Haploid Selection, Sex Ratio Bias, and Transitions Between Sex-Determination Systems

Michael F Scott∗[1], Matthew M Osmond∗[2], and Sarah P Otto[2]

∗ These authors contributed equally to this work

[1] Department of Botany, University of British Columbia, #3529 - 6270 University Boulevard, Vancouver, BC, Canada V6T 1Z4

[2] Department of Zoology, University of British Columbia, #4200 - 6270 University Boulevard, Vancouver, BC, Canada V6T 1Z4

email: mfscott@biodiversity.ubc.ca, mmosmond@zoology.ubc.ca

Contributions:

Abstract

Sex-determination systems are 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-determination 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 determination 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-determination systems cannot be simply predicted by selection to equalise the sex ratio. Overall, our models reveal that transitions between sex-determination 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-determination systems are likely to be labile and draw novel connections with sex ratio evolution

Introduction

Animals and angiosperms exhibit extremely diverse sex-determination systems (reviewed in Bull 1983, Charlesworth and Mank 2010, Beukeboom and Perrin 2014, Bachtrog et al. 2014). Among species with genetic sex determination of diploid sexes (GSD), some taxa have heterogametic males (XY) and homogametic females (XX), including mammals and most dioecious plants (Ming et al. 2011); 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 region changes. For example, transitions of the master sex-determining gene between chromosomes or the evolution of new master sex-determining genes have occurred in Salmonids (Li et al. 2011, Yano et al. 2012), Diptera (Vicoso and Bachtrog 2015), and *Oryzias* (Myosho et al. 2012). In addition, many clades exhibit transitions between male (XY) and female (ZW) heterogamety, including snakes (Gamble et al. 2017), lizards (Ezaz et al. 2009), eight of 26 teleost fish families (Mank et al. 2006), true fruit flies (Tephritids, Vicoso and Bachtrog 2015), amphibians (Hillis and Green 1990), the angiosperm genus *Silene* (Slancarova et al. 2013), the angiosperm family *Salicaceae* (Pucholt et al. 2015; 2017) and Coleoptera and Hemiptera (Beukeboom and Perrin 2014, plate 2). Indeed, in some cases, both male and female heterogametic sex-determination systems can be found in the same species, as reported in houseflies (McDonald et al. 1978), midges (Thompson 1971), frogs (Ogata et al. 2007), cichlid fish (Ser et al. 2010), tilapia (Lee et al. 2004), sea bass (Vandeputte et al. 2007), and lab-strains of Zebrafish (Liew et al. 2012, Wilson et al. 2014). In addition, multiple transitions have occurred between genetic (GSD) and environmental sex-determination (ESD) systems, e.g., in reptiles and fishes (Conover and Heins 1987, Mank et al. 2006, Pokorná and Kratochvíl 2009, Ezaz et al. 2009, Pen et al. 2010, Holleley et al. 2015).

Predominant theories accounting for the spread of new sex-determination systems by selection involve fitness differences between sexes (e.g., sexually antagonistic selection) or sex ratio selection (Blaser et al. 2012, Beukeboom and Perrin

2014, van Doorn 2014). van Doorn and Kirkpatrick (2007; 2010) and Muralidhar and Veller (2018) have shown that new sex-determining loci can be favoured if they arise 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 chromosome, for example. Such associations can favour a new partially-masculinizing or partially-feminizing allele (Muralidhar and Veller 2018), a new master sex-determining gene (van Doorn and Kirkpatrick 2007), and transitions between male and female heterogamety (trans-GSD transitions, ZW to XY or XY to ZW, van Doorn and Kirkpatrick 2010). However, any sexually-antagonistic loci that are more closely linked to the ancestral sex-determination locus will develop similar, favourable associations and are expected to hinder the spread of a new sex-determination system.

The sex ratio is directly determined by the sex-determination 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; Beukeboom and Perrin 2014, Chapter 7). 'Fisherian' sex ratio selection favours a 1:1 zygotic sex ratio when assuming that males and females are equally costly to produce (Fisher 1930, Charnov 1982). 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 (West 2009). 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. (2010) 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 (Hamilton 1967). They find that new, unlinked sex-determining loci (masculinizing or feminizing mutations, i.e., neo-Y or neo-W loci) can then spread, which restore an even sex ratio.

Here we use mathematical models to find the conditions under which new

sex-determination systems spread when individuals experience selection at both diploid and haploid stages. 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 (Mulcahy et al. 1996, Joseph and Kirkpatrick 2004). 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 (Lalanne et al. 2004, Fishman and Willis 2005, Leppälä et al. 2008; 2013, Didion et al. 2015; 2016). Where it has been characterized, meiotic drive generally occurs either during the production of male or female gametes only (Úbeda and Haig 2005, Lindholm et al. 2016). 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 random genes (Borg et al. 2009, Arunkumar et al. 2013, Gossmann et al. 2014). In addition, artificial selection pressures applied to male gametophytes are known to cause a response to selection (e.g., Hormaza and Herrero 1996, Ravikumar et al. 2003, Hedhly et al. 2004, Clarke et al. 2004). A smaller proportion of genes are thought to be expressed and selected during competition in animal sperm, although precise estimates are uncertain (Zheng et al. 2001, Joseph and Kirkpatrick 2004, Vibranovski et al. 2010). Nevertheless, recent studies have demonstrated that sperm competition in animals can alter haploid allele frequencies and increase offspring fitness (Immler et al. 2014, Alavioon et al. 2017).

There are various ways by which genes experiencing haploid selection could influence transitions between sex-determination systems. If we assume that hap-

loid 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-determination systems in a similar manner to sex-specific diploid selection (as explored by van Doorn and Kirkpatrick 2007; 2010). That is, new masculinizing mutations (neo-Y chromosomes) 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 region 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 3) or selection among X- and Y-bearing pollen (Lloyd 1974, Conn and Blum 1981, Stehlik and Barrett 2005; 2006, Field et al. 2012; 2013). It is not immediately clear how the spread of new sex-determination systems would be influenced by the combination of sex ratio biases and associations between haploid selected loci and sex-determining regions.

We find that the spread of novel sex-determiners is influenced by both Fisherian sex ratio selection and by selection on genetically-associated 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 region. Because sex-determining loci are often found within a region of suppressed recombination, there can be a significant number of tightly linked loci. We find that loci linked with the ancestral sex-determining region can drive transitions in which the heterogametic sex changes, even when the neo-sex-determining locus is less closely linked to loci under selection (either including haploid selection or not).

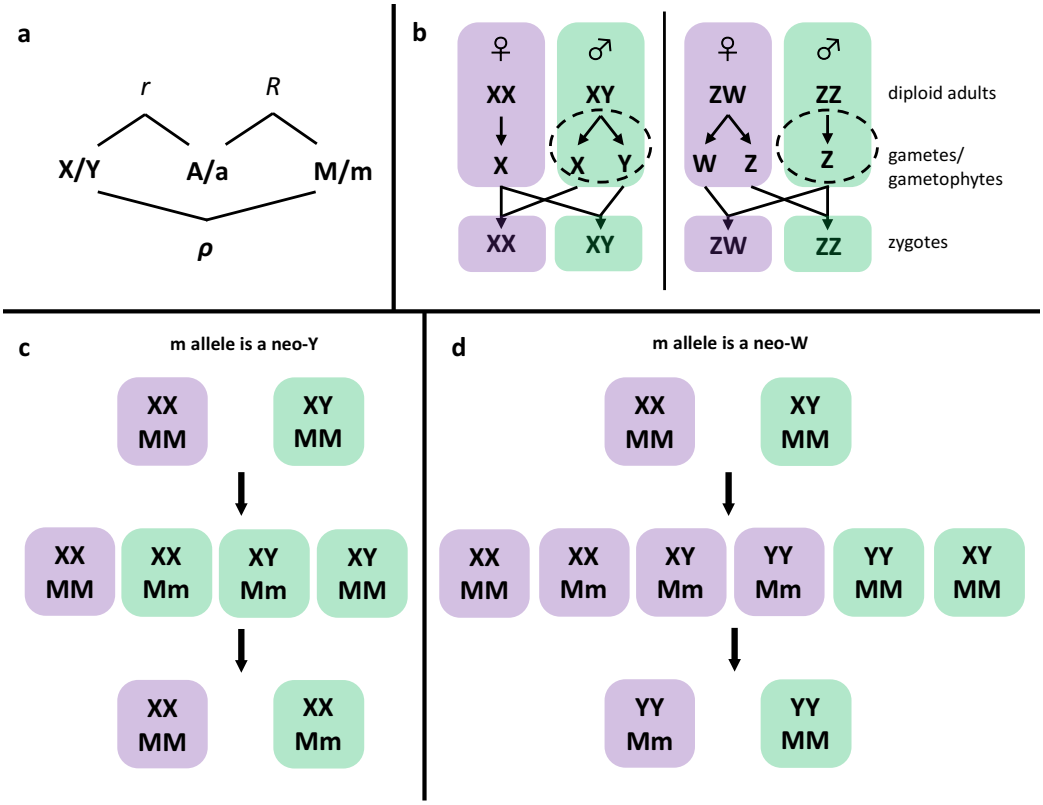

Figure 1: Outline of model features. Panel A: Recombination rate parameters between the ancestral-sex-determining locus (here, assumed to have X or Y alleles), a locus under selection (**A**, with alleles A and a), and a neo-sex-determining locus (**M**, with alleles M and m). If $r < 1/2$, then associations between ancestral-sex-determining alleles (X and Y) and **A** locus 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 male gametes/gametophytes will be abundant after haploid selection. However, the zygotic sex ratio is not biased by male haploid selection in ZW sex-determination systems. Similarly, zygotic sex ratio biases can occur if haploid selected alleles are associated with neo-sex-determining alleles (M and m, i.e., if $R < 1/2$). Panel C: During cis-GSD transitions (XY to XY or ZW to ZW, without loss of generality we assume ancestral XY sex determination here), a neo-Y allele spreads to pseudo-fixation (its maximum frequency among male gametes) and the 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 mutations allow Y-associated alleles into females, which may impede or aid their spread.

Model

We consider transitions between ancestral and novel sex-determining systems using a three-locus model, each locus having two alleles. 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-determination systems, we consider the invasion, fixation, maintenance, and/or loss of novel sex-determining alleles (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 (i.e., a neo-Y) and with $k = 1$ the m allele is a feminizer (i.e., a neo-W). 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 the 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 $w_A^{\male}$ and $w_a^{\male}$ ($\male \in \{\female, \male\}$; see table 1). We assume that all gametes compete for fertilization during gametic competition, which assumes 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, random mating occurs between male and female gametes. The resulting zygotes develop as males or females, depending on their genotypes at the **X** and **M** loci. Diploid males and females then experience selection, with relative fitnesses $w_{AA}^{\male}$, $w_{Aa}^{\male}$, and $w_{aa}^{\male}$. 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 Figure 1A and Table S.1). Individuals that are heterozygous at the **A** locus may experience meiotic drive; a gamete produced by Aa heterozgotes of sex $\mathfrak{F}$ bears allele A with probability $\alpha^{\mathfrak{F}}$. 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 $\mathfrak{F} \in \{\mathfrak{P}, \mathfrak{O}\}$

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

Results

The model outlined above describes both ancestrally-XY and ancestrally-ZW sex-determination systems if we relabel the two sexes as being ancestrally 'heterogametic' or ancestrally 'homogametic'. Without loss of generality, we primarily refer to the ancestrally heterogametic sex as male and the ancestrally homogametic sex as female. That is, we describe an ancestral XY sex-determination system but our model is equally applicable to an ancestral ZW sex-determination system (relabelling the ancestrally-heterogametic sex as female and the ancestrally-

homogametic sex as male and switching the labels of males and females throughout).

Generic invasion by a neo-Y or neo-W

The evolution of a new sex-determination system requires that a rare mutant allele at the novel sex-determining locus, m, increases in frequency when rare. The spread of a rare mutant m at the **M** locus is determined by the leading eigenvalue, λ, of the system of eight equations describing the frequency of eggs and sperm carrying the m allele in the next generation (equations S.1). This system simplifies substantially in a number of cases of interest. Dominant neo-Y (when $k = 0$) or neo-W alleles (when $k = 1$) are only found in male diploids (neo-Y) or female diploids (neo-W) such that their growth rate ultimately depends only on the change in frequency of m-bearing gametes produced by males or by females, respectively. Furthermore, if the m allele is fully epistatically dominant over the ancestral sex-determining system, phenotypes are not affected by the genotype at the ancestral sex-determining region (**X** locus). Thus, the invasion of rare dominant neo-Y or neo-W alleles is determined by the largest eigenvalue that solves the quadratic, $\lambda^2 + b\lambda + c = 0$ (see Appendix for a discussion of other roots - or Sally's proof!). Here, $b = -(\lambda_{mA} + \lambda_{ma}) + (\chi_{mA} + \chi_{ma})$ and $c = (\lambda_{mA} - \chi_{mA})(\lambda_{ma} - \chi_{ma}) - \chi_{mA}\chi_{ma}$, where λ_{mi} is the multiplicative growth rate (which we will call the "haplotypic growth rate") of the neo-sex determination allele m on background i without accounting for loss due to recombination, and χ_{mi} is the rate at which mutant haplotypes on background $i \in \{A, a\}$ recombine onto the other **A** locus background in heterozygotes (see Table 2). The λ_{mi} and χ_{mi}, and thus the spread of the mutant m allele, depend on the frequency of alleles at the **A** and **X** loci in the ancestral population. In the ancestral population, it is convenient to follow the frequency of the A allele among female gametes (eggs), $p_X^{\female}$, and among X-bearing, $p_X^{\male}$, and among Y-bearing, $p_Y^{\male}$, 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, $\hat{p}_i^{\male}$, and

Y-bearing male gametes, $\hat{q}$, when calculating the eigenvalues.

