

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

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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

32 **Introduction**

Animals and angiosperms exhibit extremely diverse sex-determination systems
34 (reviewed in Bull 1983, Charlesworth and Mank 2010, Beukeboom and Perrin
2014, Bachtrog et al. 2014). Among species with genetic sex determination of
36 diploid sexes (GSD), some taxa have heterogametic males (XY) and homogametic females (XX), including mammals and most dioecious plants (Ming et al.
38 2011); whereas other taxa have homogametic males (ZZ) and heterogametic females (ZW), including Lepidoptera and birds. Within several taxa, the chromo-
40 some that harbours the master sex-determining region changes. For example, transitions of the master sex-determining gene between chromosomes or the evolution
42 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
44 et al. 2012). In addition, many clades exhibit transitions between male (XY) and female (ZW) heterogamety, including snakes (Gamble et al. 2017), lizards (Ezaz
46 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
48 angiosperm genus *Silene* (Slancarova et al. 2013), the angiosperm family *Salicaceae* (Pucholt et al. 2015; 2017) and Coleoptera and Hemiptera (Beukeboom
50 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
52 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
54 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 environ-
56 mental 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
58 et al. 2010, Holleley et al. 2015).

Predominant theories accounting for the spread of new sex-determination sys-
60 tems 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

92 sex-determination systems spread when individuals experience selection at both
diploid and haploid stages. Even in animal and plant species that have much
94 larger and more conspicuous diploid phases than haploid phases, many loci ex-
perience significant haploid selection through gamete competition and/or meiotic
96 drive (Mulcahy et al. 1996, Joseph and Kirkpatrick 2004). We use the term ‘mei-
otic drive’ to refer to the biased (non-Mendelian) segregation of genotypes during
98 gamete production (from one parent) and the term ‘gametic competition’ to refer to
selection upon haploid genotypes within a gamete/gametophyte pool (potentially
100 from multiple parents); the term ‘haploid selection’ encompasses both processes.

Segregation distortion provides putative evidence of haploid selection and can
102 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;
104 2016). Where it has been characterized, meiotic drive generally occurs either dur-
ing the production of male or female gametes only (Úbeda and Haig 2005, Lind-
106 holm et al. 2016). Gametic competition is also typically sex specific, occurring pri-
marily among male gametes, because there are typically many more pollen/sperm
108 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,
110 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
112 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.
114 2004, Clarke et al. 2004). A smaller proportion of genes are thought to be ex-
pressed and selected during competition in animal sperm, although precise esti-
116 mates are uncertain (Zheng et al. 2001, Joseph and Kirkpatrick 2004, Vibranovski
et al. 2010). Nevertheless, recent studies have demonstrated that sperm competi-
118 tion in animals can alter haploid allele frequencies and increase offspring fitness
(Immler et al. 2014, Alavioon et al. 2017).

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

122 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
124 selection. In this respect, we might expect that haploid selection would affect
transitions between sex-determination systems in a similar manner to sex-specific
126 diploid selection (as explored by van Doorn and Kirkpatrick 2007; 2010). That is,
new masculinizing mutations (neo-Y chromosomes) could be favoured via associ-
128 ations 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
130 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
132 (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.
134 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 associa-
136 tions between haploid selected loci and sex-determining regions.

We find that the spread of novel sex-determiners is influenced by both Fisherian
138 sex ratio selection and by selection on genetically-associated alleles. Surpris-
ingly, Fisherian sex ratio selection does not dominate; it is possible for selection
140 on linked alleles to drive turnover between sex-determining systems despite caus-
ing increasingly biased sex ratios. In addition to considering haploid selection,
142 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
144 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 ances-
146 tral 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
148 under selection (either including haploid selection or not).

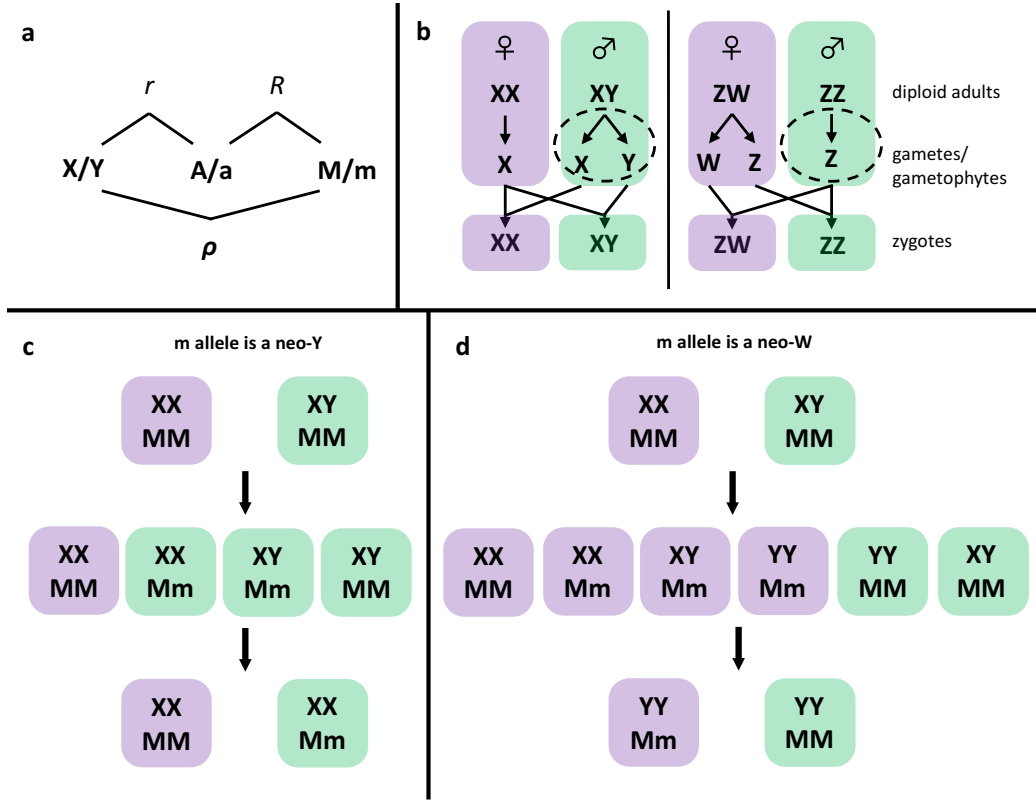


Figure 1: Outline of model features. Panel A: Recombination rate parameters between the ancestral-sex-determining locus (here, assumed to have X or Y alleles), a locus under selection (**A**, with alleles *A* and *a*), and a neo-sex-determining locus (**M**, with alleles *M* and *m*). If $r < 1/2$, then 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 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

150 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
 152 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 \mathbf{M} is a novel sex-determining region,
 154 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, \mathbf{X} ;
 156 XX genotypes become females and XY become males (or ZW become females
 and ZZ become males). To evaluate the evolution of new sex-determination sys-
 158 tems, we consider the invasion, fixation, maintenance, and/or loss of novel sex-
 determining alleles (m) at the \mathbf{M} locus. We assume that the \mathbf{M} locus is epistatically
 160 dominant over the \mathbf{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
 162 \mathbf{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
 164 interpret m as an environmental sex determination (ESD) allele, such that zygotes
 develop as females in a proportion (k) of the environments they experience.

166 In each generation, we census the genotype frequencies in male and female
 gametes/gametophytes (hereafter gametes) before gametic competition. A full de-
 168 scription of our model, including recursion equations, is given in the Appendix.
 First, competition occurs among male gametes (sperm/pollen competition) and
 170 among female gametes (egg/ovule competition) separately. Selection during ga-
 metic competition depends on the \mathbf{A} locus genotype, relative fitnesses are given
 172 by w_A^ϕ and w_a^ϕ ($\phi \in \{\varphi, \sigma\}$; see table 1). We assume that all gametes compete for
 fertilization during gametic competition, which assumes a polygamous mating sys-
 174 tem. Gametic competition in monogamous mating systems is, however, equivalent
 to meiotic drive in our model (described below), as either only alters the frequency
 176 of gametes produced by heterozygotes. After gametic competition, random mating
 occurs between male and female gametes. The resulting zygotes develop as males
 178 or females, depending on their genotypes at the \mathbf{X} and \mathbf{M} loci. Diploid males and
 females then experience selection, with relative fitnesses w_{AA}^ϕ , w_{Aa}^ϕ , and w_{aa}^ϕ . The
 180 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
 182 cross-overs) occurs between loci \mathbf{X} and \mathbf{A} with probability r , between loci \mathbf{A} and

184 **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
 186 experience meiotic drive; a gamete produced by Aa heterozygotes of sex ϕ bears allele A with probability α^ϕ . Thus, the **A** locus can experience sex-specific gametic
 188 competition, diploid selection, and/or meiotic drive.

Table 1: Relative fitness of different genotypes in sex $\phi \in \{\text{♀}, \text{♂}\}$

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

Results

190 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
 192 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-
 194 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-
 196 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 through-
 198 out).

