Haploid selection, sex ratio bias, and transitions between sex-determining systems

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Abstract

Sex determination is remarkably dynamic; many taxa display shifts in the location of sex-determining loci or the evolution of entirely new sex-determining systems. Predominant theories for why we observe such transitions generally conclude that novel sex-determining systems are favoured by selection if they equalise the sex ratio or increase linkage with a sexually-antagonistic locus. We use population genetic models to extend these theories in two ways: (1) We explicitly consider selection on loci very tightly linked to the ancestral sex-determining loci, e.g., within the non-recombining region of the ancestral sex chromosomes. Variation at such loci can favour the spread of new sex-determining systems in which the heterogametic sex changes (XY to ZW or ZW to XY) and the new sex-determining region is less closely linked (or unlinked) to the locus under selection, which is not predicted by previous theory. (2) We also consider selection upon haploid genotypes either during gametic competition (e.g., pollen/sperm competition) or meiosis (i.e., non-Mendelian segregation), selective processes that typically occur in one sex or the other. We find that associations with haploid selected loci can drive transitions between sex-determining systems, without requiring sexually-antagonistic selection in diploids. Unexpectedly, with haploid selection, transitions between male and female heterogamety can also evolve where linkage with the sex-determining locus is weakened. Furthermore, haploid selection in the heterogametic sex can cause sex ratio biases, which may increase or decrease with the spread of new sex chromosomes. Thus, we find that transitions between sex-determining systems cannot be simply predicted by selection to equalise the sex ratio. Overall, our models reveal that transitions between sex-determining systems, particularly transitions where the heterogametic sex changes, can be driven by loci in previously unpredicted genomic locations that experience selection during diploid and/or haploid phases. These results predict conditions under which sex-determining systems are likely to be labile and draw novel connections with sex ratio evolution.

Author summary

Accumulating evidence indicates that systems of sex determination are strikingly diverse and labile in many clades. This poses the question: what drives transitions between sex-determining systems? Here, we use models to derive conditions under which new sex-determining systems spread. Prevailing views suggest that new sex-determining systems are favoured when they equalize the sex ratio and/or when they are more closely linked to genes that experience differential selection in males and females. Our models extends these theories to include selection upon haploid genotypes (meiotic drive or gametic competition), which causes sex ratio biases and occurs differently in males and females. Surprisingly, we find that neither force (sex ratio selection nor associations with genes that have sex-specific effects) dominates the spread of new sex-determining systems alone. Even more unexpectedly, we find that, to spread, new sex-determining alleles do not necessarily have to arise in closer linkage with genes

that are differentially selected in males and females. Therefore, our models predict loci in previously unexpected genomic locations and/or experiencing various types of selection (including haploid selection) can now be implicated as drivers of transitions between sex-determining systems.

Introduction

Animals and angiosperms exhibit extremely diverse sex-determining systems (reviewed in [1–4]). Among species with genetic sex determination (GSD) of diploid sexes, some taxa have heterogametic males (XY) and homogametic females (XX), including mammals and most dioecious plants [5]; whereas other taxa have homogametic males (ZZ) and heterogametic females (ZW), including Lepidoptera and birds. Within several taxa, the chromosome that harbours the master sex-determining locus changes. For example, transitions of the master sex-determining locus between chromosomes or the evolution of new master sex-determining loci where the heterogametic sex does not change (hereafter 'cis-GSD transitions') have occurred in Salmonids [6, 7], Diptera [8], and *Oryzias* [9]. In addition, many clades exhibit transitions between male and female heterogamety (XY↔ZW, hereafter 'trans-GSD transitions'), including snakes [10], lizards [11], eight of 26 teleost fish families [12], true fruit flies (Tephritids, [8], amphibians [13], the angiosperm genus *Silene* [14], the angiosperm family *Salicaceae* [15, 16] and Coleoptera and Hemiptera (plate 2 [3]). Indeed, in some cases, both male and female heterogametic sex-determining systems can be found in the same species, as reported in houseflies [17], midges [18], frogs [19], cichlid fish [20], tilapia [21], sea bass [22], and lab-strains of Zebrafish [23, 24]. In addition, multiple transitions have occurred between genetic and environmental sex-determining systems (GSD↔ESD), e.g., in reptiles and fishes [11, 12, 25–28].

Predominant theories accounting for the spread of new sex-determining systems by selection involve fitness differences between sexes (e.g., sexually antagonistic selection) or sex ratio selection [3, 29, 30]. van Doorn and Kirkpatrick [31, 32] and Muralidhar and Veller [33] have shown that new sex-determining alleles can be favoured if they arise at loci in close linkage with a locus that experiences sexual antagonism. Tighter linkage allows a stronger favourable association to build up between a male-beneficial allele, and a neo-Y allele, for example. Such associations can favour cis-GSD transitions [31], trans-GSD transitions [32], and new partially-masculinizing or partially-feminizing alleles [33]. However, any sexually-antagonistic loci that are more closely linked to the ancestral sex-determining locus will develop similar, favourable associations and are expected to hinder the spread of a new sex-determining system.

The sex ratio is directly determined by the sex-determining system, and it has therefore been suggested that sex ratio selection is a dominant force in the evolution of sex determination (e.g., Bull, 1983, p 66-67 [1]; Buekeboom and Perrin, 2014, Chapter 7 [3]). 'Fisherian' sex ratio selection favours a 1:1 zygotic sex ratio when assuming that males and females are equally costly to produce [34, 35]. This follows from the fact that, for an autosomal locus, half of the genetic material is inherited from a male and half from a female [36]. Thus, if the population sex ratio is biased towards one sex, the average per-individual contribution of genetic material to the next generation from the opposite sex is greater. Therefore, a mutant that increases investment in the rarer sex will spread via the higher per-individual contributions made by that sex. In the case of sex-chromosome evolution, Kozielska et al. (2014) [37] consider systems in which the ancestral sex chromosomes experience meiotic drive (e.g., where driving X or Y chromosomes are inherited disproportionately often), which causes sex ratios to become biased [38]. They find that masculinizing or feminizing mutations that arise at a new, unlinked locus (i.e., neo-Y or neo-W chromosomes) can then spread, which restore an even sex ratio.

Here we use mathematical models to find the conditions under which new sex-determining systems spread when individuals experience selection at both diploid and haploid stages, which allows fitness differences between the sexes and sex ratio biases to occur simultaneously. Even in animal and plant species that have much larger and more conspicuous diploid phases than haploid phases, many loci experience significant haploid selection through gamete competition and/or meiotic drive [39, 40]. We use the term 'meiotic drive' to refer to the biased (non-Mendelian) segregation of genotypes during gamete production (from one parent) and the term 'gametic competition' to refer to selection upon haploid genotypes within a gamete/gametophyte pool (potentially from multiple parents); the term 'haploid selection' encompasses both processes.

Segregation distortion provides putative evidence of haploid selection and can sometimes be attributed to meiotic drive and/or gametic competition [41–46]. Where it has been characterized, meiotic drive generally occurs

either during the production of male or female gametes only [47, 48]. Gametic competition is also typically sex specific, occurring primarily among male gametes, because there are typically many more pollen/sperm than required for fertilization. Gametic competition may be particularly common in plants, in which 60-70% of all genes are expressed in the male gametophyte, and these genes exhibit stronger signatures of selection than randomly-chosen genes [49–51]. In addition, artificial selection pressures applied to male gametophytes are known to cause a response to selection (e.g., [52–55]). A smaller proportion of genes are thought to be expressed and selected during competition in animal sperm, although precise estimates are uncertain [40, 56, 57]. Nevertheless, recent studies have demonstrated that sperm competition in animals can alter haploid allele frequencies and increase offspring fitness [58, 59].

There are various ways by which genes experiencing haploid selection could influence transitions between sex-determining systems. If we assume that haploid selection at any particular locus predominantly occurs in one sex (e.g., meiotic drive during spermatogenesis), then such loci experience a form of sex-specific selection. In this respect, we might expect that haploid selection would affect transitions between sex-determining systems in a similar manner to sex-specific diploid selection (as explored in [31, 32]). That is, new masculinizing mutations (neo-Y alleles) could be favoured via associations with alleles that are beneficial in the male haploid stage. On the other hand, sex ratios can also become biased by linkage between the sex-determining locus and a locus that harbours genetic variation in haploid fitness. For example, there are several known cases of sex ratio bias caused by sex-linked meiotic drive alleles (Burt and Trivers, 2006, Chapter 6 [60]) or selection among X- and Y-bearing pollen [61–66]. It is not immediately clear how the spread of new sex-determining systems would be influenced by the combination of sex ratio biases and associations with haploid selected alleles.

We find that the spread of novel sex-determining systems is influenced by both Fisherian sex ratio selection and by selection on linked alleles. Surprisingly, Fisherian sex ratio selection does not dominate; it is possible for selection on linked alleles to drive turnover between sex-determining systems despite causing increasingly biased sex ratios. In addition to considering haploid selection, another novel development in our model is that we consider loci that are in very tight linkage with the ancestral sex-determining locus. We find that loci tightly linked with the sex-determining locus can drive transitions in which the heterogametic sex changes, even when the new sex-determining locus is less closely linked to loci under selection (either including haploid selection or not).

Model

We consider transitions between ancestral and novel sex-determining systems using a three-locus model, each locus having two alleles (Fig 1). Locus **X** is the ancestral sex-determining region, with alleles X and Y (or Z and W). Locus **A** is a locus under selection, with alleles A and a. Locus **M** is a novel sex-determining region, at which the null allele (M) is initially fixed in the population such that sex of zygotes is determined by the genotype at the ancestral sex-determining region, **X**; XX genotypes become females and XY become males (or ZW become females and ZZ become males). To evaluate the evolution of new sex-determining systems, we consider the invasion, fixation, maintenance, and/or loss of a novel sex-determining allele (m) at the **M** locus. We assume that the **M** locus is epistatically dominant over the **X** locus such that zygotes with at least one m allele develop as females with probability k and as males with probability $1 - k$, regardless of the **X** locus genotype. With $k = 0$, the m allele is a masculinizer (a neo-Y allele) and with $k = 1$ the m allele is a feminizer (a neo-W allele). With intermediate k, we can interpret m as an environmental sex-determination (ESD) allele, such that zygotes develop as females in a proportion (k) of the environments they experience.

In each generation, we census the genotype frequencies in male and female gametes/gametophytes (hereafter gametes) before gametic competition. A full description of our model, including recursion equations, is given in S1 Appendix. First, competition occurs among male gametes (sperm/pollen competition) and among female gametes (egg/ovule competition) separately. Selection during gametic competition depends on the **A** locus genotype; relative fitnesses are given by $w_A^{⚥}$ and $w_a^{⚥}$ (⚥ $\in \{♀, ♂\}$; see table 1). We assume that all gametes compete for fertilization during gametic competition, which implies a polygamous mating system. Gametic competition in monogamous mating systems is, however, equivalent to meiotic drive in our model (described below), as either only alters the frequency of gametes produced by heterozygotes. After gametic competition, conjugation between male and female gametes occurs at random. The resulting zygotes develop as males or females, depending on their

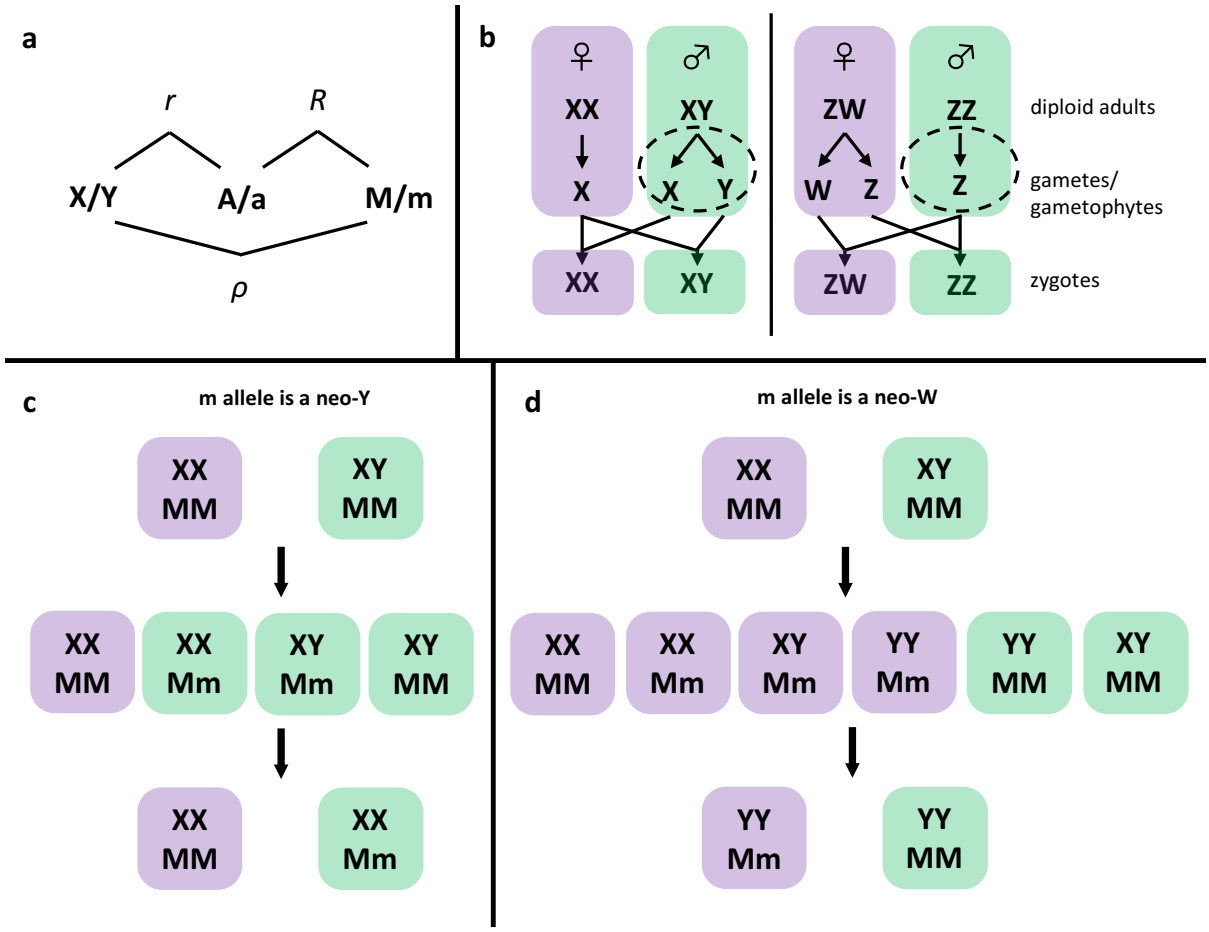

Fig 1. Outline of model features. Panel A: Recombination rate parameters between the ancestral-sex-determining locus (**X**, here assumed to have alleles X and Y), a locus under selection (**A**, with alleles A and a), and a new sex-determining locus (**M**, with alleles M and m). If $r < 1/2$, then associations between ancestral sex-determining alleles and selected alleles can be maintained past recombination in males. Panel B: Haploid selection is often sex-specific, occurring during haploid production or competition in either males or females. For example, haploid selection in males only is represented by the dashed circle. If X or Y alleles remain associated with alleles that experience haploid selection in males ($r < 1/2$), then zygotic sex ratios can become biased because either X- or Y-bearing male gametes/gametophytes will be more abundant after haploid selection. However, the zygotic sex ratio is not biased by male haploid selection in ZW sex-determining systems. Similarly, zygotic sex ratio biases can occur if haploid selected alleles are associated with new sex-determining alleles ($R < 1/2$). Panel C: During cis-GSD transitions (XY to XY or ZW to ZW), a neo-Y allele spreads to pseudo-fixation (its maximum frequency among male gametes) and the ancestral Y allele is lost. Panel D: During trans-GSD transitions (XY to ZW or ZW to XY), a neo-W allele spreads to pseudo-fixation (its maximum frequency among female gametes) and the ancestral X allele is lost. Neo-W alleles allow Y-associated alleles into females, which may impede or aid their spread.

genotypes at the **X** and **M** loci. Diploid males and females then experience selection, with relative fitnesses $w^{♀♂}_{AA}$, $w^{♀♂}_{Aa}$, and $w^{♀♂}_{aa}$. The next generation of gametes is produced by meiosis, during which recombination and sex-specific meiotic drive can occur. Recombination (i.e., an odd number of cross-overs) occurs between loci **X** and **A** with probability r, between loci **A** and **M** with probability R, and between loci **X** and **M** with probability ρ. Any linear order of the loci can be modelled with appropriate choices of r, R, and ρ (see Fig 1A and Table S1). Individuals that are heterozygous at the **A** locus may experience meiotic drive; a gamete produced by Aa

heterozgotes of sex ⚥ bears allele A with probability $\alpha^{⚥}$. Thus, the **A** locus can experience sex-specific gametic competition, diploid selection, and/or meiotic drive.

Table 1. Relative fitness of different genotypes in sex ⚥ $\in \{♀, ♂\}$

Genotype	Relative fitness during gametic competition
A	$w_A^{⚥} = 1 + t^{⚥}$
a	$w_a^{⚥} = 1$
Genotype	Relative fitness during diploid selection
AA	$w_{AA}^{⚥} = 1 + s^{⚥}$
Aa	$w_{Aa}^{⚥} = 1 + h^{⚥} s^{⚥}$
aa	$w_{aa}^{⚥} = 1$
Genotype	Transmission during meiosis in Aa heterozygotes
A	$\alpha^{⚥} = 1/2 + \alpha_{\Delta}^{⚥}/2$
a	$1 - \alpha^{⚥} = 1/2 - \alpha_{\Delta}^{⚥}/2$

Results

The model outlined above describes both ancestral XY and ZW sex-determining systems. Without loss of generality, we refer to the ancestrally heterogametic sex as male and the ancestrally homogametic sex as female. That is, we primarily describe an ancestral XY sex-determining system but our model is equally applicable to an ancestral ZW sex-determining system (relabelling the ancestrally heterogametic sex as female and the ancestrally homogametic sex as male and switching the labels of males and females throughout). We use a superscript to specify the ancestral sex-determining system described, e.g., $^{(XY)}$ for ancestral XY sex-determination.

Generic invasion by a neo-Y or neo-W

The evolution of a new sex-determining system requires that a rare mutant allele, m, at the novel sex-determining locus, **M**, increases in frequency when rare. This is determined by the leading eigenvalue ($\lambda_m^{(XY)}$) of the system of eight equations describing the frequency of eggs and sperm carrying the m allele in the next generation (equations S1.1). This system simplifies substantially for a dominant neo-Y ($k = 0$) or neo-W ($k = 1$), see S3 Appendix. The leading eigenvalue for a rare neo-Y or neo-W allele, $m \in \{Y', W'\}$, is the largest value of X that solves $x^2 + bx + c = 0$. The coefficients are $b = -(\Lambda_{mA}^{(XY)} + \Lambda_{ma}^{(XY)}) + (\chi_{mA}^{(XY)} + \chi_{ma}^{(XY)})$ and $c = (\Lambda_{mA}^{(XY)} - \chi_{mA}^{(XY)})(\Lambda_{ma}^{(XY)} - \chi_{ma}^{(XY)}) - \chi_{mA}^{(XY)}\chi_{ma}^{(XY)}$, where $\Lambda_{mi}^{(XY)} > 0$ is the multiplicative growth rate (which we will call the "haplotypic growth rate") of the neo-sex determination allele m on background $i \in \{A, a\}$ without accounting for loss due to recombination ($R = 0$), and $\chi_{mi}^{(XY)} > 0$ is the rate at which mutant haplotypes on background $i \in \{A, a\}$ recombine onto the other **A** locus background in heterozygotes (proportional to R), see Table 2. In the ancestral population, it is convenient to follow the frequency of the A allele among female gametes (eggs), $p_X^{♀}$, and among X-bearing, $p_X^{♂}$, and among Y-bearing, $p_Y^{♂}$, male gametes (sperm/pollen). We also track the fraction of male gametes that are Y-bearing, q, which may deviate from $1/2$ due to meiotic drive in males. We will consider only equilibrium frequencies of alleles, $\hat{p}_i^{⚥}$, and Y-bearing male gametes, $\hat{q}$, when calculating the eigenvalues.

The new sex-determining allele increases in frequency when rare when the largest eigenvalue is greater than one ($\lambda_m^{(XY)} > 1$). If both haplotypic growth rates are greater than one ($\Lambda_{mA}^{(XY)}, \Lambda_{ma}^{(XY)} > 1$), then the new sex-determining allele invades regardless the rate of recombination between the new sex-determining locus and the selected locus (R), see S3 Appendix for details. Conversely, if both haplotypic growth rates are less than one

Table 2. Parameters determining invasion of mutant neo-Y and neo-W alleles into an ancestrally XY system

m is a neo-Y ($k = 0$)
$\Lambda_{Y'A}^{(XY)} = (2\zeta)^{-1}\left[\hat{p}_X^{♀} w_A^{♀} w_A^{♂} w_{AA}^{♂} + (1-\hat{p}_X^{♀}) w_a^{♀} w_A^{♂} w_{Aa}^{♂}(1+\alpha_\Delta^{♂})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♂}\right)$
$\Lambda_{Y'a}^{(XY)} = (2\zeta)^{-1}\left[(1-\hat{p}_X^{♀}) w_a^{♀} w_a^{♂} w_{aa}^{♂} + \hat{p}_X^{♀} w_A^{♀} w_a^{♂} w_{Aa}^{♂}(1-\alpha_\Delta^{♂})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♂}\right)$
$\chi_{Y'A}^{(XY)} = R(2\zeta)^{-1}\left[(1-\hat{p}_X^{♀}) w_a^{♀} w_A^{♂} w_{Aa}^{♂}(1+\alpha_\Delta^{♂})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♂}\right)$
$\chi_{Y'a}^{(XY)} = R(2\zeta)^{-1}\left[\hat{p}_X^{♀} w_A^{♀} w_a^{♂} w_{Aa}^{♂}(1-\alpha_\Delta^{♂})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♂}\right)$
m is a neo-W ($k = 1$)
$\Lambda_{W'A}^{(XY)} = [2(1-\zeta)]^{-1}\left[\bar{p}^{♂} w_A^{♂} w_A^{♀} w_{AA}^{♀} + (1-\bar{p}^{♂}) w_a^{♂} w_A^{♀} w_{Aa}^{♀}(1+\alpha_\Delta^{♀})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♀}\right)$
$\Lambda_{W'a}^{(XY)} = [2(1-\zeta)]^{-1}\left[(1-\bar{p}^{♂}) w_a^{♂} w_a^{♀} w_{aa}^{♀} + \bar{p}^{♂} w_A^{♂} w_a^{♀} w_{Aa}^{♀}(1-\alpha_\Delta^{♀})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♀}\right)$
$\chi_{W'A}^{(XY)} = R[2(1-\zeta)]^{-1}\left[(1-\bar{p}^{♂}) w_a^{♂} w_A^{♀} w_{Aa}^{♀}(1+\alpha_\Delta^{♀})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♀}\right)$
$\chi_{W'a}^{(XY)} = R[2(1-\zeta)]^{-1}\left[\bar{p}^{♂} w_A^{♂} w_a^{♀} w_{Aa}^{♀}(1-\alpha_\Delta^{♀})\right] / \left(\bar{w}_H^{♀}\bar{w}_H^{♂}\bar{w}_D^{♀}\right)$

$\bar{p}^{♂} = (1-\hat{q})\hat{p}_X^{♂} + \hat{q}\hat{p}_Y^{♂}$ is the average frequency of the A allele among X- and Y-bearing male gametes. ζ is the zygotic sex ratio (fraction male). $\bar{w}_D^{♂}$ is the mean fitness of diploids of sex ♂. $\bar{w}_H^{♂}$ is the mean fitness of haploids from sex ♂, see Table S2.

($\Lambda_{mA}^{(XY)}, \Lambda_{ma}^{(XY)} < 1$), then invasion can never occur. Finally, if only one haplotypic growth rate is greater than one, the new sex-determining allele can always invade when arising at a locus that is tightly linked to the selected locus ($R \approx 0$). Furthermore, it can be shown that the leading eigenvalue declines with R, and invasion requires that R is sufficiently small such that:

$$\chi_{ma}^{(XY)} / \left(\Lambda_{ma}^{(XY)} - 1\right) + \chi_{mA}^{(XY)} / \left(\Lambda_{mA}^{(XY)} - 1\right) < 1. \tag{1}$$

This condition may or may not be satisfied for the full range of locations of the new sex-determining locus, including $R = 1/2$, depending on the nature of selection. Interpreting this condition, if we assume that only the mA haplotype would increase in frequency when $R = 0$ ($\Lambda_{ma}^{(XY)} < 1 < \Lambda_{mA}^{(XY)}$) the first term on the left-hand side of (1) is negative and invasion requires that rate of growth of mA haplotypes ($\Lambda_{mA}^{(i)} - 1 > 0$) and the rate at which mA haplotypes are produced by recombination in ma haplotypes ($\chi_{ma}^{(i)}$) are sufficiently large relative to the rate of decline of ma haplotypes ($1 - \Lambda_{ma}^{(i)} > 0$) and the rate of loss of mA haplotypes due to recombination ($\chi_{mA}^{(i)}$).

We can draw a number of key points about the invasion of neo-Y and neo-W mutations from Table 2. First, Fisherian sex ratio selection will favour the spread of a neo-Y and inhibit the spread of a neo-W if the ancestral zygotic sex ratio is biased towards females, $\zeta < 1/2$ (i.e., the first factor of the $\Lambda_{mi}^{(XY)}$ is greater than one for a neo-Y and less than one for a neo-W). However, the spread of a neo-Y (neo-W) also depends on the male (female) fitness of associated alleles (see terms involving equilibrium allele frequencies, $\hat{p}$'s). Second, invasion by a neo-Y (neo-W) does not directly depend on the fitness of female (male) diploids. This is because a dominant neo-Y (neo-W) is always found in males (females), and therefore the frequency of the neo-Y (neo-W), m, only changes in males (females), Fig 1C,D. Finally, invasions by a neo-Y and a neo-W are qualitatively different. This is because a gamete with the neo-Y always pairs with a female gamete containing an X, Fig 1C. By contrast, a gamete with a neo-W can pair with an X- or Y-bearing male gamete, Fig 1D. Consequently, neo-W-bearing females obtain a different frequency of A alleles from mating (when $\hat{p}_X^{♂} \neq \hat{p}_Y^{♂}$) compared to ancestral (MM) females.

In order to explicitly determine the conditions under which a rare new sex-determining allele spreads, we must calculate the equilibrium frequency of the A allele (i.e., $\hat{p}_X^{♀}$, $\hat{p}_X^{♂}$, and $\hat{p}_Y^{♂}$) and Y-bearing male gametes ($\hat{q}$) in the ancestral population. Since only the **A** locus experiences selection directly, any deterministic evolution requires

that there is a polymorphism at the **A** locus. Polymorphisms can be maintained by mutation-selection balance or transiently present during the spread of beneficial alleles. However, polymorphisms maintained by selection can maintain alleles at intermediate allele frequencies for longer periods. Here, we focus on polymorphisms maintained by selection, where the A allele reaches a stable intermediate equilibrium frequency under the ancestral sex-determining system before the new sex-determining allele (m) arises. Such polymorphisms can be maintained by heterozygote advantage, sexually-antagonistic selection, ploidally-antagonistic selection, or a combination [67]. We can analytically calculate the allele frequency of the A allele using two alternative simplifying assumptions: (1) the **A** locus is within (or tightly linked to) the non-recombining region around the ancestral sex-determining locus ($r \approx 0$) or (2) selection is weak relative to recombination ($s^{♀}$, $t^{♀}$, $\alpha_{\Delta}^{♂}$ of order $\epsilon << 1$).

Tight linkage with the ancestral sex-determining locus ($r \approx 0$)

The ancestral equilibrium allele frequencies and their stability conditions are given in S2 Appendix. When there is complete linkage between the ancestral sex-determining locus and the **A** locus ($r = 0$), either the A allele or the a allele must be fixed in gametes containing a Y allele. Because the labelling of alleles is arbitrary, we will assume that the a locus is fixed in gametes with a Y ($p_Y^{♂} = 0$), without loss of generality. If there are two alleles maintained at the **A** locus, the A allele can be fixed ($\hat{p}_X^{♀} = \hat{p}_X^{♂} = 1$) or segregating at an intermediate frequency ($0<\hat{p}_X^{♀}, \hat{p}_X^{♂}<1$) in gametes with an X.

We find that a neo-Y allele can never invade an ancestral XY system that already has tight linkage with the locus under selection ($\lambda_{Y'}^{(XY)} \leq 1$ when $r = 0$, for details see S1 File). When $R = 0$, a neo-Y haplotype with the same allele as the ancestral Y is neutral ($\Lambda_{Y'a}^{(XY)} = 1$) and does not change in frequency. The other neo-Y haplotype will not spread ($\Lambda_{Y'A}^{(XY)} < 1$) given that the initial equilibrium is stable. Therefore, a neo-Y mutation cannot spread in an ancestral XY system ($\lambda_{Y'}^{(XY)} \leq 1$, regardless of R) where selected loci are within or very near the non-recombining region around the sex-determining locus. In essence, through tight linkage with the **A** locus, the ancestral Y becomes strongly specialized on the allele that has the highest fitness across male haploid and diploid phases. Given that the ancestral Y is at this equilibrium, it is not possible for a neo-Y to create males that have higher fitness than the ancestral Y.

Neo-W alleles, on the other hand, can invade an ancestral XY system under some conditions (the full invasion conditions are given in S3 Appendix; equations S3.1 and S3.2). Counterintuitively, selection on loci within the non-recombining region around the sex-determining locus can favour the invasion of a less closely linked neo-W, whatever the form of selection maintaining a polymorphism (sexually-antagonistic selection, overdominance, ploidally-antagonistic selection, or some combination, Fig 2, Figure S2, Figure S8, and Figure S3). The conditions become more restrictive, however, with increasing recombination (R) between the new sex-determining locus and the selected locus. The invasion of completely unlinked neo-W alleles ($R = 1/2$) can occur with overdominance in males or with haploid selection but is not possible with only sexually-antagonistic selection if selection is directional in each diploid sex (see S1 File). To develop an intuition for how less closely linked neo-W alleles invade ($R > r$), we here focus on cases where there is no haploid selection and discuss the additional effect of haploid selection in S3 Appendix.

If we categorise the a allele as being ancestrally 'male-beneficial' via the fact that it is fixed on Y backgrounds, then $\Lambda_{W'A}^{(XY)} > 1$ indicates that the neo-W spreads when found with the ancestrally 'female-beneficial' allele. Broadly, this is possible because ancestral X alleles are sometimes in males and are therefore unable to perfectly specialise on the 'female-beneficial' allele. For example, when the a allele is favoured on ancestral X backgrounds in males, a polymorphism of A and a alleles can be maintained on the X background despite selection for the A allele in females ($s^{♀} > 0$, $0 < h^{♀} < 1$), see outlined region in Fig 3A. When the a allele is strongly favoured on the X background in males ($w_{aa}^{♂}$ sufficiently large relative to $w_{Aa}^{♂}$), neo-W-A haplotypes can spread ($\Lambda_{W'A}^{(XY)} > 1$, see grey region in Fig 3A) because they produce higher fitness females (AA or Aa genotypes) and are unleashed from counterselection in males.

When only one neo-W haplotype has growth rate greater than one (see Fig 3), a neo-W allele can invade as long as Eq (1) is satisfied, which may require that the recombination rate, R, is small enough. Nevertheless, because we assume here that r is small, these results indicate that a more loosely linked sex-determining region ($r < R$) can spread. For example, tightly sex-linked loci that experience sexually-antagonistic selection can drive trans-GSD

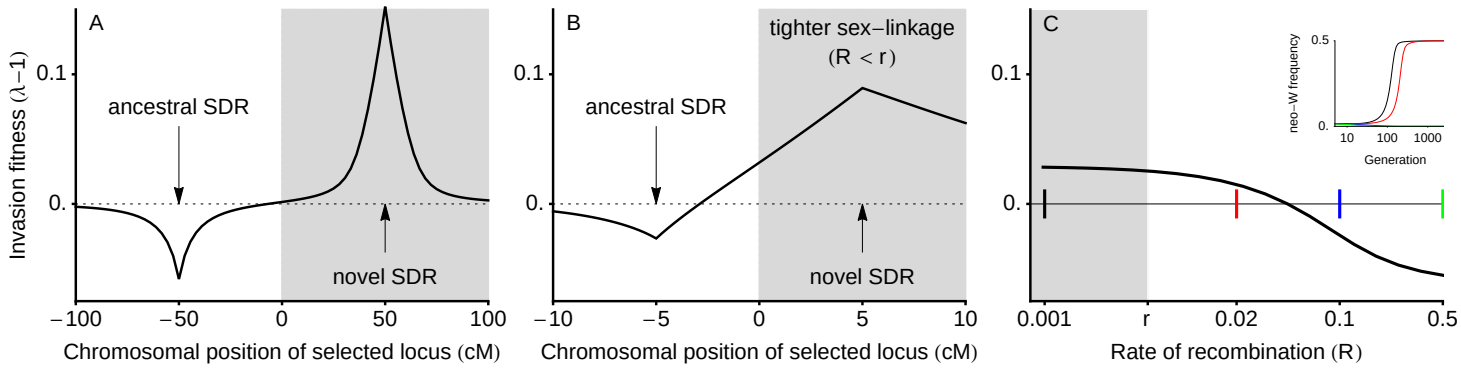

Fig 2. Transitions between XY and ZW systems can occur even when the new sex-determining locus is less tightly linked to a locus under sexually-antagonistic selection (even without haploid selection). In panel A, linkage is loose enough relative to selection that the analytical results assuming weak selection hold, and a neo-W allele can only invade when it arises at a locus more tightly linked with the selected locus ($R < r$; shaded region). In panel B, linkage is tight enough relative to selection that the analytical results assuming weak selection do not hold, and a neo-W can invade even when it is less tightly linked with the selected locus ($r < R$; unshaded region around *). In panel C we vary the recombination rate between the neo-W and the selected locus (R) for a fixed recombination rate between the ancestral sex-determining locus and the selected locus ($r = 0.005$). Coloured markers show recombination rates for which the temporal dynamics of invasion are plotted in the inset, demonstrating that neo-W alleles can reach pseudo-fixation if they are more (black) or less (red) closely linked to a locus experiencing sexually-antagonistic selection. A very loosely linked neo-W does not spread in this case (blue and green lines overlap and go to 0 in inset). Fitness parameters are: $w^{♀}_{AA} = 1.05$, $w^{♂}_{aa} = 1.2$, $w^{♀}_{aa} = w^{♂}_{AA} = 0.85$, $w^{♀}_{Aa} = 1$, $t^{♂} = \alpha^{♀}_{\Delta} = 0$.

transitions in which the new sex-determining locus is less closely linked to the locus under selection (Fig 2).

Given that the a allele can be considered ancestrally 'male-beneficial' because it is fixed on Y backgrounds, it is surprising that neo-W-a haplotypes can sometimes be favoured by selection in females ($\Lambda^{(XY)}_{W'a} > 1$). Again, this occurs because ancestral X alleles also experience selection in males, where they are ancestrally always paired with a Y-a gamete. If there is overdominance in males, X-A Y-a males have high fitness and the A allele is favoured by selection on the X background in males. Therefore, the A allele can be polymorphic or even fixed on the X background despite selection favouring the a allele in females (e.g., see outlined region in Fig 3B and [68, 69]). In such cases, neo-W-a haplotypes can spread because they create more Aa and aa females when pairing with an X-bearing gamete from males and because they bring Y-a haplotypes into females, where it has higher fitness (Fig 1D).

In some cases, both W-A and W-a haplotypes can spread. For example, when AA individuals have low fitness in females yet the A is polymorphic or fixed on the X background due to overdominance in males (Fig 3B and 3C), both neo-W-A and neo-W-a haplotypes produce fewer unfit AA females. This is true for the neo-W-A haplotype because it can pair with a Y-a haplotype and still be female. Wherever both haplotypic growth rates are greater than one, invasion by a neo-W is expected regardless of its linkage with the selected locus (i.e., for any R, see Figure S1 and Figure S2 for examples).

Assuming selection is weak relative to recombination, van Doorn and Kirkpatrick [32] showed that invasion by a neo-W allele occurs under the same conditions as 'pseudo-fixation' (at pseudo-fixation the neo-W reaches its maximum frequency among eggs, which is usually 1/2, but can deviate from 1/2 when there is haploid selection before censusing). An equivalent analysis is not possible where recombination rates are low. However, numerical simulations demonstrate that new sex-determining alleles do not necessarily reach pseudo-fixation, which can lead to the stable maintenance of a mixed sex-determining system, in which X, Y, Z, and W alleles all segregate (e.g., Figure S9B,C).

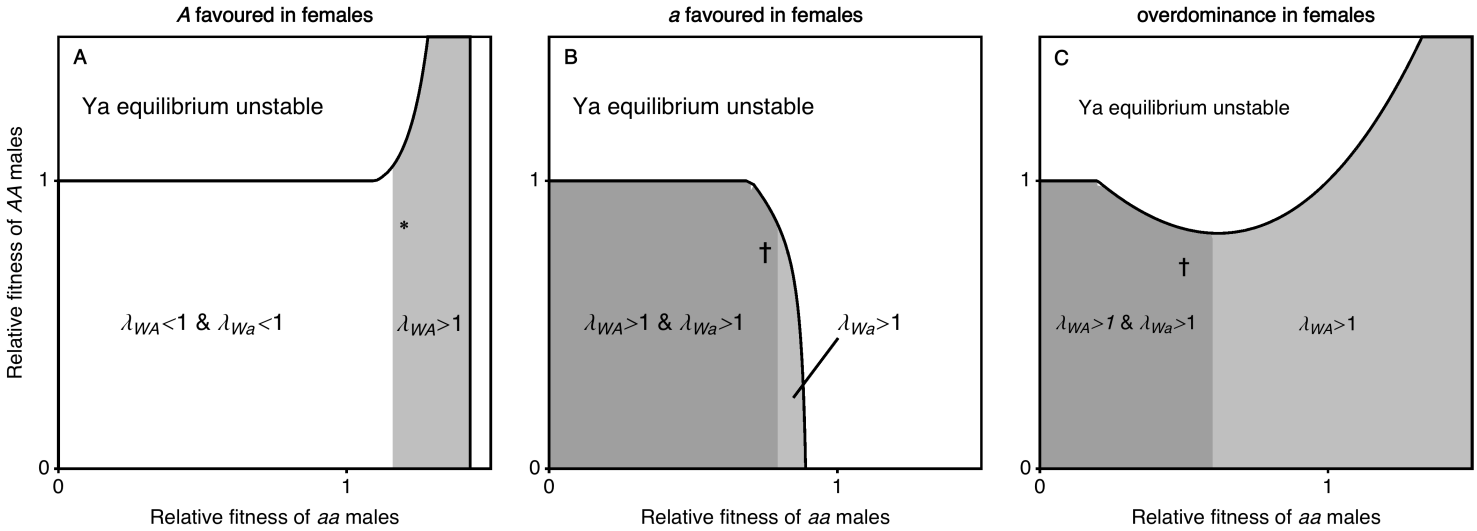

Fig 3. When the ancestral XY locus is tightly linked to a locus under selection ($r = 0$), one or both neo-W haplotypes can spread. We vary the fitness of male homozygotes relative to heterozygotes ($w^{\mathsf{G}}_{Aa} = 1$) and only consider stable equilibria at which both **A** locus alleles are maintained and the a allele is initially fixed on Y backgrounds, region outlined. Here, selection in females can favour the A allele (panel A, $w^{\mathsf{F}}_{aa} = 0.85$, $w^{\mathsf{F}}_{AA} = 1.05$), favour the a allele (panel B, $w^{\mathsf{F}}_{aa} = 1.05$, $w^{\mathsf{F}}_{AA} = 0.85$), or be overdominant (panel C, $w^{\mathsf{F}}_{aa} = w^{\mathsf{F}}_{AA} = 0.6$). If either haplotypic growth rate ($\Lambda^{(XY)}_{W'A}$ or $\Lambda^{(XY)}_{W'a}$) is greater than one, then a rare neo-W allele can spread for, at least, some values of $R > r$. The parameter values marked with an asterisk correspond to the fitnesses used in Fig 2C. Where both haplotypic growth rates are greater than one, a neo-W will spread when rare, regardless of linkage with the selected locus (for any R). Figure S1 shows the dynamics arising with the parameters marked with a dagger. Here, there is no haploid selection $t^{\mathsf{G}} = \alpha^{\mathsf{G}}_{\Delta} = 0$.

Loose linkage with the ancestral sex-determining region

Here we assume that selection is weak (s^{G}, t^{G}, $\alpha^{\mathsf{G}}_{\Delta}$ of order $\epsilon << 1$) and thus implicitly assume that all recombination rates (r, R and ρ) are large relative to selection. To leading order in selection, the leading eigenvalues are:

$$\lambda^{(XY)}_{Y'} = 1 + \frac{1}{4} V_A S_A^2 \frac{(r-R)}{rR} + O\left(\epsilon^3\right) \tag{2}$$

and

$$\lambda^{(XY)}_{W'} = \lambda^{(XY)}_{Y'} + \left(2\alpha^{\mathsf{M}}_{\Delta} - 2\alpha^{\mathsf{F}}_{\Delta} + t^{\mathsf{M}} - t^{\mathsf{F}}\right)\left(\hat{p}^{\mathsf{M}}_{Y} - \hat{p}^{\mathsf{M}}_{X}\right)/2 + O\left(\epsilon^3\right) \tag{3}$$

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the equilibrium frequency of A and $S_A = (D^{\mathsf{M}} + \alpha^{\mathsf{M}}_{\Delta} + t^{\mathsf{M}}) - (D^{\mathsf{F}} + \alpha^{\mathsf{F}}_{\Delta} + t^{\mathsf{F}})$ describes sex differences in selection for the A versus a allele across diploid selection, meiosis, and gametic competition. The diploid selection term, $D^{\mathsf{G}} = \left[\bar{p}s^{\mathsf{G}} + (1-\bar{p})h^{\mathsf{G}}s^{\mathsf{G}}\right] - \left[\bar{p}h^{\mathsf{G}}s^{\mathsf{G}} + (1-\bar{p})\right]$, is the difference in fitness between A and a alleles in diploids of sex $\mathsf{G} \in \{\mathsf{F}, \mathsf{M}\}$, where $\bar{p}$ is the leading-order probability of mating with an A-bearing gamete from the opposite sex (equation S2.3). The difference in A-allele-frequency among Y-bearing sperm versus X-bearing sperm is given by $\hat{p}^{\mathsf{M}}_{Y} - \hat{p}^{\mathsf{M}}_{X} = V_A\left(D^{\mathsf{M}} - D^{\mathsf{F}} + \alpha^{\mathsf{M}}_{\Delta} - \alpha^{\mathsf{F}}_{\Delta} + t^{\mathsf{M}} - t^{\mathsf{F}}\right)(1-2r)/(2r)$.

Eq (2) demonstrates that, under weak selection, a neo-Y allele will invade an XY system ($\lambda^{(XY)}_{Y'} > 1$) if and only if it is more closely linked to the selected locus than the ancestral sex-determining locus (i.e., if $R < r$; note that $V_A S_A^2$ is strictly positive as long as **A** is polymorphic). This echoes our results above where a neo-Y could never invade if $r \approx 0$. It is also consistent with the results of [31], who considered diploid selection only and also

found that cis-GSD transitions can only occur when the new sex-determining locus is more closely linked to a locus under sexually-antagonistic selection.

With weak selection and no haploid selection ($t^{\text{⚥}} = \alpha_{\Delta}^{\text{⚥}} = 0$), the spread of a neo-W is equivalent to the spread of a neo-Y ($\lambda_{W'}^{(XY)} = \lambda_{Y'}^{(XY)}$), such that trans-GSD transitions can also occur only if the new sex-determining locus is more closely linked to a locus under selection ($R < r$), as found by [32]. When there is haploid selection, invasion also typically occurs when the neo-W is more closely linked to the selected locus than the ancestral sex-determining region (Fig 4). For example, if the **A** locus is unlinked to the ancestral sex-determining locus ($r = 1/2$), a more closely linked neo-W ($R < 1/2$) can always invade. In this case, there is no ancestral association between **A** alleles and sex chromosomes in males, $\left(\hat{p}_Y^{\text{♂}} - \hat{p}_X^{\text{♂}}\right) = 0$, see Eq (S2.4). The second term in Eq (3) therefore disappears and invasion depends only on the sign of $(r - R)$.

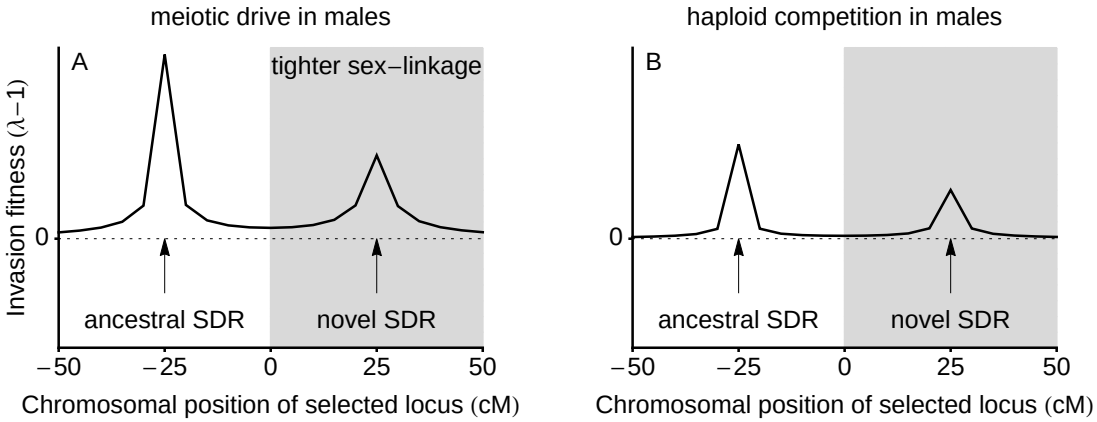

Fig 4. Ploidally-antagonistic selection allows a less tightly linked neo-W allele to invade. In panel A, male drive ($\alpha_{\Delta}^{\text{♂}} = -1/20$, $t^{\text{⚥}} = \alpha_{\Delta}^{\text{♀}} = 0$) opposes selection in diploids (no sex-differences: $s^{\text{⚥}} = 1/10$, $h^{\text{⚥}} = 7/10$), in which case the new sex-determining allele can invade regardless of its linkage with the selected locus (R). In panel B, gametic competition in males ($t^{\text{♂}} = -1/10$, $t^{\text{♀}} = \alpha_{\Delta}^{\text{⚥}} = 0$) opposes selection in diploids (sex-differences: $s^{\text{♂}} = 3/20$, $s^{\text{♀}} = 1/20$, $h^{\text{⚥}} = 7/10$), in which case the new sex-determining allele can once again invade regardless of R.

However, with haploid selection and $r < 1/2$, the additional term in Eq (3) can be positive. This can allow neo-W invasion ($\lambda_{W'}^{(XY)} > 1$), even when the new sex-determining locus is less closely linked to the selected locus ($R > r$). To clarify the parameter space under which invasion occurs despite looser sex-linkage ($\lambda_{W'}^{(XY)} > 1$ despite $R > r$), we focus on the special case where $R = 1/2$ and $r < 1/2$ (e.g., the selected locus is on the ancestral sex chromosome and the novel sex-determining locus arises on an autosome). In Table 3 we give the conditions where invasion occurs when we further assume that haploid selection only occurs in one sex (e.g., during male meiosis only) and dominance coefficients are equal in the two sexes, $h^{\text{♀}} = h^{\text{♂}}$. When there is no gametic competition and meiotic drive is in one sex only, an unlinked neo-W can invade as long as the same allele is favoured during diploid selection in males and females ($s^{\text{♀}} s^{\text{♂}} > 0$, see Fig 4A and Fig 5B). When there is no meiotic drive and gametic competition occurs in one sex only, an unlinked neo-W can invade as long as the same allele is favoured in male and female diploid selection and there are sex differences in selection of one type (e.g., $s^{\text{♀}}(s^{\text{♂}} - s^{\text{♀}}) > 0$, see Fig 4B). These special cases indicate that neo-W invasion occurs for a relatively large fraction of the parameter space, even if the neo-W uncouples the sex-determining locus from a locus under selection.

Previous research suggests that when the ancestral sex-determining locus is linked to a locus that experiences haploid selection (e.g., meiotic drive), alleles at a new, unlinked sex-determining locus invade to restore equal sex ratios [37]. Consider, for example, the case where the **A** locus is linked to the ancestral sex-determining locus ($r < 1/2$) and experiences meiotic drive in males only ($\alpha_{\Delta}^{\text{♂}} \neq 0$, $\alpha_{\Delta}^{\text{♀}} = 0$), without gametic competition ($t^{\text{♀}} = t^{\text{♂}} = 0$). In this case, the zygotic sex ratio can be initially biased only if the ancestral sex-determining system

Table 3. Invasion conditions for a neo-W allele at an unlinked locus ($R = 1/2$) into an ancestral XY system with linkage ($r < 1/2$) and one form of haploid selection

Scenario	Assumptions	neo-W spreads ($\lambda_{W'}^{(XY)} > 1$) if
male drive only	$h^{♂} = h^{♀}, t^{♀} = t^{♂} = \alpha_{\Delta}^{♀} = 0$	$s^{♀}s^{♂} > 0$
female drive only	$h^{♂} = h^{♀}, t^{♀} = t^{♂} = \alpha_{\Delta}^{♂} = 0$	$s^{♀}s^{♂} > 0$
sperm competition only	$h^{♂} = h^{♀}, t^{♀} = \alpha_{\Delta}^{♀} = \alpha_{\Delta}^{♂} = 0$	$s^{♀}(s^{♂} - s^{♀}) > 0$
egg competition only	$h^{♂} = h^{♀}, t^{♂} = \alpha_{\Delta}^{♀} = \alpha_{\Delta}^{♂} = 0$	$s^{♂}(s^{♀} - s^{♂}) > 0$

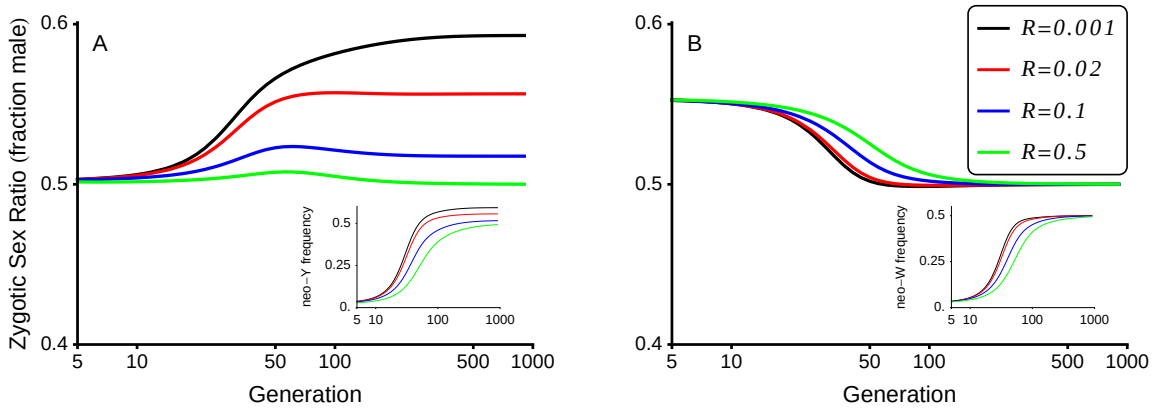

Fig 5. Fisherian sex ratio selection alone is not a good predictor of turnover between sex-determining systems. In this figure, selection is ploidally antagonistic with haploid selection favouring the a allele during male meiosis. In panel A, male meiotic drive in an ancestral XY system causes a male bias (see Fig 1B), allowing a neo-W to invade and replace the ancestral sex-determining system (inset shows neo-W frequency among female gametes, reaching pseudo-fixation), which balances the zygotic sex ratio. In panel B, male drive in an ancestral ZW system has no effect on the zygotic sex ratio yet a neo-Y can invade and replace the ancestral sex-determining system (inset shows neo-Y frequency among male gametes, reaching pseudo-fixation). Parameters: $s^{♀} = s^{♂} = 0.2$, $h^{♀} = h^{♂} = 0.7$, $t^{♀} = t^{♂} = \alpha_{\Delta}^{♀} = 0$, $\alpha_{\Delta}^{♂} = -0.1$, $r = 0.02$.

is XY (Fig 1A and Fig 5B). If Fisherian sex ratio selection were dominant, we would thus expect a difference in the potential for XY to ZW and ZW to XY transitions. However, invasion by a neo-W allele into an XY system and invasion by a neo-Y allele into a ZW system occur under the same conditions ($\lambda_{Y'}^{(XY)} = \lambda_{W'}^{(ZW)}$ and $\lambda_{W'}^{(XY)} = \lambda_{Y'}^{(ZW)}$, at least to order ϵ^2). For example, in Fig 5A neo-W alleles invade an ancestral-XY system where females are initially rare, equalizing the sex ratio. However, Fig 5B shows that a neo-Y can invade the resulting ZW system under the same conditions. When $R < 1/2$, the invading neo-Y becomes associated with the male meiotic drive allele and the zygotic sex ratio actually evolves to become male-biased.

While equalizing the sex ratio and benefiting from drive are two primary reasons why haploid selection spurs sex chromosome transitions, even when the new sex-determining allele is less closely linked to the selected locus ($r < R$), more complex situations also arise. For example with $R = 1/2$ in Fig 5B (green curve), the neo-Y allele spreads despite the fact that it cannot benefit from drive because free recombination moves it randomly between driven and non-driven backgrounds. Nevertheless, the unlinked neo-Y can spread because diploids bearing it more often carry the non-driven allele A, which is found at high frequency on the W background and has higher average diploid fitness.

Environmental sex determination

We next consider the case where the new sex-determining mutation, m, causes sex to be determined probabilistically or by heterogeneous environmental conditions (environmental sex determination, ESD), with individuals carrying allele m developing as females with probability k. Here, we do not assume that the environmental conditions that determine sex also differentially affect the fitness of males versus females. Such correlations can favour environmental sex-determining systems by allowing each sex to be produced in the environment in which it has highest fitness; in the absence of these correlations, previous theory would predict that ESD is favoured when it produces more equal sex ratios than the ancestral system (see reviews by [1, 35, 36]).

The characteristic polynomial determining the leading eigenvalue (equations S1.1) does not factor for ESD ($0 < k < 1$) as it does for a neo-Y ($k = 0$) or neo-W ($k = 1$) allele. We therefore focus on weak selection here, where the leading eigenvalue is

$$\begin{aligned}\lambda^{(XY)}_{ESD'} =& 1 + \frac{(1-2k)^2}{4} V_A {S_A}^2 \frac{r-R}{rR} \\ &+ \frac{k(\hat{p}^{♂}_Y - \hat{p}^{♂}_X)}{2}\left[k\left(2\alpha^{♂}_{\Delta} - 2\alpha^{♀}_{\Delta} + t^{♂} - t^{♀}\right) - 2(1-k)S_A\right] + O\left(\epsilon^3\right).\end{aligned} \tag{4}$$

This reduces to $\lambda^{(XY)}_{Y'}$ when $k = 0$ and $\lambda^{(XY)}_{W'}$ when $k = 1$.