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

m is a neo-Y ($k = 0$)
$\lambda_{YA} = (2\zeta)^{-1}\left[\hat{p}_X^{\varphi} w_A^{\varphi} w_A^{\sigma} w_{AA}^{\sigma} + (1-\hat{p}_X^{\varphi}) w_a^{\varphi} w_A^{\sigma} w_{Aa}^{\sigma}(1+\alpha_\Delta^{\sigma})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\sigma}\right)$
$\lambda_{Ya} = (2\zeta)^{-1}\left[(1-\hat{p}_X^{\varphi}) w_a^{\varphi} w_a^{\sigma} w_{aa}^{\sigma} + \hat{p}_X^{\varphi} w_A^{\varphi} w_a^{\sigma} w_{Aa}^{\sigma}(1-\alpha_\Delta^{\sigma})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\sigma}\right)$
$\chi_{YA} = R\,(2\zeta)^{-1}\left[(1-\hat{p}_X^{\varphi}) w_a^{\varphi} w_A^{\sigma} w_{Aa}^{\sigma}(1+\alpha_\Delta^{\sigma})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\sigma}\right)$
$\chi_{Ya} = R\,(2\zeta)^{-1}\left[\hat{p}_X^{\varphi} w_A^{\varphi} w_a^{\sigma} w_{Aa}^{\sigma}(1-\alpha_\Delta^{\sigma})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\sigma}\right)$
m is a neo-W ($k = 1$)
$\lambda_{WA} = [2(1-\zeta)]^{-1}\left[\bar{p}^{\sigma} w_A^{\sigma} w_A^{\varphi} w_{AA}^{\varphi} + (1-\bar{p}^{\sigma}) w_a^{\sigma} w_A^{\varphi} w_{Aa}^{\varphi}(1+\alpha_\Delta^{\varphi})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\varphi}\right)$
$\lambda_{Wa} = [2(1-\zeta)]^{-1}\left[(1-\bar{p}^{\sigma}) w_a^{\sigma} w_a^{\varphi} w_{aa}^{\varphi} + \bar{p}^{\sigma} w_A^{\sigma} w_a^{\varphi} w_{Aa}^{\varphi}(1-\alpha_\Delta^{\varphi})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\varphi}\right)$
$\chi_{WA} = R\,[2(1-\zeta)]^{-1}\left[(1-\bar{p}^{\sigma}) w_a^{\sigma} w_A^{\varphi} w_{Aa}^{\varphi}(1+\alpha_\Delta^{\varphi})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\varphi}\right)$
$\chi_{Wa} = R\,[2(1-\zeta)]^{-1}\left[\bar{p}^{\sigma} w_A^{\sigma} w_a^{\varphi} w_{Aa}^{\varphi}(1-\alpha_\Delta^{\varphi})\right] / \left(\bar{w}_H^{\varphi}\bar{w}_H^{\sigma}\bar{w}^{\varphi}\right)$

$\bar{p}^{\sigma} = (1-\hat{q})\hat{p}_X^{\sigma} + \hat{q}\hat{p}_Y^{\sigma}$ is the average frequency of the A allele among X- and Y-bearing male gametes.
ζ is the zygotic sex ratio (fraction male)
$\bar{w}^{\varphi}$ is the mean fitness of diploids of sex φ, see Table S.2
$\bar{w}_H^{\varphi}$ is the mean fitness of haploids from sex φ, see Table S.2

We are particularly concerned with the conditions under which a rare neo-sex-determining allele increases in frequency, which occurs when the largest eigenvalue, λ, is greater than one. The leading eigenvalue solves $f(\lambda) = \lambda^2 + b\lambda + c = 0$ and the Perron-Frobenius theorem guarantees that the leading eigenvalue is positive, unique, and real. Since $f(\lambda_{mA})$ and $f(\lambda_{ma})$ are of opposite signs, the leading eigenvalue must fall between these two quantities and is the larger of them when $R = 0$. Consequently, if both λ_{mA} and λ_{ma} are greater than one, then the leading eigenvalue will always be greater than one, regardless of the linkage between the neo-sex determination factor and the selected locus (R). In particular, having $\lambda_{mA} > 1$ and $\lambda_{ma} > 1$ thus guarantees that an unlinked sex determining factor can

invade ($R = 1/2$). Conversely, if both λ_{mA} and λ_{ma} are smaller than one, then invasion can never occur. Finally, if only one of λ_{mA} and λ_{ma} is greater than one, the new sex determining factor can always invade when tightly linked to the selected locus (R near 0). Furthermore, it can be shown that the leading eigenvalue declines with R, and invasion requires that R is sufficiently small that the following condition holds:

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

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

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 if the ancestral zygotic sex ratio is biased towards females, $\zeta < 1/2$ (i.e., the first factor of the λ_{mi} 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) allele 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) allele, m, only changes in males (females), Figure 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, and develop into males, Figure 1C. By contrast, a gamete with a neo-W can pair with an X or Y male gamete, developing into a female, Figure 1D. Consequently, neo-W bearing

females obtain a differerent frequency of A alleles from mating (when $\hat{p}_X^{\male} \neq \hat{p}_Y^{\male}$) compared to ancestral (MM) females.

In order to explicitly determine the conditions under which a rare neo-sex-determining allele spreads, we must calculate the equilibrium frequency of the A allele (i.e., $\hat{p}_X^{\female}$, $\hat{p}_X^{\male}$, and $\hat{p}_Y^{\male}$) 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-determination system before the neo-sex-determining allele (m) arises. Such polymorphisms can be maintained by heterozygote advantage, sexually-antagonistic selection, ploidally-antagonistic selection, or a combination (Immler et al. 2012). 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 SDR ($r \approx 0$) or (2) selection is weak relative to recombination ($s^{\male\female}$, $t^{\male\female}$, $\alpha_\Delta^{\male\female}$ of order $\epsilon << 1$).

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

The ancestral equilibrium allele frequencies and their stability conditions are given in the appendix. When there is complete linkage between the ancestral sex-determining region and the **A** locus ($r = 0$), either the A allele or the a allele must be fixed on the Y. Because the labelling of alleles is arbitrary, we will assume that the a locus is fixed on the Y ($p_Y^{\male} = 0$), without loss of generality. If there are two alleles maintained at the **A** locus, the X can either be fixed for the A allele ($\hat{p}_X^{\female} = \hat{p}_X^{\male} = 1$) or polymorphic ($0<\hat{p}_X^{\female}, \hat{p}_X^{\male}<1$).

We find that a neo-Y can never invade an ancestral XY system that already has tight linkage with the locus under selection ($r = 0$, for details see supplementary

296 *Mathematica* file). When $R = 0$, a neo-Y haplotype with the same allele as the ancestral Y is neutral ($\lambda_{Ya} = 1$) and does not change in frequency. The other neo-
298 Y haplotype will not spread ($\lambda_{YA} < 1$) given that the initial equilibrium is stable. Therefore, a neo-Y mutation cannot spread ($\lambda \leq 1$, regardless of R) in an ancestral
300 XY system where selected loci are within or very near the non-recombining region around the SDR. In essence, through tight linkage with the **A** locus, the ancestral Y
302 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
304 not possible for a neo-Y to create males that have higher fitness than the ancestral Y.

306 Neo-W alleles, on the other hand, can invade an ancestral XY system under some conditions (the full invasion conditions are given in the appendix; equations
308 S.6 and S.7). Counterintuitively, selection on loci within the non-recombining region of the SDR can favour the invasion of a less closely linked neo-W, whatever
310 the form of selection maintaining a polymorphism (sexually-antagonistic selection, overdominance, ploidally-antagonistic selection, or some combination, Fig-
312 ures 2, S.2, S.8, and S.3). The conditions become more restrictive, however, with increasing recombination (R) between the new sex determining region and the se-
314 lected 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
316 with only sexually-antagonistic selection if selection is directional in each diploid sex (see Supplementary *Mathematica* file). To develop an intuition for how less
318 closely linked neo-W alleles invade ($R > r$), we first focus on cases where there is no haploid selection and discuss the additional effect of haploid selection in the
320 appendix.

If we categorise the a allele as being ancestrally 'male-beneficial' via the fact
322 that it is fixed on the Y, then $\lambda_{WA} > 1$ indicates that the neo-W spreads when found with the ancestrally 'female-beneficial' allele. Broadly, this is possible because the
324 ancestral X chromosome is sometimes found in males and is therefore unable to perfectly specialise on the 'female-beneficial' allele. For example, when the a

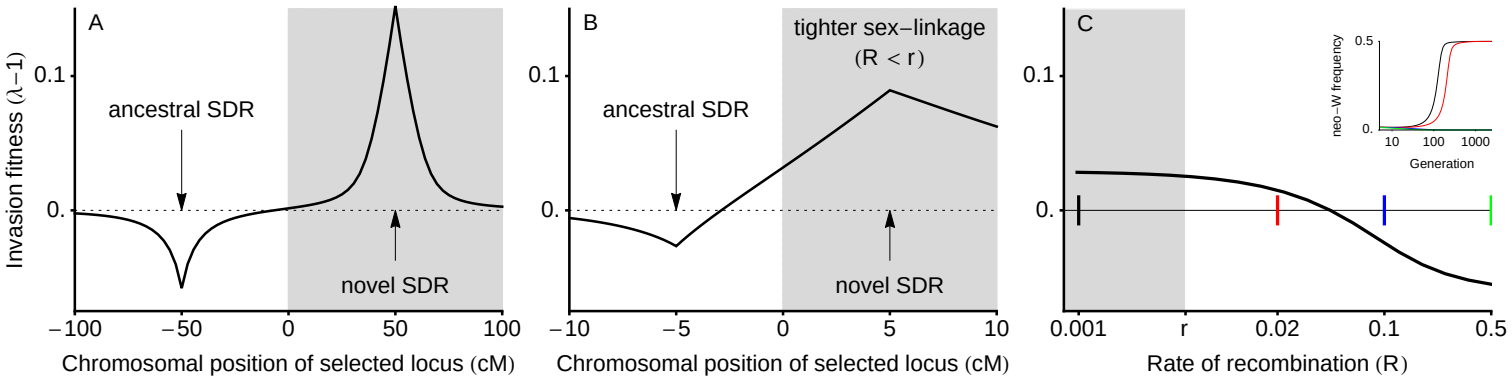

Figure 2: Transitions between XY and ZW systems can occur even when the neo-SDR is less tightly linked to a locus under sexually-antagonistic selection (here, without haploid selection). In panel A, linkage is loose enough relative to selection that the analytical results assuming weak selection hold, and a neo-W can only invade when it is 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). 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-SDR 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 fix (reach frequency 0.5 among female gametes) 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). Fitness parameters are: $w^{\female}_{AA} = 1.05$, $w^{\male}_{aa} = 1.2$, $w^{\female}_{aa} = w^{\male}_{AA} = 0.85$, $w^{\male}_{Aa} = 1$, $t^{\male} = \alpha^{\male}_{\Delta} = 0$.

allele is favoured on the ancestral X in males, a polymorphism of A and a alleles can be maintained on the X despite directional selection in favour of the A allele in females ($s^{\female} > 0$, $0 < h^{\female} < 1$), see outlined region in Figure 3A. When the a allele is strongly favoured on X chromosomes in males ($w^{\male}_{aa}$ sufficiently large relative to $w^{\male}_{Aa}$), neo-W-A haplotypes can spread ($\lambda_{WA} > 1$, see grey region in Figure 3A) because they produce hgher fitness females (AA or Aa genotypes) and are unleashed from counterselection in males.

When only one neo-W haplotype has a positive growth rate (see Figure 3), a neo-W can invade as long as equation (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. Therefore, tightly sex-linked loci that experience sexually-antagonistic selection can drive trans-GSD transitions in which the neo-SDR is

less closely linked to the locus under selection (Figure 2).

Given that the *a* allele can be considered ancestrally 'male-beneficial' because it is fixed on the Y, it is surprising that neo-W-*a* haplotypes can sometimes be favoured by selection in females ($\lambda_{Wa} > 1$). Again, this occurs because ancestral X's also experience selection in males, in which they will always be paired with a Y-*a*. 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 in males. Therefore, the X can be polymorphic or even fixed for the *A* allele despite favouring the *a* allele during selection in females (e.g., see outlined region in Figure 3B and Lloyd and Webb 1977, Otto 2014). In such cases, neo-W-*a* haplotypes can spread because they create more *Aa* and *aa* females when pairing with an X from males and because they bring Y-*a* haplotypes into females, where it has higher fitness (Figure 1D).

In some cases, both W-*A* and W-*a* haplotypes can spread, e.g., when *AA* individuals have low fitness in females yet the *A* is polymorphic or fixed on the X due to overdominance in males (Figure 3B and 3C). Both neo-W-*A* and neo-W-*a* haplotypes then 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 haplotypes have positive growth rates, invasion by a neo-W is expected regardless of its linkage with the selected locus (i.e., even unlinked neo-W alleles can invade, see Figures S.1 and S.2 for examples).

Assuming that linkage is not tight, van Doorn and Kirkpatrick (2010) showed that invasion by a neo-W occurs under the same conditions as 'pseudo-fixation' (at pseudo-fixation the neo-W reaches its maximum frequency among eggs, which is 1/2). An equivalent analysis is not possible where we assume that linkage is tight. However, numerical simulations with tight linkage demonstrate that the neo-SDR does not necessarily reach pseudo-fixation, leading to the stable maintenance of a mixed sex-determining system, in which X, Y, Z, and W alleles all segregate (e.g., Figure S.9B,C).

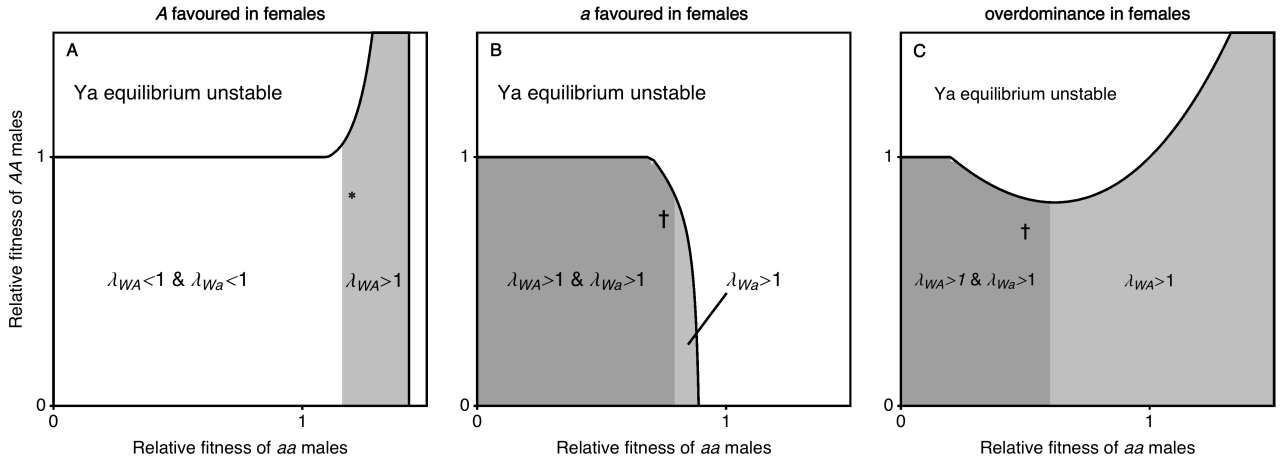

Figure 3: When the ancestral-XY locus is tightly linked to a locus under selection ($r = 0$), one or both neo-W haplotypes can spread. We vary the fitness of male homozygotes relative to heterozygotes ($w^{\male}_{Aa} = 1$) and only consider stable equilibria at which both **A** locus alleles are maintained and the *a* allele is initially fixed on the Y, region outlined. Here, selection in females can favour the *A* allele (panel A, $w^{\female}_{aa} = 0.85$, $w^{\female}_{AA} = 1.05$), favour the *a* allele (panel B, $w^{\female}_{aa} = 1.05$, $w^{\female}_{AA} = 0.85$), or be overdominant (panel C, $w^{\female}_{aa} = w^{\female}_{AA} = 0.6$). If λ_{wA} or λ_{wa} is greater than one, then a rare neo-W can spread for, at least, some values of $R > r$. The parameter values marked with an asterisk correspond to the fitnesses used in Figure 2C. Where both λ_{wA} and λ_{wa} are greater than one, a neo-W will spread when rare, regardless of linkage with the selected locus (for any R). Figure S.1 shows the dynamics using the parameters marked with a dagger. Here, there is no haploid selection $t^{\male} = \alpha^{\male}_{\Delta} = 0$.

Loose linkage with the ancestral sex-determining region

Assuming that selection is weak ($s^{\male}$, $t^{\male}$, $\alpha^{\male}_{\Delta}$ of order $\epsilon << 1$) and thus implicitly assuming that all recombination rates (r, R and ρ) are large relative to selection, we denote the leading eigenvalues describing the invasion of a neo-Y ($k = 0$) and a neo-W ($k = 1$) into an ancestrally XY system by $\lambda_{Y',XY}$ and $\lambda_{W',XY}$, respectively. To leading order in selection, these are:

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

and

$$\lambda_{W',XY} = \lambda_{Y',XY} + \left(2\alpha^{\male}_{\Delta} - 2\alpha^{\female}_{\Delta} + t^{\male} - t^{\female}\right)\left(\hat{p}^{\male}_{Y} - \hat{p}^{\male}_{X}\right)/2 + O\left(\epsilon^3\right) \tag{3}$$

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the equilibrium frequency of A and $S_A = (D^{♂} + \alpha_{\Delta}^{♂} + t^{♂}) - (D^{♀} + \alpha_{\Delta}^{♀} + t^{♀})$ describes sex differences in selection for the A versus a allele across diploid selection, meiosis, and gametic competition. The diploid selection term, $D^{⚥} = \left[\bar{p}s^{⚥} + (1-\bar{p})h^{⚥}s^{⚥}\right] - \left[\bar{p}h^{⚥}s^{⚥} + (1-\bar{p})\right]$, is the difference in fitness between A and a alleles in diploids of sex $⚥ \in \{♀, ♂\}$, where $\bar{p}$ is the leading-order probability of mating with an A-bearing gamete from the opposite sex (equation S.4). The difference in A-allele-frequency among Y-bearing sperm versus X-bearing sperm is given by $\hat{p}_Y^{♂} - \hat{p}_X^{♂} = V_A\big(D^{♂} - D^{♀} + \alpha_{\Delta}^{♂} - \alpha_{\Delta}^{♀} + t^{♂} - t^{♀}\big)(1-2r)/(2r)$.

The neo-sex-determining allele, m, will spread if $\lambda_{m,XY} > 1$. Equation (2) demonstrates that, under weak selection, a neo-Y will invade an XY system if and only if it is more closely linked to the selected locus than the ancestral sex-determining region (i.e., if $R < r$; note that $V_A S_A^2$ is strictly positive as long as **A** is polymorphic). This echoes our tight linkage results above where a neo-Y could never invade if $r \approx 0$. It is also consistent with the results of van Doorn and Kirkpatrick (2007), who considered diploid selection only and also found that cis-GSD transitions (XY to XY or ZW to ZW) can only occur when the neo-sex-determining locus is more closely linked to a locus under sexually-antagonistic selection.

With weak selection and no haploid selection ($t^{⚥} = \alpha_{\Delta}^{⚥} = 0$), 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 (XY to ZW or ZW to XY) can also occur only if the neo-sex-determining region is more closely linked to a locus under selection ($R < r$), as found by van Doorn and Kirkpatrick (2010). With haploid selection, however, the additional term in equation (3) can be positive, which can allow, for example, neo-W invasion ($\lambda_{W',XY} > 1$) even when the neo-sex-determining region is less closely linked to the selected locus ($R > r$).

Equation (3) shows that, with weak selection, neo-W alleles can invade an XY system for a large number of selective regimes. To clarify the parameter space under which $\lambda_{W',XY} > 1$, we consider several special cases. Firstly, if the **A** locus is

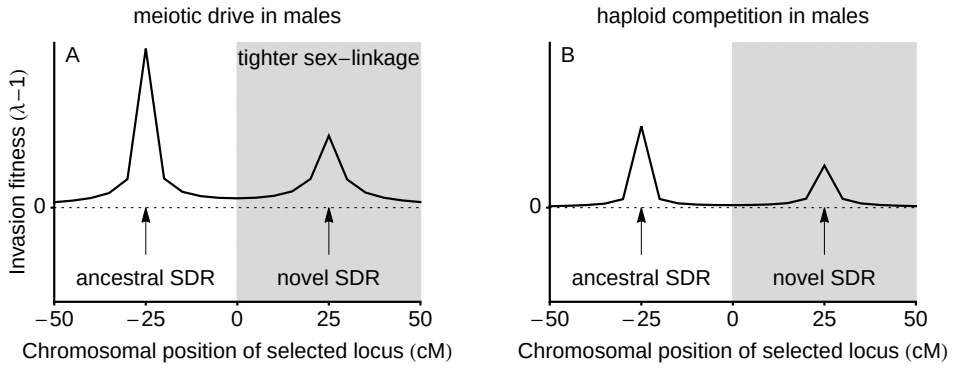

Figure 4: Ploidally-antagonistic selection allows a less tightly linked neo-W to invade. In panel A, male drive ($\alpha_\Delta^{\male} = -1/20$, $t^{\male} = \alpha_\Delta^{\female} = 0$) opposes selection in diploids (no sex-differences: $s^{\male} = 1/10$, $h^{\male} = 7/10$), in which case the neo-sex-determining allele can invade regardless of linkage. In panel B, gametic competition in males ($t^{\male} = -1/10$, $t^{\female} = \alpha_\Delta^{\male} = 0$) opposes selection in diploids (sex-differences: $s^{\male} = 3/20$, $s^{\female} = 1/20$, $h^{\male} = 7/10$), in which case the neo-sex-determining allele can once again invade regardless of linkage. We use Haldane's map function (Equation 3 in Haldane 1919) to convert from map distance (centiMorgans, cM) to the probability of recombination (an odd number of cross-over events).

unlinked to the ancestral sex-determining region ($r = 1/2$), a more closely linked neo-W ($R < 1/2$) can always invade because there is no ancestral association between A alleles and sex chromosomes in males, $\left(\hat{p}_Y^{\male} - \hat{p}_X^{\male}\right) = 0$, see equation (S.5). The second term in equation (3) therefore disappears and invasion depends only on the sign of $(r - R)$, as in the case of the neo-Y. Indeed, invasion typically occurs when the neo-W is more closely linked to the selected locus than the ancestral sex-determining region (Figure 4).

Secondly, we can simplify the discussion of cases where invasion occurs despite looser sex-linkage, $R > r$, by focusing 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, $h^{\female} = h^{\male}$. 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 ($s^{\female} s^{\male} > 0$, see Figure 4A

and Figure 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., $s^{\varphi}(s^{\sigma} - s^{\varphi}) > 0$, see Figure 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.

Table 3: Invasion conditions for unlinked neo-W ($R = 1/2$, $r < 1/2$) into ancestral XY with one form of haploid selection

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

Previous research suggests that when the ancestral sex-determining locus is linked to a locus that experiences haploid selection (e.g., meiotic drive), a new, unlinked sex-determining locus invades in order to restore equal sex ratios (Kozielska et al. 2010). Consider, for example, the case where the **A** locus is linked to the ancestral-SDR ($r < 1/2$) and experiences meiotic drive in males only ($\alpha_{\Delta}^{\sigma} \neq 0$, $\alpha_{\Delta}^{\varphi} = 0$), without gametic competition ($t^{\varphi} = t^{\sigma} = 0$). In this case, the zygotic sex ratio can be initially biased only if the ancestral sex-determining system is XY (Figure 1B and Figure 5B). If Fisherian sex ratio selection were dominant, we would expect a difference in the potential for XY to ZW and ZW to XY transitions. However, invasion by a neo-W into an XY system and invasion by a neo-Y into a ZW system occur under the same conditions ($\lambda_{Y',XY} = \lambda_{W',ZW}$ and $\lambda_{Y',ZW} = \lambda_{W',XY}$, at least to order ϵ^2). For example, in Figure 5A neo-W alleles invade an ancestral-XY system where females are initially rare. However, Figure 5B shows that a neo-Y can invade an ancestral-ZW system under the same conditions. As a consequence, whenever $R < 1/2$, the neo-Y becomes associated with the male meiotic drive allele such that the zygotic sex ratio actually evolves to become biased to-

wards males.