Generic invasion by a neo-Y or neo-W

200 The evolution of a new sex-determination system requires that a rare mutant al-
 allele at the novel sex-determining locus, m , increases in frequency when rare. The
 202 spread of a rare mutant m at the \mathbf{M} locus is determined by the leading eigenvalue,
 λ , of the system of eight equations describing the frequency of eggs and sperm
 204 carrying the m allele in the next generation (equations S.1). This system simpli-
 fies substantially in a number of cases of interest. Dominant neo-Y (when $k = 0$)
 206 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
 208 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-
 210 determining system, phenotypes are not affected by the genotype at the ancestral
 sex-determining region (\mathbf{X} locus). Thus, the invasion of rare dominant neo-Y or
 212 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!](#)).
 214 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
 216 growth rate”) of the neo-sex determination allele m on background i without ac-
 counting for loss due to recombination, and χ_{mi} is the rate at which mutant haplo-
 218 types on background $i \in \{A, a\}$ recombine onto the other \mathbf{A} locus background in
 heterozygotes (see Table 2). The λ_{mi} and χ_{mi} , and thus the spread of the mutant
 220 m allele, depend on the frequency of alleles at the \mathbf{A} and \mathbf{X} loci in the ancestral
 population. In the ancestral population, it is convenient to follow the frequency
 222 of the A allele among female gametes (eggs), p_X^ϕ , and among X-bearing, p_X^δ , and
 among Y-bearing, p_Y^δ , male gametes (sperm/pollen). We also track the fraction of
 224 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^ϕ , and

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

$\bar{p}^{\delta} = (1 - \hat{q})\hat{p}_X^{\delta} + \hat{q}\hat{p}_Y^{\delta}$ 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}^{\varnothing} is the mean fitness of diploids of sex \varnothing , see Table S.2

\bar{w}_H^{\varnothing} is the mean fitness of haploids from sex \varnothing , see Table S.2

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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 $R = 0$ (see supplementary Mathematica file). 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 un-

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linked 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:

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

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

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

270 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^q , \hat{p}_X^δ , and \hat{p}_Y^δ) 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 272 can be maintained by mutation-selection balance or transiently present during the spread of beneficial alleles. However, polymorphisms maintained by selection can 274 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 276 maintained by heterozygote advantage, sexually-antagonistic selection, ploidy-antagonistic selection, or a combination (Immler et al. 2012). We can analytically 278 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 280 (s^δ , t^δ , α_Δ^δ of order $\epsilon \ll 1$).

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

The ancestral equilibrium allele frequencies and their stability conditions are given 288 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 290 is fixed on the Y ($p_Y^\delta = 0$), without loss of generality. If there are two alleles maintained at the **A** locus, the X can either be fixed for the A allele ($\hat{p}_X^q = \hat{p}_X^\delta = 1$) or polymorphic ($0 < \hat{p}_X^q, \hat{p}_X^\delta < 1$). 292

294 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 re-
gion 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 selec-
tion, overdominance, ploidy-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*

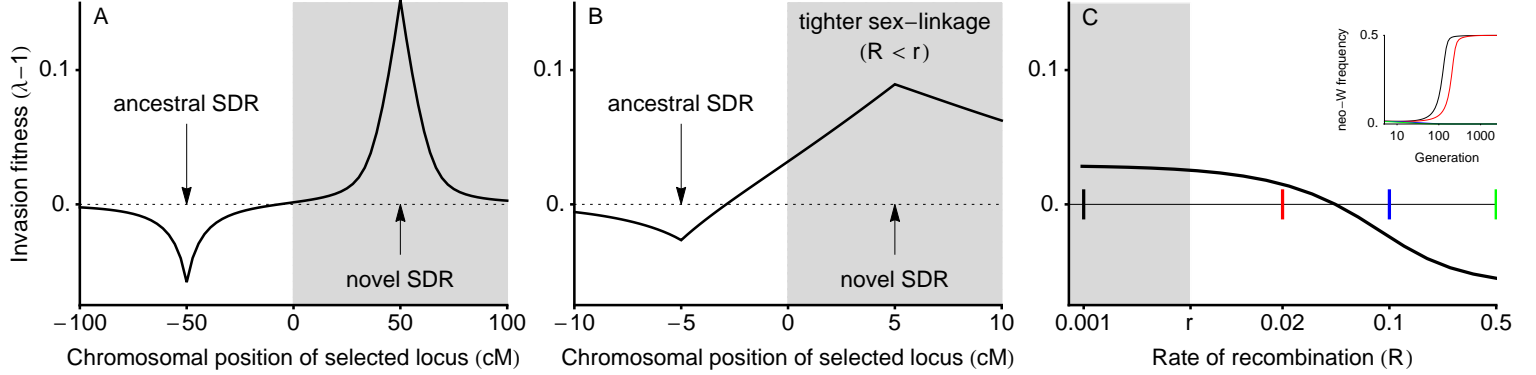


Figure 2: Transitions between XY and ZW systems can occur even when the neo-SDR is less tightly linked to a locus under sexually-antagonistic selection (here, without haploid selection). In panel A, linkage is loose enough relative to selection that the analytical results assuming weak selection hold, 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: $w_{AA}^{\circ} = 1.05$, $w_{aa}^{\delta} = 1.2$, $w_{aa}^{\circ} = w_{AA}^{\delta} = 0.85$, $w_{Aa}^{\delta} = 1$, $r^{\delta} = a_{\Delta}^{\delta} = 0$.

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 ($s^{\circ} > 0$, $0 < h^{\circ} < 1$), see outlined region in Figure 3A. When the a allele is strongly favoured on X chromosomes in males (w_{aa}^{δ} sufficiently large relative to w_{Aa}^{δ}), neo-W- A haplotypes can spread ($\lambda_{WA} > 1$, see grey region in Figure 3A) because they produce higher fitness females (AA or Aa genotypes) and are unleashed from counterselection in males.

When only one neo-W haplotype has 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).

340 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
342 favoured by selection in females ($\lambda_{W_a} > 1$). Again, this occurs because ancestral
X’s also experience selection in males, in which they will always be paired with
344 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
346 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
348 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
350 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 in-
352 dividuals 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
354 haplotypes then produce fewer unfit AA females. This is true for the neo-W- A hap-
lotype because it can pair with a Y- a haplotype and still be female. Wherever both
356 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,
358 see Figures S.1 and S.2 for examples).

Assuming that linkage is not tight, van Doorn and Kirkpatrick (2010) showed
360 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
362 $1/2$). An equivalent analysis is not possible where we assume that linkage is tight.
However, numerical simulations with tight linkage demonstrate that the neo-SDR
364 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.,
366 Figure S.9B,C).

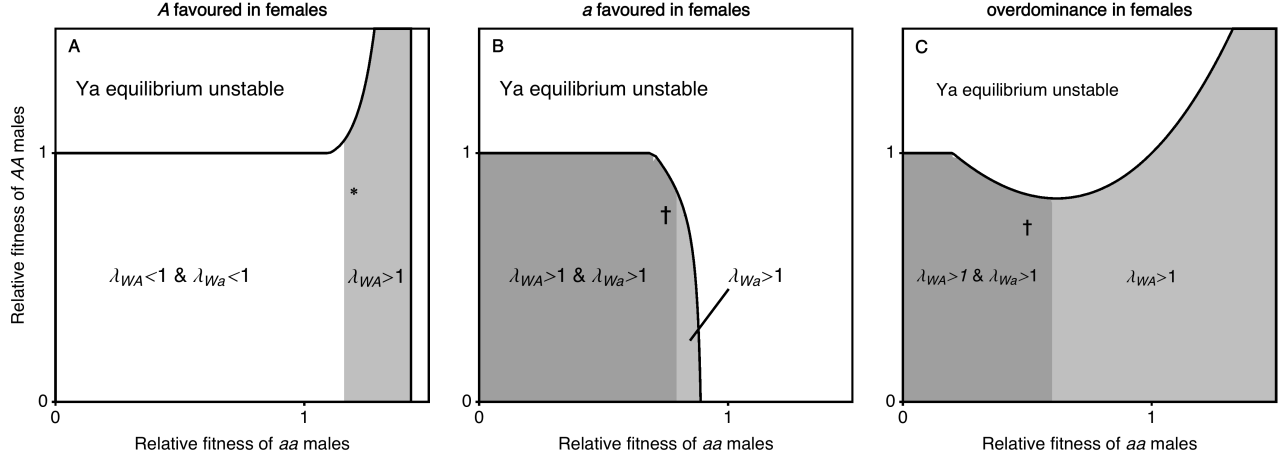


Figure 3: When the ancestral-XY locus is tightly linked to a locus under selection ($r = 0$), one or both neo-W haplotypes can spread. We vary the fitness of male homozygotes relative to heterozygotes ($w_{Aa}^{\delta} = 1$) and only consider stable equilibria at which both A locus alleles are maintained and the a allele is initially fixed on the Y, region outlined. Here, selection in females can favour the A allele (panel A, $w_{aa}^{\delta} = 0.85$, $w_{AA}^{\delta} = 1.05$), favour the a allele (panel B, $w_{aa}^{\delta} = 1.05$, $w_{AA}^{\delta} = 0.85$), or be overdominant (panel C, $w_{aa}^{\delta} = w_{AA}^{\delta} = 0.6$). 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 $t^{\delta} = \alpha_{\Delta}^{\delta} = 0$.

Loose linkage with the ancestral sex-determining region

Assuming that selection is weak (s^{δ} , t^{δ} , α_{Δ}^{δ} of order $\epsilon \ll 1$) 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:

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

and

$$\lambda_{W',XY} = \lambda_{Y',XY} + (2\alpha_{\Delta}^{\delta} - 2\alpha_{\Delta}^{\delta} + t^{\delta} - t^{\delta}) (\hat{p}_Y^{\delta} - \hat{p}_X^{\delta}) / 2 + O(\epsilon^3) \quad (3)$$

374 where $V_A = \bar{p}(1 - \bar{p})$ is the variance in the equilibrium frequency of A and $S_A =$
 $(D^\delta + \alpha_\Delta^\delta + t^\delta) - (D^\varphi + \alpha_\Delta^\varphi + t^\varphi)$ describes sex differences in selection for the
 376 A versus a allele across diploid selection, meiosis, and gametic competition. The
 diploid selection term, $D^\varphi = [\bar{p}s^\varphi + (1 - \bar{p})h^\varphi s^\varphi] - [\bar{p}h^\varphi s^\varphi + (1 - \bar{p})]$, is the difference
 378 in fitness between A and a alleles in diploids of sex $\varphi \in \{\varphi, \delta\}$, where \bar{p} is the
 leading-order probability of mating with an A -bearing gamete from the opposite
 380 sex (equation S.4). The difference in A -allele-frequency among Y-bearing sperm
 versus X-bearing sperm is given by $\hat{p}_Y^\delta - \hat{p}_X^\delta = V_A(D^\delta - D^\varphi + \alpha_\Delta^\delta - \alpha_\Delta^\varphi + t^\delta -$
 382 $t^\varphi)(1 - 2r)/(2r)$.

