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Authors: Wedekind C.

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Demographic and genetic consequences of disturbed sex determination

Claus Wedekind
Department of Ecology and Evolution, Biophore, University of Lausanne, 1015 Lausanne, Switzerland
claus.wedekind@unil.ch

Abstract

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

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

1. Introduction

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

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

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

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

2. Sex determination in disturbed and undisturbed environments

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

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

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

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

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

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

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

3. Relevance of different mating types after disturbed sex determination

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

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

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

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

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

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

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

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

4. Demographic and genetic consequences of phenotype-genotype mismatches

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

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

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

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

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

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

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

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

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

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

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

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

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

6. Rapid evolutionary responses to environmentally disturbed sex determination?

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

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

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

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

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

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

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

7. Conclusions and implications for conservation and pest management

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

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

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

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

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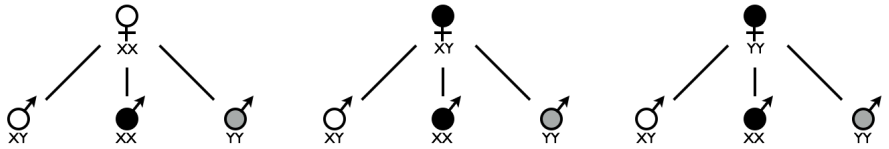
Box 1: Settings of the model

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

The effects environmental feminization and a ceasing of sex reversal are then analyzed with regard to the population census sizes (N_c) and the genetically effective population sizes (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 effects of variation of population size over time, e.g. of population bottlenecks, by using the harmonic mean each over all N_e since generation 0 [57].

Table 1 Mating types with XY sex determination and environmental sex reversal

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

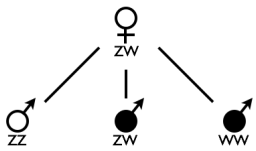
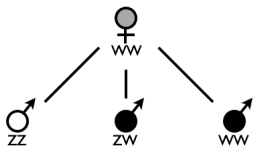
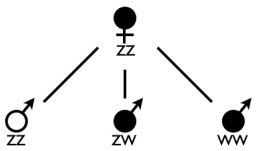


Frequency of										
	♀ XX	50%	100%	0%	25%	50%	0%	0%	0%	0%
	♂ XY	50%	0%	100%	50%	50%	50%	50%	100%	0%
	♂ YY	0%	0%	0%	25%	0%	50%	50%	0%	100%
	Y-chromosomes	25%	0%	50%	50%	25%	75%	75%	50%	100%
	male phenotype*	50%	0%	100%	75%	50%	100%	100%	100%	100%
	Mating scenario	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)

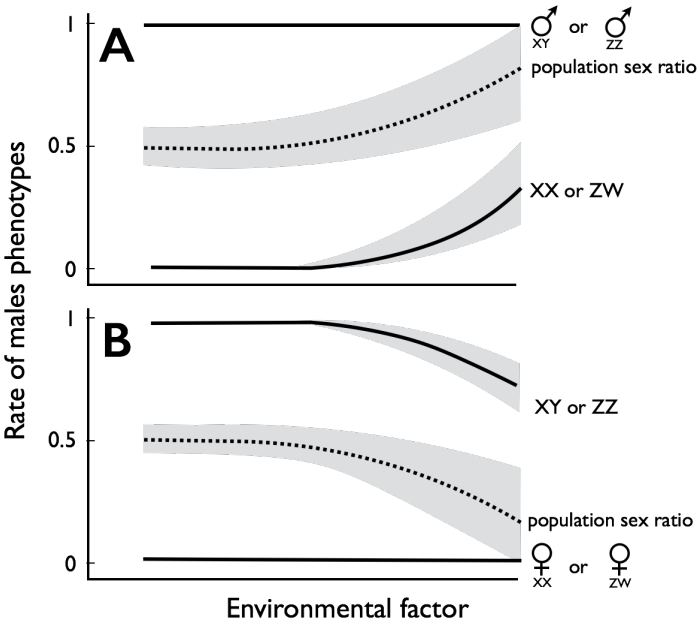
*before possible futher sex reversal

Table 2 Mating types with ZW sex determination and environmental sex reversal

The expected consequences of all possible mating types in a ZW sex determination system, analogous to Table 1 (assuming that the WW genotype naturally leads to the female phenotype, i.e. sex reversal is necessary to produce WW males). See text for a discussion of the mating scenarios.

		Mating type								
										
		♂ZZ	♀ZW	♂WW	♂ZZ	♀WW	♂WW	♂ZZ	♀ZZ	♂WW
Frequency of	♂ZZ	50%	25%	0%	0%	0%	0%	100%	50%	0%
	♀ZW	50%	50%	50%	100%	50%	0%	0%	50%	100%
	♀WW	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)

*before possible futher sex reversal



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692
693 **Figure 1. Illustrating the continuum of genetic and environmental sex determination**.
694 Examples of possible effects of environmental factors (e.g. temperature or concentration of
695 endocrine-disrupting micropollutants) on sex determination in (A) a hypothetical population
696 with genetic sex determination and the female genotype being susceptible to environmental
697 factors that masculinize (i.e. turning some XX or ZW individuals into males), and (B) a
698 population with genetic sex determining factors and the male genotype being susceptible to
699 environmental factors that feminize (i.e. turning some XY or ZZ individuals into females).
700 The shaded area indicates the within-population variance that could be due to additive genetic
701 variance in the reaction norms or due to random effects at the start of the sex determination
702 cascade. The hatched line gives the population sex ratio (proportion of males) if all clutches
703 experience the same environmental conditions. This population sex ratio will equal adult sex
704 ratio (ASR) if there is no sex-specific mortality.