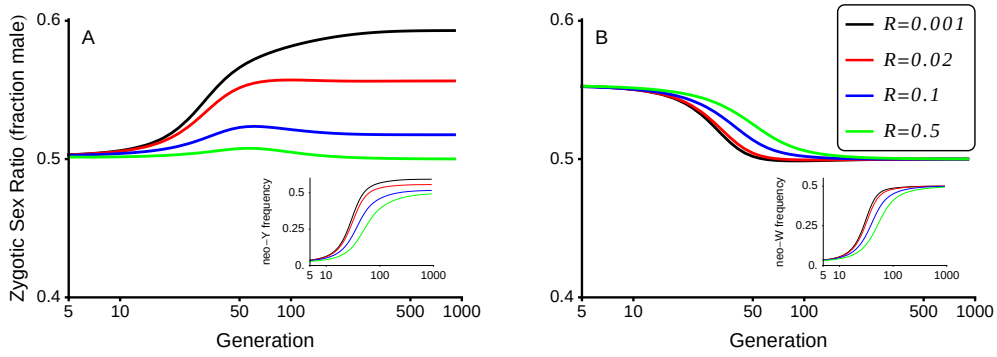

Figure 5: Fisherian sex ratio selection alone is not a good predictor of turnover between sex-determining systems. In this figure, selection is ploidally antagonistic with haploid selection favouring the a allele during male meiosis. In panel A, male drive in an ancestral ZW system has no affect on the zygotic sex ratio (see Figure 1B) yet a neo-Y can invade and replace the ancestral sex-determination system (inset shows neo-Y frequency among male gametes, the ancestral W also goes to fixation during this transition). When $R < 1/2$, the neo-Y becomes associated with the allele favoured by drive, causing the zygotic sex ratio to become biased, hence the frequency of neo-Y among male gametes can be higher than 0.5 (inset). In panel B, male drive in an ancestral XY system causes a male bias, allowing a neo-W to invade and replace the ancestral sex-determination system (inset shows neo-W frequency among female gametes, the ancestral Y also goes to fixation), which balances the zygotic sex ratio. Parameters: $s^{\varphi} = s^{\sigma} = 0.2$, $h^{\varphi} = h^{\sigma} = 0.7$, $t^{\varphi} = t^{\sigma} = \alpha_{\Delta}^{\varphi} = 0$, $\alpha_{\Delta}^{\sigma} = -0.1$, $r = 0.02$.

Why can new sex-determining regions invade when more loosely linked to selected loci ($R > r$)? Consider first the case where both loci are linked to the selected locus ($r < R < 1/2$). In an XY system, haploid selection in males can facilitate the spread of a neo-W because the zygotic sex ratio is ancestrally biased and the W helps to equalize the sex ratio (Figure 5A). A new sex determining region can also, however, benefit from becoming more associated with drive. For example in a ZW system with the same selection regime (haploid selection in males), a neo-Y can spread despite the fact that the zygotic sex is initially even; in this case, the neo-Y spreads because it is often found in males and can, if it carries the driven allele a, benefit from haploid selection (Figure 5B). While equalizing the sex ratio and benefiting from drive are two primary reasons why haploid selection spurs sex chromosome transitions, more complex situations also arise. For example with $R = 1/2$ in Figure 5B (green curve), the neo-Y 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 found at high frequency on the W background, which has higher average diploid fitness to balance the haploid advantage of the a allele at equilibrium.

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-determination systems that allow 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 Charnov 1982, Bull 1983, West 2009).

The characteristic polynomial determining the eigenvalues (equations S.1) does not factor for ESD mutants as it does for $k = 0$ or $k = 1$. We therefore focus on weak selection here. Assuming weak selection, the spread of the new sex-determining region is given by

$$\begin{aligned}\lambda_{ESD',XY} =& 1 + \frac{(1-2k)^2}{4} V_A {S_A}^2 \frac{r-R}{rR} \\ &+ \frac{k(\hat{p}_Y^{\male} - \hat{p}_X^{\male})}{2} \left[k\left(2\alpha_\Delta^{\male} - 2\alpha_\Delta^{\female} + t^{\male} - t^{\female}\right) - 2(1-k)S_A \right] + O\left(\epsilon^3\right),\end{aligned} \tag{4}$$

which reduces to $\lambda_{Y',XY}$ when $k = 0$ and $\lambda_{W',XY}$ 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 which is given by

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

where $\lambda_{Y',XY|R=1/2}$ and $\lambda_{W',XY|R=1/2}$ represent $\lambda_{Y',XY}$ and $\lambda_{W',XY}$ when evaluated at $R = 1/2$ (Equations 2 and 3). That is, recombination between the selected locus and the novel sex-determining locus, R, doesn't enter into the $k = 1/2$ results. This is because sex is essentially randomized each generation, preventing associations from building up between allele A and sex. Equation (5) shows that the neo-ESD 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, $\lambda_{Y',XY|R=1/2}$ is necessarily less than one, but $\lambda_{W',XY|R=1/2}$ can be greater than one if there is haploid selection. That is, when there is haploid selection, ESD mutations can invade an ancestrally-XY system because they generate females that are either rare or have high fitness, in the same manner as a neo-W.

Significantly, equation (5) is the same whether ESD is invading an ancestrally XY or ZW system (because $\lambda_{Y',XY} = \lambda_{W',ZW}$ and $\lambda_{W',XY} = \lambda_{Y',ZW}$). Thus, Fisherian sex ratio selection alone does not explain the invasion of ESD under weak selection because the sex ratio is only biased by male haploid selection when the ancestral sex-determination system is XY. Specifically, with male haploid selection, the neo-ESD is equally likely to invade when it equalizes the zygotic sex ratio (through $\lambda_{W',XY}$) and when it doesn't (through $\lambda_{Y',ZW}$). In addition, we note that ESD may not invade, even if the sex ratio is initially biased (e.g., with drive in males only, $r < 1/2$, $h^{\female} = h^{\male}$, and $s^{\female}s^{\male} < 0$, then $\lambda_{W',XY} < 1$, see Table 3). We conclude that, as with neo-W and neo-Y loci, associations with selected loci mean that the evolution of neo-ESD systems 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-determination systems are sexually-antagonistic selection and sex ratio selection (reviewed in Blaser et al. 2012, van Doorn 2014). The former predicts that neo-sex-determining alleles can invade when they arise in closer linkage with a sexually-antagonistic locus (van Doorn and Kirkpatrick 2007; 2010, Muralidhar and Veller 2018). 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 region can favour trans-GSD transitions (XY to ZW or ZW to XY) to new sex-determining systems that are less closely linked to the selected loci (e.g., see Figure 2). Similarly, even when linkage is weak relative to selection, we show that trans-GSD transitions (XY to ZW or ZW to XY) can occur where the new sex-determining region is less closely linked to the locus under selection if there is haploid selection (e.g., Figures 4 and 5).

We find that the spread of neo-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 GSD-ESD transitions between sex-determining systems. For instance, alleles favoured by haploid selection in males often become associated with the Y, which leads to a male-biased zygotic sex ratio. This male bias increases the potential for a neo-W to invade (Table 2), which can equalize the sex ratio (e.g., see Figure 5B, for related examples see Kozielska et al. 2010). 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., Figure 5A and step 1 in Úbeda et al. 2015). Significantly, with weak selection, we find that there is no difference in conditions allowing XY to ZW and ZW to XY transi-

tions, 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 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 neo-sex-determining allele, and these selective pressures are often predicted to be of equal magnitude.

We have shown that the spread of new sex determination systems can be driven by loci experiencing haploid selection. In agreement with this hypothesis, a recent transcriptome analysis in *Rumex* shows that Y-linked genes have higher expression in haploid pollen than autosomal genes (check this is accurate). Interestingly, haploid-expression is also more common on the autosome that is orthologous to the sex chromosomes in closely related species suggesting that new sex chromosomes may have been favoured through their association with haploid selected alleles on these chromosomes (Sandler et al., 2018, Personal Communication). In general, we predict that haploid selection increases lability of sex-determination systems, particularly because haploid selection can cause transitions that increase or decrease sex-linkage (e.g., the final state of the red line in Figure 5B is the starting state in Figure 5A). 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 (XY to ZW or ZW to XY) are favoured more strongly than cis-GSD transitions, with transitions to ESD intermediate (e.g., with $|D^{\male} - D^{\female}| << |\alpha_{\Delta}^{\male} - \alpha_{\Delta}^{\female} + t^{\male} - t^{\female}|$ we have $\lambda_{W',XY} > \lambda_{Y',XY}$; Equations 3 and S.5). Among the relatively few dioecious clades in which multiple species have well characterized sex chromosomes (Ming et al. 2011), trans-GSD transitions have been inferred in *Silene* subsection *Otites* (Slancarova et al. 2013) and in *Salicaceae* (Pucholt et al. 2015; 2017). 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 (Käfer et al. 2017, Goldberg et al. 2017).

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 (Lindholm and Breden 2002, Tripathi et al. 2009, Ser et al. 2010). Our results show, however, that tight ancestral-linkage of polymorphic loci 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., Figures S.9B and S.9C), which is not possible with loose linkage (van Doorn and Kirkpatrick 2010). 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 (Kallman 1965; 1968, Volff and Schartl 2001, Schulteis et al. 2006). Several rodent species also maintain feminizing alleles along with the ancestral X and Y sex-determination alleles (reviewed in Fredga 1994). For example, in nine *Akadon* species, it appears that male-determining-*sry* expression is suppressed by an autosomal feminizing allele, creating XY females (Bianchi 2002, Sánchez et al. 2010), which have increased fitness relative to XX females (Hoekstra and Hoekstra 2001). In *Mus microtoides*, females can have XX, XX* or X*Y genotypes (Veyrunes et al. 2010). 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 (Saunders et al. 2014; 2016, Veyrunes and Perez 2017). Although Y-linkage of female-beneficial alleles is counterintuitive, our tight linkage 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 around the Y or W sex-determining regions (Rice 1996, Charlesworth and Charlesworth 2000, Bachtrog 2006, Marais et al. 2008). During trans-GSD transitions (XY to ZW or ZW to XY), but not cis-GSD transitions (XY to XY or ZW to ZW), any recessive deleterious alleles linked to the Y or W are revealed to selection in YY or WW individuals (Bachtrog et al. 2014). This phenomenon was studied by van Doorn and Kirkpatrick (2010), who found that degeneration can prevent fixation of a neo-W or a neo-Y allele, leading to a mixed sex-determination 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 region 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, Vicoso and Bachtrog (2015) found a dozen sex chromosome configurations among Dipteran species but only one transition between male and female heterogamety.

In this study, we have only considered neo-sex-determining alleles of large effect. However, we expect similar selective forces to act on masculinizing/feminizing alleles of weaker effect. For example, Muralidhar and Veller (2018) consider small effect masculinizing/feminizing alleles within a threshold model of sex determination, finding that they can be favoured when linked to loci that experience sexually-antagonistic selection. These results echo those for large-effect neo-Y/neo-W alleles (van Doorn and Kirkpatrick 2007; 2010). Finally, while we have considered cis-GSD, trans-GSD, and GSD to ESD transitions, we have not explicitly consid-

ered ESD to GSD transitions. Recent models of ESD to GSD transitions (Úbeda et al. 2015, Muralidhar and Veller 2018) 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.

We have shown that tight sex-linkage and haploid selection can drive previously unexpected transitions between sex-determination systems. In particular, both can select for neo-sex-determining loci that are more loosely linked. 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-determination systems. Perhaps counterintuitively, transitions involving haploid selection can be driven by sex ratio selection or cause sex ratio biases to evolve and Fisherian sex ratio selection is not an overwhelming force. Overall, our results suggest several new scenarios under which new sex-determination systems are favoured, which could help to explain why the evolution of sex-determination systems is so dynamic.

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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 $x_i^{\male}$ and $y_i^{\male}$. The superscript $\male \in \{\male, \female\}$ 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, $\sum_i x_i^{\male} + y_i^{\male} = 1$.

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 ($w_1^{\male} = w_3^{\male} = w_A^{\male}$, $w_2^{\male} = w_4^{\male} = w_a^{\male}$, see Table 1). The genotype frequencies after gametic competition are $x_i^{\male,s} = w_i x_i^{\male} / \bar{w}_H^{\male}$ and $y_i^{\male,s} = w_i y_i^{\male} / \bar{w}_H^{\male}$, where $\bar{w}_H^{\male} = \sum_i w_i x_i^{\male} + w_i y_i^{\male}$ is the mean fitness of male ($\male = \male$) or female ($\male = \female$) 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, $xx_{ij} = (x_i^{\female,s} x_j^{\male,s} + x_j^{\female,s} x_i^{\male,s})/2$ and $yy_{ij} = (y_i^{\female,s} y_j^{\male,s} + y_j^{\female,s} y_i^{\male,s})/2$.