The neo-sex-determining allele, m , will spread if $\lambda_{m,XY} > 1$. Equation (2)
 384 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-
 386 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
 388 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
 390 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
 392 selection.

With weak selection and no haploid selection ($t^\varphi = \alpha_\Delta^\varphi = 0$), the spread of a
 394 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-
 396 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
 398 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
 400 linked to the selected locus ($R > r$).

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

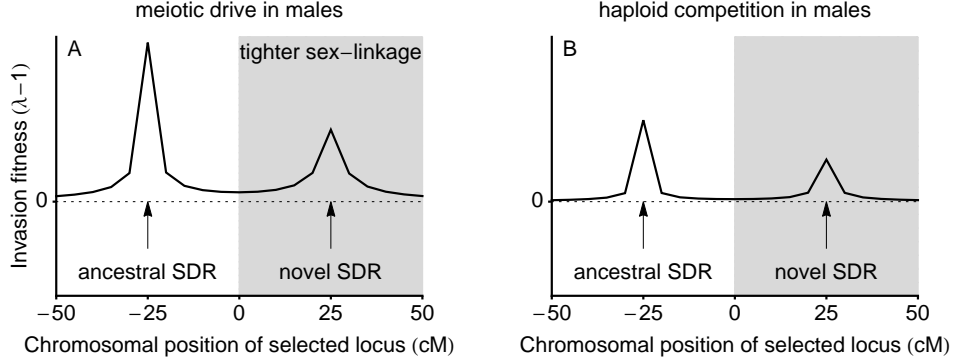


Figure 4: Ploidally-antagonistic selection allows a less tightly linked neo-W to invade. In panel A, male drive ($\alpha_{\Delta}^{\delta} = -1/20$, $r^{\delta} = \alpha_{\Delta}^{\delta} = 0$) opposes selection in diploids (no sex-differences: $s^{\delta} = 1/10$, $h^{\delta} = 7/10$), in which case the neo-sex-determining allele can invade regardless of linkage. In panel B, gametic competition in males ($t^{\delta} = -1/10$, $r^{\delta} = \alpha_{\Delta}^{\delta} = 0$) opposes selection in diploids (sex-differences: $s^{\delta} = 3/20$, $s^{\varnothing} = 1/20$, $h^{\delta} = 7/10$), 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).

404 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 be-
406 tween A alleles and sex chromosomes in males, $(\hat{p}_Y^{\delta} - \hat{p}_X^{\delta}) = 0$, see equation (S.5).
The second term in equation (3) therefore disappears and invasion depends only
408 on the sign of $(r - R)$, as in the case of the neo-Y. Indeed, invasion typically oc-
curs when the neo-W is more closely linked to the selected locus than the ancestral
410 sex-determining region (Figure 4).

Secondly, we can simplify the discussion of cases where invasion occurs de-
412 spite 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
414 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
416 in one sex (e.g., during male meiosis only) and dominance coefficients are equal
in the two sexes, $h^{\varnothing} = h^{\delta}$. When there is no gametic competition and meiotic
418 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 ($s^{\varnothing}s^{\delta} > 0$, see Figure 4A

420 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
 422 in male and female diploid selection and there are sex differences in selection of
 one type (e.g., $s^{\varphi}(s^{\delta} - s^{\varphi}) > 0$, see Figure 4B). These special cases indicate that
 424 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	$h^{\delta} = h^{\varphi}, t^{\varphi} = t^{\delta} = \alpha_{\Delta}^{\varphi} = 0$	$s^{\varphi}s^{\delta} > 0$
female drive only	$h^{\delta} = h^{\varphi}, t^{\varphi} = t^{\delta} = \alpha_{\Delta}^{\delta} = 0$	$s^{\varphi}s^{\delta} > 0$
sperm competition only	$h^{\delta} = h^{\varphi}, t^{\varphi} = \alpha_{\Delta}^{\varphi} = \alpha_{\Delta}^{\delta} = 0$	$s^{\varphi}(s^{\delta} - s^{\varphi}) > 0$
egg competition only	$h^{\delta} = h^{\varphi}, t^{\delta} = \alpha_{\Delta}^{\varphi} = \alpha_{\Delta}^{\delta} = 0$	$s^{\delta}(s^{\varphi} - s^{\delta}) > 0$

426 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,
 428 unlinked sex-determining locus invades in order to restore equal sex ratios (Koziel-
 ska et al. 2010). Consider, for example, the case where the **A** locus is linked to the
 430 ancestral-SDR ($r < 1/2$) and experiences meiotic drive in males only ($\alpha_{\Delta}^{\delta} \neq 0$,
 $\alpha_{\Delta}^{\varphi} = 0$), without gametic competition ($t^{\varphi} = t^{\delta} = 0$). In this case, the zygotic sex
 432 ratio can be initially biased only if the ancestral sex-determining system is XY (Fig-
 ure 1B and Figure 5B). If Fisherian sex ratio selection were dominant, we would
 434 expect a difference in the potential for XY to ZW and ZW to XY transitions. How-
 ever, invasion by a neo-W into an XY system and invasion by a neo-Y into a ZW
 436 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-
 438 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 conse-
 440 quence, 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-

442 wards males.

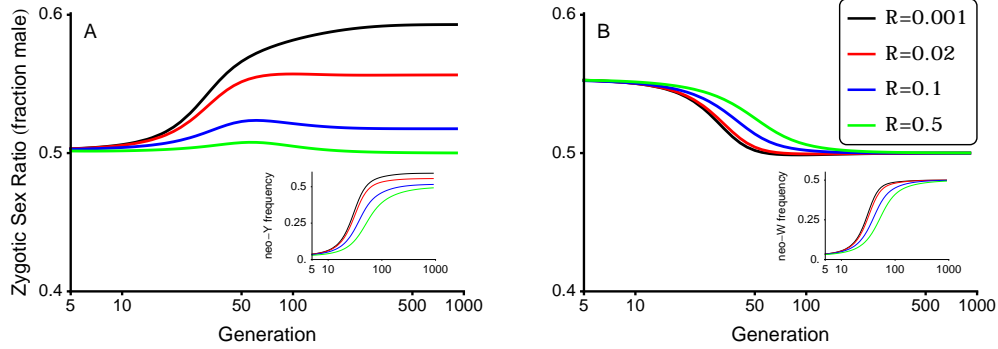


Figure 5: Fisherian sex ratio selection alone is not a good predictor of turnover between sex-determining systems. In this figure, selection is ploidy antagonistic with haploid selection favouring the a allele during male meiosis. In panel A, male drive in an ancestral ZW system has no effect on the 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: $s^{\varnothing} = s^{\sigma} = 0.2$, $h^{\varnothing} = h^{\sigma} = 0.7$, $t^{\varnothing} = t^{\sigma} = \alpha_{\Delta}^{\varnothing} = 0$, $\alpha_{\Delta}^{\sigma} = -0.1$, $r = 0.02$.

Why can new sex-determining regions invade when more loosely linked to
 444 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 fa-
 446 cilitate 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
 448 can also, however, benefit from becoming more associated with drive. For exam-
 ple in a ZW system with the same selection regime (haploid selection in males),
 450 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
 452 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
 454 spurs sex chromosome transitions, more complex situations also arise. For exam-
 ple with $R = 1/2$ in Figure 5B (green curve), the neo-Y spreads despite the fact
 456 that it cannot benefit from drive because free recombination moves it randomly

between driven and non-driven backgrounds. Nevertheless, the unlinked neo-Y
 458 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
 460 fitness to balance the haploid advantage of the a allele at equilibrium.

Environmental sex determination

462 We next consider the case where the new sex-determining mutation, m , causes sex
 to be determined probabilistically or by heterogeneous environmental conditions
 464 (environmental sex determination, ESD), with individuals carrying allele m devel-
 oping as females with probability k . Here, we do not assume that the environmen-
 466 tal conditions that determine sex also differentially affect the fitness of males versus
 females. Such correlations can favour environmental sex-determination systems
 468 that allow each sex to be produced in the environment in which it has highest fit-
 ness; in the absence of these correlations, previous theory would predict that ESD
 470 is favoured when it produces more equal sex ratios than the ancestral system (see
 reviews by Charnov 1982, Bull 1983, West 2009).

472 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
 474 on weak selection here. Assuming weak selection, the spread of the new sex-
 determining region is given by

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

476 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
 478 develop as females and half as males ($k = 1/2$, creating equal sex ratios), the

spread of which is given by

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

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, $r < 1/2$, $h^\varnothing = h^\delta$, and $s^\varnothing s^\delta < 0$, 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 ploidy-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
 536 by their effect on the sex ratio (i.e., the sex ratio bias created by male haploid se-
 lection facilitates the spread of a neo-W into an XY system to the same degree that
 538 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
 540 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.

