate (ranging from 0.005 to 0.1, in accordance with the literature (Keightley
171 and Bataillon 2000; Shaw *et al.* 2002; Haag-Liautard *et al.* 2007)). The additive value of a
172 new mutant allele is drawn from a Normal distribution of mean 0 and variance a^2. We use
173 parameter set values similar to those in Bürger *et al.* (1989) and Ronce *et al.* (2009), with the
174 number of freely recombining loci under selection $L = 50$, $a^2 = 0.05$, $V_E = 1$, $\omega^2 = 1$ (and hence
175 $V_S = \omega^2 + V_E$ is equal to 2). The mean deleterious effect of mutations $\bar{s}$ ($\bar{s} = a^2 / 2V_S$, Martin
176 and Lenormand 2006) is equal to 0.0125. Although simulations were run over a large range of
177 selfing values, throughout the manuscript we show results run principally for three rates of
178 self-fertilisation, $\sigma = 0$, 0.5 and 0.95, representing outcrossing, mixed-mating and
179 predominantly selfing respectively. They are representative of the three main patterns
180 observed over the whole range (σ from 0 to 1). We also considered two population sizes $N =$
181 250 and 1000.

182

Simulation program:

At the start of a simulation, all N individuals are homozygous for allele 0 at all L loci and are thus at the fitness optimum. To form the next generation, N new zygotes are produced through selfing with probability σ, and through random mating with probability 1-σ. Selection occurs during the sampling of parental individuals, occurring with probabilities proportional to their fitness. During meiosis, the number of cross-overs is sampled from a Poisson distribution with parameter R (which represents the genome map length), and the position of each cross-over along the chromosome is sampled from an uniform distribution. According to Haldane's mapping function, the recombination rate between two adjacent loci is $r = \frac{1}{2}\left[1 - exp\left(\frac{-2R}{L-1}\right)\right]$, with R = 50 in our simulations. Mutation occurs after recombination: the number of new mutations per chromosome per generation is sampled from a Poisson distribution with parameter U, the haploid genomic mutation rate ($U = L\mu$, with μ being the per locus mutation rate). The additive value of a new mutant allele is drawn from a Normal distribution of mean 0 and variance a^2.

After reaching the M-S-D equilibrium, we introduce an environmental change by shifting the phenotypic optimum. The only source of genetic variability to reach the new optimum is the standing variation accumulated at M-S-D equilibrium (after the shift, U is set to 0). We then let the population evolve for 200 generations.

Effect of selfing on genetic variance structuration at Mutation-Selection-Drift equilibrium

Following Turelli & Barton (Turelli and Barton 1990), we decompose the genetic variance of a polygenic trait using the following equation:

$$V_A = 2\sum_j^L (C_{jj} + C_{j,j}) + 2\sum_{j\neq k}^L (C_{jk} + C_{j,k}), \quad (3)$$

with

$$C_{j\,j} = \frac{1}{2} E[\,(g^M{}_j - \bar{g}_j)^2 + (g^P{}_j - \bar{g}_j)^2] \quad (4)$$

and

$$C_{j,j} = E[\,(g^M{}_j - \bar{g}_j)\,.\,(g^P{}_j - \bar{g}_j)], \quad (5)$$

where $\bar{g}_j$ is the mean allelic effect on the phenotype at locus j and $g^M{}_j$ (respectively $g^P{}_j$) is the allelic effect at locus j inherited from the maternal (respectively paternal) gamete. The sum of all values of C_{jj} represents the variance of allelic effects (the genic variance V_{genic}, the genetic variance of a trait in a population harboring the same allelic frequencies as the population under study, but without any genetic association between loci) and is computed from simulation outputs following equation (4). The sum of all values of $C_{j,j}$ represents the covariance in allelic effects on the maternally and paternally inherited chromosomes at locus j, and represents the fraction of the genetic variance due to excess of homozygosity (named V_{inbred}); we compute it following equation (5). This quantity represents $F.V_{genic}$, where F is the inbreeding coefficient of the population. These first term of equation (3) ($2\sum_j^L (C_{jj} + C_{j,j})$) represents the genetic variance due to within locus variation. The second term ($2\sum_{j\neq k}^L (C_{jk} + C_{j,k})$) represents the component of the variance due to associations between loci (noted V_{LD}), and is obtained by subtracting V_{genic} and V_{inbred} from the total additive genetic variance. This component is proportional to linkage disequilibrium (LD), and tends to be negative under stabilizing selection due to associations between alleles from different loci with compensatory

effects (*i.e.* the allele on one locus is positive, the other negative, their effects on the phenotype thus cancel out when both are present).

Analyses after the environmental change

Due to an increased probability of extinction during long periods of maladaptation, it seems more relevant to focus only on the dynamics of adaptation during the first generations after an environmental change. We follow the temporal dynamics of the additive variance and its components, the dynamic of the mean population phenotype, and the dynamic of the mean population fitness, as a function of the mating system and the mutation rate, over 20 generations.

In addition, and in order to test if remobilization of V_{LD} plays a role in the adaptation of selfing populations, we computed the slope of the trait mean dynamics just after the environmental change (during the first five generations) as a function of the amount of additive variance available at M-S-D equilibrium. If remobilization of V_{LD} is involved in the adaptive process of selfing populations, the initial slope, for a similar amount of additive variance, should be higher in selfing populations compared to mixed mating and outcrossing ones.

RESULTS

Below we present results only for N = 250 and L = 50, as larger population sizes and more loci did not qualitatively change the results. Results for N = 1000, as well as L = 500 are given in the supplementary materials section (Figures S1-S6).

DECOMPOSITION OF THE GENETIC VARIANCE AT EQUILIBRIUM

As predicted, the additive genetic variance present at M-S-D equilibrium in our simulations is negatively correlated with the selfing rate (figure 1A, see Abu Awad and Roze 2018 for the analytical model). By examining each component of the additive variance, we can see that the variance due to within loci variation (V_{genic} + V_F) is higher in selfing populations due to the higher rate of homozygosity (figure 1 B & C). These two components, as well as the total additive variance, increase linearly with increasing mutation rates (figure 1 A, B & C). The among-loci component (V_{LD}) is negative (figure 1D), due to the build-up of linkage disequilibrium between alleles with different signs, allowing phenotypes to be close to the phenotypic optimum (0). Because recombination is less effective under selfing, this negative component is responsible for the smaller additive variance observed under predominant selfing. It also contributes significantly to the variance observed in mixed mating and outcrossing populations with moderate to high mutation rates (figure 1D). Larger population sizes or more loci do not change the results for outcrossing and mixed mating populations (Figures S1-S2). For selfing populations, larger population sizes and higher per locus mutation rates contribute to increasing negative linkage disequilibrium (V_{LD}) due to negative linkage disequilibrium (Figure S3).

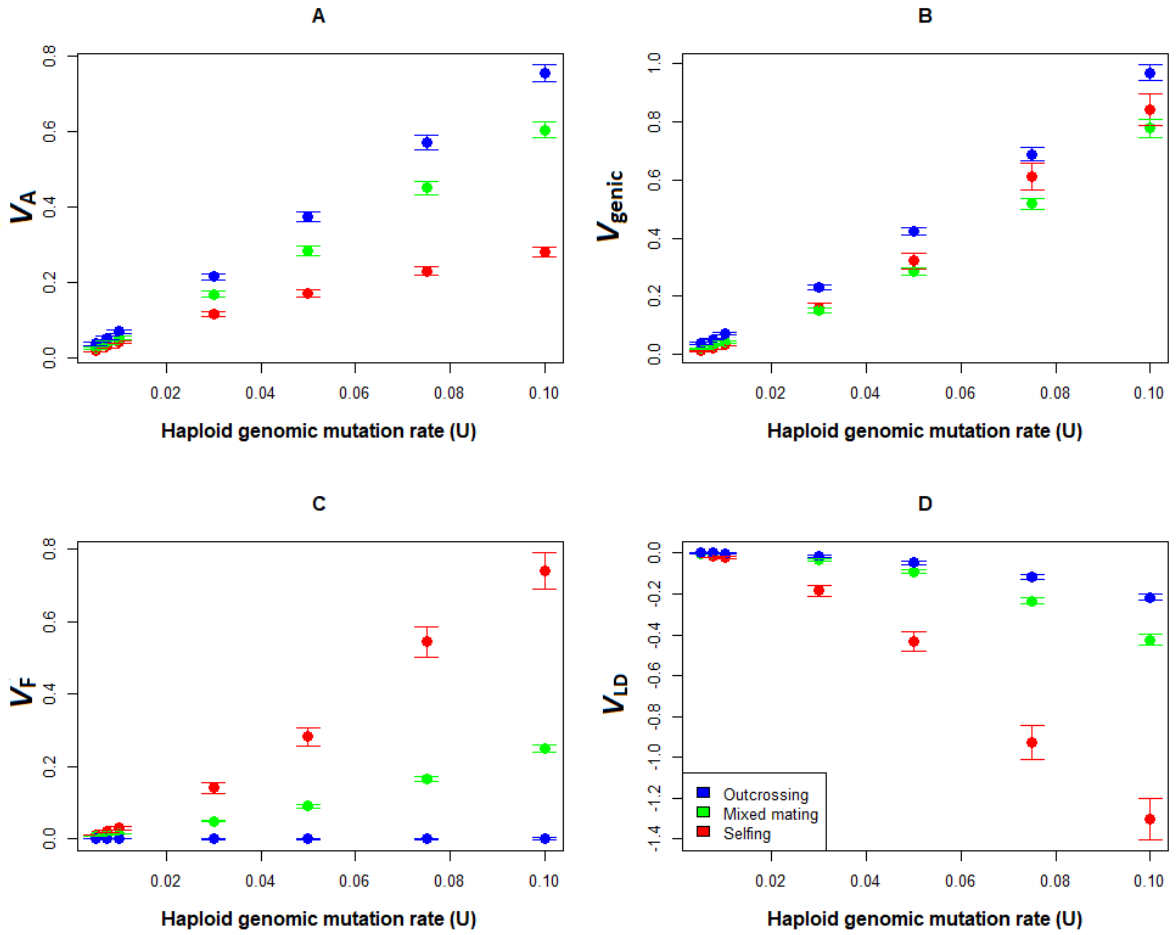

Figure 1. Additive genetic variance and its components as a function of the genomic mutation rate and the mating system. **A.** Observed additive variance for the phenotypic trait. **B.** Genic variance for the phenotypic trait (V_{genic}). **C.** Genetic variance due to inbreeding (V_F). **D.** Genetic variance due to linkage disequilibrium (V_{LD}). Error bars stand for 95% confidence interval (n = 100).

ADAPTATION THROUGH STANDING GENETIC VARIATION:

For simplicity, we focus on four mutation rates (U = 0.005; 0.03; 0.05; 0.1), representing the different patterns of genetic variance observed at M-S-D equilibrium for the

outcrossing, mixed mating and selfing populations mentioned above. We first describe the dynamics observed for outcrossing populations, which will serve as a reference for comparison with the dynamics of selfing populations. We generally find that the dynamics for mixed mating populations are similar to those of outcrossing populations (Figure S4).

DYNAMICS OF THE ADDITIVE VARIANCE AND OF ITS COMPONENTS:

In outcrossing populations, the additive variance exhibits very tiny changes during the adaptation process, so do its components (Figure 2). In all cases, the observed additive genetic variance slightly increases during the first generations of adaptation (Figure 2A), then, it either reaches an equilibrium (Figure 2A, $U < 0.1$) or slowly begins to decrease (Figure 2A, $U = 0.1$). When V_{LD} is small at M-S-D equilibrium ($U < 0.1$), the observed increase of the additive variance is mainly due to an increase of the genic variance (Figure 2B), probably due to successive sweeps of rare alleles during the adaptation process. In these situations, V_{LD} slightly decreases with time (Figure 2C), indicating that some associations between loci are building up. When V_{LD} is significant at M-S-D equilibrium ($U = 0.1$), the genic variance remains constant during the first generations (Figure 2B), but V_{LD} increases slightly (Figure 2C), contributing to the increase of the additive variance. The second phase during which the observed additive variance decreases can be explained by the decrease of genic variance with time, due to the purging of deleterious mutations (Figure 2B).

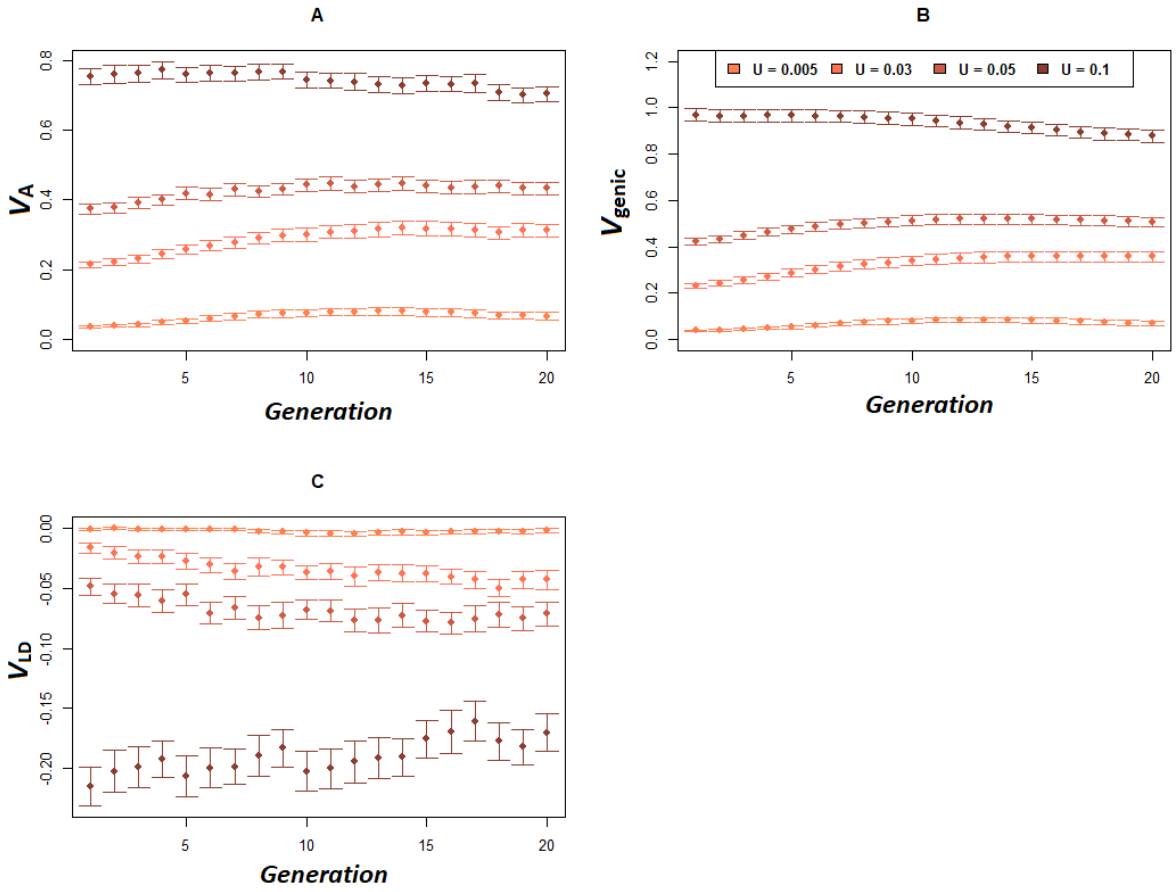

Figure 2. Dynamics of additive genetic variance and its components in function of the haplotypic trait mutation rate, for outcrossing populations. **A.** Observed additive variance for the phenotypic trait. **B.** Genic variance for the phenotypic trait (V_{genic}). **C.** Genetic variance of the phenotype due to linkage disequilibrium (V_{LD}). Error bars stand for 95% confidence interval (n=100).

Contrary to the dynamics observed in outcrossing populations, additive variance substantially varies during the adaptation process in selfing populations. For small mutation rates ($U \leq 0.03$), the dynamics are very similar to those observed in outcrossing populations (figure 3). The observed additive variance slightly increases during the first generations (Figure 3A). This increase is due to a rise of the genic variance (Figure 3B), associated with a

315 decrease of V_{LD} (Figure 3C), probably due to an interaction between sweeps of beneficial
316 mutations that were rare before the environmental change and the creation of new beneficial
317 associations between loci. For higher mutation rates ($U \geq 0.05$), the dynamics are different.
318 The genic variance remains constant during the first generations and then decreases (figure
319 3B), whereas V_{LD} increases faster than the decrease of V_{genic} (figure 3C), explaining the
320 overall increase of additive variance. This behaviour can be explained as follows: there is a
321 complex interaction between the purging of deleterious mutations due to selfing, which tends
322 to quickly fix the best multi-locus genotypes, eroding genetic diversity and residual allogamy,
323 which allows the mobilization of a small fraction of the hidden genetic diversity. The outcome
324 of this interaction is an increase of the genetic diversity and of the populations' adaptive
325 potential. The fact that the rate of adaptation (*i.e* the slope of the change in the trait values
326 during the first generations) as a function of the initial level of additive variance is higher for
327 selfing populations when V_{LD} is large, confirms that the remobilisation of the hidden diversity
328 plays a role in the adaptation process (figure S5).

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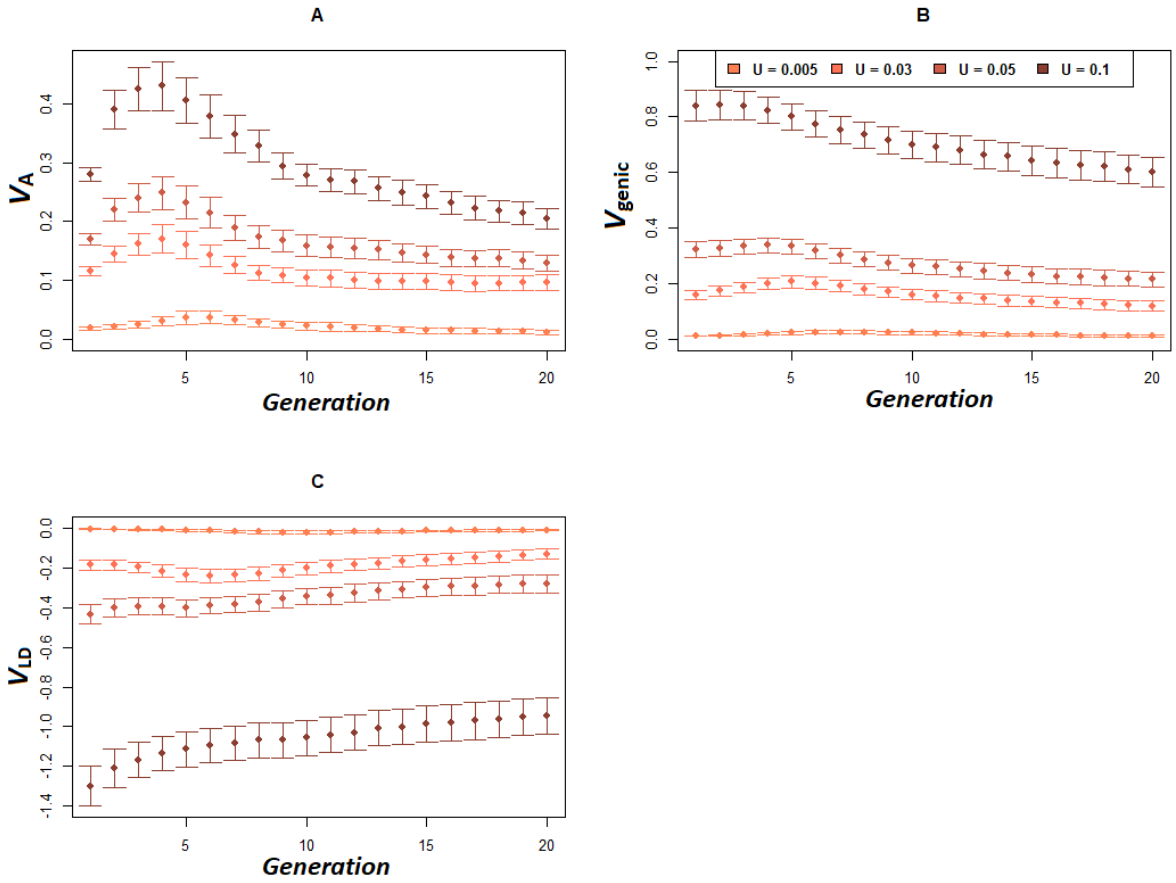

Figure 3. Dynamics of additive genetic variance and its components in function of the haplotypic trait mutation rate, for selfing populations. **A.** Observed additive variance for the phenotypic trait. **B.** Genic variance for the phenotypic trait (V_{genic}). **C.** Genetic variance of the phenotype due to linkage disequilibrium (V_{LD}). Error bars stand for 95% confidence interval (n=100).

TRAIT AND FITNESS DYNAMICS DURING ADAPTATION PROCESS:

Here, we consider that there is adaptation if populations reach a similar level of fitness as that observed before the environmental change. In all cases, compared to selfing

populations, outcrossing and mixed mating population respond better to selection, by being closer to the new phenotypic optimum (figure 4). When the mutation rate is weak (U = 0.005), none of the populations are able to adapt, and thus the fitness remains low (figure 4). For higher mutation rates (U > 0.005), outcrossing and mixed mating populations are always close to the new optimum, and are able to return to fitness levels similar to those observed at M-S-D equilibrium. Selfing populations require that the mutation rate is high enough ($U \geq$ 0.05, figure 4) in order to reach similar fitness levels as those observed in outcrossing populations. Interestingly, in some cases, adaptation occurs more rapidly in selfing populations, despite the higher genetic diversity of outcrossing populations. The larger the population size and the higher the per-locus mutation rate, the higher the level of potentially usable hidden genetic diversity, and the smaller the genomic mutation rate necessary to reach similar levels of fitness in selfing populations (figures S6-S7).

Nevertheless, different mating systems exhibit different dynamics of adaptation. Outcrossing populations adapt by reaching a new phenotypic optimum, but they also maintain a high level of genetic diversity (figure 3), resulting in populations having both mal-adapted and well-adapted individuals. Selfing populations are always further away from the new phenotypic optimum (figure 4), but both the remobilization of the V_{LD}, and the fast fixation of the “best” phenotypes allow for the production of close-to-optimum individuals. These phenotypes will then quickly increase in frequency, leading to more homogenous populations than observed for an outcrossing mating system (figure 4).

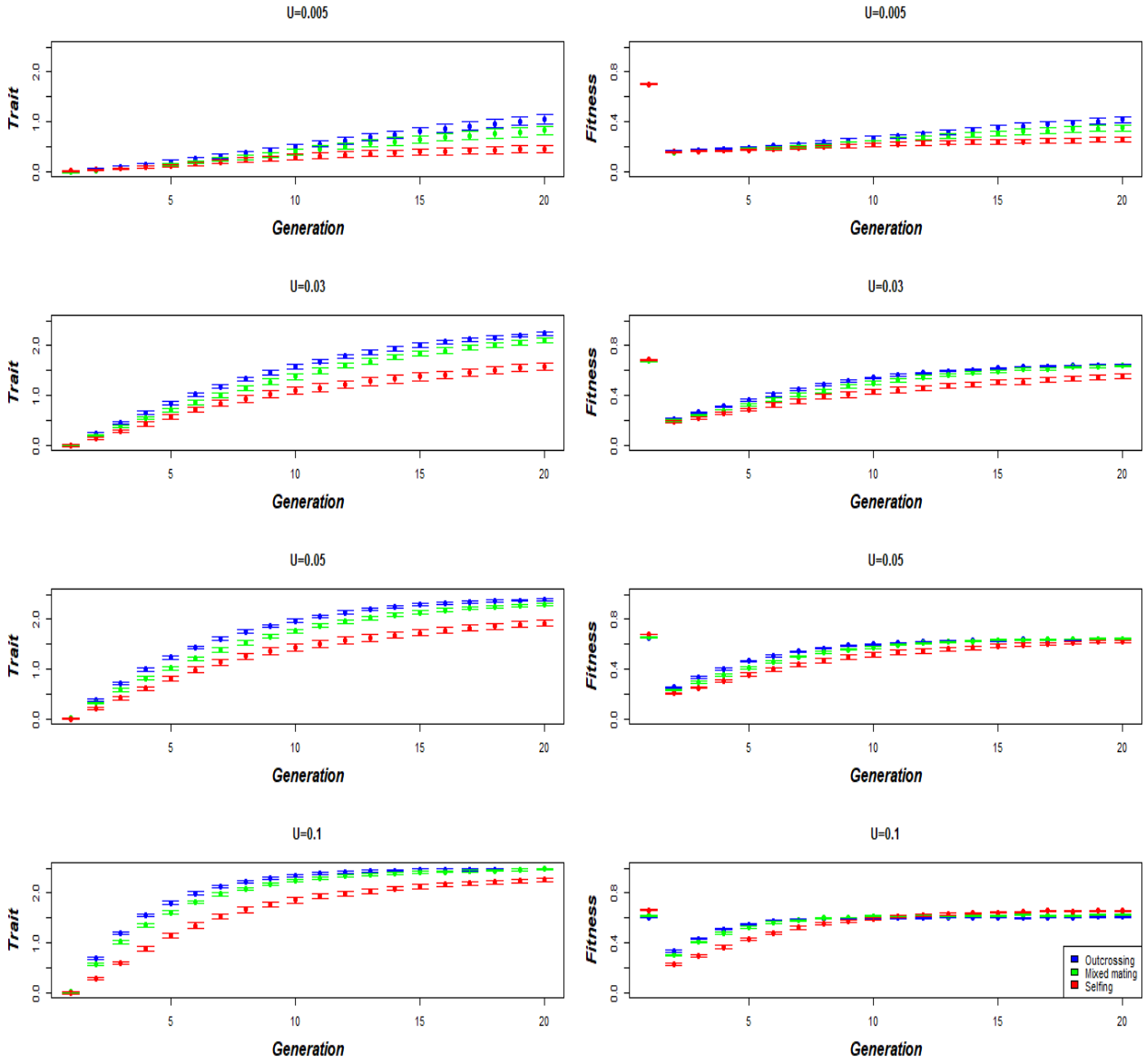

Figure 4. Dynamics of the trait and fitness, in function of the trait haplotypic mutation rate and the mating system. Error bars stand for 95% confidence interval (n=100).

DISCUSSION

In accordance with Stebbins' definition of the dead-end hypothesis (Stebbins 1957), single-locus models predict that adaptation from standing genetic variation is less likely in

selfing populations compared to outcrossing ones, notably due to the reduced genetic variation resulting from purging (Glémin and Ronfort 2013). Considering a polygenic trait, and associated interactions among loci, we find that this is not always the case. Indeed, we find that for low mutation rates, our results support the expectations of single locus models. However, for higher mutation rates, and as predicted by previous work (Abu Awad and Roze 2018), associations between loci are no longer negligible. In this case, stabilizing selection shelters an important amount of hidden additive variance, especially in self-fertilising populations. We show that some of this variance can be released during phases of directional selection to new environmental conditions. Our results support that it is possible to observe similar levels of adaptation in selfing and outcrossing populations, despite unconditionally lower levels of observed additive variance under predominant selfing.

Hidden genetic variation, its remobilization and genotypic selection

Stabilizing selection is expected to favour the build-up and maintenance of co-adapted gene complexes, and this will structure the additive variance into positive within-loci components and negative among-loci components, reducing the observed additive variance (Abu Awad and Roze 2018). In a changing environment, alleles involved in the negative among loci component of variance may be unveiled and mobilized to respond to directional selection (Le Rouzic and Carlborg 2008). Our analysis shows that such associations between loci, coupled with hidden genetic variation, are more likely to emerge in selfing than in outcrossing populations, because of less efficient recombination under selfing (Lande and Porcher 2015; Abu Awad and Roze 2018). This prediction is in accordance with empirical observations of more frequent transgressive segregation (progeny of a cross being outside the

phenotypic parental range) in inbred compared to outbred species (Rieseberg *et al.* 1999; Johansen-Morris and Latta 2006). Our analysis also shows that the less effective recombination rate associated with selfing avoids the complete release of the negative linkage disequilibria and thus limits the response to selection. As a result, selection mostly operates at the genotypic level while allelic selection is more prevalent in more recombining populations (Neher and Shraiman 2009). Interestingly, if the rate of self-fertilization is changed during the adaptation process (σ changing from 0.95 to zero after the environmental change), the dynamics of the fitness remains similar (figures S8-S9). Indeed, under complete outcrossing all the hidden genetic variance can be mobilized and this allows initially selfing populations to reach the new phenotypic optimum but recombination also generates less adapted genotypes which reduces the mean population fitness.

De novo mutations _vs._ standing genetic variation: rethinking adaptation in selfing species?

It has been a long accepted paradigm that the advantage procured by selfing, was the rapid fixation of *de novo* mutations more efficiently than in outcrossing populations, independently of the dominance of new mutations, a process known has “Haldane sieve” (Haldane 1927). Indeed, from one locus theory, adaptation through new mutations is more likely in selfing species, and is more likely than adaptation from standing genetic variation (Glémin and Ronfort 2013). However, recent works have suggested that the reduced effective recombination rate of selfing populations adds a disadvantage even when it comes to the fixation of new mutations. Unlike what is expected in outcrossing populations, the fixation of beneficial mutations in selfing populations can be hindered if they appear during the selective

418 sweep triggered by a beneficial allele at another locus (Hartfield and Glémin 2016). This
419 observation as well as the results presented here show that predictions from the point of view
420 of polygenic models are less dichotomist: the ability of selfing populations to adapt from
421 either *de novo* mutations or standing variation strongly depends on the parameters considered
422 (the mutation rate in particular), with selfers being often as able to adapt as outcrossers, even
423 if the underlying mechanisms strongly differ.

424 We have only considered a simple architecture of quantitative traits in which epistatic
425 interactions emerge naturally. Epistasis, and notably its directionality, is known to play a key
426 role in adaptation (Hansen 2013). Positive epistasis, with genes that reinforce each other's
427 effects in the direction of selection, inflate the additive variance and thus the ability of
428 populations to adapt to an environmental change (Carter *et al.* 2005; Monnahan and Kelly
429 2015), contrary to the non-directional epistatic scenario (Carter *et al.* 2005). Negative
430 epistasis, where genes tend to mute each other's effects, reduces the additive variance of the
431 character, thus limiting adaptive potential (Carter *et al.* 2005). Few empirical estimations of
432 the directionality of epistasis are available in literature (Le Rouzic 2014; Monnahan and Kelly
433 2015; Oakley *et al.* 2015, all detecting positive epistatic interactions), despite numerous
434 methods and the diversity of data used to infer it (Le Rouzic 2014). Developing methods to
435 detect and measure the directionality of epistatic interactions in relation to the mating system
436 may bring us closer to understanding the differences in patterns of adaptation observed in
437 selfing and outcrossing populations.

438

439 **New insights into the role of standing genetic variation in the adaptation dynamics of**
440 **selfing populations**

441

The overwhelming success of selfing species in the domestication process and as invasive species is not considered as resulting from a higher adaptive ability of selfing species compared to outcrossing ones. For instance, the invasive success of selfing populations is attributed to reproductive assurance, since a single individual is able to colonize a new environment (Rambuda and Johnson 2004; van Kleunen *et al.* 2008), and to reduce gene flow which are expected to limit maladapted gene exchanges between populations (Levin 2010). Regarding domestication, it has been argued that selection in selfing populations is most probably due to new mutations, because the standing genetic variation is lower in such populations due to more efficient purging of deleterious mutations that could be involved in the domestication process (Glémin and Bataillon 2009). This idea is reinforced by the fact that selfing species are expected to quickly fix a rare beneficial mutation, independently from its dominance level (Ross-Ibarra 2005). In their review on mating system variation in domesticated plant species, Glémin and Bataillon (2009) have suggested that the high frequency of self-fertilising crop species could be related to an increase in additive variance during domestication; this idea has however never been tested theoretically or empirically. Here we show that this increase in additive variance could indeed be an advantage when selfing species are faced with new environments. However, our results hold true only if bottlenecks during the domestication and invasion processes are not too strong or if mutation rates are high.

CONCLUSION AND PERSPECTIVES

In this work, we argue that selfing populations under stabilizing selection are able to accumulate hidden genetic variation through negative linkage disequilibrium. Thanks to this

hidden variation, adaptation under high self-fertilisation rates is not always limited by the expected reduction in additive genetic variance due to purging. We therefore suggest that a simple estimation of additive variance of quantitative traits is not adequate when speculating on the long-term adaptive capacity of a population. Complementary analyses should also be carried out when quantifying the long-term evolvability of a population. Such analyses include looking for transgressive segregation, or carrying out experimental evolutionary experiments in which directional selection is induced. More empirical evidence is required to determine how frequent is cryptic diversity in natural populations of selfing species, and whether or not this property is sufficient to allow for selfing species to adapt to a changing environment.

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