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 $xx_{ij}^{\female} = k_{bc} xx_{ij}$, XY females are given by $xy_{ij}^{\female} = k_{bc} xy_{ij}$, and YY females are given by $yy_{ij}^{\female} = k_{bc} yy_{ij}$. Similarly, XX male frequencies are $xx_{ij}^{\male} = (1 - k_{bc}) xx_{ij}$, XY male frequencies are $xy_{ij}^{\male} = (1 - k_{bc}) xy_{ij}$, and YY males frequencies are $yy_{ij}^{\male} = (1 - k_{bc}) yy_{ij}$. 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 $\male$ are given by $xx_{ij}^{\male,s} = w_l^{\male} xx_{ij}/\bar{w}^{\male}$, $xy_{ij}^{\male,s} = w_l^{\male} xy_{ij}/\bar{w}^{\male}$, and $yy_{ij}^{\male,s} = w_l^{\male} yy_{ij}/\bar{w}^{\male}$, where $\bar{w}^{\male} = \sum_{i=1}^{4}\sum_{j=1}^{4} w_l^{\male} xx_{ij} + w_l^{\male} xy_{ij} + w_l^{\male} yy_{ij}$ is the mean fitness of individuals of sex $\male$.

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 SDR, **A**, and **M** loci by using three parameters to describe the recombination rates between them. R is the recombination rate between the **A** locus and the **M** locus, ρ is the recombination rate between the **M** locus and the **X** locus, and r is the recombination rate between the **A** locus and the **X** locus. Table S.1 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 $\male$, meiotic drive occurs such that, in Aa heterozygotes, a fraction $\alpha^{\male}$ of gametes produced carry the A allele and $(1 - \alpha^{\male})$ carry the a allele.

Table S.1: 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	$R = r(1-\rho) + \rho(1-r)$

Among gametes from sex $\male$, the frequencies of haplotypes (before gametic

competition) in the next generation are given by

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

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

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

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

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

$$
\begin{aligned}
y_2^{\male'} =& yy_{22}^{\male,s} + yy_{24}^{\male,s}/2 + (yy_{12}^{\male,s} + yy_{23}^{\male,s})\alpha^{\male} \\
& - R(yy_{23}^{\male,s} - yy_{14}^{\male,s})\alpha^{\male} \\
& (xy_{22}^{\male,s} + xy_{42}^{\male,s})/2 + (xy_{12}^{\male,s} + xy_{32}^{\male,s})(1-\alpha^{\male}) \\
& - r(xy_{12}^{\male,s} - xy_{21}^{\male,s})(1-\alpha^{\male}) - \rho(xy_{42}^{\male,s} - xy_{24}^{\male,s})/2 \\
& + \big[-(R+r+\rho)xy_{32}^{\male,s} + (R+\rho-r)xy_{23}^{\male,s} \\
& + (R+r-\rho)xy_{41}^{\male,s} + (R+\rho-r)xy_{14}^{\male,s}\big](1-\alpha^{\male})/2
\end{aligned} \tag{S.1f}
$$

$$
\begin{aligned}
y_3^{\male'} =& yy_{33}^{\male,s} + yy_{13}^{\male,s}/2 + (yy_{23}^{\male,s} + yy_{34}^{\male,s})\alpha^{\male} \\
& - R(yy_{23}^{\male,s} - yy_{14}^{\male,s})\alpha^{\male} \\
& (xy_{33}^{\male,s} + xy_{13}^{\male,s})/2 + (xy_{23}^{\male,s} + xy_{43}^{\male,s})\alpha^{\male} \\
& - r(xy_{43}^{\male,s} - xy_{34}^{\male,s})\alpha^{\male} - \rho(xy_{13}^{\male,s} - xy_{31}^{\male,s})/2 \\
& + \big[-(R+r+\rho)xy_{23}^{\male,s} + (R+\rho-r)xy_{32}^{\male,s} \\
& + (R+r-\rho)xy_{14}^{\male,s} + (R+\rho-r)xy_{41}^{\male,s}\big]\alpha^{\male}/2
\end{aligned} \tag{S.1g}
$$

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

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-determination systems. For example, with the M allele fixed and an ancestral XY sex-determining system, there are XX males, XY females, or YY females ($x_3^{\varphi} = x_4^{\varphi} = y_4^{\varphi} = y_3^{\varphi} = y_i^{\male} = 0$). In this case, the system only involves six recursion equations, which we assume below to calculate the equilibria.

Resident equilibria and stability

In the resident population (allele M fixed), we follow the frequency of A in X-bearing female gametes, $p_X^{\male}$, and X-bearing male gametes, p_X^{φ}, and Y-bearing male gametes, p_Y^{φ}. 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: $x_1^{\male} = \hat{p}_X^{\male}$, $x_2^{\male} = 1 - \hat{p}_X^{\male}$, $x_1^{\varphi} = (1-q)\hat{p}_X^{\varphi}$, $x_2^{\varphi} = (1-q)(1-\hat{p}_X^{\varphi})$, $y_1^{\varphi} = q\hat{p}_Y^{\varphi}$, and $y_2^{\varphi} = q(1-\hat{p}_Y^{\varphi})$. Mean fitnesses in the resident population are given in table S.2.

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 antagonistic selection, Immler et al. 2012), or a combination of these selective regimes (see below).

In particular special cases, e.g., no sex-differences in selection or meiotic drive ($s^{\varphi} = s^{\male}$, $h^{\varphi} = h^{\male}$, and $\alpha^{\varphi} = \alpha^{\male} = 1/2$), the equilibrium allele frequency and sta-

Table S.2: Mean fitnesses and zygotic sex ratio in the resident population (M fixed, XY sex determination).

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

bility can be calculated analytically without assuming anything about the relative strengths of selection and recombination. However, here, we focus on two regimes (tight linkage and weak selection) in order to make fewer assumptions about fitnesses.

Recombination weak relative to selection (tight linkage between A and X)

We first calculate the equilibrium frequency of the Y and A alleles 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:

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

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

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

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

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

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

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

A fifth equilibrium (C) also exists where A is present at an intermediate frequency on the Y chromosome ($0 < \hat{p}_Y^{\male} < 1$). However, equilibrium (C) is never locally stable when $r \approx 0$ and is therefore not considered further. Thus, the Y can either be fixed for the a allele (equilibria A and B) or the A allele (equilibria A' and B'). The X chromosome 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 is fixed for the a allele. If there is no haploid selection ($\alpha_\Delta^{\male\female} = 0$, $w_A^{\male\female} = w_a^{\male\female} = 1$), these equilibria are equivalent to those found by Lloyd and Webb (1977) and Otto (2014).

We next calculate when (A) and (B) are locally stable for $r = 0$. According to the 'small parameter theory' (Karlin and McGregor 1972*a*;*b*), these stability prop-

erties are unaffected by small amounts of recombination between the SDR and **A** locus, although equilibrium frequencies may be slightly altered. For the a allele to be stably fixed on the Y we need $\bar{w}^{\male}_{Ya} > \bar{w}^{\male}_{YA}$ where $\bar{w}^{\male}_{Ya} = w^{\male}_{a}\left[\hat{p}^{\female}_{X}(1-\alpha^{\male}_{\Delta})w^{\female}_{A}w^{\male}_{Aa} + (1-\hat{p}^{\female}_{X})w^{\female}_{a}w^{\male}_{aa}\right]$ and $\bar{w}^{\male}_{YA} = w^{\male}_{A}\left[\hat{p}^{\female}_{X}w^{\female}_{A}w^{\male}_{AA} + (1-\hat{p}^{\female}_{X})(1+\alpha^{\male}_{\Delta})w^{\female}_{a}w^{\male}_{Aa}\right]$. That is, Y-$a$ haplotypes must have higher fitness than Y-A haplotypes. Substituting in $\hat{p}^{\female}_{X}$ from equation (S.2), fixation of the a allele on the Y requires that $\gamma_i > 0$ where $\gamma_{(A)} = w^{\male}_{a}\left[(1-\alpha^{\male}_{\Delta})w^{\male}_{Aa}\phi + w^{\male}_{aa}\psi\right] - w^{\male}_{A}\left[w^{\male}_{AA}\phi + (1+\alpha^{\male}_{\Delta})w^{\male}_{Aa}\psi\right]$ for equilibrium (A) and $\gamma_{(B)} = (1-\alpha^{\male}_{\Delta})w^{\male}_{a}w^{\male}_{Aa} - w^{\male}_{A}w^{\male}_{AA}$ for equilibrium (B). Stability of a polymorphism on the X chromosome (equilibrium A) further requires that $\phi > 0$ and $\psi > 0$. Fixation of the a allele on the X (equilibrium B) can be stable only if equilibrium (A) is not, as it requires $\psi < 0$.

Selection weak relative to recombination (weak selection)

Here, we assume that selection and meiotic drive are weak relative to recombination ($s^{\female}$, $t^{\female}$, $\alpha^{\female}_{\Delta}$ of order ϵ). The maintenance of a polymorphism at the **A** locus then requires that

$$\begin{aligned} 0 &< -\left[(1-h^{\female})s^{\female} + (1-h^{\male})s^{\male} + t^{\female} + t^{\male} + \alpha^{\female}_{\Delta} + \alpha^{\male}_{\Delta}\right] \\ \text{and} \quad 0 &< h^{\female}s^{\female} + h^{\male}s^{\male} + t^{\female} + t^{\male} + \alpha^{\female}_{\Delta} + \alpha^{\male}_{\Delta}. \end{aligned} \tag{S.3}$$

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 ($\hat{p}^{\female}_{X} = \hat{p}^{\male}_{X} = \hat{p}^{\male}_{Y} = \bar{p}$) and given, to leading order, by

$$\bar{p} = \frac{h^{\female}s^{\female} + h^{\male}s^{\male} + t^{\female} + t^{\male} + \alpha^{\female}_{\Delta} + \alpha^{\male}_{\Delta}}{(2h^{\female}-1)s^{\female} + (2h^{\male}-1)s^{\male}} + O(\epsilon). \tag{S.4}$$

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

$$\begin{aligned}
\hat{p}_X^{\male} - \hat{p}_X^{\female} &= V_A\left(D^{\male} - D^{\female} + \alpha_\Delta^{\male} - \alpha_\Delta^{\female}\right) + O(\epsilon^2) \\
\hat{p}_Y^{\male} - \hat{p}_X^{\female} &= V_A\left[D^{\male} - D^{\female} + \alpha_\Delta^{\male} - \alpha_\Delta^{\female} + (1-2r)(t^{\male} - t^{\female})\right]/2r + O(\epsilon^2) \\
\hat{p}_Y^{\male} - \hat{p}_X^{\male} &= V_A\left(D^{\male} - D^{\female} + \alpha_\Delta^{\male} - \alpha_\Delta^{\female} + t^{\male} - t^{\female}\right)(1-2r)/2r + O(\epsilon^2)
\end{aligned} \tag{S.5}$$

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $D^{\mathfrak{s}} = \left[\bar{p}s^{\mathfrak{s}} + (1-\bar{p})h^{\mathfrak{s}}s^{\mathfrak{s}}\right] - \left[\bar{p}h^{\mathfrak{s}}s^{\mathfrak{s}} + (1-\bar{p})\right]$ corresponds to the difference in fitness between A and a alleles in diploids of sex $\mathfrak{s} \in \{\female, \male\}$ ($\bar{p}$ is the leading-order probability of mating with an A-bearing gamete from the opposite sex). The frequency of Y among 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, $q = 1/2 + \alpha_\Delta^{\male}(\hat{p}_Y^{\male} - \hat{p}_X^{\male})/2 + O(\epsilon^3)$. Without gametic competition or drive ($\alpha_\Delta^{\mathfrak{s}} = t^{\mathfrak{s}} = 0$) our results reduce to those of van Doorn and Kirkpatrick (2007).

Invasion conditions

Cover the other parts of the characteristic polynomial here. Waiting for Sally's proof!

A rare neo-Y or neo-W will spread from a given ancestral equilibrium when the leading eigenvalue, λ, of the Jacobian matrix derived from the eight mutant recursion equations (given by S.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, we need only two recursion equations (e.g., tracking the change in the frequency of neo-Y-A and neo-Y-a gametes from males) and thus the leading eigenvalue is the largest solution the polynomial $\lambda^2 + b\lambda + c = 0$ as described in the text (Table 2).

The general conditions for the invasion of a neo-sex-determining allele are given in the main text, in terms of the growth rates of the mutant haplotypes in the absence of recombination (λ_{mi}) and the rate that recombination destroys them

(χ_{mi}). For tight linkage between the ancestral sex-determining locus and the selected locus we can calculate these terms explicitly (see below). For weak selection we can take a Taylor series of the leading eigenvalue. The leading eigenvalue, λ, for any k, is given up to order ϵ^2 by equation (4).

Tight linkage between A and X (recombination weak relative to selection)

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 region ($r \approx 0$). We disregard neo-Y mutations, which never spread given that the ancestral population is at a stable equilibrium (see supplementary *Mathematica* notebook for proof).

