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

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

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40    **Abstract:** Standing genetic variation is considered a major contributor to the adaptive

41    potential of species. The low heritable genetic variation observed in self-fertilising

42    populations has led to the hypothesis that species with this particular mating system would be

43    less likely to adapt. However, a non-negligible amount of cryptic genetic variation for

44    polygenic traits, accumulated through negative linkage disequilibrium, could prove to be an

45    important source of standing variation in self-fertilising species. Using a classical quantitative

46    genetics model, we demonstrate that selfing populations are better able to store cryptic genetic

47    variance than outcrossing populations, notably due to their lower recombination rate.

48    Following a shift in the environment, this hidden diversity can be partially released,

49    increasing the additive variance and adaptive potential of selfing populations. In such

50    conditions, even though the process of adaptation itself is mating system dependant, selfers

51    reach levels of fitness that are equal to or higher than outcrossing populations within a few

52    generations. Outcrossing populations respond better to selection for the new optimum, but

53    they maintain more genetic diversity resulting in a higher genetic load. In selfing populations,

54    genetic diversity is remobilised, and new close-to-optimum genotypes are generated and

55    quickly increase in frequency, leading to more homogenous populations. Our results bring

56    new insights into the role of standing genetic variation for adaptation in selfing populations.

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58    *INTRODUCTION*

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60           Natural populations harbour a significant amount of genetic variation, especially at

61    loci governing polygenic traits (Mittell *et al.* 2015; Wood *et al.* 2016; Clo *et al.* 2019). This

62    variation, known as standing genetic variation, has been considered to be an important

63    predictor for the adaptive potential of populations (Orr and Betancourt 2001; Hermisson and

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64    Pennings 2005; Barrett and Schluter 2008; Pritchard *et al.* 2010; Glémin and Ronfort 2013;

65    Matuszewski *et al.* 2015). Indeed, standing variation represents an easily accessible, hence

66    non-negligible, source of genetic variation, available for adaptation to changing conditions

67    (Hermisson and Pennings 2005; Barrett and Schluter 2008). Contrary to adaptation from *de*

68    *novo* mutations, the probability to adapt from standing variation is higher simply because

69    beneficial mutations already segregating in a population are expected to be present at higher

70    frequencies (Innan and Kim 2004; Barrett and Schluter 2008). It has also been suggested that

71    populations adapting from standing genetic variation can cope with more severe and more

72    rapid environmental change, as they are able to cross larger distances in phenotype space

73    (Matuszewski *et al.* 2015). The amount of heritable variance is thus expected to play a key

74    role in adaptation, and any forces affecting it may greatly influence whether or not

75    populations are able to survive environmental changes.

76         An important characteristic of populations, known to greatly affect the amount of

77    genetic variance, is the mating system. From both theoretical (Charlesworth and Charlesworth

78    1995; Lande and Porcher 2015; Abu Awad and Roze 2018) and empirical works

79    (Charlesworth and Charlesworth 1995; Geber and Griffen 2003; Clo *et al.* 2019), it is known

80    that, compared to outcrossing populations, self-fertilization reduces, on average, the amount

81    of additive genetic variance for polygenic or quantitative traits under stabilizing selection.

82    This diminution is due to more efficient purifying selection under selfing and linkage

83    disequilibria maintained between alleles at different loci: the so-called Bulmer effect (Lande

84    and Porcher 2015; Abu Awad and Roze 2018). Because of the low genetic variance

85    maintained in self-fertilizing populations, this mating system has been qualified as an

86    evolutionary dead-end (Stebbins 1957; Takebayashi and Morrell 2001; Igic and Busch 2013).

87    However, theoretical and some empirical works are now pointing towards the existence of

88    cryptic genetic variability (see Paaby and Rockman 2014 for a review), which should, in

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89    addition to the "visible" genetic variation, contribute to the adaptive potential of natural

90    populations. Cryptic genetic variation has been defined as a part of a population's standing

91    genetic variation that does not affect phenotypic variation in a stable environment, but can

92    increase heritable variation in environmental conditions rarely experienced (Gibson and

93    Dworkin 2004; Paaby and Rockman 2014). In other words, it defines a source of variability

94    that is not expressed in stable conditions (due to conditional neutrality, the genetic structure of

95    the population, etc), but which can contribute to adaptation in new conditions. Such "hidden"

96    variability has been detected in both outcrossing (in sticklebacks (McGuigan *et al.* 2011),

97    cavefish (Rohner *et al.* 2013), dung flies (Berger *et al.* 2011), gulls (Kim *et al.* 2013) or

98    spadefoot toads (Ledon-Rettig *et al.* 2010)) and selfing species (*Caenorhabditis elegans*,

99    Milloz *et al.* 2008; *Arabidopsis thaliana,* Queitsch *et al.* 2002). Two main mechanisms could

100   explain the accumulation and the release of such variance: interactions between loci (Badano

101   and Katsanis 2002; Carter *et al.* 2005; Shao *et al.* 2008), and phenotypic plasticity (Anderson

102   *et al.* 2013). In this paper, we focus on interactions between loci.

103        To maintain the population as close as possible to the phenotypic optimum, stabilizing

104   selection disfavors apparent genetic and phenotypic diversity (Lande and Porcher 2015; Abu

105   Awad and Roze 2018). However, the structuration of the additive variance also strongly

106   depends on the trait mutation rate and the prevalence of pleiotropy (Lande and Porcher 2015;

107   Abu Awad and Roze 2018). When the per-trait mutation rate is weak, associations between

108   loci are negligible, but when the rate increases, the creation and maintenance of co-adapted

109   gene complexes structure the additive variance into positive within-loci components and

110   negative among-loci components, reducing the observed additive variance (Abu Awad and

111   Roze 2018). The remobilization of alleles contributing to this last component of variance

112   could boost the evolvability of populations forced to undergo directional selection after a

113   change in the phenotypic optimum (Le Rouzic and Carlborg 2008). Indeed, if associations

114    between loci are broken, segregating alleles could express some or all of their additive effects

115    in new-genetic backgrounds. Classical models analyzing the effect of selfing on adaptation

116    from standing genetic variation have considered a single locus (Glémin and Ronfort 2013),

117    thus neglecting interactions among loci that could result in other forms of standing genetic

118    variation. As self-fertilization reduces the effective recombination rate (Nordborg 2000),

119    allowing the maintenance of co-adapted gene complexes, the storage of hidden genetic

120    diversity should be stronger in selfing populations (as suggested in Lande and Porcher 2015;

121    Abu Awad and Roze 2018), potentially increasing their probability to adapt to an

122    environmental change beyond that expected from single-locus models.

123       In this paper, we explore this hypothesis, using a quantitative genetics framework. We

124    describe and quantify how, to what degree, and under which conditions populations

125    accumulate hidden genetic variation in this theoretical framework of polygenic traits. Though

126    these polygenic trait models are based on simple hypotheses, they have so far proven to be

127    surprisingly accurate in predicting the distribution of epistatic coefficients (Martin *et al.* 2007)

128    andI inferring the mean dominance coefficient of mutations (Manna *et al.* 2011). We show

129    that, in models allowing for hidden genetic diversity and when adaptation is only possible

130    from pre-existing standing genetic variation, selfing populations are able to perform just as

131    well as their mixed-mating and outcrossing counterparts.

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133    *MATERIAL AND METHODS*

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135    **General assumptions**

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137    We consider the evolution of a quantitative trait $Z$ in a population of size $N$, made of

138    diploid individuals reproducing through partial self-fertilization, with a constant selfing rate $\sigma$.

139    The phenotypic value $z$ of an individual is determined by the additive action of $L$ loci each

140    with an infinite possible number of alleles and is given by

141                                  $$z = g + e, (1)$$

142    where $g$ is the genetic component of the individual's phenotype, and is given by $g = \sum_j^L g_j^M +$

143    $g_j^P$, with $g^M{}_j$ (respectively $g^P{}_j$) the additive allelic effect at locus $j$ inherited from the maternal

144    (respectively paternal) gamete. The random environmental effect, $e$, is drawn from a Gaussian

145    distribution of mean 0 and variance $V_E$, and is considered to be independent from the genetic

146    components of fitness. The trait initially undergoes stabilizing selection around an optimal

147    phenotypic value (set arbitrarily at 0). The fitness value $W_Z$ of an individual with phenotype $z$

148    is thus described by the Gaussian function:

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

150    where $d$ is the distance between the individual's phenotype $z$ and the optimum trait value and

151    $\omega^2$ is the width of the fitness function, and represents the strength of selection.

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153    **Simulation model**

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155    We implement the model described above into an individual based simulation model

156    written in C++, a modified version of the "continuum of alleles" program provided in Abu

157    Awad and Roze (2018). The simulation program is available in File S1 and online

158    (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 $L . a^2$).

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 ($\sigma$ from 0 to 1). We also considered two population sizes $N =$

181  250 and 1000.

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183 **Simulation program:**

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185        At the start of a simulation, all *N* individuals are homozygous for allele 0 at all *L* loci

186    and are thus at the fitness optimum. To form the next generation, *N* new zygotes are produced

187    through selfing with probability σ, and through random mating with probability 1-σ. Selection

188    occurs during the sampling of parental individuals, occurring with probabilities proportional

189    to their fitness. During meiosis, the number of cross-overs is sampled from a Poisson

190    distribution with parameter *R* (which represents the genome map length), and the position of

191    each cross-over along the chromosome is sampled from an uniform distribution. According to

192    Haldane's mapping function, the recombination rate between two adjacent loci is $r =$

193    $\frac{1}{2}\left[1 - exp\left(\frac{-2R}{L-1}\right)\right]$, with $R = 50$ in our simulations. Mutation occurs after recombination: the

194    number of new mutations per chromosome per generation is sampled from a Poisson

195    distribution with parameter *U*, the haploid genomic mutation rate ($U = L\mu$, with $\mu$ being the

196    per locus mutation rate). The additive value of a new mutant allele is drawn from a Normal

197    distribution of mean 0 and variance $a^2$.

198        After reaching the M-S-D equilibrium, we introduce an environmental change by

199    shifting the phenotypic optimum. The only source of genetic variability to reach the new

200    optimum is the standing variation accumulated at M-S-D equilibrium (after the shift, *U* is set

201    to 0). We then let the population evolve for 200 generations.

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

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205    Following Turelli & Barton (Turelli and Barton 1990), we decompose the genetic variance of

206    a polygenic trait using the following equation:

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

208    with

209
$$C_{jj} = \frac{1}{2} E[\, (g^\text{M}_j - \bar{g}_j)^2 + (g^\text{P}_j - \bar{g}_j)^2 ] \quad (4)$$

210    and

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

212    where $\bar{g}_j$ is the mean allelic effect on the phenotype at locus $j$ and $g^\text{M}_j$ (respectively $g^\text{P}_j$) is the

213    allelic effect at locus $j$ inherited from the maternal (respectively paternal) gamete. The sum of

214    all values of $C_{jj}$ represents the variance of allelic effects (the genic variance $V_\text{genic}$, the genetic

215    variance of a trait in a population harboring the same allelic frequencies as the population

216    under study, but without any genetic association between loci) and is computed from

217    simulation outputs following equation (4). The sum of all values of $C_{j,j}$ represents the

218    covariance in allelic effects on the maternally and paternally inherited chromosomes at locus

219    $j$, and represents the fraction of the genetic variance due to excess of homozygosity (named

220    $V_\text{inbred}$); we compute it following equation (5). This quantity represents $F.V_\text{genic}$, where $F$ is the

221    inbreeding coefficient of the population. These first term of equation (3) ($2 \sum_j^L (C_{jj} + C_{j,j})$)

222    represents the genetic variance due to within locus variation. The second term ($2 \sum_{j \neq k}^L (C_{jk} + $

223    $C_{j,k})$) represents the component of the variance due to associations between loci (noted $V_\text{LD}$),

224    and is obtained by subtracting $V_\text{genic}$ and $V_\text{inbred}$ from the total additive genetic variance. This

225    component is proportional to linkage disequilibrium (LD), and tends to be negative under

226    stabilizing selection due to associations between alleles from different loci with compensatory

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227    effects (*i.e.* the allele on one locus is positive, the other negative, their effects on the

228    phenotype thus cancel out when both are present).

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230    *Analyses after the environmental change*

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232         Due to an increased probability of extinction during long periods of maladaptation, it

233    seems more relevant to focus only on the dynamics of adaptation during the first generations

234    after an environmental change. We follow the temporal dynamics of the additive variance and

235    its components, the dynamic of the mean population phenotype, and the dynamic of the mean

236    population fitness, as a function of the mating system and the mutation rate, over 20

237    generations.

238         In addition, and in order to test if remobilization of $V_{LD}$ plays a role in the adaptation

239    of selfing populations, we computed the slope of the trait mean dynamics just after the

240    environmental change (during the first five generations) as a function of the amount of

241    additive variance available at M-S-D equilibrium. If remobilization of $V_{LD}$ is involved in the

242    adaptive process of selfing populations, the initial slope, for a similar amount of additive

243    variance, should be higher in selfing populations compared to mixed mating and outcrossing

244    ones.

245

246    **RESULTS**

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248   Below we present results only for $N = 250$ and $L = 50$, as larger population sizes and

249 more loci did not qualitatively change the results. Results for $N = 1000$, as well as $L = 500$ are

250 given in the supplementary materials section (Figures S1-S6).

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252 **DECOMPOSITION OF THE GENETIC VARIANCE AT EQUILIBRIUM**

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254   As predicted, the additive genetic variance present at M-S-D equilibrium in our

255 simulations is negatively correlated with the selfing rate (figure 1A, see Abu Awad and Roze

256 2018 for the analytical model). By examining each component of the additive variance, we

257 can see that the variance due to within loci variation ($V_{\text{genic}} + V_{\text{F}}$) is higher in selfing

258 populations due to the higher rate of homozygosity (figure 1 B & C). These two components,

259 as well as the total additive variance, increase linearly with increasing mutation rates (figure 1

260 A, B & C). The among-loci component ($V_{\text{LD}}$) is negative (figure 1D), due to the build-up of

261 linkage disequilibrium between alleles with different signs, allowing phenotypes to be close to

262 the phenotypic optimum (0). Because recombination is less effective under selfing, this

263 negative component is responsible for the smaller additive variance observed under

264 predominant selfing. It also contributes significantly to the variance observed in mixed mating

265 and outcrossing populations with moderate to high mutation rates (figure 1D). Larger

266 population sizes or more loci do not change the results for outcrossing and mixed mating

267 populations (Figures S1-S2). For selfing populations, larger population sizes and higher per

268 locus mutation rates contribute to increasing negative linkage disequilibrium ($V_{\text{LD}}$) due to

269 negative linkage disequilibrium (Figure S3).

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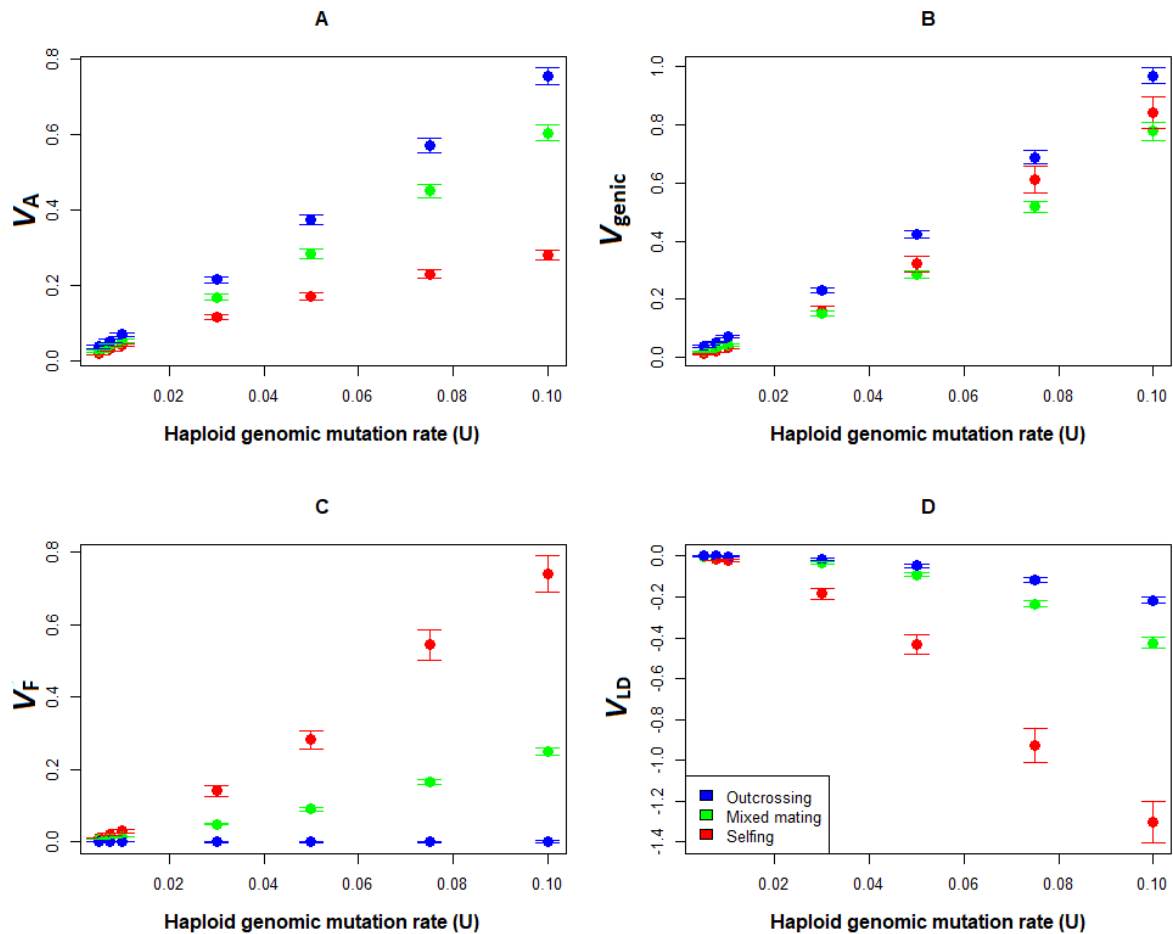
**Figure 1.** Additive genetic variance and its components as a function of the genomic mutation rate and the mating system. **A.** Observed additive variance for the phenotypic trait. **B.** Genic variance for the phenotypic trait ($V_{genic}$). **C.** Genetic variance due to inbreeding ($V_F$). **D.** 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

282   outcrossing, mixed mating and selfing populations mentioned above. We first describe the

283   dynamics observed for outcrossing populations, which will serve as a reference for

284   comparison with the dynamics of selfing populations. We generally find that the dynamics for

285   mixed mating populations are similar to those of outcrossing populations (Figure S4).

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287   **DYNAMICS OF THE ADDITIVE VARIANCE AND OF ITS COMPONENTS:**

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289   In outcrossing populations, the additive variance exhibits very tiny changes during the

290   adaptation process, so do its components (Figure 2). In all cases, the observed additive genetic

291   variance slightly increases during the first generations of adaptation (Figure 2A), then, it

292   either reaches an equilibrium (Figure 2A, $U < 0.1$) or slowly begins to decrease (Figure 2A, $U$

293   $= 0.1$). When $V_{LD}$ is small at M-S-D equilibrium ($U < 0.1$), the observed increase of the

294   additive variance is mainly due to an increase of the genic variance (Figure 2B), probably due

295   to successive sweeps of rare alleles during the adaptation process. In these situations, $V_{LD}$

296   slightly decreases with time (Figure 2C), indicating that some associations between loci are

297   building up. When $V_{LD}$ is significant at M-S-D equilibrium ($U = 0.1$), the genic variance

298   remains constant during the first generations (Figure 2B), but $V_{LD}$ increases slightly (Figure

299   2C), contributing to the increase of the additive variance. The second phase during which the

300   observed additive variance decreases can be explained by the decrease of genic variance with

301   time, due to the purging of deleterious mutations (Figure 2B).

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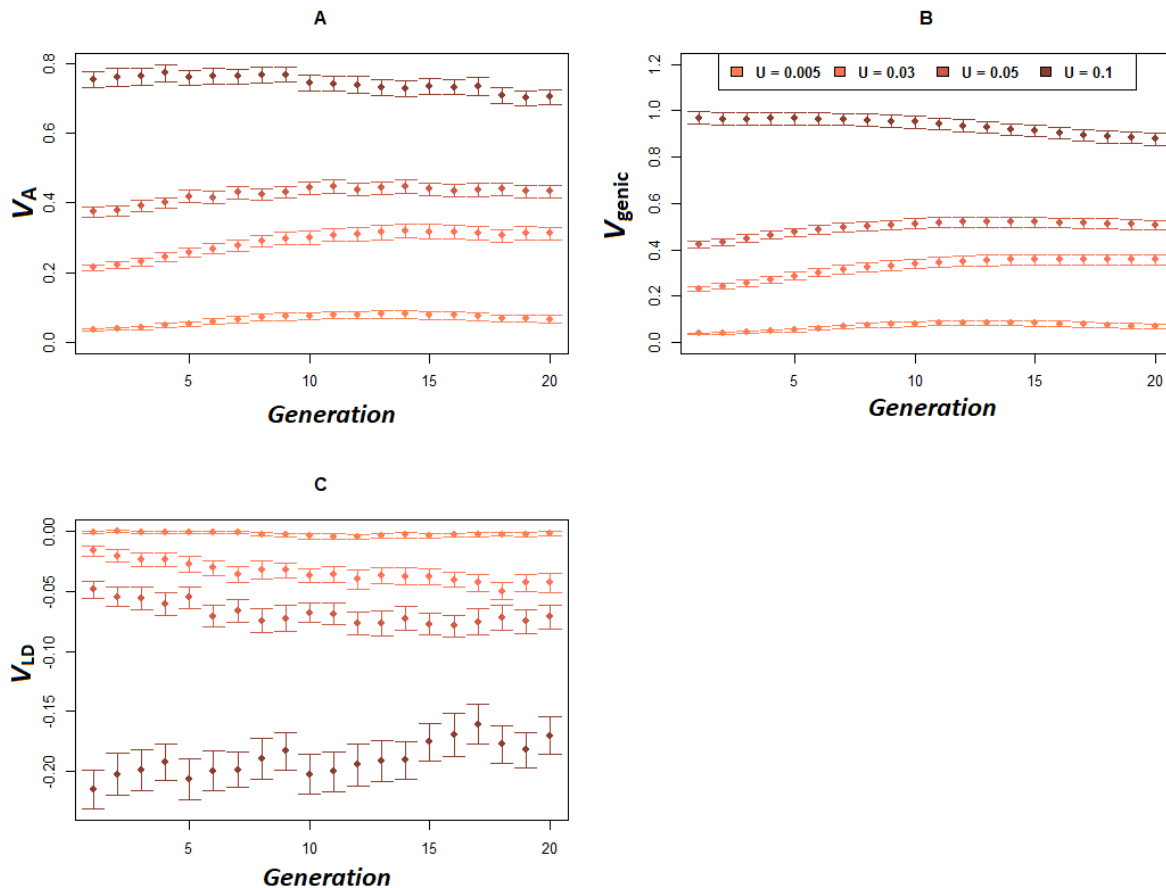
**Figure 2.** Dynamics of additive genetic variance and its components in function of the haplotypic trait mutation rate, for outcrossing populations. **A.** Observed additive variance for the phenotypic trait. **B.** Genic variance for the phenotypic trait ($V_{genic}$). **C.** Genetic variance of the 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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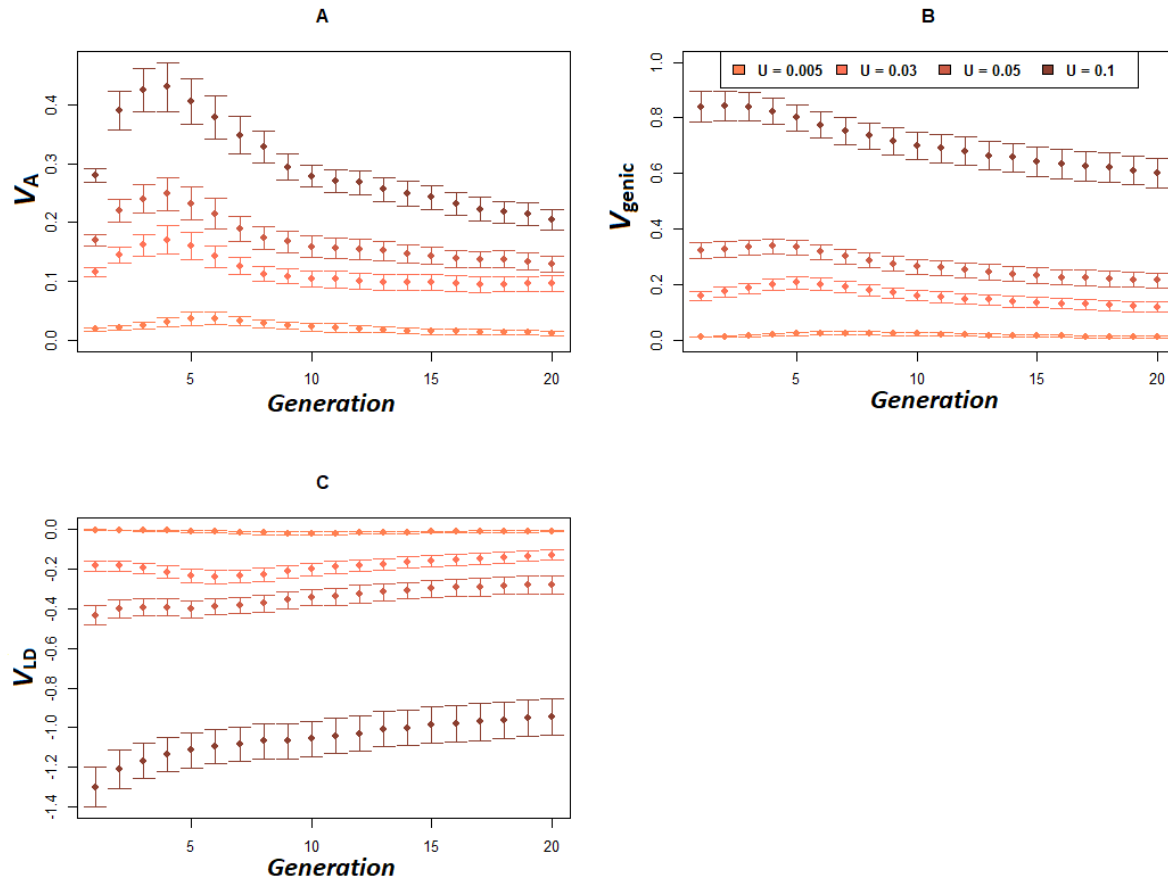
**Figure 3.** Dynamics of additive genetic variance and its components in function of the haplotypic trait mutation rate, for selfing populations. **A.** Observed additive variance for the phenotypic trait. **B.** Genic variance for the phenotypic trait ($V_{genic}$). **C.** Genetic variance of the phenotype 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

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341  populations, outcrossing and mixed mating population respond better to selection, by being

342  closer to the new phenotypic optimum (figure 4). When the mutation rate is weak ($U$ =

343  0.005), none of the populations are able to adapt, and thus the fitness remains low (figure 4).

344  For higher mutation rates ($U > 0.005$), outcrossing and mixed mating populations are always

345  close to the new optimum, and are able to return to fitness levels similar to those observed at

346  M-S-D equilibrium. Selfing populations require that the mutation rate is high enough ($U \geq$

347  0.05, figure 4) in order to reach similar fitness levels as those observed in outcrossing

348  populations. Interestingly, in some cases, adaptation occurs more rapidly in selfing

349  populations, despite the higher genetic diversity of outcrossing populations. The larger the

350  population size and the higher the per-locus mutation rate, the higher the level of potentially

351  usable hidden genetic diversity, and the smaller the genomic mutation rate necessary to reach

352  similar levels of fitness in selfing populations (figures S6-S7).

353       Nevertheless, different mating systems exhibit different dynamics of adaptation.

354  Outcrossing populations adapt by reaching a new phenotypic optimum, but they also maintain

355  a high level of genetic diversity (figure 3), resulting in populations having both mal-adapted

356  and well-adapted individuals. Selfing populations are always further away from the new

357  phenotypic optimum (figure 4), but both the remobilization of the $V_{LD}$, and the fast fixation of

358  the "best" phenotypes allow for the production of close-to-optimum individuals. These

359  phenotypes will then quickly increase in frequency, leading to more homogenous populations

360  than observed for an outcrossing mating system (figure 4).

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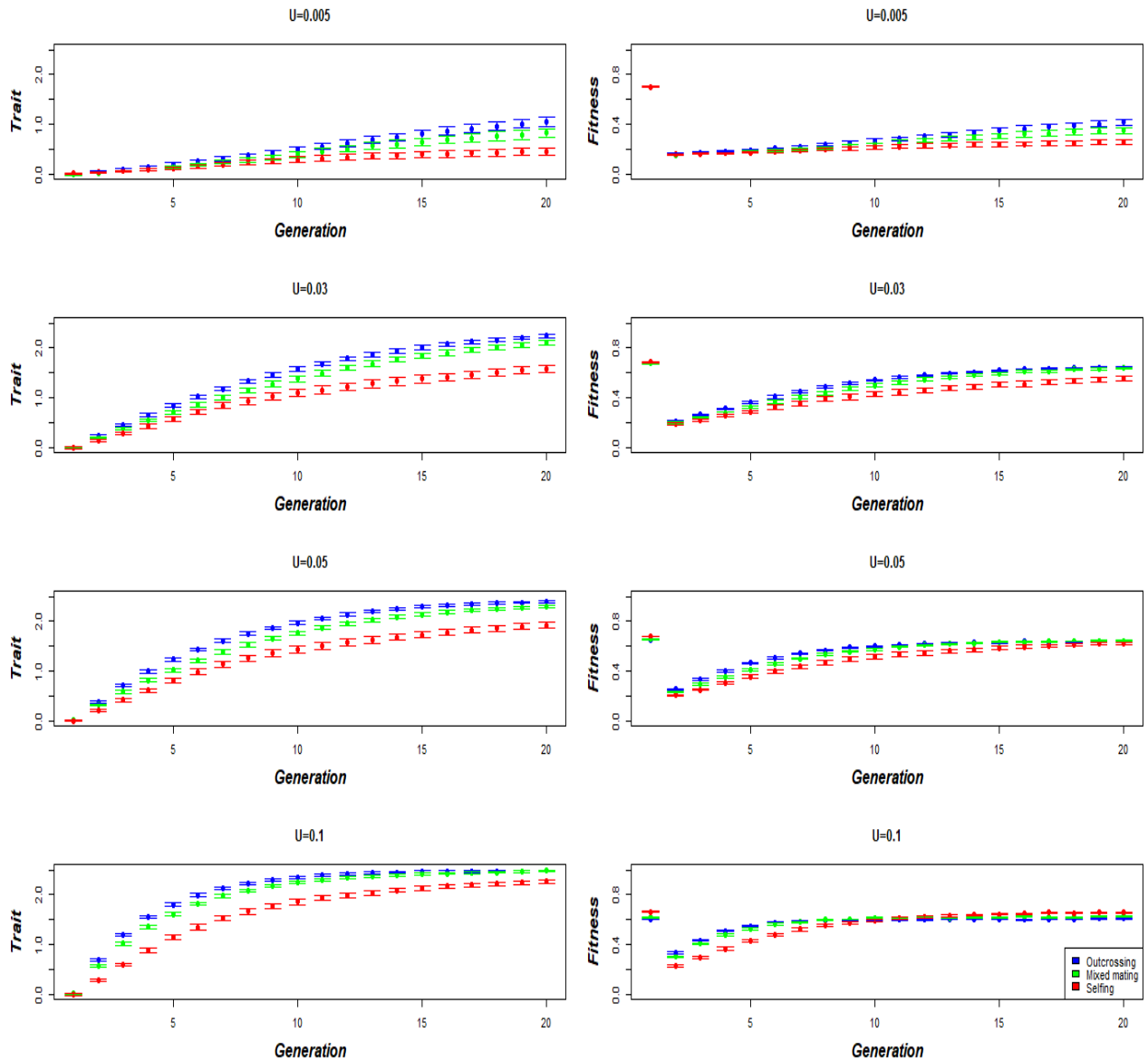
**Figure 4.** Dynamics of the trait and fitness, in function of the trait haplotypic mutation rate and the mating system. Error bars stand for 95% confidence interval (n=100).

*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

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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

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394   phenotypic parental range) in inbred compared to outbred species (Rieseberg *et al.* 1999;

395   Johansen-Morris and Latta 2006). Our analysis also shows that the less effective

396   recombination rate associated with selfing avoids the complete release of the negative linkage

397   disequilibria and thus limits the response to selection. As a result, selection mostly operates at

398   the genotypic level while allelic selection is more prevalent in more recombining populations

399   (Neher and Shraiman 2009). Interestingly, if the rate of self-fertilization is changed during the

400   adaptation process (σ changing from 0.95 to zero after the environmental change), the

401   dynamics of the fitness remains similar (figures S8-S9). Indeed, under complete outcrossing

402   all the hidden genetic variance can be mobilized and this allows initially selfing populations

403   to reach the new phenotypic optimum but recombination also generates less adapted

404   genotypes which reduces the mean population fitness.

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406   ***De novo* mutations *vs*. standing genetic variation: rethinking adaptation in selfing**

407   **species?**

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409       It has been a long accepted paradigm that the advantage procured by selfing, was the

410   rapid fixation of *de novo* mutations more efficiently than in outcrossing populations,

411   independently of the dominance of new mutations, a process known has "Haldane sieve"

412   (Haldane 1927). Indeed, from one locus theory, adaptation through new mutations is more

413   likely in selfing species, and is more likely than adaptation from standing genetic variation

414   (Glémin and Ronfort 2013). However, recent works have suggested that the reduced effective

415   recombination rate of selfing populations adds a disadvantage even when it comes to the

416   fixation of new mutations. Unlike what is expected in outcrossing populations, the fixation of

417   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**

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442    The overwhelming success of selfing species in the domestication process and as

443    invasive species is not considered as resulting from a higher adaptive ability of selfing species

444    compared to outcrossing ones. For instance, the invasive success of selfing populations is

445    attributed to reproductive assurance, since a single individual is able to colonize a new

446    environment (Rambuda and Johnson 2004; van Kleunen *et al.* 2008), and to reduce gene flow

447    which are expected to limit maladapted gene exchanges between populations (Levin 2010).

448    Regarding domestication, it has been argued that selection in selfing populations is most

449    probably due to new mutations, because the standing genetic variation is lower in such

450    populations due to more efficient purging of deleterious mutations that could be involved in

451    the domestication process (Glémin and Bataillon 2009). This idea is reinforced by the fact that

452    selfing species are expected to quickly fix a rare beneficial mutation, independently from its

453    dominance level (Ross-Ibarra 2005). In their review on mating system variation in

454    domesticated plant species, Glémin and Bataillon (2009) have suggested that the high

455    frequency of self-fertilising crop species could be related to an increase in additive variance

456    during domestication; this  idea has however never been tested theoretically or empirically.

457    Here we show that this increase in additive variance could indeed be an advantage when

458    selfing species are faced with new environments. However, our results hold true only if

459    bottlenecks during the domestication and invasion processes are not too strong or if mutation

460    rates are high.

461

## CONCLUSION AND PERSPECTIVES

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464    In this work, we argue that selfing populations under stabilizing selection are able to

465    accumulate hidden genetic variation through negative linkage disequilibrium. Thanks to this

23

466   hidden variation, adaptation under high self-fertilisation rates is not always limited by the

467   expected reduction in additive genetic variance due to purging. We therefore suggest that a

468   simple estimation of additive variance of quantitative traits is not adequate when speculating

469   on the long-term adaptive capacity of a population. Complementary analyses should also be

470   carried out when quantifying the long-term evolvability of a population. Such analyses

471   include looking for transgressive segregation, or carrying out experimental evolutionary

472   experiments in which directional selection is induced. More empirical evidence is required to

473   determine how frequent is cryptic diversity in natural populations of selfing species, and

474   whether or not this property is sufficient to allow for selfing species to adapt to a changing

475   environment.

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