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Héloïse Bastide, David Ogereau, Catherine Montchamp-Moreau, Pierre R
Gérard

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1 The fate of a suppressed X-linked meiotic driver: experimental evolution
2 in *Drosophila simulans*

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4 Héloïse Bastide, David Ogereau, Catherine Montchamp-Moreau and Pierre R. Gérard

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6

7 **Authors information**

8 Héloïse Bastide

9 Université Paris-Saclay, CNRS, IRD, UMR Évolution, Génomes, Comportement et Écologie,
10 91272

11 Gif-sur- Yvette, France.

12 <https://orcid.org/0000-0003-4553-4738>

13

14 David Ogereau

15 Université Paris-Saclay, CNRS, IRD, UMR Évolution, Génomes, Comportement et Écologie,
16 91272, Gif-sur-Yvette, France.

17

18 Catherine Montchamp-Moreau

19 Université Paris-Saclay, CNRS, IRD, UMR Évolution, Génomes, Comportement et Écologie,
20 91272, Gif-sur-Yvette, France.

21 <https://orcid.org/0000-0002-5044-9709>

22

23 Pierre R. Gérard

24 Université Paris-Saclay, INRAE, CNRS, AgroParisTech, UMR Génétique Quantitative et
25 Evolution, 91272, Gif-sur-Yvette, France.

26 <https://orcid.org/0000-0001-5859-3476>

27

28

29

30

31 Corresponding authors:

32 Pierre R. Gérard (pierre.gerard@agroparistech.fr) and

33 Héloïse Bastide (heloise.bastide@universite-paris-saclay.fr)

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41

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43 formed research; P.R.G., H.B. and C.M.M. analyzed the data and wrote the paper.

44 **Abstract**

45 *Sex-ratio* (SR) meiotic drivers are X-linked selfish genetic elements that promote their own
46 transmission by preventing the production of Y-bearing sperm, which usually lowers male
47 fertility. The spread of SR drivers in populations is expected to trigger the evolution of
48 unlinked drive suppressors, a theoretically predicted co-evolution that has been observed in
49 nature. Once completely suppressed, the drivers are expected either to decline if they still
50 affect the fitness of their carriers, or to evolve randomly and possibly get fixed if the
51 suppressors eliminate their deleterious effects. To explore this issue, we used the Paris *sex-*
52 *ratio* system of *Drosophila simulans* in which drive results from the joint effect of two
53 elements on the X chromosome: a segmental duplication and a deficient allele of the *HP1D2*
54 gene. We set up six experimental populations starting with 2/3 of X chromosomes carrying
55 both elements (X^{SR}) in a fully suppressing background. We let them evolve independently
56 during almost a hundred generations under strong sexual competition, a condition known to
57 cause the rapid disappearance of unsuppressed Paris X^{SR} in previous experimental
58 populations. In our study, the fate of X^{SR} chromosomes varied among populations, from
59 extinction to their maintenance at a frequency close to the starting one. While the reasons for
60 these variable outcomes are still to be explored, our results show that complete suppression
61 can prevent the demise of an otherwise deleterious X^{SR} chromosome, turning a genetic
62 conflict into cooperation between unlinked loci. Observations in natural populations suggest a
63 contrasting fate of the two elements: disappearance of the duplication and maintenance of
64 deficient *HP1D2* alleles.

65

66

67 Key words: meiotic drive, drive suppression, *Drosophila*, sex ratio, experimental evolution

68

69 Introduction

70 X-linked meiotic drivers favor the transmission of their carriers at the expense of the Y
71 chromosome in heterogametic males, thus producing female-biased sex ratios. At the
72 population level, they are predicted to rapidly spread and eventually lead to extinction if the
73 driver is strong and males become too rare.

74 However, a stable polymorphism of X-linked drivers has been observed in natural populations
75 of several *Drosophila* species (e.g., James and Jaenike 1990; Beckenbach 1996; Dyer 2012).
76 Although this could be due to an observational bias, it reveals the existence of mechanisms
77 that tend to balance the transmission advantage of the drivers (Jaenike 2001; Helleu et al.
78 2015; Price et al. 2020). First, in a number of species, it has been shown that the loss of Y-
79 bearing sperm is not compensated by an overproduction of X-bearing sperm, which lowers
80 male fertility (e.g., Policansky and Ellison 1970; Hauschteck-Jungen and Maurer 1976; Wu
81 1983b; Montchamp-Moreau and Joly 1997; Presgraves et al. 1997). This, and probably other
82 pleiotropic effects, makes *Drosophila sex-ratio* (SR) males poor competitors against standard
83 males (e.g., Wilkinson et al. 2006; Angelard et al. 2008; Price et al. 2008a). Second, when the
84 driver is located in low recombination regions or within inversions, linked deleterious
85 mutations can hitchhike and lower the fitness of the carriers, as it has been documented in
86 *Drosophila recens* (Dyer et al. 2007). Several adaptations have also been proposed as
87 countervailing processes against drivers (Presgraves 2008), such as polyandry (e.g., Angelard
88 et al. 2008; Price et al. 2008b 2010a; Pinzone and Dyer 2013; reviewed in Wedell 2013) or
89 mate preference (e.g., Wilkinson et al. 1998). The spread of strong X-linked drivers can also
90 be halted by the evolution of drive resistance on the Y chromosome and/or drive suppressors
91 on the autosomes (Price et al. 2020). When a population is highly female-biased, any variant
92 that produces more males will be favored through a frequency-dependent selective process
93 towards a balanced sex ratio (Fisher 1930; Bull and Charnov 1988). In particular, Y-linked
94 resistance should rapidly spread to fixation (Thomson and Feldman 1975; Clark 1987) but can
95 be maintained at a stable equilibrium depending on frequency-dependent interactions between
96 the driving X chromosome (X^{SR}) and the resistant Y (Carvalho et al. 1997) or cycle with the
97 X^{SR} (Hall 2004). An autosomal suppressor of drive is also predicted to be selected and reach
98 fixation (Hamilton 1967). It can also stay at an equilibrium frequency with the driver when
99 there is overdominance in females (Wu 1983a) or when the driver is slightly deleterious (Vaz
100 and Carvalho 2004). In the latter case, an autosomal suppressor should go to fixation only if
101 the driver is neutral in fitness (Vaz and Carvalho 2004). A similar qualitative prediction can
102 be made for a resistant Y chromosome, with an higher fixation probability even in the

103 presence of a deleterious driver (Carvalho and Vaz 1999). The fate of the driver and
104 suppressor will depend on several parameters, such as the fitness cost associated with drive
105 and suppression in males and females, the time at which the suppressor arises during the
106 spread of the driver, or the population structure (Carvalho and Vaz 1999; Hall 2004; Vaz and
107 Carvalho 2004). Under complete suppression, the driver frequency is expected to decline if
108 costly or to evolve stochastically if neutral. This process can generate evolutionary cycles of
109 drive and suppression (Hall 2004), or cryptic meiotic drive systems like the *Drosophila*
110 *simulans* Winters system (Tao et al. 2007a,b; Kingan et al. 2010; Helleu et al. 2015).

111 Resistant Y and autosomal suppressors have been detected in a number of *Drosophila* species
112 exhibiting SR drive (e.g., Stalker 1961; Voelker 1972; Carvalho and Klaczko 1993; Carvalho
113 et al. 1997; Cazemajor et al. 1997; Jaenike 1999; Montchamp-Moreau et al. 2001; Courret et
114 al. 2019), but the dynamics of drive and suppression has rarely been assessed in natural
115 populations. In *Drosophila mediopunctata*, X^{SR} frequency had not changed within 10 years in
116 the 1990s, suggesting that the driver was kept at an equilibrium frequency reflecting a balance
117 between partial suppression and natural selection (Carvalho and Vaz 1999).