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

$$\lambda_{mA} = \left[w_A^{\male}(1+\alpha_\Delta^{\male})\right]^{-1} \frac{w_A^{\female}}{w_A^{\female}} \frac{\left[w_A^{\male}(1+\alpha_\Delta^{\male})w_{AA}^{\female} + w_a^{\male}(1-\alpha_\Delta^{\male})w_{Aa}^{\female}(1+\alpha_\Delta^{\female})\right]}{2w_{AA}^{\female}} \tag{S.6a}$$

$$\lambda_{ma} = \left[w_A^{\male}(1+\alpha_\Delta^{\male})\right]^{-1} \frac{w_a^{\female}}{w_A^{\female}} \frac{\left[w_A^{\male}(1+\alpha_\Delta^{\male})w_{Aa}^{\female}(1-\alpha_\Delta^{\female}) + w_a^{\male}(1-\alpha_\Delta^{\male})w_{aa}^{\female}\right]}{2w_{AA}^{\female}} \tag{S.6b}$$

$$\chi_{mA} = \frac{1}{2}\left[w_A^{\male}(1+\alpha_\Delta^{\male})\right]^{-1} \frac{w_A^{\female}}{w_A^{\female}} \frac{\left[w_a^{\male}(1-\alpha_\Delta^{\male})w_{Aa}^{\female}(1+\alpha_\Delta^{\female})\right]}{w_{AA}^{\female}} \frac{R}{2} \tag{S.6c}$$

$$\chi_{ma} = \frac{1}{2}\left[w_A^{\male}(1+\alpha_\Delta^{\male})\right]^{-1} \frac{w_a^{\female}}{w_A^{\female}} \frac{\left[w_A^{\male}(1+\alpha_\Delta^{\male})w_{Aa}^{\female}(1-\alpha_\Delta^{\female})\right]}{w_{AA}^{\female}} \frac{R}{2} \tag{S.6d}$$

Haploid selection impacts the spread of neo-W haplotypes in three ways. 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 $1-\zeta = w_A^{\male}(1+\alpha_\Delta^{\male})/(2\bar{w}_H^{\male})$ where $2\bar{w}_H^{\male} = \left[w_a^{\male}(1-\alpha_\Delta^{\male}) + w_A^{\male}(1+\alpha_\Delta^{\male})\right]$ has been canceled out in equations (S.6) to leave the term $\left[w_A^{\male}(1+\alpha_\Delta^{\male})\right]^{-1}$. 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 $w_A^{\female}$ such that the relative fitnesses of neo-W-A and neo-W-a haplotypes during female gametic competition are $w_A^{\female}/w_A^{\female}$ and $w_a^{\female}/w_A^{\female}$ (see terms in equation S.6). 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 $(1+\alpha_\Delta^{\female})/2$ and $(1-\alpha_\Delta^{\female})/2$, respectively. These terms are only associated with heterozygous females, i.e., they are found alongside $w_{Aa}^{\female}$.

Thirdly, haploid selection in males affects the diploid genotypes of females by altering the allele frequencies in the male gametes that female gametes pair with. At equlibrium (***B***), neo-W female gametes will mate with X-A male gametes with probability $w_A^{\male}(1+\alpha_\Delta^{\male})/(2\bar{w}_H^{\male})$ and Y-a male gametes with probability $w_a^{\male}(1-\alpha_\Delta^{\male})/(2\bar{w}_H^{\male})$, where the $2\bar{w}_H^{\male}$ terms have been canceled in equation (S.6) (as mentioned above). Thus, for example, neo-W-A haplotypes are found in AA female diploids with probability $w_A^{\male}(1+\alpha_\Delta^{\male})/(2\bar{w}_H^{\male})$ (first term in square brackets in the numerator of equation S.6a) and in Aa female diploids with probability $w_a^{\male}(1-\alpha_\Delta^{\male})/(2\bar{w}_H^{\male})$ (see equation S.6c and the second term in square brackets in the numerator of equation S.6a).

The other terms in equations (S.6) are more easily interpreted if we assume that there is no haploid selection in either sex, in which case $\lambda_{mA} = (w_{AA}^{\female}+w_{Aa}^{\female})/2w_{AA}^{\female}$ and $\lambda_{ma} = (w_{aa}^{\female}+w_{Aa}^{\female})/2w_{AA}^{\female}$. Neither haplotype can spread under purely sexually-antagonistic selection, where A is directionally favoured in females ($w_{AA}^{\female} > w_{Aa}^{\female} > w_{aa}^{\female}$) and a is directionally favoured in males ($w_{AA}^{\male} > w_{Aa}^{\male} > w_{aa}^{\male}$). Essentially, the X is then already as specialized as possible for the female beneficial allele (A is fixed on the X), 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 hap-

lotypes and/or neo-W-a haplotypes can spread ($\lambda_{mA} > 1$ and/or $\lambda_{ma} > 1$). A neo-W-A haplotype can spread ($\lambda_{mA} > 1$) when $w^{\female}_{Aa} > w^{\female}_{AA}$, 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. 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 $w^{\female}_{Aa} < 2w^{\female}_{AA}$ and $w^{\male}_{Aa}/\left[(w^{\male}_{aa} + w^{\male}_{Aa})/2\right] > w^{\female}_{Aa}/w^{\female}_{AA}$.

Still considering $w^{\female}_{Aa} > w^{\female}_{AA}$, the neo-W can also spread alongside the a allele ($\lambda_{ma} > 1$) if $w^{\female}_{aa}$ is large enough such that $(w^{\female}_{Aa} + w^{\female}_{aa})/2 > w^{\female}_{AA}$. This can occur with overdominance or directional selection for a in females (Figure 3B,C). In this case, a is favoured in females (comparing Aa to AA genotypes in females) but A is fixed on the X 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 allele frequencies into Table 2

$$\lambda_{mA} = \frac{a}{b}\left[w^{\female}_{AA}w^{\male}_{Aa}w^{\male}_{A}(1+\alpha^{\male}_{\Delta})\phi + w^{\female}_{Aa}(1+\alpha^{\female}_{\Delta})w^{\male}_{a}c\right]/(2w^{\female}_{a}) \tag{S.7a}$$

$$\lambda_{ma} = \frac{a}{b}\left[w^{\female}_{Aa}(1-\alpha^{\female}_{\Delta})w^{\male}_{Aa}w^{\male}_{A}(1+\alpha^{\male}_{\Delta})\phi + w^{\female}_{aa}w^{\male}_{a}c\right]/(2w^{\female}_{A}) \tag{S.7b}$$

$$\chi_{mA} = \frac{a}{b}\frac{R}{2}\left[w^{\female}_{Aa}(1+\alpha^{\female}_{\Delta})w^{\male}_{a}c\right]/w^{\female}_{a} \tag{S.7c}$$

$$\chi_{ma} = \frac{a}{b}\frac{R}{2}\left[w^{\female}_{Aa}(1-\alpha^{\female}_{\Delta})w^{\male}_{Aa}w^{\male}_{A}(1+\alpha^{\male}_{\Delta})\phi\right]/w^{\female}_{A} \tag{S.7d}$$

where

$$a = w_a^{\female}\phi + w_A^{\female}\psi \tag{S.8a}$$

$$b = w_{AA}^{\female}\left[w_{Aa}^{\male}w_A^{\male}(1+\alpha_\Delta^{\male})\right]\phi^2 + w_{Aa}^{\female}\left[w_{Aa}^{\male}w_A^{\male}(1+\alpha_\Delta^{\male}) + w_{aa}^{\male}w_a^{\male}\right]\psi\phi + w_{aa}^{\female}\left(w_{aa}^{\male}w_a^{\male}\right)\psi^2 \tag{S.8b}$$

$$c = w_{Aa}^{\male}(1-\alpha_\Delta^{\male})\phi + 2w_{aa}^{\male}\psi \tag{S.8c}$$

As with equilibrium (B), haploid selection again modifies invasion fitnesses by altering the sex ratio and the diploid genotypes of females and directly selecting upon female gametes. 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 ($\lambda_{mA} > 1$) if and only if

$$2(w_{Aa}^{\female} - w_{aa}^{\female})w_{aa}^{\male}\psi^2 > (w_{AA}^{\female} - w_{Aa}^{\female})w_{Aa}^{\male}\phi(\phi-\psi) \tag{S.9}$$

where $\phi - \psi = w_{AA}^{\female}w_{Aa}^{\male} - w_{aa}^{\female}w_{aa}^{\male}$ 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 ($w_{aa}^{\female} < w_{Aa}^{\female} < w_{AA}^{\female}$ and $w_{AA}^{\male} < w_{Aa}^{\male} < w_{aa}^{\male}$). The neo-W-$A$ can spread as long as it becomes associated with females that bear more A alleles than observed at equilibrium (A).

Without haploid selection, the neo-W-a haplotype spreads ($\lambda_{ma} > 1$) if and only if

$$(w_{aa}^{\female} + w_{Aa}^{\female} - 2w_{AA}^{\female})w_{Aa}^{\male}\phi^2 + (w_{aa}^{\female} - w_{Aa}^{\female})(w_{Aa}^{\male} + 2w_{aa}^{\male})\phi\psi > 0 \tag{S.10}$$

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 X chromosomes 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. This scenario selects for a modifier that increases recombination between the sex chromosomes (e.g., blue region of Figure 2d in Otto 2014) and facilitates the spread of neo-W-a haplotypes, which create more females bearing more a alleles than the ancestral X chromosome does.

Role of Haploid Selection with Tight Linkage

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 unlinked alleles - can spread (Figure S.8). Second, even when diploid selection could itself maintain a polymorphism, haploid selection can increase the conditions under which transitions among sex chromosomes are possible. Of particularly importance, when selection is sexually-antagonistic in diploids ($s^{\varphi}s^{\sigma} < 0$ and $0 < h^{\varphi} < 1$), an unlinked neo-W ($R = 1/2$) cannot invade unless there is also haploid selection (see proof in supplementary *Mathematica* file; Figures 2 and S.3). More generally, haploid selection alters the conditions under which neo-W chromosomes can spread (compare Figures S.4-S.7 to Figure 3).

Male haploid selection in favour of the a allele ($\alpha_{\Delta}^{\sigma} < 0$, $w_A^{\sigma} < w_a^{\sigma}$) generates male-biased sex ratios at equilibria (A) and (B), where Y-a is fixed ($\hat{p}_Y^{\sigma} = 0$). Male-biased sex-ratios facilitate the spread of neo-W-A and neo-W-a haplotypes (increasing λ_{mA} and λ_{ma}). Panels A-C in Figures S.4 and S.5 show that neo-W

haplotypes tend to spread for a wider range of parameters when sex ratios are male biased, compared to Figure 3 without haploid selection. By contrast, male haploid selection in favour of the A allele generates female-biased sex ratios and reduces λ_{mA} and λ_{ma}, as demonstrated by panels D-F in Figures S.4 and S.5.

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 λ_{ma} and decrease λ_{mA}, as shown by panels A-C in Figures S.6 and S.7. Conversely, female haploid selection in favour of the A allele increases λ_{mA} and decreases λ_{ma}, see panels D-F in Figures S.6 and S.7.

Thus, the impact of haploid selection on sex chromosome transitions must be considered as two sides of a coin: it can generate sex ratio biases that drive sex chromosome transitions to equalize the sex ratio, but it can also drive in new sex chromosomes and thereby cause sex ratios to become biased.

Supplementary Figures

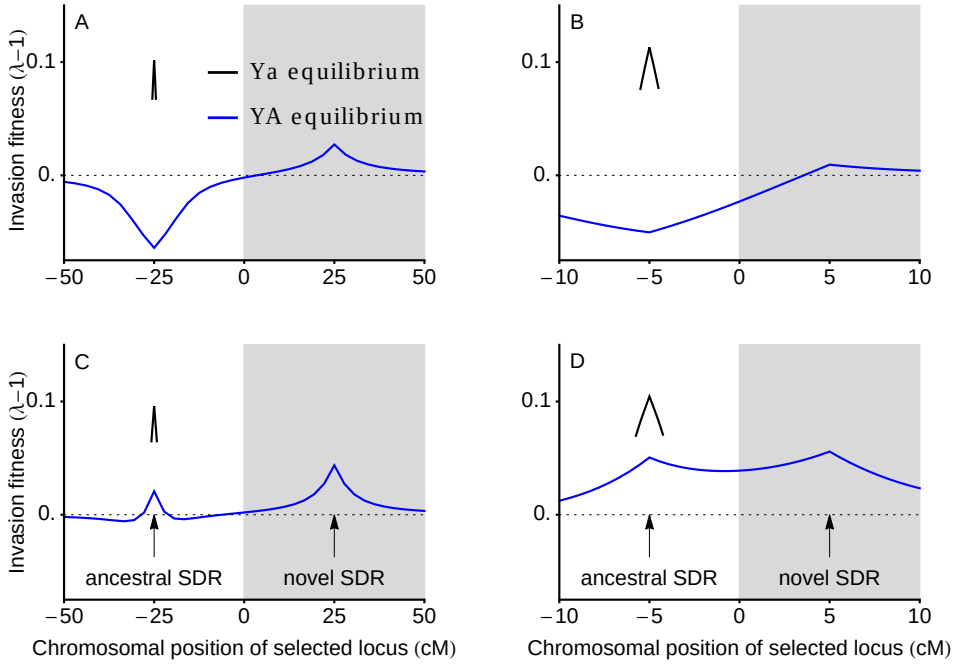

Figure S.1: Neo-W alleles can spread when loci under diploid selection are tightly linked to the ancestral sex determining locus ($r \approx 0$). In panels A and B, the a allele is favoured in females ($w^{\varphi}_{aa} = 1.05$, $w^{\varphi}_{Aa} = 1$, $w^{\varphi}_{AA} = 0.85$) and selection in males is overdominant ($w^{\sigma}_{aa} = w^{\sigma}_{AA} = 0.75$). In panels C and D, selection in males and females is overdominant ($w^{\varphi}_{aa} = w^{\varphi}_{AA} = 0.6$, $w^{\sigma}_{aa} = 0.5$, $w^{\sigma}_{AA} = 0.7$, $w^{\sigma}_{Aa} = 1$). There is no haploid selection $t^{\varphi}_{\sigma} = \alpha^{\varphi}_{\Delta} = 0$. These parameters are marked by daggers in Figure 3B and C, which show that neo-W invasion is expected for any R ($\lambda_{WA}, \lambda_{Wa} > 1$) when 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). The weak selection approximation holds when all recombination rates are large relative to selection (around 0 in panels A and C), in which case, in the absence of haploid selection, neo-W alleles should spread if and only if they are more tightly linked to the selected locus (positive invasion fitness if and only if the selected locus is in the grey region). However, when linkage is tight (panels B and D and when the selected locus is near the SDRs in all panels), this weak selection prediction can break down.

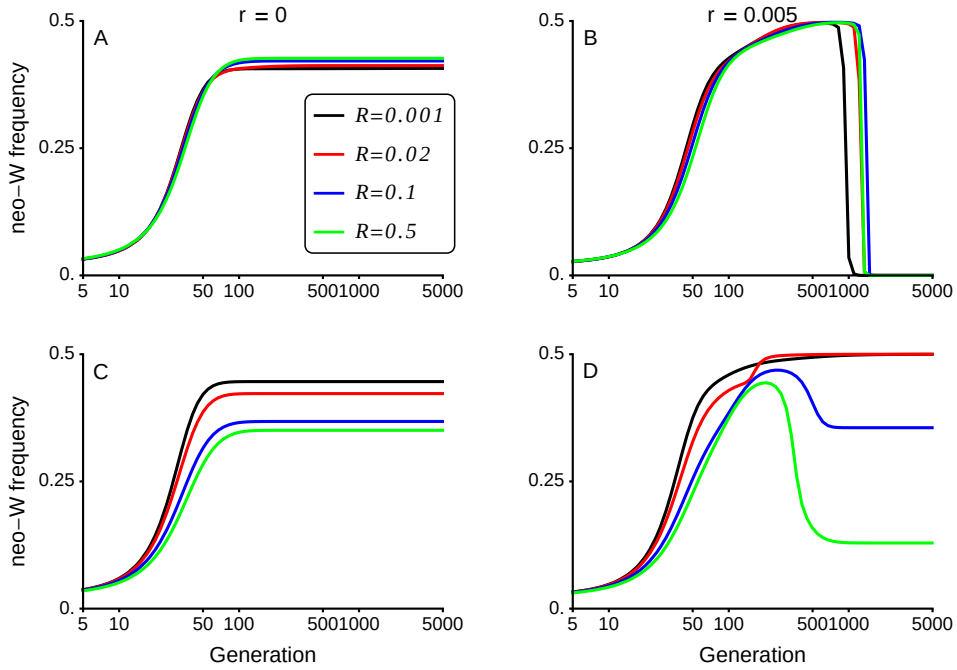

Figure S.2: Following invasion by a neo-W allele, there can be a complete transition to a new sex-determination system, maintenance of polymorphism at both ancestral-XY and neo-ZW sex determining regions, or loss of the new sex-determining allele. Here we plot the frequency of the neo-W allele among female gametes; as the neo-W reaches frequency 0.5, polymorphism at the ancestral XY locus is lost with Y becoming fixed such that sex is determined only be the ZW allele carried by a female gamete. 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 (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 (see blue lines in Figure S.1A and S.1B near the ancestral SDR). In contrast, the neo-W is not lost in panel D as it is favoured near $r \approx 0$ (see blue lines in Figure S.1C and S.1D near the ancestral SDR). Fitness parameters are the same as in Figure S.1; in panels A and B the a allele is favoured in females ($w^{\varphi}_{aa} = 1.05$, $w^{\varphi}_{Aa} = 1$, $w^{\varphi}_{AA} = 0.85$) while there is overdominance in males ($w^{\sigma}_{aa} = w^{\sigma}_{AA} = 0.75$) and in panels C and D, there is overdominance in both sexes ($w^{\varphi}_{aa} = w^{\varphi}_{AA} = 0.6$, $w^{\sigma}_{aa} = 0.5$, $w^{\sigma}_{AA} = 0.7$, $w^{\varphi}_{Aa} = 1$). These parameters are marked by a dagger in Figure 3. Here, there is no haploid selection $t^{\varphi} = \alpha^{\varphi}_{\Delta} = 0$.

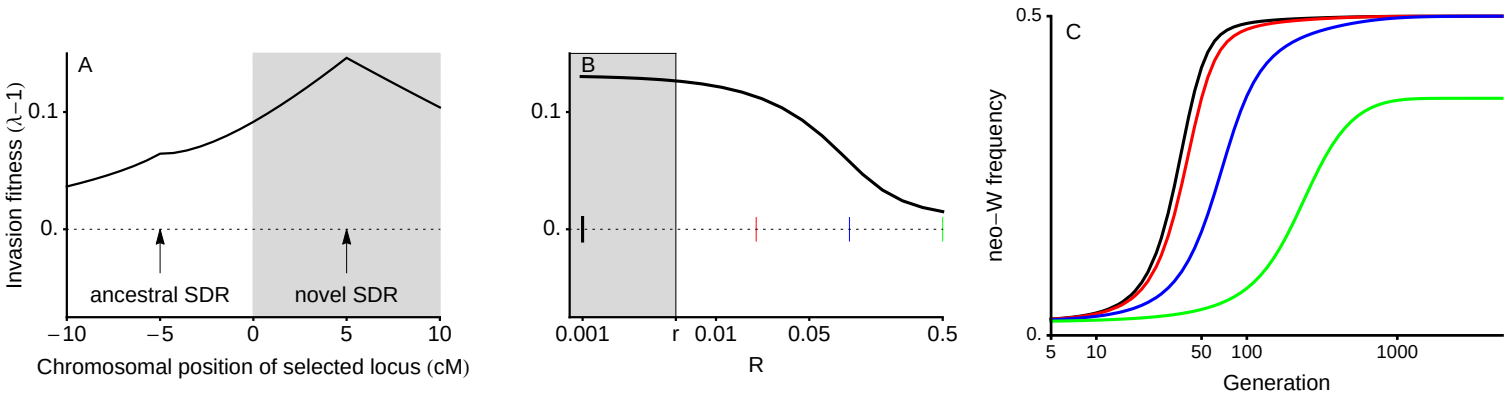

Figure S.3: When there is sexually-antagonistic selection and haploid selection, a neo-W may invade for any R. Panel A shows that the invasion fitness of a neo-W is positive where linkage is tight, even when $r < R$ (unshaded region). In panel B, we vary the recombination rate between the neo-W and the selected locus (R) for a fixed recombination rate between the ancestral-SDR 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 Figure 2. There is also meiotic drive in males favouring a ($\alpha_{\Delta}^{\sigma} = -0.08$), this full set of parameters is marked by an asterisk in Figure S.4A. 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 S.9C.

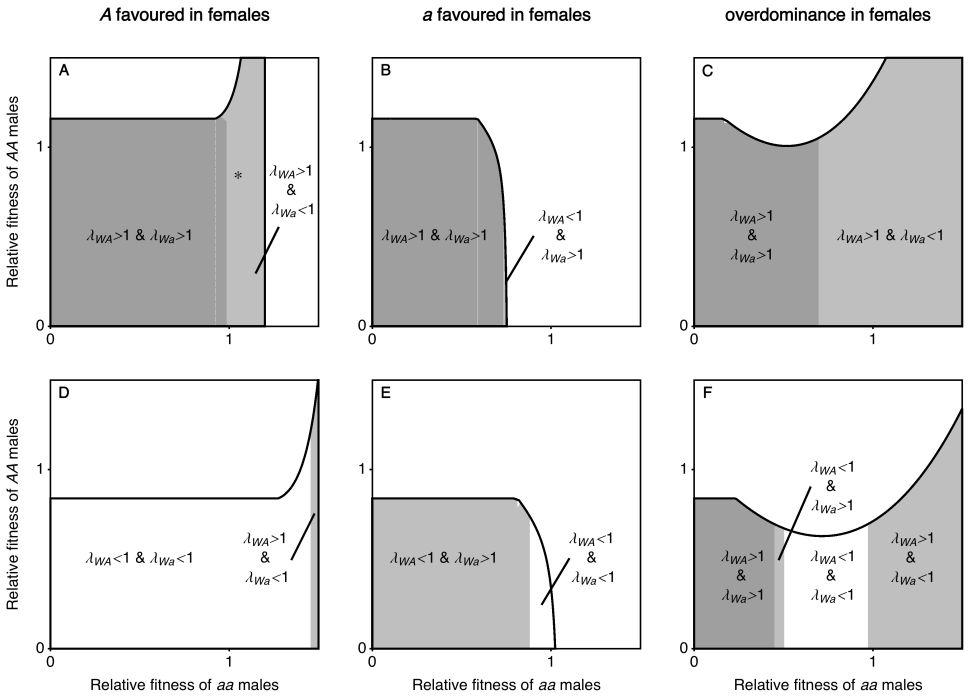

Figure S.4: Meiotic drive in males affects whether neo-W-*A* and neo-W-*a* haplotypes spread when the ancestral-XY locus is tightly linked to a locus under selection ($r = 0$). We vary the fitness of male homozygotes relative to heterozygotes ($w^{\male}_{Aa} = 1$) and only consider stable equilibria at which both **A** locus allele are maintained and the *a* allele is initially fixed on the Y, region outlined. In panels A-C, meiotic drive in males favours the *a* allele ($\alpha^{\male}_{\Delta} = -0.16$), creating male-biased sex ratios and generally increasing λ_{WA} and λ_{Wa}. By contrast, λ_{WA} and λ_{Wa} tend to be reduced when meiotic drive in males favours the *A* allele ($\alpha^{\male}_{\Delta} = 0.16$), panels D-F. We consider three forms of selection in females: directional selection in favour of the *A* allele (panels A and D, $w^{\female}_{aa} = 0.85$, $w^{\female}_{AA} = 1.05$), direction selection in favour of the *a* allele (panels B and E, $w^{\female}_{aa} = 1.05$, $w^{\female}_{AA} = 0.85$), and overdominance (panels C and F, $w^{\female}_{aa} = w^{\female}_{AA} = 0.6$).

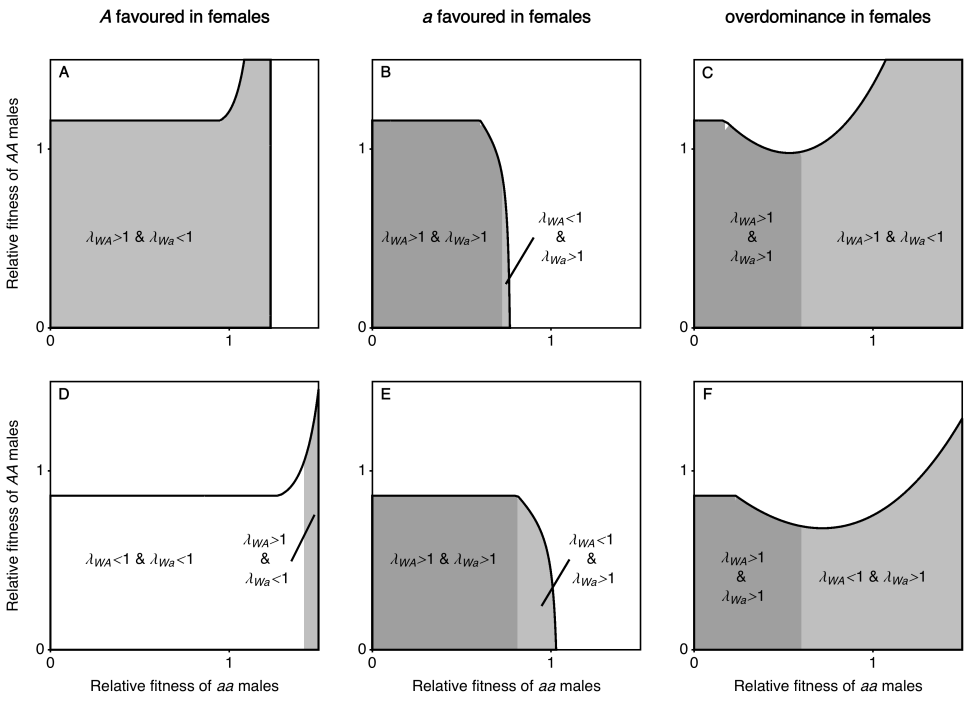

Figure S.5: Parameters for which neo-W-*A* and neo-W-*a* haplotypes spread when there is male gametic competition at a locus that is tightly linked to the ancestral-XY locus. Diploid selection parameters (w_{ij}^{δ}) are the same as those in Figure S.4. The *a* allele is favoured during male gametic competition in Panels A-C ($w_a^{\delta} = 1.16$, $w_A^{\delta} = 1$), which creates male biased sex ratios and increases λ_{WA} and λ_{Wa}. On the other hand, the *A* allele is favoured during male gametic competition in Panels D-F ($w_a^{\delta} = 1$, $w_A^{\delta} = 1.16$) and λ_{WA} and λ_{Wa} tend to be reduced. Compared to the meiotic drive parameters in Figure S.4, the effect of these male gametic competition parameters on the sex ratio is smaller. For example, in Figure S.4A-C, the ancestral sex ratio is $\alpha^{\delta} = 0.58$ at equilibrium (B) and in panels A-C of this plot, the ancestral sex ratio is $w_a^{\delta}/(w_A^{\delta} + w_a^{\delta}) = 0.537$ at equilibrium (B).

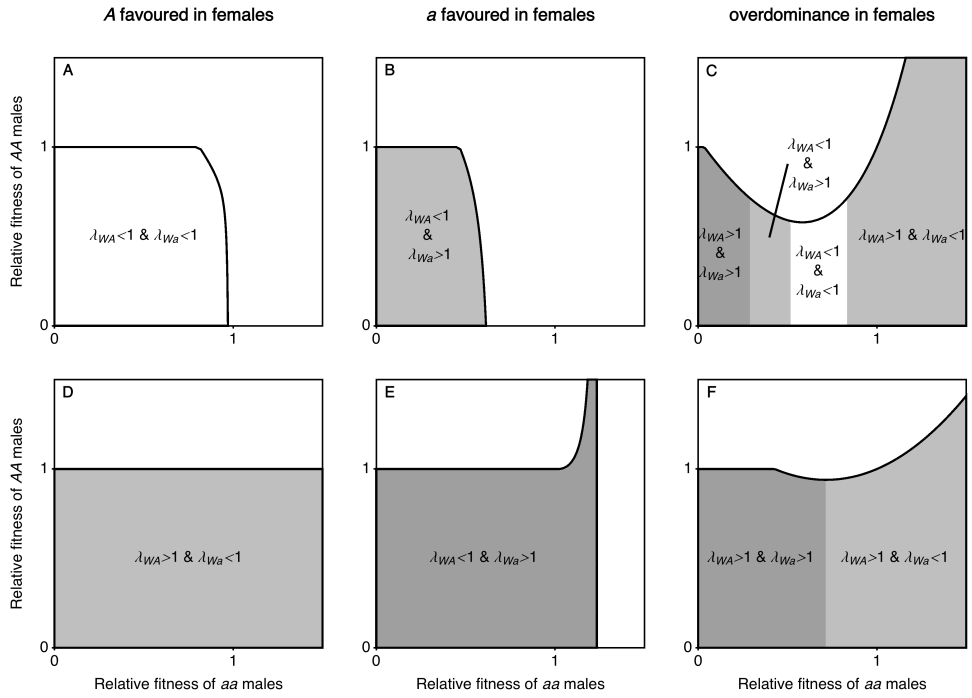

Figure S.6: Parameters for which neo-W-A and neo-W-a haplotypes spread when there is female meiotic drive at a locus that is tightly linked to the ancestral-XY locus. Diploid selection parameters (w_{ij}^{δ}) are the same as those in Figure S.4 and S.5. The a allele is favoured by meiotic drive in females in Panels A-C ($\alpha_{\Delta}^{\varphi} = -0.16$), which increases λ_{Wa} and decreases λ_{WA}. Female meiotic drive in favour of the A allele (panels D-F, $\alpha_{\Delta}^{\varphi} = -0.16$) has the opposite effect.

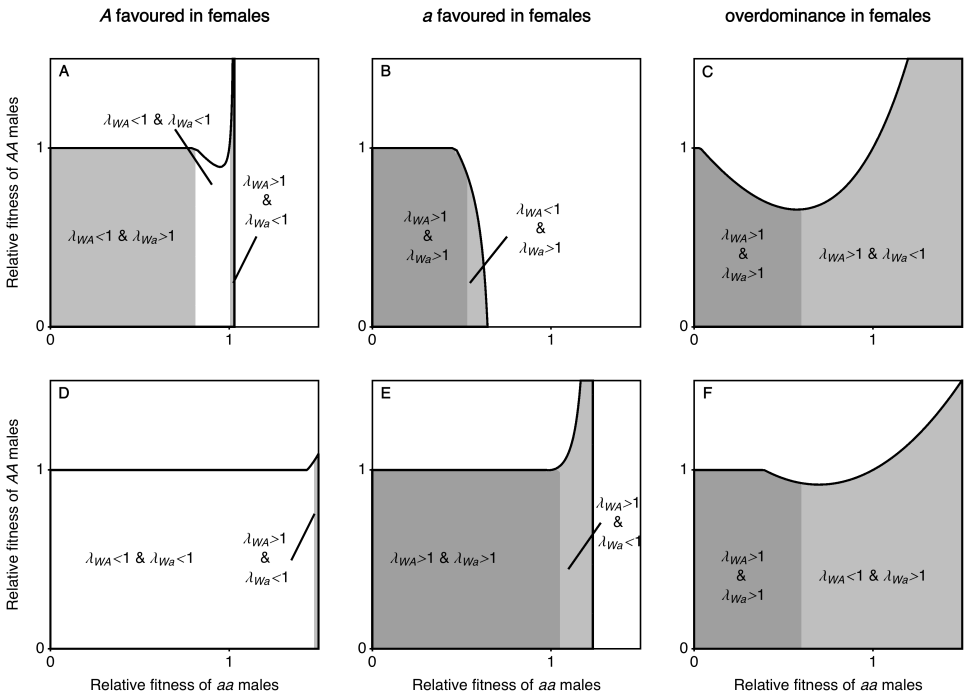

Figure S.7: Parameters for which neo-W-A and neo-W-a haplotypes spread when there is female gametic competition at a locus that is tightly linked to the ancestral-XY locus. Diploid selection parameters (w_{ij}^{δ}) are the same as those in Figure S.4, S.5, and S.6. The a allele is favoured during female gametic competition in females in Panels A-C ($w_a^{\varphi} = 1.16$, $w_A^{\varphi} = 1$), which increases λ_{Wa} and decreases λ_{WA}. The A allele is favoured during gametic competition in panels D-F ($w_a^{\varphi} = 1$, $w_A^{\varphi} = 1.16$), giving the opposite effect on λ_{Wa} and λ_{WA}.

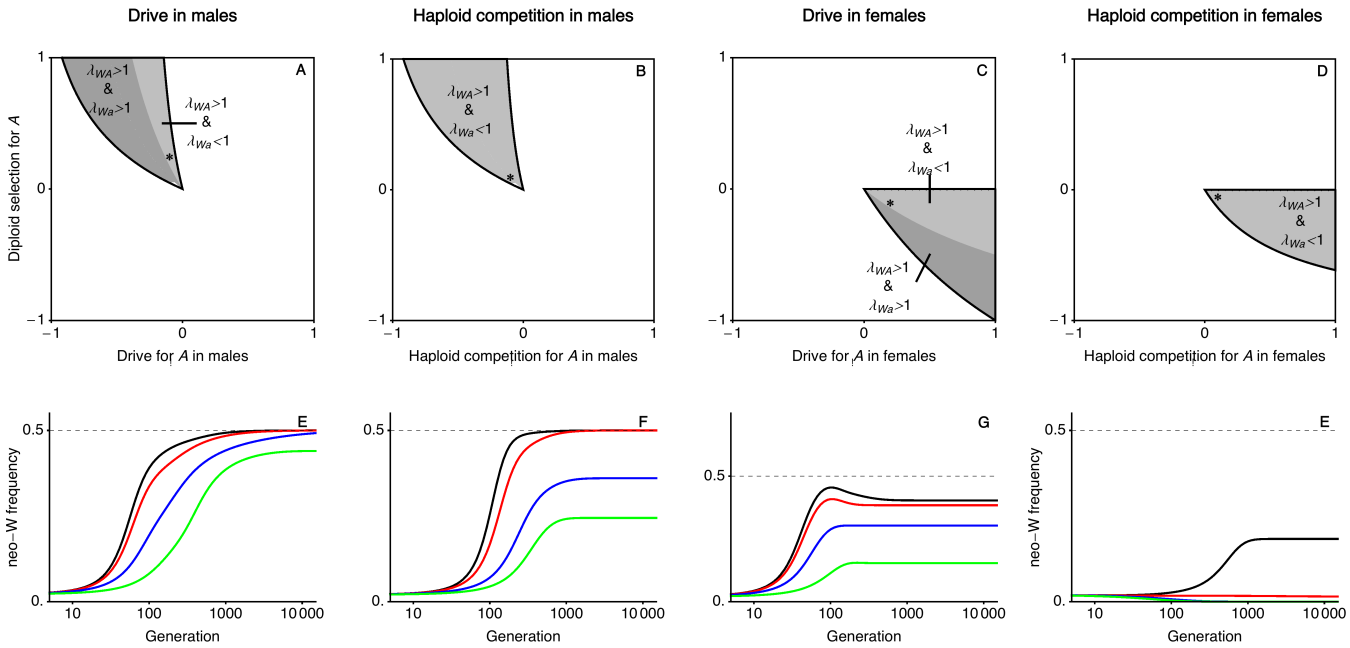

Figure S.8: A-D show when each of the neo-W haplotypes invade an internally stable equilibrium with a fixed on the Y (found by setting $r = 0$). The y-axis shows directional selection in diploids of both sexes, $s^{♀} = s^{♂}$, and the x-axes show sex-specific drive, $\alpha_{\Delta}^{♀♂}$, or haploid 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 $R = 1/2$.

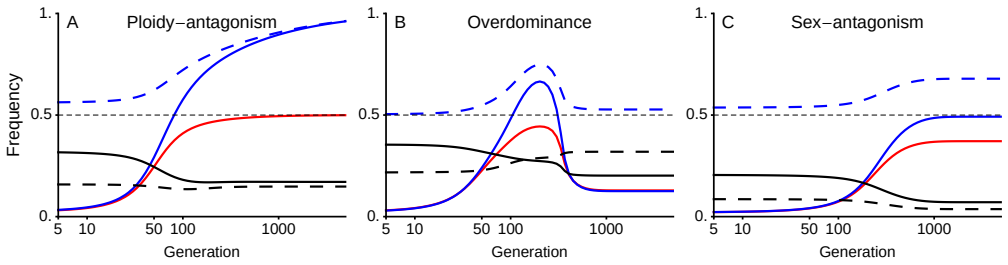

Figure S.9: Fixation of neo-W or maintenance of multiple sex-determining systems. The curves show the frequencies of the neo-W (red), ancestral-Y (blue), and *A* allele (black) among female gametes (solid curves) and among male gametes (dashed curves). In panel A, there is a complete transition from 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 neo-ZW locus, such that there are males with genotypes XY-ZZ or YY-ZZ and females with genotypes XX-ZZ, XX-ZW, XY-ZW, or YY-ZW. In panel A, selection is ploidally antagonistic with drive in males (parameters as in the green curve in Figure 5B). In panel B, there is overdominance in both sexes and no haploid selection (parameters as in the green curve in Figure S.2C). In panel C, there is sexually-antagonistic selection in diploids with drive in males (parameters as in the green curve in Figure S.4C). In all cases, the initial equilibrium frequency has *a* near fixation on the Y.

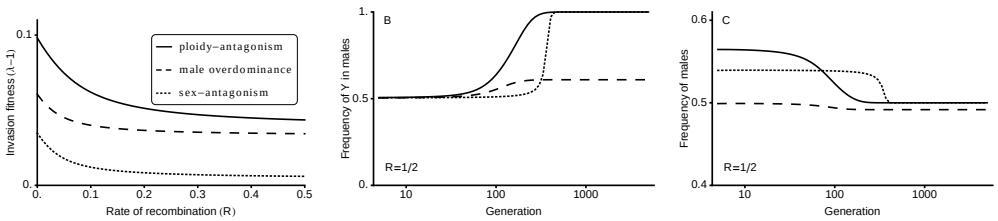

Figure S.10: An unlinked neo-W can invade a perfectly linked system with overdominance or haploid selection. Here overdominance leads to a polymorphic sex-determining system. Before invasion the population is at equilibrium B. Parameters: