

1 The genetics of assisted gene flow: immediate costs and long-term benefits

2

3

4 Jared A. Grummer^{1,6,*}, Tom R. Booker^{1,2,*}, Remi Matthey-Doret^{1,3,*}, Pirmin Nietlisbach^{1,4,*}, Andréa
5 T. Thomaz^{1,5,*}, Michael C. Whitlock¹

6

7 ¹ Biodiversity Research Centre and Department of Zoology, University of British Columbia, 6270
8 University Blvd., Vancouver, BC, V6T 1Z4, Canada

9 ² Department of Biological Sciences, University of Calgary, Calgary, AB, T2N 1N4, Canada

10 ³ Institute of Ecology and Evolution, University of Bern, CH-3012 Bern, Switzerland

11 ⁴ School of Biological Sciences, Illinois State University, Normal, IL 61790-4120, USA

12 ⁵ Facultad de Ciencias Naturales, Universidad del Rosario, Bogotá DC, 111221, Colombia

13 ⁶ Corresponding author: grummer@zoology.ubc.ca

14 * Authors contributed equally

15

16

17 Running title: The genetics of assisted gene flow

2

18

ABSTRACT

19 Plant and animal populations are facing several novel risks such as human-mediated habitat
20 fragmentation and climate change that threaten their long-term productivity and persistence.
21 With the genetic health of many populations deteriorating due to climate change outpacing
22 physiological adaptation, human interventions in the form of assisted gene flow (AGF) may
23 provide genetic variation to adapt populations to predicted climate change scenarios and result
24 in more robust and productive populations. We ran genetic simulations to mimic a variety of AGF
25 scenarios and measured their outcomes on population-level fitness to answer the question: in
26 which circumstances is it worthwhile to perform AGF? Based on the parameters we explored,
27 AGF may be harmful in certain situations over the short term (e.g., the first ~10-20 generations),
28 due to outbreeding depression and introducing deleterious genetic variation. Moreover, under
29 many parameter sets, the benefits of AGF were relatively weak or took many generations to
30 accrue. In general, when the adaptive trait is controlled by many loci of small effect, the benefits
31 of assisted gene flow take much longer to realize—potentially too long for most climate-related
32 management decisions. We also show that when translocation effort is divided across several
33 generations and outbreeding depression is strong, the recipient population experiences a
34 smaller decrease in fitness as compared to moving all individuals in a single effort. Importantly,
35 in most cases, we show that the genomic integrity of the recipient population remains relatively
36 intact following AGF; the amount of genetic material from the donor population typically ends up
37 constituting no more of the recipient population's genome than the fraction introduced. Our
38 results will be useful for conservation practitioners and silviculturists, for instance, aiming to
39 intervene and adaptively manage so that populations maintain a robust genetic health and
40 maintain productivity into the future given anthropogenic climate change.

41

3

42 **Keywords:** local adaptation, assisted gene flow, conservation genetics, outbreeding depression,

43 assisted migration, translocation

44 INTRODUCTION

45 Natural populations are currently facing a multitude of anthropogenic threats, such as climate
46 change and habitat loss, alteration, and fragmentation, that lead to fitness reductions and
47 population declines (Klenner and Arsenault, 2009; Pacifici et al. 2017). In many species, a once
48 suitable environment becomes of lower quality and the local population is either forced to
49 migrate, adapt, exhibit phenotypic plasticity, or become extinct (Hamilton and Miller 2016). Many
50 populations cannot easily adjust to climate change because migration to suitable habitat is not
51 possible due to habitat fragmentation and the lack of suitable habitat corridors (Hoffman and
52 Sgrò 2011). Phenotypic plasticity may provide temporary relief (Levis and Pfennig 2016).
53 However, rapid anthropogenically-based climate change is outpacing the natural process of
54 environmental adaptation through natural selection (Gonzalez et al. 2013).

55 Natural selection allows populations to adapt to environmental conditions, but adaptation
56 requires genetic variation that may be lacking in certain populations. Particularly when
57 environmental conditions are changing rapidly, populations may experience a lag in adaptation
58 to the environmental conditions they experience, and thereby suffer fitness reductions (e.g.,
59 Browne et al. 2019). Recently, human activities have caused the climate to change particularly
60 fast (Stocker et al. 2014). As a consequence of changing climates and environments, an
61 increasing number of populations experience an evolutionary lag and struggle with the pace of
62 environmental change (e.g., Uecker et al. 2014; Wilczek et al. 2014; Radchuk et al. 2019;
63 Klausmeier et al. 2020).

64 Many commercially relevant species such as crop plants and trees for timber production have
65 been studied for their capacity to adapt to changing climates (Anderson 2016). For instance,
66 Wang et al. (2010) showed that greater harvests of lodgepole pine (*Pinus contorta*), a
67 commercially harvested tree species in British Columbia, Canada, could be achieved when

5

68 planting efforts account for genetic and predicted climatic effects. Similarly, many marine
69 organisms of economic importance for harvesting or ecotourism, such as coral reefs, are also
70 under threat due to ocean acidification and rising temperatures resulting from acute and severe
71 episodic ocean-climate events (Baker et al. 2008). In some systems, natural populations show
72 differential responses to bleaching (Hughes et al. 2003), suggesting that gene flow from other
73 populations could be beneficial for those populations suffering more severely from bleaching
74 events. Indeed, genomic data and biophysical modeling for a coral in the Great Barrier Reef
75 suggest that gene flow from lower to higher latitude populations can provide beneficial heat-
76 tolerant alleles as the climate warms (Matz et al. 2018), in spite of moderate levels of selection
77 against migrants in other coral systems (Kenkel et al. 2015). In terrestrial populations, gene flow
78 from populations in drier regions could help populations in more mesic regions that are predicted
79 to experience a higher frequency of droughts via climate change (e.g., Exposito-Alonso et al.
80 2018). However, natural gene flow may not always be possible because of natural dispersal
81 barriers or anthropogenic habitat fragmentation. Over recent decades, habitat fragmentation has
82 increased considerably, both in terrestrial (Haddad et al. 2015) and aquatic (Grill et al. 2019)
83 habitats, likely often inhibiting the natural process of adaptation via gene flow.

84 Assisted gene flow (AGF), i.e., human-mediated translocation of individuals from other
85 populations to pre-adapt a population to a changing environment, has been proposed as a way
86 to introduce genetic variation into populations experiencing fitness declines via maladaptation
87 (Aitken and Whitlock 2013; Uecker et al. 2014; Tomasini and Peischl 2020). AGF is a specific
88 type of assisted migration. Assisted migration includes translocations both within and outside of
89 species' ranges but is typically focused on movement of individuals outside of current species'
90 ranges, whereas AGF refers to translocations among existing populations. Although related
91 concepts, a distinction should be made between AGF, genetic rescue, and evolutionary rescue.
92 Genetic rescue is an increase in the fitness of small populations owing to the immigration of new

6

93 alleles (Tallmon et al. 2004), and is generally considered to occur when population fitness
94 increases by more than what can be attributed to the demographic contribution of immigrants
95 (Ingvarsson 2001). Thereby, genetic rescue alleviates the deleterious consequences of
96 inbreeding in small populations. Evolutionary rescue occurs when a population adapts, through
97 natural selection, to a changing environment and results in demographic stabilization, population
98 persistence and rescue from extinction (Bell 2013). Thus, evolutionary rescue is typically invoked
99 in large populations and includes adaptation to a changing environment, whereas genetic rescue
100 occurs in small populations by reducing inbreeding depression and promoting heterosis.

101 While the intended consequences of genetic or evolutionary rescue are to prevent a population
102 from going extinct, AGF aims to prevent extinction of threatened species or to promote
103 productivity in a species of economic importance (e.g., Aitken and Bemmels 2016). AGF is
104 typically invoked as a management action when a population is no longer adapted to its
105 environment. To achieve this goal, individuals harboring pre-adaptive alleles (alleles that cause
106 local adaptation to a particular environmental trait) are translocated to rescue an imperiled
107 population (Aitken and Whitlock 2013). Even if their environment has been stable, small
108 populations that suffer from inbreeding depression and fixed deleterious genetic variation may
109 benefit from genetic rescue via AGF (Gaggiotti and Hanski 2004).

110 The introduction of genotypes from foreign sources poses its own risks. For instance, genetic
111 swamping resulting from “hybridization” between distinct populations can lead to the loss of a
112 population’s genetic integrity and potentially genomic extinction (Todesco et al. 2016).

113 Additionally, individuals from foreign populations may carry alleles which are maladaptive under
114 the local conditions or that may create outbreeding depression in combination with local alleles.
115 Locally deleterious variation could be responsible for adaptation to environmental dimensions
116 other than the ones of interest (e.g., Etterson and Shaw 2001). For example, AGF may be
117 planned with the aim of aiding adaptation to warming temperatures, but the source or “donor”

7

118 population may be adapted to a different seasonal cycle and thus exhibit a phenology that is
119 incompatible with the conditions at the new location. Similar differences between the
120 environments of the source and recipient populations may exist in precipitation, exposure to the
121 weather, or other circadian and circannual (day length, seasonality) traits. Furthermore, although
122 populations may be selected for their ability to handle warmer temperatures, light limitations from
123 lower latitude populations may restrict their use in poleward assisted migrations (Wadgyamar et
124 al. 2015; Huffeldt 2020). Finally, because alleles sometimes interact poorly with alleles from
125 other populations (outbreeding depression), some alleles that work well in one genetic context
126 can cause fitness declines in a novel genetic context (Templeton et al. 1986, Frankham et al.
127 2011). Such locally deleterious alleles will initially be in strong linkage disequilibrium with the
128 introduced beneficial alleles, making them even more potentially consequential. For reasons
129 such as this, it is important to take into consideration the level of population relatedness and
130 environmental differences between donor and recipient populations, but it is currently unclear
131 how these negative effects can reverse or ameliorate the benefits of AGF.