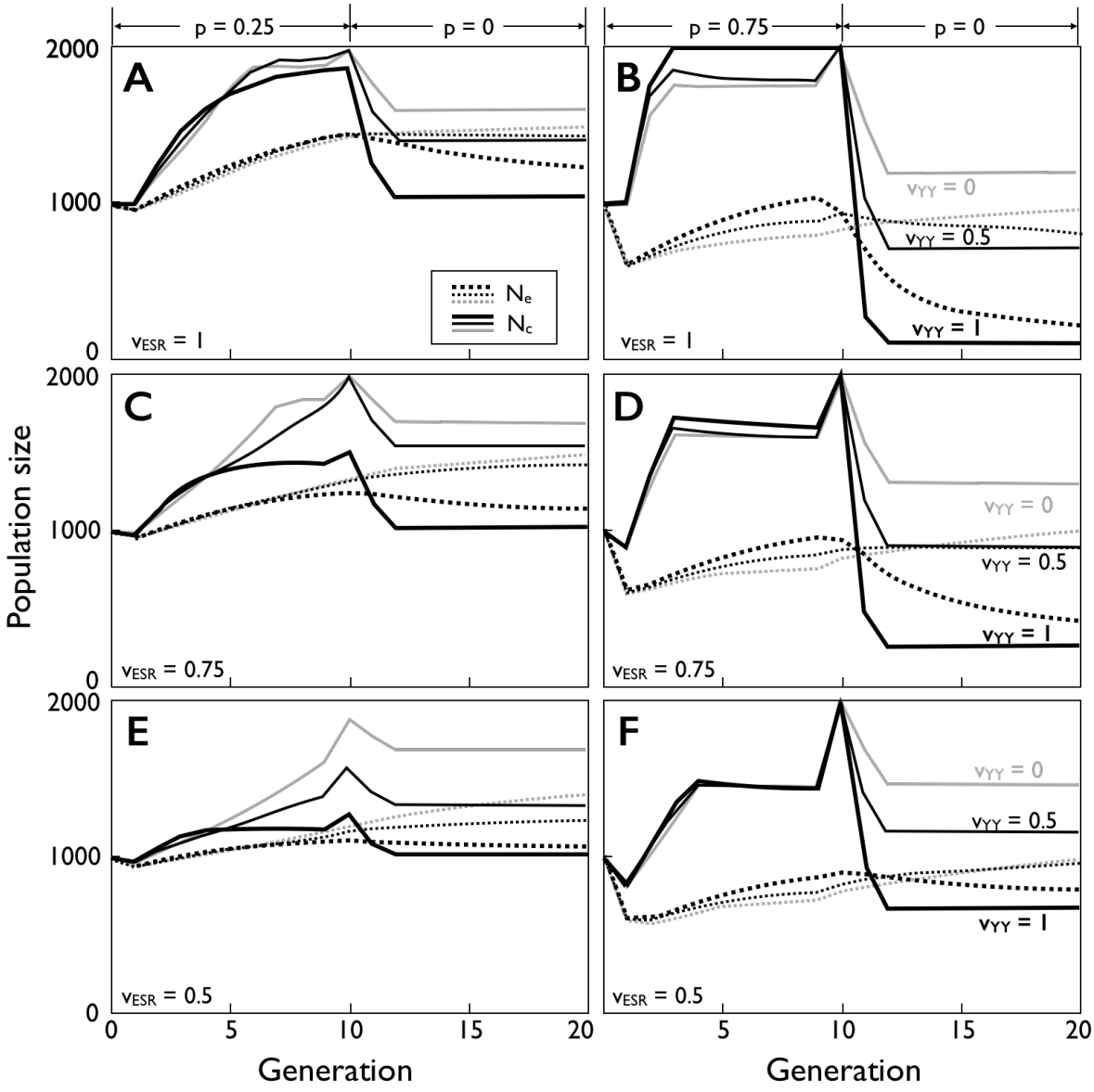


Figure 2. The effects of environmental feminization and various types of fitness reduction on population size and genetics

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.

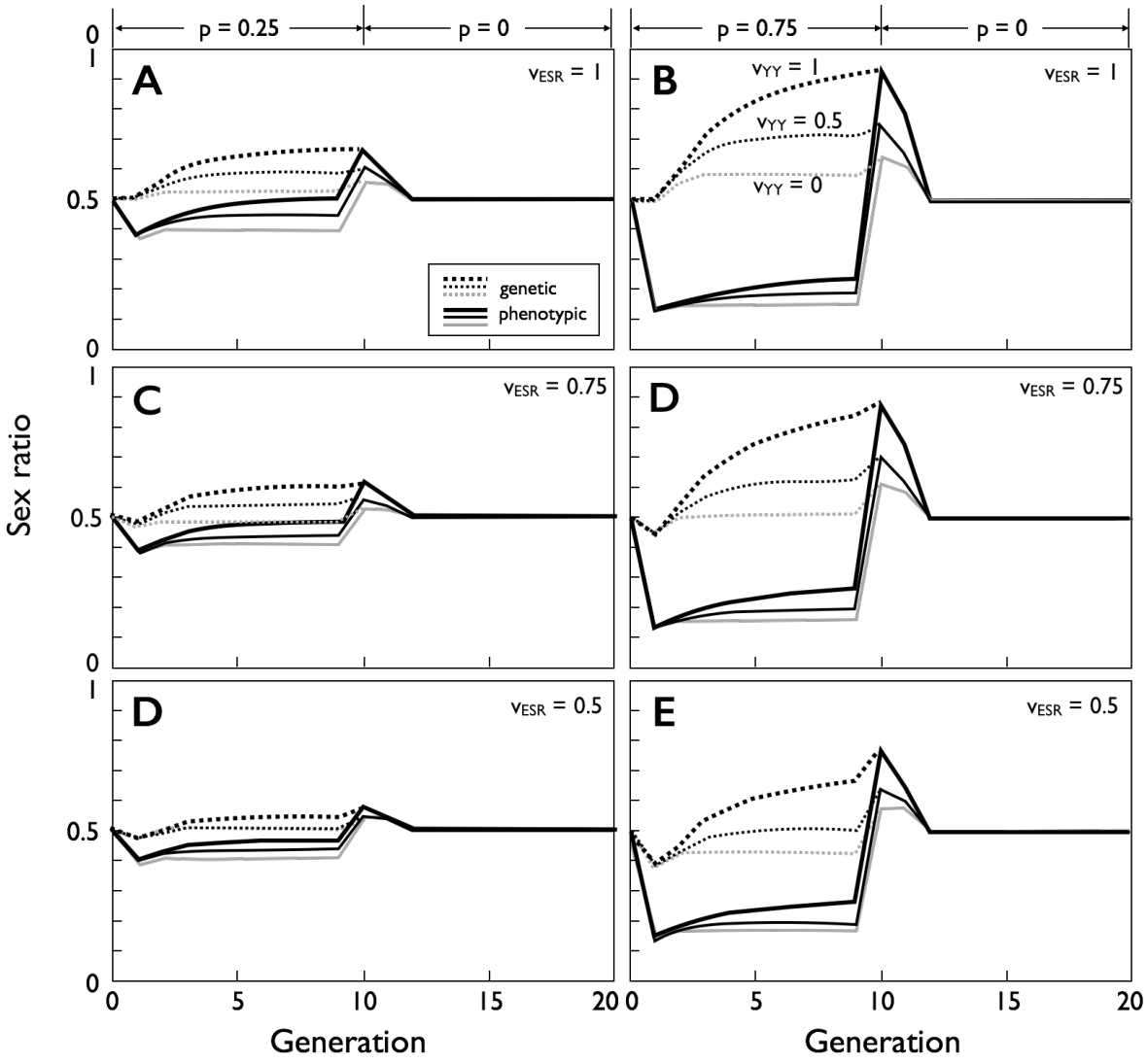


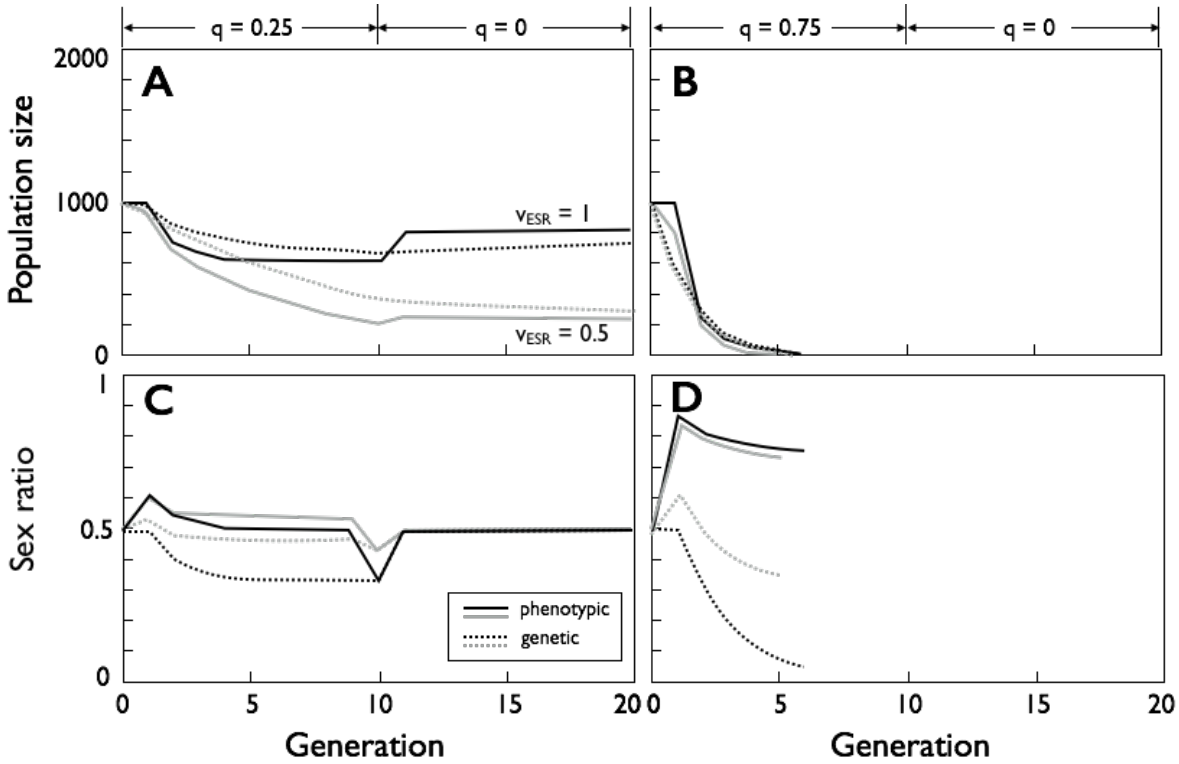
Figure 3. The effects of environmental feminization and various types of fitness reduction on phenotypic and genetic sex ratio

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

Supplementary Material

Demographic and genetic consequences of disturbed sex determination

Claus Wedekind
Department of Ecology and Evolution, Biophore, University of Lausanne, 1015 Lausanne, Switzerland; claus.wedekind@unil.ch



Supplementary Figure S1. The effects of environmental masculinization on demography and genetics.
The population size (panels A and B) as census sizes N_c (non-hatched lines) and effective sizes N_e (hatched lines), and the population sex ratios (panels C and D) when $v_{ESR} = 1$ (black lines) or $v_{ESR} = 0.5$ (grey lines), and when masculinization is weak ($q = 0.25$; panels A and C) or strong ($q = 0.75$; panels B and D) during the first 10 generations. Masculinization ceases from generation 10 on ($q = 0$). Panels C and D give the phenotypic sex ratio (proportion of males; non-hatched lines) and the genetic sex ratio, i.e. the rate of individuals with Y chromosomes (hatched lines). All other parameters are set as in Fig. 2 (but $p = 0$).