

Effect of partial selfing and polygenic selection on establishment in a new habitat

Himani Sachdeva

Institute of Science and Technology Austria (IST Austria), Am Campus 1,
Klosterneuburg A-3400, Austria

Abstract

This paper analyzes how partial selfing in a large source population influences its ability to colonize a new habitat via the introduction of a few founder individuals. Founders experience inbreeding depression due to partially recessive deleterious alleles as well as maladaptation to the new environment due to selection on a large number of additive loci. I first introduce a simplified version of the Inbreeding History Model (Kelly , 2007) in order to characterize mutation-selection balance in a large, partially selfing source population under selection involving multiple non-identical loci. I then use individual-based simulations to study the eco-evolutionary dynamics of founders establishing in the new habitat under a model of hard selection. The study explores how selfing rate shapes establishment probabilities of founders via effects on both inbreeding depression and adaptability to the new environment, and also distinguishes the effects of selfing on the initial fitness of founders from its effects on the long-term adaptive response of the populations they found. A high rate of (but not complete) selfing is found to aid establishment over a wide range of parameters, even in the absence of mate limitation. The sensitivity of the results to assumptions about the nature of polygenic selection are discussed.

1 Introduction

Peripheral habitats such as islands and geographic range limits present demographic and adaptive challenges to the establishment of new populations (Kawecki , 2008). Natural habitats often span environmental gradients, resulting in different selection pressures at the core and peripheries of the habitat. Peripheral habitats may also be subject to asymmetric gene flow, resulting in swamping, maladaptation and the emergence of ‘demographic sinks’ (Bridle and Vines , 2006). Alternatively, habitats colonized by a single long-distance dispersal event may be effectively isolated from the core, in which case the establishing population is strongly influenced by founder effects and prone to stochastic extinction. Other challenges

32 stem from the low population densities that characterize initial phases of establishment.
33 These result in increased inbreeding and associated fitness costs, while also rendering the
34 population vulnerable to mate limitation and demographic Allee effects (Courchamp et al ,
35 1999).

36 Several empirical studies have suggested a causal link between the mating system of a pop-
37 ulation and its establishment success in a new habitat. In a highly influential paper, Baker
38 (1955) hypothesized that self-fertilizing species should be more adept at long-distance coloni-
39 sation, and presented evidence for the over-representation of selfers on islands in comparison
40 to the mainland. Subsequent work has revealed other examples of this general pattern
41 (Barrett , 1996; Grossenbacher et al , 2017), but also important exceptions, notably the
42 abundance of dioecious plants on the Hawaiian archipelago (Carlquist , 1966).

43 Arguments linking selfing to colonizing ability are primarily based on reduced mate lim-
44 itation in selfing populations (Baker , 1955). Selfing, or more generally uniparental re-
45 production, provides *reproductive assurance*, allowing colonizers to survive the initial low-
46 density phase (Pannell et al , 2015). However, mating systems affect several other aspects
47 of establishment— complete or partial selfing changes the average heterozygosity along the
48 genome, the extent of linkage and identity disequilibrium between loci under selection, and
49 the amount of genetic variation in the population. These characteristics of the source pop-
50 ulation influence its adaptive potential in a new habitat, as well as the degree of inbreeding
51 depression it might experience during the establishment bottleneck. Further, mating systems
52 modulate outbreeding depression in the establishing population in the face of recurrent, mal-
53 adaptive gene flow from the core habitat and thus, have the potential to themselves evolve
54 under selection during establishment.

55 Given the many and possibly conflicting effects of mating system on establishment, the-
56 oretical models can play a crucial role in clarifying the range of environmental conditions
57 and genetic parameters for which mating strategies such as increased selfing augment es-
58 tablishment success (Glémin and Ronfort , 2013; Uecker , 2017). An important challenge
59 is to integrate polygenic architectures that often underlie adaptation into eco-evolutionary
60 models that consider how population size and genotypic frequencies co-evolve.

61 Most theoretical work on the effects of polygenic adaptation during range expansions or
62 the colonisation of new habitats has focused on *randomly mating* populations (Kirkpatrick
63 and Barton , 1997; Polechova and Barton , 2015; Tufto , 2001; Barton and Etheridge , 2018).
64 These models give insight into whether and how interactions and associations between loci-
65 generated either by selection or due to mixing of diverged populations- impact evolutionary
66 dynamics during establishment.

67 However, selfing and other forms of non-random mating also generate strong multi-locus
68 associations. These have two major effects on a population under selection. First, correla-

69 tions between homozygosity at different loci cause most deleterious alleles to be masked from
70 selection in outcrossing or weakly selfing populations, but efficiently purged at higher selfing
71 rates. Thus, allele frequencies and inbreeding depression exhibit a non-linear dependence on
72 the selfing rate, especially when deleterious alleles are nearly recessive and the total muta-
73 tion rate is high (Lande and Schemske , 1985; Lande et al , 1994). Second, selfing reduces
74 homozygosity and the within-family variance of quantitative traits, while increasing their
75 between-family variance (Wright , 1951). While the precise effect of selfing on quantitative
76 trait variation depends on the magnitude and type of selection on the trait (Charlesworth
77 and Charlesworth , 1995; Kelly , 1999; Lande and Porcher , 2015), adaptive response from
78 quantitative variation is expected to be generally different in selfed versus outcrossed popu-
79 lations.

80 In this paper, I investigate how selfing within a large source population (e.g., on a main-
81 land) influences its ability to colonize a new habitat (such as an island) in a scenario where
82 the establishing population experiences both inbreeding depression and maladaptation to
83 the new habitat due to selection on a large number of loci. For simplicity, it is assumed
84 that environmental adaptation and inbreeding depression are affected by two *different* sets
85 of unlinked loci. Alleles at the first set of loci have partially recessive effects and are uncondi-
86 tionally deleterious on both the mainland and the island. Alleles at the second set of loci have
87 co-dominant effects and additively determine a trait which is under environment-dependent
88 selection. The environmental trait is assumed to be under directional selection on both the
89 mainland and island, but in opposite directions. The implications of these assumptions are
90 explored in detail in the Discussion.

91 The study has two parts: I first use a simplified version of the inbreeding history model
92 (Kelly , 2007) to characterize mutation-selection balance involving non-identical, unlinked
93 loci under multiplicative selection in a large, partially selfing source population. The focus
94 is on elucidating the extent to which associations between loci are explained by differences
95 in *recent* selfed versus outcrossed ancestry of individuals.

96 In the second part, I explore how the genetic composition of a large source population in-
97 fluences establishment probabilities on the island, following the introduction of a few founder
98 individuals from the source. Successful establishment requires that the population both sur-
99 vive increased inbreeding depression (due to higher levels of inbreeding in small populations,
100 and segregation of partially recessive alleles) and adapt (via a response from existing ge-
101 netic variation or new mutations). The goal is to understand how selfing within the source
102 population affects both these aspects of the establishment process, and explain the resulting
103 dependence of establishment probabilities on selfing rate. Another goal is to distinguish the
104 effect of selfing on the *initial fitness* of founders from its effect on how variable or inbred
105 their descendants are, which determines the long-term *adaptive potential* of the population.

106 The interplay between partial selfing and polygenic selection in large populations has been
107 analysed using different theoretical approaches (Kondrashov , 1985; Charlesworth et al , 1990,
108 1991; Lande et al , 1994; Kelly , 1999, 2007; Roze , 2015; Lande and Porcher , 2015; Awad
109 and Roze , 2018). The main challenge is to find tractable and accurate approximations
110 for the multi-locus associations that emerge due to partial selfing even in the absence of
111 linkage. Roze (2015) and Awad and Roze (2018) derive analytical expressions for allele
112 frequencies under different kinds of selection by assuming that these are only affected by
113 *pairwise* associations between loci. This analysis is thus applicable for low genome-wide
114 mutation rates, nearly co-dominant loci, and weak selfing, but becomes inaccurate if these
115 conditions are not met (see fig. 4 in Roze (2015)), which generates significant multi-locus
116 disequilibria between loci.

117 An interesting approach by Kelly (1999, 2007) classifies individuals according to their
118 *selfing age*, i.e., the number of generations of continuous selfing in the lineage leading up to
119 the individual. The partially selfing population can then be viewed as a structured population
120 consisting of groups or cohorts of individuals of different selfing ages. Kelly (2007) used
121 this approach to analyse a model with identical loci subject to partially recessive, deleterious
122 mutations. He derived recursions for the mean and variance of (and the correlation between)
123 the number of loci that are homozygous and heterozygous for the deleterious allele within
124 each selfing age cohort by assuming that associations, i.e., linkage and identity disequilibria
125 *within* cohorts are weak. The underlying assumption is that in the absence of linkage and
126 epistasis, variation of inbreeding coefficients between individuals in the population is mostly
127 due to differences in their recent selfing histories.

128 The present work employs a simpler approximation which neglects disequilibria within
129 cohorts altogether, but accounts for disequilibria that emerge across the whole population
130 due to differences in average allele frequencies or average homozygosity between cohorts.
131 This approximation is thus slightly less accurate than that of Kelly (2007), but has the
132 advantage of yielding simpler recursions which can be easily generalized to describe the
133 evolution of *non-identical* loci. As shown below, ignoring associations within cohorts yields
134 reasonably accurate predictions for allele frequencies, pairwise associations between loci, and
135 mean fitness and inbreeding depression in the population across a range of parameters. This
136 also allows us to predict the genetic composition of source populations with different selfing
137 fractions, without directly simulating large numbers of individuals with many selected loci.

138 While the effects of inbreeding *during* establishment have been studied in recent theoretical
139 work (Barton and Etheridge , 2018), the implications of having systematic deviations from
140 panmixia in the source population itself remain largely unexplored. Dornier et al (2008)
141 consider how inbreeding depression and Allee effects shape the establishment potential of
142 partially selfing populations by assuming a fixed level of inbreeding depression. However,
143 as demonstrated below, establishment success depends on the interplay between inbreeding
144 depression and the fitness of founders, which are correlated in a complex way when the

145 total genomic mutation rate is high. Moreover, establishment often involves adaptation to
146 a new environment via response from quantitative genetic variation. The consideration of
147 source populations with complex genetic architectures and non-random mating is thus an
148 important step towards modeling more realistic population establishment or evolutionary
149 rescue scenarios.

150 Since the main goal is to understand how selfing affects establishment probability via
151 the genetic composition of founding individuals subject to polygenic selection, we will only
152 consider a single bout of migration. We thus ignore the effect of selfing on outbreeding
153 depression as well as heterosis, which may, however, be important when the establishing
154 population is subject to continuous gene flow from a divergent source population. Further,
155 the analysis will focus on *initial* establishment: this distinction is important, since selfing
156 may have different effects in small and growing versus large and equilibrated populations.
157 Finally, selfing rates on the island are assumed to be the same as in the source population.
158 Thus, the model does not allow for mating system plasticity or the evolution of selfing rates
159 in the new habitat, which could, however, be important during the establishment of natural
160 populations (Peterson and Kay , 2014).

161 Model and Methods

162 Source population.

163 Consider a large, partially selfing source population with N diploid, hermaphroditic indi-
164 viduals. Each individual genome has L_A loci (referred to as additive loci henceforth) which
165 undergo mutation between two alternative alleles with *co-dominant* effects, and L_R loci
166 (referred to as recessive loci) which undergo mutation to deleterious alleles with *partially*
167 *recessive* effects. The co-dominant alleles contribute additively to a trait z under directional
168 selection. All loci are unlinked, and there is no epistasis between loci. Mutation between
169 the two alternative allelic states occurs at rates μ_A and μ_R per locus per generation for the
170 additive and partially recessive loci respectively.

171 For simplicity, effect sizes of the two alternative alleles are set to $-\alpha/2$ and $\alpha/2$ at each
172 additive locus (though the approximations and results generalize to the case where effect sizes
173 are unequal across loci). The trait value z thus ranges from $z_{min} = -\alpha L_A$ to $z_{max} = \alpha L_A$.
174 The effect α can be arbitrarily set to $1/\sqrt{L_A}$ in accordance with the usual quantitative
175 genetics convention. For simplicity, it is assumed that all deleterious recessive alleles are
176 also characterised by the same selective disadvantage s and dominance coefficient h , with
177 $h < 1/2$. Individual fitness is then given by $W = \exp[-\beta(z - z_{min}) - s \sum_{i=1}^{L_R} (X_i + hY_i)]$,
178 where X_i and Y_i are equal to 1 respectively if the individual is homozygous or heterozygous
179 for the recessive allele at locus i , and zero otherwise. The strength of selection per allele at
180 each additive locus is thus $\tilde{s} = \beta\alpha$. It is sometimes convenient to use the negative log fitness

181 $G = -\ln(W)$, which is the genetic load associated with an individual, and which is the sum
182 of two components: $\beta(z - z_{min})$ and $s \sum_{i=1}^{LR} (X_i + hY_i)$.

183 Generations are assumed to be non-overlapping. The lifecycle in each generation consists
184 of mutation, followed by selection, and then mating via partial self-fertilization (in which a
185 fraction r_s of individuals self). Since fitness is *multiplicative* across both types of loci, and
186 loci are unlinked, there should be no multi-locus associations in a sufficiently large population
187 that is either purely outcrossing ($r_s = 0$) or purely selfing ($r_s = 1$). However, partial selfing
188 ($0 < r_s < 1$) generates associations between allelic states (linkage disequilibrium or LD) as
189 well as between homozygosity (identity disequilibrium or ID) at different loci even in the
190 absence of epistasis, linkage and drift (Weir and Cockerham, 1973).

191 **Identity and Linkage Equilibrium within Cohorts (ILEC) approximation.** Such
192 associations arise due to differences in selfing histories and the resultant variation in homozy-
193 gosity across individuals in a partially selfing population. Following Kelly (2007), we can
194 define the *selfing age* of an individual as the number of generations back to its most recent
195 outcrossing ancestor, or equivalently, the number of generations of continuous selfing in the
196 lineage leading up to the individual. Thus, an individual produced by outcrossing in the
197 present generation has selfing age 0, the selfed offspring of a parent produced via outcrossing
198 in the previous generation has selfing age 1, and so on. Individuals with higher selfing ages
199 have higher homozygosity on average.

200 Let the proportion of individuals with selfing age i be f_i , and the average frequency of
201 homozygous loci (with two ‘1’ alleles) among these individuals be $p_{11}^{(i)}$. Then, under the
202 assumption that the states of different loci are uncorrelated within cohorts, the identity
203 disequilibrium between a pair of loci (of the same type) across the whole population is given
204 by (Supporting Information):

$$(ID)_{pair} = \sum_i \sum_{j < i} f_i f_j [p_{11}^{(i)} - p_{11}^{(j)}]^2 \quad (1)$$

205 Here, the double summation is over all possible pairs of selfing ages. Thus, population-wide
206 disequilibria arise due to the presence of cohorts with different average homozygosities and
207 allele frequencies per locus, even when there are no associations within cohorts.

208 In general, each such cohort is itself characterized by some population structure— for in-
209 stance, the cohort with selfing age zero consists of outcrossed offspring of parents with diverse
210 selfing histories (and hence slightly different allele frequencies), which generates LD within
211 this cohort. However, in the present approximation, all multi-locus associations (LD and
212 ID) within a cohort are neglected. Then the state of the population is completely specified
213 by the fraction f_i of individuals belonging to cohort i , the frequencies of homozygous and
214 heterozygous additive loci (denoted by $p_{11,A}^{(i)}$ and $p_{01,A}^{(i)}$ respectively) within the i^{th} cohort, and

215 the corresponding frequencies $p_{11,R}^{(i)}$ and $p_{01,R}^{(i)}$ for partially recessive loci. This will be referred
216 to this as the Identity and Linkage Equilibrium within Cohorts (ILEC) approximation, to
217 distinguish it from the inbreeding history model (IHM) introduced by Kelly (2007). Note
218 that the latter also accounts for weak, pairwise disequilibria within cohorts.

219 Under the ILEC approximation, the evolution of the partially selfing population is de-
220 scribed by specifying how the proportions f_i , and the frequencies $p_{11,A}^{(i)}$, $p_{01,A}^{(i)}$, $p_{11,R}^{(i)}$ and
221 $p_{01,R}^{(i)}$ change due to mutation, selection and partial selfing in each generation (see SI). These
222 *deterministic* equations ignore allele frequency changes due to drift, as well as stochastic
223 fluctuations of the proportions f_i , and are thus only applicable for large source populations.
224 These equations can be iterated over generations, until equilibrium is attained. The equi-
225 librium frequencies within each cohort and the corresponding fractions f_i can then be used
226 to calculate all population-wide disequilibria (e.g., eq. (1), see also SI), as well as the full
227 fitness distribution in the population, under the ILEC assumption.

228 **Individual-based simulations.** The key assumption underlying the ILEC approximation
229 is that a single round of outcrossing is sufficient to erase most associations between loci, and
230 that the residual associations can be ignored for prediction of population attributes. This
231 assumption is tested by simulating large populations for various parameter combinations.

232 Simulations are initialized by choosing the allelic state of each locus for each of the N
233 individuals independently. The population is evolved in discrete generations as follows—
234 first, all individuals undergo mutation, where the allelic state of each locus is flipped ($0 \leftrightarrow$
235 1) with probability μ_R for a recessive locus and probability μ_A for an additive locus. N
236 individuals are then chosen for mating by sampling (with replacement) from the population
237 with probabilities proportional to individual fitness. Each individual is then allowed to self
238 with probability r_s or outcross with probability $1 - r_s$. For outcrossing individuals, the mating
239 partner is chosen by again sampling individuals in proportion to their fitness. All parental
240 individuals produce gametes via free recombination of their diploid genomes. Selfed offspring
241 are then created by pairing gametes from the same individual and outcrossed offspring by
242 pairing gametes from the two (different) parental individuals.

243 The population is evolved for a few thousand generations until there is no further change
244 in allele frequencies and disequilibria. For each set of parameters, reliable estimates of
245 various quantities of interest are obtained by averaging over several replicates. All statistics
246 are measured at the end of the generation. Comparisons with individual-based simulations
247 show that the ILEC approximation predicts detailed attributes of the source population
248 such as pairwise disequilibria between loci, as well as the *distribution* of genetic load among
249 individuals in the population with reasonable accuracy (figs. 1 and 2 below).

250 Population establishment in the new habitat.

251 In the second part of the paper, I investigate how founders from source populations with
252 different selfing fractions colonize a new environment. Since establishment typically involves
253 a few individuals and proceeds via a phase of small population size, we cannot use the
254 deterministic ILEC approximation and must explicitly account for drift and demographic
255 stochasticity by simulating individuals.

256 However, founders from a large source population can still be drawn using the ILEC ap-
257 proximation: each founder is assigned a selfing age i with probability equal to the proportion
258 f_i of individuals belonging to cohort i in the population. The proportions $\{f_j\}$ depend on
259 selection, dominance and mutation parameters, and the selfing rate in the source population,
260 and can be obtained from the ILEC approximation, as described above (see also SI). Then,
261 each of the L_A additive loci in the founder genome is independently assigned one of three
262 possible genotypes: 00, 01/10 or 11 (corresponding to two possible alleles) with probabilities
263 $1 - p_{01,A}^{(i)} - p_{11,A}^{(i)}$, $p_{01,A}^{(i)}$ or $p_{11,A}^{(i)}$ respectively. Here, $p_{01,A}^{(i)}$ and $p_{11,A}^{(i)}$ denote the frequency of
264 additive loci that are heterozygous and homozygous for the ‘1’ allele, within the i^{th} cohort.
265 Recessive loci are assigned genotypes similarly, i.e., based on the equilibrium heterozygote
266 and homozygote frequencies $p_{01,R}^{(i)}$ and $p_{11,R}^{(i)}$ in cohort i . Choosing genotypes independently
267 at each locus reflects the simplifying assumption that there are no associations between loci
268 within cohorts of individuals with a given selfing age.

269 Establishment is initiated by a single founder event in which N_0 individuals from the
270 source population are introduced all at once into the new habitat. There is no subsequent
271 migration. The direction of selection on the additive trait is reversed in the new habitat
272 (with respect to the source population), such that individual fitness in the new habitat is:
273 $\exp[-\beta_1(z_{max} - z) - s \sum_{i=1}^{L_R} (X_i + hY_i)]$, where β_1 is positive, and is typically different from
274 β_0 , the strength of selection in the source population. Contrast this with the fitness function
275 in the source population: while partially recessive alleles are unconditionally deleterious in
276 both the source population and the new habitat, different additive alleles are favoured in the
277 new habitat versus the source population. Thus, additive alleles have *environment-dependent*
278 fitness effects. The establishing population is subject to *hard* selection in the new habitat,
279 such that mean fitness influences population size.

280 Establishment in the new habitat is studied via individual-based simulations. These are
281 initialized by randomly sampling N_0 founder genomes from the source population, as de-
282 scribed above. Mutation is implemented as before. Hard selection is enforced by assuming
283 that the total number N_{t+1} of offspring produced in generation $t + 1$ is a Poisson-distributed
284 random variable with mean given by $\exp[r_0(1 - N_t/K)]\bar{W}$. Here, r_0 is the intrinsic rate of
285 growth of the population, N_t is the number of individuals prior to selection, K is the carrying
286 capacity of the new habitat, and \bar{W} is the mean population fitness, obtained by averaging
287 over the fitness of all N_t individuals in the new habitat.

288 Each of the N_{t+1} offspring is assumed to be produced via selfing (with probability r_s) or
289 outcrossing (probability $1-r_s$). One (or two) parent(s) of each selfed (or outcrossed) offspring
290 are chosen from among the N_t individuals by sampling with probabilities proportional to
291 fitness. Note that if $N(t)$ is small, then the same individual may be drawn both times while
292 sampling the two parents of an outcrossed offspring. Thus, the realised selfing fraction may
293 be much higher than r_s — being 1 if there is a single individual in the parental generation, and
294 approaching r_s as population size increases. Gametes are generated via free recombination,
295 and paired to produce the next generation of individuals, as in the source population.

296 To assess the colonisation potential of a source population, a thousand independent coloni-
297 sation events are simulated. Each event involves N_0 founders, independently sampled from
298 the source. Establishment probability in the new habitat is then computed as the fraction of
299 ‘successful’ establishment events among these. Establishment is considered successful if the
300 population size is at least $K/10$ individuals at the end of a certain time period (here taken
301 to be 100 generations) after the founder event. Since density-dependence has little effect in
302 such small populations ($N/K \sim 0.1$), these simulations yield approximately the same results
303 as a simpler model where each individual has a Poisson-distributed number of offspring with
304 mean equal to its fitness multiplied by the growth rate r_0 (Barton and Etheridge , 2018).

305 Results

306 Mutation-selection balance in the source population: ILEC approx- 307 imation.

308 We will first analyze attributes of a large source population (neglecting drift) under partial
309 selfing and polygenic selection. Figures 1a and 1b show the equilibrium frequencies of the
310 negatively selected allele at the two types of loci, in an example where fitness is affected
311 by both. Allele frequencies obtained from simulations of 10000 individuals (points) are in
312 close agreement with predictions of the ILEC approximation for both $h = 0.1$ and $h = 0.02$,
313 across a range of selfing fractions.