118 The only documented example of ongoing SR drive/suppression co-evolution in natural
119 populations is that of the Paris SR system of *D. simulans*. In this system, the drive is caused
120 by the joint effect of two X-linked elements: a young segmental duplication, estimated less
121 than 500 years old (Fouvry et al. 2011) and dysfunctional alleles of the *HPID2* gene (Helleu
122 et al. 2016). A first survey of natural populations 25 years ago revealed a sharp contrast
123 between sub-Saharan Africa and Indian Ocean, where a complete drive suppression along
124 with various frequencies of X^{SR} (up to 60%) were observed, and the rest of the world where
125 X^{SR} were rare or absent with no or only a slight drive suppression (Atlan et al. 1997). Since
126 then, X^{SR} have been found to steadily decrease in East Africa and Indian Ocean, whereas drive
127 suppression has been persistent (Bastide et al. 2011; 2013). In contrast, the driver has been
128 rising in frequency together with drive suppression around the Mediterranean sea, from
129 Middle East to North Africa and Europe (Bastide et al. 2013; Helleu et al. 2019). In the two
130 species *D. mediopunctata* and *D. simulans*, the rise of suppression when X^{SR} is fixed was
131 demonstrated in experimental populations (Carvalho et al. 1998; Capillon and Atlan 1999). In
132 contrast, the Paris driver of *D. simulans* was unable to invade laboratory populations when
133 introduced at a 25% (or 67%) frequency and was even lost in very few generations in the
134 absence of suppressors, suggesting the existence of strong deleterious effects (Capillon and
135 Atlan 1999). Yet in nature, X^{SR} chromosomes are able to invade rapidly (Derome et al. 2008;
136 Bastide et al. 2011). We can thus hypothesize that in the wild, Paris X^{SR} are much less

137 deleterious than in experimental populations where there is a strong competition between
138 males, and/or that their detrimental effects are at least partly rescued by the coevolution of
139 suppressors. This last assumption is supported by experimental data showing that X^{SR}
140 chromosomes have no effect on cyst number or cyst length in the male testis (Montchamp-
141 Moreau and Joly 1997).

142 Here, we have studied the effect of suppressors on the dynamics of the Paris drivers by
143 following the evolution of X^{SR} chromosomes in experimental populations similar to those in
144 Capillon and Atlan (1999) but set up with complete suppression. This means that the drivers
145 did not benefit from any segregation advantage from the beginning. We obtained contrasting
146 results depending on the replicates, which could partly reflect the variable dynamics observed
147 in natural populations. Most importantly, we demonstrate that suppression slows down and
148 can sometimes prevent the elimination of an otherwise deleterious X^{SR} chromosome.

149

150 **Materials and Methods**

151 **Drosophila strains:**

152 - SR is a reference strain for the Paris *sex-ratio* system. It originates from flies collected in the
153 Seychelles archipelago in 1981 (Atlan et al. 1997). A *sex-ratio* X chromosome (X^{SR}) is fixed
154 in the SR strain. It carries the two elements required to induce the drive: the tandem
155 duplication Dp^{SR} and a distorter allele at the *HPID2* locus ($HPID2^{SR}$). It induces a strong
156 female-biased sex ratio in a suppressor- and resistance-free background (90% of females in
157 the progeny) but the SR strain contains a resistant Y chromosome and autosomal suppressors
158 that together make X^{SR} fully suppressed (Cazemajor et al. 1997). The SR stock thus shows a
159 1:1 sex ratio.

160 - Seych1 and Seych3 are two isofemale lines with standard (i.e. non-driving) X chromosomes
161 (X^{ST}). Each line was obtained from the progeny of a single female collected by D. Lachaise in
162 the Seychelles (Mahé island) in 2003. The X chromosomes of Seych1 and Seych3 do not
163 carry the Dp^{SR} duplication associated with Paris *sex-ratio* drive but display the same $HPID2^{SR}$
164 allele than the one found in the SR strain (see molecular tests below). While both lines did not
165 show any SR activity, they were found to completely suppress the *Paris* sex-ratio drive
166 similarly to the SR strain (Table S1, S2 and S3, $\chi^2_{2\text{ df}} = 1.06$; $P = 0.59$).

167

168 **Experimental populations**

169 Three replicate populations were set up by crossing 100 virgin females from the SR strain

170 with 100 males from the Seych1 line. The same procedure was used with the Seych3 line to
171 set up three other replicate populations. In all six populations, the initial frequency of the X^{SR}
172 chromosomes was then 2/3. Each population was made evolving with non-overlapping
173 generations in a 500 mL bottle containing 100 mL axenic cornmeal-yeast medium (David
174 1962). At each generation, adults were allowed to emerge for a few days before being
175 transferred into a new bottle for egg laying during half a day. At least 500 eggs were then
176 randomly collected in each population to produce the next generation. All six populations
177 were kept at 25°C during the whole experiment. The experimental procedure is described in
178 Fig S1.