542 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
 544 transcriptome analysis in *Rumex* shows that Y-linked genes have higher expres-
 sion in haploid pollen than autosomal genes (check this is accurate). Interestingly,
 546 haploid-expression is also more common on the autosome that is orthologous to
 the sex chromosomes in closely related species suggesting that new sex chromo-
 548 somes may have been favoured through their association with haploid selected
 alleles on these chromosomes (Sandler et al., 2018, Personal Communication). In
 550 general, we predict that haploid selection increases lability of sex-determination
 systems, particularly because haploid selection can cause transitions that increase
 552 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
 554 explain the relative rarity of heteromorphic sex chromosomes in plants, which
 are thought to experience more selection during their multicellular haploid stage.
 556 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)
 558 are favoured more strongly than cis-GSD transitions, with transitions to ESD in-
 termediate (e.g., with $|D^\delta - D^\varnothing| \ll |\alpha_\Delta^\delta - \alpha_\Delta^\varnothing + t^\delta - t^\varnothing|$ we have $\lambda_{W',XY} > \lambda_{Y',XY}$;
 560 Equations 3 and S.5). Among the relatively few dioecious clades in which mul-
 tiple species have well characterized sex chromosomes (Ming et al. 2011), trans-
 562 GSD transitions have been inferred in *Silene* subsection *Otites* (Slancarova et al.
 2013) and in *Salicaceae* (Pucholt et al. 2015; 2017). Assuming that transitions
 564 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 *Akodon* 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
596 in these rodent species.

We note that we assume that sex-determining alleles do not experience direct
598 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
600 or W) in the ancestral sex-determining region because recessive deleterious mu-
tations and/or deletions accumulate around the Y or W sex-determining regions
602 (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
604 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.
606 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
608 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
610 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 tran-
612 sitions 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
614 conditions, especially with haploid selection. For example, Vicoso and Bachtrog
(2015) found a dozen sex chromosome configurations among Dipteran species but
616 only one transition between male and female heterogamety.

In this study, we have only considered neo-sex-determining alleles of large ef-
618 fect. However, we expect similar selective forces to act on masculinizing/feminizing
alleles of weaker effect. For example, Muralidhar and Veller (2018) consider small
620 effect masculinizing/feminizing alleles within a threshold model of sex determina-
tion, finding that they can be favoured when linked to loci that experience sexually-
622 antagonistic selection. These results echo those for large-effect neo-Y/neo-W al-
leles (van Doorn and Kirkpatrick 2007; 2010). Finally, while we have considered
624 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

914 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^{ϕ} and y_i^{ϕ} . The superscript $\phi \in \{\sigma, \varphi\}$ 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, $\sum_i x_i^{\phi} + y_i^{\phi} = 1$.

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

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

Finally, these diploids undergo meiosis to produce the next generation of ga-
metes. 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 param-
eters 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 possi-
ble ordering of the loci assuming that there is no cross-over interference. During
meiosis in sex ϕ , meiotic drive occurs such that, in Aa heterozygotes, a fraction
 α^{ϕ} of gametes produced carry the A allele and $(1 - \alpha^{\phi})$ 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 ϕ , the frequencies of haplotypes (before gametic

competition) in the next generation are given by

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

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

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

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

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

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

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

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

966

The full system is therefore described by 16 recurrence equations (three diallelic
968 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
970 ancestral XY sex-determining system, there are XX males, XY females, or YY
females ($x_3^{\sigma} = x_4^{\sigma} = y_4^{\sigma} = y_3^{\sigma} = y_i^{\sigma} = 0$). In this case, the system only involves six
972 recursion equations, which we assume below to calculate the equilibria.

Resident equilibria and stability

974 In the resident population (allele M fixed), we follow the frequency of A in X-
bearing female gametes, p_X^{σ} , and X-bearing male gametes, p_X^{σ} , and Y-bearing male
976 gametes, p_Y^{σ} . 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 deter-
978 mine the frequencies of the six resident gamete types: $x_1^{\sigma} = \hat{p}_X^{\sigma}$, $x_2^{\sigma} = 1 - \hat{p}_X^{\sigma}$,
 $x_1^{\sigma} = (1 - q)\hat{p}_X^{\sigma}$, $x_2^{\sigma} = (1 - q)(1 - \hat{p}_X^{\sigma})$, $y_1^{\sigma} = q\hat{p}_Y^{\sigma}$, and $y_2^{\sigma} = q(1 - \hat{p}_Y^{\sigma})$. Mean
980 fitnesses in the resident population are given in table S.2.

Various forms of selection can maintain a polymorphism at the A locus, in-
982 cluding sexually antagonistic selection, overdominance, conflicts between diploid
selection and selection upon haploid genotypes (ploidy antagonistic selection,
984 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
986 ($s^{\sigma} = s^{\sigma}$, $h^{\sigma} = h^{\sigma}$, and $\alpha^{\sigma} = \alpha^{\sigma} = 1/2$), 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}_H^\varnothing)	$p_X^\varnothing w_A^\varnothing + (1 - p_X^\varnothing) w_a^\varnothing$
male gametes (\bar{w}_H^δ)	$\bar{p}^\delta w_A^\delta + (1 - \bar{p}^\delta) w_a^\delta$
females (\bar{w}^\varnothing)	$(1 - \zeta)^{-1} [p_X^\varnothing w_A^\varnothing p_X^\delta w_A^\delta w_{AA}^\varnothing +$ $(1 - p_X^\varnothing) w_a^\varnothing p_X^\delta w_A^\delta w_{Aa}^\varnothing +$ $p_X^\varnothing w_A^\varnothing (1 - p_X^\delta) w_a^\delta w_{Aa}^\varnothing +$ $(1 - p_X^\varnothing) w_a^\varnothing (1 - p_X^\delta) w_a^\delta w_{aa}^\varnothing] / (\bar{w}_H^\varnothing \bar{w}_H^\delta)$
males (\bar{w}^δ)	$\zeta^{-1} [p_X^\varnothing w_A^\varnothing p_Y^\delta w_A^\delta w_{AA}^\delta +$ $(1 - p_X^\varnothing) w_a^\varnothing p_Y^\delta w_A^\delta w_{Aa}^\delta +$ $p_X^\varnothing w_A^\varnothing (1 - p_Y^\delta) w_a^\delta w_{Aa}^\delta +$ $(1 - p_X^\varnothing) w_a^\varnothing (1 - p_Y^\delta) w_a^\delta w_{aa}^\delta] / (\bar{w}_H^\varnothing \bar{w}_H^\delta)$
fraction zygotes male (ζ)	$q [p_Y^\delta w_A^\delta + (1 - p_Y^\delta) w_a^\delta] / \bar{w}_H^\delta$

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

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

992 We first calculate the equilibrium frequency of the **Y** and **A** alleles in the ances-
tral population when the recombination rate between the **X** and **A** loci is small
994 (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
996 on the five equilibria that maintain both **A** and **a** alleles, four of which are given to
leading order by:

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

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

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

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

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

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

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

998 A fifth equilibrium (C) also exists where A is present at an intermediate frequency
on the Y chromosome ($0 < \hat{p}_Y^\delta < 1$). However, equilibrium (C) is never locally
1000 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
1002 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
1004 (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
1006 a allele. If there is no haploid selection ($\alpha_\Delta^\delta = 0$, $w_A^\delta = w_a^\delta = 1$), these equilibria
are equivalent to those found by Lloyd and Webb (1977) and Otto (2014).

1008 We next calculate when (A) and (B) are locally stable for $r = 0$. According to
the ‘small parameter theory’ (Karlin and McGregor 1972a;b), these stability prop-

1010 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
 1012 be stably fixed on the Y we need $\bar{w}_{Ya}^\delta > \bar{w}_{YA}^\delta$ where $\bar{w}_{Ya}^\delta = w_a^\delta [\hat{p}_X^\varphi (1 - \alpha_\Delta^\delta) w_A^\varphi w_{Aa}^\delta +$
 $(1 - \hat{p}_X^\varphi) w_a^\varphi w_{aa}^\delta]$ and $\bar{w}_{YA}^\delta = w_A^\delta [\hat{p}_X^\varphi w_A^\varphi w_{AA}^\delta + (1 - \hat{p}_X^\varphi)(1 + \alpha_\Delta^\delta) w_a^\varphi w_{Aa}^\delta]$. That is,
 1014 Y- a haplotypes must have higher fitness than Y- A haplotypes. Substituting in \hat{p}_X^φ
 from equation (S.2), fixation of the a allele on the Y requires that $\gamma_i > 0$ where
 1016 $\gamma_{(A)} = w_a^\delta [(1 - \alpha_\Delta^\delta) w_{Aa}^\delta \phi + w_{aa}^\delta \psi] - w_A^\delta [w_{AA}^\delta \phi + (1 + \alpha_\Delta^\delta) w_{Aa}^\delta \psi]$ for equilibrium
 (A) and $\gamma_{(B)} = (1 - \alpha_\Delta^\delta) w_a^\delta w_{Aa}^\delta - w_A^\delta w_{AA}^\delta$ for equilibrium (B). Stability of a poly-
 1018 morphism 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
 1020 equilibrium (A) is not, as it requires $\psi < 0$.

Selection weak relative to recombination (weak selection)

1022 Here, we assume that selection and meiotic drive are weak relative to recombina-
 tion ($s^\varphi, t^\varphi, \alpha_\Delta^\varphi$ of order ϵ). The maintenance of a polymorphism at the **A** locus
 1024 then requires that

$$\begin{aligned}
 0 &< -[(1 - h^\varphi)s^\varphi + (1 - h^\delta)s^\delta + t^\varphi + t^\delta + \alpha_\Delta^\varphi + \alpha_\Delta^\delta] \\
 \text{and } 0 &< h^\varphi s^\varphi + h^\delta s^\delta + t^\varphi + t^\delta + \alpha_\Delta^\varphi + \alpha_\Delta^\delta.
 \end{aligned} \tag{S.3}$$

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

1026 Given that a polymorphism is maintained at the **A** locus by weak selection, the
 frequencies of A in each type of gamete are the same ($\hat{p}_X^\varphi = \hat{p}_X^\delta = \hat{p}_Y^\delta = \bar{p}$) and
 1028 given, to leading order, by

$$\bar{p} = \frac{h^\varphi s^\varphi + h^\delta s^\delta + t^\varphi + t^\delta + \alpha_\Delta^\varphi + \alpha_\Delta^\delta}{(2h^\varphi - 1)s^\varphi + (2h^\delta - 1)s^\delta} + O(\epsilon). \tag{S.4}$$

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

$$\begin{aligned}
\hat{p}_X^\delta - \hat{p}_X^\varphi &= V_A (D^\delta - D^\varphi + \alpha_\Delta^\delta - \alpha_\Delta^\varphi) + O(\epsilon^2) \\
\hat{p}_Y^\delta - \hat{p}_X^\varphi &= V_A [D^\delta - D^\varphi + \alpha_\Delta^\delta - \alpha_\Delta^\varphi + (1 - 2r)(t^\delta - t^\varphi)] / 2r + O(\epsilon^2) \quad (\text{S.5}) \\
\hat{p}_Y^\delta - \hat{p}_X^\delta &= V_A (D^\delta - D^\varphi + \alpha_\Delta^\delta - \alpha_\Delta^\varphi + t^\delta - t^\varphi) (1 - 2r) / 2r + O(\epsilon^2)
\end{aligned}$$

1030 where $V_A = \bar{p}(1 - \bar{p})$ is the variance in the frequency of A and $D^\varphi = [\bar{p}s^\varphi + (1 - \bar{p})h^\varphi s^\varphi] - [\bar{p}h^\varphi s^\varphi + (1 - \bar{p})]$ corresponds to the difference in fitness between A and
 1032 a alleles in diploids of sex $\varphi \in \{\varphi, \delta\}$ (\bar{p} is the leading-order probability of mating with an A -bearing gamete from the opposite sex). The frequency of Y among male
 1034 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
 1036 allele in males, $q = 1/2 + \alpha_\Delta^\delta(\hat{p}_Y^\delta - \hat{p}_X^\delta)/2 + O(\epsilon^3)$. Without gametic competition or drive ($\alpha_\Delta^\varphi = t^\varphi = 0$) our results reduce to those of van Doorn and Kirkpatrick
 1038 (2007).

Invasion conditions

1040 [Cover the other parts of the characteristic polynomial here.](#) [Waiting for Sally's proof!](#)

1042 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
 1044 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)
 1046 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
 1048 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).

1050 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
 1052 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

$$\lambda_{mA} = [w_A^\delta(1 + \alpha_\Delta^\delta)]^{-1} \frac{w_A^\varnothing [w_A^\delta(1 + \alpha_\Delta^\delta)w_{AA}^\varnothing + w_a^\delta(1 - \alpha_\Delta^\delta)w_{Aa}^\varnothing(1 + \alpha_\Delta^\varnothing)]}{w_A^\varnothing 2w_{AA}^\varnothing} \quad (\text{S.6a})$$

$$\lambda_{ma} = [w_A^\delta(1 + \alpha_\Delta^\delta)]^{-1} \frac{w_a^\varnothing [w_A^\delta(1 + \alpha_\Delta^\delta)w_{Aa}^\varnothing(1 - \alpha_\Delta^\varnothing) + w_a^\delta(1 - \alpha_\Delta^\delta)w_{aa}^\varnothing]}{w_A^\varnothing 2w_{AA}^\varnothing} \quad (\text{S.6b})$$

$$\chi_{mA} = \frac{1}{2} [w_A^\delta(1 + \alpha_\Delta^\delta)]^{-1} \frac{w_A^\varnothing [w_a^\delta(1 - \alpha_\Delta^\delta)w_{Aa}^\varnothing(1 + \alpha_\Delta^\varnothing)]}{w_A^\varnothing w_{AA}^\varnothing} \frac{R}{2} \quad (\text{S.6c})$$

$$\chi_{ma} = \frac{1}{2} [w_A^\delta(1 + \alpha_\Delta^\delta)]^{-1} \frac{w_a^\varnothing [w_A^\delta(1 + \alpha_\Delta^\delta)w_{Aa}^\varnothing(1 - \alpha_\Delta^\varnothing)]}{w_A^\varnothing w_{AA}^\varnothing} \frac{R}{2} \quad (\text{S.6d})$$

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 $1 - \zeta = w_A^\delta(1 + \alpha_\Delta^\delta)/(2\bar{w}_H^\delta)$ where $2\bar{w}_H^\delta = [w_a^\delta(1 - \alpha_\Delta^\delta) + w_A^\delta(1 + \alpha_\Delta^\delta)]$ has been canceled out in equations (S.6) to leave the term $[w_A^\delta(1 + \alpha_\Delta^\delta)]^{-1}$. Male biased sex

ratios facilitate the spread of a neo-W because neo-W alleles cause the zygotes that
 1072 carry them to develop as the rarer, female, sex.

Secondly, haploid selection in females selects on neo-W haplotypes directly. At
 1074 equilibrium (B), the fitness of female gametes under the ancestral sex-determining
 system is w_A^\varnothing such that the relative fitnesses of neo-W- A and neo-W- a haplotypes
 1076 during female gametic competition are $w_A^\varnothing/w_A^\varnothing$ and $w_a^\varnothing/w_A^\varnothing$ (see terms in equation
 S.6). Meiotic drive in females will also change the proportion of gametes that carry
 1078 the A versus a alleles, which will be produced by heterozygous females in propor-
 tions $(1 + \alpha_\Delta^\varnothing)/2$ and $(1 - \alpha_\Delta^\varnothing)/2$, respectively. These terms are only associated with
 1080 heterozygous females, i.e., they are found alongside w_{Aa}^\varnothing .

Thirdly, haploid selection in males affects the diploid genotypes of females
 1082 by altering the allele frequencies in the male gametes that female gametes pair
 with. At equilibrium (B), neo-W female gametes will mate with X- A male ga-
 1084 metes with probability $w_A^\delta(1 + \alpha_\Delta^\delta)/(2\bar{w}_H^\delta)$ and Y- a male gametes with probability
 $w_a^\delta(1 - \alpha_\Delta^\delta)/(2\bar{w}_H^\delta)$, where the $2\bar{w}_H^\delta$ terms have been canceled in equation (S.6)
 1086 (as mentioned above). Thus, for example, neo-W- A haplotypes are found in AA
 female diploids with probability $w_A^\delta(1 + \alpha_\Delta^\delta)/(2\bar{w}_H^\delta)$ (first term in square brack-
 1088 ets in the numerator of equation S.6a) and in Aa female diploids with probability
 $w_a^\delta(1 - \alpha_\Delta^\delta)/(2\bar{w}_H^\delta)$ (see equation S.6c and the second term in square brackets in
 1090 the numerator of equation S.6a).

The other terms in equations (S.6) are more easily interpreted if we assume that
 1092 there is no haploid selection in either sex, in which case $\lambda_{mA} = (w_{AA}^\varnothing + w_{Aa}^\varnothing)/2w_{AA}^\varnothing$
 and $\lambda_{ma} = (w_{aa}^\varnothing + w_{Aa}^\varnothing)/2w_{AA}^\varnothing$. Neither haplotype can spread under purely sexually-
 1094 antagonistic selection, where A is directionally favoured in females ($w_{AA}^\varnothing > w_{Aa}^\varnothing >$
 w_{aa}^\varnothing) and a is directionally favoured in males ($w_{AA}^\delta > w_{Aa}^\delta > w_{aa}^\delta$). Essentially, the
 1096 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,
 1098 increasing the flow of a alleles into females, which reduces the fitness of those
 females.

1100 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
 1102 neo-W-*A* haplotype can spread ($\lambda_{mA} > 1$) when $w_{Aa}^{\varphi} > w_{AA}^{\varphi}$, despite the fact that
 a neo-W brings Y-*a* haplotypes into females. In this case the *a* allele is favoured
 1104 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
 1106 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
 1108 have $w_{Aa}^{\varphi} < 2w_{AA}^{\varphi}$ and $w_{Aa}^{\delta} / [(w_{aa}^{\delta} + w_{Aa}^{\delta})/2] > w_{Aa}^{\varphi} / w_{AA}^{\varphi}$.

Still considering $w_{Aa}^{\varphi} > w_{AA}^{\varphi}$, the neo-W can also spread alongside the *a* allele
 1110 ($\lambda_{ma} > 1$) if w_{aa}^{φ} is large enough such that $(w_{Aa}^{\varphi} + w_{aa}^{\varphi})/2 > w_{AA}^{\varphi}$. This can occur
 with overdominance or directional selection for *a* in females (Figure 3B,C). In this
 1112 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
 1114 because it produces females with higher fitness *Aa* and *aa* genotypes.