314 The high rate of recessive mutations ($U_R = 2\mu_R L_R = 1$) relative to the (weak) selective
315 effect per allele ($U_R/h s$ equal to 200 and 1000 in figs. 1a and 1b respectively), results in the
316 segregation of a large number of recessive alleles. This generates substantial fitness differences
317 between selfed and outcrossed individuals within a population, especially in weakly selfing
318 populations (see also fig. 2d). Thus selfers tend to be significantly under-represented (relative
319 to the selfing fraction r_s) among parents of the next generation of offspring. This implies
320 that most deleterious alleles are masked from selection, since selection against deleterious
321 alleles is less effective within the outcrossing cohort as compared to selfing cohorts, especially
322 for low r_s and when the average heterozygosity is high. As a consequence of this kind of
323 *selective interference* between alleles, deleterious alleles are purged efficiently only at high
324 selfing fractions, when selfed individuals make a non-negligible genetic contribution to the

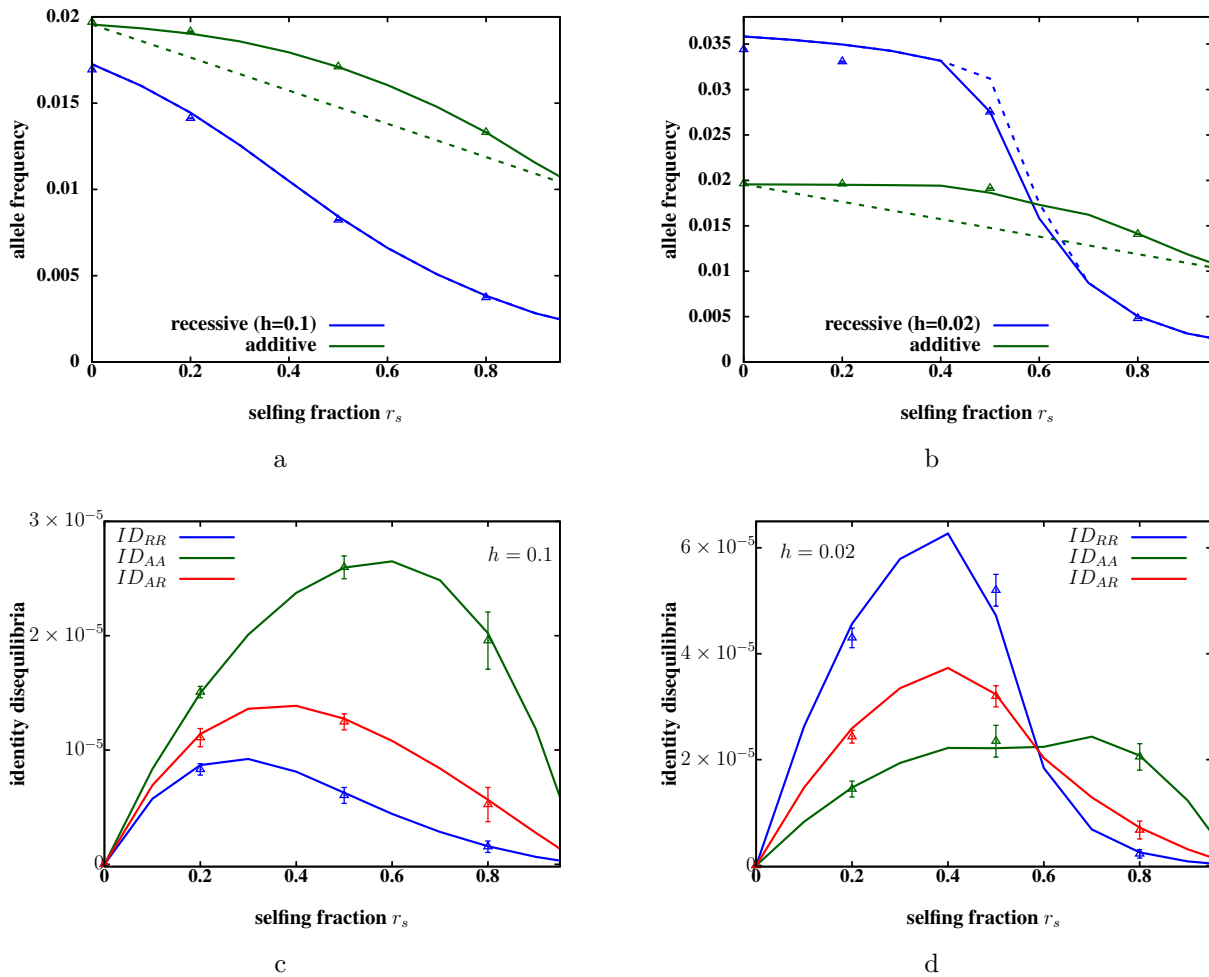


Figure 1: (A)-(B) Equilibrium allele frequencies at partially recessive (blue) and additive (green) loci versus selfing fraction r_s , when the genome has $L_A = 1000$ additive and $L_R = 5000$ partially recessive loci. The dominance coefficient of partially recessive alleles is $h = 0.1$ in fig. A, and $h = 0.02$ in fig. B. All loci are unlinked. Predictions of the ILEC approximation (solid lines) agree closely with results from simulations of $N = 10,000$ individuals (triangles). Dashed lines are the corresponding allele frequencies (obtained from the ILEC approximation) when only one type of loci is present— thus, the green dashed line represents additive allele frequencies in a genome with 1000 additive loci (and no recessive loci). Presence of unlinked deleterious recessive mutations inflates the frequency of the unfavourable additive allele (dashed vs. solid green lines), especially for intermediate selfing fractions. However, the frequency of recessive alleles is not strongly affected by unlinked additive alleles (dashed and solid blue lines are indistinguishable in fig. A). (C)-(D) Various pairwise identity disequilibria versus r_s for $h = 0.1$ (fig. C) and $h = 0.02$ (fig. D) respectively. Green, red and blue solid lines show the ILEC predictions for ID between two additive loci on the genome (ID_{AA}), or two recessive loci on the genome (ID_{RR}), or between an additive and a recessive locus (ID_{AR}); triangles show the corresponding disequilibria, as obtained from individual-based simulations of a population with $N = 10000$. The mutation rate per locus is $\mu_A = \mu_R = 10^{-4}$, selection against partially recessive deleterious alleles is $s = 0.05$ and against additive alleles is $\tilde{s} = \beta\alpha = 0.005$.

325 next generation of offspring (Lande et al , 1994). The ILEC approximation captures the
326 threshold selfing fraction, beyond which purging is effective, with reasonable accuracy (fig.
327 1b), unlike calculations that only include corrections due to pairwise disequilibria (Roze ,
328 2015).

329 A related effect is observed at additive loci, where the frequency of unfavourable alleles is
330 *inflated* by unlinked deleterious recessives segregating in the population (in figs. 1a and 1b,
331 compare solid lines which represent allele frequencies in a genome having both additive and
332 recessive loci with dashed lines which represent allele frequencies in a genome with only one
333 type of locus). This is again a consequence of high inbreeding depression due to recessive
334 alleles, which strongly reduces the contribution of selfed individuals to the gametic pool
335 from which the next generation of offspring is formed. As a result, the effective selection
336 against unfavourable additive alleles is weaker than it would be in the absence of recessive
337 alleles. This effect is typically quite modest, and is most significant at intermediate r_s , for
338 which the mean and variance of the additive trait may increase by as much as 20 – 25%
339 due to unlinked deleterious recessive alleles. More generally, unlinked recessive alleles affect
340 additive trait variation in a complex way that depends qualitatively on U_R (to be explored
341 in detail elsewhere).

342 The ILEC approximation is inaccurate for r_s close to 1: purely selfing populations tend to
343 fix deleterious alleles due to smaller effective population sizes N_e (Charlesworth et al , 1993).
344 In particular, N_e is strongly reduced close to $r_s = 1$, when the total genomic mutation
345 rate is high relative to selection, i.e., $U_R/s \gg 1$. This builds up negative disequilibria
346 between deleterious alleles, which decreases fitness variance and the efficacy of selection
347 in the population (Kamran-Disfani and Agrawal , 2014). This effect is not captured by
348 the deterministic ILEC approximation, which does not account for LD due to drift. Thus,
349 equilibrium allele frequencies are several times higher than the ILEC prediction for $r_s \sim 1$
350 and $U_R/s = 20$ (not shown in figs. 1a and 1b), even for population sizes as large as 10000.

351 The ILEC approximation also predicts identity and linkage disequilibria between alleles
352 at different loci. Figures 1c and 1d compare pairwise ID obtained from simulations with
353 the corresponding ILEC prediction, and show that the approximation is accurate for ID
354 between two loci of the same type (blue and green triangles), as well as between loci of
355 different types (red triangles). As expected, ID is strongest for intermediate selfing fractions
356 when the distribution of selfing ages and inbreeding coefficients in the population is widest,
357 resulting in maximally structured populations. Pairwise linkage disequilibria are found to
358 be negligible for the same parameters (except for $r_s \sim 1$) both in simulations and according
359 to the ILEC prediction.

360 The ILEC approximation can also predict the average population fitness \bar{W} and the in-
361 breeding depression δ , defined as $1 - \bar{W}_{self}/\bar{W}_{oc}$ (where \bar{W}_{self} or \bar{W}_{oc} is the average fitness
362 of a randomly chosen selfed or outcrossed individual). Note that \bar{W} and δ depend on the

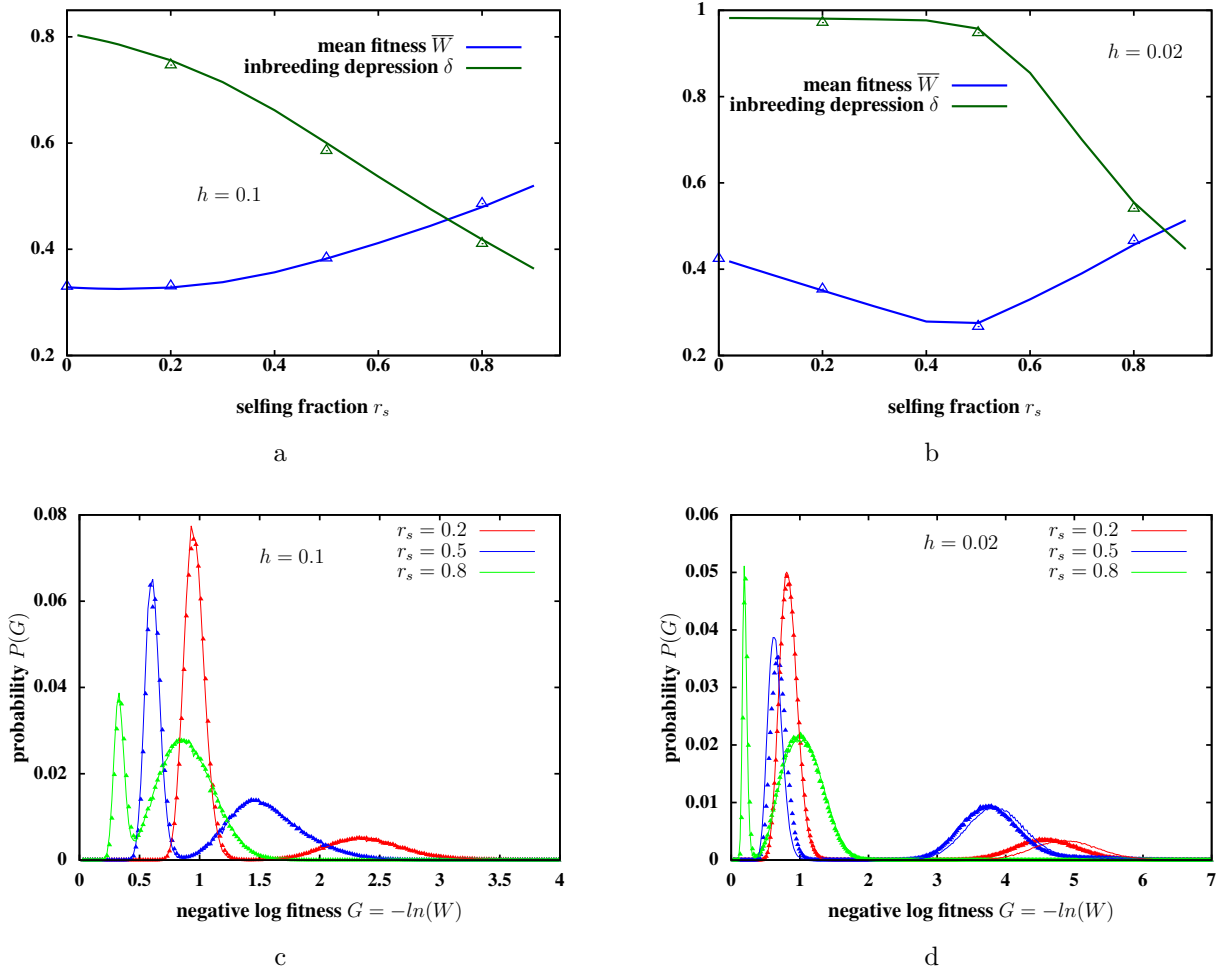


Figure 2: (A)-(B) Mean population fitness \bar{W} and inbreeding depression δ versus selfing fraction r_s , when the genome has $L_A = 1000$ additive and $L_R = 5000$ partially recessive loci. The dominance coefficient of partially recessive alleles is $h = 0.1$ in fig. A, and $h = 0.02$ in fig. B. Solid lines represent predictions of the ILEC approximation, triangles depict results from simulations of $N = 10000$ individuals. (C)-(D) Comparison of simulation results (triangles) and ILEC predictions (lines) for the probability distributions of genetic load G (defined as negative log fitness $G = -\ln(W)$) in the source population. The plots show load distributions for three different selfing fractions: $r_s = 0.2, 0.5, 0.8$, and for two different dominance values of the recessive allele: $h = 0.1$ (fig. C) and $h = 0.02$ (fig. D). The distribution of G is bimodal due to significantly higher number of homozygous deleterious, recessive alleles in the genomes of selfed versus outcrossed offspring. Mutation rates per locus are $\mu_A = \mu_R = 10^{-4}$, selection against partially recessive deleterious alleles is $s = 0.05$ and the strength of directional selection is $\tilde{s} = \beta\alpha = 0.005$.

363 full genotypic distribution, and are thus affected by all disequilibria (at least when selective
364 interference between loci is strong). As before, there is good agreement between simulation
365 results (triangles) and ILEC predictions (lines) for various selfing fractions and dominance
366 values (figs. 2a and 2b).

367 For $h = 0.02$, the mean fitness is minimum at intermediate selfing fractions (fig. 2b). An
368 increase in r_s reduces the frequency of deleterious alleles (which tends to increase fitness),
369 while increasing the average homozygosity (which tends to reduce fitness). Since highly
370 recessive alleles are effectively masked from selection at low selfing fractions in the selective
371 interference ($U_R/h_s \gg 1$) regime, the reduction in deleterious allele frequency with r_s is
372 quite modest (see fig. 1b). Thus, increased selfing reduces fitness at low r_s primarily by
373 generating excess homozygosity. The ineffectiveness of selection at low r_s is also reflected in
374 the fact that inbreeding depression only starts falling beyond a threshold r_s (fig. 2b).

375 Further, we can use the ILEC approximation to generate the *distribution* of load in
376 the population (see SI for details) and compare this with equilibrium distributions from
377 individual-based simulations (figs. 2c and 2d). Here, load is simply negative log fitness
378 $G = -\ln(W) = \beta(z - z_{min}) + s \sum_{i=1}^{L_R} (X_i + hY_i)$, and is the sum of two components, the
379 first due to additive alleles that influence environmental adaptation, and the second due to
380 unconditionally deleterious recessive mutations. The ILEC prediction is very accurate for
381 higher dominance ($h = 0.1$) but slightly less so when alleles are more recessive ($h = 0.02$).

382 A key feature of the load distribution is that it is bimodal, with outcrossed individuals
383 having significantly lower load due to recessive alleles than individuals with one or more
384 generation(s) of continuous selfing in their lineage. This difference is especially marked
385 when alleles are highly recessive and selfing fractions small or intermediate. Note that
386 cohorts with different selfing have different average homozygosity. However, these differences
387 are comparable to the variance of homozygosity within each cohort, so that the fitness
388 distributions of cohorts with different *non-zero* selfing ages overlap significantly, resulting in
389 a single broad peak at high load (figs. 2c and 2d).

390 **Population establishment in the new habitat.**

391 To understand how selfing influences establishment in the new habitat, it is useful to con-
392 sider scenarios where genetic load is either only due to unconditionally deleterious recessive
393 alleles or only due to locally maladaptive additive alleles, and then analyse a scenario with
394 selection on both. We will investigate establishment for a range of selfing fractions from
395 $r_s = 0$ to $r_s = 0.9$, but will not consider complete selfing ($r_s = 1$), as this leads to high
396 fixation rates of deleterious mutations, even in large source populations (Kamran-Disfani
397 and Agrawal, 2014).

398 **Establishment scenario with environment-independent selection on recessive al-**
399 **leles.** For simplicity, deleterious alleles at each locus are assumed to have the same se-
400 lective effect s and dominance value h , in each source population. Moreover, s and h are
401 environment-independent, i.e., are the same in the new habitat. Thus, in this scenario, es-
402 tablishment does not involve adaptation to a new environmental optimum, but only requires
403 that the establishing population purge the excess genetic load that arises from increased
404 inbreeding just after colonisation.

405 Since the N_0 founder genomes are generated using the deterministic ILEC approximation,
406 there is no identity by descent in the population at $t = 0$. I further consider only those
407 parameters U_R , s and h for which a large source population would be viable under hard
408 selection (with the same intrinsic growth rate r_0). This is ensured by testing that for each
409 parameter combination, a population with $N_0 = 100$ individuals doubles with probability
410 greater than 0.95 within 100 generations, for very large K . In principle, $N_0 = 100$ is small
411 enough that drift, stochastic fluctuations and inbreeding may be significant. Thus, this is a
412 rather conservative criterion for testing the viability of a *large* population.

413 Figure 3a shows how the establishment probability P_{est} varies with the selfing fraction r_s
414 of the source population in an example with $N_0 = 10$ founders. Note how the dependence
415 of P_{est} on r_s changes qualitatively with the recessivity and selective effect of deleterious
416 alleles. When genetic load is due to nearly recessive, weakly selected deleterious alleles, then
417 P_{est} is minimum for intermediate r_s . By contrast, when populations undergo mutation to
418 less recessive or more strongly deleterious alleles, then P_{est} increases monotonically with r_s
419 (neglecting the $r_s \sim 1$ behaviour).

420 Since selection pressures on the mainland and island are identical, and we have only
421 considered parameter combinations for which a large source population would be viable
422 under hard selection, failure to establish in the new habitat must arise solely from inbreeding
423 depression due to the small number of founders, and cannot be due to their low initial fitness.
424 However, the extent to which inbreeding depression reduces establishment probability does
425 depend on the initial fitness of founders— even moderate inbreeding depression can prevent
426 establishment if the initial founder fitness is close to the threshold of viability ($e^{r_0 \bar{W}} \sim 1$),
427 while very fit founders ($e^{r_0 \bar{W}} \gg 1$) would establish despite high inbreeding depression.

428 Thus, the complex dependence of P_{est} on selfing fraction reflects the underlying depen-
429 dence of both the initial fitness of founders and the magnitude of inbreeding depression on
430 r_s . For highly recessive alleles and high genomic mutation rates U_R , fitness is minimum at
431 intermediate selfing fractions in a large population (fig. 2b). Moreover, inbreeding depres-
432 sion shows little dependence on r_s for weak selfing. Thus, founders with intermediate r_s are
433 least fit and experience similar levels of inbreeding depression as founders with $r_s = 0$, which
434 explains the minimum in P_{est} at intermediate r_s for $h = 0.02$ (fig. 3a). For less recessive
435 alleles or lower mutation rates U_R , the mean fitness of a large partially selfing population

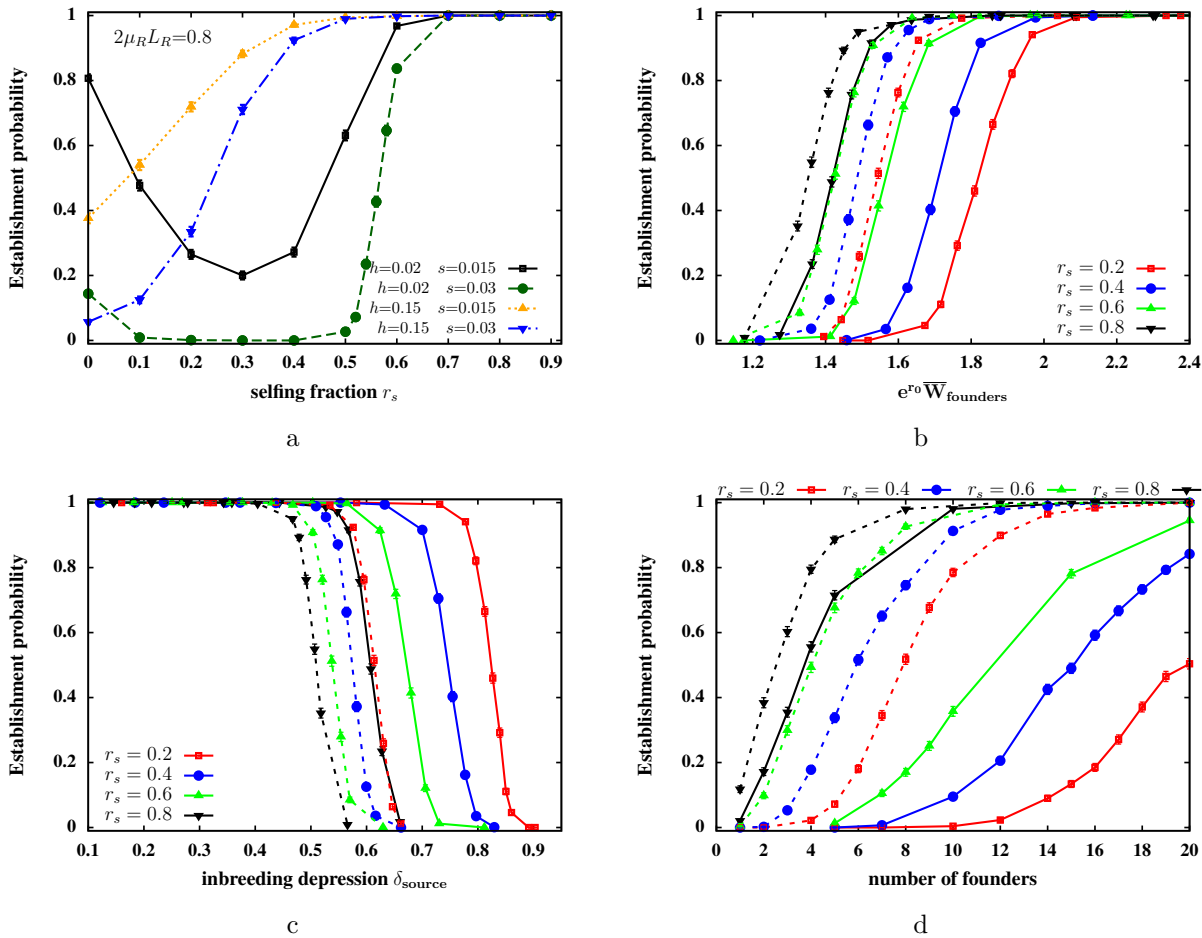


Figure 3: Establishment probabilities P_{est} in the new habitat in a scenario where founders only carry deleterious recessive alleles with environment-independent selective effects. (A) P_{est} versus selfing fraction r_s for different selective effects s and dominance values h of deleterious mutations. P_{est} is minimum at intermediate r_s if genetic load is due to weakly selected, nearly recessive alleles, but increases monotonically with r_s for larger h . Simulation parameters: $L_R = 4000$, $\mu_R = 10^{-4}$. (B)-(C) P_{est} as a function of the initial growth rate of founders (fig. B) and as a function of inbreeding depression in the source population (fig. C), for different selfing fractions (represented by different colors) and different dominance coefficients (solid lines for $h = 0.02$ versus dashed lines for $h = 0.1$). The initial growth rate of the founders and inbreeding depression in the source are tuned by changing the total mutation rate U_R . The number of founders is $N_0 = 10$. (D) P_{est} versus the number of founders N_0 for source populations with different r_s and different dominance values (solid and dashed lines for $h = 0.02$ and $h = 0.1$ respectively). The mutation rate U_R is chosen independently for each source population such that all populations have the same mean fitness $e^{r_0} \bar{W}_{founders} = 1.6$. Simulation parameters in figs. (B)-(D): $L_R = 4000$, $s = 0.02$. P_{est} is the fraction of successful establishment events among 1000 independent simulation runs, each initialized by generating N_0 founders from the source population using the ILEC approximation. Growth rate is $r_0 = 1.1$ in the new habitat; carrying capacity is $K = 1000$.

436 increases and the inbreeding depression decreases with r_s (fig. 2b). Thus, outcrossing pop-
437 ulations are at maximum disadvantage, resulting in a monotonic increase in P_{est} with r_s for
438 $h = 0.15$ in fig. 3a.

439 To further disentangle the effects of selfing fraction on founder fitness and inbreeding
440 depression, we can plot P_{est} as a function of the initial growth rate of the founders (fig.
441 3b). The initial growth rate is e^{r_0} multiplied by the mean fitness of the founders in the new
442 habitat, which, in this scenario, is just their mean fitness in the source population. Figure
443 3b shows that P_{est} becomes non-zero above a threshold founder fitness which depends on
444 both r_s and the dominance coefficient h . For a given h , the threshold fitness required for
445 establishment decreases with r_s . This just reflects the fact that a strongly selfing population
446 with the same mean fitness as a weakly selfing population, must have lower heterozygosity,
447 and hence, experience a lower level of inbreeding depression. Similarly, for a given selfing
448 fraction, the threshold founder fitness is lower when mutations are less recessive (solid versus
449 dashed lines), due to the lower inbreeding depression associated with higher values of h . The
450 dependence on h is especially marked in weakly selfing populations.

451 It is also informative to plot P_{est} as a function of inbreeding depression δ_{source} in the source
452 population (fig. 3c). As expected, establishment is successful only below a threshold value of
453 δ_{source} . Figure 3c further shows that this threshold for inbreeding depression is actually *lower*
454 for populations with higher selfing fractions. This is due to the fact that a strongly selfing
455 population must harbour more deleterious alleles on average and thus have lower fitness than
456 a weakly selfing source population with the same level of inbreeding depression. In addition,
457 populations with the same selfing fraction r_s and the same level of inbreeding depression
458 have establishment probabilities which depend on the recessivity of alleles contributing to
459 inbreeding depression: P_{est} is higher if alleles are *more* recessive (dashed vs. solid lines).

