Sexual antagonism can explain why major-effect sex determining genes are zygotically and not maternally expressed

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In species for which sex is determined by a single gene or chromosome, sex may be determined either by zygotic or maternal expression of a gene. The zygotic case, with XY males and XX females or ZZ males and ZW females, is widely known; the maternal case, for instance with Z'W' and Z'Z' females producing all daughters and all sons, respectively, is much less familiar. This difference in familiarity reflects difference in incidence: the many known cases of single-locus sex determination (slSD) are dominated by zygotic effect genes. This imbalance exists despite apparent selection in many lineages for mothers to determine the sex of their offspring. While previous models convincingly show an advantage for zygotic slSD under many circumstances, under many other cases, including local research enhancement or sex differences in optimal rearing conditions, maternal slSD is expected to be favored. Thus the remarkable general dominance of zygotic slSD remains unexplained. This manuscript provides three contributions. First, I note that some previous arguments for split sex broods are more limited in scope than is widely appreciated; these models thus cannot explain the general lack of maternal slSD. Second, I note that under standard assumptions for the spread of a novel slSD alleles, maternal slSD alleles but not zygotic slSD are expected to be ultraselfish, increasing the fitness of the offspring to which they are transmitted but reducing the total fitness of the mother's brood. Thus the dearth of maternal slSD systems across nature may reflect the difficulty of initial establishment of maternal slSD. Third, I consider the subsequent evolution of an established maternal slSD system. I show that under maternal slSD, accumulation of sexually antagonistic linked mutations is expected to lead to suboptimal sex determination for many progeny, driving selection for modifiers. I consider the fates of various classes of potential modifiers and discuss the variety of paths by which maternal slSD is expected to evolve into zygotic slSD. I note that this model predicts the observed concentration of maternal slSD in species with paternal genome elimination and discuss the implications of the model.

1. Introduction

The genomic era has brought a wealth of knowledge about the mechanisms of sex determination across animals and plants (Bachtrog et al. 2014; Charlesworth 2019; Capel et al. 2017). Particularly large strides have been made in understanding the diversity of single-locus sex determination (slSD) – that is, loci whose expression leads with high penetrance to development as one sex, rather than instances of probabilistic, polygenic, or facultative sex determination. This work has revealed an

unappreciated diversity of mechanisms and inheritance patterns and shown a remarkable dynamism of sex determination, with turnover of the loci responsible for sexual expression within genera and sometimes within populations (Dubendorfer et al. 2003; Liew and Orbán 2014; Peichel et al. 2004). These studies have also revealed additional axes of diversity of sex determination, including the extent of the sex-linked region (from a single nucleotide difference to the entire X and Y chromosomes), as well as the number of genes involved in sex determination present in the locus (from the single-locus case of mammalian SRY to the multi-gene mechanism of *Drosophila;* Bachtrog et al. 2014).

Even while detailing this exuberance of mechanisms and evolutionary turnover, these studies have underscored a remarkable rarity of one mode of sex determination: single locus sex determination through maternal expression of a gene (maternal slSD) (Vitagliano et al. 1996; Juchault and Legrand 1989; Tabadkani et al. 2011; Stuart et al. 1991). That is, nearly all described cases of slSD involve zygotic gene action, with XX or ZW females and XY or ZZ males (Figure 1a,b) . Nearly no cases resemble the case seen in hessian fly, wherein presence or absence of a dominant allele in mothers (Z'W') leads to production of all daughters (Figure 1c) or all sons (Z'Z' mothers) (Stuart et al. 1991), or the hypothetical case in which presence or absence of a dominant allele leads a mother to produce all sons (X'Y') or all daughters (X'X') (Figure 1d). The dearth of known cases of simple maternal slSD is all the more striking given a readily observable expected phenotype: monogenic (single-sex) broods. Indeed, known cases of monogenic broods appear to be largely limited to species with otherwise atypical genetics, including two families of dipteran flies that undergo paternal genome elimination, haplodiploid species, species harboring feminizing endosymbionts, and armadillos, the last of which produce broods of genetically-identical quadruplets. The only exception of which I am aware is in blowflies, the full understanding of which awaits further investigation (Ullerich 1975). This dearth of maternal slSD stands both in striking contrast to both the wealth of zygotic slSD as well as to abundant evidence for smaller effect maternal alleles that adjust the probability of male versus female sex determination, for instance alleles that affect temperature sensitivity under environmental temperature-dependent sex determination and alleles that that facilitate facultative adjustment of offspring sex (e.g., Butka et al. 2019; Duffy et al. 2015; Richardson et al. 2014).

The absence of maternal slSD loci lies in contrast to a wealth of theoretical and empirical support for selection on mothers to control offspring sex (West 2009). Indeed, the active and storied field of sex ratio evolution, which has been called the most successful field of evolutionary biology, is largely focused on maternal control of sex ratios (West 2009). Proposed and empirically supported causes of selection for maternal control of offspring sex include female bias under inbreeding, biasing towards or away from the sex more likely to help the mother, biasing towards or away from the sex with higher variance in fitness based on maternal condition, biasing towards the sex best fit to the local environment, production of sex-biased

cohorts under within-sex cooperation, and many others (West 2009; Werren et al. 1998; Uller 2006).

Several previous theoretical arguments have been put forward to explain the lack of maternal slSD. Among early commenters, Verner (1965) argued that selection favored a strategy of equal sex ratios within broods, and Taylor and Sauer (1980) took this further to argue that exact equality of sex ratios is favored over random production of sex ratios. Both of these ideas argue for maternal control of sex ratio even while arguing against the monogenic broods produced by slSD maternal control. However, as I show here, the strength of both of these arguments rests on the assumption of partial inbreeding; in the absence of inbreeding, the former argument does not support either maternal or zygotic slSD over the other, while the latter in fact predicts the evolution of maternal slSD.

More recently, Werren (2002) showed that zygotic sex determination is expected to outcompete maternal sex determination under a variety of conditions, and Uller et al. (2007) emphasized the generality of these arguments. These arguments do indeed predict a preponderance of zygotic slSD under a wide variety of conditions in which relatives interact, including local mate or resource competition. However these cases are not entirely general. Studies of organisms in the wild indicate that there exist many conditions under which the above conditions do not apply. These include: (i) local resource enhancement through cooperation between same-sex siblings (Packer and Pusey 1987; Varndell and Godfray 1996; West 2009); (ii) sex differences in effects of environmental parameters on early development of males and females, such that production of monogenic but not split broods could allow adjustment of offspring microenvironment to optimal development (e.g., Navara 2018); and (iii) selection for inbreeding avoidance (Pusey 1987; Freeman 1997). Given that such conditions seem likely to apply to a wide variety of taxa, previous arguments fail to explain the general dearth of maternal slSD.

Here, I provide a new model to explain the dominance of zygotic slSD over maternal slSD. I first revisit the early arguments that have been taken as support for the general evolution of split sex ratios and show that: (i) these models, like Werren's (2002), depend on an assumption of local mating; and (ii) in the absence of local mating, the argument of Taylor and Sauer (1980) in fact supports the evolution of either zygotic or maternal slSD. I then develop a new argument for the preponderance of zygotic slSD. I first show that at the time of invasion of the population, newly-arising slSD alleles are ultraselfish from the perspective of the mother, leading to selection for suppressors of slSD function, which could explain why slSD systems do not frequently evolve. I then consider evolution of established slSD systems. I show that ongoing accumulation of sexually antagonistic alleles leads to selection for a variety of modifiers of the maternal slSD system, and discuss a variety of likely evolutionary pathways from maternal slSD to zygotic slSD systems. Finally, I point out that that the main exceptional case, Z'W' systems in species with paternal genome elimination, are not expected to experience the

described sexual antagonism dynamics, which could help to explain why these lineages are exceptional.

2. Results

2.1 Reconsideration of earlier arguments for split sex broods

Fisherian population-wide sex ratio balance needn't imply within-brood balance, as balance could also be achieved through a wealth of scenarios including equal numbers of male and female monogenic broods. However, Verner (1965) used an example with five mothers to argue that mothers producing equal sex ratio broods have a selective advantage. Taylor and Sauer (1980) then derived general equations to argue further that mothers producing precisely equal sex ratios (i.e., with variance less than expected from a binomial distribution) would have an advantage over mothers in which offspring sex is independent and thus binomially distributed.