Similar equations can be derived for equilibrium (A) by substituting the equi-
 1116 librium allele frequencies into Table 2

$$\lambda_{mA} = \frac{a}{b} [w_{AA}^{\varphi} w_{Aa}^{\delta} w_A^{\delta} (1 + \alpha_{\Delta}^{\delta}) \phi + w_{Aa}^{\varphi} (1 + \alpha_{\Delta}^{\varphi}) w_a^{\delta} c] / (2w_a^{\varphi}) \quad (\text{S.7a})$$

$$\lambda_{ma} = \frac{a}{b} [w_{Aa}^{\varphi} (1 - \alpha_{\Delta}^{\varphi}) w_{Aa}^{\delta} w_A^{\delta} (1 + \alpha_{\Delta}^{\delta}) \phi + w_{aa}^{\varphi} w_a^{\delta} c] / (2w_a^{\varphi}) \quad (\text{S.7b})$$

$$\chi_{mA} = \frac{a}{b} \frac{R}{2} [w_{Aa}^{\varphi} (1 + \alpha_{\Delta}^{\varphi}) w_a^{\delta} c] / w_a^{\varphi} \quad (\text{S.7c})$$

$$\chi_{ma} = \frac{a}{b} \frac{R}{2} [w_{Aa}^{\varphi} (1 - \alpha_{\Delta}^{\varphi}) w_{Aa}^{\delta} w_A^{\delta} (1 + \alpha_{\Delta}^{\delta}) \phi] / w_a^{\varphi} \quad (\text{S.7d})$$

where

$$a = w_a^\varnothing \phi + w_A^\varnothing \psi \quad (\text{S.8a})$$

$$b = w_{AA}^\varnothing [w_{Aa}^\delta w_A^\delta (1 + \alpha_\Delta^\delta)] \phi^2 + w_{Aa}^\varnothing [w_{Aa}^\delta w_A^\delta (1 + \alpha_\Delta^\delta) + w_{aa}^\delta w_a^\delta] \psi \phi + w_{aa}^\varnothing (w_{aa}^\delta w_a^\delta) \psi^2 \quad (\text{S.8b})$$

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

1118 As with equilibrium (B), haploid selection again modifies invasion fitnesses
by altering the sex ratio and the diploid genotypes of females and directly select-
1120 ing 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 .
1122 Thus the effect of haploid selection in males is reduced, as is the difference in fit-
ness between neo-W haplotypes and resident X haplotypes, as both can be on any
1124 diploid or haploid background.

The other terms are easier to interpret in the absence of haploid selection. For
1126 instance, without haploid selection, the neo-W- A haplotype spreads ($\lambda_{mA} > 1$) if
and only if

$$2(w_{Aa}^\varnothing - w_{aa}^\varnothing)w_{aa}^\delta \psi^2 > (w_{AA}^\varnothing - w_{Aa}^\varnothing)w_{Aa}^\delta \phi(\phi - \psi) \quad (\text{S.9})$$

1128 where $\phi - \psi = w_{AA}^\varnothing w_{Aa}^\delta - w_{aa}^\varnothing w_{aa}^\delta$ and both ϕ and ψ are positive when equilibrium
(A) is stable. In contrast to equilibrium (B), a neo-W haplotype can spread under
1130 purely sexually-antagonistic selection ($w_{aa}^\varnothing < w_{Aa}^\varnothing < w_{AA}^\varnothing$ and $w_{AA}^\delta < w_{Aa}^\delta < w_{aa}^\delta$).
The neo-W- A can spread as long as it becomes associated with females that bear
1132 more A alleles than observed at equilibrium (A).

Without haploid selection, the neo-W- a haplotype spreads ($\lambda_{ma} > 1$) if and
1134 only if

$$(w_{aa}^\varnothing + w_{Aa}^\varnothing - 2w_{AA}^\varnothing)w_{Aa}^\delta \phi^2 + (w_{aa}^\varnothing - w_{Aa}^\varnothing)(w_{Aa}^\delta + 2w_{aa}^\delta)\phi\psi > 0 \quad (\text{S.10})$$

This condition cannot be met with purely sexually antagonistic selection (as both
 1136 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
 1138 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
 1140 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
 1142 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.

1144 **Role of Haploid Selection with Tight Linkage**

Haploid selection generally expands the conditions under which neo-W alleles can
 1146 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
 1148 a polymorphism to be maintained when it would not under diploid selection alone
 (e.g., with directional selection in diploids). In cases of ploidy-antagonistic se-
 1150 lection, 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).
 1152 Second, even when diploid selection could itself maintain a polymorphism, hap-
 loid selection can increase the conditions under which transitions among sex chro-
 1154 mosomes are possible. Of particularly importance, when selection is sexually-
 antagonistic in diploids ($s^{\text{♀}}s^{\text{♂}} < 0$ and $0 < h^{\text{♂}} < 1$), an unlinked neo-W ($R = 1/2$)
 1156 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
 1158 conditions under which neo-W chromosomes can spread (compare Figures S.4-S.7
 to Figure 3).

1160 Male haploid selection in favour of the a allele ($\alpha_{\Delta}^{\text{♂}} < 0$, $w_A^{\text{♂}} < w_a^{\text{♂}}$) generates
 male-biased sex ratios at equilibria (A) and (B), where Y- a is fixed ($\hat{p}_Y^{\text{♂}} = 0$).
 1162 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

1164 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
1166 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.

1168 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
1170 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
1172 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
1174 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
1176 chromosomes and thereby cause sex ratios to become biased.

Supplementary Figures

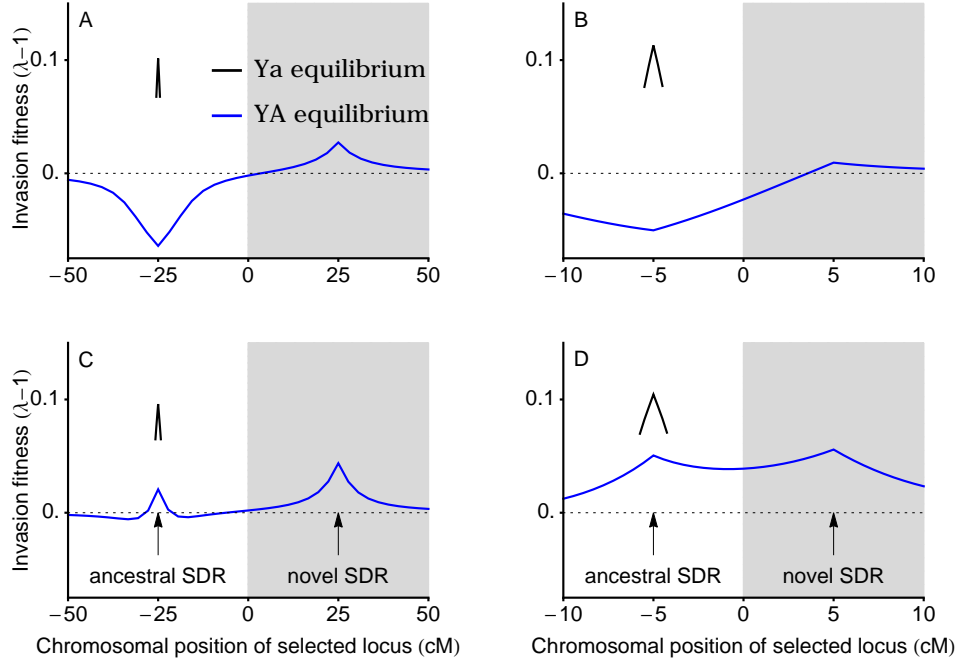


Figure S.1: Neo-W alleles can spread when loci under diploid selection are tightly linked to the ancestral sex determining locus ($r \approx 0$). In panels A and B, the a allele is favoured in females ($w_{aa}^{\varnothing} = 1.05$, $w_{Aa}^{\varnothing} = 1$, $w_{AA}^{\varnothing} = 0.85$) and selection in males is overdominant ($w_{aa}^{\sigma} = w_{AA}^{\sigma} = 0.75$). In panels C and D, selection in males and females is overdominant ($w_{aa}^{\varnothing} = w_{AA}^{\varnothing} = 0.6$, $w_{aa}^{\sigma} = 0.5$, $w_{AA}^{\sigma} = 0.7$, $w_{Aa}^{\sigma} = 1$). There is no haploid selection $r^{\varnothing} = \alpha_{\Delta}^{\varnothing} = 0$. These parameters are marked by daggers in Figure 3B and C, which show that neo-W invasion is expected for any \bar{R} ($\lambda_{W_A}, \lambda_{W_a} > 1$) when the a allele is nearly fixed on the Y (black lines in this figure; not stable for $r \gg 0$). 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.

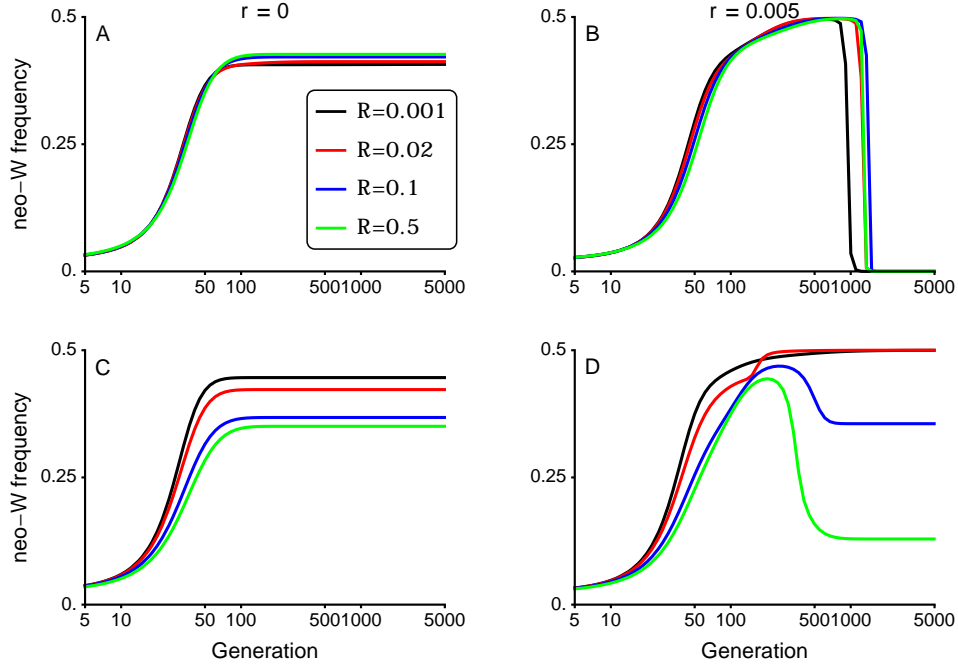


Figure S.2: Following invasion by a neo-W allele, there can be a complete transition to a new sex-determination system, maintenance of polymorphism at both ancestral-XY and neo-ZW sex determining regions, or loss of the new sex-determining allele. Here we plot the frequency of the neo-W allele among 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 by 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 ($w_{aa}^{\varnothing} = 1.05$, $w_{Aa}^{\varnothing} = 1$, $w_{AA}^{\varnothing} = 0.85$) while there is overdominance in males ($w_{aa}^{\delta} = w_{AA}^{\delta} = 0.75$) and in panels C and D, there is overdominance in both sexes ($w_{aa}^{\varnothing} = w_{AA}^{\varnothing} = 0.6$, $w_{aa}^{\delta} = 0.5$, $w_{AA}^{\delta} = 0.7$, $w_{Aa}^{\delta} = 1$). These parameters are marked by a dagger in Figure 3. Here, there is no haploid selection $I^{\delta} = \alpha_{\Delta}^{\delta} = 0$.