Of particular interest are ESD mutations that cause half of their carriers to develop as females and half as males ($k = 1/2$), creating equal sex ratios. The spread of such ESD is determined by

$$\lambda^{(XY)}_{ESD'} = 1 + \frac{1}{2}\frac{(\lambda^{(XY)}_{Y'|R=1/2} - 1) + (\lambda^{(XY)}_{W'|R=1/2} - 1)}{2} + O\left(\epsilon^3\right), \tag{5}$$

where $\lambda^{(XY)}_{Y'|R=1/2}$ and $\lambda^{(XY)}_{W'|R=1/2}$ represent $\lambda^{(XY)}_{Y'}$ and $\lambda^{(XY)}_{W'}$ when evaluated at $R = 1/2$ (Equations 2 and 3). That is, recombination between the selected locus and the novel sex-determining locus, R, does not enter into the $k = 1/2$ results. This is because sex is essentially randomized each generation, preventing associations from building up between alleles at locus **A** and sex. Eq (5) shows that the ESD mutation gets half of the fitness of a feminizing mutation (neo-W) and half of the fitness of a masculinizing mutation (neo-Y), but only has an effect one half of the time (the other half of the time it produces the same sex as the ancestral system would have). As discussed above, $\lambda^{(XY)}_{Y'|R=1/2}$ is necessarily less than one, but $\lambda^{(XY)}_{W'|R=1/2}$ can be greater than one if there is haploid selection. That is, when there is haploid selection, ESD can invade an ancestrally-XY system because it generates females that are either rare or have high fitness, in the same manner as a neo-W.

Significantly, Eq (5) is the same whether ESD is invading an ancestrally XY or ZW system (because $\lambda^{(XY)}_{Y'} = \lambda^{(ZW)}_{W'}$ and $\lambda^{(XY)}_{W'} = \lambda^{(ZW)}_{Y'}$). Thus, Fisherian sex ratio selection alone does not easily explain GSD to ESD transitions. For example, when the ancestral sex-determining system is XY, but not ZW, the sex ratio is biased by male haploid selection. Nevertheless, ESD is equally likely to invade when it equalizes the zygotic sex ratio (through $\lambda^{(XY)}_{W'}$) as when it doesn't (through $\lambda^{(ZW)}_{Y'}$). In addition, we note that ESD may not invade, even if the sex ratio is initially biased (e.g., with drive in males only, $r < 1/2$, $h^{♀} = h^{♂}$, and $s^{♀}s^{♂} < 0$, then $\lambda^{(XY)}_{W'} < 1$, see Table 3). We conclude that, as with neo-W and neo-Y loci, associations with selected loci mean that the evolution of ESD is not straightforwardly predicted by selection to balance the zygotic sex ratio when haploid selection is present.

Discussion

Two predominant theories explaining the remarkably high frequency of transitions between sex-determining systems are sexually-antagonistic selection and sex ratio selection (reviewed in [29, 30]). The former predicts that new sex-determining alleles can invade when they arise in closer linkage with a sexually-antagonistic locus ($r < R$, [31–33]). The latter predicts that new sex-determining systems are generally favoured if they result in more equal sex ratios than the ancestral system. In contrast to these prevailing views, we show that selection (including sexually-antagonistic selection, overdominance, and/or ploidally-antagonistic selection) on loci tightly linked to the

ancestral sex-determining locus can favour trans-GSD transitions (XY↔ ZW) to new sex-determining systems that are less closely linked to the selected loci (e.g., see Fig 2). Similarly, even when linkage is weak relative to selection, we show that trans-GSD transitions can occur where the new sex-determining locus is less closely linked to the locus under selection if there is haploid selection (e.g., Figs 4 and 5).

We find that the spread of new sex-determining systems cannot be simply predicted from their effect on the sex ratio. On one hand, sex ratio biases caused by haploid selection can facilitate trans-GSD transitions or transitions from genetic to environmental sex determination. For instance, alleles favoured by haploid selection in males often become associated with the Y allele, which leads to a male-biased zygotic sex ratio. This male bias increases the potential for a neo-W allele to invade (Table 2), which can equalize the sex ratio (e.g., see Fig 5B, for related examples see [37]). On the other hand, sex ratio selection can be overwhelmed by additional selective effects, preventing a neo-W or ESD allele from invading, even if it would balance the sex ratio (e.g., when selection acts in opposite directions in male and female diploids, Table 3). Indeed, transitions between sex-determining systems can generate stronger sex ratio biases (e.g., Fig 5A and step 1 in [70]). Significantly, with weak selection, we find that there is no difference in conditions allowing XY to ZW and ZW to XY transitions, indicating that sex chromosome transitions are not predominantly predicted by their effect on the sex ratio (i.e., the sex ratio bias created by male haploid selection facilitates the spread of a neo-W allele into an XY system to the same degree that male haploid selection drives the spread of a neo-Y into a ZW system with a 1:1 sex ratio). Thus, haploid selection can favour trans-GSD transitions both via sex ratio selection and via selection on alleles associated with the new sex-determining allele, and these selective pressures are often predicted to be of equal magnitude.

We have shown that the spread of new sex-determining systems can be driven by loci experiencing haploid selection. In agreement with this hypothesis, a recent transcriptome analysis in Rumex shows that pollen-biased expression (relative to expression in flower buds or leaves) is enhanced among XY-linked genes compared to autosomal genes or compared to hemizygous genes that are only linked to the X (Sandler et al., 2018, personal communication). In addition, Y-linked genes are over-expressed relative to X-linked genes in pollen (but not in flower buds or leaves). This suggests that the spread of neo-Y chromosomes in this clade could have been favoured through linkage with haploid selected genes. In general, we predict that haploid selection increases lability of sex-determining systems, particularly because haploid selection can cause transitions that increase or decrease sex-linkage (e.g., the final state of the red line in Fig 5B is the starting state in Fig 5A). Frequent turnovers driven by haploid selection may help to explain the relative rarity of heteromorphic sex chromosomes in plants, which are thought to experience more selection during their multicellular haploid stage.

If haploid selection is strong but selective differences between male and female diploids are weak, we find that trans-GSD transitions are favoured more strongly than cis-GSD transitions, with transitions to ESD intermediate (e.g., with $|D^{♂} - D^{♀}| << |\alpha_{\Delta}^{♂} - \alpha_{\Delta}^{♀} + t^{♂} - t^{♀}|$ we have $\lambda_{W'}^{(XY)} > \lambda_{Y'}^{(XY)}$; Equations 3 and S2.4). Among the relatively few dioecious clades in which multiple species have well characterized sex chromosomes [5], trans-GSD transitions have been inferred in *Silene* subsection *Otites* [14] and in *Salicaceae* [15, 16]. Assuming that transitions from dioecy to hermaphroditism (equal parental investment in male and female gametes) are favoured in a similar manner to the ESD examined here (equal probability of zygotes developing as males or females), our results suggest that competition during the haploid stage could also drive transitions between dioecy and hermaphroditism, which are frequent in plants [71, 72].

In support of their role in sex chromosome turnover, genes expected to be under sexually-antagonistic selection (e.g., those causing bright male colouration) have been found on recently derived sex chromosomes [20, 73, 74]. Our results show, however, that tight ancestral-linkage of polymorphic loci, maintained by sexually-antagonistic selection or otherwise, can also drive trans-GSD transitions. In addition, we find that polymorphic sex determining systems (X, Y, W, and Z alleles all present) can be maintained when a selected locus is tightly linked to the ancestral sex-determining system (e.g., Figure S9B and Figure S9C), which is not possible with loose linkage [32]. For example, our results suggest a potential mechanism maintaining multiple sex determining alleles in the platyfish (*Xiphophorus maculatus*), in which X,Y, and W alleles segregate at one locus (or two closely-linked loci) near to potentially sexually-antagonistic genes for pigmentation and sexual maturity [75–78]. Several rodent species also maintain feminizing alleles along with the ancestral X and Y sex-determination alleles (reviewed in [79]). For example, in nine *Akadon* species, it appears that male-determining-*sry* expression is suppressed by an autosomal feminizing allele, creating XY females [80, 81], which have increased fitness relative to XX females [82]. In *Mus microtoides*, females can have XX, XX* or X*Y genotypes [83]. Previous theory would

predict that the X^* chromosome (or the autosome it is fused to) harbours female beneficial alleles, driving its spread. However, XX and XX^* females have similar fitness, whereas X^*Y female fitness is enhanced [84–86]. Although Y-linkage of female-beneficial alleles is counterintuitive, our model suggests that it can be stably maintained and then favour new feminizing mutations, which is a parsimonious explanation for the spread of feminizing alleles in these rodent species.

We note that we assume that sex-determining alleles do not experience direct selection except via their associations with sex and selected alleles. However, in some cases, there may be significant degeneration around the sex-limited allele (Y or W) in the ancestral sex-determining region because recessive deleterious mutations and/or deletions accumulate in this non-recombining regions [87–90]. During trans-GSD transitions, but not cis-GSD transitions, any recessive deleterious alleles linked to the Y or W are revealed to selection in YY or WW individuals [4]. This phenomenon was studied by van Doorn and Kirkpatrick (2010) [32], who found that degeneration can prevent fixation of a neo-W or a neo-Y allele, leading to a mixed sex-determining system where the ancestral and new sex-determining loci are both segregating. However, they noted that very rare recombination events around the ancestral sex-determining locus can allow these trans-GSD transitions to complete. Degeneration around the Y or W could explain why trans-GSD transitions are not observed to be much more common than cis-GSD transitions despite the fact that our models demonstrate that they are favoured under a wider range of conditions, especially with haploid selection. For example, there are a dozen sex chromosome configurations among Dipteran species but only one transition between male and female heterogamety [8].

In this study, we have only considered new sex-determining alleles of large effect. However, we expect similar selective forces to act on masculinizing/feminizing alleles of weaker effect. For example, small effect masculinizing/feminizing alleles within a threshold model of sex determination can be favoured when linked to loci that experience sexually-antagonistic selection [33]. These results echo those for large-effect neo-Y/neo-W alleles [31, 32]. Finally, while we have considered cis-GSD, trans-GSD, and GSD to ESD transitions, we have not explicitly considered ESD to GSD transitions. Recent models of ESD to GSD transitions [33, 70] show that that neo-Y/neo-W alleles can be favoured when they arise near to haploid and/or diploid selected loci, which also occurs in our model.

Conclusion

We have shown that tight sex-linkage and haploid selection can drive previously unexpected transitions between sex-determining systems. In particular, both can select for new sex-determining loci that are more loosely linked to loci under selection. In addition, haploid selection can cause transitions analogous to those caused by purely sexually-antagonistic selection, eliminating the need for differences in selection between male and female diploids. We conclude that haploid selection should be considered as a pivotal factor driving transitions between sex-determining systems. Perhaps counterintuitively, transitions involving haploid selection can be driven by sex ratio selection or cause sex ratio biases to evolve; we do not find Fisherian sex ratio selection to be an overwhelming force. Overall, our results suggest several new scenarios under which new sex-determining systems are favoured, which could help to explain why the evolution of sex-determining systems is so dynamic.

Acknowledgments

This project was supported by the Natural Sciences and Engineering Research Council of Canada (CGS-D 6564 to MMO; RGPIN-2016-03711 to SPO).

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Supporting information

S1 Appendix

Recursion equations

In each generation we census the genotype frequencies in male and female gametes/gametophytes (hereafter, gametes) between meiosis (and any meiotic drive) and gametic competition. At this stage we denote the frequencies of X- and Y-bearing gametes from males and females $x_i^{⚥}$ and $y_i^{⚥}$. The superscript $⚥ \in \{♂, ♀\}$ specifies the sex of the diploid that the gamete came from. The subscript $i \in \{1, 2, 3, 4\}$ specifies the genotype at the selected locus **A** and at the novel sex-determining locus **M**, where $1 = AM$, $2 = aM$, $3 = Am$, and $4 = am$. The gamete frequencies from each sex sum to one, $\sum_i x_i^{⚥} + y_i^{⚥} = 1$.

Competition then occurs among gametes of the same sex (e.g., among eggs and among sperm separately) according to the genotype at the **A** locus ($w_1^{⚥} = w_3^{⚥} = w_A^{⚥}$, $w_2^{⚥} = w_4^{⚥} = w_a^{⚥}$, see Table 1). The genotype frequencies after gametic competition are $x_i^{⚥,s} = w_i^{⚥} x_i^{⚥} / \bar{w}_H^{⚥}$ and $y_i^{⚥,s} = w_i^{⚥} y_i^{⚥} / \bar{w}_H^{⚥}$, where $\bar{w}_H^{⚥} = \sum_i w_i^{⚥} x_i^{⚥} + w_i^{⚥} y_i^{⚥}$ is the mean fitness of male ($⚥ = ♂$) or female ($⚥ = ♀$) gametes.

Random mating then occurs between gametes to produce diploid zygotes. The frequencies of XX zygotes are then denoted as xx_{ij}, XY zygotes as xy_{ij}, and YY zygotes as yy_{ij}, where **A** and **M** locus genotypes are given by $i, j \in \{1, 2, 3, 4\}$, as above. In XY zygotes, the haplotype inherited from an X-bearing gamete is given by i and the haplotype from a Y-bearing gamete is given by j. In XX and YY zygotes, individuals with diploid genotype ij are equivalent to those with diploid genotype ji; for simplicity, we use xx_{ij} and yy_{ij} with $i \neq j$ to denote the average of these frequencies, $xx_{ij} = (x_i^{♀,s} x_j^{♂,s} + x_j^{♀,s} x_i^{♂,s})/2$ and $yy_{ij} = (y_i^{♀,s} y_j^{♂,s} + y_j^{♀,s} y_i^{♂,s})/2$.

Denoting the **M** locus genotype by $b \in \{MM, Mm, mm\}$ and the **X** locus genotype by $c \in \{XX, XY, YY\}$, zygotes develop as females with probability k_{bc}. Therefore, the frequencies of XX females are given by $xx_{ij}^{♀} = k_{bc} xx_{ij}$, XY females are given by $xy_{ij}^{♀} = k_{bc} xy_{ij}$, and YY females are given by $yy_{ij}^{♀} = k_{bc} yy_{ij}$. Similarly, XX male frequencies are $xx_{ij}^{♂} = (1 - k_{bc}) xx_{ij}$, XY male frequencies are $xy_{ij}^{♂} = (1 - k_{bc}) xy_{ij}$, and YY males frequencies are $yy_{ij}^{♂} = (1 - k_{bc}) yy_{ij}$. This notation allows both the ancestral and novel sex-determining regions to determine zygotic sex according to an XY system, a ZW system, or an environmental sex-determining system. In addition, we can consider any epistatic dominance relationship between the two sex-determining loci. Here, we assume that the ancestral sex-determining system (**X** locus) is XY ($k_{MMXX} = 1$ and $k_{MMXY} = k_{MMYY} = 0$) or ZW ($k_{MMZZ} = 0$ and $k_{MMZW} = k_{MMWW} = 1$) and epistatically recessive to a dominant novel sex-determining locus, **M** ($k_{Mmc} = k_{mmc} = k$).

Selection among diploids then occurs according to the diploid genotype at the **A** locus, $l \in \{AA, Aa, aa\}$, for an individual of type ij (see Table 1). The diploid frequencies after selection in sex $⚥$ are given by $xx_{ij}^{⚥,s} = w_l^{⚥} xx_{ij} / \bar{w}_D^{⚥}$, $xy_{ij}^{⚥,s} = w_l^{⚥} xy_{ij} / \bar{w}_D^{⚥}$, and $yy_{ij}^{⚥,s} = w_l^{⚥} yy_{ij} / \bar{w}_D^{⚥}$, where $\bar{w}_D^{⚥} = \sum_{i=1}^{4} \sum_{j=1}^{4} w_l^{⚥} xx_{ij} + w_l^{⚥} xy_{ij} + w_l^{⚥} yy_{ij}$ is the mean fitness of diploids of sex $⚥$.

Finally, these diploids undergo meiosis to produce the next generation of gametes. Recombination and sex-specific meiotic drive occur during meiosis. Here, we allow any relative locations for the **X**, **A**, and **M** loci by using three parameters to describe the recombination rates between them. R is the recombination rate between the **A** and **M** loci, ρ is the recombination rate between the **M** and **X** loci, and r is the recombination rate between the **A** and **X** loci (Fig 1). Table S1 shows replacements that can be made for each possible ordering of the loci assuming that there is no cross-over interference. During meiosis in sex $⚥$, meiotic drive occurs such that, in Aa heterozygotes, a fraction $\alpha^{⚥}$ of gametes produced carry the A allele and $(1 - \alpha^{⚥})$ carry the a allele.

Among gametes from sex $⚥$, the frequencies of haplotypes (before gametic competition) in the next generation

are given by

$$
\begin{aligned}
x_1^{\mathrm{♂}\prime} =& xx_{11}^{\mathrm{♂},s} + xx_{13}^{\mathrm{♂},s}/2 + (xx_{12}^{\mathrm{♂},s} + xx_{14}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - R(xx_{14}^{\mathrm{♂},s} - xx_{23}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& + (xy_{11}^{\mathrm{♂},s} + xy_{13}^{\mathrm{♂},s})/2 + (xy_{12}^{\mathrm{♂},s} + xy_{14}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - r(xy_{12}^{\mathrm{♂},s} - xy_{21}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} - \rho(xy_{13}^{\mathrm{♂},s} - xy_{31}^{\mathrm{♂},s})/2 \\
& + \big[-(R+r+\rho)xy_{14}^{\mathrm{♂},s} + (R+\rho-r)xy_{41}^{\mathrm{♂},s} \\
& + (R+r-\rho)xy_{23}^{\mathrm{♂},s} + (R+\rho-r)xy_{32}^{\mathrm{♂},s}\big]\alpha^{\mathrm{♂}}/2
\end{aligned} \tag{S1.1a}
$$

$$
\begin{aligned}
x_2^{\mathrm{♂}\prime} =& xx_{22}^{\mathrm{♂},s} + xx_{24}^{\mathrm{♂},s}/2 + (xx_{12}^{\mathrm{♂},s} + xx_{23}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - R(xx_{23}^{\mathrm{♂},s} - xx_{14}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& (xy_{22}^{\mathrm{♂},s} + xy_{24}^{\mathrm{♂},s})/2 + (xy_{21}^{\mathrm{♂},s} + xy_{23}^{\mathrm{♂},s})(1-\alpha^{\mathrm{♂}}) \\
& - r(xy_{21}^{\mathrm{♂},s} - xy_{12}^{\mathrm{♂},s})(1-\alpha^{\mathrm{♂}}) - \rho(xy_{24}^{\mathrm{♂},s} - xy_{42}^{\mathrm{♂},s})/2 \\
& + \big[-(R+r+\rho)xy_{23}^{\mathrm{♂},s} + (R+\rho-r)xy_{32}^{\mathrm{♂},s} \\
& + (R+r-\rho)xy_{14}^{\mathrm{♂},s} + (R+\rho-r)xy_{41}^{\mathrm{♂},s}\big](1-\alpha^{\mathrm{♂}})/2
\end{aligned} \tag{S1.1b}
$$

$$
\begin{aligned}
x_3^{\mathrm{♂}\prime} =& xx_{33}^{\mathrm{♂},s} + xx_{13}^{\mathrm{♂},s}/2 + (xx_{23}^{\mathrm{♂},s} + xx_{34}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - R(xx_{23}^{\mathrm{♂},s} - xx_{14}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& (xy_{33}^{\mathrm{♂},s} + xy_{31}^{\mathrm{♂},s})/2 + (xy_{32}^{\mathrm{♂},s} + xy_{34}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - r(xy_{34}^{\mathrm{♂},s} - xy_{43}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} - \rho(xy_{31}^{\mathrm{♂},s} - xy_{13}^{\mathrm{♂},s})/2 \\
& + \big[-(R+r+\rho)xy_{32}^{\mathrm{♂},s} + (R+\rho-r)xy_{23}^{\mathrm{♂},s} \\
& + (R+r-\rho)xy_{41}^{\mathrm{♂},s} + (R+\rho-r)xy_{14}^{\mathrm{♂},s}\big]\alpha^{\mathrm{♂}}/2
\end{aligned} \tag{S1.1c}
$$

$$
\begin{aligned}
x_4^{\mathrm{♂}\prime} =& xx_{44}^{\mathrm{♂},s} + xx_{34}^{\mathrm{♂},s}/2 + (xx_{14}^{\mathrm{♂},s} + xx_{24}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - R(xx_{14}^{\mathrm{♂},s} - xx_{23}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& (xy_{44}^{\mathrm{♂},s} + xy_{42}^{\mathrm{♂},s})/2 + (xy_{41}^{\mathrm{♂},s} + xy_{43}^{\mathrm{♂},s})(1-\alpha^{\mathrm{♂}}) \\
& - r(xy_{43}^{\mathrm{♂},s} - xy_{34}^{\mathrm{♂},s})(1-\alpha^{\mathrm{♂}}) - \rho(xy_{42}^{\mathrm{♂},s} - xy_{24}^{\mathrm{♂},s})/2 \\
& + \big[-(R+r+\rho)xy_{41}^{\mathrm{♂},s} + (R+\rho-r)xy_{14}^{\mathrm{♂},s} \\
& + (R+r-\rho)xy_{32}^{\mathrm{♂},s} + (R+\rho-r)xy_{23}^{\mathrm{♂},s}\big](1-\alpha^{\mathrm{♂}})/2
\end{aligned} \tag{S1.1d}
$$

$$
\begin{aligned}
y_1^{\mathrm{♂}\prime} =& yy_{11}^{\mathrm{♂},s} + yy_{13}^{\mathrm{♂},s}/2 + (yy_{12}^{\mathrm{♂},s} + yy_{14}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - R(yy_{14}^{\mathrm{♂},s} - yy_{23}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& (xy_{11}^{\mathrm{♂},s} + xy_{31}^{\mathrm{♂},s})/2 + (xy_{21}^{\mathrm{♂},s} + xy_{41}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} \\
& - r(xy_{21}^{\mathrm{♂},s} - xy_{12}^{\mathrm{♂},s})\alpha^{\mathrm{♂}} - \rho(xy_{31}^{\mathrm{♂},s} - xy_{13}^{\mathrm{♂},s})/2 \\
& + \big[-(R+r+\rho)xy_{41}^{\mathrm{♂},s} + (R+\rho-r)xy_{14}^{\mathrm{♂},s} \\
& + (R+r-\rho)xy_{32}^{\mathrm{♂},s} + (R+\rho-r)xy_{23}^{\mathrm{♂},s}\big]\alpha^{\mathrm{♂}}/2
\end{aligned} \tag{S1.1e}
$$

$$
\begin{aligned}
y_2^{\text{⚥}\prime} =& y y_{22}^{\text{⚥},s} + y y_{24}^{\text{⚥},s}/2 + (y y_{12}^{\text{⚥},s} + y y_{23}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& - R(y y_{23}^{\text{⚥},s} - y y_{14}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& (x y_{22}^{\text{⚥},s} + x y_{42}^{\text{⚥},s})/2 + (x y_{12}^{\text{⚥},s} + x y_{32}^{\text{⚥},s})(1-\alpha^{\text{⚥}}) \\
& - r(x y_{12}^{\text{⚥},s} - x y_{21}^{\text{⚥},s})(1-\alpha^{\text{⚥}}) - \rho(x y_{42}^{\text{⚥},s} - x y_{24}^{\text{⚥},s})/2 \\
& + \big[-(R+r+\rho) x y_{32}^{\text{⚥},s} + (R+\rho-r) x y_{23}^{\text{⚥},s} \\
& + (R+r-\rho) x y_{41}^{\text{⚥},s} + (R+\rho-r) x y_{14}^{\text{⚥},s}\big](1-\alpha^{\text{⚥}})/2
\end{aligned} \tag{S1.1f}
$$

$$
\begin{aligned}
y_3^{\text{⚥}\prime} =& y y_{33}^{\text{⚥},s} + y y_{13}^{\text{⚥},s}/2 + (y y_{23}^{\text{⚥},s} + y y_{34}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& - R(y y_{23}^{\text{⚥},s} - y y_{14}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& (x y_{33}^{\text{⚥},s} + x y_{13}^{\text{⚥},s})/2 + (x y_{23}^{\text{⚥},s} + x y_{43}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& - r(x y_{43}^{\text{⚥},s} - x y_{34}^{\text{⚥},s})\alpha^{\text{⚥}} - \rho(x y_{13}^{\text{⚥},s} - x y_{31}^{\text{⚥},s})/2 \\
& + \big[-(R+r+\rho) x y_{23}^{\text{⚥},s} + (R+\rho-r) x y_{32}^{\text{⚥},s} \\
& + (R+r-\rho) x y_{14}^{\text{⚥},s} + (R+\rho-r) x y_{41}^{\text{⚥},s}\big]\alpha^{\text{⚥}}/2
\end{aligned} \tag{S1.1g}
$$

$$
\begin{aligned}
y_4^{\text{⚥}\prime} =& y y_{44}^{\text{⚥},s} + y y_{34}^{\text{⚥},s}/2 + (y y_{14}^{\text{⚥},s} + y y_{24}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& - R(y y_{14}^{\text{⚥},s} - y y_{23}^{\text{⚥},s})\alpha^{\text{⚥}} \\
& (x y_{44}^{\text{⚥},s} + x y_{24}^{\text{⚥},s})/2 + (x y_{14}^{\text{⚥},s} + x y_{34}^{\text{⚥},s})(1-\alpha^{\text{⚥}}) \\
& - r(x y_{34}^{\text{⚥},s} - x y_{43}^{\text{⚥},s})(1-\alpha^{\text{⚥}}) - \rho(x y_{24}^{\text{⚥},s} - x y_{42}^{\text{⚥},s})/2 \\
& + \big[-(R+r+\rho) x y_{14}^{\text{⚥},s} + (R+\rho-r) x y_{41}^{\text{⚥},s} \\
& + (R+r-\rho) x y_{23}^{\text{⚥},s} + (R+\rho-r) x y_{32}^{\text{⚥},s}\big](1-\alpha^{\text{⚥}})/2.
\end{aligned} \tag{S1.1h}
$$

The full system is therefore described by 16 recurrence equations (three diallelic loci in two sexes, $2^3 \times 2 = 16$). However, not all diploid types are produced under certain sex-determining systems. For example, with the M allele fixed and an ancestral XY sex-determining system, there are XX females and XY males ($x_3^{\text{⚥}} = x_4^{\text{⚥}} = y_3^{\text{♂}} = y_4^{\text{♂}} = y_i^{\text{♀}} = 0,\ \forall\ i$). In this case, the system only involves six recursion equations, which we assume below to calculate the equilibria.

S2 Appendix

Resident equilibria and stability

In the resident population (allele M fixed), we follow the frequency of A in X-bearing female gametes, $p_X^{♀}$, and X-bearing male gametes, $p_X^{♂}$, and Y-bearing male gametes, $p_Y^{♂}$. We also track the total frequency of Y among male gametes, q, which may deviate from $1/2$ due to meiotic drive in males. These four variables determine the frequencies of the six resident gamete types, which sum to one in each sex: $x_1^{♀} = \hat{p}_X^{♀}$, $x_2^{♀} = 1 - \hat{p}_X^{♀}$, $x_1^{♂} = (1-q)\hat{p}_X^{♂}$, $x_2^{♂} = (1-q)(1-\hat{p}_X^{♂})$, $y_1^{♂} = q\hat{p}_Y^{♂}$, and $y_2^{♂} = q(1-\hat{p}_Y^{♂})$. Mean fitnesses in the resident population are given in Table S2.

Various forms of selection can maintain a polymorphism at the **A** locus, including sexually antagonistic selection, overdominance, conflicts between diploid selection and selection upon haploid genotypes (ploidally-antagonsitic selection, [67]), or a combination of these selective regimes (see below).

In particular special cases, e.g., no sex-differences in selection or meiotic drive ($s^{♂} = s^{♀}$, $h^{♂} = h^{♀}$, and $\alpha^{♂} = \alpha^{♀} = 1/2$), the equilibrium allele frequency and stability can be calculated analytically without assuming anything about the relative strengths of selection and recombination. However, here, we focus on two regimes (tight linkage between **A** and **X** and weak selection) in order to make fewer assumptions about fitnesses.

Tight linkage between X and A loci

We first calculate the equilibria in the ancestral population when the recombination rate between the **X** and **A** loci is small (r of order ϵ). Selection at the **A** locus will not affect evolution at the novel sex-determining locus, **M**, if one allele is fixed on all backgrounds. We therefore focus on the five equilibria that maintain both A and a alleles, four of which are given to leading order by:

$$(A)\quad \hat{p}_Y^{♂} = 0,\ \hat{q} = \frac{1}{2}\left(1 - \alpha_\Delta^{♂}\frac{w_{Aa}^{♂}\phi}{w_{Aa}^{♂}\phi + w_{aa}^{♂}\psi}\right), \tag{S2.1a}$$

$$\hat{p}_X^{♀} = \frac{w_a^{♀}\phi}{w_a^{♀}\phi + w_A^{♀}\psi},\ \hat{p}_X^{♂} = \frac{(1+\alpha_\Delta^{♂})w_{Aa}^{♂}\phi}{(1+\alpha_\Delta^{♂})w_{Aa}^{♂}\phi + w_{aa}^{♂}\psi}$$

$$(A')\quad \hat{p}_Y^{♂} = 1,\ \hat{q} = \frac{1}{2}\left(1 + \alpha_\Delta^{♂}\frac{w_{Aa}^{♂}\phi'}{w_{Aa}^{♂}\phi' + w_{AA}^{♂}\psi'}\right), \tag{S2.1b}$$

$$\hat{p}_X^{♀} = 1 - \frac{w_A^{♀}\phi'}{w_A^{♀}\phi' + w_a^{♀}\psi'},\ \hat{p}_X^{♂} = 1 - \frac{(1-\alpha_\Delta^{♂})w_{Aa}^{♂}\phi'}{(1-\alpha_\Delta^{♂})w_{Aa}^{♂}\phi' + w_{AA}^{♂}\psi'}$$

$$(B)\quad \hat{p}_Y^{♂} = 0,\ \hat{p}_X^{♀} = 1,\ \hat{p}_X^{♂} = 1,\ \hat{q} = (1-\alpha_\Delta^{♂})/2 \tag{S2.1c}$$

$$(B')\quad \hat{p}_Y^{♂} = 1,\ \hat{p}_X^{♀} = 0,\ \hat{p}_X^{♂} = 0,\ \hat{q} = (1+\alpha_\Delta^{♂})/2 \tag{S2.1d}$$

$$\begin{aligned}
\phi =&(1+\alpha_\Delta^{♀})w_A^{♀}w_{Aa}^{♀}\left[w_a^{♂}w_{aa}^{♂} + (1+\alpha_\Delta^{♂})w_A^{♂}w_{Aa}^{♂}\right]/2 - w_a^{♂}w_a^{♀}w_{aa}^{♂}w_{aa}^{♀}\\
\psi =&(1-\alpha_\Delta^{♀})w_a^{♀}w_{Aa}^{♀}\left[w_a^{♂}w_{aa}^{♂} + (1+\alpha_\Delta^{♂})w_A^{♂}w_{Aa}^{♂}\right]/2 - (1+\alpha_\Delta^{♂})w_A^{♂}w_A^{♀}w_{Aa}^{♂}w_{AA}^{♀}\\
\phi' =&(1-\alpha_\Delta^{♀})w_a^{♀}w_{Aa}^{♀}\left[w_A^{♂}w_{AA}^{♂} + (1-\alpha_\Delta^{♂})w_a^{♂}w_{Aa}^{♂}\right]/2 - w_A^{♂}w_A^{♀}w_{AA}^{♂}w_{AA}^{♀}\\
\psi' =&(1+\alpha_\Delta^{♀})w_A^{♀}w_{Aa}^{♀}\left[w_A^{♂}w_{AA}^{♂} + (1-\alpha_\Delta^{♂})w_a^{♂}w_{Aa}^{♂}\right]/2 - (1-\alpha_\Delta^{♂})w_a^{♂}w_a^{♀}w_{Aa}^{♂}w_{aa}^{♀}.
\end{aligned}$$

A fifth equilibrium (C) also exists where A is present at an intermediate frequency on the Y background ($0 < \hat{p}_Y^{♂} < 1$). However, equilibrium (C) is never locally stable when $r \approx 0$ and is therefore not considered further. Thus, the Y background can either be fixed for the a allele (equilibria (A) and (B)) or the A allele (equilibria (A') and (B')). The X background can then either be polymorphic (equilibria (A) and (A')) or fixed for the alternative allele (equilibria (B) and (B')). Since equilibria (A) and (B) are equivalent to equilibria (A') and (B') with the labelling of A and a alleles interchanged, we discuss only equilibria (A) and (B), in which the Y background is

fixed for the a allele. If there is no haploid selection ($\alpha_\Delta^{\mathsf{F}} = 0$, $w_A^{\mathsf{F}} = w_a^{\mathsf{F}} = 1$), these equilibria are equivalent to those found by [68] and [69].

We next calculate when equilibria (A) and (B) are locally stable for $r = 0$. According to the 'small parameter theory' [91, 92], these stability properties are unaffected by small amounts of recombination between the sex-determining locus and the **A** locus, although equilibrium frequencies may be slightly altered. For the a allele to be stably fixed on the Y background we need $\bar{w}_{Ya}^{\mathsf{M}} > \bar{w}_{YA}^{\mathsf{M}}$ where $\bar{w}_{Ya}^{\mathsf{M}} = w_a^{\mathsf{M}}\left[\hat{p}_X^{\mathsf{F}}(1-\alpha_\Delta^{\mathsf{M}})w_A^{\mathsf{F}}w_{Aa}^{\mathsf{M}} + (1-\hat{p}_X^{\mathsf{F}})w_a^{\mathsf{F}}w_{aa}^{\mathsf{M}}\right]$ and $\bar{w}_{YA}^{\mathsf{M}} = w_A^{\mathsf{M}}\left[\hat{p}_X^{\mathsf{F}}w_A^{\mathsf{F}}w_{AA}^{\mathsf{M}} + (1-\hat{p}_X^{\mathsf{F}})(1+\alpha_\Delta^{\mathsf{M}})w_a^{\mathsf{F}}w_{Aa}^{\mathsf{M}}\right]$. That is, Y-$a$ haplotypes must have higher fitness than Y-A haplotypes. Substituting in $\hat{p}_X^{\mathsf{F}}$ from Eq (S2.1), fixation of the a allele on the Y background requires that $\gamma_i > 0$ where $\gamma_{(A)} = w_a^{\mathsf{M}}\left[(1-\alpha_\Delta^{\mathsf{M}})w_{Aa}^{\mathsf{M}}\phi + w_{aa}^{\mathsf{M}}\psi\right] - w_A^{\mathsf{M}}\left[w_{AA}^{\mathsf{M}}\phi + (1+\alpha_\Delta^{\mathsf{M}})w_{Aa}^{\mathsf{M}}\psi\right]$ for equilibrium (A) and $\gamma_{(B)} = (1-\alpha_\Delta^{\mathsf{M}})w_a^{\mathsf{M}}w_{Aa}^{\mathsf{M}} - w_A^{\mathsf{M}}w_{AA}^{\mathsf{M}}$ for equilibrium (B). Stability of a polymorphism on the X background (equilibrium (A)) further requires that $\phi > 0$ and $\psi > 0$. Fixation of the a allele on the X background (equilibrium (B)) can be stable only if equilibrium (A) is not, as it requires $\psi < 0$.

Selection weak relative to recombination

Here, we assume that selection is weak relative to recombination (s^{F}, t^{F}, $\alpha_\Delta^{\mathsf{F}}$ of order ϵ). The maintenance of a polymorphism at the **A** locus then requires that

$$\begin{aligned} & 0 < -\left[(1-h^{\mathsf{F}})s^{\mathsf{F}} + (1-h^{\mathsf{M}})s^{\mathsf{M}} + t^{\mathsf{F}} + t^{\mathsf{M}} + \alpha_\Delta^{\mathsf{F}} + \alpha_\Delta^{\mathsf{M}}\right] \\ \text{and} \quad & 0 < h^{\mathsf{F}}s^{\mathsf{F}} + h^{\mathsf{M}}s^{\mathsf{M}} + t^{\mathsf{F}} + t^{\mathsf{M}} + \alpha_\Delta^{\mathsf{F}} + \alpha_\Delta^{\mathsf{M}}. \end{aligned} \tag{S2.2}$$

which indicates that a polymorphism can be maintained by various selective regimes.

Given that a polymorphism is maintained at the **A** locus by weak selection, the frequencies of A in each type of gamete are the same ($\hat{p}_X^{\mathsf{F}} = \hat{p}_X^{\mathsf{M}} = \hat{p}_Y^{\mathsf{M}} = \bar{p}$) and given, to leading order, by

$$\bar{p} = \frac{h^{\mathsf{F}}s^{\mathsf{F}} + h^{\mathsf{M}}s^{\mathsf{M}} + t^{\mathsf{F}} + t^{\mathsf{M}} + \alpha_\Delta^{\mathsf{F}} + \alpha_\Delta^{\mathsf{M}}}{(2h^{\mathsf{F}}-1)s^{\mathsf{F}} + (2h^{\mathsf{M}}-1)s^{\mathsf{M}}} + O(\epsilon). \tag{S2.3}$$

Differences in frequency between gamete types are of $O(\epsilon)$:

$$\begin{aligned} \hat{p}_X^{\mathsf{M}} - \hat{p}_X^{\mathsf{F}} &= V_A\left(D^{\mathsf{M}} - D^{\mathsf{F}} + \alpha_\Delta^{\mathsf{M}} - \alpha_\Delta^{\mathsf{F}}\right) + O(\epsilon^2) \\ \hat{p}_Y^{\mathsf{M}} - \hat{p}_X^{\mathsf{F}} &= V_A\left[D^{\mathsf{M}} - D^{\mathsf{F}} + \alpha_\Delta^{\mathsf{M}} - \alpha_\Delta^{\mathsf{F}} + (1-2r)(t^{\mathsf{M}} - t^{\mathsf{F}})\right]/2r + O(\epsilon^2) \\ \hat{p}_Y^{\mathsf{M}} - \hat{p}_X^{\mathsf{M}} &= V_A\left(D^{\mathsf{M}} - D^{\mathsf{F}} + \alpha_\Delta^{\mathsf{M}} - \alpha_\Delta^{\mathsf{F}} + t^{\mathsf{M}} - t^{\mathsf{F}}\right)(1-2r)/2r + O(\epsilon^2), \end{aligned} \tag{S2.4}$$

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $D^{\mathsf{F}} = \left[\bar{p}s^{\mathsf{F}} + (1-\bar{p})h^{\mathsf{F}}s^{\mathsf{F}}\right] - \left[\bar{p}h^{\mathsf{F}}s^{\mathsf{F}} + (1-\bar{p})\right]$ corresponds to the difference in fitness between A and a alleles in diploids of sex $\mathsf{F} \in \{\mathsf{F}, \mathsf{M}\}$. The frequency of Y-bearing male gametes depends upon the difference in the frequency of the A allele between X- and Y-bearing male gametes and the strength of meiotic drive in favour of the A allele in males, $q = 1/2 + \alpha_\Delta^{\mathsf{M}}(\hat{p}_Y^{\mathsf{M}} - \hat{p}_X^{\mathsf{M}})/2 + O(\epsilon^3)$. Without gametic competition or drive ($\alpha_\Delta^{\mathsf{F}} = t^{\mathsf{F}} = 0$) our results reduce to those of [31].

S3 Appendix

Invasion conditions

A rare neo-Y or neo-W allele, m, will spread in an XY sex-determining system when the leading eigenvalue, $\lambda_m^{(XY)}$, of the Jacobian matrix derived from the eight mutant recursion equations (given by S1.1c,d,g,h), evaluated at the ancestral equilibrium, is greater than one. However, because a neo-Y (neo-W) is always in males (females) and is epistatically dominant to the ancestral sex-determining locus, the characteristic polynomial factors into two quadratics times $(\lambda_m^{(XY)})^4$. One quadratic governs the change in the frequency of the new sex determination factor associated with the A and a allele frequencies, summing across backgrounds at the old sex-determining locus (i.e., summing haplotypes bearing the original X and Y alleles). The second quadratic describes the dynamics of the difference in the m-A and m-a haplotypes between X and Y backgrounds. Asymptotically, this difference is constrained to grow at a rate equal to or less than the sum while the m allele is rare, because the frequencies can never become negative. We therefore focus on the leading eigenvalue, $\lambda_m^{(XY)}$, which is the largest root of the first quadratic $f(x) = x^2 + bx + c = 0$, as described in the text (details in S1 File).

When $R = 0$ the two roots are $\Lambda_{mA}^{(XY)}$ and $\Lambda_{ma}^{(XY)}$, and the leading eigenvalue is the larger of the two. When $R > 0$ then $f(\Lambda_{mA}^{(XY)})$ and $f(\Lambda_{ma}^{(XY)})$ are of opposite signs, and the leading eigenvalue must fall between these two quantities (details in S1 File). Thus, $\lambda_m^{(XY)} > 1$ if both $\Lambda_{mA}^{(XY)} > 1$ and $\Lambda_{ma}^{(XY)} > 1$; similarly, $\lambda_m^{(XY)} < 1$ if both $\Lambda_{mA}^{(XY)} < 1$ and $\Lambda_{ma}^{(XY)} < 1$. If only one haplotypic growth rate is greater than one ($\Lambda_{ma}^{(XY)} < 1 < \Lambda_{mA}^{(XY)}$ or $\Lambda_{mA}^{(XY)} < 1 < \Lambda_{ma}^{(XY)}$), then $\lambda_m^{(XY)}$ is greater than one when condition (1) is met. Thus, the invasion of a new sex-determining allele is determined by the haplotypic growth rates ($\Lambda_{mj}^{(XY)}$ terms), which do not account for loss due to recombination, and the rates at which recombination between the **M** and **A** loci breaks apart these haplotypes ($\chi_{mj}^{(XY)}$). For tight linkage between the ancestral sex-determining locus (**X**) and the selected locus (**A**) we can calculate these terms explicitly (see below). For weak selection we approximate the leading eigenvalue with a Taylor series. The leading eigenvalue for any k is given up to order ϵ^2 by Eq (4).

Tight linkage between A and X ($r \approx 0$)

Here, we explore the conditions under which a neo-W invades an XY system assuming that the **A** locus is initially in tight linkage with the ancestral sex-determining locus ($r \approx 0$). We disregard neo-Y mutations, which never spread given that the ancestral population is at a stable equilibrium (see S1 File for proof).

Starting with the simpler (B) equilibrium, the terms that determine the leading eigenvalue are

$$\Lambda_{W'A}^{(XY)} = \left[w_A^{♂}(1+\alpha_\Delta^{♂})\right]^{-1} \frac{w_A^{♀}}{w_A^{♀}} \frac{\left[w_A^{♂}(1+\alpha_\Delta^{♂})w_{AA}^{♀} + w_a^{♂}(1-\alpha_\Delta^{♂})w_{Aa}^{♀}(1+\alpha_\Delta^{♀})\right]}{2w_{AA}^{♀}} \tag{S3.1a}$$

$$\Lambda_{W'a}^{(XY)} = \left[w_A^{♂}(1+\alpha_\Delta^{♂})\right]^{-1} \frac{w_a^{♀}}{w_A^{♀}} \frac{\left[w_A^{♂}(1+\alpha_\Delta^{♂})w_{Aa}^{♀}(1-\alpha_\Delta^{♀}) + w_a^{♂}(1-\alpha_\Delta^{♂})w_{aa}^{♀}\right]}{2w_{AA}^{♀}} \tag{S3.1b}$$

$$\chi_{W'A}^{(XY)} = \frac{1}{2}\left[w_A^{♂}(1+\alpha_\Delta^{♂})\right]^{-1} \frac{w_A^{♀}}{w_A^{♀}} \frac{\left[w_a^{♂}(1-\alpha_\Delta^{♂})w_{Aa}^{♀}(1+\alpha_\Delta^{♀})\right]}{w_{AA}^{♀}} \frac{R}{2} \tag{S3.1c}$$

$$\chi_{W'a}^{(XY)} = \frac{1}{2}\left[w_A^{♂}(1+\alpha_\Delta^{♂})\right]^{-1} \frac{w_a^{♀}}{w_A^{♀}} \frac{\left[w_A^{♂}(1+\alpha_\Delta^{♂})w_{Aa}^{♀}(1-\alpha_\Delta^{♀})\right]}{w_{AA}^{♀}} \frac{R}{2}. \tag{S3.1d}$$

Haploid selection impacts the spread of neo-W haplotypes in three ways (also seen in Table 2). Firstly, the zygotic sex ratio becomes male biased, $\zeta > 1/2$, when the a allele (which is fixed on the Y) is favoured during competition among male gametes or by meiotic drive in males. Specifically, at equilibrium (B), female zygote frequency is $1 - \zeta = w_A^{♂}(1+\alpha_\Delta^{♂})/(2\bar{w}_H^{♂})$ where $2\bar{w}_H^{♂} = \left[w_a^{♂}(1-\alpha_\Delta^{♂}) + w_A^{♂}(1+\alpha_\Delta^{♂})\right]$ has been canceled out in equations (S3.1) to leave the term $\left[w_A^{♂}(1+\alpha_\Delta^{♂})\right]^{-1}$. Male biased sex ratios facilitate the spread of a neo-W because neo-W alleles cause the zygotes that carry them to develop as the rarer, female, sex.

Secondly, haploid selection in females selects on neo-W haplotypes directly. At equilibrium (B), the fitness of female gametes under the ancestral sex-determining system is $w_A^{♀}$ such that the relative fitnesses of neo-W-A and neo-W-a haplotypes during female gametic competition are $w_A^{♀}/w_A^{♀}$ and $w_a^{♀}/w_A^{♀}$ (see terms in equation S3.1). Meiotic drive in females will also change the proportion of gametes that carry the A versus a alleles, which will be produced by heterozygous females in proportions $(1+\alpha_\Delta^{♀})/2$ and $(1-\alpha_\Delta^{♀})/2$, respectively. These terms are only associated with heterozygous females, i.e., they are found alongside $w_{Aa}^{♀}$.

Thirdly, haploid selection in males affects the diploid genotypes of females by altering the allele frequencies in the male gametes with which female gametes pair. At equlibrium (B), neo-W female gametes will mate with X-A male gametes with probability $w_A^{♂}(1+\alpha_\Delta^{♂})/(2\bar{w}_H^{♂})$ and Y-a male gametes with probability $w_a^{♂}(1-\alpha_\Delta^{♂})/(2\bar{w}_H^{♂})$, where the $2\bar{w}_H^{♂}$ terms have been canceled in Eq (S3.1) (as mentioned above). Thus, neo-W-A haplotypes are found in AA female diploids with probability $w_A^{♂}(1+\alpha_\Delta^{♂})/(2\bar{w}_H^{♂})$ (e.g., first term in square brackets in the numerator of equation S3.1a) and in Aa female diploids with probability $w_a^{♂}(1-\alpha_\Delta^{♂})/(2\bar{w}_H^{♂})$ (e.g., the second term in square brackets in the numerator of equation S3.1a).

The other terms in equations (S3.1) are more easily interpreted if we assume that there is no haploid selection in either sex, in which case $\Lambda_{W'A}^{(XY)} = (w_{AA}^{♀}+w_{Aa}^{♀})/2w_{AA}^{♀}$ and $\Lambda_{W'a}^{(XY)} = (w_{aa}^{♀}+w_{Aa}^{♀})/2w_{AA}^{♀}$. Neither haplotype can spread under purely sexually-antagonistic selection at equilibrium (B), with directional selection in each sex. Essentially, the X is then already as specialized as possible for the female beneficial allele (A is fixed on the X background), and the neo-W often makes daughters with the Y-a haplotype, increasing the flow of a alleles into females, which reduces the fitness of those females.

If selection doesn't uniformly favour A in females, however, neo-W-A haplotypes and/or neo-W-a haplotypes can spread ($\Lambda_{W'A}^{(XY)} > 1$ and/or $\Lambda_{W'a}^{(XY)} > 1$). A neo-W-A haplotype can spread ($\Lambda_{W'A}^{(XY)} > 1$) when $w_{Aa}^{♀} > w_{AA}^{♀}$, despite the fact that a neo-W brings Y-a haplotypes into females. In this case the a allele is favoured by selection in females despite A being fixed on the X background. For this equilibrium to be stable (i.e., to keep A fixed on the X), X-a cannot be overly favoured in females and X-A must be sufficiently favoured in males (for example, by overdominance in males). Specifically, from the stability conditions for equilibrium (B), we must have $w_{Aa}^{♀} < 2w_{AA}^{♀}$ and $w_{Aa}^{♂}/\left[(w_{aa}^{♂}+w_{Aa}^{♂})/2\right] > w_{Aa}^{♀}/w_{AA}^{♀}$.

Still considering $w_{Aa}^{♀} > w_{AA}^{♀}$, the neo-W can also spread alongside the a allele ($\Lambda_{W'a}^{(XY)} > 1$) if $w_{aa}^{♀}$ is large enough such that $(w_{Aa}^{♀}+w_{aa}^{♀})/2 > w_{AA}^{♀}$. This can occur with overdominance or directional selection for a in females (Fig 3B,C). In this case, a is favoured on the ancestral Y background in males and on the ancestral X background in females (comparing Aa to AA genotypes in females) but A is fixed on the X background due to selection in males. The neo-W-a haplotype can spread because it produces females with higher fitness Aa and aa genotypes.

Similar equations can be derived for equilibrium (A) by substituting the equilibrium frequencies into Table 2

$$\Lambda_{W'A}^{(XY)} = \frac{a}{b}\left[w_{AA}^{♀}w_{Aa}^{♂}w_A^{♂}(1+\alpha_\Delta^{♂})\phi + w_{Aa}^{♀}(1+\alpha_\Delta^{♀})w_a^{♂}c\right]/(2w_a^{♀}) \tag{S3.2a}$$

$$\Lambda_{W'a}^{(XY)} = \frac{a}{b}\left[w_{Aa}^{♀}(1-\alpha_\Delta^{♀})w_{Aa}^{♂}w_A^{♂}(1+\alpha_\Delta^{♂})\phi + w_{aa}^{♀}w_a^{♂}c\right]/(2w_A^{♀}) \tag{S3.2b}$$

$$\chi_{W'A}^{(XY)} = \frac{a}{b}\frac{R}{2}\left[w_{Aa}^{♀}(1+\alpha_\Delta^{♀})w_a^{♂}c\right]/w_a^{♀} \tag{S3.2c}$$

$$\chi_{W'a}^{(XY)} = \frac{a}{b}\frac{R}{2}\left[w_{Aa}^{♀}(1-\alpha_\Delta^{♀})w_{Aa}^{♂}w_A^{♂}(1+\alpha_\Delta^{♂})\phi\right]/w_A^{♀}, \tag{S3.2d}$$

where

$$a = w_a^{♀}\phi + w_A^{♀}\psi \tag{S3.3a}$$

$$b = w_{AA}^{♀}\left[w_{Aa}^{♂}w_A^{♂}(1+\alpha_\Delta^{♂})\right]\phi^2 + w_{Aa}^{♀}\left[w_{Aa}^{♂}w_A^{♂}(1+\alpha_\Delta^{♂}) + w_{aa}^{♂}w_a^{♂}\right]\psi\phi + w_{aa}^{♀}\left(w_{aa}^{♂}w_a^{♂}\right)\psi^2 \tag{S3.3b}$$

$$c = w_{Aa}^{♂}(1-\alpha_\Delta^{♂})\phi + 2w_{aa}^{♂}\psi. \tag{S3.3c}$$

As with equilibrium (B), haploid selection again modifies invasion fitnesses by altering the ancestral sex ratio, ζ (see Table 2), and directly selecting upon female gametes, through $w_i^{♀}$. The only difference is that resident XX

females are no longer always homozygote AA and males are no longer always heterozygote Aa. Thus the effect of haploid selection in males is reduced, as is the difference in fitness between neo-W haplotypes and resident X haplotypes, as both can be on any diploid or haploid background.

The other terms are easier to interpret in the absence of haploid selection. For instance, without haploid selection, the neo-W-A haplotype spreads ($\Lambda^{(XY)}_{W'A} > 1$) if and only if

$$2(w^{♀}_{Aa} - w^{♀}_{aa})w^{♂}_{aa}\psi^2 > (w^{♀}_{AA} - w^{♀}_{Aa})w^{♂}_{Aa}\phi(\phi - \psi), \tag{S3.4}$$

where $\phi - \psi = w^{♀}_{AA}w^{♂}_{Aa} - w^{♀}_{aa}w^{♂}_{aa}$ and both ϕ and ψ are positive when equilibrium (A) is stable. In contrast to equilibrium (B), a neo-W haplotype can spread under purely sexually-antagonistic selection ($w^{♀}_{aa} < w^{♀}_{Aa} < w^{♀}_{AA}$ and $w^{♂}_{AA} < w^{♂}_{Aa} < w^{♂}_{aa}$). The neo-W-$A$ can spread as long as it becomes associated with females that bear more A alleles than observed at equilibrium (A), effectively specializing on female fitness.

Without haploid selection, the neo-W-a haplotype spreads ($\Lambda^{(XY)}_{W'a} > 1$) if and only if

$$(w^{♀}_{aa} + w^{♀}_{Aa} - 2w^{♀}_{AA})w^{♂}_{Aa}\phi^2 + (w^{♀}_{aa} - w^{♀}_{Aa})(w^{♂}_{Aa} + 2w^{♂}_{aa})\phi\psi > 0. \tag{S3.5}$$

This condition cannot be met with purely sexually antagonistic selection (as both terms on the left-hand side would then be negative), but it can be met under other circumstances. For example, with overdominance in males there is selection for increased A frequencies on the X background in males, which are always paired with Y-a haplotypes. Directional selection for a in females can then maintain a polymorphism at the **A** locus on the X background. This scenario selects for a modifier that increases recombination between the sex chromosomes (e.g., blue region of Fig 2d in [69]) and facilitates the spread of neo-W-a haplotypes, which create females bearing more a alleles than the ancestral X haplotype does.

Role of haploid selection with tight linkage between X and A loci

Haploid selection generally expands the conditions under which neo-W alleles can spread within ancestral systems that have evolved tight linkage between the sex-determining locus and a selected locus ($r \approx 0$). First, haploid selection can allow a polymorphism to be maintained when it would not under diploid selection alone (e.g., with directional selection in diploids). In cases of ploidally-antagonistic selection, where there is a balance between alleles favored in the haploid stage and the diploid stage, neo-W alleles - even if unlinked to the selected locus - can spread (Figure S8). Second, even when diploid selection could itself maintain a polymorphism, haploid selection can increase the conditions under which transitions among sex-determining systems are possible. Of particularly importance, when selection is sexually-antagonistic in diploids ($s^{♀}s^{♂} < 0$ and $0 < h^{♂}_{♀} < 1$), an unlinked neo-W ($R = 1/2$) cannot invade unless there is also haploid selection (see proof in S1 File; Fig 2 and Figure S3). More generally, haploid selection alters the conditions under which neo-W alleles can spread (compare Figure S4-Figure S7 to Fig 3).

Male haploid selection in favour of the a allele ($\alpha^{♂}_{\Delta} < 0$, $w^{♂}_{A} < w^{♂}_{a}$) generates male-biased sex ratios at equilibria (A) and (B), where Y-a is fixed ($\hat{p}^{♂}_{Y} = 0$). Male-biased sex ratios facilitate the spread of neo-W-A and neo-W-a haplotypes (increasing $\Lambda^{(XY)}_{W'A}$ and $\Lambda^{(XY)}_{W'a}$). Panels A-C in Figure S4 and S5 show that neo-W haplotypes tend to spread for a wider range of parameters when sex ratios are male biased, compared to Fig 3 without haploid selection. By contrast, male haploid selection in favour of the A allele generates female-biased sex ratios and reduces $\Lambda^{(XY)}_{W'A}$ and $\Lambda^{(XY)}_{W'a}$, as demonstrated by panels D-F in Figure S4 and Figure S5.

Female haploid selection generates direct selection on the neo-W-A and neo-W-a haplotypes as they spread in females. Thus, female haploid selection in favour of the a allele tends to increase $\Lambda^{(XY)}_{W'a}$ and decrease $\Lambda^{(XY)}_{W'A}$, as shown by panels A-C in Figure S6 and Figure S7. Conversely, female haploid selection in favour of the A allele increases $\Lambda^{(XY)}_{W'A}$ and decreases $\Lambda^{(XY)}_{W'a}$, see panels D-F in Figure S6 and Figure S7.

Thus, the impact of haploid selection on transitions between sex-determining systems must be considered as two sides of a coin: it can generate sex ratio biases that promote transitions that equalize the sex ratio, but it can also direct select for transitions that cause sex ratios to become biased.

Supplementary Files

S1 File. Supplementary *Mathematica* file. This file can be used to re-derive our results and generate figures. Please contact authors for access.

Supplementary Tables

Table S1. Substitutions for different loci orders assuming no interference.

Order of loci	
SDR-A-M	$\rho = r(1-R) + R(1-r)$
SDR-M-A	$r = \rho(1-R) + R(1-\rho)$
A-SDR-M	$R = r(1-\rho) + \rho(1-r)$

Table S2. Mean fitnesses and zygotic sex ratio in the resident population (M fixed, XY sex determination).

Sex & Life Cycle Stage	Mean Fitness
female gametes ($\bar{w}^{♀}_{H}$)	$p^{♀}_{X} w^{♀}_{A} + (1-p^{♀}_{X}) w^{♀}_{a}$
X-bearing male gametes ($\bar{w}^{♂}_{HX}$)	$p^{♂}_{X} w^{♂}_{A} + (1-p^{♂}_{X}) w^{♂}_{a}$
Y-bearing male gametes ($\bar{w}^{♂}_{HY}$)	$p^{♂}_{Y} w^{♂}_{A} + (1-p^{♂}_{Y}) w^{♂}_{a}$
male gametes ($\bar{w}^{♂}_{H}$)	$(1-q)\bar{w}^{♂}_{HX} + q\bar{w}^{♂}_{HY}$
females ($\bar{w}^{♀}$)	$\big[p^{♀}_{X} w^{♀}_{A} p^{♂}_{X} w^{♂}_{A} w^{♀}_{AA} + (1-p^{♀}_{X}) w^{♀}_{a} p^{♂}_{X} w^{♂}_{A} w^{♀}_{Aa} + p^{♀}_{X} w^{♀}_{A} (1-p^{♂}_{X}) w^{♂}_{a} w^{♀}_{Aa} + (1-p^{♀}_{X}) w^{♀}_{a} (1-p^{♂}_{X}) w^{♂}_{a} w^{♀}_{aa}\big] / \left(\bar{w}^{♀}_{H} \bar{w}^{♂}_{HX}\right)$
males ($\bar{w}^{♂}$)	$\big[p^{♀}_{X} w^{♀}_{A} p^{♂}_{Y} w^{♂}_{A} w^{♂}_{AA} + (1-p^{♀}_{X}) w^{♀}_{a} p^{♂}_{Y} w^{♂}_{A} w^{♂}_{Aa} + p^{♀}_{X} w^{♀}_{A} (1-p^{♂}_{Y}) w^{♂}_{a} w^{♂}_{Aa} + (1-p^{♀}_{X}) w^{♀}_{a} (1-p^{♂}_{Y}) w^{♂}_{a} w^{♂}_{aa}\big] / \left(\bar{w}^{♀}_{H} \bar{w}^{♂}_{HY}\right)$
fraction zygotes male (ζ)	$q\left[p^{♂}_{Y} w^{♂}_{A} + (1-p^{♂}_{Y}) w^{♂}_{a}\right] / \bar{w}^{♂}_{H}$

Supplementary Figures

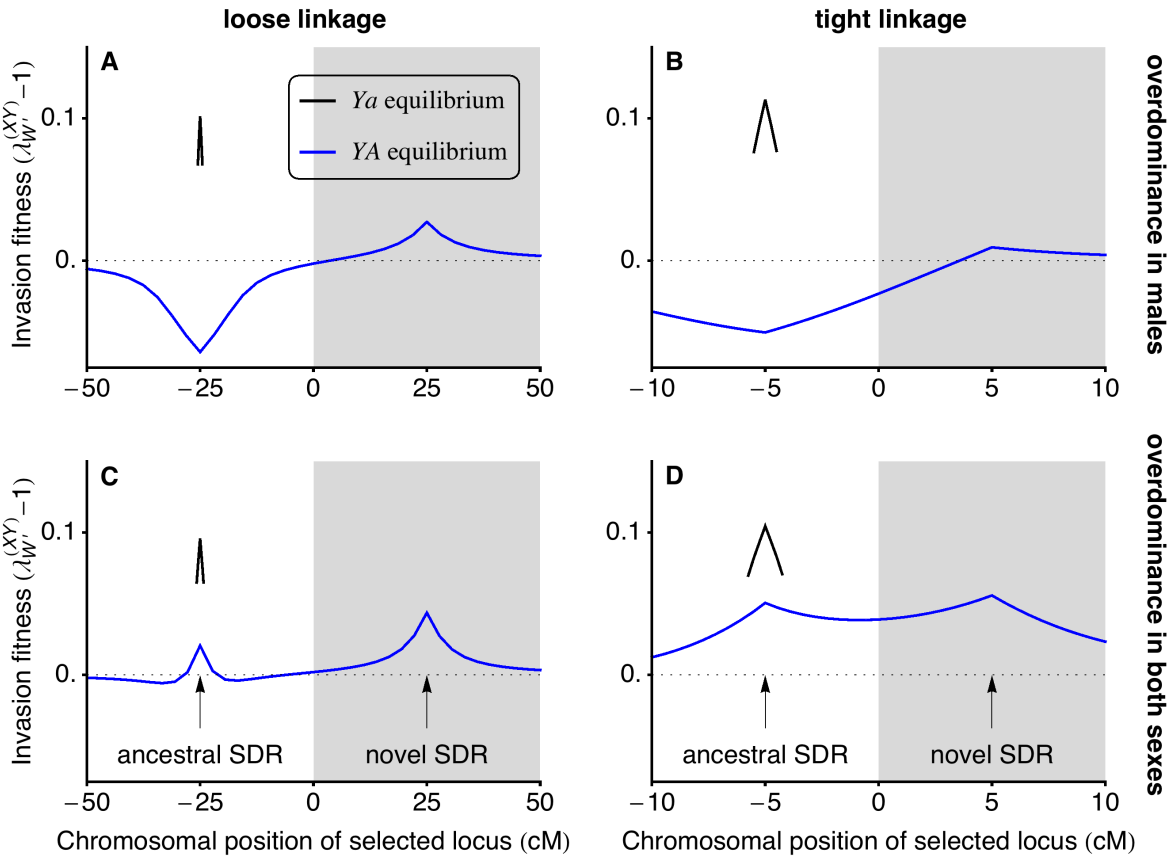

Fig S1. With overdominance, loci near to the ancestral sex-determining locus ($r \approx 0$) can favour neo-W alleles that are less tightly linked ($R > r$). In panels A and B, the a allele is favoured in females ($w^{♀}_{aa} = 1.05$, $w^{♀}_{Aa} = 1$, $w^{♀}_{AA} = 0.85$) and selection in males is overdominant ($w^{♂}_{aa} = w^{♂}_{AA} = 0.75$). In panels C and D, selection in males and females is overdominant ($w^{♀}_{aa} = w^{♀}_{AA} = 0.6$, $w^{♂}_{aa} = 0.5$, $w^{♂}_{AA} = 0.7$, $w^{♂}_{Aa} = 1$). There is no haploid selection $t^{♂} = \alpha^{♂}_{\Delta} = 0$. These parameters are marked by daggers in Fig 3B and C, which show that neo-W invasion is expected for any R ($\Lambda^{(XY)}_{W'A}, \Lambda^{(XY)}_{W'a} > 1$) if the a allele is nearly fixed on the Y (black lines in this figure; not stable for $r >> 0$). Equilibria where the A allele is more common among Y-bearing male gametes can also be stable and allow neo-W invasion for these parameters (blue lines).

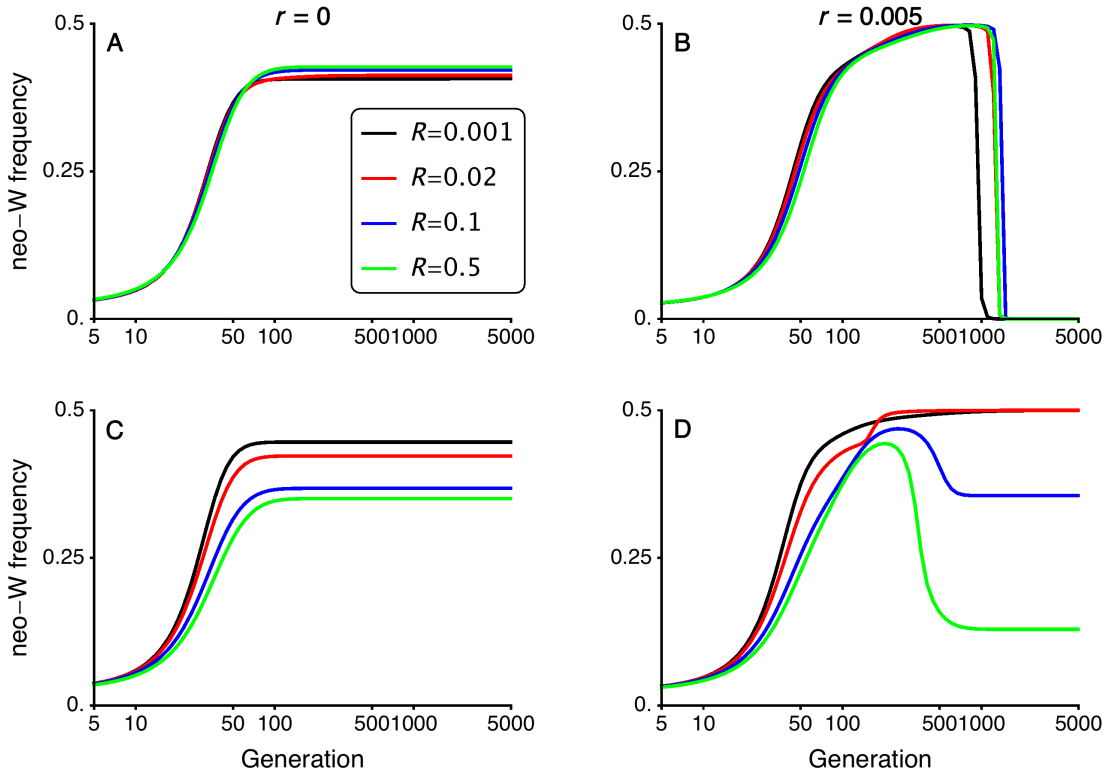

Fig S2. Following invasion by a neo-W allele, there can be a complete transition to a new sex-determining system, maintenance of both ancestral-XY and neo-ZW sex determining systems, or loss of the new sex-determining allele. Here, we plot the frequency of the neo-W allele among female gametes. Panels A, C and D show cases where a steady state is reached with the neo-W at a frequency below 0.5, in which case ancestral-X and Y alleles also both segregate. In all cases, we assume that the *a* allele is initially more common than the *A* allele on the Y background (Y-*a* is fixed when $r = 0$). When $r > 0$ (panels B and D), Y-*A* haplotypes created by recombination can become more common than Y-*a* haplotypes as the neo-W spreads. In B, this leads to loss of the neo-W and the system goes to an equilibrium with X-*a* and Y-*A* haplotypes fixed (equilibrium A'), such that all females have the high fitness genotype *aa* and all males are *Aa*. For the parameters in B, neo-W alleles have negative invasion fitness when the Y-*A* haplotype is ancestrally more common than Y-*a* (compare blue to black curves in Figure S1A and Figure S1B near the ancestral sex-determining locus). In contrast, the neo-W is not lost in panel D as it is favoured regardless of whether Y-*A* or Y-*a* haplotypes predominate (again, compare blue to black curves in Figure S1C and Figure S1D).

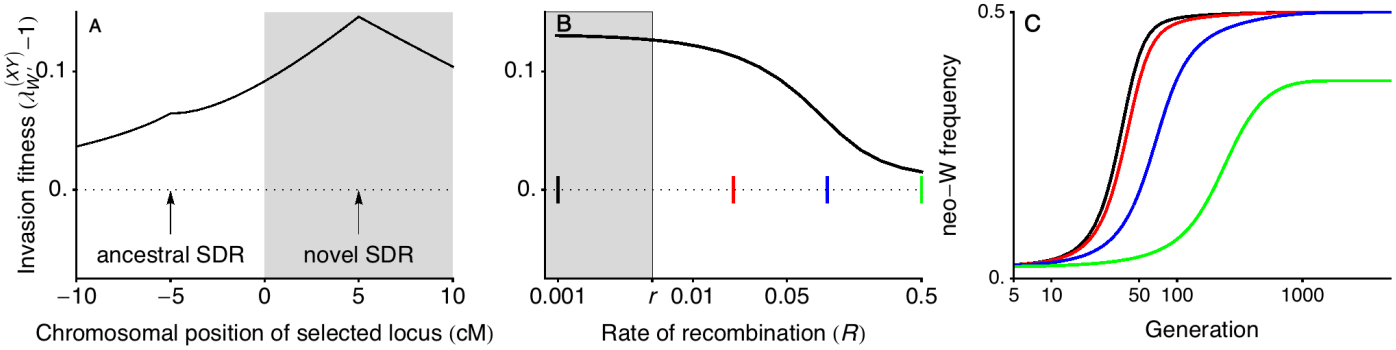

Fig S3. When there is sexually-antagonistic selection and haploid selection, a neo-W allele may invade for any R. Panel A shows that the invasion fitness of a neo-W is positive, even when $r < R$ (unshaded region). In panel B, we vary the recombination rate between the neo-W and the selected locus (R) for a fixed recombination rate between the ancestral sex-determining locus and the selected locus ($r = 0.005$). Coloured markers show recombination rates for which the temporal dynamics of neo-W invasion are plotted in panel C (black $R = 0.001$, red $R = 0.02$, blue $R = 0.1$, green $R = 0.5$). The diploid selection parameters used in this plot are the same as in Fig 2. There is also meiotic drive in males favouring a ($\alpha_{\Delta}^{\delta} = -0.08$), this full set of parameters is marked by an asterisk in Figure S4A. When $R = 0.5$ (green curve), the neo-W does not reach fixation and X, Y, Z, and W alleles are all maintained in the population, see Figure S9C.

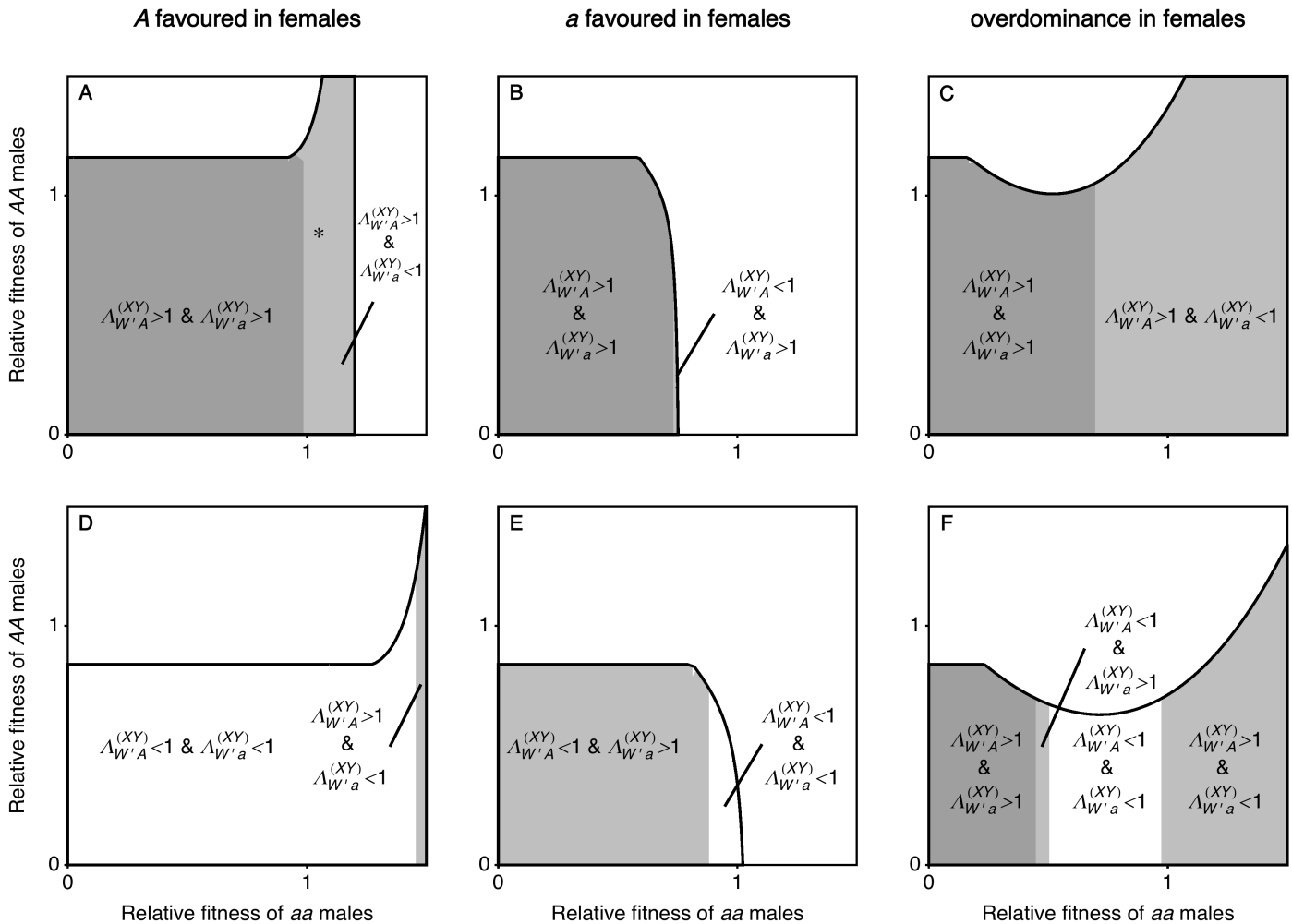

Fig S4. Parameters for which neo-W-*A* and neo-W-*a* haplotypes spread when there is male meiotic drive at a locus that is tightly linked to the ancestral XY locus ($r = 0$). This figure is equivalent to Fig 3 but with meiotic drive in males. In panels A-C, meiotic drive in males favours the *a* allele ($\alpha^{♂}_{\Delta} = -0.16$), creating male-biased sex ratios and generally increasing $\Lambda^{(XY)}_{W'A}$ and $\Lambda^{(XY)}_{W'a}$. By contrast, $\Lambda^{(XY)}_{W'A}$ and $\Lambda^{(XY)}_{W'a}$ tend to be reduced when meiotic drive in males favours the *A* allele ($\alpha^{♂}_{\Delta} = 0.16$), panels D-F.

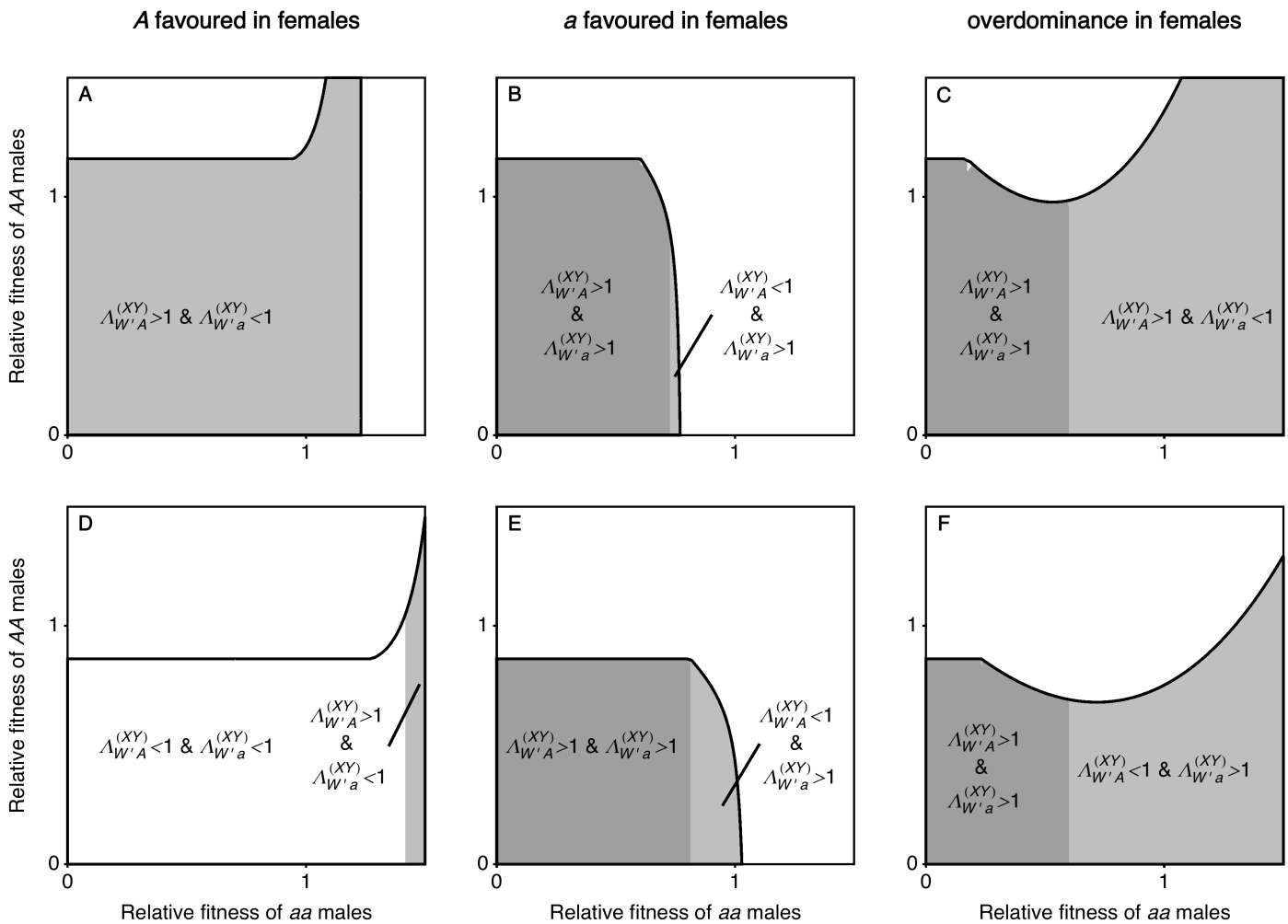

Fig S5. Parameters for which neo-W-*A* and neo-W-*a* haplotypes spread when there is male gametic competition at a locus that is tightly linked to the ancestral XY locus ($r = 0$). This figure is equivalent to Fig 3 but with gametic competition in males. The *a* allele is favoured during male gametic competition in Panels A-C ($w_a^{♂} = 1.16$, $w_A^{♂} = 1$), which creates male biased sex ratios and increases $\Lambda^{(XY)}_{W'A}$ and $\Lambda^{(XY)}_{W'a}$. By contrast, $\Lambda^{(XY)}_{W'A}$ and $\Lambda^{(XY)}_{W'a}$ tend to be reduced when the *A* allele is favoured during male gametic competition, panels D-F. Compared to the meiotic drive parameters in Figure S4, the effect of these male gametic competition parameters on the sex ratio is smaller. For example, in Figure S4A-C, the ancestral sex ratio is $\alpha^{♂} = 0.58$ at equilibrium (B) and in panels A-C of this plot, the ancestral sex ratio is $w_a^{♂}/(w_A^{♂} + w_a^{♂}) = 0.537$ at equilibrium (B).

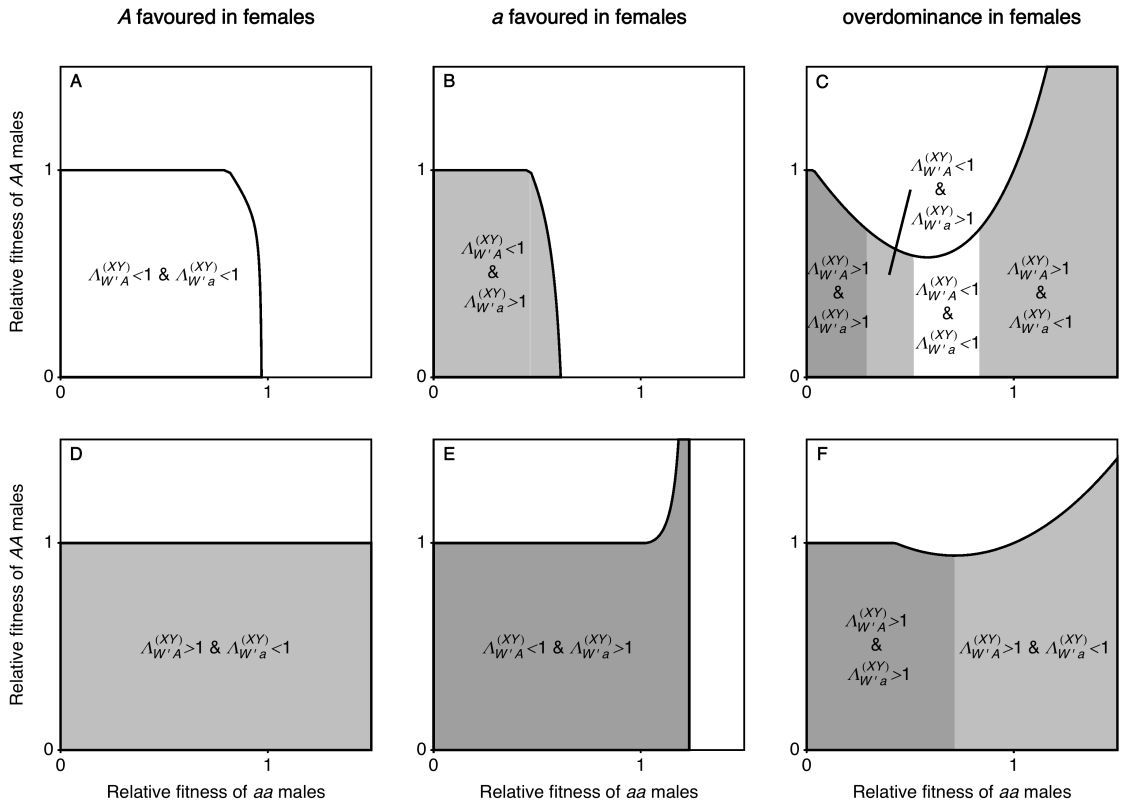

Fig S6. Parameters for which neo-W-A and neo-W-a haplotypes spread when there is female meiotic drive at a locus that is tightly linked to the ancestral XY locus ($r = 0$). This figure is equivalent to Fig 3 but with meiotic drive in females. The a allele is favoured by meiotic drive in females in Panels A-C ($\alpha^{♀}_{\Delta} = -0.16$), which increases $\Lambda^{(XY)}_{W'a}$ and decreases $\Lambda^{(XY)}_{W'A}$. Female meiotic drive in favour of the A allele (panels D-F, $\alpha^{♀}_{\Delta} = -0.16$) has the opposite effect.

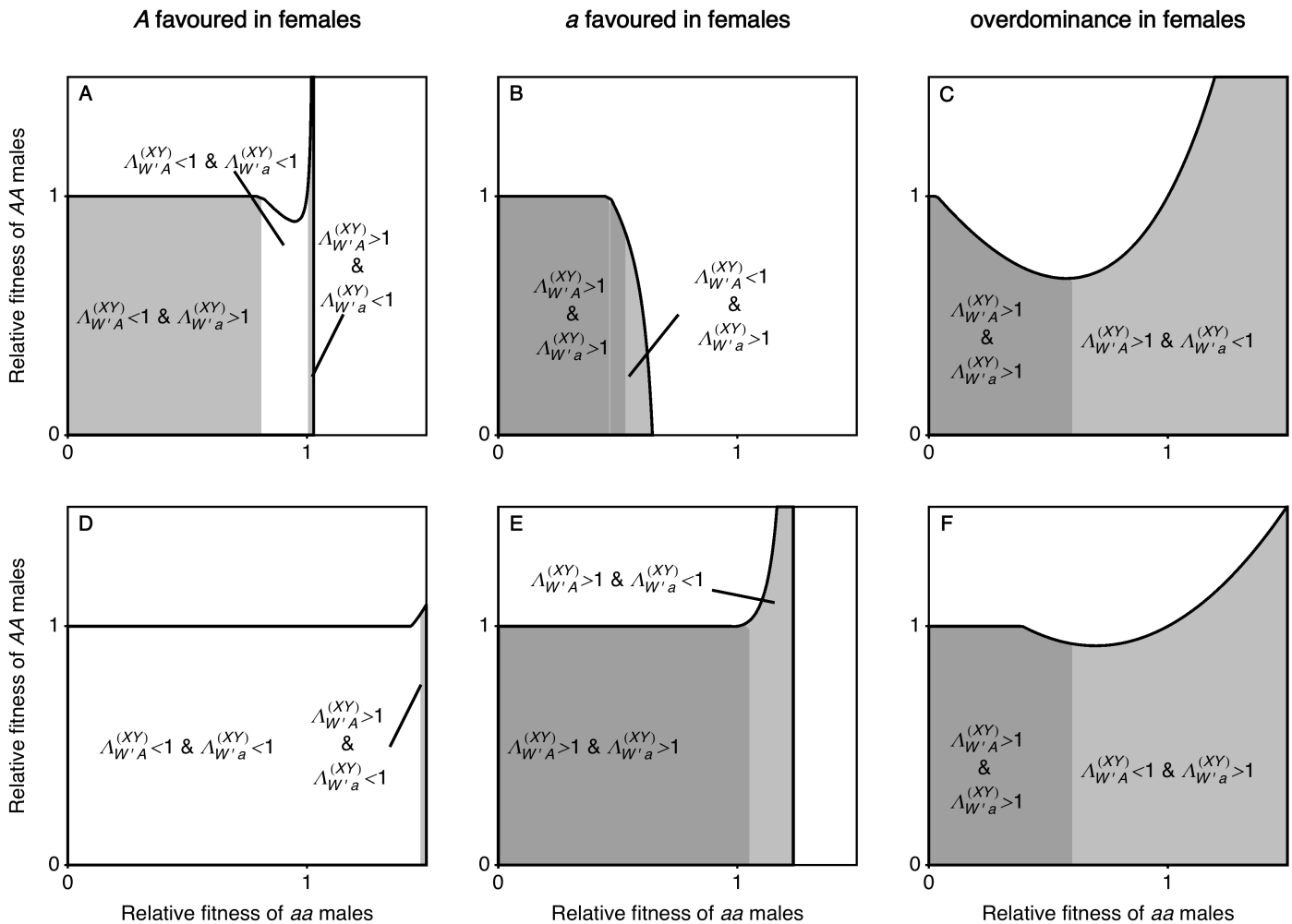

Fig S7. Parameters for which neo-W-A and neo-W-a haplotypes spread when there is female gametic competition at a locus that is tightly linked to the ancestral XY locus ($r = 0$). This figure is equivalent to Fig 3 but with gametic competition in females. The a allele is favoured during female gametic competition in females in Panels A-C ($w_a^{♀} = 1.16$, $w_A^{♀} = 1$), which increases $\Lambda^{(XY)}_{W'a}$ and decreases $\Lambda^{(XY)}_{W'A}$. The A allele is favoured during gametic competition in panels D-F ($w_a^{♀} = 1$, $w_A^{♀} = 1.16$), giving the opposite effect on $\Lambda^{(XY)}_{W'a}$ and $\Lambda^{(XY)}_{W'A}$.

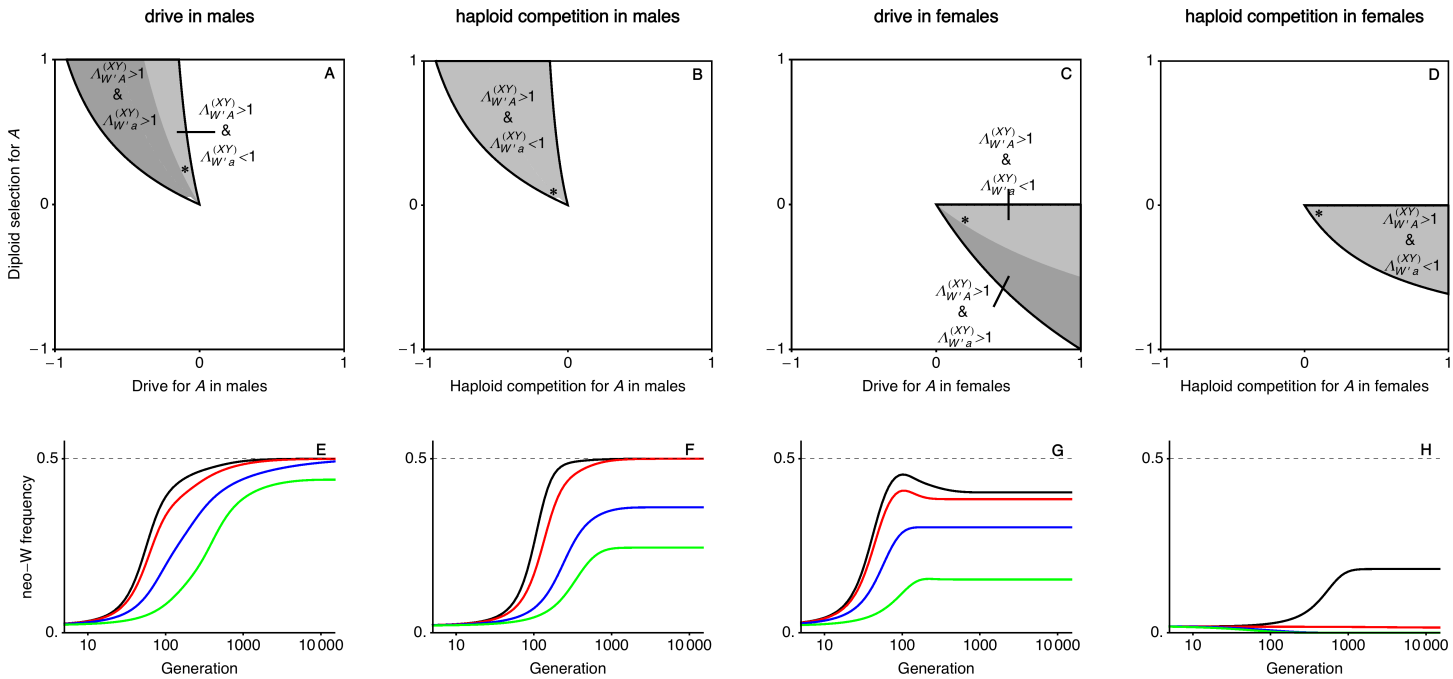

Fig S8. Ploidally-antagonistic selection can drive the spread of neo-W alleles. A-D show when each of the neo-W haplotypes invades an internally stable equilibrium with a fixed on the Y (found by setting $r = 0$). The y-axis shows directional selection in diploids of both sexes, $s^{♀} = s^{♂}$, and the x-axes show sex-specific drive, $\alpha_{\Delta}^{♀♂}$, or haploid competition, $t^{♀♂}$. The top left and bottom right quadrants therefore imply ploidally-antagonistic selection (and these are the only places where neo-W haplotypes can invade). Dominance is equal in both sexes, $h^{♀} = h^{♂} = 3/4$. E-F show the temporal dynamics of neo-W frequency in females with parameters given by the asterisks in the corresponding A-D plot, with $r = 1/200$, for four different R. Black $R = 1/1000$, Red $R = 2/100$, Blue $R = 1/10$, Green $R = 1/2$.

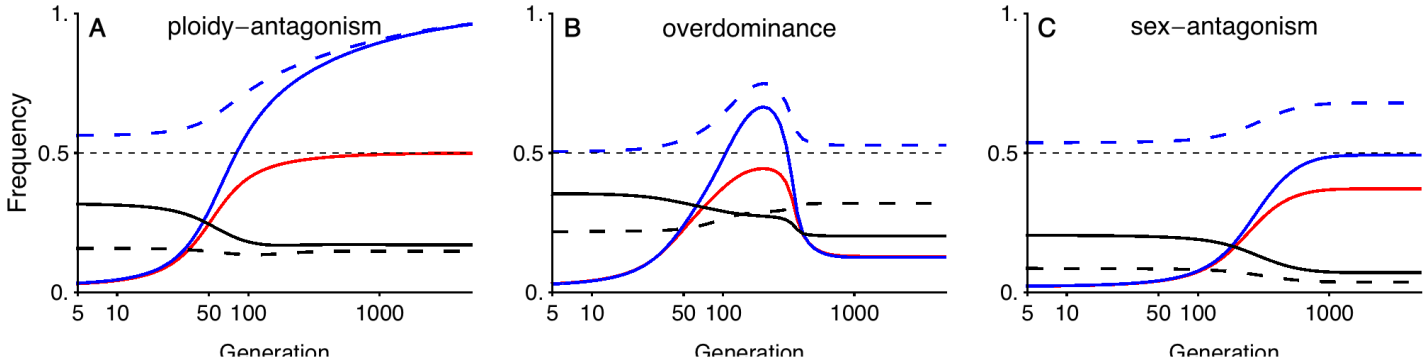

Fig S9. Pseudo-fixation of neo-W or maintenance of multiple sex-determining alleles. The curves show the frequencies of the neo-W (red), ancestral Y (blue), and *A* allele (black) among female gametes (solid curves) and among male gametes (dashed curves). In panel A, there is a complete transition from XY sex determination (XX-ZZ females and XY-ZZ males) to ZW sex determination (YY-ZW females and YY-ZZ males). In panels B and C a polymorphism is maintained at both the ancestral XY locus and the new ZW locus, such that there are males with genotypes XY-ZZ and YY-ZZ and females with genotypes XX-ZZ, XX-ZW, XY-ZW, and YY-ZW. In panel A, selection is ploidally-antagonistic with drive in males (parameters as in the green curve in Fig 5B). In panel B, there is overdominance in both sexes and no haploid selection (parameters as in the green curve in Figure S2C). In panel C, there is sexually-antagonistic selection in diploids with drive in males (parameters as in the green curve in Figure S4C). In all cases, the initial equilibrium frequency has *a* near fixation on the Y.