Discussion of the power and limits of these arguments will be aided by deriving the general fitness of various mothers under their assumpations. Consider a population consisting of some number of breeding populations, each consisting of Mn individuals descended from M mothers each of whom produced n offspring, and which will yield M dispersing, mated females. We consider the various potential strategies of a focal female carrying a rare allele that causes her to play a novel strategy. We assume each of the other contributing mothers produce a sex ratio with an average of 0.5 and a variance of v (with no assumptions about the magnitude of v). We denote the probability that the M-1 non-focal mothers produce a fraction of males of r as $p(r)$ and the probability that the focal mother produces a sex ratio of r_f as $p_f(r_f)$. Thus exactly 1:1 ratio corresponds to $p_f(0.5) = 1$, and the case of all female broods corresponds to $p_f(0) = 1$. The overall sex ratio r_{tot} is thus distributed as $\left((M-1)p(r) + p_f(r_f)\right)/M$, giving average fitness for sons and daughters of:

$$\omega_s(r, r_f) = \frac{0.5}{\left((1 - 1/M)p(r) + (1/M)p_f\left(r_f\right)\right)}$$

and

$$\omega_d(r, r_f) = \frac{0.5}{1 - \left((1 - 1/M)p(r) + (1/M)p_f\left(r_f\right)\right)}$$

respectively. The average fitness for offspring of our focal female is thus:

$$\int_0^1 \int_0^1 p(r)p_f\left(r_f\right)\left(r\omega_s\left(r, r_f\right) + (1-r)\omega_d(r, r_f)\right)drdr_f$$

For the case where the focal female produces exactly equal numbers of daughters and sons,

$$\omega_s(r, 0.5) = \frac{0.5}{\left(\left(1 - \frac{1}{M}\right)r + \frac{0.5}{M}\right)} \approx \frac{0.5}{M} + \frac{0.5}{r}\frac{1}{(1 - 1/M)}$$

and

$$\omega_d(r, 0.5) \approx \frac{0.5}{M} + \frac{0.5}{(1-r)}\frac{1}{\left(1 - \frac{1}{M}\right)}$$

Whereas for females who produce only daughters the values are

$$\omega_s(r, 0.5) = \frac{0.5}{\left(\left(1 - \frac{1}{M}\right)r + \frac{0.5}{M}\right)} \approx \frac{0.5}{r}\frac{M-1}{M}$$

and

$$\omega_d(r, 0.5) \approx \frac{1}{M} + \frac{0.5}{(1-r)}\frac{M-1}{M}$$

Thus for mothers that produce precisely equal numbers of males and females the average offspring fitness is:

$$\int_0^1 \int_0^1 p(r)p_f(r_f)\left(r\omega_s(r,r) + (1-r)\omega_d(r,r)\right)dr dr_f$$
$$= 0.5\int_0^1 p(r)\frac{M-1}{M}\left(r_f\left(\frac{0.5}{r}\right) + \left(1 - r_f\right)\left(\frac{0.5}{1-r}\right)\right)dr$$

Assuming the sex ratio distribution for non-focal individuals (r) is symmetrical around 0.5, and defining $q(e) = p(0.5+e)$, this is

$$0.5\frac{M-1}{M}\int_0^1 q(e)\left(r_f\left(\frac{0.5}{0.5+e}\right) + \left(1 - r_f\right)\left(\frac{0.5}{0.5-e}\right)\right)de$$

Becaues q is symmetrical, this is equal to

$$0.25\frac{M-1}{M}\int_0^1 q(e)\left(r_f\left(\frac{0.5}{0.5+e}+\frac{0.5}{0.5-e}\right)+(1-r_f)\left(\frac{0.5}{0.5-e}+\frac{0.5}{0.5+e}\right)\right)de =$$

$$0.25\frac{M-1}{M}\int_0^1 q(e)\left(r_f\left(\frac{2}{1+4e^2}\right)+(1-r_f)\left(\frac{2}{1+4e^2}\right)\right)de$$

$$\approx 0.5\frac{M-1}{M}\int_0^1 q(e)\,(1+4e^2)de = 1+v\frac{M-1}{M}$$

A similar train of thought leads to values for females producing monogenic broods (either all sons or all daughters) of

$$1-\frac{1}{M}+v\frac{M-1}{M}$$

These values are to be compared to average offspring fitness values of for a focal female that produces the same distribution of sex ratios as the non-focal females, which is necessarily 1 by symmetry. Thus, as previously emphasized by Taylor and Sauer (1980), a female producing exactly equal broods benefits by a positive value close to the variance in the sex ratio across generations or breeding subpopulations produced by wildtype females. However, this cannot be extended to a general argument for equal sex ratios across broods since, when *M* is large, females producing monogenic broods benefit by an equal amount as do females producing strictly equal sex ratios. Of course, as a monogeic allele rises in frequency, it will be subject to increased costs due to skewed sex ratio; however this is also the case for zygotic slSD alleles, and thus is not a clear argument for split brood ratios over monogeny. In addition, these results clarify Verner's example of $M = 5$, under which the cost of producing skewed broods is indeed expected to be large ($s = 0.2$ for monogenic broods).

In general, the fitness differential relative to wildtype experienced by mothers producing monogenic broods may be understood as a tradeoff between: (i) the fact that having one's siblings be the same sex as oneself biases the local sex ratio against oneself; and (ii) the fact that lack of covariance with the population sex ratio in fact produces an overall advantage. The latter point is due to the fact that individuals benefit more when they are rare the rare sex than they suffer when they are the common sex, due to the simple fact that $1/(2+x) + 1/(2-x) > 1$). By noting that $1/M$ is the fraction of individuals that one encounters that are one's siblings, we can see that this deficit of $1/M$ in fact resonates with previous general discussions of monogenic broods: alleles producing monogenic broods suffer insofar as competitive interactions occur between relatives (Werren 2002; Uller et al. 2007).

The above indicates that previous arguments taken to support generally split sex broods are more limited than previously noted, and that the previous arguments

only apply insofar as there is competition between siblings, as noted more recently by Werren.

2.2 Newly-arising maternal slSD alleles are ultraselfish, driving selection for suppressors

Let us turn now to the evolution of slSD genes acting at the maternal or zygotic levels. The origins of novel sex determining genes may be seen as a puzzle. Beginning with an even sex ratio, spread of a gene that biases offspring sex ratio is expected to bias population sex ratio in the exact direct that selects against the spreading gene: for example, spread of a male determinant leads to increased production of males, leading to decreased fitness of males, including those carrying the gene (Rice 1987).

The most influential solution to this puzzle posits that novel sex determining genes often overcome this challenge by being linked to sexually antagonistic alleles, that is alleles that are beneficial in one sex and deleterious in the other (Rice 1987). Thus, novel sex determinating genes overcome skewed sex ratios because individuals carrying the novel SD gene and its linked SA mutations are more fit than are other individuals of the same sex. Let us call these linked pairs of mutations SD-SA alleles. Such SD-SA alleles can spread in the population until their spread has biased the population to the extent that this sex ratio-driven cost balances the sex-specific advantage of the alleles. If the SD-SA allele is at frequency p, the sex ratio is expected to be $0.5+p/2$, and the fitness of SD-SA-containing and individuals of the commoner sex is close to $\frac{1}{1+p}\frac{1+s}{1+sp} \approx 1+s-p$, predicting an equilibrium when the allelic frequency is close to the allelic benefit (Figure 2a).

Though more complex than the classic case of a beneficial allele, such SD-SA alleles retain the classic mode of allelic spread: they benefit by increasing the total fitness of parents that carry them, and then by increasing the total fitness of the offspring that inherit them (Table 1). Relative to wildtype mothers, mothers carrying the SD-SA allele either have higher fitness (when p is less than the equilibrium frequency) or equal fitness (at equilibrium). This can be seen in Figure 2b, where the fitness of mutant mothers (solid black line) is higher than that of WT mothers (solid gray line) when p is less than the equilibrium value. This may also be seen in the 'Zygotic' section of Table 1, which shows production of mutant-carrying and wildtype offspring of common and rare sex, individual offspring fitnesses, and mean offspring fitness for wildtype mothers and mothers heterozygous for the SD-SA allele (WT mom and MUT mom, respectively). Thus, when rare or at equilibrium SD-SA alleles either increase or do not affect maternal fitness. That is, they are selfish in the classic sense of Dawkins and so many others, but they do not meet the definition of ultraselfish, that is: they do not decrease the total fitness of parents that carry them by increasing the total fitness of the offspring that carry them (Burt and Trivers 2009).