179 **Molecular tests**

180 - Dp^{SR} : DNA was extracted using a classical protocol and a PCR test was performed to detect
181 the presence of Dp^{SR} , with primers specific to the junction region between the two paralogous
182 segments (Bastide et al. 2011; Fouvry et al. 2011). Individual molecular tests of the presence
183 of Dp^{SR} were performed on 20 males per population until G_{10} , and then on 20-60 males per
184 population at generations G_{15} , G_{17} , G_{22} , G_{32} , G_{48} , G_{60} , G_{72} , G_{80} , G_{88} and G_{94} .

185 In addition, we checked for the *Trf2* gene copy number by real-time qPCR (Bastide et al.
186 2013) using subsamples of males with or without the duplication.

187 - $HPID2^{SR}$: We sequenced two markers in the second drive element region from the three
188 parental strains: the markers GA17 and GA19 spanning a total of 2 kb including the driving
189 gene *HPID2* (described in Table S7 in Helleu et al. 2016).

190 Sequences were aligned and edited with Geneious version R6 (Kearse et al. 2012).

191

192 **Drive and suppression assays**

193 Tests of drive and suppression abilities were conducted using the crossing procedures
194 previously described (e.g. Montchamp-Moreau and Cazemajor 2002). In short, drive ability
195 was assessed by measuring the sex ratio in the progeny of males carrying the X chromosome
196 under study and a drive sensitive background (Y chromosome and autosomes). Suppression
197 ability was assessed by measuring the sex ratio in the progeny of males carrying the
198 autosomes and the Y chromosome under study and a reference X^{SR} chromosome.

199

200

201

202 **Data analysis**

203 We estimated the 95% confidence intervals on a binomial distribution of the X^{SR}
 204 chromosomes (i.e. that carry the SR duplication) with the Wilson's score method (Brown et al.
 205 2001). We used Pearson's chi-squared tests or Kruskal-Wallis rank sum tests for comparing
 206 sex ratio and X^{SR} distributions.

207 We also estimated selection coefficients in the six replicate experimental populations through
 208 a maximum likelihood procedure, in the same way as Bastide et al (2011). Briefly, the
 209 evolution of X^{SR} and X^{ST} frequencies under natural selection is modelled in a classical
 210 deterministic framework for a biallelic X-linked locus (Haldane and Jayakar 1964). We
 211 considered recessive deleterious effects of X^{SR} that lower the fitness of homozygous SR/SR
 212 females or SR males by s . The likelihood of s given the data from experimental populations is
 213 calculated by multiplying the binomial probabilities of obtaining the observed number of X^{SR}
 214 in males given the frequency predicted by the deterministic model at every generation
 215 sampled. 95% confidence intervals were computed with the values of s that correspond to a
 216 log-likelihood drop-off of 1.92 (half of a 1-df chi-squared random variable corresponding to a
 217 P-value of 5%) on each side of the maximum.

218

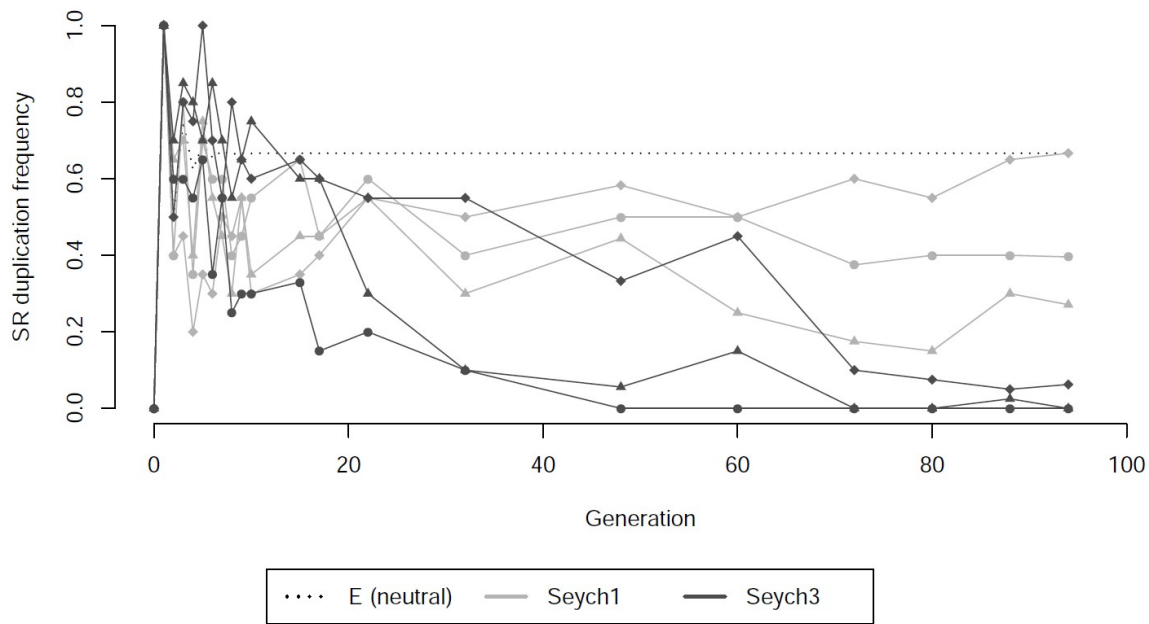
219 **Results**

220 **Evolution of Dp^{SR} in a context of total suppression**

221 Given that suppression is complete in the SR, Seych1 and Seych3 strains (Table S1, S2 and
 222 S3) and that all three lines carry the same $HP1D2^{SR}$ deficient allele, the Dp^{SR} duplication was
 223 used as a proxy to follow the evolution of X^{SR} chromosomes in each of the six populations.

224 The results are shown in Figure 1 and Table S6, and a subsample of the data with confidence
 225 intervals is presented in Table S7. The final Dp^{SR} frequencies in G_{94} were significantly
 226 different within Seych1 replicates ($\chi^2_{2\text{ df}} = 15.92$; $P < 10^{-3}$) and marginally significantly
 227 different within Seych3 replicates ($\chi^2_{2\text{ df}} = 1.13$; $P = 0.047$). The distributions of Dp^{SR}
 228 frequencies were also marginally significantly different between the replicate populations
 229 from the two lines (Kruskal-Wallis $\chi^2_{1\text{ df}} = 3.97$; $P = 0.046$).

230



231

232

233 Figure 1: Evolution of the frequency of males carrying Dp^{SR} in the six experimental
 234 populations (E: expected frequency if neutral, also corresponding to the frequency of X^{SR}
 235 under a neutral Wright-Fisher model with infinite population size). Large fluctuations were
 236 expected during the first five generations, due to the exclusively maternal origin of the X^{SR}
 237 chromosome among the founders. Triangles represent the first replicates of each line (Seych1-
 238 1 and Seych3-1), diamonds the second replicates (Seych1-2 and Seych3-2), and circles the
 239 third replicates (Seych1-3 and Seych3-3).

240

241

242

243 **Control of the strict association of the drive phenotype with Dp^{SR}**

244 At G_{88} , we checked for the distortion phenotype associated with the X chromosomes carrying
 245 Dp^{SR} in the two populations where it was at its highest frequencies (i.e. the two replicates
 246 Seych1-2 and Seych1-3). According to the crossing procedure described above, 26 X
 247 chromosomes from population Seych1-2 and 24 X chromosomes from population Seych1-3
 248 carrying Dp^{SR} were tested for drive ability and all of them produced significantly female-
 249 biased progenies. A sub-sample of X chromosomes that were used as control and were devoid
 250 of Dp^{SR} at G_{88} , did not show any sex ratio bias (Tables 1 and 2).

251 Whether an X chromosome is SR or not, recombination occurs freely between the two loci

252 involved in drive (they are located about 1cM apart). Consequently, the complete association

253 observed between Dp^{SR} and the SR phenotype after 88 generations of experimental evolution
 254 in populations Seych1-2 and Seych1-3 is consistent with our observation that the Seych1 line
 255 carries an $HP1D2^{SR}$ allele.

256

257 **Control of the persistence of complete suppression**

258 We also checked for the persistence of total suppression in populations Seych1-2 and Seych1-
 259 3 by measuring the sex ratio in the progeny of males sampled at G_{93} (Tables S4 and S5).

260 Among 61 males from population Seych1-2, 44 (72%) were found to carry Dp^{SR} , and thus a
 261 putative X^{SR} chromosome. The mean percentage of females in progenies was not different
 262 between Dp^{SR} and non- Dp^{SR} males (51.2% and 51.5% females respectively, Kruskal-Wallis χ^2_{1}
 263 $df = 0.92$; $P = 0.34$). Similarly we did not find any significant difference between 27 males
 264 carrying Dp^{SR} and 25 males devoid of Dp^{SR} that were sampled in population Seych1-3 (52.7 %
 265 and 51,1% females respectively, Kruskal-Wallis $\chi^2_{1 df} = 1.40$; $P = 0.24$).

266

267 **Are suppressed X^{SR} neutral or deleterious?**

268 The evolution of Dp^{SR} was very different across populations, especially after the 20th
 269 generation. It showed a marked decline in all three Seych3 replicates: Dp^{SR} disappeared or
 270 nearly disappeared from Seych3-1 and Seych3-3 around G_{48} , and became at very low
 271 frequency in Seych3-2 around G_{70} . In contrast, Dp^{SR} was maintained at a moderate to high
 272 frequency in the three Seych1 replicates, particularly in Seych1-2 where its frequency stood
 273 close to the expected value under a neutral Wright-Fisher model (0.66). The mean frequency
 274 of Dp^{SR} among the six populations headed steady at around 0.25 from G_{72} to G_{94} .

275 We assessed potential deleterious effects of X^{SR} by estimating selection coefficients from Dp^{SR}
 276 frequency data in every replicate. They are significantly different from 0 for all populations
 277 but Seych1-2 (Table 3). The estimates range from 0.021 to 0.053 for Seych1-1, Seych1-3 and
 278 Seych3-2, which correspond to moderate deleterious effects. The estimate for Seych3-2 is
 279 significantly different from the other two. The estimates for Seych3-1 and Seych3-3 are
 280 significantly higher (0.1 and 0.201 respectively). It is worth noting that we obtain similar
 281 values of \hat{s} and of confidence intervals when considering dominant deleterious effects of X^{SR}
 282 in females (not shown).

283

284

285

286

287 **Discussion**

288 **Dynamics of drivers and suppressors in experimental populations**

289 A few experimental evolution experiments have been carried out to assess the dynamics of SR
290 drive in *Drosophila*. A very valuable piece of work has been made in *D. pseudoobscura*, a
291 species devoid of drive suppressor where it has been shown that SR drive promotes
292 countervailing mechanisms such as polyandry (Price et al. 2008b), which in turn prevents
293 extinction of the populations by strong drive (Price et al. 2010a). In addition, non-SR males
294 from SR populations evolve to suppress female remating when high rates of polyandry occur
295 (Price et al. 2010b). In an earlier study in this species, Curtsinger and Feldman (1980) showed
296 that SR drive disappeared very quickly from experimental populations set up with 70% of X^{SR}
297 chromosomes: as early as 7 generations in two cases, the X^{SR} frequency being very low after
298 12 generations in all other cases. The estimated selection coefficients due to deleterious
299 effects of the driving chromosomes were very high (0.3-0.4) and mainly associated with
300 fertility defects. In similar experiments with the Paris system of *D. simulans*, Capillon and
301 Atlan (1999) showed that unsuppressed X^{SR} almost disappeared from experimental
302 populations after 17 generations when starting at a 25% frequency, even though it benefited
303 from a strong transmission rate in the carrier males (90% on average). It is supposed to be
304 also lost with an initial frequency of 67% (Capillon and Atlan 1999), but the data are not
305 available. Besides, theory that has been developed to describe the population genetics of *sex-*
306 *ratio* systems in *Drosophila* usually considered the drive suppressors as brakes that convert
307 spreading unbalanced distorters into balanced ones (Carvalho and Vaz 1999). This view is
308 based on the assumption that the frequency of X^{SR} chromosomes is primarily controlled by
309 their segregation distortion rate, in other terms that the deleterious effects associated with X^{SR}
310 are of a similar magnitude whether drive is suppressed or not. Our results show that it is
311 clearly not the case for the Paris SR system. Here, starting at a frequency of 66%, a
312 completely suppressed Paris X^{SR} still persists at a substantial frequency in half of the six
313 experimental populations after nearly one hundred generations. We do not know how quickly
314 it disappeared when unsuppressed and starting at the same frequency (2/3), but we can
315 suppose that it happened earlier than in our experiment. The comparison with *D.*
316 *pseudoobscura* is probably limited because of a much more ancient origin of the SR drive
317 system in this species. Yet, our selection coefficient estimations seem to be always lower than
318 those from Curtsinger and Feldman (1980), where there was no suppressor but supposedly a
319 slight overdominance.

320 While deleterious effects associated with X^{SR} are much lower when fully suppressed, they still
 321 exist. All estimates of s are positive, and only one is not significantly different from 0 (in
 322 Seych1-2, for which the X^{SR} frequency is close to the starting one at G_{94}). In addition, under a
 323 neutral Wright-Fisher model the probability of fixation will depend on the initial frequency
 324 when we start the experiment. The time to fixation will depend on the effective population
 325 size, which in our case would have been moderate (less than 500 individuals). Then X^{SR} is
 326 expected to fix in 4 populations and X^{ST} in only 2. After almost a hundred generations, X^{SR}
 327 has never reached fixation and X^{ST} has fixed or nearly fixed in 3 populations. We can surely
 328 reject the hypothesis of complete neutrality, and suppose that X^{SR} has deleterious effects *per*
 329 *se*, even if suppression moderates these effects.

330

331 **Comparison with natural populations**

332 The Paris driver has been found to decrease in frequency and likely disappear in natural
 333 populations where suppression is complete (Bastide et al. 2011). In our experimental
 334 populations, estimates of the selection coefficient in 3 replicates are very close to the value
 335 estimated in Madagascar on data from a period of 8 years. Only one replicate shows a much
 336 lower estimate, and the two others show a much higher estimate. We cannot exclude the
 337 possibility that X^{SR} dynamics are very similar in natural and experimental populations, but the
 338 reasons why they are apparently variable in the latter are unclear. In at least some cases, the
 339 higher deleterious effects observed could be associated with a higher male competition in
 340 bottles (Atlan et al. 2004; Angelard et al. 2008), which could also reduce the effective
 341 population size.

342 Besides, we looked for the presence of Dp^{SR} and surveyed the $HPID2$ alleles in a sample of
 343 22 F_1 males from 11 isofemale lines (2 F_1 males per line) collected in the Seychelles in 2011.
 344 None of them carried Dp^{SR} but we found the $HPID2^{SR}$ allele in all tested males, suggesting a
 345 persistence of this potentially driving allele even when Dp^{SR} has long disappeared. A sample
 346 of X chromosomes from 72 males (collected in Mayotte in 2009 by CMM and François
 347 Wurmser) showed a similar trend, with 6 chromosomes (8%) carrying Dp^{SR} while 28
 348 chromosomes (39%) carried a well-characterized $HPID2^{SR}$ allele. This is in line with a
 349 spatiotemporal analysis of molecular data, prior to the characterization of $HPID2$ as the
 350 second driving element of the Paris system (Bastide et al. 2011). This analysis highlighted a
 351 discrepancy in the evolution of the two drivers, strongly suggesting that the counter-selection
 352 in natural populations acts mainly, if not exclusively, on Dp^{SR} .

353

354 Conclusion

355 We conclude that much of the deleterious effects associated with the Paris X^{SR} are a direct
356 consequence of the drive, which is consistent with the high cost on male fertility observed
357 when competition occurs (Atlan et al. 2004; Angelard et al. 2008). Thus, our present
358 knowledge on the Paris system, which is of very recent origin (Fouvry et al. 2011) is
359 consistent with the hypothesis proposed by Keais et al. (2020) about X^{SR} evolution, in which
360 the dynamics of young X^{SR} are primarily governed by fitness consequences in males.

361 We have obtained here contrasting results depending on the replicates, which could partly
362 reflect the variable dynamics observed in natural populations where complete suppression has
363 evolved (Bastide et al. 2011). But importantly, we demonstrate that suppression slows down
364 and could sometimes prevent the elimination of an otherwise deleterious X^{SR} chromosome.
365 This is consistent with the concomitant rise of X^{SR} and drive suppressors observed in the wild
366 (Bastide et al. 2013; Helleu et al. 2019). We can suppose that each of them takes advantage of
367 the presence of the other to increase in frequency. The strongly biased transmission,
368 associated with lower deleterious effects entailed by the suppressors, allows the driver to
369 quickly rise in frequency. As for the suppressors, their frequency probably increases by
370 frequency-dependent selection associated with drive. Thus, this genetic conflict appears to
371 convert into a cooperation between alleles at unlinked loci.

372

373

374

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Dp^{SR}	chromosome	n	Female %	
			M	SE
-	2-7	5	49.4	1.8
	2-10	3	51.8	3.9
	2-25	5	53.4	7.0
	2-31	4	50.6	8.1
	2-43	3	54.1	7.7
	2-57	2	53.8	3.8
+	2-1	5	92.9	2.7
	2-5	3	88.3	8.5
	2-6	6	94.1	1.8
	2-9	5	95.8	1.9
	2-12	5	93.7	1.8
	2-14	3	89.4	6.3
	2-21	5	92.3	5.1
	2-23	5	94.2	3.0
	2-26	4	89.2	6.8
	2-28	4	92.5	3.5
	2-33	3	95.4	2.6
	2-35	3	93.9	3.4
	2-37	5	95.3	3.2
	2-38	4	93.3	3.6
	2-39	2	89.2	3.9
	2-41	5	89.8	5.8
	2-44	4	90.9	2.1
	2-47	3	92.3	5.7
	2-49	4	90.4	7.4
	2-51	3	89.4	6.7
	2-52	2	92.7	0.3
	2-53	5	94.8	1.1
	2-54	3	84.9	8.1
	2-58	5	92.5	0.9
2-59	4	91.3	2.9	
2-60	5	93.7	5.4	

542 Table 1: Assessment of the drive activity of X chromosomes with (+) or without (-) the SR
543 duplication (Dp^{SR}) in Seych1-2 at G88. n : number of full-sib F1 males tested, M: mean
544 percentage of females in the progeny, SE: standard error.

Dp^{SR}	chromosome	n	Female %	
			M	SE
-	3-6	3	51.5	3.3
	3-15	4	52.2	4.9
	3-25	4	50.7	4.4
	3-37	3	55.7	4.2
	3-45	3	50.3	4.5
	3-60	4	50.8	4.8
+	3-1	5	90.9	6.8
	3-3	4	94.6	2.2
	3-8	4	91.3	3.9
	3-9	4	89.8	5.7
	3-10	5	92.4	2.4
	3-16	3	90.9	4.4
	3-19	3	85.5	9.0
	3-20	5	85.9	9.2
	3-22	5	89.5	6.2
	3-24	3	81.0	6.8
	3-27	4	92.6	1.7
	3-28	5	91.5	7.5
	3-30	3	87.4	8.6
	3-31	3	93.5	3.0
	3-33	3	87.2	5.4
	3-34	5	94.4	1.9
	3-35	4	95.3	1.0
	3-36	5	90.6	7.4
	3-39	5	93.8	3.8
	3-43	3	94.7	1.4
3-46	5	93.8	2.6	
3-49	3	93.1	3.3	
3-51	4	93.1	5.7	
3-56	3	95.2	1.4	

546 Table 2: Assessment of the drive activity of X chromosomes with (+) or without (-) the SR
547 duplication (Dp^{SR}) in Seych1-3 at G88. n : number of full-sib F1 males tested, M: mean
548 percentage of females in the progeny, SE: standard error.

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Strain	Replicate population	\hat{s}	CI _{95%}
Seych1	1	0.039	[0.029 – 0.05]
	2	0.007	[0 – 0.014]
	3	0.021	[0.013 – 0.029]
Seych3	1	0.1	[0.077 – 0.13]
	2	0.053	[0.04 – 0.067]
	3	0.201	[0.149 – 0.266]

555 Table 3: Estimates of the selection coefficient (\hat{s}) in each of the six experimental populations,
 556 and 95% confidence intervals (see text for details).