460 Since the transient increase in inbreeding just after colonisation depends crucially on the
461 number N_0 of founders, it is useful to consider how P_{est} varies with N_0 , for founders drawn
462 from source populations which have the same mean fitness but different selfing fractions (fig.
463 3d). Consistent with 3b, high rates of selfing allow for establishment with fewer founders,
464 because of the lower inbreeding depression δ_{source} associated with these founders. Further,
465 P_{est} increases more slowly with N_0 for more recessive alleles, again because of higher δ_{source}
466 associated with smaller values of h .

467 **Establishment scenario with environment-dependent selection on additive alleles.**

468 Consider now a scenario where individuals only carry loci that mutate between alternative
469 co-dominant alleles that additively determine a trait z . The fitness of an individual with trait
470 value z is proportional to $\exp[-\beta_0(z - z_{min})]$ in the source population, and $\exp[-\beta_1(z_{max} - z)]$
471 in the new habitat, where β_0 and β_1 are both positive. Thus, in this scenario, establishment
472 is primarily constrained by maladaptation of the founders to the new environment, and is
473 aided by the ability of the population to adapt from standing variation. Figure 4a shows how

474 P_{est} varies with the selfing fraction of the source population, following a single colonisation
475 event involving $N_0 = 10$ founders.

476 In the absence of deleterious recessive mutations, the frequency of the locally unfavourable
477 additive allele is approximately $\sim (\mu_A/2\tilde{s}_0)(2 - r_s)$ in the source population (Ohta and
478 Cockerham (1974), see also dashed lines in figures 1a and 1b). As a result, stronger selfing
479 reduces the frequency of alleles that are selected against in the source and conversely, favoured
480 in the new habitat (where the direction of selection on the additive trait is reversed). Thus,
481 other parameters being the same, founder fitness in the new environment declines with r_s ,
482 which causes establishment probabilities to also decline with r_s (fig. 4a). This dependence on
483 selfing fraction arises only close to a threshold value of $\tilde{s}_1 = \beta_1\alpha$, for which the genetic load
484 of founders in the new habitat, given by $2\tilde{s}_1L_A[1 - (\mu_A/2\tilde{s}_0)(2 - r_s)]$, is comparable to the
485 growth rate r_0 . Populations fail to establish, irrespective of selfing fraction, when selection
486 in the new habitat is very strong ($2\tilde{s}_1L_A \gg r_0$). Conversely, for $2\tilde{s}_1L_A \ll r_0$, founders from
487 any source population have high establishment success.

488 As before, we can ask: does selfing influence establishment probability predominantly
489 through the initial fitness of founders or more via its effect on the rate of adaptation of the
490 establishing population? Figure 4b shows P_{est} as a function of initial fitness of founders,
491 which is varied by varying the mutation target $U_A = 2\mu_AL_A$ for the additive trait. For a
492 given number of founders N_0 , the curves for different values of r_s appear to collapse onto
493 a single curve, suggesting that in this situation, establishment probabilities depend on the
494 selfing fraction only via its effect on the fitness of the founders. Contrast this with the
495 previous scenario with deleterious recessive mutations, where the threshold fitness required
496 for establishment exhibited a marked dependence on r_s (fig. 3b).

497 This is surprising at first glance since it suggests that adaptation plays little role during
498 establishment. To investigate this further, we can follow the dynamics of the average popula-
499 tion size \bar{N} and the average genetic load $\bar{G}(t) = -\ln[W]$ (figures 4c and 4d) for four different
500 groups of founders with different r_s but the same mean fitness (here $e^{r_0}W_{founders} = 1.16$).
501 Note that the genetic load declines (or equivalently, the frequency of the favoured alleles in-
502 creases) faster in the more strongly selfing populations, from the outset (fig. 4c). However,
503 this does not affect the *initial* growth rate of the population (fig. 4d). More precisely, if the
504 initial growth rate of founders $r_0 - G_0$ is high compared to the rate of adaptation $-dG(t)/dt$,
505 populations rapidly attain a size $\sim K(1 - G(0)/r_0)$, more or less independently of the actual
506 rate of adaptation. As a result, initial establishment (which is defined here as reaching a
507 minimum size of $\sim K/10$) depends only on the initial fitness of the founders in fig. 4d (where
508 $(1 - G(0)/r_0) \sim 0.135$). However, *long-term* population growth does depend on the rate of
509 adaptation and is thus faster in populations with higher selfing fractions.

510 The above reasoning suggests that when the initial fitness advantage of founders is com-
511 parable to the rate of adaptation, then selfing fraction should influence initial establishment

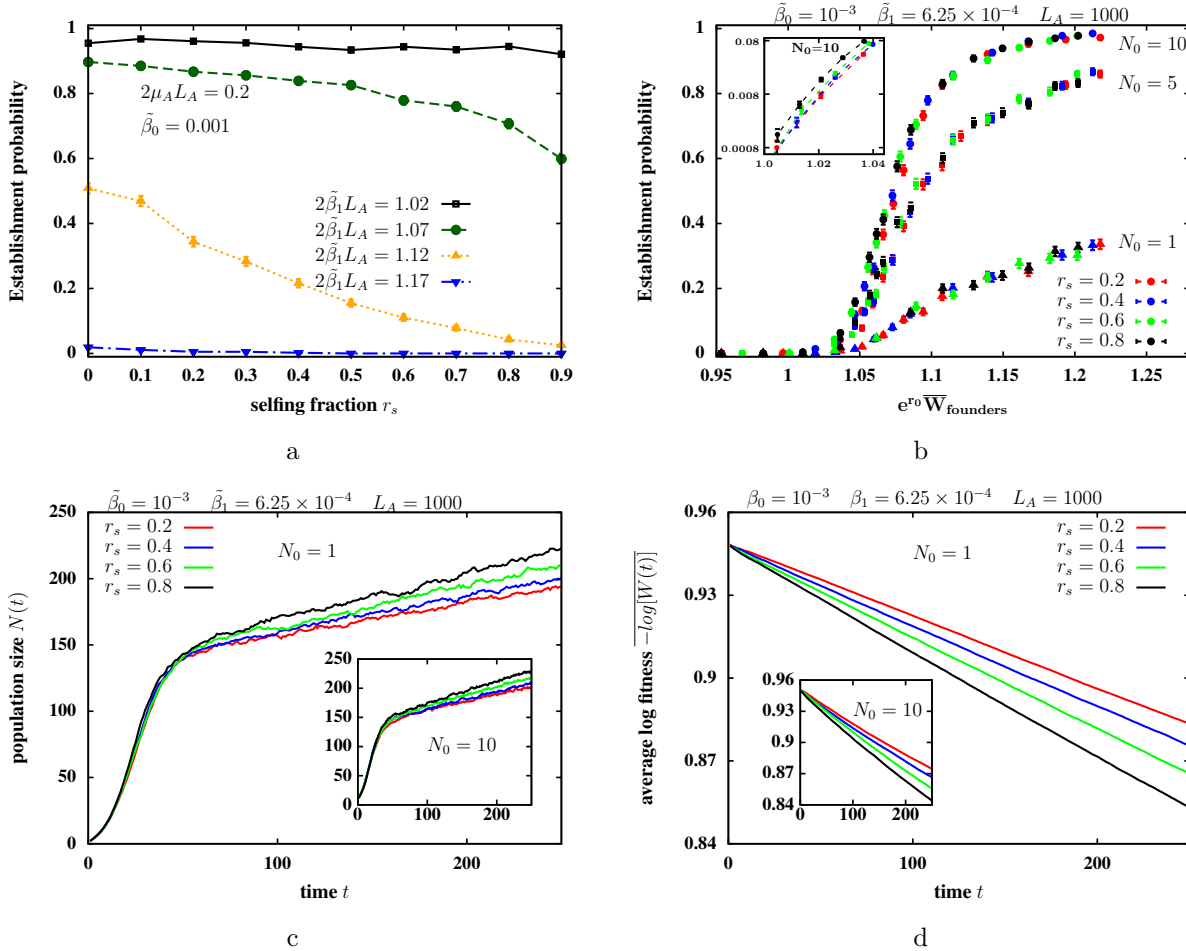


Figure 4: Establishment probabilities P_{est} in the new habitat in a scenario where founders only carry co-dominant alleles that additively determine a trait under environment-dependent selection. (A) P_{est} versus selfing fraction r_s for different selection strengths (expressed as $2\tilde{\beta}_1 L_A$) in the new habitat with $N_0 = 10$ founders. P_{est} declines with increasing r_s for intermediate $2\tilde{\beta}_1 L_A$. Simulation parameters: $L_A = 1000$, $\mu_A = 10^{-4}$, $\tilde{\beta}_0 = 0.001$. (B) P_{est} as a function of the initial growth rate of founders in the new habitat for various r_s (represented by different colors) and various values of N_0 (represented by different symbols). The initial growth rate of the founders is varied by changing the total mutation rate $U_A = 2\mu_A L_A$, which changes the minor allele frequency. The inset zooms into the parameter region with rare establishment ($P_{est} \ll 1$) for $N_0 = 10$. (C)-(D) Average population size $N(t)$ (fig. C) and average load or negative log fitness $-\log[W(t)]$ (fig. D) in the new habitat versus time t , when founders have the same mean fitness ($e^{r_0} \overline{W}_{founders} = 1.16$) in the new habitat, but different selfing fractions r_s and genomic mutation rates U_A . The quantities $N(t)$ and $-\log[W(t)]$ are calculated by averaging over those replicates in which the population is not extinct until 250 generations. Main plots and insets depict dynamics for $N_0 = 1$ and $N_0 = 10$ respectively. Genetic load decreases faster in highly selfing populations but population growth is insensitive to r_s at short time scales. Simulation parameters for figs. (B)-(D): $L_A = 1000$, $\beta_0 = 10^{-3}$, $\beta_1 = 6.25 \times 10^{-4}$. Intrinsic growth rate is $r_0 = 1.1$ in the new habitat; carrying capacity is $K = 1000$. 18

512 more strongly. However, for weak selection per locus (which implies slow adaptation), this
513 is precisely the condition under which establishment would be improbable. To test this, we
514 zoom into the parameter region with $e^{r_0} \bar{W}_{founders} \sim 1$ (see inset of fig. 4b), and find that
515 selfing has a more significant effect on P_{est} when establishment is rare. For instance, in the
516 inset of fig. 4b, the establishment probability of founders drawn from a source population
517 with $r_s = 0.8$ is ~ 1.75 times that of founders with $r_s = 0.2$ that have the same fitness in
518 the new habitat.

519 **Establishment scenario with both types of alleles.** Finally consider establishment
520 scenarios where founders carry both unconditionally deleterious, partially recessive alleles
521 and additive alleles under environment-dependent selection. Figure 5 compares source pop-
522 ulations with different total mutation rates U_R , and hence different magnitudes of genetic
523 load due to partially recessive variants. For each U_R , we can find the critical environmental
524 selection strength $\beta_{1,c}$, such that P_{est} is significant (greater than 0.05), as long as the selection
525 strength in the new habitat is weaker than $\beta_{1,c}$ (see fig. 5a). A high value of $\beta_{1,c}$ signifies
526 that the population can establish despite a large reversal of environmental selection.

527 As expected, for any selfing fraction, the range of environmental selection strengths, to
528 which a population can adapt, shrinks as U_R increases. When U_R is close to zero, outcrossing
529 populations ($r_s \sim 0$) are able to adapt to slightly larger shifts than highly selfing populations
530 ($r_s = 0.8$). However, for any other small, non-zero value of U_R , founders from the $r_s = 0.8$
531 population establish over a larger range of β_1 . This is due to the lower deleterious recessive
532 load and lower inbreeding depression in large, highly selfing populations. Note that this is
533 true for almost completely recessive alleles ($h = 0.02$, solid lines in fig. 5a) as well as partially
534 recessive alleles ($h = 0.2$, dotted lines).

535 We can also measure different components of the genetic load (negative log fitness $-\ln(W)$)
536 associated with founders, for parameter combinations with $P_{est} > 0.05$. The genetic load
537 is the sum of two components— one arising from deleterious recessive mutations, and the
538 other from local maladaptation of the additive trait. The first component has average value
539 $Ls[p_{11}^R + hp_{01}^R]$ (where p_{11}^R and p_{01}^R are the homozygote and heterozygote frequencies of the
540 recessive allele in the source), and the second component has average value $\beta_1(z_{max} - \bar{z})$
541 (where \bar{z} is the population average of the additive trait in the source). Figure 5b depicts the
542 values of these two components on a two dimensional phase plot: for instance, 10 founders
543 drawn from a source population with $r_s = 0$ and dominance $h = 0.02$ of the recessive alleles,
544 establish a colony in the new habitat with probability greater than 0.05, only for points
545 (representing the two load components) lying below the solid red line.

546 Figure 5b shows that the total load is a good predictor of establishment success when
547 deleterious mutations are less recessive and source populations strongly selfing. However,
548 for weakly selfing populations, which suffer significant inbreeding depression due to highly
549 recessive alleles, establishment success cannot be predicted on the basis of the total genetic

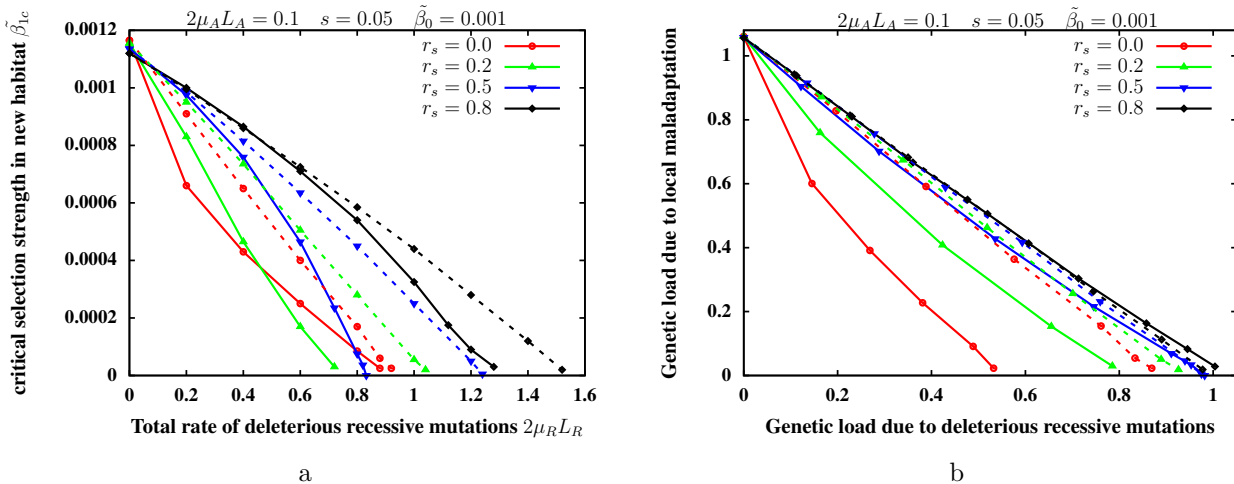


Figure 5: Phase diagrams showing parameter combinations for which the establishment probability P_{est} is greater than 0.05, when individual genomes contain both partially recessive alleles with environment-independent deleterious effects, and additive alleles with environment-dependent effects. (A) Critical selection strength $\tilde{\beta}_{1,c}$ on the additive trait in the new habitat versus the total mutation rate U_R for the partially recessive alleles for different r_s and h . For a given U_R , the establishment probability P_{est} is greater than 0.05 only if $\tilde{\beta}_1 < \tilde{\beta}_{1,c}$, i.e., in the parameter regions below the corresponding line. (B) The maximum (average) genetic load due to maladaptation in the new habitat for which establishment is possible ($P_{est} > 0.05$), as a function of the genetic load due to deleterious recessive alleles. Solid and dashed lines depict phase boundaries when deleterious alleles have dominance values $h = 0.02$ and $h = 0.2$ respectively; different colors show phase boundaries for different values of r_s . Establishment probabilities are obtained as the fraction of successful establishment events out of 1000 independent simulation runs, each initialized by sampling $N_0 = 10$ founders from the source population. Growth rate is $r_0 = 1.1$ in the new habitat; carrying capacity is $K = 1000$. Other parameters are: $L_A = 500$, $\mu_A = 10^{-4}$, $L_R = 2000$, $s = 0.05$, $\tilde{\beta}_0 = 0.001$.

550 load of the founders, but requires a consideration of the different contributions to load.
 551 Thus, for low values of r_s and h , the threshold total fitness required for establishment is
 552 significantly higher (or maximum possible load significantly lower) when there is a high rate
 553 of deleterious recessive mutations.

554 Discussion

555 Partial selfing is common across a variety of taxa, with some analyses reporting interme-
 556 diate selfing rates (between 0.2 and 0.8) in as many as 40 – 50% of seed plants (Goodwillie
 557 et al , 2005) and hermaphroditic animal species (Jarne and Auld , 2006). The extent of in-
 558 breeding depression in populations with intermediate selfing rates may be similar to that in

559 outcrossers, especially among long-lived taxa such as gymnosperms with high per-generation
560 mutation rates (Winn et al , 2011). This suggests a highly polygenic architecture of in-
561 breeding depression, characterized by selective interference between recessive alleles (Lande
562 et al , 1994), in many natural populations. Extensive work on the genetics of inbreeding
563 depression points towards an important role of both highly recessive lethals and moderately
564 recessive, weakly deleterious alleles (Charlesworth and Willis , 2009). More generally, esti-
565 mates in *Drosophila melanogaster* and *Saccharomyces cerevisiae* reveal a wide distribution
566 of dominance values of deleterious alleles, with a mean of 0.1-0.2 (Agrawal and Whitlock ,
567 2011; Peters et al , 2003), and also suggest a negative correlation between the dominance
568 values of deleterious alleles and selection against them (Charlesworth , 1979).

569 The present study represents a preliminary attempt to understand how the interplay of
570 selfing and polygenic architecture shapes the eco-evolutionary dynamics of a population
571 establishing in a new habitat. Our model makes several assumptions about the genetic
572 architecture of the establishing population, whose implications are examined below. First,
573 the model assumes that inbreeding depression and response to environmental selection are
574 due to distinct, non-overlapping sets of unlinked loci. Founders are drawn from source
575 populations in mutation-selection balance, with directional selection on the environment-
576 dependent trait. Further, source populations are assumed to be large enough that mutation-
577 selection balance is essentially deterministic, with a negligible role for drift. Under these
578 assumptions, high rates of (but not complete) selfing is found to facilitate establishment in
579 several distinct ways.

580 **Establishment in the presence of deleterious recessive mutations.** Large popula-
581 tions harbour a substantial number of deleterious recessive alleles when the genomic rate
582 of deleterious mutations U_R is high with respect to the typical selective effect hs . In this
583 scenario, colonies founded by a small number of individuals may fail due to a kind of ge-
584 netic Allee effect, wherein an increase in the fraction of selfed individuals (over and above
585 r_s) or increased mating between related individuals depresses fitness, which reduces popula-
586 tion size and further increases inbreeding, ultimately resulting in extinction. This effect is
587 ameliorated if the source population is itself highly selfing— inbreeding depression declines
588 significantly with r_s for $U_R \gg hs$, which gives highly selfing founders an advantage over
589 equally fit, weakly selfing founders (fig. 3b).

590 More generally, our analysis points towards the difficulty of predicting establishment suc-
591 cess based only on average fitness of the source population or on inbreeding depression alone.
592 In a partially selfing population, these two quantities bear no simple relationship to each
593 other, when selective interference between loci is strong, unlike in the case with $U_R/hs \sim 1$
594 (Bataillon and Kirkpatrick , 2000). Founders with the same initial fitness show different
595 degrees of inbreeding depression δ that depend on s , h , r_s and U_R . Conversely, founders
596 drawn from populations with the same δ have different mean fitness and thus are affected by
597 inbreeding depression to different extents. In particular, the threshold value of inbreeding

598 depression δ_c , beyond which establishment becomes unlikely, is higher in outcrossing versus
599 selfing populations with the same mean fitness (fig. 3c).

600 The success of highly selfing founders in establishing despite the initial bottleneck hinges on
601 the effective purging of deleterious variants in large source populations with high r_s . Purging
602 is less effective, however, when the source population is itself small (Glémin, 2003), as is
603 often the case in human-assisted re-introduction of endangered species into new habitats.
604 Understanding how the genetic composition of *small* source populations influences their
605 establishment potential remains an important challenge in conservation biology.

606 The realised rate of selfing or biparental inbreeding during initial establishment depends
607 crucially on the effective number of founders. In the present model, this is equal to or less
608 than $2N_0$ — this could describe, for instance, the establishment of a diploid plant population
609 via dispersal of seeds into a new habitat. In an alternative scenario, where populations are
610 founded by N_0 fertilized adults (carrying sperm from one or many fathers), the effective
611 number of founders could be larger than $2N_0$. Importantly, in our model, founders are *not*
612 obligate outcrossers; thus, founders from source populations with $r_s = 0$, can nevertheless
613 self under conditions of mate limitation, resulting in a severe *genetic* Allee effect. If the
614 source population is self-incompatible, then the realised rate of selfing in the new habitat is
615 zero, irrespective of N_0 . In this case, outcrossers suffer much less from inbreeding depression
616 during establishment, but are subject to a *demographic* Allee effect, wherein population
617 growth rate is strictly zero for $N_0 = 1$. This leads to an even stronger advantage for self-
618 compatible founders for low N_0 .

619 **Establishment with adaptation from standing additive variation.** Selfing has a
620 qualitatively different effect when the establishing population must adapt to a different
621 environment via a response from standing variation and new mutations at additive loci. We
622 have analysed a specific scenario in which the direction of selection on the environmental
623 trait is reversed in the new habitat, so that the response to selection occurs only via rare
624 alleles. In this scenario, if the number of loci L_A is large, then selection per locus must
625 be correspondingly weak for initial founder fitness to be in a range where establishment
626 is possible. As a consequence, adaptation is too slow to significantly affect establishment,
627 which is instead determined essentially by the initial fitness advantage of founders. Thus,
628 the selfing fraction in the source population influences establishment probability only via
629 founder fitness, except when P_{est} is small (fig. 4b).

630 In an alternative scenario, where the trait is under stabilizing selection towards different
631 optima in the two habitats, adaptation to the new habitat would involve a response from both
632 rare and common alleles. In this scenario, if the difference between the two selection optima is
633 small relative to the standard deviation of trait values among founders, then adaptation can
634 play a more important role during initial establishment than in the present model. As before,
635 adaptation should be faster in more strongly selfing populations due to stronger effective

636 selection per favourable allele. However, with strong stabilizing selection, co-dominant alleles
637 also generate inbreeding depression: selfed cohorts have higher trait variance and lower
638 fitness than outcrossed cohorts, and thus may make little genetic contribution to the next
639 generations. As a result, trait variance is unaffected by selfing at low selfing rates but
640 purged at higher selfing rates (Lande and Porcher , 2015). Understanding how selfing in a
641 source population under stabilizing selection influences its colonisation potential via effects
642 on genetic variation, effective population size and rate of adaptation is an interesting avenue
643 for future work.

644 More generally, when the trait is determined by a large number of small-effect loci, the
645 genotypic values of the offspring of any two individuals are approximately normally dis-
646 tributed (Barton et al. , 2017). In the absence of selfing, this allows for a description of the
647 eco-evolutionary dynamics of an establishing population within an infinitesimal framework
648 (Barton and Etheridge , 2018), which is characterised by relatively few parameters such as
649 the population size, the mean and variance of the trait under selection, and the distribution
650 of inbreeding coefficients in the population. In principle, this framework can be extended
651 to include selfing (although incorporating dominance within the infinitesimal model is more
652 challenging). A key feature of selfing is that it *redistributes* variance (from within families to
653 between families), unlike inbreeding due to small population sizes (as considered by Barton
654 and Etheridge (2018)) which reduces both within and between family variance. Thus, the
655 two forms of inbreeding are expected to have qualitatively different effects on establishment.

656 **Establishment involving both inbreeding depression and adaptation to a new**
657 **environment.** Under the assumptions of this model, highly selfing populations establish
658 over a wider parameter region, especially when the total rate U_R of deleterious mutations is
659 large, and mutations highly recessive. Importantly, with low or intermediate r_s , establish-
660 ment success depends not only on founder fitness, but also on what proportion of fitness loss
661 is due to recessive alleles (fig. 5b).

662 The present model is relatively easy to analyse since it makes the convenient assumption
663 that the alleles that contribute to local adaptation and the alleles that are unconditionally
664 deleterious are distinct and unlinked. In reality, variants that affect fitness are often highly
665 pleiotropic. Thus, an alternative model would be one where alleles at a large number of loci
666 affect multiple traits under stabilizing selection. In this case, most alleles are deleterious
667 and have recessive effects on fitness *on average*, though with a wide variance of dominance
668 coefficients (Manna et al , 2011). A shift in the selection optima for one or more traits in the
669 new habitat would then necessitate a response from variants with a range of adaptive effects
670 and contributions to inbreeding depression. This model could thus provide an alternative
671 framework for studying the interplay between inbreeding depression and polygenic adaptive
672 response during establishment.

673 Linkage between adaptive and deleterious alleles could also qualitatively change our results.
674 In particular, strong selfing significantly reduces the effective rate of recombination when
675 loci are tightly linked. This generates Hill-Robertson interference between adaptive alleles,
676 which reverses the advantage selfers experience during adaptation from co-dominant or even
677 mildly recessive alleles (Hartfield and Glémin , 2016). Linkage also increases hitchhiking
678 of deleterious variants with adaptive alleles, especially in highly selfing populations, which
679 reduces the fixation probability of even slightly recessive adaptive alleles (Hartfield and
680 Glémin , 2014; Kamran-Disfani and Agrawal , 2014). An interesting question is whether
681 linkage could thus reduce the selfing fraction that is ‘optimal’ for establishment in new
682 habitats.

683 Our analysis focuses on establishment that involves a single founder event. A natural ex-
684 tension is to study establishment via recurrent migration from the source population (Barton
685 and Etheridge , 2018). Continual gene flow is expected to alleviate the high inbreeding de-
686 pression experienced by predominantly outcrossing populations via heterosis, and thus reduce
687 the advantage of highly selfing founders during initial establishment. On the other hand, a
688 highly selfing population, once established, might better withstand maladaptive gene flow
689 from the mainland and experience less outbreeding depression. An interesting question is
690 whether different mating strategies might be favoured by natural selection during different
691 phases of establishment.

692 For simplicity, the analysis included only two kinds of loci. However, the ILEC approx-
693 imation provides a computationally frugal way of studying multiple loci with a distribu-
694 tion of selective and dominance effects. Understanding multi-locus associations in terms of
695 population structure arising from recent selfing history (Kelly , 1999, 2007) is a powerful
696 but relatively under-utilized approach for studying partially selfing populations (though see
697 (Lande and Porcher , 2015)). Extension of the ILEC (or similar) approximations to predict
698 multi-locus associations under more complex forms of selection can provide general insight
699 into how the interaction between population structure and polygenic selection shapes the
700 eco-evolutionary dynamics of partially selfing populations.

701 **Acknowledgement.** I thank Nick Barton for very useful suggestions on the model and
702 critical comments on the manuscript.

703 **Supporting Information**

704 **Identity and Linkage Equilibrium within Cohorts (ILEC) approxi-** 705 **mation**

706 This paper introduces the Identity and Linkage Equilibrium within Cohorts (ILEC) ap-
707 proximation, which is a simplified version of the Inbreeding History Model (Kelly , 2007).
708 The basic idea is to approximate the state of a large partially selfing population by neglecting

709 correlations among the allelic states and homozygosity of different loci within each cohort
 710 of individuals who have the same *selfing age*. The selfing age of an individual is defined
 711 as the number of generations back in time to its most recent outcrossing ancestor. Thus,
 712 an individual produced by an outcrossing event in the present generation has selfing age 0,
 713 an individual produced via selfing from a parent who was itself produced by an outcrossing
 714 event in the previous generation has selfing age 1, and so on.

715 Individuals with higher selfing ages have a higher number of homozygous loci; this results
 716 in differences in the average fitness of cohorts of different selfing ages, if most segregating
 717 alleles are recessive. As a result, any single allele (additive or recessive) experiences effective
 718 selection that varies across cohorts, resulting in allele frequency differences between cohorts.
 719 Thus a partially selfing population can be viewed as a *structured* population consisting of
 720 cohorts with different selfing ages (or more generally different selfing histories). A structured
 721 population has non-zero linkage and identity disequilibria, even when there are *no associa-*
 722 *tions* between loci within the sub-groups of the population, simply due to allele frequency
 723 or homozygosity differences between sub-groups. This is demonstrated below for the case of
 724 identity disequilibria between a pair of identical loci.

725 For simplicity, consider the case where individuals have only one type of locus, with one
 726 effect size. Assume that a fraction f_i of individuals in the population have selfing age
 727 i , and the average frequency of homozygous loci within the cohort with selfing age i is
 728 $p_{11}^{(i)}$. Assuming that the allelic states of loci within a cohort are uncorrelated, the fraction
 729 of individuals within cohort i who are homozygous at both loci for the 1 allele is $[p_{11}^{(i)}]^2$.
 730 Thus, the frequency of single-locus homozygotes across the whole population is $\sum_i f_i p_{11}^{(i)}$, and
 731 the corresponding frequency of double homozygotes is $\sum_i f_i (p_{11}^{(i)})^2$. The pairwise identity
 732 disequilibrium, which is just the difference between the population-wide frequency of the
 733 double homozygote and the square of the single-locus homozygote frequency, is given by:

$$\begin{aligned}
 (ID)_{pair} &= \sum_i f_i [p_{11}^{(i)}]^2 - \sum_i \sum_j f_i f_j p_{11}^{(i)} p_{11}^{(j)} \\
 &= \sum_i f_i (1 - f_i) [p_{11}^{(i)}]^2 - \sum_i \sum_{j \neq i} f_i f_j p_{11}^{(i)} p_{11}^{(j)} \\
 &= \sum_i f_i \sum_{j \neq i} f_j [p_{11}^{(i)}]^2 - \sum_i \sum_{j \neq i} f_i f_j p_{11}^{(i)} p_{11}^{(j)} \\
 &= \sum_i \sum_{j < i} f_i f_j ([p_{11}^{(i)}]^2 + [p_{11}^{(j)}]^2) - 2 \sum_{j < i} f_i f_j p_{11}^{(i)} p_{11}^{(j)} \\
 &= \sum_i \sum_{j < i} f_i f_j [p_{11}^{(i)} - p_{11}^{(j)}]^2
 \end{aligned} \tag{2}$$

734 where the double summation is over all possible selfing ages. Thus, positive population-
 735 wide ID emerges, as long as the average homozygosity is different across cohorts. A similar

736 expression for pairwise LD can also be obtained.

737 The assumption that the allelic states of loci within a cohort are uncorrelated is an approx-
 738 imation. The underlying assumption is that a single generation of outcrossing erases most
 739 associations between loci, such that the cohort of outcrossed offspring is a well-mixed group
 740 with little or no population structure. This assumption would be clearly untenable if loci are
 741 linked, or if there are epistatic interactions between loci (for example, if there were strong sta-
 742 bilizing selection on the additive trait). Even in the present scenario involving multiplicative
 743 selection across unlinked loci, this assumption is not strictly true, as outcrossing individuals
 744 with different selfing histories have different allele frequencies and homozygosities (resulting
 745 in differences in segregation variance among different outcrossing pairs), which can generate
 746 some structure within the cohort of outcrossed offspring. Nevertheless, this approximation
 747 generates predictions for detailed attributes of large populations, which agree quite well with
 748 results of individual-based simulations.

749 Under the ILEC approximation, the population is described completely by the fractions f_i
 750 of individuals who belong to each selfing age cohort i , and the frequency of heterozygous and
 751 homozygous alleles for each type of locus within each cohort. Let us denote the frequencies
 752 of homozygous and heterozygous additive loci (carrying the ‘1’ allele) within the i^{th} cohort
 753 by $p_{11,A}^{(i)}$ and $p_{01,A}^{(i)}$, and the corresponding frequencies at partially recessive loci by $p_{11,R}^{(i)}$ and
 754 $p_{01,R}^{(i)}$. The evolution of f_i , $p_{11,A}^{(i)}$, $p_{01,A}^{(i)}$, $p_{11,R}^{(i)}$ and $p_{01,R}^{(i)}$ under mutation, selection and partial
 755 selfing can then be described using the following equations:

Mutation

$$\begin{aligned} p_{11,A}^{(i)} &\rightarrow (1 - \mu_A)^2 p_{11,A}^{(i)} + \mu_A(1 - \mu_A) p_{01,A}^{(i)} + \mu_A^2 (1 - p_{11,A}^{(i)} - p_{01,A}^{(i)}) \\ p_{01,A}^{(i)} &\rightarrow 2\mu_A(1 - 2p_{01,A}^{(i)}) + p_{01,A}^{(i)} \end{aligned} \quad (3a)$$

756

$$f^{(i)} \rightarrow f^{(i)} \quad (3b)$$

757 Equations (3a) represents the change in homozygote and heterozygote frequencies due to
 758 mutation at a single additive locus. A similar equation can be written for frequency changes
 759 at recessive loci, by replacing μ_A by μ_R . The fraction of individuals in each cohort itself
 760 remains unchanged by mutation (eq. (3b)).

Selection

$$\begin{aligned} p_{11,A}^{(i)} &\rightarrow e^{-\tilde{s}} p_{11,A}^{(i)} / \overline{W}_A^{(i)} & p_{01,A}^{(i)} &\rightarrow e^{-\tilde{s}/2} p_{01,A}^{(i)} / \overline{W}_A^{(i)} \\ \text{where } \overline{W}_A^{(i)} &= (1 - p_{11,A}^{(i)} - p_{01,A}^{(i)}) + e^{-\tilde{s}} p_{11,A}^{(i)} + e^{-\tilde{s}/2} p_{01,A}^{(i)} & \tilde{s} &= \alpha s \end{aligned} \quad (4a)$$

761

$$p_{11,R}^{(i)} \rightarrow e^{-s} p_{11,R}^{(i)} / \overline{W}_R^{(i)} \quad p_{01,R}^{(i)} \rightarrow e^{-hs} p_{01,R}^{(i)} / \overline{W}_R^{(i)} \quad (4b)$$

where $\overline{W}_R^{(i)} = (1 - p_{11,R}^{(i)} - p_{01,R}^{(i)}) + e^{-s} p_{11,R}^{(i)} + e^{-hs} p_{01,R}^{(i)}$

762

$$f^{(i)} \rightarrow \frac{f^{(i)} \left[\overline{W}_A^{(i)} \right]^{L_A} \left[\overline{W}_R^{(i)} \right]^{L_R}}{\sum_j f^{(j)} \left[\overline{W}_A^{(j)} \right]^{L_A} \left[\overline{W}_R^{(j)} \right]^{L_R}} \quad (4c)$$

763 Equations (4a) and (4b) represent the effect of selection on heterozygote and homozygote
 764 frequencies at an additive locus and a recessive locus respectively, within a selfing-age cohort
 765 i . Equation (4c) shows how selection causes the proportions of different cohorts within the
 766 population to change in proportion to the average fitness of its members. The average fitness
 767 is determined multiplicatively by the additive and recessive loci—the fitness contribution of
 768 a single additive locus in the i^{th} cohort is denoted by $\overline{W}_A^{(i)}$; the contribution of all additive
 769 loci is $\left[\overline{W}_A^{(i)} \right]^{L_A}$, and similarly for recessive loci.

770 Mating

$$p_{11,A}^{(i+1)} \rightarrow p_{11,A}^{(i)} + \frac{p_{01,A}^{(i)}}{4} \quad p_{01,A}^{(i+1)} \rightarrow \frac{p_{01,A}^{(i)}}{2} \quad (5a)$$

771

$$p_{11,A}^{(0)} \rightarrow p_A^2 \quad p_{01,A}^{(0)} \rightarrow 2p_A(1 - p_A) \quad \text{where } p_A = \sum_i f^{(i)} (p_{11,A}^{(i)} + p_{01,A}^{(i)}/2) \quad (5b)$$

772

$$f^{(0)} \rightarrow 1 - r_s \quad f^{(i+1)} \rightarrow r_s f^{(i)} \quad (5c)$$

773 Equation (5a) shows how homozygote and heterozygote frequencies at an additive locus
 774 change due to selfing: note that the new frequencies within the $(i + 1)^{th}$ cohort depend on
 775 the old frequencies within the i^{th} cohort. Equation (5b) shows the new heterozygote and
 776 homozygote frequencies within the outcrossing cohort: these depend only on the population-
 777 wide allele frequency p_A , and not on the frequencies of the additive allele within each cohort
 778 separately. Equations identical to (5a) and (5b) can be written down for frequency changes
 779 at recessive loci. Equation (5c) shows the proportion of individuals belonging to different
 780 selfing age cohorts after mating; the fraction of outcrossed individuals (with selfing age 0) is
 781 just $1 - r_s$.

782 Equations (3)-(5) can be iterated over generations, until the proportions f_i , and the ho-
 783 mozygote and heterozygote allele frequencies $p_{11,A}^{(i)}$, $p_{01,A}^{(i)}$, $p_{11,R}^{(i)}$ and $p_{01,R}^{(i)}$ reach stationary
 784 (equilibrium) values. Note that the concept of equilibrium or steady state is not strictly
 785 well-defined for this model: starting with a fully outcrossed population (i.e., $f_0 = 1$, $f_i = 0$
 786 for all $i > 0$) at $t = 0$, cohorts with higher and higher selfing ages are generated in each

787 generation. Thus, in principle, f_i can be non-zero for all cohorts i with selfing ages $0, 1, \dots, t$
 788 in generation t . However, the proportions f_i become vanishingly small for $i \gg -1/\log(r_s)$
 789 even in the absence of selection, while f_i show a steeper decline with i when there is selec-
 790 tion against partially recessive alleles. Thus, in practice, all cohorts reach equilibrium if the
 791 above recursions are iterated sufficiently long. The fact that only the first few cohorts have
 792 non-zero occupancy makes this a relatively economical way of approximating population
 793 structure in a highly polygenic context.

794 Under the ILEC approximation, we can express the frequency of any multi-locus genotype
 795 in terms of the proportions f_i and the homozygote and heterozygote frequencies in each
 796 cohort. The probability $P(m_{11,A}, m_{01,A}, m_{11,R}, m_{01,R})$, that an individual has $m_{11,A}$ homozy-
 797 gous and $m_{01,A}$ heterozygous loci for the additive ‘1’ allele, and $m_{11,R}$ and $m_{01,R}$ homozygous
 798 and heterozygous loci respectively for the partially recessive allele, is given by:

$$\begin{aligned}
 P(m_{11,A}, m_{01,A}, m_{11,R}, m_{01,R}) = & \\
 \sum_i f_i \left\{ \binom{L_A}{m_{11,A}} \binom{L_A - m_{11,A}}{m_{01,A}} [p_{11,A}^{(i)}]^{m_{11,A}} [p_{01,A}^{(i)}]^{m_{01,A}} [1 - p_{11,A}^{(i)} - p_{01,A}^{(i)}]^{L_A - m_{11,A} - m_{01,A}} \right. & \\
 \left. \times \binom{L_R}{m_{11,R}} \binom{L_R - m_{11,R}}{m_{01,R}} [p_{11,R}^{(i)}]^{m_{11,R}} [p_{01,R}^{(i)}]^{m_{01,R}} [1 - p_{11,R}^{(i)} - p_{01,R}^{(i)}]^{L_R - m_{11,R} - m_{01,R}} \right\} & \quad (6)
 \end{aligned}$$

799 where the sum is over all selfing ages i for which f_i is non-zero. The equation above sim-
 800 ply reflects the ILEC assumption that the states of loci within any selfing age cohort are
 801 statistically independent: then the numbers of loci (of a particular type) with states ‘00’,
 802 ‘01’ and ‘11’ must have a trinomial distribution across individuals within a particular selfing
 803 age. Equation 6 allows us to calculate any pairwise associations, as in eq. (2) above. We
 804 can also use eq. (6) to generate founder genotypes when simulating colonisation from a
 805 source population. Approximate distributions of genetic load in the population under the
 806 ILEC approximation (shown by lines in figs. 2c and 2d in the main text) were obtained
 807 by first sampling a large numbers of genotypes according to eq. (6) and then plotting the
 808 distribution of load among these.

809 References

- 810 Agrawal, A. F., and M. C. Whitlock. 2011. Inferences about the distribution of dominance
 811 drawn from yeast gene knockout data. *Genetics* 187(2):553-566.
- 812 Awad, D.A., and D. Roze. 2018. Effects of partial selfing on the equilibrium genetic variance,
 813 mutation load, and inbreeding depression under stabilizing selection. *Evolution* 72(4):751-
 814 769.
- 815 Baker, H. G. 1955. Self-compatibility and establishment after long-distance dispersal. *Evo-*
 816 *lution* 9:347-349.

- 817 Barrett, S.C.H. 1996. The reproductive biology and genetics of island plants. *Philos. Trans.*
818 *R. Soc. Lond. B Biol. Sci.* 351:725-733.
- 819 Barton, N. H. 2001. Adaptation at the edge of a species range. In: *Integrating Ecology and*
820 *Evolution in a Spatial Context* (eds J Silvertown, J Antonovics), pp. 365-392. Blackwell,
821 London.
- 822 Barton, N. H., and A. M. Etheridge. 2018. Establishment in a new habitat by polygenic
823 adaptation. *Theor. Popul. Biol.* 122:110-127.
- 824 Barton, N. H., Etheridge, A. M., and A. Véber. 2017. The infinitesimal model: Definition,
825 derivation, and implications. *Theor. Popul. Biol.* 118:50-73.
- 826 Bataillon, T., and M. Kirkpatrick. 2000. Inbreeding depression due to mildly deleterious
827 mutations in finite populations: size does matter. *Genet. Res.* 75:75-81.
- 828 Bridle, J. R., and T. H. Vines. 2006. Limits to evolution at range margins: when and why
829 does adaptation fail? *Trends Ecol. Evol.* 22:140-147.
- 830 Carlquist, S. 1966. The biota of long-distance dispersal. IV. Genetic systems in the floras of
831 oceanic islands. *Evolution* 20:433-455.
- 832 Charlesworth, B. 1979. Evidence against Fisher's theory of dominance. *Nature* 278: 848-849.
- 833 Charlesworth, B. 1992. Evolutionary rates in partially self-fertilizing species. *Am. Nat.*
834 140:126-148.
- 835 Charlesworth, B., Morgan, M. T., and D. Charlesworth. 1991. Multilocus models of inbreed-
836 ing depression with synergistic selection and partial self-fertilization. *Genetical Research*
837 57:177-194.
- 838 Charlesworth, D., and B. Charlesworth. 1995. Quantitative genetics in plants: the effect of
839 the breeding system on genetic variability. *Evolution* 49:911-920.
- 840 Charlesworth, D., Morgan, M. T., and B. Charlesworth. 1990. Inbreeding depression, ge-
841 netic load, and the evolution of out-crossing rates in a multilocus system with no linkage.
842 *Evolution* 44:1469-1489.
- 843 Charlesworth, D., Morgan, M. T., and B. Charlesworth. 1993. Mutation accumulation in
844 finite outbreeding and inbreeding populations. *Genetical Research* 61:39-56
- 845 Charlesworth, D., and J. H. Willis. 2009. The genetics of inbreeding depression. *Heredity*
846 10:783-796.
- 847 Courchamp, F., Clutton-Brock, T., and B. Grenfell. 1999. Inverse density dependence and
848 the Allee effect. *Trends Ecol. Evol.* 14:405-410

- 849 Dornier, A., Munoz, F., and P. O. Cheptou. 2008. Allee effect and self-fertilization
850 in hermaphrodites: Reproductive assurance in a structured metapopulation *Evolution*
851 62(10):2558-2569.
- 852 Glémin, S. 2003. How are deleterious mutations purged? Drift versus nonrandom mating.
853 *Evolution* 57:2678-2687.
- 854 Glémin, S., and J. Ronfort. 2013. Adaptation and maladaptation in selfing and outcrossing
855 species: new mutations versus standing genetic variation. *Evolution* 67:225-240.
- 856 Goodwillie, C., Kalisz, S., and C. G. Eckert. 2005. The evolutionary enigma of mixed mating
857 systems in plants: occurrence, theoretical explanations, and empirical evidence. *Annu. Rev.*
858 *Ecol. Evol. Syst.* 36:4779.
- 859 Grossenbacher, D. L., Brandvain, Y., Auld, J. R., Burd, M., Cheptou, P. O., Conner, J.
860 K., Grant, A. G., Hovick, S. M., Pannell, J. R., Pauw, A., Petanidou, T., Randle, A. M.,
861 Rubio de Casas, R., Vamosi, J., Winn, A., Iqbal, B., Busch, J. W., Kalisz, S., and E. E.
862 Goldberg. 2017. Self-compatibility is overrepresented on islands. *New Phytol.* 215:469-478.
- 863 Hartfield, M., and S. Glémin. 2014. Hitchhiking of deleterious alleles and the cost of adap-
864 tation in partially selfing species. *Genetics* 196:281-293.
- 865 Hartfield, M., and S. Glémin. 2016. Limits to adaptation in partially selfing species. *Genetics*
866 203:959-974.
- 867 Jarne, P., and J. R. Auld. 2006. Animals mix it up too: the distribution of self-fertilization
868 among hermaphroditic animals. *Evolution* 60:1816-1824
- 869 Kamran-Disfani, A., and A. F. Agrawal. 2014. Selfing, adaptation and background selection
870 in finite populations. *J. Evol. Biol.* 27:1360-1371.
- 871 Kawecki, T.J. 2008. Adaptation to marginal habitats. *Annu. Rev. Ecol. Syst.* 39:321-342
- 872 Kelly, J. K. 1999. Response to selection in partially self-fertilizing populations. I. Selection
873 on a single trait. *Evolution* 53:336-349.
- 874 Kelly, J. K. 2007. Mutation-selection balance in mixed mating populations. *J. Theor. Biol.*
875 246:355-365.
- 876 Kirkpatrick, M., and N.H. Barton. 1997. Evolution of a species range. *Am. Nat.* 150:1-23
- 877 Kondrashov, A. S. 1985. Deleterious mutations as an evolutionary factor. II. Facultative
878 apomixis and selfing. *Genetics* 111:635-653.
- 879 Lande, R., and E. Porcher. 2015. Maintenance of quantitative genetic variance under partial
880 self-fertilization, with implications for the evolution of selfing. *Genetics* 200:891-906.

- 881 Lande, R., and D. W. Schemske. 1985. The evolution of self-fertilization and inbreeding
882 depression in plants. I. Genetic models. *Evolution* 39:24-40.
- 883 Lande, R., Schemske, D.W., and S. T. Schultz. 1994. High inbreeding depression, selective in-
884 terference among loci, and the threshold selfing rate for purging recessive lethal mutations.
885 *Evolution* 48:965-978.
- 886 Manna, F., G. Martin, and T. Lenormand. 2011. Fitness landscapes: an alternative theory
887 for the dominance of mutation. *Genetics* 189:923-937.
- 888 Ohta, T., and C. C. Cockerham. 1974. Detrimental genes with partial selfing and effects on
889 a neutral locus. *Genetical Research* 23:191-200.
- 890 Pannell, J. R., Auld, J. R., Brandvain, Y., Burd, M., Busch, J. W., Cheptou, P., Conner,
891 J. K., Goldberg, E. E., Grant, A., Grossenbacher, D. L., , S. M. et al. 2015. The scope of
892 Baker's law. *New Phytol.* 208:656-667.
- 893 Peters, A. D., Halligan, D. L., Whitlock, M. C., and P.D. Keightley. 2003. Dominance and
894 overdominance of mildly deleterious induced mutations for fitness traits in *Caenorhabditis*
895 *elegans*. *Genetics* 165:589-599.
- 896 Peterson, M. L., and K. M. Kay. 2014. Mating system plasticity promotes persistence and
897 adaptation of colonizing populations of hermaphroditic angiosperms. *Am. Nat.* 185:28-43.
- 898 Polechova, J., and N.H. Barton. 2015. Limits to adaptation along environmental gradients.
899 *Proc. Natl. Acad. Sci. USA*, 112:6401-6406.
- 900 Roze, D. 2015. Effects of interference between selected loci on the mutation load, inbreeding
901 depression and heterosis. *Genetics* 201:745-757.
- 902 Tufto, J. 2001. Effects of releasing maladapted individuals: a demographic- evolutionary
903 model. *Am. Nat.* 158:331-340.
- 904 Uecker, H., 2017. Evolutionary rescue in randomly mating, selfing, and clonal populations.
905 *Evolution.* 71:845-858
- 906 Weir, B. S., and C. C. Cockerham. 1973. Mixed self and random mating at two loci. *Genet.*
907 *Res.* 21:247-262.
- 908 Winn, A. A., Elle, E., Kalisz, S., Cheptou, P. O., Eckert, C. G., Goodwillie, C., Johnston,
909 M. O., Moeller, D. A., Ree, R. H., Sargent, R. D. et al . 2011. Analysis of inbreeding
910 depression in mixedmating plants provides evidence for selective interference and stable
911 mixed mating. *Evolution* 65:3339-3359.
- 912 Wright, S. 1951. The genetical structure of populations. *Ann. Eugen.* 15:323-354.