What of the case of maternal slSD alleles? As is the case for zygotic SD alleles, in an ancestral population with even sex ratios, the spread of such alleles biases the population sex ratio against themselves. Thus maternal SD alleles are expected to spread only in the presence of some mitigating force. As in the case for zygotic SD, perhaps the likeliest possibility is linkage to a SA allele. Thus, novel sex determining genes overcome skewed sex ratios because individuals carrying the novel SD gene and its linked SA mutations are more fit than are other individuals of the same sex (Figure 2b). If the SD-SA allele is at frequency p, the sex ratio is expected to be $0.5+p$, and the fitness of SD-SA-containing and individuals of the commoner sex is close to $\frac{1}{1+2p}\frac{1+s}{1+sp} \approx 1 + s - 2p$, predicting an equilibrium when the allelic frequency is close to one-half the allelic benefit (Figure 2b). Note that the equilibrium value is lower for maternal slSD than for zygotic slSD, because maternal effect alleles determine the sex of twice as many offspring per copy (all offspring instead of only those carrying the allele), thus biasing the sex ratio by twice as much for a given p.

A crucial difference, however, comes when considering the total fitness of the parent (Figure 2b and 'Maternal' section of Table 1). When the allele is rare, population sex ratio is expected to be balanced. From a perspective of a mother heterozygous for the allele, half of her offspring have increased fitness from carrying the SD-SA allele, while the half that do not carry the SD-SA allele pay no cost since males and females have equal average fitness. Thus she has increased average offspring fitness relative to a wildtype female However, as the sex ratio becomes skewed through spread of the allele, the size of the benefit remains constant while the cost of producing the commoner sex increases. At equilibrium, the one-half of the offspring that inherit the SD gene have average fitness of 1, representing a balance between the fitness advantage of the linked SA alleles and the fitness cost of being the commoner sex. However the other half of the offspring now suffer from being the commoner sex without the benefit of the SA alleles. Thus, at equilibrium, mothers carrying the SD gene have lower fitness than those that do not. In general, the fitness of SD-SA-containing and –lacking individuals of the commoner sex are close to $\frac{1}{1+2p}\frac{1+s}{1+sp} \approx 1 + s - 2p$ and $\frac{1}{1+2p}\frac{1}{1+sp} \approx 1 - 2p$, thus the average fitness for offspring of an SD-SA-allele carrying mother is close to $\frac{1}{1+2p}\frac{1+s}{1+sp} \approx 1 + s/2 - 2p$, meaning that the mother benefits only when $p < s/4$, i.e., half of the equilibrium frequency. This can be seen in Figure 2b, where the fitness of mutant mothers (solid black line) is less than that of WT mothers (solid gray line) when p is more than one-half of the equilibrium value.

Thus, as the maternal SD-SA allele approaches equilibrium, selection will tend to drive the emergence of suppressors. The simplest and perhaps most feasible mechanism of suppression would be direct repression of activity of the SD gene in the mother's reproductive tract, leading to equal sex ratio for both SD-SA-containing and –lacking offspring. This has the effect of converting one-half of progeny of SD-SA mothers to the commoner sex. Upon conversion, offspring that do not carry the SD-SA allele are expected to have average fitness of $\frac{1}{1-2p} \approx 1 + 2p$, while those that

do carry the SD-SA allele are expected to have average fitness of $\frac{1}{1-2p}\frac{1+sf_{opp}}{1+sp} \approx 1 - sf_{opp} + 2p$, for an average of $1 - sf_{opp}/2 + 2p$. The mother benefits when this fitness is higher than the fitness in the absence of a suppressor, $1 - sf_{opp}/2 + 2p > 1 + s/2 - 2p$, yielding the condition $s(1+f_{opp})/2 < 4p$. At equilibrium, $p \sim s/2$, yielding the condition $f_{opp} < 3$ – that is, the suppressor provides a benefit so long as the SA's selective benefit in one sex is at least one-third its cost in the other. Thus, for many SA mutations, a suppressor is expected to invade the population, at which point the SD-SA allele carries a net disadvantage and is expected to be driven from the population.

Cases where $f_{opp} > 3$ provide an interesting case. In these cases, a direct suppressor is not expected to benefit, since the costs of producing highly unfit SD-SA-containing offspring of the 'wrong' sex outweighs the benefit of producing offspring of the rarer sex. Under these circumstances, zygotic-acting modifiers that increase the chance that specifically non-SD-SA-containing offspring develop as the rarer sex are expected to be favored. I consider the various evolutionary trajectories under this case in detail below.

The above considerations suggest that the evolution of maternal slSD systems may often be thwarted in their initial stages. However, another possibility is that the skewed sex ratio selects for a complementary SD mutation elsewhere in the genome that causes production of the rarer sex. As this second mutation rises in frequency in the population the threshold for selection for suppressors ($s(1+f_{opp})/2 < 4p$) could be passed, in which case suppressors are not expected to be favored. In this case, the two complementary SD alleles could spread in the population, under conditions identical (or nearly so) to the case for zygotic slSD discussed previously (REF), leading to an established sex maternal slSD system.

2.3 Fitness of various individuals under established maternal slSD systems

I next consider the expected evolutionary trajectories of established maternal slSD, allowing for the possibility of sexually antagonistic alleles. First, I consider equilibrium populations in which mothers produce either all males or all daughters, and further subdivide the phenomenon into cases in which daughter production is dominant or recessive.

Forms of slSD and notation

I use the standard notation for zygotic slSD systems, namely either XX females and XY males or ZW females or ZZ males. As is the case of zygotic slSD, maternal slSD can take on two forms. The daughter-producing allele can be dominant over the son-producing allele (Z'W' and Z'Z' females produce all daughters and all sons, respectively) or the son-producing allele can be dominant (X'X' and X'Y' females produce all daughters and all sons, respectively.) (Figure 1). Note that I follow the

convention of using primes to indicate maternal effect, thus a W' is similar to a W except that whereas the presence of a W in the zygote to is associated with female development of the zygote, the presence of a W' in the mother is associated with female development of all offspring.

It is also of importance which chromosome expresses the gene product responsible for sex determination. In the simplest case, it is expected that sex is determined by gene products from one of the alleles (e.g., either the W' or Z') but not both, as is the case for characterized zygotic slSD systems. Thus for both Z'W'/Z'Z' and X'Y'/X'X' systems, the active allele is either the dominant (W'/Y') or recessive (Z'/X') allele, assumed to be a product maternally deposited in all eggs (recall that 'dominance' is a description of the genotype-phenotype map and a separate issue from which chromosome encodes the SD gene product – thus the Y' is the dominant allele regardless of whether the X' or Y' encodes the SD gene). Thus when the SD gene is on the dominant chromosome sex is determined by presence/absence of gene expression while in the recessive system sex is determined by amount of gene expression, in the simplest case. I refer to the chromosome on which the SD gene resides as the X'-, Y'-, Z'- or W'-linked cases. An illustration of these cases is shown in Figure 3.

Sex-biased transmission, sexually antagonistic selection and the production of unfit offspring

For a Z'W' system, at equilibrium we expect even sex ratios with equal numbers of Z'W' and Z'Z' females and all Z'Z' males, meaning that the W' allele is always transmitted through females while the Z' allele is transmitted through males 4/7 of the time (Figure 1c). For a X'Y' system, at equilibrium we expect even sex ratios with equal numbers of X'Y' and X'X' females and a 1:2:1 ratio of X'X', X'Y' and Y'Y' males, meaning that Y' alleles are transmitted through males 2/3 of the time while x' alleles are transmitted through females 3/5 of the time (Figure 1d).

Because of their strongly biased transmission, the dominant allele (W' or Y') is expected to accumulate sexually antagonistic alleles, namely alleles that are beneficial in one sex and deleterious in the other. In a Z'W'/Z'Z' system, female-beneficial sexually antagonistic (SA) mutations tightly linked to the W' allele experience increased fitness every generation and may rapidly fix (slightly male-biased SA alleles linked to the Z' allele may also fix). Similarly, in a X'Y'/X'X' system, SA mutations tightly linked to the Y' will experience increased average fitness so long as the benefit in males is more than one-half the cost in females; SA mutations tightly linked to the X' will experience increased average fitness so long as the benefit in females is more than two-thirds the cost in males. The expected consequence of these dynamics is the accumulation of SA mutations at the slSD locus (Figure 3).

Deviations from the optimal genotype-phenotype map under maternal slSD

As a consequence of accumulation of linked SA mutations, at equilibrium and equal sex ratios, the fitness of individuals of a given genotype depends on sex. I use notation in which the dominant (W' or Y') allele imparts sex-specific fitness effects relative to the recessive allele (Z' or W'), which difference indicates the entire divergence between the alleles regardless of whether these represent changes on the dominant or recessive allele relative to the ancestral autosome. For notation, I use effect s subscripted by the sex (f/m) and chromosome (W/Y): s_{fW}, s_{mW}, s_{fY} *and* s_{mY}. Results are constructed such that s values are always positive. For a Z'W' system, at equilibrium Z'W' females and (hypothetical) males have fitnesses of $(1+s_{fW})/(1+s_{fW}/2)$ and $1-s_{mW}$, and Z'Z' females and males have fitnesses of $1/(1+s_{fW}/2)$ and 1. Thus Z'W' and Z'Z' individuals' fitness is optimized by female and male development, respectively, and the fitness effect of converting the sex of an individual is of a magnitude close to $s_{mW} - s_{fW}/2$ for Z'W' individuals and close to $s_{fW}/2$ for Z'Z' individuals (Table 1). For a X'Y' system, at equilibrium X'X' males and females have fitnesses of $1/(1+s_{mY})$ and $1/(1-s_{fY}/2)$, X'Y' females and males have fitness of $(1+ s_{mY})/(1+s_{mY})$ and $(1-s_{fY})/(1-s_{fY}/2)$, and Y'Y' males and (hypothetical) females have fitness of $(1+2s_{mY})/(1+s_{mY})$ and $(1-2s_{fY})/(1-s_{fY}/2)$. At equilibrium and for small s values, this is close to $1-s_{mY}$ and $1+s_{fY}/2$ for X'X', 1 and $1-s_{fY}/2$ for X'Y', and $1+s_{mY}$ and $1-3s_{fY}/2$ for Y'Y', respectively. Thus X'X' and X'Y' individuals' fitnesses are optimized by female and male development, respectively, and the fitness effect of converting the sex of an individual is of a magnitude close to $s_{mY}-s_{fY}/2$ for X'X' individuals, $s_{fY}/2$ for X'Y' individuals, and $3s_{fY}/2 + s_{mY}$ for Y'Y' individuals.

Under maternal slSD, then, many individuals' sexual expression leads to suboptimal reproductive fitness. This effect depends on maternal genotype, thus it is useful to introduce the following notation. Throughout, I use notation in which normal text represent offspring genotype, while superscript to represent maternal genotype and sex (F/M) under the slSD system. Thus for a Z'W' system we have three classes of offspring, namely $Z'Z'^{Z'Z'\text{-}M}$, $Z'Z'^{Z'W'\text{-}F}$ and $Z'Z'W'^{W'\text{-}F}$ and for an X'Y' system we have five classes of offspring, namely $X'Y'^{X'X'\text{-}F}$, $X'X'^{X'X'\text{-}F}$, $Y'Y'^{X'Y'\text{-}M}$, $X'Y'^{X'Y'\text{-}M}$ and $X'X'^{X'Y'\text{-}M}$. Thus, using this notation, in a Z'W' system, $Z'Z'^{Z'W'\text{-}F}$ females would benefit from instead developing as males. Under a X'Y' system, $X'X'^{X'Y'\text{-}M}$ males would benefit from converting to females, while $X'Y'^{X'X'\text{-}F}$ females would benefit from converting to males.

2.4 Evolution of modifiers of established slSD systems

This general dynamic of suboptimality in the genotype-phenotype map is expected to produce selection for a range of modifiers. Potential modifiers are diverse: they may be generally selected or may favor the mutation to the detriment of family fitness and thus be expected to attract suppressors (which may be complete or partial, general or conditional); they may be favored only when rare or favored generally; and they may produce selective environments that favor or disfavor and equally diverse array of secondary modifiers. Features of the alleles that may affect these dynamics include genomic location of the modifier (*cis* or *trans*), at which time expression is affected (maternal and/or zygotic), the magnitude of change in

expression, the dominance of the mutation, etc. It is difficult *a priori* to predict the rate of random occurrence of various types of mutations and thus to choose which possibilities to emphasize in this discussion. I have chosen to focus on some of the simplest and most intuitive possibilities, which may also be among the mutationally most accessible to evolution; however, the following is not intended to represent a comprehensive treatment. Below, I treat the four most intuitive cases for initial evolutionary changes in some depth – zygotic expression of the SD gene, altered maternal expression of the SD gene, zygotic degradation of the maternal product, and origins of a new SD locus.

Modifiers 1: Induction of zygotic expression by cis changes to the SD gene

The simplest potential solution to the genotype-phenotype mismatches would be increased expression of the SD gene in the zygote through a *cis* change in the SD gene. The simplest case is for a *cis* mutation at a W'-linked SD allele. Because W' alleles are only present in Z'W' females, zygotic expression of the W' product would not change the sex of any offspring and thus would not disrupt the Z'W' system. Thus *cis* modifiers are not expected to arise in a W'-linked SD case.

For a *cis* mutation at a Y'-linked SD allele that causes zygotic expression leading to masculinization (converting the Y' into a Y), the effect is simply to convert X'Y'$^{X'X'\text{-}F}$ individuals into males, which is expected to enjoy a benefit when rare because X'Y' males are more fit than X'Y' females at equilibrium. Such a mutation is expected to be able to invade a population, leading to equal numbers of X'Y' males and X'X' females, i.e. the features of a novel zygotic slSD system.

A *cis* mutation at a X'-linked SD allele that causes zygotic expression and thus feminization (converting the X' into a W) immediately becomes confined to females. The effect of such a mutation is to convert equal numbers of X'X'$^{X'Y'\text{-}M}$ and X'Y'$^{X'Y'\text{-}M}$ offspring into females, with a benefit close to $s_{fY}/2+s_{mY}$ and a cost close to $s_{fY}/2$, respectively, for an overall benefit of $s_{mY}/2$. Simulation indicate that such a mutation can rise in the population, displacing the ancestral X' allele and leading to an equilibrium with X'Y' females and Y'Y' males, thus producing a novel ZW system, with the novel W and Z chromosomes derived from the ancestral X' and Y' chromosomes, respectively.

A *cis* mutation at a Z'-linked SD allele that causes zygotic expression and thus masculinization (converting the Z' into a Y) immediately becomes confined to males. The effect of such a mutation is to convert equal numbers of Z'Z'$^{Z'W'\text{-}F}$ and Z'W'$^{Z'W'\text{-}F}$ offspring into males, with a benefit close to $s_{fW}/2$ and a cost close to s_{mW}, respectively. Thus the condition for invasion is $s_{mW} < s_{fW}/2$. Given its restriction to females, the W' chromosome is expected to be very poorly suited to presence in males for well-established Z'W' systems (i.e., s_{mY} is expected to be relatively large). In general, the distinctive feature of the W' haplotype is that mutations can fix there even when $s_{mW} >> s_{fW}$, thus it would be unlikely if the selective differences at this locus were dominated by mutations that could fix anywhere in the genome (since

autosomal mutations enjoy a net benefit when $s_m < s_f/2$). Thus zygotic expression-inducing *cis* mutations near a Z'-linked SD allele are unlikely to succeed.

In total, then, we expect maternal X'Y' systems to be vulnerable to invasion of *cis* changes that induce zygotic expression, with the SD-determining allele (X' or Y') being converted into the new dominant SD gene for the novel zygotic slSD system. By contrast, maternal Z'W' systems are not expected to be vulnerable to invasion of *cis* changes that induce zygotic expression.

Modifiers 2: Induction of zygotic expression of the SD gene by trans changes

The case for *trans* changes that lead to zygotic expression of the SD allele is somewhat different. For the W'-linked case, zygotic expression of the W' product does not change sex determination in any offspring, thus neither *cis* nor *trans* changes that alter W' expression are expected to be favored. For, the Y'-linked case, the *trans* case resembles the *cis* case: the effect is simply to convert X'Y'$^{X'X'\text{-F}}$ individuals into males. As the *trans* modifier allele rises in frequency, the Y' is expected to become confined to males (because most X'Y' offspring will develop as males regardless of parentage), eventually leading to equal numbers of X'Y' males and X'X' females, i.e. the features of a novel zygotic XY slSD system.

More consideration is necessary for the Z'- and W'-linked cases. For the Z'-linked case, *trans* changes of strong and dominant effect would lead to conversion of both Z'Z'$^{Z'W'\text{-F}}$ and Z'W'$^{Z'W'\text{-F}}$ individuals to males. As with the *cis* case above, the fitness cost to Z'W' males is expected to outweigh the fitness benefit to Z'Z' males, thus such a *trans* change cannot invade the population. However, a *trans* change with a subtler effect could potentially invade. If we can define m as the quantity of maternal product deposited in the egg for each copy of the gene, then the expected expression levels in zygotes are m and $2m$ for offspring of Z'W'/X'Y' females and m for offspring of Z'Z'/X'X' females. Thus the sex determination threshold must be at some intermediate level of $m(1+h)$. Under outbreeding, a rare change in *trans* leading to total expression levels of z per Z' allele would lead to expression levels of $m+2z$ and $m+z$ in Z'Z' and Z'W' offspring of Z'W' females, respectively. Such an allele can convert Z'Z'$^{Z'W'\text{-F}}$ but not Z'W'$^{Z'W'\text{-F}}$ offspring, thus enjoying benefits without costs, so long as $tm/2 < z < tm$. Such an allele is expected to be able to rise to high frequency in the population, leading to an equilibrium of equal numbers of Z'W' females and Z'Z' males – i.e., the phenomenon of simple zygotic slSD.

The case is similar for the X'-linked case: feminization of X'X' but not X'Y' males can be achieved for *trans*-specific changes of intermediate effect with the same conditions as above, leading to benefits without costs. As with the *cis* case, fixation of such a *trans* allele is expected to produce an equilibrium of equal numbers of X'Y' females and Y'Y' males, thus producing a novel zygotic ZW SD system.

In total, then, we expect maternal slSD systems to be vulnerable to invasion of *trans* changes that induce zygotic expression in three out of four cases, namely when the SD gene is on the X', Y', or Z' allele, but not when it is on the W' allele.

Modifiers 3: Changes in maternal expression of the SD gene

Another possible class of modifier is a change in maternal expression of the SD product, either increasing or decreasing maternal expression. As opposed to changes in zygotic expression, such changes are expected to change the sex of offspring both carrying- and not-carrying the change, potentially leading to ultraselfish behavior. Such changes could occur in either *cis* or *trans*.

For the W'-linked case, no advantage is expected for *cis* change to a SD allele that changes its expression, since the W' allele is never present in genotype-phenotype mismatched offspring, and the Y' allele is only present in genotype-phenotype mismatched offspring when it is paternally inherited (which are not affected by changes in maternal Y' expression). Thus increases in maternal expression are not expected to have a fitness effect on individuals carrying the mutation while decreases in maternal expression (for instance converting X'Y'/Y'Y' offspring into females or Z'W' offspring into females) are expected to be disfavored.

For the Z'-linked case, increased maternal expression due to a *cis* change could lead Z'W' females to produce only sons, essentially converting the Z' into a Y'. Such a change would convert genotype-phenotype mismatched Z'Z' daughters into sons and thus enjoy an advantage and invade the population. However, from the perspective of the mother, such an allele is likely to be ultraselfish, since the advantage accruing to Z'Z' sons is offset by a disadvantage for Z'W' sons, which are expected to have low fitness (as discussed above) . Thus, such a *cis* change can invade the population but is expected to attract maternally-expressed suppressors.

The case is somewhat more complex for the X'-linked case. In this case, increased expression due to a *cis* change could lead X'Y' females to produce only daughters, essentially converting the X' into a W'. When rare, such an allele will have the effect of converting two classes of offspring carrying the allele into daughters, namely X'Y' and X'X' offspring (due to equal chance of acquiring an X' or Y' allele in the sperm). The effect of such a mutation is to convert equal numbers of $X'X'^{X'Y'-M}$ and $X'Y'^{X'Y'-M}$ offspring into females, with a benefit close to $s_{fY}/2+s_{mY}$ and a cost close to $s_{fY}/2$, respectively, for an overall benefit of $s_{mY}/2$. Thus the allele itself experiences a net benefit. However, from the perspective of mothers, the allele has the effect of feminizing three classes of offspring, $X'X'^{X'Y'-M}$, $X'Y'^{X'Y'-M}$ and $Y'Y'^{X'Y'-M}$, at a 1:2:1 ratio, with a per-individual benefit of $s_{fY}/2+s_{mY}$ for $X'X'^{X'Y'-M}$ individuals, and per-benefit costs of $s_{fY}/2$ and $s_{fY} - s_{mY}$ for Y'Y' individuals. Thus on balance the cost-benefit ratio for mothers is dependent on the quantity $s_{fY}/2+s_{mY} - 2s_{fY}/2 - 3s_{fY}/2-s_{mY} = -2s_{fY}$, implying a net cost to mothers. Thus, as with the Z'-linked case, such a *cis* change can invade the population but is expected to attract maternally-expressed suppressors.

Another possibility would be change in maternal expression through *trans* changes. The case of *trans* changes is simplified in two ways relative to that of *cis* changes. First, *trans* changes can have similar effects regardless of the location of the SD gene (for instance, for a Z'W' system a *trans* change could masculinize Z'W' progeny either by reducing expression of a W'-linked SD gene or increasing expression of a Z'-linked one). Second, because a *trans* change is equally likely to be inherited by all offspring, analyzing the case of a *trans* change is equivalent to considering the impact on mothers of a *cis* change, as discussed directly above. Thus, *trans* changes are expected to be disfavored in all cases because the benefits are outweighed by the costs associated with masculinization of Z'W'$^{Z'W'\text{-}F}$ offspring or feminization of X'Y'$^{X'Y'\text{-}M}$ and Y'Y'$^{X'Y'\text{-}M}$ offspring.

In total, then, we expect modification of maternal expression to be a less simple evolutionary path. *Trans* modifiers are not expected to invade the population regardless of the position of the SD gene. *Cis* modifiers can invade the population for X' or Z' changes, but not for W' or Y' changes, however these modifiers are costly to mothers that carry them and thus are expected to attract suppressors, calling into question their importance for the subsequent evolution of maternal slSD systems.

Modifiers 4: Degradation of the maternal product in zygotes

Another possibility is that a modifier could arise that acts in the zygote to degrade the maternal product. If dominant and not linked to the SD locus, such a change will have the effect of changing the sex of all offspring of a subset of mothers. The effect is thus similar to the case of a maternally-expressed *trans* modifier: namely, the change is not expected to be favored on balance.

Alternatively, a modifier could arise in *cis* to the SD locus but on the non SD gene-containing allele (linked to the X' in the case where the SD gene is Y'-linked, etc.; called 'cis-opposite' in Table 3). For the X'- and Z'-linked cases, modifiers linked to the W' and Y' alleles are not expected to arise because these alleles are never present in phenotype-genotype mismatched offspring. On the other hand, for the W'-linked case, a Z'-linked modifier that converted Z'Z'$^{Z'W'\text{-}F}$ individuals into males would benefit. Such a modifier could invade the population and rise in frequency, leading to a new equilibrium case with equal numbers of Z'Z' males and Z'W' females, that is a new ZW zygotic slSD system. For the Y'-linked case, a X'-linked modifier would immediately become confined to females, converting the X' into a W. Such an allele would experience a benefit from feminizing X'X'$^{X'Y'\text{-}M}$ offspring, but would also experience a cost from feminizing an equal number of X'Y'$^{X'Y'\text{-}M}$ offspring. As calculated above, this amounts to a net benefit of $s_{mY}/2$. Such an allele could thus invade the population, displacing the ancestral X' allele and potentially reaching an equilibrium with equal numbers of X'Y' females and Y'Y' males, thus a new stable ZW system.

In total, then, zygotic modifiers of maternal slSD products are not expected to arise in *trans* but may arise in *cis* for the W'-linked and Y'-linked cases, converting the system into a novel ZW zygotic slSD system.

Modifiers 5: Origins of a new SD locus

Notably, the presence of phenotype-genotype mismatched individuals under maternal slSD implies that novel sex determining loci may be more likely to evolve under maternal slSD systems than under zygotic slSD systems. Under zygotic systems, there is a complete match between SD gene complement and sex, with the associated sex-specific optimization of regions linked to the SD. Thus, each time it causes sex conversion, it is changing an individual from the sex for which its ancestral SD locus is optimized to the opposite sex: in the simplest case, in converting an XY male into a female, it is paying the costs s_{mY} associated with Y presence in a female. Thus to succeed a novel sex determining gene must provide a strong sex-specific advantage to overcome this deficit.

By contrast, in the case of a maternal slSD system, the presence of genotype-phenotype mismatched individuals in the population implies that the conversion will sometimes be favored. For instance, for an ancestral Z'W' system a zygotically-acting dominant male-determining gene arising at a novel locus will benefit from masculinizing Z'Z' individuals, even while suffering from masculinizing Z'W' individuals. It is simple to work out the conditions under which a novel dominant SD gene will benefit from Table 2. For a Z'W' system, a masculinizing zygotic-acting mutation that is epistatic on the ancestral locus can benefit so long as the selective benefit in males of the new SD locus is greater than $s_{mW}/2$, whereas a feminizing mutation is not expected to benefit (since there are no phenotype-genotype mismatched males). For a X'Y' system, a masculinizing mutation can benefit so long as the benefit is greater than $s_{mY}/2$ whereas a feminizing mutation can benefit so long as the benefit is greater than $s_{fY}/2$.

The dynamics following invasion of such a mutation are expected to be complex since as the allele rises in frequency, the distribution of genetic backgrounds in which it is found will shift, in some cases leading to balancing selection while in others conceivably leading to extinction of the ancestral system. However, regardless of the eventual resolution, the enhanced ability of novel zygotic slSD genes to invade maternal slSD systems provides yet another force that is expected to be involved in the destabilization of zygotic slSD.

Discussion

Single locus sex determining systems of varying age and character have been characterized across a wide and increasing diversity of animal and plant species (Capel 2017; Bachtrog et al. 2014). Here I address a remarkable but largely overlooked characteristic of these systems: the dearth of maternal effect systems, despite the seeming theoretical possibility of these systems and their observation in

a small number of exceptional species (see below). I show that, unlike zygotic systems, maternal slSD systems may be unlikely to get established since newly arising maternal slSD genes, from the perspective of the mother, are ultraselfish, i.e., reducing maternal fitness. Such alleles are thus expected to attract suppressors, presumably reducing their probability of becoming established in the population. In addition, I show that established maternal slSD systems are vulnerable to invasion by various classes of alleles from *cis* and *trans* modifiers of expression of the SD product to zygotic degradation of gene products to origins of new SD loci.

Summary of modifiers

I have argued that maternal slSD is expected to be highly unstable due to a diversity of different classes of mutation that can benefit due to phenotype-genotype mismatch under slSD. The number of classes of mutation that are available depend on whether the system is Z'W' or X'Y', whether the SD gene falls on the dominant or recessive allele, and in some cases on the specific selective impacts of the different alleles. In most cases, the expected outcome is the origins of a new zygotic slSD system encoded by the same locus as the ancestral maternal slSD system, though the barrier to turnover of SD locus is also lowered in maternal slSD systems relative to zygotic ones. The above considerations suggest that a X'Y' systems may be more susceptible to turnover whereas the W'-linked Z'W' system may be more stable than others, however even in this most stable system multiple pathways to turnover exist (Table 3).

Dynamics of subsequent evolution

I have sketched potential initial evolutionary steps beginning from an established maternal slSD system. In some cases, these initial steps may comprise the entire trajectory of the slSD system: for instance, a Z'-linked zygotic suppressor of a W'-expressed SD gene product can invade the population and displace the ancestral Z' allele, potentially rapidly leading to a stable ZW system without further steps. At the other extreme, evolution following the invasion of the population by a novel SD gene at a new locus is expected to be complex and involve complex equilibria between alleles at multiple loci and subsequent modifiers. The specific equilibria expected and the classes of modifiers most likely to arise are expected to depend on the conditional fitness benefits and costs of the various alleles, the epistatic dynamics of the multiple SD loci, and other features not considered here including population structure. While such dynamics are potentially of interest, given the dearth of empirical data on segregating maternal slSD systems, understanding the complex dynamics of systems that are not observed may not be of great importance. The central conclusion that can be drawn from the dynamics described here is that maternal slSD systems are expected to be readily destabilized by diverse mutations; even if the complex dynamics eventually lead back to new or restored slSD systems, the considerations shown here suggest the new equilibrium will also be short-lived, with the general expectation that such dynamics will eventually lead to the

replacement of the unstable maternal slSD system with a more stable zygotic slSD system or another alternative.

Phylogenetic distribution of slSD

The above arguments suggest that maternal slSD is unlikely to arise, and that even if it does arise and reach equilibrium it is unlikely to be susceptible to extinction by the invasion of modifiers. This then raises the question of why those few instances in which maternal slSD systems are observed are exceptional.

Maternal slSD systems are observed primarily in certain types of organisms: (i) those with feminizing endosymbionts; (ii) Z'W' systems in species with paternal genome elimination; and (iii) possibly, haplodiploid species (e.g., Werren et al. 2002; Vitagliano et al. 1996; Juchault et al. 1989; Tabadkani et al. 2011; Stuart et al. 1991). It is not surprising that the first case is exceptional: because endosymbionts are expected to favor heavily female-biased sex ratios, the Fisherian balancing dynamics assumed in this analysis do not apply – instead, such feminizing elements can spread through the population because of, not despite, the sex ratio bias produced (e.g., Werren 1987; Burt and Trivers 2009). Under such circumstances, maternally-acting nuclear suppressors of feminizing activity are expected to be favored, likely leading to a balance between feminizing endosymbionts and suppressors. Thus the dynamics imposed by intragenomic conflict are likely to explain the existence of maternal genotype-dependent monogenic broods in these species.

What of the second and third cases, paternal genome elimination and haplodiploidy? Maternal Z'W' slSD has been described in multiple groups with paternal genome elimination, and may exist in haplodiploids (Figure 4a; Stuart et al. 1991; Binns 1980). One compelling possibility is that because of the paternally-inherited genome loses all of its reproductive fitness if a zygote develops as male, there is intense conflict between the maternally- and paternally-inherited genomes over sex determination, which selects for strong maternal control of sexual development (e.g., Haig 1993; see also Ross et al. 2010). The strength of this selection certainly seems capable of overcoming the dynamics described here, and may indeed explain these exceptional cases. However, the model here in fact arguably provides an alternative explanation for why paternal genome elimination may be exceptional, and predicts the mode of maternal slSD. Under paternal genome elimination (as well as haplodiploidy), because males do not transmit their maternal genome, the transmission dynamics of such systems are considerably different. Z' chromosomes are expected to be transmitted through the female germline 3/5 of the time. Thus less conflict is expected due to SA alleles, since both Z' and W' chromosomes are selected to be female optimized. On the other hand, conflict persists in X'Y' systems (Figure 4b): since the X' experiences female-biased transmission while the Y' experienced balanced transmission, the system is similar to the Z'W' diploid system, with one (almost) unbiased and one biased chromosome. These primarily verbal arguments are thus consistent with the current model predicting both the overrepresentation of slSD systems within paternal genome elimination systems as

well as the observation of Z'W' rather than X'Y' systems. However, caution is necessary since the differences in bias for transmission of W' and Z' still raise the possibility of conflict (strongly SA mutations will still only succeed on the W'), and future work will be necessary to understand the conditions under which a Z'W' system can remain stable under paternal genome elimination.

Alternative explanations for the dearth of maternal systems

The dynamics described here are unlikely to be the entire explanation for the preponderance of zygotic-acting factors among slSD systems. The incidence of maternal effect traits remains unclear, and the evolvability of maternal versus zygotic factors may also differ insofar as both represent crucial developmental stages. Indeed, zygotic-acting factors seem to dominate among characterized alleles of large phenotypic effect, though it is of note that the earliest developmental events, such as sex determination, may be more amenable to maternal effect actors; indeed, insofar as the zygote can benefit from early sex determination, availability of the SD product prior to activation of the zygotic genome could carry benefits. Nonetheless, while it is possible to imagine several reasons why we might expect maternal effect slSD systems to be less common than zygotic ones, the near absence of slSD systems across life is nonetheless remarkable, suggesting that fundamental dynamics such as those discussed here may be a key part of the explanation.

Concluding remarks

I have argued here that maternal effect slSD systems, by virtue of containing ultraselfish alleles, may be unlikely to establish in populations, and that if established may be likely to be unstable due to invading modifiers. Future work should explore to what extent similar considerations may apply to more complex maternal SD systems that lead to skewed but not monogenic brood sex ratios.

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	ZYGOTIC			MATERNAL		
	Fitness	WT Mom	MUT Mom	Fitness	WT Mom	MUT Mom
Common sex, MUT	1-*p+s*	0	1/2	1-2*p+s*	0	1/2
Common sex, WT	1-*p*	1/2	1/4	1-*2p*	1/2	1/2
Rare sex, WT	1+*p*	1/2	1/4	1+*2p*	1/2	0
Mean offspring fitness		1	1-*p/2+s/2*		1	1-*2p+s/2*
... at equilibrium		1	1		1	1-*s/2*

Table 1. Fitnesses and frequencies for offspring of different sexes and genotypes for dominant sex determination genes acting zygotically (left) or maternally (right). Values are given for (i) the fitnesses of offspring of the common or rare sex with either wildtype genotype (WT) or which are heterozygous for the sex determining allele (MUT); (ii) frequencies of the three types of offspring for mothers either either wildtype genotype (WT) or which are heterozygous for the sex determining allele (MUT); and (iii) mean fitness for mothers for arbitrary *p* or at equilibrium. *p* indicates the frequency of the sex determining allele.

W'Z' system

	Male	Female	Difference
W' allele	($-s_{mW}$)	$+s_{fW}$	
Z' allele	-	-	
Z'W'	($1-s_{mW}$)	$1+s_{fW}/2$	$s_{mW}+s_{fW}/2$
Z'Z'	1	$1-s_{fW}/2$	$s_{fW}/2$
Mean offspring of...			
Z'W' mom (1:1 Z'W':Z'Z')	($1-s_{mW}/2$)	1	$s_{mW}/2$
Z'Z' mom (Z'Z')	1	($1-s_{fW}/2$)	$s_{fW}/2$

X'Y' system

	Male	Female	Difference
Y' allele	$+s_{mY}$	$-s_{fY}$	
X' allele	-	-	
X'X'	1-smY	$1+s_{fY}/2$	$s_{fY}/2+s_{mY}$
X'Y'	1	$1-s_{fY}/2$	$s_{fY}/2$
Y'Y'	1+smY	1-3sfY/2	$s_{mY}+3s_{fY}/2$
Mean offspring of...			
X'X mom (1:1 X'X':X'Y')	($1-s_{mY}/2$)	1	$s_{mY}/2$
X'Y' mom (1:2:1 X'X':X'Y':Y'Y')	1	($1-s_{fY}/2$)	$s_{fY}/2$

Table 2. Fitness values for alleles, offspring and broods. 'Allele' values show the non-normalized per-generation effect of each allele on fitness, as parameterized. Diploid genotypes show the expected fitnesses at population equilibrium (see Figure 1), and mean offspring values show the same averaged across broods. 'Difference' shows the magnitude of the selective impact for converting an individual or brood from one sex to the other. Parentheses indicate individuals not observed in the absence of modifiers (e.g., Z'W' do not produce sons).

	Zygotic expression		Maternal expression		Degrade maternal product		New SD
	cis	trans	cis	trans	cis-opposite	trans	locus
W-LINKED	-	-	-	-	Z'W'>ZW	-	Complex
Z-LINKED	-	Z'W'>ZW (tm/2<z<tm)	Z'>Y' (ultraselfish)	-	-	-	Complex
Y-LINKED	X'Y'>XY	X'Y'>XY	-	-	X'Y'>WZ	-	Complex
X-LINKED	X'Y'>WZ	X'Y'>WZ	X'>W' (ultraselfish)	-	-	-	Complex

Table 3. Summary of expected outcome for different classes of modifiers of established maternal-effect sex determination system, as described in the text. Classes include increased zygotic or maternal expression of the sex determining product (columns 1-4), zygotic degradation of the maternally expressed product at the zygotic stage (5-6), or origins of a novel sex determining locus. Expected outcome of an invading allele is indicated (e.g., X'Y'>XY indicates the ancestral X'Y' system is converted into a XY system), as are specific conditions (i.e., $tm/2<z<tm$) or instances in which the modifier is expected to be ultraselfish.

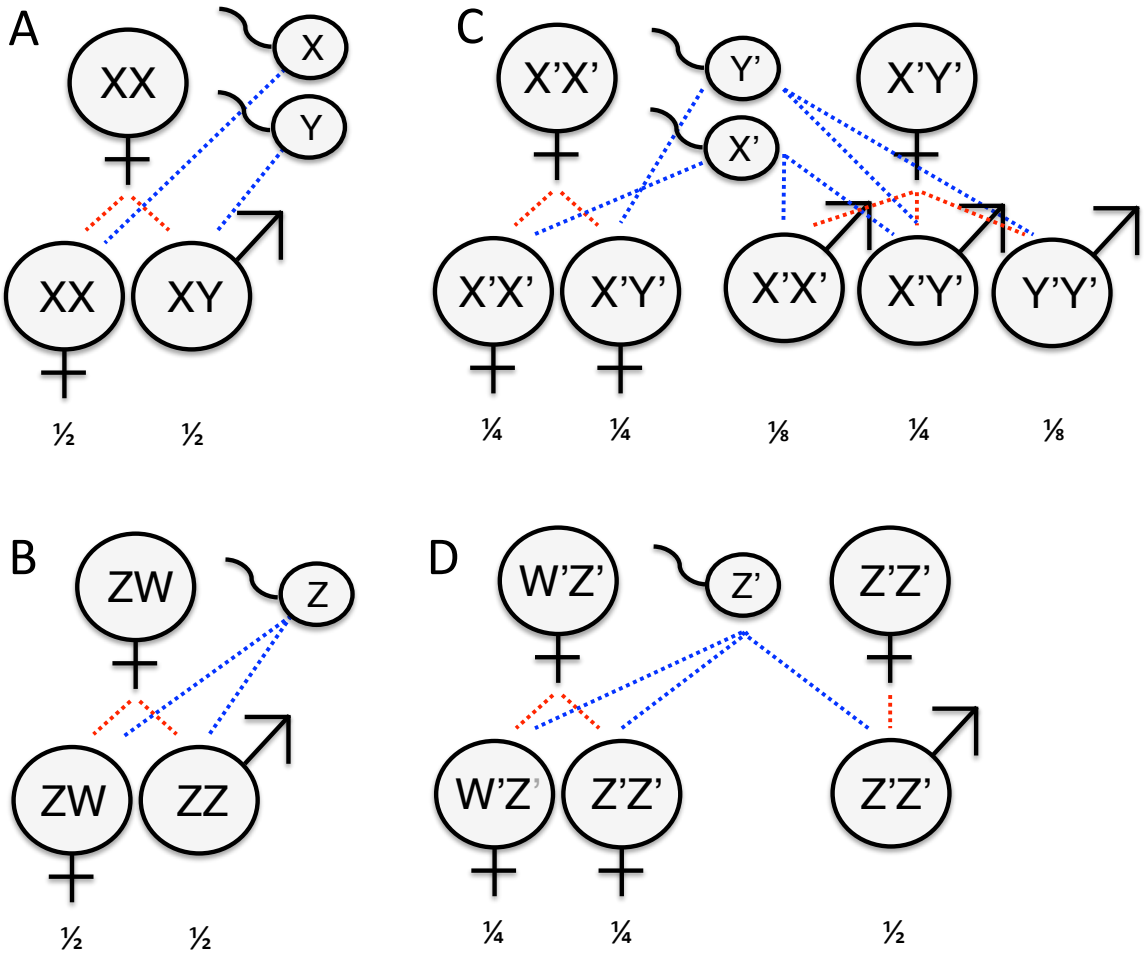

Figure 1. Schematic for four forms of single locus sex determination. Two forms of zygotic (A,B) and maternal (C,D) sex determination are shown, along with transmission lines (dotted lines) and sex of offspring. Fractions show the frequencies of individuals of each class at equilibrium.

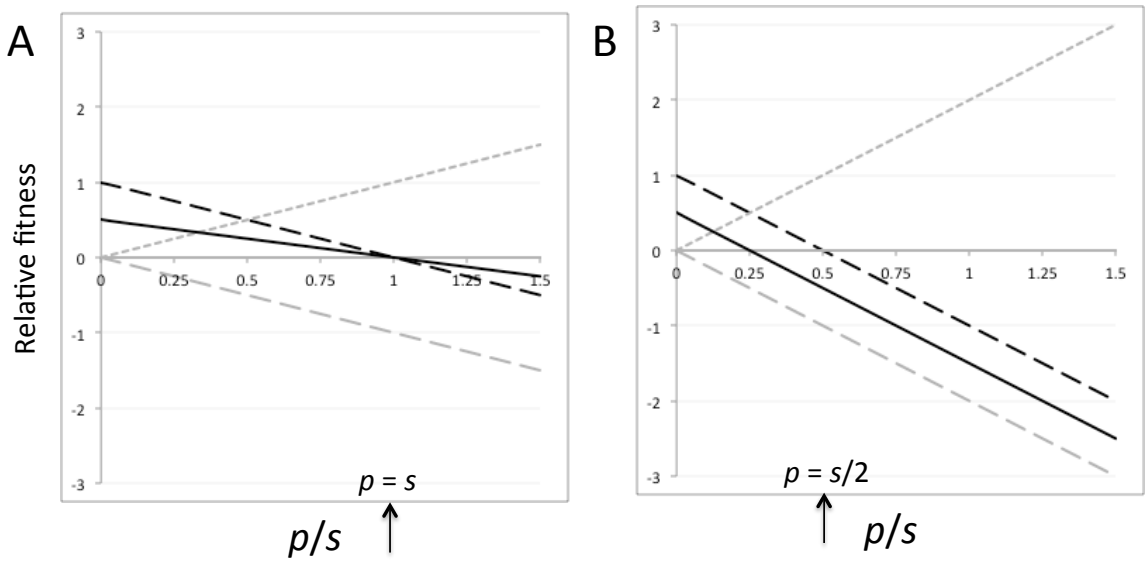

Figure 2. Individual and brood fitness for invading sex determination alleles. Relative fitness (defined here as fitness minus the population mean fitness) is shown as a function of the frequency of the sex determination allele. Results are shown for alleles that act at the zygotic (A) and maternal (B) stage. Both relative fitness and sex determination are shown in units of *s*, the selective advantage of the invading sex determination allele. Dashed lines show fitness values for wildtype individuals of the rare or common sex (grey short-dash and long-dash lines) and of individuals heterozygous for the sex determining allele (and thus of the common sex; black dashe). Solid lines show the average fitness for offspring of mothers heterozygous for the sex determining allele. Positions of equilibrium frequency values are indicated by arrows. Plots are approximations assuming $s << 1$, as discussed in the text.

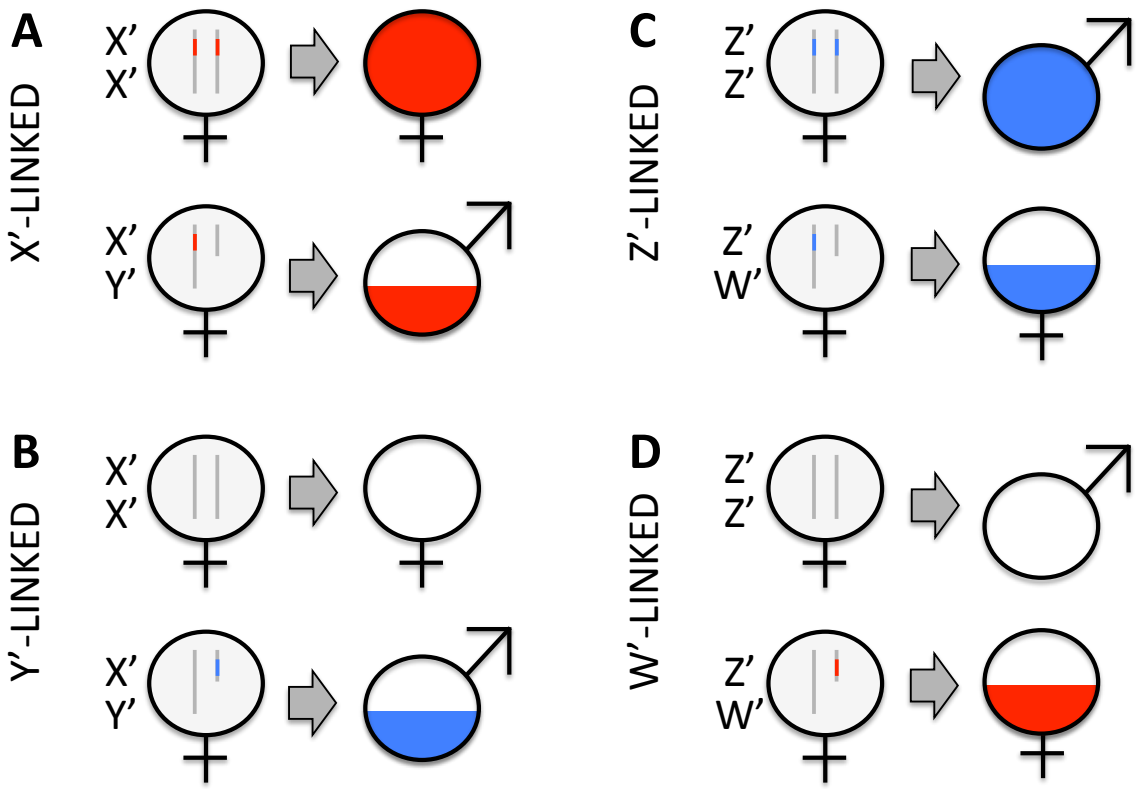

Figure 3. Depiction of four different sex determination mechanisms differing in position of the sex determining allele. Features of the mother (left of arrow) and offspring (right of arrow) are shown. Red and blue indicate genes that promote female and male development, respectively. Line lengths in mothers indicates either Y/W (short) or X/Z (long) chromosomes. Shading of offspring represents either zero (empty), one (half full) or two (full) doses of the product. Offspring sex is determined either by presence/absence of product (for Y- and W-linked cases) or one or two doses (for X- and Z-linked cases).

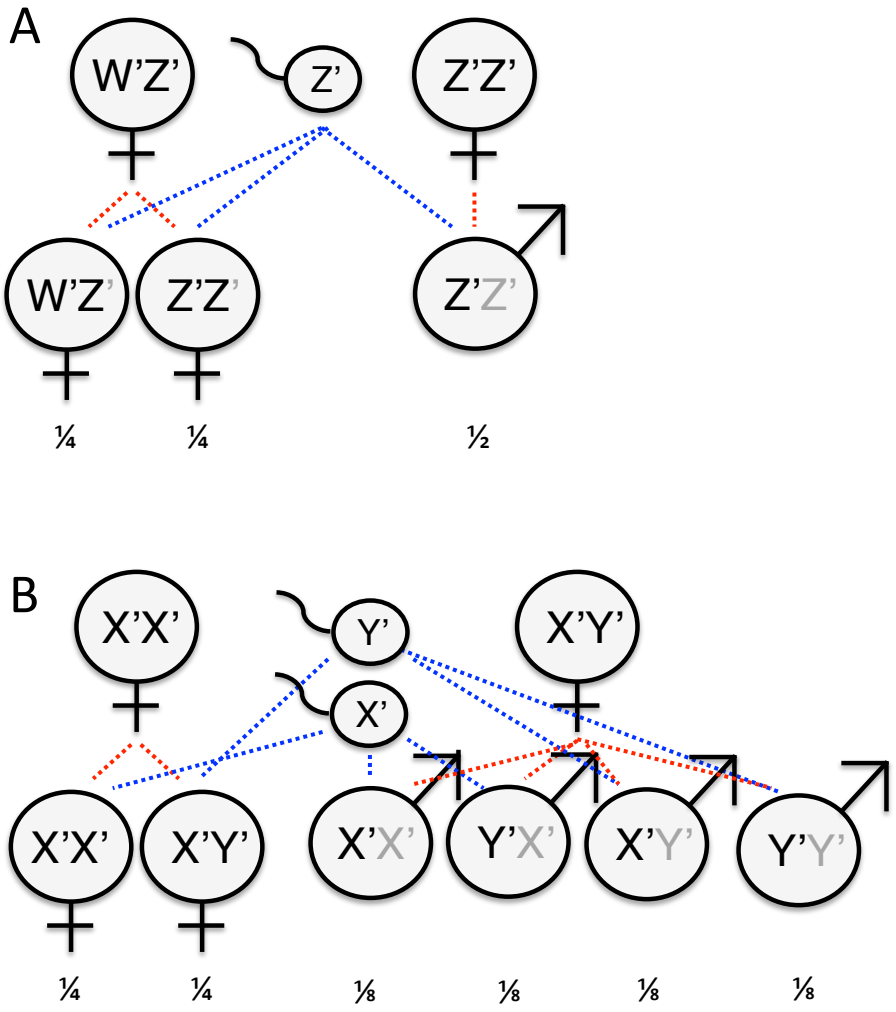

Figure 4.
Schematic for observed W'Z' (A) and hypothetical alternative X'Y' (B) maternal sex determination cases under paternal genome elimination. Depictions are as in Figure 1, with the addition that grey text indicates paternally-inherited chromosomes in sons, which are not transmitted to the following generation.