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# 1 Demographic and genetic consequences of disturbed sex determination

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11

## 12 Abstract

13 During sex determination, genetic and/or environmental factors determine the cascade of  
14 processes of gonad development. Many organisms therefore have a developmental window in  
15 which their sex determination can be sensitive to, for example, unusual temperatures or  
16 chemical pollutants. Disturbed environments can distort population sex ratios and may even  
17 cause sex reversal in species with genetic sex determination. The resulting genotype-  
18 phenotype mismatches can have long-lasting effects on population demography and genetics.  
19 I review the theoretical and empirical work in this context and explore in a simple population  
20 model the role of the fitness  $v_{yy}$  of chromosomally aberrant YY genotypes that are a  
21 consequence of environmentally-induced feminization. Low  $v_{yy}$  is mostly beneficial for  
22 population growth. During feminization, low  $v_{yy}$  reduces the proportion of genetic males and  
23 hence accelerates population growth, especially at low rates of feminization and at high  
24 fitness costs of the feminization itself (i.e. when feminization would otherwise not affect  
25 population dynamics much). When sex reversal ceases, low  $v_{yy}$  mitigates the negative effects  
26 of feminization and can even prevent population extinction. Little is known about  $v_{yy}$  in  
27 natural populations. The available models now need to be parametrized in order to better  
28 predict the long-term consequences of disturbed sex determination.

29

30 **Keywords:** sex determination, environmental sex reversal, climate change, endocrine  
31 disrupting chemicals, population growth, extinction

32

33

## 33 1. Introduction

34 Sex determination is strictly genetic in nearly all mammals and birds, mostly with male (XY)  
35 or female (ZW) heterogamety, and purely environmental in, for example, many reptiles.  
36 However, in various taxa sex determination is neither purely genetic nor purely environmental  
37 [1, 2]. It is therefore often useful to see the phenotypic sex as the result of the three major  
38 drivers of phenotypic variation, namely genes, the environment, and developmental noise  
39 (stochasticity due to random factors) [3]. It is then easy to see why disturbed environments  
40 can affect sex determination and hence population sex ratios. Such disturbances have genetic  
41 and demographic consequences that can sometimes threaten the viability of populations.

42 Authors often make a distinction between sex determination, i.e. the developmental step  
43 that decides whether an individual becomes female or male, and sex differentiation, i.e. the  
44 subsequent steps in developmental pathways during which the female or male phenotype is  
45 built up after the initial step of sex determination has occurred. However, abandoning a  
46 fundamental distinction between sex determination and gonad differentiation may help to  
47 better understand the evolution of sex determining systems [1, 4]. Sex is then still a threshold  
48 trait, with processes early in development regulating later processes, and with some of these  
49 processes occurring directly in the gonads, while others occurring elsewhere in the organism.  
50 While sex is often a trait that has a single main trigger (e.g. DMRT1 expression above critical

51 level in chicken [5]), there are many species with several master triggers, for example, in  
52 plants [6], fishes [7] or gastropods [8]. It is therefore more useful to understand sex  
53 determination as a developmental switch that is composed of various regulatory elements.  
54 These elements can be both genetic and non-genetic and may even include maternal strategies  
55 [1, 4].

56 Thinking of sex determination as a developmental process with one or several initial  
57 triggers raises interesting questions, including (i) what prevents in some taxa the emergence  
58 of a single master trigger of sex, i.e. why do so many species have several types of factors that  
59 determine sex [9], (ii) how do novel sex determining systems arise from existing single or  
60 multi-factorial systems, and (iii) what are the demographic and genetic consequences of  
61 different sex-determining systems in changing environments? This article focuses on the latter  
62 question.

63

## 64 **2. Sex determination in disturbed and undisturbed environments**

65 Many environmental factors can affect sex determination in species with primarily  
66 environmental or genetic sex determination. Temperature is certainly the most important  
67 environmental factor that can potentially influence sex determination and hence adult sex  
68 ratios (ASR) in undisturbed environments [2, 10, 11]. In pure temperature-dependent sex  
69 determination (TSD), temperature during a thermosensitive period triggers male or female  
70 gonad development. TSD occurs in crocodiles, most turtles, and some fish [12, 13]. Other  
71 factors that drive environmental sex determination in undisturbed environments are  
72 photoperiod in some amphipods and barnacles [14], social influences in some fish and aquatic  
73 snails [15, 16], pathogens [17], and pH or oxygen levels [13]. Temperature often acts in  
74 combination with other environmental effects on sex determination [1, 18]. These other  
75 factors include maternal environmental effects like egg size [19] and yolk steroid hormones  
76 [20], which appear to reflect differential maternal investment [21, 22]. It may therefore not be  
77 surprising that several endocrine disrupting chemicals have also been found to interfere with  
78 sex determination in species with TSD [23]. For instance, embryos of the turtle *Trachemys*  
79 *scripta* that are incubated at male-producing temperatures often turn into females when  
80 exposed to estradiol [24], different types of PCBs [25], the herbicide atrazine [26], or other  
81 compounds of which the insecticide chlordane is synergistic with estradiol when applied in  
82 combination [24].

83 Sex determination can also be altered in species with genetic sex determination. In this  
84 context, the most important anthropogenic changes to the environment are temperature (due  
85 to climate change or, for example, power plants that increase river water temperatures) and  
86 micropollutants [27]. Various endocrine disrupting chemicals have been shown to interfere  
87 with the endocrine system and affect sex determination. Exogenous chemicals are therefore  
88 often used in aquaculture and research to override genetic sex determination [28]. Piferrer  
89 [28] lists over 50 fish species and hybrids whose sex determination has been successfully  
90 manipulated. The estrogens used most often in such treatments are natural estrone (E1), 17 $\beta$ -  
91 estradiol (E2), the synthetic 17 $\alpha$ -ethinylestradiol (EE2). However, fishes vary in their  
92 susceptibility to exogenous chemicals, i.e. the potential of a given estrogen to feminize needs  
93 to be separately evaluated for each species [13, 28].

94 While many of these estrogens usually play a minor role in aquatic systems because of  
95 their low prevalence and relatively short half-life, EE2, is a prevalent pollutant that is globally  
96 relevant. It is used in most formulations of oral contraceptives, and its half-life in aquatic  
97 environments is around 14 days [29]. EE2 is now commonly found in surface and  
98 groundwater at concentrations around 1 ng/L [30], but concentrations of up to 273 ng/L have  
99 been reported [31]. Concentrations as low as 1 ng/L are known to affect embryo growth and

100 to induce vitellogenin production, i.e. the precursor protein of egg yolk, in fish [32-34]. EE2  
101 is also a potential endocrine disrupting chemical in amphibians [35].

102 Other micropollutants that can affect sex determination are pesticides, including atrazine  
103 that has been shown to interfere with sex determination ([36, 37], see also [38] and  
104 subsequent discussion in the same journal), polychlorinated biphenyls (PCBs)[23], and some  
105 of the most widely used plasticizers (additives that increase the viscosity or plasticity of  
106 certain industrial products), including phthalates and bisphenol A (BPA) that can interfere  
107 with hormone systems and may hence affect sex determination [39]. Within aquatic systems,  
108 molluscs, crustacean, and amphibians generally seem to be more susceptible to these  
109 plasticizers than fish, but disturbance of fish spermatogenesis has also been found even at low  
110 concentrations of BPA [39].

111 There are many cases of unusual temperatures or micropollutants overriding genetic  
112 factors of sex determination and causing environmental sex reversal, resulting in a mismatch  
113 between an organism's phenotype and genotype. Figure 1 illustrates possible patterns of  
114 genetic versus environmental contributions to sex determination. The figure only illustrates  
115 the principles. The link between sex determination and environment need not be linear or  
116 even continuous, the variance need not be constant in different environments, and  
117 environmental inputs may completely override genetic sex determining factors. The resulting  
118 phenotype-genotype mismatches can then affect sex ratios in subsequent generations, as  
119 explained below. The potential significance of the interaction between genetic and  
120 environmental factors is further explored in Bokony et al. [11] who argue that male  
121 heterogametic and female heterogametic amphibians are likely to respond differently to  
122 temperature-induced sex reversal.

123 There are other types of anthropogenic changes of the environment that can influence  
124 individual sex determination and hence population sex ratios, for example, non-random  
125 exploitation of sequential hermaphrodites that can affect their life history and their timing of  
126 sex change [40]. These other anthropogenic changes will not be further discussed here. In the  
127 following section I concentrate on environmental changes that override genetic sex  
128 determination.

129

### 130 **3. Relevance of different mating types after disturbed sex determination**

131 While environmental sex reversal can immediately affect the phenotypic sex ratio of a  
132 population, it also creates phenotype-genotype mismatches that can have potentially counter-  
133 intuitive consequences for future generations (e.g. environmental feminization may  
134 sometimes explain male-biased ASR). Such long-term consequences depend on the various  
135 possible mating types. Some of these mating types can therefore be relevant for the  
136 management of wild and captive populations.

137 Table 1 shows the effect of environmental sex reversal on all possible mating types in an  
138 XY sex determination system with environmental sex reversal (ESR; both masculinization  
139 and feminization), the frequency of the sex chromosomes in the resulting offspring, and the  
140 family sex ratios (here defined as frequency of the male phenotype before possible further sex  
141 reversal; assuming that the YY genotype naturally leads to the male phenotype). These family  
142 sex ratios will equal the ASR in the F1 if there is no further sex reversal and no sex-specific  
143 mortality.

144 Apart from the  $F_{XX} \times M_{XY}$  mating (scenario 1 in Table 1), there are 8 further possible  
145 mating types that can result from ESR. Some scenarios are only possible after sex reversal  
146 occurs in a previous generation (e.g.  $M_{YY}$  and  $F_{YY}$  must be offspring of sex-reversed  $F_{YY}$  or  
147  $F_{XY}$ ). The 9 scenarios vary in their genetic and demographic effects on future generations [41,  
148 42]. They also vary in their potential relevance for population management, including the  
149 management of threatened wild populations that may [43] or may not suffer from distorted

150 sex ratio [44], the management of undesired populations (e.g. invasive species) [45], and the  
151 management of captive populations (e.g. in aquaculture) [28].

152 In aquaculture, one-generation mono-sex cultures are often economically advantageous  
153 because, for example, they avoid the problems of early maturation and uncontrolled  
154 reproduction [28]. Masculinization of XX individuals (via hormone treatment) and mating  
155 scenario 2 could be relevant for the production of female mono-sex cultures in fish farming  
156 [46]. They may also be relevant in managing wild populations, for example, for boosting  
157 population growth to above-critical levels in order to reduce the risk of extinction [44].  
158 Scenarios 3, 4, 6, 7 and 9 (all based on feminization of XY or YY individuals, e.g. via  
159 hormones) pertain to population management that is based on “Trojan Y chromosomes” [45,  
160 47]. The idea here is to produce YY individuals and release them into natural populations in  
161 order to distort population sex ratios towards the male sex in order to control growth of  
162 undesired populations (e.g. of invasive fish or amphibians). This type of population  
163 management would ideally be based on broodstocks of YY males and YY females (if males  
164 are the heterogametic sex) or of ZZ males and ZZ females (if females are the normally  
165 heterogametic sex, see below).

166 YY-broodstocks would ideally aim for mating scenario 3 in Table 1 if the release of  
167 hormone-treated individuals into a natural population is to be avoided, for example, to avoid  
168 anglers catching and consuming hormone-treated fish [48]. Consumption of non-treated  
169 offspring of hormone-treated fish seems accepted from a food-safety standpoint, as made  
170 evident by the large amounts of commercially grown offspring of sex-reversed fish that have  
171 been consumed over the last decades [49]. Scenarios 7 and 9 could become relevant if  
172 progeny of a YY-broodstock can be released after hormone-treatment [45, 47], with scenario  
173 9 as a possibility when wild-born offspring of  $F_{YY}$  mate with introduced  $F_{YY}$ . Scenarios 4 and  
174 9 also describe stages in a YY broodstock production [48]. Scenarios 5 and 8 seem to have no  
175 or limited relevance in aquaculture or for the control of undesired natural populations but  
176 could be used in experimental research to study, for example, viability effects of sex reversal  
177 in the different karyotypes. These are crucial parameters in various types of population  
178 models [41, 42, 45, 50]. Scenario 6 could become relevant if the second phase in a YY-  
179 broodstock production needs to be repeated, for example, in order to increase the genetic  
180 diversity of the broodstock.

181 Table 2 shows the analogous demographic and genetic effects of all other possible mating  
182 types in a ZW sex determination system with wild-type and artificially constructed genotype-  
183 phenotype combinations on the subsequent generation, assuming that the WW genotype  
184 naturally leads to the female phenotype (analogous to the assumption above that the YY  
185 genotype naturally leads to the male genotype). Scenario 10 describes the natural  $F_{ZW} \times M_{ZZ}$   
186 mating. The release of sex-reversed ZW and WW individuals into a natural population with  
187 ZW females (scenarios 11 and 12) would be expected to bias the population sex ratio towards  
188 the female sex and hence boost population growth. This could potentially be an option for  
189 boosting population growth to above-critical levels in order to reduce the risk of extinction  
190 [44], analogously to scenario 2 in Table 1. Scenario 13 offers such a potential boost in  
191 population growth while avoiding the release of hormone-treated individuals. Such non-  
192 hormone treated  $F_{WW}$  would ideally be produced in scenario 15. Scenarios 12, 13, 14, 15, and  
193 18 would be possible broodstocks for mono-sex cultures in fish farming if females are the  
194 preferred sex. Scenarios 17 seems of no or limited relevance in aquaculture or for the  
195 management of natural populations but could potentially be used in experimental research to  
196 study viability effects of sex reversal in the different karyotypes, analogously to scenarios 5  
197 and 8 in Table 1. Scenario 16 is an interesting one: it may not only be the ideal broodstock for  
198 mono-sex cultures if males are the preferred sex in fish farming, but it could also describe the  
199 type of mating that a release of sex-reversed ZZ individuals into a natural population with ZZ

200 males would lead to if the Z-chromosome is used as Trojan element to control the growth of  
201 an undesired population.

202

#### 203 **4. Demographic and genetic consequences of phenotype-genotype mismatches**

204 If sex determination is predominantly genetic but can be reversed by environmental factors,  
205 immediate shifts in population sex ratios and in the frequencies of the sex chromosomes are  
206 likely and can extend over several generations [51, 52]. The demographic and genetic  
207 consequences then need to be modelled. They depend on the frequencies of the all possible  
208 mating types that were discussed in section 3 (Relevance of different mating types after  
209 disturbed sex determination) and that are likely to change over time, depending on the fitness  
210 (viability and reproductive success) of the various possible combinations of phenotypes and  
211 genotypes. The present section summarizes the available models and later meta-analyses and  
212 case studies that help to better define the relevant parameter space of such models. Recent  
213 empirical work suggests that the fitness of sex-reversed individuals is probably not as decisive  
214 as previously assumed in some models. However, the fitness of aberrant karyotypes (YY and  
215 WW) may be more important than sometimes assumed. Section 5 (Modelling effects of ESR  
216 and YY karyotypes on population dynamics) will therefore focus on the fitness of aberrant  
217 karyotypes and demonstrate its relevance for demographic and population-genetic models.

218 Environmental masculinization (Fig. 1a) reduces the proportion of genetic males and  
219 can eventually lead to the extinction of Y-chromosomes, while environmental feminization  
220 (Fig. 1b) can elevate the proportion of genetic males and can theoretically drive X-  
221 chromosomes to extinction [41, 42, 53] (but extinction of X chromosomes requires far  
222 stronger rates of ESR than extinction of Y chromosomes [42]). Ceasing sex reversal (e.g. by  
223 stopping pollution) could then lead to extreme population sex ratios and quickly drive  
224 populations to extinction [42]. Another important consequence of environmentally induced  
225 sex reversal can be a switching between sex-determination systems, for example, switching  
226 from XY/XX to ZW/ZZ or from genetic to environmental sex determination [11, 54-56].

227 Apart from these extreme scenarios, ESR can have marked effects on population  
228 growth, depending on the kind of sex reversal and on the fitness costs of the sex reversal [42].  
229 If these fitness costs are small and males are not needed for parental care, population census  
230 sizes ( $N_c$ ) tend to react positively to environmental feminization. Genetically effective  
231 population sizes ( $N_e$ , i.e. the size of a model population that loses genetic variation at the same  
232 rate as the study population [57]) suffer from distorted sex ratios. However, this effect is  
233 likely to be compensated in subsequent generations by increased census sizes [58, 59]. On the  
234 other hand, masculinization is generally expected to reduce population growth [42].  
235 Moreover,  $N_e$  is negatively affected if masculinization increases the variance in reproductive  
236 success among phenotypic males, for example, because sexual selection may act differently  
237 on XX- and XY- males or because of possible effects of distorted sex ratios on male and  
238 female life history [60, 61]. This is because  $N_e$  also decreases with increasing variation in  
239 family size among males [57].

240 The viability of sex-reversed individuals has been assumed to be a key variable  
241 determining the dynamics of populations that are exposed to ESR [42, 62]. However, a first  
242 meta-analysis of the available data concluded that ESR by itself does generally not seem to  
243 significantly reduce individual health and vigor [62]. Exposure to endocrine-disrupting  
244 chemicals often reduces individual growth during some developmental stages, but individuals  
245 seem often able to recover from such temporary effects [62]. In a more recent review, Senior  
246 et al. [63] found little evidence for significant effects of ESR on sperm characteristics. They  
247 concluded that "...masculinized genotypic females may enjoy reproductive success  
248 comparable to genotypic males" [63], and hence that ESR is more likely to influence the  
249 genetics and demography of wild populations than has previously been assumed. On the same

250 line, Holleley *et al.* [64] argue in their review that ESR is unlikely to reduce viability and  
251 fertility in reptiles.

252 While the effects of masculinization or feminization on individual viability and  
253 fertility may typically be smaller than previously assumed [42], the effects of aberrant  
254 karyotypes (YY or WW) on viability and fertility can still be significant. Sex chromosomes  
255 evolve from autosomes and are likely to become heteromorphic because of repressed  
256 recombination on Y and W chromosomes [65]. Repressed recombination reduces the  
257 efficiency of natural selection and is expected to cause the kind of degeneration of Y and W  
258 chromosomes that is observed in many taxa, including humans [66].

259 Taxa in which ESR occasionally occurs under natural conditions (e.g. many fish and  
260 amphibians) typically show lower levels of degeneration of Y and W chromosomes than taxa  
261 that are less susceptible to ESR (e.g. birds and mammals). This may be because such taxa  
262 benefit from phenotype-specific recombination of sex chromosomes (e.g. X-Y recombination  
263 in  $F_{XY}$ ). Perrin [9] suggested that this phenotype-specific recombination in sex-reversed  
264 individuals (e.g. recombination between X and Y in phenotypic females), followed by  
265 selection, is a “fountain of youth” for sex chromosomes and may explain the high rate of  
266 homomorphic sex chromosomes in fish and amphibians. Indeed, viable and fertile YY and  
267 WW genotypes could repeatedly be produced in some fish and amphibians [13, 67]. Such  
268 aberrant genotypes could even be sex-reversed for subsequent breeding programs (recent  
269 examples include Liu *et al.* [68] and Schill *et al.* [48]). However, because of their reduced  
270 recombination rate and their relatively small effective size compared to X and Z  
271 chromosomes (Y and W are rarer in natural populations than X and Z), Y and W  
272 chromosomes will generally show higher levels of degeneration than X and Z chromosomes.  
273 Therefore, the aberrant YY and WW karyotypes usually suffer from reduced individual  
274 fitness as compared to the XX, XY, ZZ, and ZW genotypes.

275 Not much is known about the relative viability and reproductive success of karyotypes  
276 within fishes and amphibians. When Schill *et al.* [48] produced a YY-broodstock of brook  
277 trout (*Salvelinus fontinalis*) for potential use in eradication programs, they found the expected  
278 number of YY offspring in  $F_{XY} \times M_{XY}$  matings, i.e. YY individuals did not seem to suffer  
279 from higher embryo or juvenile mortality under the protected hatchery conditions. However,  
280 feminization of YY individuals was more difficult than feminization of XY individuals, and  
281 E2-treatment led to higher rates of individuals with intersex characteristics among the YY  
282 than the XY individuals. Theoretical treatments of the long-term demographic and genetic  
283 effects of environmentally induced sex reversal should therefore distinguish between (the  
284 possibly minor) fitness effects on sex-reversed normal genotypes (e.g.  $F_{XY}$  or  $M_{XX}$ ) and (the  
285 possibly higher) fitness effects of chromosomally aberrant individuals (e.g.  $M_{YY}$  or the sex-  
286 reversed  $F_{YY}$ ). Fitness reduction in aberrant karyotypes are predicted to affect an evolutionary  
287 transition from one sex-determining system to another [55, 69]. They have also been  
288 predicted to affect population sex ratios [41].

289

## 290 **5. Modelling effects of ESR and YY karyotypes on population dynamics**

291 To study the demographic and genetic effects of reduced fitness in chromosomally aberrant  
292 individuals, I adopt Cotton and Wedekind’s [42] deterministic model and largely followed  
293 their settings (Box 1). Cotton and Wedekind’s [42] analyses were based on the assumption  
294 that ESR-linked individual fitness was identical for YY and XY genotypes. In order to relax  
295 this assumption, YY genotypes now have a fitness of  $v_{YY} \leq 1$ . I analyzed 20 generations, with  
296 a constant feminization rate during the first 10 generations and no feminization in the  
297 remaining 10 generations (i.e. a cease of ESR at generation 10).

298 Environmental feminization has first a positive effect on the population census sizes  
299  $N_c$  (Fig. 2). However, ESR changes the population sex ratio and hence reduces the genetically

300 effective population size  $N_e$ , at least in the first generation after ESR has started (Fig. 2).  
301 Environmental masculinization generally reduces population sizes (both  $N_c$  and  $N_e$ ) because of  
302 the high rate of males in the population [42], and, at the present parameter setting, quickly  
303 leads to population extinction at high rates of masculinization (Supplementary Fig. S1). In  
304 environmental feminization, the negative effects on  $N_e$  can be compensated later by the  
305 increased  $N_c$ , depending on the strength of the feminization and the population's carrying  
306 capacity (Fig. 2). However, ceasing sex reversal after generation 10 reduces population sizes  
307 (both  $N_c$  and  $N_e$ ). The higher the feminization rate in the first 10 generations, the more  
308 pronounced is this drop in population sizes (approaching  $N_c = 0$  with high  $p$ ,  $v_{ESR}$ , and  $v_{YY}$ ; Fig.  
309 2b). This effect is mitigated with increased reduction of  $v_{ESR}$ , and especially so with increased  
310 reduction of  $v_{YY}$  (Fig. 2), because low  $v_{YY}$  cause low ratios of genetic males (Y-carriers) in the  
311 population during feminization (Fig. 3).

312 The role of  $v_{YY}$  on population growth during feminization depends both on  $p$  and  $v_{ESR}$ .  
313 At high  $p$ , variation in  $v_{YY}$  has little effects on population growth during feminization. At low  
314  $p$  and low  $v_{ESR}$ , overall population growth is nearly unaffected by the feminization when  $v_{YY}$  is  
315 high. However, population growth then increases with declining  $v_{YY}$  (Fig. 2e) because  
316 declining  $v_{YY}$  reduce the rate of male genotypes in the population (Fig. 3).

317

## 318 **6. Rapid evolutionary responses to environmentally disturbed sex determination?**

319 The mechanisms of sex determination are rapidly evolving in many animal and plant clades  
320 [2]. The diversity of sex determination systems within fish, for example, extends deep into  
321 families [13], and there are several cases of within-species population differences in fish and  
322 other taxa [70]. Pen et al. [71] found, for example, sex determination to be mostly  
323 temperature-dependent in snow skink (*Niveoscincus ocellatus*) living in the lowlands of  
324 Tasmania, while it was predominantly genetic in adjacent highland populations. The authors  
325 argued that warm incubation temperatures lead to earlier births in the year and hence an  
326 improved opportunity for growing to large body until maturation. In lowland populations,  
327 females seem to profit more from large body sizes than males, and this might have selected  
328 for TSD. In their simulation models they assumed sex to be determined by a combination of  
329 incubation temperature and of the alleles at four diploid loci. Under lowland conditions,  
330 genetic sex determination is then likely to turn into TSD within few thousands generations  
331 [71].

332 Such a transition from genetic to temperature-dependent sex determination can be  
333 dramatically faster if temperature induces sex reversal. The Australian bearded dragon  
334 (*Pogona vitticeps*), for example, has a ZW sex determination system that can be overridden  
335 by warm temperatures such that ZZ individuals turn into females who seem to be at least as  
336 viable and fertile as the wildtype ZW females [56]. By mating sex-reversed individuals,  
337 Holleley et al. [56] could experimentally induce a transition from genetic to solely  
338 temperature-dependent sex determination within only one generation (because sex-reversed  
339 ZZ females mated to wild-type ZZ males can only produce ZZ offspring). The environmental  
340 temperatures that allow for such transitions are within the range the species is currently  
341 exposed to, i.e. sex-reversed ZZ female bearded dragons can be found in the wild, and  
342 probably in increasing frequencies as observations between 2003 and 2011 suggest [56]. This  
343 species is hence susceptible to local extinction of W chromosomes due to extreme  
344 environmental conditions, especially if combined with small population sizes (drift effects).  
345 Analogous rapid transitions are possible in a XY sex determination system when XX  
346 individuals are masculinized and mate with wild-type XX females to produce only XX  
347 offspring [41, 42, 69].

348 Further examples of diversity in sex determination system within species include the  
349 recent work of Rodrigues et al. [72, 73] who found significant difference in sex determination



350 among populations of the common frog (*Rana temporaria*), Ribas et al. [74] who found the  
351 masculinizing effects of elevated environmental temperatures to be family-specific in zebra  
352 fish (*Danio rerio*), and Shen et al. [75] who found strain-specific reaction norms in TSD in  
353 four strains of bluegill sunfish (*Lepomis macrochirus*). In the latter example, the authors  
354 suggested that the genotype-temperature interactions they found could be exploited to more  
355 efficiently manipulate sex determination in aquaculture, because males grow faster and larger  
356 than females in this species.

357 Given that even populations of the same species can differ in sex determination, it  
358 seems unsurprising that closely related species often differ in their reaction norms in  
359 feminization rate after exposure to micropollutants. A recent example includes Tamschick et  
360 al. [35] who found species-specific reaction norms in the response of three amphibians to  
361 exposure to EE2. Mizoguchi and Valenzuela [23] discuss possible species-specific reaction  
362 norms to various micropollutants in reptiles.

363 The evolutionary potential of natural populations to adapt to anthropogenic changes in  
364 the environment critically depends on the existence of additive genetic variation in the  
365 response to the change [76, 77]. Such heritabilities are typically difficult to estimate,  
366 especially in the presence of non-genetic parental effects [78]. However, recent analyses of  
367 genome sequences and transcriptomes of Atlantic killifish (*Fundulus heteroclitus*) and of blue  
368 mussel (*Mytilus edulis*) populations sampled from polluted sites and from geographically  
369 paired non-polluted sites suggest pollution-induced genetic differentiation [79, 80]. Brazzola  
370 et al. [32] used full-factorial *in vitro* breeding experiments (i.e. several males crossed with  
371 several females in all possible combination to control for maternal environmental effects and  
372 for any form of differential parental investments) and found significant additive genetic  
373 variance in the tolerance to EE2 pollution within two whitefish species (*Coregonus* sp.). And  
374 Hamilton et al. [81] found roach (*Rutilus rutilus*) populations to be self-sustaining in heavily  
375 polluted habitats of Southern England despite widespread feminization (see also discussion in  
376 [82, 83]).

377 These examples suggest that rapid genetic adaptation to some forms of pollution could be  
378 possible in some taxa. The basis of such tolerances needs to be further studied in order to  
379 better understand the potential for rapid adaptive evolution in response to environmentally  
380 disrupted sex determination. Data about the lability of sex determination and about the critical  
381 heritabilities are often lacking, and it is possible that many taxa might not be capable of rapid  
382 adaptation to environments that disturb sex determination [84].

383

## 384 **7. Conclusions and implications for conservation and pest management**

385 Fishes, amphibians, and reptiles are often susceptible to anthropogenic disturbance of sex  
386 determination caused either by extreme temperatures or various types of micropollutants. This  
387 may occur either because their sex determination is environmental, or because their sex  
388 determination has a genetic basis that can be overruled. Such environmental sex reversal  
389 creates phenotype-genotype mismatches that are often exploited in aquaculture to produce  
390 more profitable mono-sex cultures. In natural populations, phenotype-genotype mismatches  
391 can sometimes boost population growth if they reduce the ratio of males in the population and  
392 if females are limiting population growth. However, in most cases, disturbed sex  
393 determination and environmental sex reversal is a threat to natural populations because it  
394 distorts the rates of sex chromosomes. Distorted rates of sex chromosomes can severely affect  
395 population growth and even cause extinction, for example, during masculinization or when an  
396 environmental force that induces feminization ceases after sex reversal over several  
397 generations.

398 Recent meta-analyses suggest that environmental sex reversal has little effect on  
399 individual survival and reproduction, and that the significance of  $v_{ESR}$  for population

400 dynamics is sometimes overrated. However, the extended model presented here reveals that  
401 the fitness (survival and reproduction) of individuals with the aberrant YY genotype ( $v_{yy}$ )  
402 plays an important role especially when feminization ceases and populations experience a  
403 sudden consequent drop in  $N_c$  and  $N_e$ . Low  $v_{yy}$  significantly mitigates population decline.  
404 During feminization,  $v_{yy}$  has little effect on population growth except when the rate of  
405 feminization is small and feminization affects individual fitness. Low  $v_{yy}$  then boosts  
406 population growth because it reduces the rate of individuals carrying Y chromosomes.

407 While environmental sex reversal commonly threatens natural populations, it also  
408 creates interesting management options for problem populations, such as invasive fish or  
409 amphibians. This is true for both species with a ZW/ZZ and species with a XY/XX sex  
410 determination system. In ZW/ZZ species, the release of sex-reversed ZZ females into natural  
411 populations (and the subsequent mating of ZZ females with wild-type ZZ males) is expected  
412 to increase the rate of males in future generations and hence to reduce population growth.  
413 Analogously, in XY/XX species, the release of sex-reversed XY females and especially of  
414 YY males or even of sex-reversed YY females into a natural population is also expected to  
415 increase the ratio of males to females in future generations and to reduce population growth.  
416 This idea is based on the assumption that  $v_{ESR}$  and  $v_{yy}$  are high, which is often the case for  
417  $v_{ESR}$ , but needs to be further examined for  $v_{yy}$ . The potential of this “Trojan Y chromosome  
418 hypothesis” then needs to be evaluated in field trials.

419

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425

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








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- 653

654 **Box 1: Settings of the model**

655 The present analysis of potential effects of ESR and YY karyotypes on population dynamics  
656 is based on Cotton and Wedekind's [42] deterministic model (i.e. excluding mutation-based  
657 evolution and random sex determination). Their settings were as follows: discrete generations,  
658 male heterogamety, population size at generation 0 = 1000, initial 1:1 sex ratio, random  
659 mating, females mate only once and contribute  $r$  offspring to the next generation,  
660 environmental feminization  $p \leq 1$  (identical for YY and XY genotypes), environmental  
661 masculinization  $q \leq 1$ , and ESR-linked individual fitness  $v_{ESR} \leq 1$  (with fitness including  
662 survival and reproduction). In the new model, YY genotypes have a fitness of  $v_{YY} \leq 1$ , and the  
663 following simplifications are implemented: (i) no limitations on male mating ability  
664 (including the extreme case when one male is sufficient to fertilize all available eggs), (ii)  
665 carrying capacity  $K = 2000$ , and (iii) number of offspring per female  $r = 2$  when  $N_F \leq K/2$ ,  
666 otherwise  $r = K/N_F$  (ceiling model of density dependent reproduction).

667 The effects environmental feminization and a ceasing of sex reversal are then analyzed  
668 with regard to the population census sizes ( $N_c$ ) and the genetically effective population sizes  
669 ( $N_e$ ).  $N_e$  corrects for the effects of unequal sex ratios by  $N_e = 4N_M N_F / (N_M + N_F)$  and for the  
670 effects of variation of population size over time, e.g. of population bottlenecks, by using the  
671 harmonic mean each over all  $N_e$  since generation 0 [57].













672 **Table 1 Mating types with XY sex determination and environmental sex reversal**  
 673 The expected consequences of all possible mating types in a XY sex determination system,  
 674 i.e. of males or females with no phenotype-genotype mismatch (open symbols), sex-reversed  
 675 individuals (black symbols), or with karyotypes that can results from sex reversal in the  
 676 parental generation (gray symbols), assuming that all mating types are possible and have the  
 677 same effect on the viability of all types of offspring, and that the YY genotype naturally leads  
 678 to the male phenotype, i.e. sex reversal is necessary to produce YY females. The figure gives  
 679 the expected frequencies of XX-female, XY-male, and YY-male offspring, the expected  
 680 frequencies of Y chromosomes, and the expected frequencies of male phenotypes in the F1.  
 681 See text for a discussion of the various mating scenarios.  
 682

		Mating type								
										
Frequency of		50%	100%	0%	25%	50%	0%	0%	0%	0%
		50%	0%	100%	50%	50%	50%	50%	100%	0%
		0%	0%	0%	25%	0%	50%	50%	0%	100%
	Y-chromosomes	25%	0%	50%	50%	25%	75%	75%	50%	100%
	male phenotype*	50%	0%	100%	75%	50%	100%	100%	100%	100%
	Mating scenario	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)

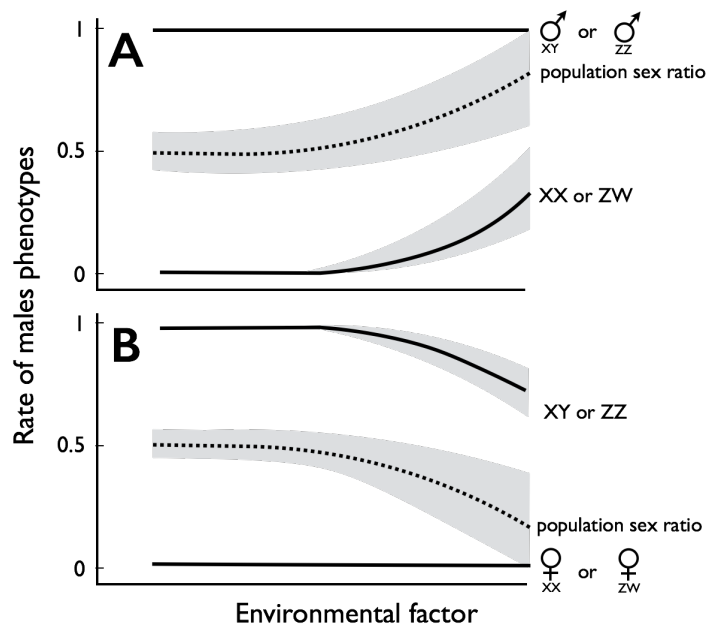
683 \*before possible futher sex reversal



684 **Table 2 Mating types with ZW sex determination and environmental sex reversal**  
 685 The expected consequences of all possible mating types in a ZW sex determination system,  
 686 analogous to Table 1 (assuming that the WW genotype naturally leads to the female  
 687 phenotype, i.e. sex reversal is necessary to produce WW males). See text for a discussion of  
 688 the mating scenarios.  
 689

		Mating type								
										
Frequency of		50%	25%	0%	0%	0%	0%	100%	50%	0%
		50%	50%	50%	100%	50%	0%	0%	50%	100%
		0%	25%	50%	0%	50%	100%	0%	0%	0%
	Z chromosomes	75%	50%	25%	50%	25%	0%	100%	75%	50%
	male phenotype*	50%	25%	0%	0%	0%	0%	100%	50%	0%
	Mating scenario	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)

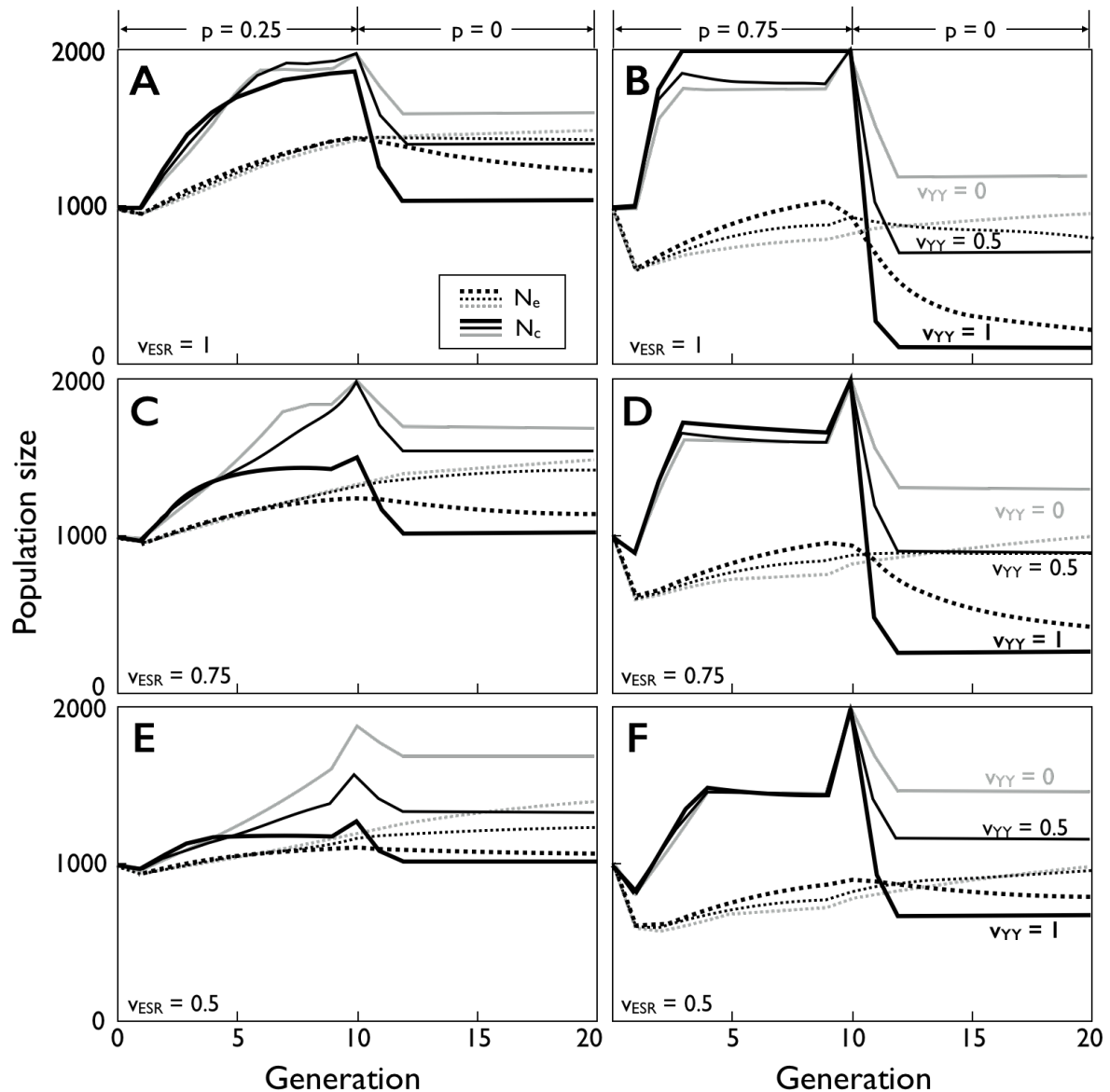
690 \*before possible further sex reversal



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**Figure 1. Illustrating the continuum of genetic and environmental sex determination.**

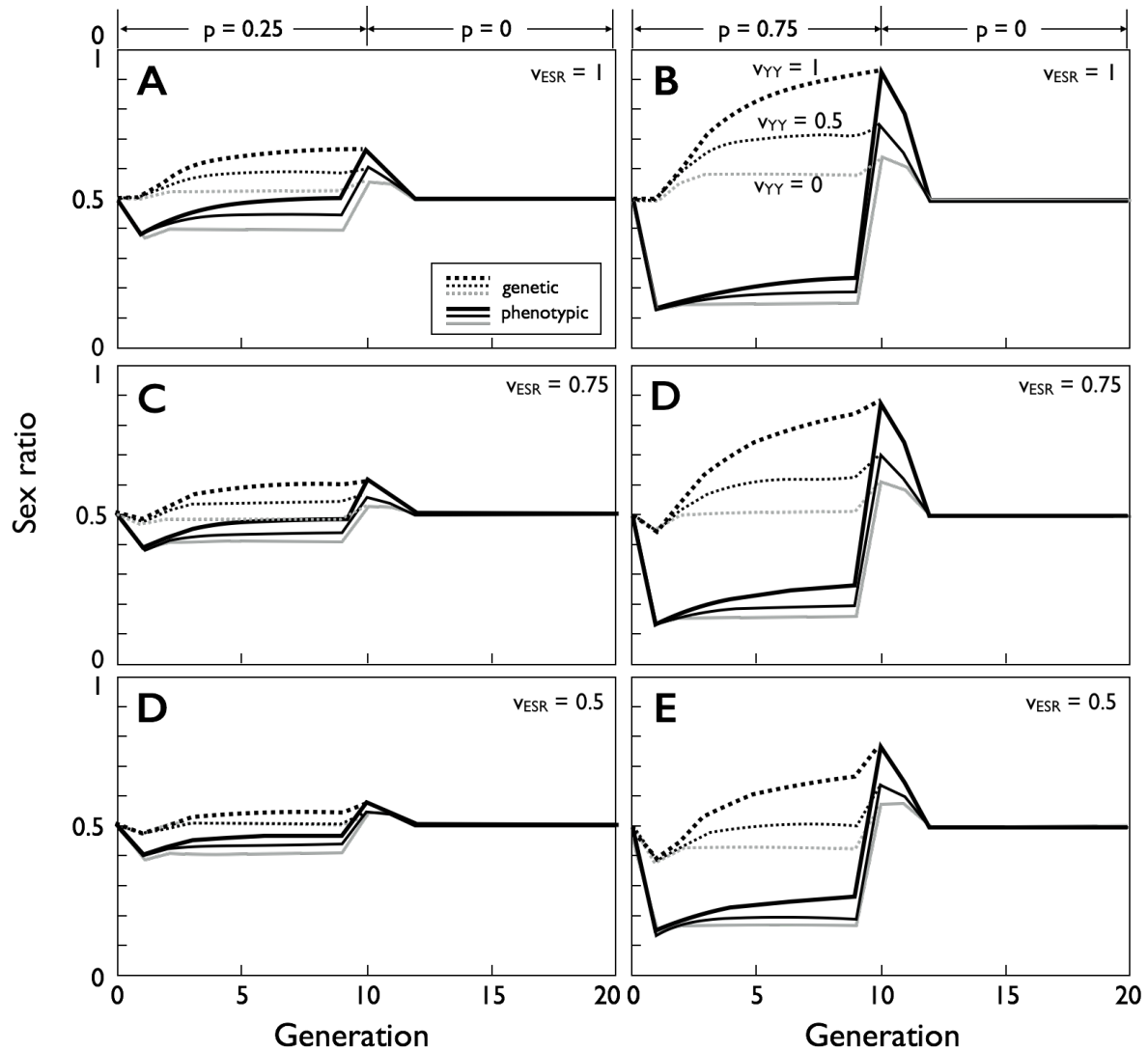
Examples of possible effects of environmental factors (e.g. temperature or concentration of endocrine-disrupting micropollutants) on sex determination in (A) a hypothetical population with genetic sex determination and the female genotype being susceptible to environmental factors that masculinize (i.e. turning some XX or ZW individuals into males), and (B) a population with genetic sex determining factors and the male genotype being susceptible to environmental factors that feminize (i.e. turning some XY or ZZ individuals into females). The shaded area indicates the within-population variance that could be due to additive genetic variance in the reaction norms or due to random effects at the start of the sex determination cascade. The hatched line gives the population sex ratio (proportion of males) if all clutches experience the same environmental conditions. This population sex ratio will equal adult sex ratio (ASR) if there is no sex-specific mortality.



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**Figure 2. The effects of environmental feminization and various types of fitness reduction on population size and genetics**

Low fitness of YY genotypes ( $v_{YY}$ ) can significantly mitigate the negative long-term effects of feminization when sex reversal ceases. Low  $v_{YY}$  can also produce positive effects on population growth during feminization, especially at low rates and high costs of feminization. The figure shows the population census sizes  $N_c$  (non-hatched lines) and the genetically effective population sizes  $N_e$  (hatched lines) when sex reversal (here only feminization, i.e.  $q = 0$ ) causes no fitness reduction ( $v_{ESR} = 1$ ; panels A and B) or fitness reductions of  $v_{ESR} = 0.75$  (panels C and D) or  $v_{ESR} = 0.5$  (panels E and F). Feminization is either weak ( $p = 0.25$ ; panels A, C, and E) or strong ( $p = 0.75$ ; panels B, D and F) during the first 10 generations ( $q$  always = 0). Feminization ceases from generation 10 on ( $p = 0$ ). The aberrant YY karyotype either causes no additional fitness reduction ( $v_{YY} = 1$ ; thick black lines) or a fitness of  $v_{YY} = 0.5$  (thin black lines) or  $v_{YY} = 0$  (thin gray lines). See Box 1 for the settings of the model.



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723 **Figure 3. The effects of environmental feminization and various types of fitness**  
 724 **reduction on phenotypic and genetic sex ratio**

725 Feminization reduces the proportion of phenotypic males while it increases the proportion of  
 726 genetic males. Both effects are dependent on the fitness of YY genotypes ( $v_{YY}$ ). Low  $v_{YY}$  can  
 727 significantly reduce the proportion of genetic males, especially so at high rates of  
 728 feminization. The figure shows the phenotypic population sex ratio (proportion of males; non-  
 729 hatched lines) and the genetic sex ratio, i.e. the rate of individuals with Y chromosomes  
 730 (hatched lines). The parameter setting are as in Fig. 2, i.e. the fitness effect of sex reversal is  
 731 either  $v_{ESR} = 1$  (panels A and B),  $v_{ESR} = 0.75$  (panels C and D), or  $v_{ESR} = 0.5$  (panels E and F),  
 732 feminization is either weak ( $p = 0.25$ ; panels A, C, E) or strong ( $p = 0.75$ ; panels B, D, F)  
 733 during the first 10 generations, feminization ceases from generation 10 on ( $p = 0$ ), and the  
 734 aberrant YY karyotype has a fitness of either  $v_{YY} = 1$  (thick black lines),  $v_{YY} = 0.5$  (thin black  
 735 lines), or  $v_{YY} = 0$  (thin gray lines).

736 **Supplementary Material**

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738 **Demographic and genetic consequences of disturbed sex determination**

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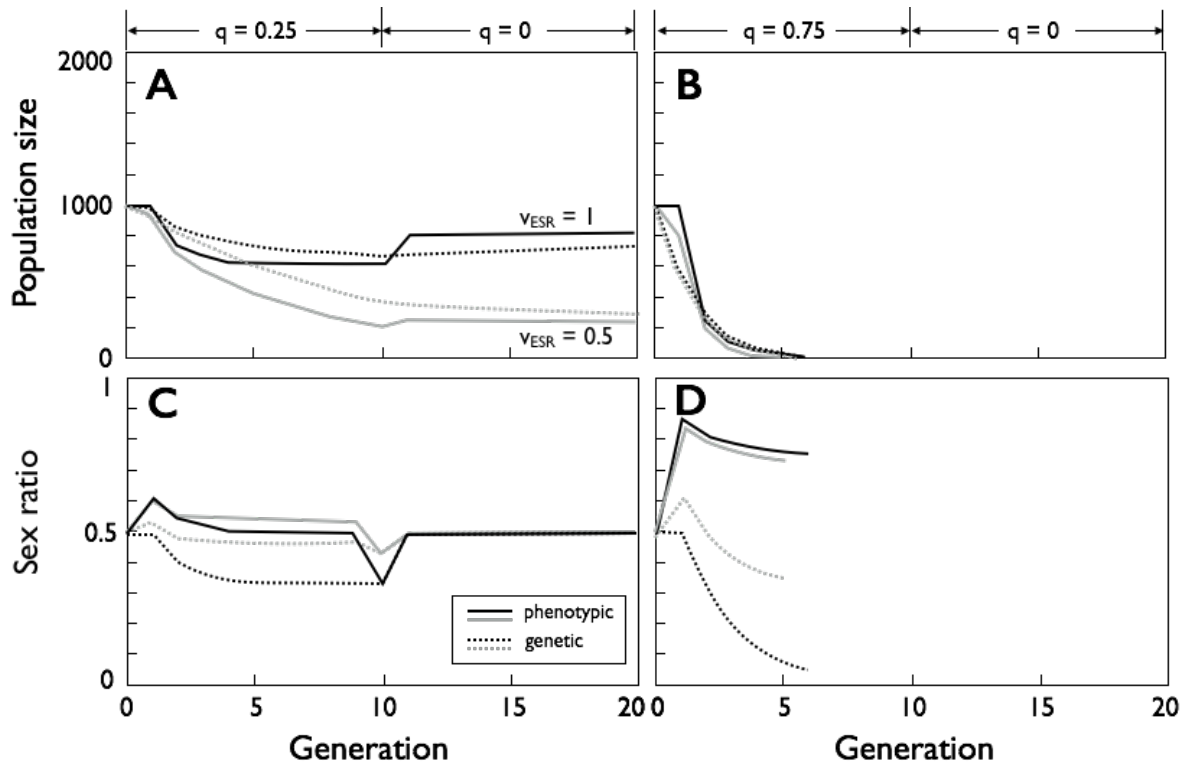
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748 **Supplementary Figure S1. The effects of environmental masculinization on demography**  
 749 **and genetics.**

750 The population size (panels A and B) as census sizes  $N_c$  (non-hatched lines) and effective  
 751 sizes  $N_e$  (hatched lines), and the population sex ratios (panels C and D) when  $v_{ESR} = 1$  (black  
 752 lines) or  $v_{ESR} = 0.5$  (grey lines), and when masculinization is weak ( $q = 0.25$ ; panels A and C)  
 753 or strong ( $q = 0.75$ ; panels B and D) during the first 10 generations. Masculinization ceases  
 754 from generation 10 on ( $q = 0$ ). Panels C and D give the phenotypic sex ratio (proportion of  
 755 males; non-hatched lines) and the genetic sex ratio, i.e. the rate of individuals with Y  
 756 chromosomes (hatched lines). All other parameters are set as in Fig. 2 (but  $p = 0$ ).