132 Conservation managers have several practical decisions to make when considering whether to
133 invoke assisted gene flow or not:

134 *Migration effort*—how many individuals to translocate? Translocating a high number of
135 individuals to increase the odds of allele frequency change in the recipient population
136 could come at a high financial cost. Moreover, the resulting high proportion of foreign
137 individuals may dilute or even completely replace the “native” composition of the recipient
138 gene pool. Conversely, adding too few individuals might not introduce the pre-adaptive
139 alleles at a high enough frequency to remain in the population.

140 *Translocation strategy*—translocate all individuals at once, or over several generations (a
141 “pulsed” strategy)? Will a pulsed translocation effort spread across several generations
142 ease the transition of translocated individuals into a foreign ecosystem?

143 *Fitness reductions*—does the long-term gain outweigh the short-term loss? Outbreeding
144 depression and maladaptive alleles can lead to a sharp reduction in population-level
145 fitness following translocation; is this “fitness valley” so deep that it can impair fitness
146 recovery and potentially lead to local extinction, or shallow enough to be transcended
147 and ultimately lead to long-term improvements in fitness?

148 In this study, we investigated under which genetic circumstances it is worthwhile to perform
149 assisted gene flow using forward-in-time individual-based simulations. We assessed the
150 combined effect of alleles that are pre-adapted to a changing climatic variable (i.e., lead to local
151 adaptation), maladaptive alleles (i.e., alleles that are fixed in the donor population but deleterious
152 in the recipient population), and alleles that cause outbreeding depression through the
153 breakdown of epistatic interactions. We simulated various genetic architectures of these traits
154 that have positive (“pre-adaptation”) and negative (maladaptation, outbreeding depression)
155 consequences on the fitness of the recipient population. We then tracked population mean
156 fitness over time to determine how different genetic architectures affected the short- and long-
157 term fitness of the recipient population. We end by discussing the implications of these results
158 for natural resource managers and conservation practitioners.

159 MATERIALS & METHODS

160 We conducted population genetic simulations using SimBit v4.9.30 (Matthey-Doret 2020). A
161 glossary of terms and default parameter values for variables are listed in Table 1. We simulated
162 the translocation of individuals from a donor population into a recipient population of either 1,000
163 or 10,000 diploid individuals. Individuals from the donor population were fixed for alleles that

164 were pre-adaptive or maladaptive in the recipient population (see below). We modelled a
165 translocation fraction (T_f) of either 5% or 50% (simulation results of $T_f = 0.5\%$ are available in the
166 Supplement). Although a translocation fraction of 50% may be unrealistic in certain scenarios, it
167 serves as an extreme example to help visualize trends of the impact of translocation effort on
168 fitness and the maintenance of local genetic identity. We modelled selection on fecundity so the
169 first round of selection in all simulations occurred at the time that generation 1 was produced.
170 Individuals were translocated in a single pulse or in five pulses separated by either 1, 2, or 4
171 generations, each pulse representing 20% of the total number of individuals translocated. After
172 the introduction, the simulated recipient population evolved for 100 generations.

173 Our simulations modelled alleles that were both locally pre-adapted and maladapted to the
174 climate experienced by the recipient population. We modelled alleles that were selectively
175 favored in the donor population (and therefore fixed there). Some of these alleles would be
176 adaptive in the new environment of the recipient population (“pre-adapted alleles”) and other
177 alleles have low fitness in that new environment (“maladaptive alleles”). We assumed that these
178 alleles were absent in the recipient population until they were introduced by AGF. We
179 parameterized the selective effects of pre-adaptive and maladaptive alleles by focusing on the
180 overall effect of 0, 1, 5 or 50 selected loci. If an individual in the recipient population was
181 homozygous for all pre-adaptive alleles, its relative fitness would be increased by Δ_{PA} . Similarly,
182 if an individual in the recipient population was homozygous for all maladaptive alleles, its relative
183 fitness would be decreased by Δ_{MA} . We simulated cases with Δ_{PA} of 10% or 50% and $\Delta_{MA} =$
184 $\sim 9.1\%$ and 50%. Note that these Δ_{PA} and Δ_{MA} values represent the *maximum* change in fitness,
185 e.g., when an individual is homozygous for all pre-adaptive or maladaptive alleles. As a
186 consequence, for a given Δ_{PA} or Δ_{MA} , the higher the number of loci, the lower the selection
187 coefficient per locus. The values were chosen so that Δ_{PA} of 10% will compensate $\Delta_{MA} \approx 9.1\%$ in
188 individuals homozygous for either all PA or MA alleles. The dominance coefficient was set to 0.5

10

189 for PA loci and 0.5 for MA loci (0 dominance for MA loci is shown in the Supplementary
190 Material).

191 Outbreeding depression poses an additional genetic risk of translocating individuals from other
192 populations (Frankham et al. 2011). For example, epistatic interactions among pairs of loci may
193 considerably reduce the fitness of some double homozygotes (Orr 1995, 1996). At equilibrium,
194 these strongly deleterious double homozygotes rarely occur in a population. However, they may
195 occur more commonly in individuals with mixed ancestry from differentiated populations.

196 Outbreeding depression (OD) was modelled by simulating pairs of loci with additive-by-additive
197 epistasis. An individual homozygous for either foreign or local alleles at both loci in a pair had
198 fitness of $1 + s_{OD}$ relative to the double heterozygote (double heterozygote fitness = 1).

199 Individuals homozygous for local alleles at one locus and foreign alleles at the other had a
200 fitness of $1 - s_{OD}$ relative to the double heterozygote. All other genotype combinations (i.e., at
201 least one heterozygote in a pair) had a fitness of 1.0. We modelled either 0, 2, 10, or 100 pairs of
202 such epistatic OD loci.

203 Following Aitken & Whitlock (2013), we parameterized outbreeding depression by focusing on
204 the overall fitness reduction across all pairs of loci. Individuals heterozygous for all epistatic pairs
205 had a fitness reduction of Δ_{OD} relative to the fittest homozygotes. We simulated cases where
206 outbreeding depression resulted in fitness reductions of either $\Delta_{OD} = 20\%$ or 60% in
207 heterozygotes relative to the fittest double homozygotes. By way of illustration, when simulating
208 $\Delta_{OD} = 20\%$ across 2 pairs of epistatic loci, $s_{OD} \approx 0.1180$, for 10 pairs $s_{OD} \approx 0.0226$, and for 100
209 pairs $s_{OD} = 0.0022$. A fitness reduction of 60% resulted from 2 pairs of epistatic loci with $s_{OD} \approx$
210 0.5811 , 10 pairs with $s_{OD} \approx 0.0960$, or 100 pairs with $s_{OD} \approx 0.0092$. Though likely not
211 indicative of intraspecific population pairings, a Δ_{OD} of 60% illustrates an extreme case to
212 visualize the effect of outbreeding depression on fitness.

11

213 For the simulation results with PA and MA loci presented in the main text, we assumed
214 multiplicative fitness effects among loci and additive interactions between alleles within loci.
215 Fitness effects of OD loci pairs also interact multiplicatively with all other pairs and the PA and
216 MA loci. All loci were randomly distributed onto 10 chromosomes of 10 centimorgans each with a
217 uniform recombination rate. Thus, pairs of loci causing outbreeding depression were randomly
218 distributed in the genome and therefore often not closely linked.

219 Local genomic replacement (LGR) may occur as introduced haplotypes spread to fixation in the
220 recipient population, replacing local genetic diversity. Given the concern that an increase in local
221 fitness may be due to a proportionate change in non-local ancestry (e.g., Harris et al. 2019), we
222 measured local genomic replacement by including 100 neutral loci in all simulations that were
223 reciprocally fixed in the source and recipient populations; these were placed at random along the
224 genome. At every generation of a simulation run, we calculated the mean allele frequency
225 across all the neutral markers to obtain a measure of the average proportion of alleles in the
226 local population that derived from alleles introduced during AGF. Our measure of LGR therefore
227 varies from 0.0 to 1.0, where 1.0 indicates that all neutral alleles in the recipient population are
228 derived from the donor population.

229 For each combination of all parameter values summarized in Table 1, we performed 50
230 simulation replicates on a total of 1,536 unique parameter combinations. We measured relative
231 fitness in the recipient population and calculated the mean fitness across replicates. We used
232 the mean frequency of neutral alleles as a measure of local genomic replacement.

233 **Data availability statement**

234 Code to perform and analyze the simulations as well as to plot the results are available at
235 <https://github.com/TBooker/Assisted-Gene-Flow> and in the Dryad data repository (link to be
236 added upon acceptance for publication). The results of all our simulations can be visualized

12

237 using a Shiny App (<https://shiny.zoology.ubc.ca/whitlock/AGF/>), the code for which is available
238 in the github repository.

239 RESULTS

240 One of the goals of assisted gene flow is to provide populations with alleles that may help them
241 cope with a changing environment. In the absence of maladaptive alleles or outbreeding
242 depression, introducing pre-adaptive alleles always increased the fitness of recipient
243 populations, as expected (Fig. 1A, black lines, left column). For natural systems, though,
244 outbreeding depression and/or maladaptive alleles may be difficult to identify, which motivated
245 us to examine a wide variety of parameter combinations. Here, we show the results from 10,000
246 individuals, but the results for 1,000 individuals were qualitatively similar and are available for
247 exploration in the Shiny App. Furthermore, simulations showed little inter-replicate variation (Fig.
248 S1), so we present our results as the means of 50 simulation replicates per parameter
249 combination.

250 Under a variety of outbreeding depression and maladaptation scenarios, we found that there
251 was an initial reduction in relative fitness after a translocation replacing $T_f = 5\%$ of the recipient
252 population, but the recipient population fitness typically recovered within 100 generations, and
253 often within 20 generations (Fig. 1A upper half; Fig. S2). This was true across a range of
254 different selection strengths and also for $T_f = 0.5\%$ (Fig. S3). However, with the high value $T_f =$
255 50% , fitness recovery was often quite delayed (Fig. 1A lower half) and did not always recover to
256 pre-translocation levels within 100 generations when OD was $> 0\%$ and maladaptation was
257 weak (Fig. S3). The effect of genetic incompatibilities on fitness mainly depended on the total
258 effect across all loci rather than the number of pairs of epistatic alleles. For instance, in cases
259 with high migration ($T_f = 50\%$), scenarios with outbreeding depression of 20% frequently took

13

260 longer to fully recover than with outbreeding depression of 60%, regardless of genetic
261 architecture (Fig. 1A; Fig. S3).

262 The dynamics of fitness change after assisted gene flow were driven in part by the total strength
263 of selection acting on pre-adaptive alleles (Δ_{PA}). In the cases where the overall fitness benefit of
264 pre-adaptive alleles was greater than or equal to the effect of maladaptation, the deleterious
265 alleles were purged and the pre-adaptive alleles rose in frequency, increasing population mean
266 fitness. The presence of maladaptation did not prevent pre-adaptive alleles from rising in
267 frequency and increasing population mean fitness (Figs. 1A, S2 and S3). However, when
268 maladaptation was stronger than the fitness benefit of the pre-adaptive alleles, the translocated
269 individuals were purged and the assisted gene flow had negligible long-term fitness
270 consequences for the recipient population.

271 The fitness consequences of the interplay between positive and negative selection were
272 dependent on the number of individuals moved (translocation fraction). When the translocation
273 fraction was 5% or smaller (i.e., 0.5%), a stronger selection on maladaptive alleles (Δ_{MA}) led to
274 slower fitness recoveries and with less ultimate increases in fitness, as mentioned above (Figs.
275 1A, S2 and S3). In the cases of $T_f = 50\%$, increasing selection strength on pre-adaptive alleles
276 led to fewer generations of greatly reduced fitness when selection is weak on maladaptive alleles
277 ($\Delta_{MA} = 0$).

278 The magnitude of population-level fitness increase due to assisted gene flow was highly
279 dependent upon the genomic architecture underlying the traits of interest. Specifically, the
280 strength of selection on pre-adaptive alleles had a noticeable impact on how long it took for
281 mean fitness to increase (Fig. 2). When there was only a single large-effect pre-adaptive allele,
282 fitness increased to the maximum possible value within ~50 generations. However, fitness gains
283 occurred much more slowly with genetic architectures that had more loci of weaker effect.

14

284 In contrast to the pre-adaptive alleles, the architecture of maladaptation and outbreeding
285 depression had relatively little effect on long-term population fitness, when the translocation
286 fraction is small (Figs. 2, S2). However, for a given strength of outbreeding depression and Δ_{MA} ,
287 the mean fitness was slightly higher in cases with fewer outbreeding depression pairs and/or
288 maladaptive alleles with larger effects, even though the total strength of selection was equal
289 regardless of the number of loci (Fig. S2).

290 One possible concern surrounding assisted gene flow is the replacement of native genetic
291 variation in the recipient population. We measured local genomic replacement (LGR) by
292 calculating the proportion of donor population ancestry in the recipient population at neutral sites.
293 We observed that local genomic replacement varies over time, but it will be less than the fraction
294 of individuals translocated (T_f) when maladaptation is strong (Figs. S4 and S5). When
295 maladaptation was comparatively weak ($\Delta_{MA} < 10\%$), the strengths of outbreeding depression,
296 pre-adaptive, and maladaptive alleles determined whether LGR was greater than T_f (Figs. 1B,
297 S4).

298 The interaction of outbreeding depression and adaptation was highly dependent on the
299 proportion of translocated individuals. For instance, when translocating a modest number of
300 individuals ($T_f = 5\%$, shown in Fig. 1B), local genomic replacement was highest when the effects
301 of positive selection (Δ_{PA}) outweigh negative selection (Δ_{MA} and Δ_{OD} ; Fig. 1B). Qualitatively
302 similar results were obtained with a lower translocation fraction ($T_f = 0.5\%$) and are presented in
303 the Supplementary Materials (Fig. S5). When the translocation fraction was very large ($T_f =$
304 50%), local genomic replacement exceeded the translocation fraction value when Δ_{MA} was low
305 and Δ_{OD} was high, presumably because with 50% introduction, the outbreeding depression loci
306 are exactly at a fitness saddle and genetic hitchhiking from the PA alleles causes an increase in
307 introduced OD alleles, leading to resolution of those loci towards introduced alleles. When the
308 selection strengths on pre-adaptive and maladaptive alleles exactly equaled each other ($\Delta_{PA} =$

15

309 10% and $\Delta_{MA} = \sim 9.1\%$, or both equal 0.0), a stable equilibrium was reached and LGR remained
310 at 0.5 for all outbreeding depression levels (Fig. 1B). These results were independent of
311 dominance patterns of maladaptive loci and the number of pre-adaptive, maladaptive and
312 outbreeding depression loci (Figs. S6, S7).

313 Our simulations included scenarios where the total number of introduced individuals was divided
314 among five pulses introduced at five evenly spaced time points. We found that this pulsed
315 migration resulted in a lower fitness reduction (e.g., relatively higher fitness) than when
316 translocating all individuals in a single event. Indeed, we found that, when $\Delta_{OD} = 60\%$, the fitness
317 reduction experienced by populations was about half that of a single translocation event (Fig.
318 3A); this same effect was seen with $\Delta_{OD} = 20\%$, but to a lesser extent (Fig. 3A). In general, the
319 architecture of loci contributing to outbreeding depression (e.g., number of pairs of loci) had less
320 of an impact on fitness and local genomic replacement than the overall strength of outbreeding
321 depression (Figs. S8, S9). Additionally, with outbreeding depression, local genomic replacement
322 (LGR) was lower in pulsed scenarios in the short-term given the smaller number of individuals
323 introduced at each event and the frequency of introductions (Fig. 3B). It is important to note,
324 however, that although pulsing may decrease the minimum fitness experienced (Fig. 3C),
325 relative fitness may stay decreased for a longer period of time in comparison to when all
326 individuals are moved at a single time (Figs. 3A, S8). After the short-term effects of pulsing have
327 subsided, both local genomic replacement and relative fitness values of single translocation or
328 pulsed translocation events converge on the same values after approximately 30 generations
329 (Fig. 3A).

330 In absence of outbreeding depression, introducing foreign individuals over many generations in a
331 “pulsed” manner did not offer any measurable benefit over translocating all individuals at once
332 ($\Delta_{OD} = 0\%$; Fig. 3C). Overall, changing the frequency of translocation events—whether every
333 one, two, or four generations—offered marginal decreases in the amount of overall population

16

334 fitness reduction. In these cases, considering the organismal generation time will be important—
335 from a practical, applied perspective—in determining the frequency of translocation events.
336 Specifically, it may be impractical to spread out translocation efforts across decades for species
337 with long generation times.

338 DISCUSSION

339 We have found that assisted gene flow can in some cases be a useful and powerful tool for
340 conservation and production management. However, in many cases the advantages are small or
341 take several generations to accrue, and the disadvantages of AGF caused by outbreeding
342 depression and the introduction of locally maladapted alleles may have short-term
343 consequences that need to be overcome.

344 *Assisted Gene Flow Leads to Modest Increases in Fitness in the Short Term*

345 Assisted gene flow, while sometimes causing a reduction in fitness immediately following
346 translocation, often increases population-level fitness in the long term. However, even in most
347 beneficial scenarios, AGF does not often provide measurable benefits in the short term (e.g., the
348 first ~10 generations following translocation). In general, the exact fitness response resulted
349 from a complex interplay between selection on loci with deleterious (maladaptive alleles and
350 outbreeding depression loci) and beneficial (pre-adaptive alleles) genetic variation and their
351 genomic architectures. The number of individual migrants (translocation fraction) had a
352 significant impact on both the fitness response and amount of genome replaced in the recipient
353 population. Specifically, both positive and negative fitness effects were exaggerated in the cases
354 of higher migration levels. When the translocation effort was divided into discrete "pulses" across
355 generations as opposed to a single translocation event, fitness reductions and genomic
356 replacement were mitigated (particularly when outbreeding depression was strong).

357 Our results indicate that the conservation outcomes of AGF may be fairly modest. In our
358 simulations, we assumed a rather extreme situation where all fitness-affecting alleles were
359 reciprocally fixed in the donor and recipient populations. While extreme, reciprocal fixation
360 allowed us to understand the maximum effect that AGF may have on population mean fitness. In
361 many of the cases we tested, we found that population mean fitness had not appreciably
362 increased even 40 generations after AGF, particularly when there were many pre-adapted loci of
363 small effect (Figs. 1, 2, and S2A). With a translocation fraction of 5% or less, AGF was only
364 effective when there was an oligogenic architecture of adaptation (i.e., 1 or 5 preadapted alleles)
365 and a 50% fitness difference between the recipient and donor populations. If conservation
366 practitioners are considering AGF as a management tool to buffer populations against the effects
367 of anthropogenic climate change, an understanding of the genetic architecture of adaptation
368 would be very useful. The effects of AGF on population mean fitness in long-lived species such
369 as trees or corals, many of which are reported to have generation times in excess of decades
370 (Babcock 1991; Howe et al. 2008), may be too slow to help populations cope with rapidly
371 changing climates.

372 *The Genomic Architecture of Adaptation and Maintaining Local Identity*

373 We examined the fitness effects resulting from different genomic architectures of three types of
374 loci: pre-adaptive alleles, maladaptive alleles, and those causing outbreeding depression. In
375 addition to modifying the number of these loci across the genome, we also varied their total
376 effect. A key finding of our analysis is that the long-term fitness outcome of AGF is highly
377 dependent upon the architecture of pre-adaptive alleles. Fitness gains were rapid when the
378 selected trait is controlled by one or few loci of large effect. Conversely, when the trait is
379 controlled by many loci of small effect, fitness gains were very slow and of limited benefit, even
380 when the total possible benefit for pre-adaptive loci was the strongest (50 pre-adaptive loci and
381 $\Delta_{PA} = 50\%$; Figs. 2 and S2). A similar result was found when examining the effects of genetic

18

382 architecture of heat tolerance in coral, where simulated populations went extinct more quickly
383 and had higher reductions in population size when thermal tolerance was controlled by many loci
384 (Bay et al. 2017).

385 Regarding this point, it is important to understand the specific causes of fitness gains resulting
386 from AGF. When translocating beneficial mutations only, an initial increase in fitness of the
387 recipient population results from the translocation itself as the population now includes
388 individuals with novel beneficial alleles. Subsequent fitness gains following this initial “fitness
389 bump” result from selection. The change in fitness due to selection will be directly proportional to
390 the magnitude of the selective effect on the loci controlling the trait for the following reason.
391 Fisher’s fundamental theorem states that the change in fitness Δ_W is equal to the additive
392 genetic variance in fitness V_A (Fisher 1930; Grafen 2018). Assuming random mating, the additive
393 genetic variance equals

394
$$V_A = 2p(1 - p)\alpha^2,$$

395 with p being the allele frequency, and α representing the slope of a regression of genotypic
396 value on allele count (Falconer 1985; Falconer and Mackay 1996 [Fig. 7.2 therein]). Without
397 dominance effects and with s being the single locus homozygous selection coefficient, this slope
398 is $\frac{s}{2}$, and thus

399
$$V_A = 2p(1 - p)\left(\frac{s}{2}\right)^2,$$

400
$$V_A = \frac{p(1 - p)s^2}{2}.$$

401 In our calculations, we held the total possible fitness benefit constant, meaning that we modelled
402 cases with either few large-effect loci or many small-effect loci. In this case, the value of s
403 decreases with the number of loci n_{PA} for a given total effect Δ_{PA} . Although in our simulations all

19

404 loci interact multiplicatively, we use the approximation of additivity in the following calculations.

405 The approximation suffices for the illustrative purpose here. With that approximation,

406
$$s \cong \frac{\Delta_{PA}}{n_{PA}}.$$

407 Given that we assume that the relevant alleles are reciprocally fixed in the recipient and donor

408 populations, the initial allele frequency p equals the translocation fraction T_f , and thus

409
$$V_A = \frac{T_f(1 - T_f) \left(\frac{\Delta_{PA}}{n_{PA}}\right)^2}{2},$$

410
$$V_A = \frac{T_f(1 - T_f)\Delta_{PA}^2}{2 n_{PA}^2}.$$

411 In the absence of gametic phase disequilibrium, total V_A is the sum of the contributions from

412 different loci (Falconer and Mackay 1996, pg. 132):

413
$$V_A = \frac{n_{PA} T_f(1 - T_f)\Delta_{PA}^2}{2 n_{PA}^2},$$

414
$$V_A = \frac{T_f(1 - T_f)\Delta_{PA}^2}{2 n_{PA}}.$$

415 Gametic phase disequilibrium will increase additive genetic variance particularly in the early

416 generations in our simulations (Lynch and Walsh 1998, pg. 102). However, our simulations show

417 that this effect is not strong enough to affect the conclusion that the change in fitness decreases

418 when an increasing number of loci are responsible for a given cumulative effect.

419 It follows that the change in fitness is slower for traits controlled by many loci of small effect,

420 because additive genetic variance is smaller for these traits. An important result therefore is that

421 for such traits, AGF is not likely to confer practically relevant benefits within a few generations for

20

422 the range of parameters simulated here. On the other hand, simulations using assisted gene
423 flow to pre-adapt *Acropora* coral to a warming climate showed that translocating as few as 10
424 migrants per year (with population sizes of fewer than 1,000 individuals, 114 SNPs associated
425 with thermal tolerance, and no maladaptive loci) increased population sizes within ~30 years,
426 approximately 10 *Acropora* generations, of migration onset (in relation to no AGF; Bay et al.
427 2017).

428 The result that fitness gains are slow for traits controlled by many loci of small effect is an
429 important consideration when implementing AGF, given that empirical studies have shown
430 climate-related traits are often controlled by many small-effect loci (e.g., Rose et al. 2018; Fuller
431 et al. 2020). For instance, drought tolerance in European populations of *Arabidopsis thaliana*
432 was shown to be polygenic and associated with 151 SNPs (Single Nucleotide Polymorphisms;
433 Exposito-Alonso et al. 2018). Similarly, tolerance to warm marine temperatures in *Acropora*
434 corals was shown to be associated with variation at 114 SNPs (Bay and Palumbi, 2014).
435 Although managers without genomic resources are at a disadvantage, it bears reminding that
436 AGF rarely results in long-term fitness declines (Fig. S2). Furthermore, other simulations have
437 shown little difference in the outcome of AGF when thermal tolerance is controlled by more than
438 ca. 150 loci (Bay et al. 2017). Thus, a rough estimate of a trait's genetic architecture or an
439 estimation based on related species or similar traits may under some circumstances already be
440 helpful. We also observed that the overall selection strength on maladaptive alleles (Δ_{MA}) had a
441 larger effect on fitness than the number of maladaptive alleles; the same pattern was seen in
442 outbreeding depression loci (Fig. S2).

443 One concern that AGF raises is the loss of local genetic identity in the recipient population due to
444 genetic swamping from the donor population, a process we term "local genomic replacement".
445 Through the process of AGF, some fraction of the local genome will come to be derived from
446 outside sources, representing a change from the natural state of the population. In extreme

447 cases, “hybridization” between donor and recipient populations could lead to the recipient
448 population’s genomic extinction and therefore the loss of its genetic integrity (Todesco et al.
449 2016). Maintaining such genetic integrity (e.g., Hauskeller 2008) may be more important in some
450 conditions (conservation) than others (optimizing resource extraction), but the case-by-case
451 need for maintaining genetic integrity is a philosophical question beyond what we consider here
452 (but see Rohwer and Marris 2015 for an in-depth treatment of this topic).

453 In the cases we simulated, the amount of local genomic replacement was largely a function of
454 translocation fraction (T_f). Under likely more realistic levels of translocation ($T_f \leq 5\%$), the amount
455 of local genomic replacement was typically less than the translocation fraction. However, this
456 replacement of local genetic variation by translocated alleles is greatest when there are the
457 greatest fitness benefits of AGF. The exceptions were the combinations of weak total selection
458 strength on maladaptive alleles ($\Delta_{MA} < 10\%$) while selection was strong on pre-adaptive alleles
459 ($\Delta_{PA} = 50\%$; Fig. S5). When a large number of individuals was translocated ($T_f = 50\%$), the
460 amount of genomic turnover exceeded 80% in some cases (Fig. S5). It is important to note,
461 however, that such a large translocation fraction is likely not realistic in a management scenario.
462 In large populations, it is likely unfeasible to move so many individuals, and in small populations
463 where this fraction can be achieved, inbreeding depression will likely become an issue and the
464 results here may be inapplicable. In some real-world cases, such as reforestation of harvested
465 sites following clearcutting, many millions of individuals may be replanted across a species
466 range in a year. In British Columbia, for example, 259 million trees of various species were
467 replanted in 2016 (<https://news.gov.bc.ca/factsheets/factsheet-reforestation-in-bc>), so a
468 simulated translocation fraction of 50% helps illustrate fitness trends for management
469 considerations.

470 *Pulsed Translocation Efforts*

471 We examined whether dividing the translocation effort into discrete “pulses”, here represented as
472 20% of the total number of individuals to be moved in five separate events, had an effect on the
473 recipient population’s fitness response. Overall, in comparison to translocating all individuals in a
474 single effort, pulsing alleviated some of the negative fitness effects resulting from assisted gene
475 flow. In particular, translocating individuals every four generations resulted in marked decreases
476 in fitness reductions (e.g., relatively higher fitness) compared to more frequent pulses or a single
477 migration (Fig. 3C). As new deleterious genotypes are introduced in each pulse, selection
478 reduces their frequency over the subsequent generations until the next pulse of individuals
479 arrives. This pattern, however, is largely, but not exclusively, driven by scenarios with high levels
480 of outbreeding depression (60%). Such high levels of genomic incompatibilities via epistatic
481 interactions are not likely to result from inter-population matings within a species; this level of
482 outbreeding depression is more likely to result from interspecific matings and therefore not
483 applicable to many cases where AGF may be implemented. However, the potentially unrealistic
484 value of outbreeding depression demonstrates an extreme and shows a trend of its effect on
485 fitness.

486 The genomic architecture of loci causing outbreeding depression also interacted with pulsing the
487 translocation effort. In general, the overall strength of outbreeding depression (Δ_{OD}) had a larger
488 effect on the resulting fitness than the number of pairs of outbreeding depression loci (Fig. S8).
489 Nonetheless, within a given strength of outbreeding depression, populations with fewer pairs of
490 outbreeding depression loci experienced faster gains in fitness and higher levels of local
491 genomic replacement (Fig. S8). This is likely because selection can more easily remove
492 individuals from the population with fewer pairs of outbreeding depression loci, each with a
493 higher s_{OD} value, than when many weaker pairs of outbreeding depression loci are spread
494 across the genome and potentially linked with beneficial (e.g., pre-adaptive) alleles.

23

495 Although populations show reduced levels of both fitness reductions and local genomic
496 replacement as a result of pulsing (Fig. 3), they also experience these depressed levels for a
497 longer period of time. In other words, translocating individuals in a single effort might lead to
498 lower fitness and higher local genomic replacement, but both levels recover (towards 1.0 and
499 0.0, respectively) more quickly. Similarly, whereas pulsing can mitigate fitness reductions when
500 outbreeding depression is strong, it can also delay the fitness benefits of gene flow when
501 introduced individuals have a high fitness (high Δ_{PA} , low Δ_{MA}) and weak outbreeding depression
502 (low Δ_{OD}). Hence, if pulsing helps reduce fitness reductions in some scenarios, it also delays
503 fitness gains in other scenarios. Given that fitness and local genomic replacement levels
504 converge on the same values regardless if pulsing was performed or not, it becomes important
505 to consider the more critical state—a more severe fitness reduction for less time, or a less
506 severe reduction in fitness for more time.

507 *Considerations for Resource Managers*

508 We simulated a fitness increase of 50% owing to pre-adaptive alleles, meaning that individuals
509 from the donor population would have a 50% higher fitness in the new environment. Empirical
510 studies in natural populations have found that the strength of local adaptation is of that order in a
511 wide variety of species (Bontrager et al. 2020). Similarly, Exposito-Alonso et al. (2019) reported
512 strong climate-mediated natural selection in *A. thaliana* from common garden transplants where
513 > 60% of populations were killed due to non-native (hot and dry) conditions. However, estimating
514 the beneficial effect of pre-adaptive alleles in a novel ecological and genomic context is
515 extremely difficult in natural settings. Furthermore, if an environment is predicted to change in a
516 particular direction over time (e.g., trend of climatic warming), the selective benefits of pre-
517 adaptive traits may increase in the future. In general, the benefits of pre-adaptive alleles from
518 assisted gene flow may take many generations to realize (Figs. 1, S2), and an important

24

519 consideration must be made as to whether the long-term gains outweigh the short-term fitness
520 costs.

521 Assisted gene flow has been proposed as part of a decision-tree for managing coral reef
522 restoration (Van Oppen et al. 2017). In such systems, our results can be used to guide decisions
523 for managers, but we are aware that estimates for many of the parameters we have simulated
524 here will not be available in most systems. It is therefore important to consider the results
525 presented here qualitatively and in relative terms. For instance, little is known about outbreeding
526 depression and its underlying genetic mechanisms in many systems. Our results show that
527 outbreeding depression should be a consideration mainly when it is strong, e.g., between very
528 divergent populations representative of interspecific crosses (Fig. S2). Given that assisted gene
529 flow is typically done with closely related populations, outbreeding depression is not likely to play
530 a strong role in reducing the benefits of AGF. Similarly, little is known about alleles originating in
531 source populations that are deleterious in the recipient population. Our results highlight that this
532 parameter (Δ_{MA} , the maximum possible fitness reduction in an individual with all maladaptive
533 alleles) matters when it is strong, e.g., when fitness is reduced in an individual by >10%.

534 This research has also generated some suggestions for managers considering assisted gene
535 flow. First, performing controlled breeding trials before going “all-in” at the population-scale in the
536 wild may be helpful. Many problems resulting from outbreeding depression or maladaptive
537 alleles could be screened by measuring growth and fitness in F_1 (and F_2 and beyond) individuals
538 resulting from donor-recipient crosses. Indeed, using F_1 individuals in AGF attempts may help
539 reduce the fitness reduction the population may experience. Second, translocating fewer
540 individuals at a time (i.e., a smaller translocation fraction) is one way to mitigate population-level
541 harm if breeding trials are not able to occur before translocation and unforeseen risks manifest in
542 reductions of individual-level fitness and fecundity. Furthermore, translocating fewer individuals
543 per translocation event mimics our pulsing scenarios that resulted in benefits previously

25

544 mentioned. And lastly, if these options are not available, landscape genomic techniques that
545 merge species distribution models with the knowledge of adaptive loci can generate
546 recommendations for assisted migrations (Shryock et al. 2020).

547 In spite of a broad parameter space that we explored in our simulations, we did not examine all
548 factors that might be considered while deciding to perform assisted gene flow or not. For
549 instance, we did not model carrying capacity or a fluctuating population size. Secondly, we did
550 not consider other consequences of translocations, such as disease/parasites or disruptions of
551 social structures. Furthermore, even though adaptive genetic variation may help a population
552 cope with environmental change, climatically-induced range shifts may increase interspecific
553 competition in certain contexts (Razgour et al. 2019), which is a factor we did not consider.

554 *Future Work*

555 Our study has provided a deepened understanding of some of the genetic factors determining
556 the outcomes of assisted gene flow. Nonetheless, the results and parameter choices we made
557 have exposed some avenues that future research should pursue. First, we assumed that the
558 beneficial (pre-adaptive) alleles were reciprocally fixed between donor and recipient populations.
559 This is likely to be an oversimplification—it is possible that these pre-adaptive alleles may
560 already be present at a low frequency in the recipient population. Thus, what is the benefit of
561 assisted gene flow when the pre-adaptive alleles are already present in the recipient population?
562 Exploring the cases in which a translocation fraction (T_i) of 0.5% was simulated may give an
563 approximate representation of pre-adaptive alleles being present at a low frequency. In this
564 case, however, the pre-adaptive alleles will be in linkage disequilibrium (at least in the early
565 generations following translocation), which might not be an accurate representation of these
566 alleles existing at low frequencies in natural populations. On a related point, further research is
567 necessary into the uncertainty of positive selection strength of pre-adaptive loci. We modeled a

26

568 constant positive selection strength over time, but selection strength may increase in the future
569 with a changing environment. In such cases, the benefits from AGF may be more frequent or
570 strong than our results imply.

571 Although we were primarily concerned with assisted gene flow as a means to improve the overall
572 genetic health and productivity of a population and therefore measured relative fitness, it would
573 also be worthwhile to explore the impacts of assisted gene flow on population size. Given that
574 increasing population size is one of the principal goals of genetic rescue, population size is
575 perhaps more comprehensible than fitness and almost certainly to be of interest to resource
576 managers. Future research might consider allowing population size to fluctuate instead of
577 maintaining a fixed size, and might explicitly model the possibility of population extinction.

578 Lastly, much remains to be explored in terms of interactions between divergent genomes and
579 the effects of outbreeding. Although we modeled such genomic interactions as only having zero
580 or negative consequences (e.g., outbreeding depression), we did not explore how “hybrids”
581 between donor and recipient individuals may have hybrid vigor (e.g., heterosis). Although
582 relatively little is known about heterosis in natural populations, it is expected to be strongest in
583 small populations (Whitlock 2002). Although our study was concerned with large populations, the
584 use of translocations to promote genetic rescue in small populations has recently received
585 increasing attention (Bell et al. 2020).

586 *Conclusions*

587 As climate change intensifies and populations experience fitness reductions and/or local
588 extinctions, management strategies such as assisted gene flow will become a more widely
589 considered tool for “prescriptive evolution” (Smith et al. 2014). Our results indicate that the
590 conservation outcomes of AGF may be fairly modest in real world settings. In our simulations,

27

591 we assumed a rather extreme situation where all fitness-affecting alleles were reciprocally fixed
592 in the donor and recipient populations; this allowed us to understand the maximum effect that
593 AGF may have on population mean fitness. In many of the cases we tested, we found that
594 population mean fitness had not appreciably increased even 40 generations after AGF,
595 particularly when there were many pre-adapted loci of small effect (Figs 1, 2, and S2A). If the
596 alleles that contribute to local adaptation have individually weak fitness effects, the effects of
597 AGF on population mean fitness in long-lived species may be too slow to help populations cope
598 with rapidly changing climates. With a translocation fraction of 5% or less, our simulations
599 showed AGF to be effective only with a 50% fitness difference between the recipient and donor
600 populations and when an oligogenic architecture of adaptation underlied the adaptive trait (i.e., 1
601 or 5 preadapted alleles) Fig. 2).

602 Although detailed knowledge of outbreeding depression and the genetic architecture of adaptive
603 (both pre- and maladaptive) traits would greatly improve predictions regarding the long-term
604 success of assisted gene flow, such knowledge is often rudimentary at best, and often limited to
605 model systems. However, tools such as controlled breeding trials or landscape genomics can
606 help inform managers before conducting AGF. Although assisted gene flow has the potential to
607 lead to negative short-term fitness consequences, its long-term benefits suggest it may be a
608 useful management tool moving forward to help populations adapt to a changing climate.

609 *Acknowledgements*

610 Thanks to Sally Aitken for discussion and thanks to Sam Yeaman and Moisés Expósito-Alonso
611 for comments on the manuscript. Additionally, comments from UBC Biodiversity Research
612 Centre participants of an early presentation of this work increased its quality and clarity.
613 Funding for parts of this study was provided by a Genome Canada Large-Scale Applied
614 Research Project in Natural Resources and the Environment (Project code 242RTE) to JAG;

28

615 TRB was funded by the CoAdapTree project which is funded by Genome Canada (241REF),
616 Genome BC and 16 other sponsors (<http://coadaptree.forestry.ubc.ca/sponsors/>); the Swiss
617 National Science Foundation (SNF) Doc. Mobility fellowship to RMD (P1SKP3_168393); the
618 Swiss National Science Foundation to PN (P400PB_180870); a BRITE postdoctoral fellowship to
619 ATT from the Biodiversity Research Centre at the University of British Columbia; and an NSERC
620 Discovery Grant to MCW.

621 *Author Contributions*

622 MCW conceived of the study. RMD performed genetic simulations, TB analyzed the data and AT
623 and TB made the figures. JAG led the manuscript writing. All authors designed the study and
624 contributed to manuscript writing and editing.

625

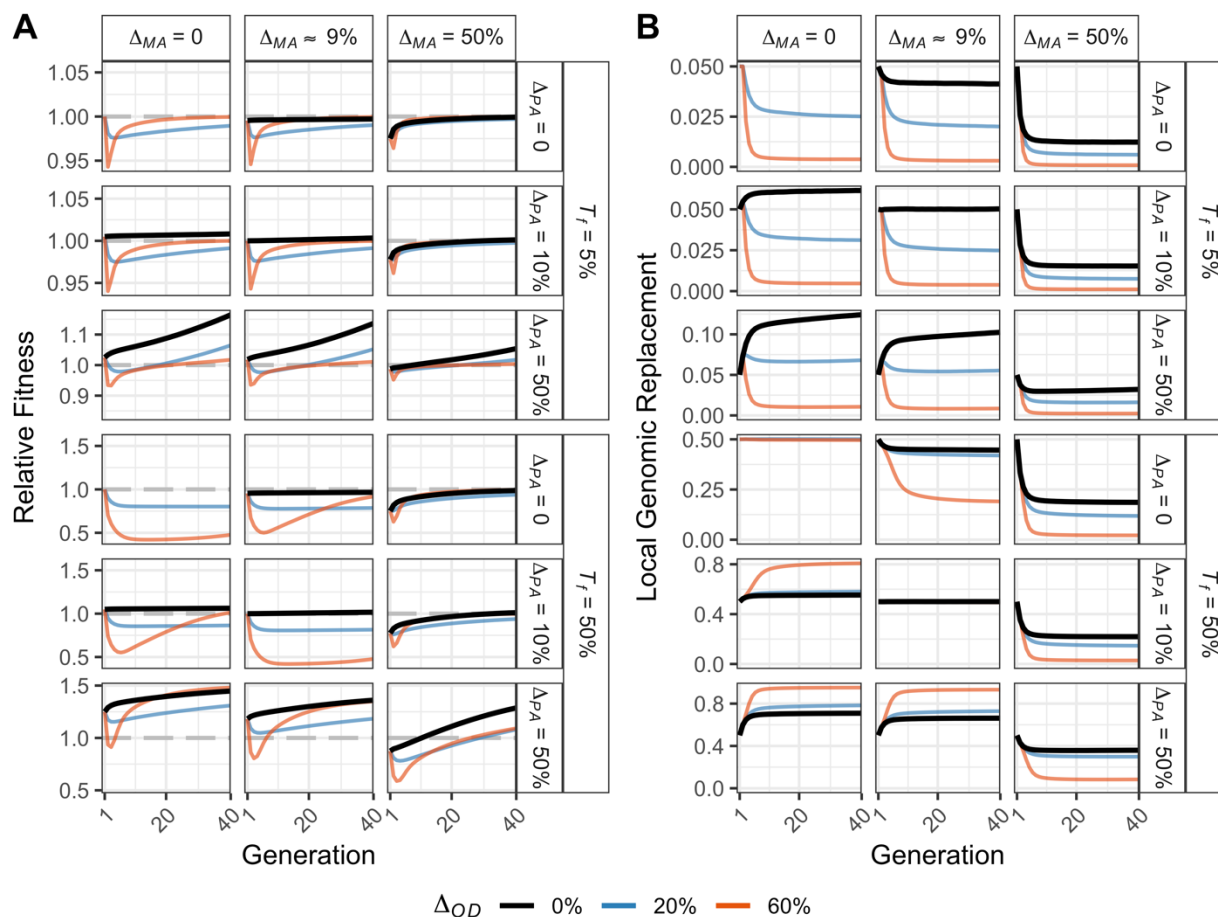
626 **Table 1** A glossary of terms and the parameters used in this study. For simulation parameters,
 627 we include the values used in our factorial simulation analysis.

628

Term	Definition	Values Used
Assisted gene flow (AGF)	The process of translocating individuals with the aim of increasing the frequency of beneficial alleles in the recipient population	N/A
Donor population	The population that supplies individuals for translocation	N/A
Recipient population	The population that receives translocated individuals	N/A
Local genomic replacement (LGR)	The proportion of the recipient genome derived from alleles introduced from the donor population (averaged across all individuals in the population)	N/A
Translocation fraction (T_f)	The proportion of the recipient population replaced by translocated individuals at the time of introduction	0.5%; 5%; 50%
Translocation pulses	Number of discrete translocation events	Either a single pulse or five pulses each comprising 20% of T_f every 1, 2, or 4 generations
Recipient population size	Number of diploid individuals in recipient population (remains constant)	1,000; 10,000
PA alleles	Pre-adaptive (beneficial) alleles coming from translocated individuals	0; 1; 5; 50
PA dominance coefficient	Dominance of PA alleles	0.5 (= additive gene action)
Δ_{PA}	Maximum possible fitness increase in an individual carrying all pre-adaptive alleles	0; 10%; 50%
Maladaptive (MA) alleles	Maladaptive alleles coming from translocated individuals	0; 1; 5; 50
MA dominance coefficient	Dominance of MA alleles	0 (= MA alleles are recessive); 0.5 (= additive gene action)
Δ_{MA}	Maximum possible fitness reduction in an individual carrying all maladaptive alleles	0; ~9.1%; 50%
OD (outbreeding depression)		
loci	Pairs of loci with additive-by-additive epistasis	0; 2; 10; 100
Δ_{OD}	The fitness reduction of a genotype heterozygous for all loci relative to local or foreign double homozygotes due to outbreeding depression	0; 20%; 60%
Neutral loci	Neutral loci used to calculate LGR	100

30

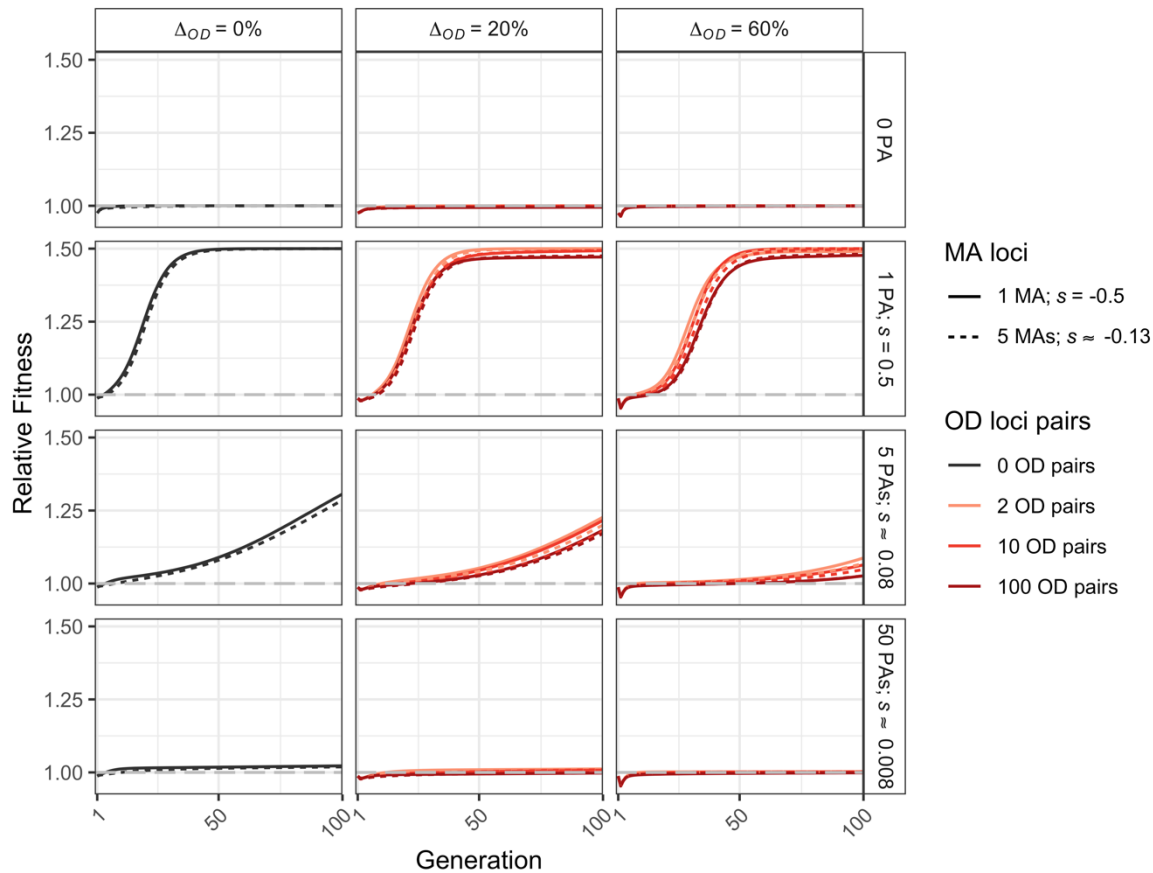
629 Figure Captions



630
 631 Figure 1. Assisted gene flow is beneficial in the long term with moderate translocation fractions
 632 (T_f), although the mean fitness of recipient populations can be reduced for a large number of
 633 generations. (A) Relative fitness (B) and local genomic replacement fraction for the first 40
 634 generations under $T_f = 5\%$ and 50% following a single translocation event in generation 1. In all
 635 cases with beneficial alleles, the mean fitness of the recipient population increased to greater
 636 than 1.0 after several generations, but the initial drop in fitness can be substantial. For this
 637 figure, genomes included ten pairs of outbreeding depression loci, and in the scenarios where
 638 pre-adaptive and maladaptive alleles occurred, five of each were present with variable selection
 639 strengths in both cases (Δ_{PA} and Δ_{MA} ; maladaptive with 0.5 dominance). Relative fitness value of
 640 1.0 is indicated with a grey dashed line. Note that the scale of the y-axis changes for different
 641 rows and the y-axis limits vary in panel (B). Cases with $\Delta_{PA} = \Delta_{MA} = 0$ are not shown because
 642 they were not simulated (relative fitness would stay at 1.0).
 643

31

644



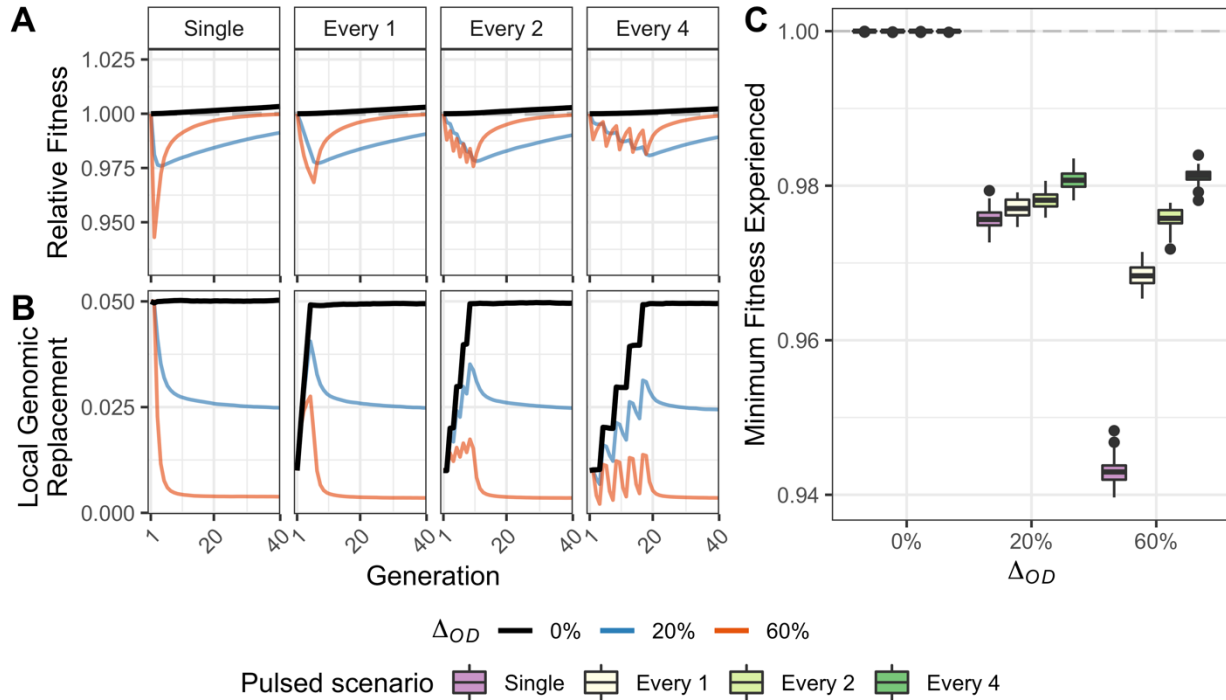
645

646 Figure 2. When the fitness changes of introduced alleles are the result of many loci of weak
647 effect, the response to selection is much slower than when fewer alleles of larger effect are
648 present. In each of these cases, the total immediate fitness effect of introduced individuals is
649 held constant, and fitness contributions are set up as $1 + s$ per locus. Note that all plots have the
650 same y-axis limits, and a relative fitness value of 1.0 is indicated with a grey dashed line. Results
651 are shown for a single translocation event with $T_f = 5\%$, $\Delta_{PA} = 50\%$ and $\Delta_{MA} = 50\%$ (with 0.5
652 dominance). Different colours denote numbers of outbreeding depression (OD) loci pairs, and
653 the continuous and dashed lines indicate variable numbers of maladaptive alleles (MA). Note
654 that unlike Figures 1 and 3, the x-axis on this plot extends to generation 100.

655

656

32



657

658

659 **Figure 3.** When populations suffer from outbreeding depression, pulsed introductions can
660 decrease fitness reductions. (A) Relative fitness and (B) local genomic replacement by
661 outbreeding depression level are shown over the first 40 generations for each translocation
662 scenario (i.e., single translocation and five events of pulsed translocations every one, two or four
663 generations). Note that the total number of individuals translocated was the same in each
664 scenario (e.g., each “pulsed” introduction was one fifth the size of the single one-time
665 introduction). Panel (C) shows the variation across 50 replicates of each translocation scenario,
666 using the same data as in (A). Results are shown for a total migration rate of 5%, five adaptive
667 and maladaptive alleles with a $\Delta_{PA} = 10\%$, $\Delta_{MA} \approx 9.1\%$ (dominance coefficient of 0.5), and 10
668 pairs of outbreeding depression loci.

669

670

671

672

673

674

References

- 675 Aitken, S. N., & Whitlock, M. C. (2013). Assisted gene flow to facilitate local adaptation to climate
676 change. *Annual Review of Ecology, Evolution, and Systematics*, 44, 367-388.
- 677 Aitken, S. N., & Bemmels, J. B. (2016). Time to get moving: assisted gene flow of forest trees.
678 *Evolutionary Applications*, 9(1), 271-290.
- 679 Anderson, J. T. (2016). Plant fitness in a rapidly changing world. *New Phytologist*, 210(1), 81-87.
- 680 Babcock, R. C. (1991). Comparative demography of three species of scleractinian corals using
681 age-and size-dependent classifications. *Ecological Monographs*, 61(3), 225-244.
- 682 Baker, A. C., Glynn, P. W., & Riegl, B. (2008). Climate change and coral reef bleaching: An
683 ecological assessment of long-term impacts, recovery trends and future outlook. *Estuarine,
684 Coastal and Shelf Science*, 80(4), 435-471.
- 685 Bay, R. A., & Palumbi, S. R. (2014). Multilocus adaptation associated with heat resistance in
686 reef-building corals. *Current Biology*, 24(24), 2952-2956.
- 687 Bay, R. A., Rose, N. H., Logan, C. A., & Palumbi, S. R. (2017). Genomic models predict
688 successful coral adaptation if future ocean warming rates are reduced. *Science Advances*, 3(11),
689 e1701413.
- 690 Bell, G. (2013). Evolutionary rescue and the limits of adaptation. *Philosophical Transactions of
691 the Royal Society B: Biological Sciences*, 368(1610), 20120080.
- 692 Bell, D. A., Robinson, Z. L., Funk, W. C., Fitzpatrick, S. W., Allendorf, F. W., Tallmon, D. A., &
693 Whiteley, A. R. (2019). The exciting potential and remaining uncertainties of genetic rescue.
694 *Trends in Ecology & Evolution*, 34(12), 1070-1079.
- 695 Bontrager, M., Muir, C. D., Mahony, C. R., Gamble, D. E., Germain, R. M., Hargreaves, A. L., ...
696 & Angert, A. L. (2020). Climate warming weakens local adaptation. *bioRxiv*.
- 697
- 698 Browne, L., Wright, J. W., Fitz-Gibbon, S., Gugger, P. F., & Sork, V. L. (2019). Adaptational lag
699 to temperature in valley oak (*Quercus lobata*) can be mitigated by genome-informed assisted
700 gene flow. *Proceedings of the National Academy of Sciences*, 116(50), 25179-25185.
- 701 Etterson, J. R., & Shaw, R. G. (2001). Constraint to adaptive evolution in response to global
702 warming. *Science*, 294(5540), 151-154.
- 703 Exposito-Alonso, M., Vasseur, F., Ding, W., Wang, G., Burbano, H. A., & Weigel, D. (2018).
704 Genomic basis and evolutionary potential for extreme drought adaptation in *Arabidopsis
705 thaliana*. *Nature Ecology & Evolution*, 2(2), 352-358.

- 706 Exposito-Alonso, M., Burbano, H. A., Bossdorf, O., Nielsen, R., & Weigel, D. (2019). Natural
707 selection on the *Arabidopsis thaliana* genome in present and future climates. *Nature*, 573(7772),
708 126-129.
- 709 Falconer, D. S. (1985). A note on Fisher's 'average effect' and 'average excess'. *Genetics*
710 *Research*, 46(3), 337-347.
- 711 Falconer, D. S., & Mackay, T. F. C. (1996). Introduction to quantitative genetics. Longman:
712 Harlow, UK.
- 713 Fisher RA (1930). The Genetical Theory of Natural Selection. Clarendon Press: Oxford, UK.
- 714 Frankham, R., Ballou, J. D., Eldridge, M. D., Lacy, R. C., Ralls, K., Dudash, M. R., & Fenster, C.
715 B. (2011). Predicting the probability of outbreeding depression. *Conservation Biology*, 25(3),
716 465-475.
- 717 Fuller, Z. L., Mocellin, V. J., Morris, L. A., Cantin, N., Shepherd, J., Sarre, L., ... & Matz, M.
718 (2020). Population genetics of the coral *Acropora millepora*: Toward genomic prediction of
719 bleaching. *Science*, 369(6501).
- 720 Gaggiotti, O. E., & Hanski, I. (2004). Mechanisms of population extinction. In *Ecology, Genetics*
721 *and Evolution of Metapopulations* (pp. 337-366). Academic Press.
- 722 Gonzalez, A., Ronce, O., Ferriere, R., & Hochberg, M. E. (2013). Evolutionary rescue: an
723 emerging focus at the intersection between ecology and evolution. *Philosophical Transactions of*
724 *the Royal Society B*, 368: 20120404.
- 725 Grafen, A. (2018). The left hand side of the fundamental theorem of natural selection. *Journal of*
726 *Theoretical Biology*, 456, 175-189.
- 727 Grill, G., Lehner, B., Thieme, M., Geenen, B., Tickner, D., Antonelli, F., ... & Zarfl, C. (2019).
728 Mapping the world's free-flowing rivers. *Nature*, 569(7755), 215-221.
- 729 Haddad, N. M., Brudvig, L. A., Clobert, J., Davies, K. F., Gonzalez, A., Holt, R. D., ... & Cook, W.
730 M. (2015). Habitat fragmentation and its lasting impact on Earth's ecosystems. *Science*
731 *Advances*, 1(2), e1500052.
- 732 Hall, A. E., Karkare, K., Cooper, V. S., Bank, C., Cooper, T. F., & Moore, F. B. G. (2019).
733 Environment changes epistasis to alter trade-offs along alternative evolutionary paths. *Evolution*,
734 73(10), 2094-2105.
- 735 Hamilton, J. A., & Miller, J. M. (2016). Adaptive introgression as a resource for management and
736 genetic conservation in a changing climate. *Conservation Biology*, 30(1), 33-41.
- 737 Harris, K., Zhang, Y., & Nielsen, R. (2019). Genetic rescue and the maintenance of native
738 ancestry. *Conservation Genetics*, 20(1), 59-64.

- 739 Hauskeller, M. (2007). *Biotechnology and the integrity of life: taking public fears seriously*.
740 Ashgate Publishing, Ltd.
- 741 Hoffmann, A. A., & Sgrò, C. M. (2011). Climate change and evolutionary adaptation. *Nature*,
742 *470*(7335), 479-485.
- 743 Holt, R. D., Barfield, M., & Gomulkiewicz, R. (2005). Theories of niche conservatism and
744 evolution: could exotic species be potential tests. *Species Invasions: Insights Into Ecology*,
745 *Evolution, and Biogeography*, 259-290.
- 746 Howe, G. T., Johnson, G. R., & Wheeler, N. C. (2008). Breeding Douglas-Fir. In *Plant Breeding*
747 *Reviews* (Vol. 30), Ed. Janick, J. John Wiley & Sons.
- 748 Huffeldt, N. P. (2020). Photoc barriers to poleward range-shifts. *Trends in Ecology & Evolution*,
749 *35*(8), 652-655.
- 750 Hughes, T. P., Baird, A. H., Bellwood, D. R., Card, M., Connolly, S. R., Folke, C., ... & Lough, J.
751 M. (2003). Climate change, human impacts, and the resilience of coral reefs. *Science*,
752 *301*(5635), 929-933.
- 753 Ingvarsson, P. K. (2001). Restoration of genetic variation lost—the genetic rescue hypothesis.
754 *Trends in Ecology & Evolution*, *16*(2), 62-63.
- 755 Kenkel, C. D., Almanza, A. T., & Matz, M. V. (2015). Fine-scale environmental specialization of
756 reef-building corals might be limiting reef recovery in the Florida Keys. *Ecology*, *96*(12), 3197-
757 3212.
- 758 Klausmeier, C. A., Osmond, M. M., Kremer, C. T., & Litchman, E. (2020). Ecological limits to
759 evolutionary rescue. *Philosophical Transactions of the Royal Society B*, *375*(1814), 20190453.
- 760 Klenner, W., & Arsenault, A. (2009). Ponderosa pine mortality during a severe bark beetle
761 (Coleoptera: Curculionidae, Scolytinae) outbreak in southern British Columbia and implications
762 for wildlife habitat management. *Forest Ecology and Management*, *258*, S5-S24.
- 763 Levis, N. A., & Pfennig, D. W. (2016). Evaluating ‘plasticity-first’ evolution in nature: key criteria
764 and empirical approaches. *Trends in Ecology & Evolution*, *31*(7), 563-574.
- 765 Lynch, M., & Walsh, B. (1998). *Genetics and analysis of quantitative traits*. Sinauer: Sunderland,
766 MA, USA.
767
- 768 Matthey-Doret, R. (2021), SimBit: A high performance, flexible and easy-to-use population genetic
769 simulator. *Molecular Ecology Resources*. Advance online publication. [https://doi.org/10.1111/1755-
770 0998.13372](https://doi.org/10.1111/1755-0998.13372)
- 771 Matz, M. V., Trembl, E. A., Aglyamova, G. V., & Bay, L. K. (2018). Potential and limits for rapid
772 genetic adaptation to warming in a Great Barrier Reef coral. *PLoS Genetics*, *14*(4), e1007220.

- 773 Orr, H. A. (1995). The population genetics of speciation: the evolution of hybrid incompatibilities.
774 *Genetics*, 139(4), 1805-1813.
- 775 Orr, H. A. (1996). Dobzhansky, Bateson, and the genetics of speciation. *Genetics*, 144(4), 1331.
- 776 Pacifici, M., Visconti, P., Butchart, S. H., Watson, J. E., Cassola, F. M., & Rondinini, C. (2017).
777 Species' traits influenced their response to recent climate change. *Nature Climate Change*, 7(3),
778 205-208.
- 779 Radchuk, V., Reed, T., Teplitsky, C., Van De Pol, M., Charmantier, A., Hassall, C., ... & Kramer-
780 Schadt, S. (2019). Adaptive responses of animals to climate change are most likely insufficient.
781 *Nature Communications*, 10(1), 1-14.
- 782 Razgour, O., Forester, B., Taggart, J. B., Bekaert, M., Juste, J., Ibáñez, C., ... & Manel, S.
783 (2019). Considering adaptive genetic variation in climate change vulnerability assessment
784 reduces species range loss projections. *Proceedings of the National Academy of Sciences*,
785 116(21), 10418-10423.
- 786 Rohwer, Y., & Marris, E. (2015). Is there a prima facie duty to preserve genetic integrity in
787 conservation biology?. *Ethics, Policy & Environment*, 18(3), 233-247.
- 788 Rose, N. H., Bay, R. A., Morikawa, M. K., & Palumbi, S. R. (2018). Polygenic evolution drives
789 species divergence and climate adaptation in corals. *Evolution*, 72(1), 82-94.
- 790 Shryock, D. F., Washburn, L. K., DeFalco, L. A., & Esque, T. C. (2020). Harnessing landscape
791 genomics to identify future climate resilient genotypes in a desert annual. *Molecular Ecology*,
792 30(2021), 698-717.
- 793 Smith, T. B., Kinnison, M. T., Strauss, S. Y., Fuller, T. L., & Carroll, S. P. (2014). Prescriptive
794 evolution to conserve and manage biodiversity. *Annual Review of Ecology, Evolution, and*
795 *Systematics*, 45, 1-22.
- 796 Stocker, T. F., Qin, D., Plattner, G. K., Tignor, M. M., Allen, S. K., Boschung, J., ... & Midgley, P.
797 M. (2014). Climate Change 2013: The physical science basis. contribution of working group I to
798 the fifth assessment report of IPCC the intergovernmental panel on climate change.
- 799 Tallmon, D. A., Luikart, G., & Waples, R. S. (2004). The alluring simplicity and complex reality of
800 genetic rescue. *Trends in Ecology & Evolution*, 19(9), 489-496.
- 801 Templeton, A. R., Hemmer, H., Mace, G., Seal, U. S., Shields, W. M., & Woodruff, D. S. (1986).
802 Local adaptation, coadaptation, and population boundaries. *Zoo Biology*, 5(2), 115-125.
- 803 Todesco, M., Pascual, M. A., Owens, G. L., Ostevik, K. L., Moyers, B. T., Hübner, S., ... &
804 Rieseberg, L. H. (2016). Hybridization and extinction. *Evolutionary Applications*, 9(7), 892-908.
- 805 Tomasini, M., & Peischl, S. (2020). When does gene flow facilitate evolutionary rescue? *BioRxiv*,
806 622142.

- 807 Uecker, H., Otto, S. P., & Hermisson, J. (2014). Evolutionary rescue in structured populations.
808 *The American Naturalist*, 183(1), E17-E35.
- 809 Van Oppen, M. J., Gates, R. D., Blackall, L. L., Cantin, N., Chakravarti, L. J., Chan, W. Y., ... &
810 Putnam, H. M. (2017). Shifting paradigms in restoration of the world's coral reefs. *Global Change*
811 *Biology*, 23(9), 3437-3448.
- 812 Wadgyamar, S. M., Cumming, M. N., & Weis, A. E. (2015). The success of assisted colonization
813 and assisted gene flow depends on phenology. *Global Change Biology*, 21(10), 3786-3799.
- 814 Wang, T., O'Neill, G. A., & Aitken, S. N. (2010). Integrating environmental and genetic effects to
815 predict responses of tree populations to climate. *Ecological Applications*, 20(1), 153-163.
- 816 Whitlock, M. C. (2002). Selection, load and inbreeding depression in a large metapopulation.
817 *Genetics*, 160(3), 1191-1202.
- 818 Wilczek, A. M., Cooper, M. D., Korves, T. M., & Schmitt, J. (2014). Lagging adaptation to
819 warming climate in *Arabidopsis thaliana*. *Proceedings of the National Academy of Sciences*,
820 111(22), 7906-7913.