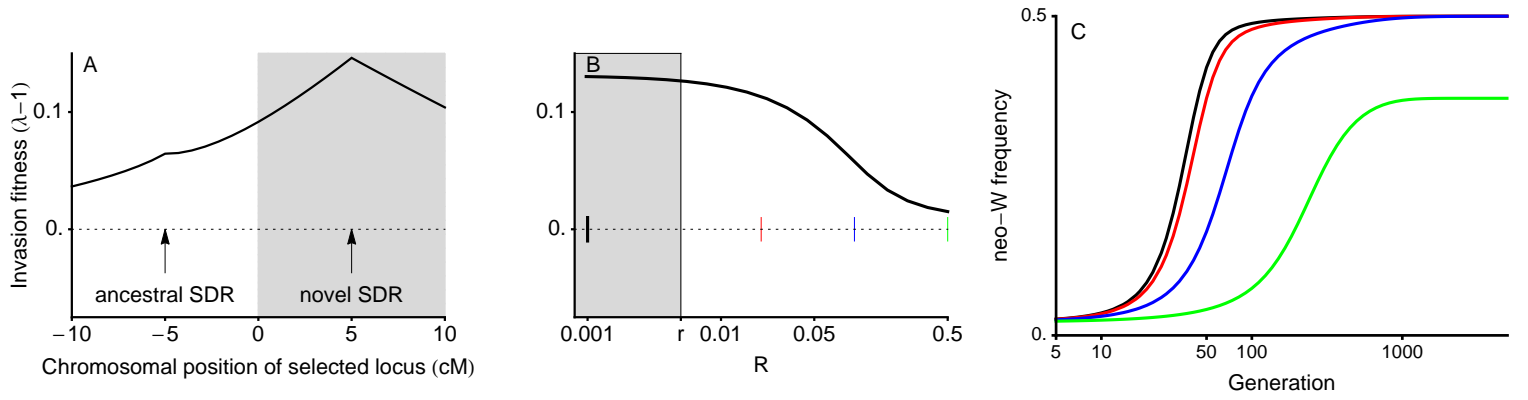


Figure S.3: When there is sexually-antagonistic selection and haploid selection, a neo-W may invade for any R . Panel A shows that the invasion fitness of a neo-W is positive where linkage is tight, even when $r < R$ (unshaded region). In panel B, we vary the recombination rate between the neo-W and 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 ($\alpha_{\Delta}^{\delta} = -0.08$), 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.

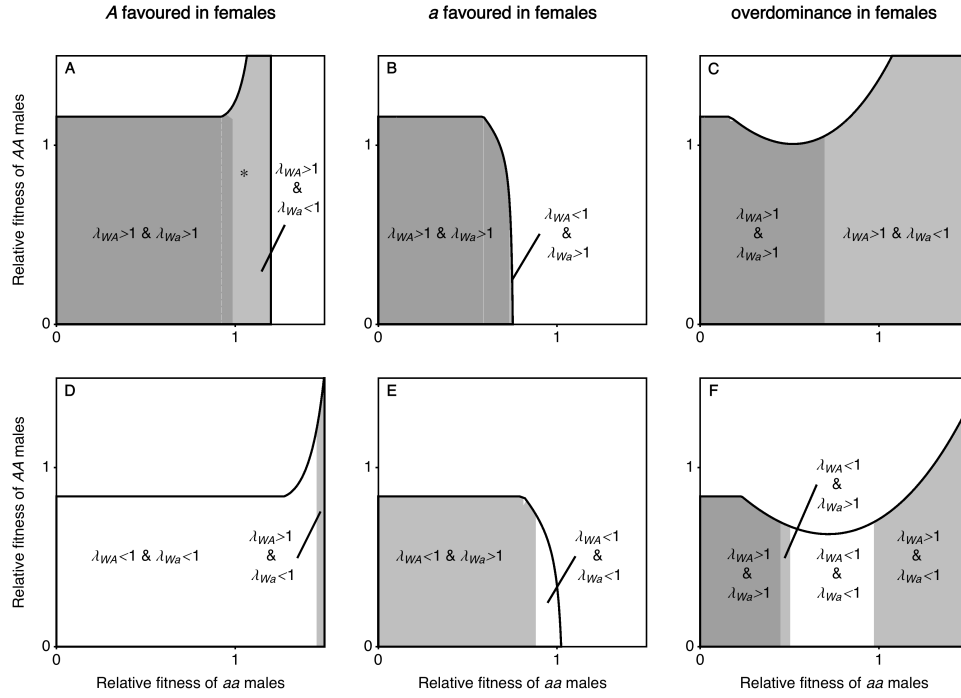


Figure S.4: Meiotic drive in males affects whether neo-W-A and neo-W-a haplotypes spread when the ancestral-XY locus is tightly linked to a locus under selection ($r = 0$). We vary the fitness of male homozygotes relative to heterozygotes ($w_{Aa}^{\varnothing} = 1$) and only consider stable equilibria 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 ($\alpha_{\Delta}^{\delta} = -0.16$), 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 ($\alpha_{\Delta}^{\delta} = 0.16$), panels D-F. We consider three forms of selection in females: directional selection in favour of the *A* allele (panels A and D, $w_{aa}^{\varnothing} = 0.85$, $w_{AA}^{\varnothing} = 1.05$), direction selection in favour of the *a* allele (panels B and E, $w_{aa}^{\varnothing} = 1.05$, $w_{AA}^{\varnothing} = 0.85$), and overdominance (panels C and F, $w_{aa}^{\varnothing} = w_{AA}^{\varnothing} = 0.6$).

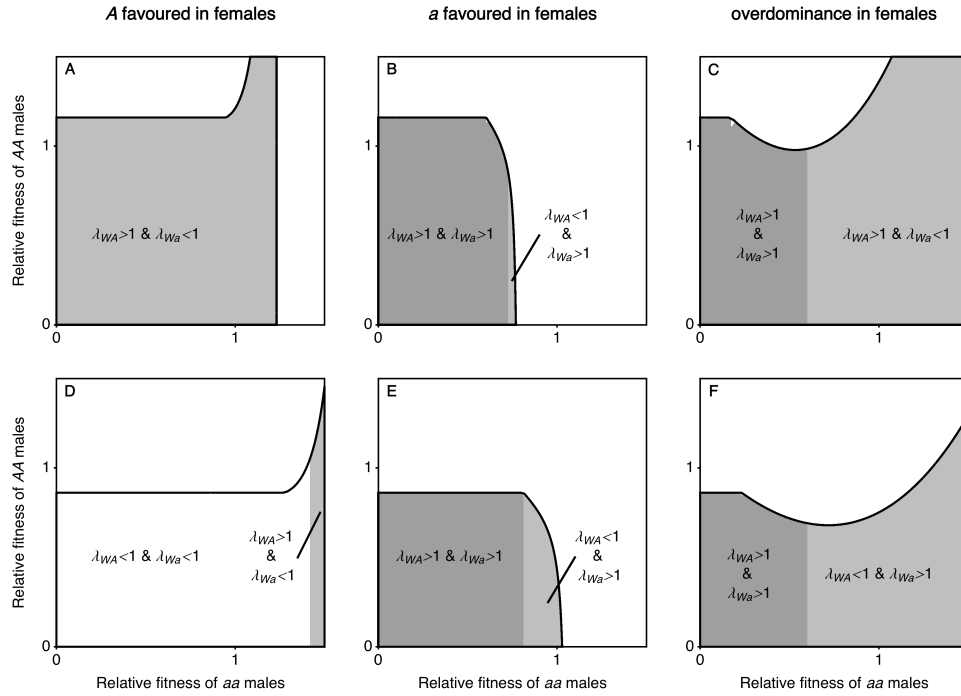


Figure S.5: Parameters for which neo-W-A and neo-W-a haplotypes spread when there is male gametic competition at a locus that is tightly linked to the ancestral-XY locus. Diploid selection parameters (w_{ij}^δ) are the same as those in Figure S.4. The *a* allele is favoured during male gametic competition 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).

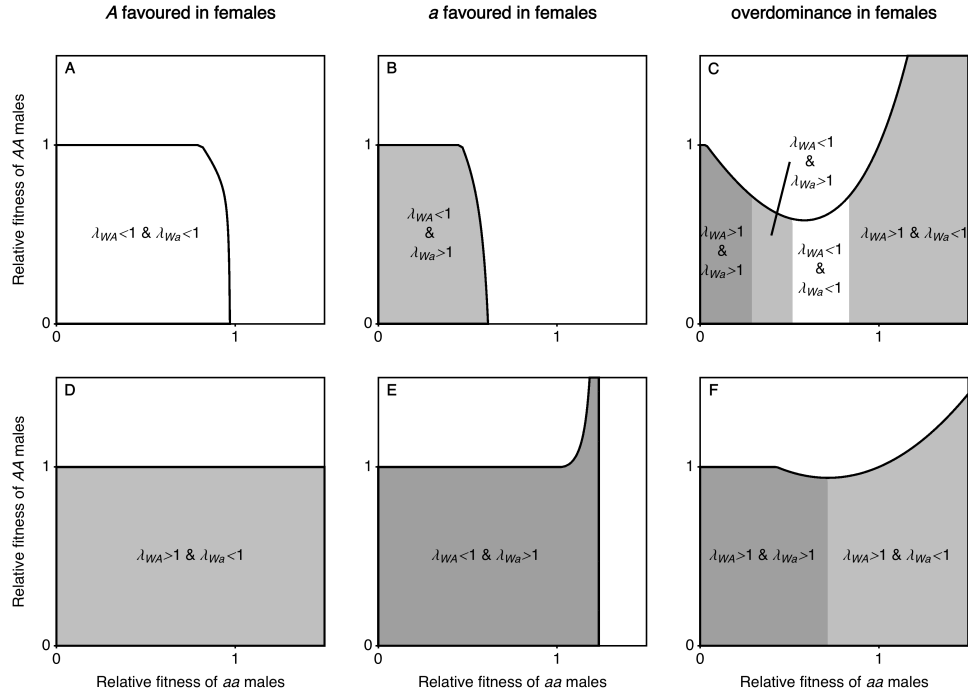


Figure S.6: Parameters for which neo-W-*A* and neo-W-*a* haplotypes spread when there is female meiotic drive at a locus that is tightly linked to the ancestral-XY locus. Diploid selection parameters (w_{ij}^{δ}) are the same as those in Figure S.4 and S.5. The *a* allele is favoured by meiotic drive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

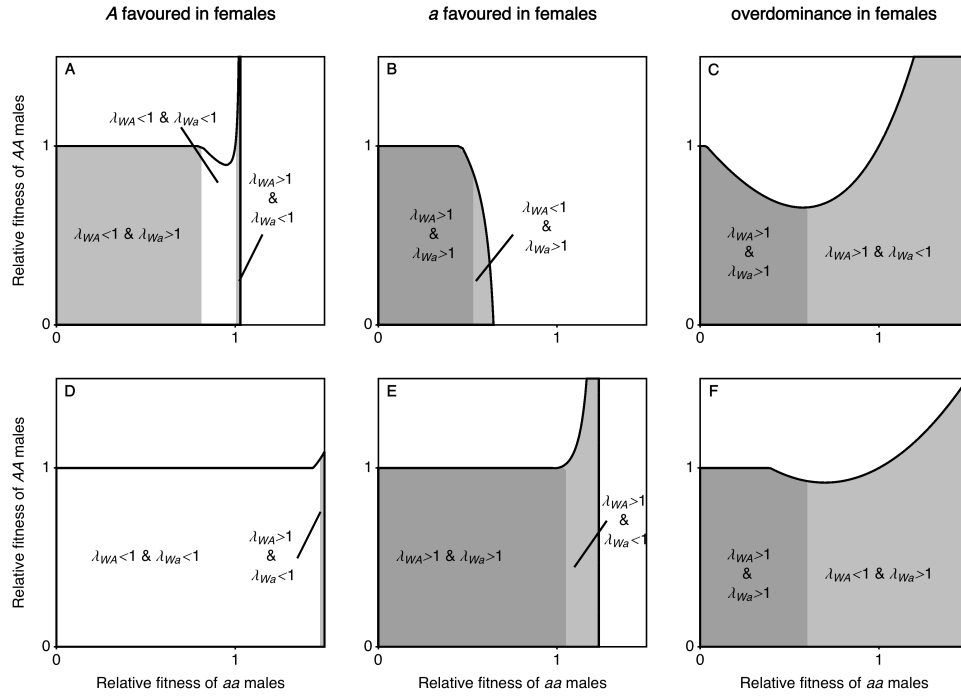


Figure S.7: Parameters for which neo-W-A and neo-W-a haplotypes spread when there is female gametic competition at a locus that is tightly linked to the ancestral-XY locus. Diploid selection parameters (w_{ij}^{ϕ}) are the same as those in Figure S.4, S.5, and S.6. The *a* allele is favoured during female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

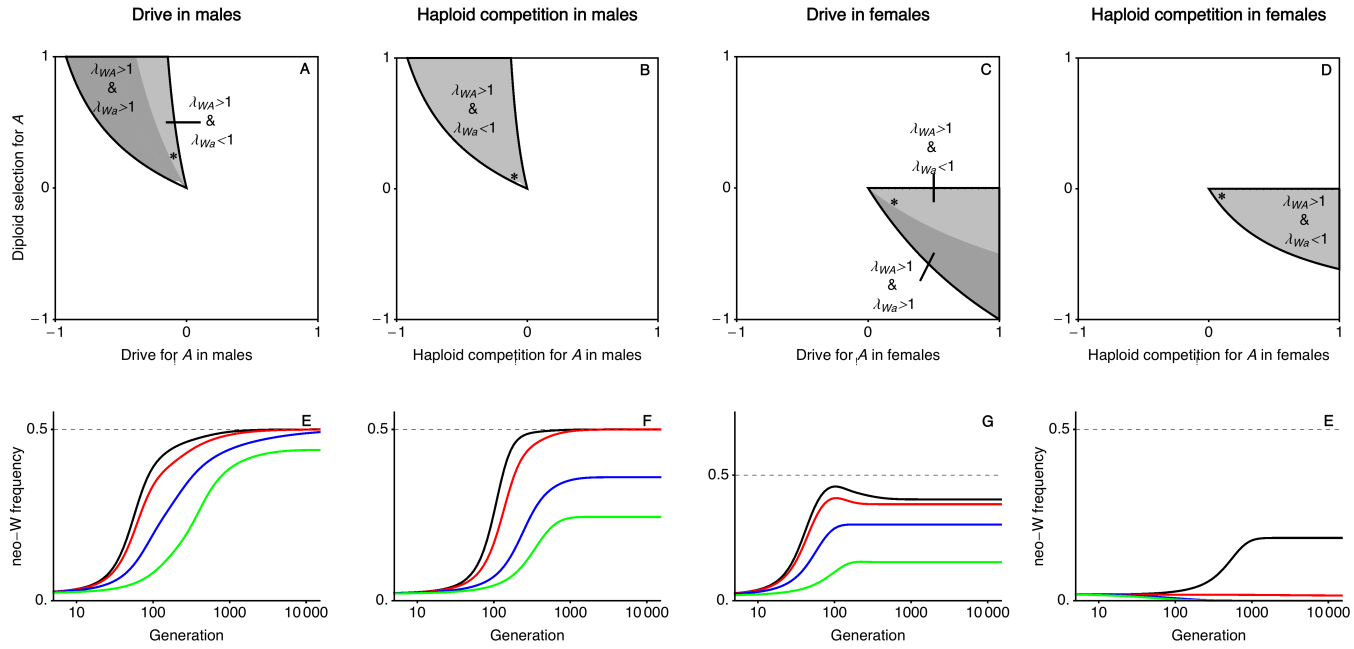


Figure S.8: A-D show when each of the neo-W haplotypes invade an internally stable equilibrium with a fixed on the Y (found by setting $r = 0$). The y-axis shows directional selection in diploids of both sexes, $s^{\varnothing} = s^{\delta}$, and the x-axes show sex-specific drive, α_{Δ}^{δ} , or haploid competition, t^{δ} . 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, $h^{\varnothing} = h^{\delta} = 3/4$. 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 $R = 1/2$.

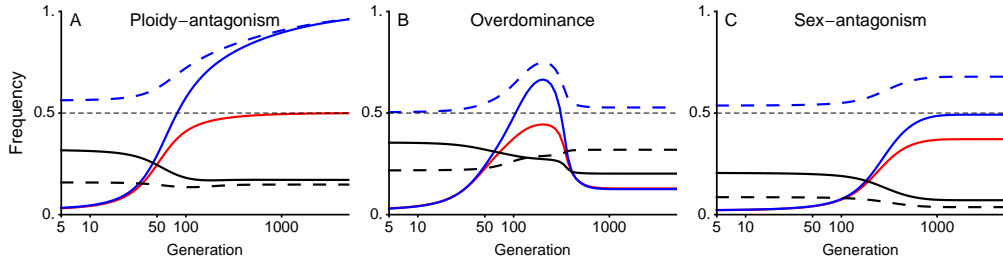


Figure S.9: Fixation of neo-W or maintenance of multiple sex-determining systems. The curves show the frequencies of the neo-W (red), ancestral-Y (blue), and A allele (black) among female gametes (solid curves) and among male gametes (dashed curves). In panel A, there is a complete transition from XY 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 ploidy 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.

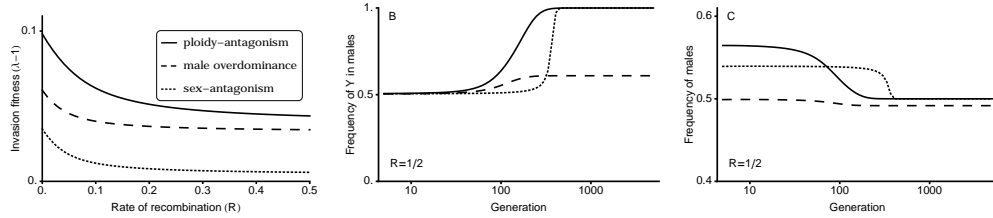


Figure S.10: An unlinked neo-W can invade a perfectly linked system with overdominance or haploid selection. Here overdominance leads to a polymorphic sex-determining system. Before invasion the population is at equilibrium B. Parameters: