

Gametic Selection, Meiotic Drive, 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 how selection on very tightly sex-linked loci influences the spread of novel sex-determiners. We find that tightly sex-linked genetic variation 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 sex-linked locus under selection; a result that is not found with loose sex-linkage. (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. As well as having sex-specific fitness consequences, haploid selection can cause the zygotic sex ratio to become biased because sex ratios are determined by the production and fertilization success of X- versus Y-bearing pollen/sperm (or Z- versus W-bearing ovules/eggs). Consequently, selection for XY to ZW transitions and ZW to XY transitions can be asymmetrical when linkage between the ancestral sex-determining locus and a locus under haploid selection is tight, in which case ancestral sex ratio biases can be strong. With looser linkage and haploid selection, we again find that transitions between male and female heterogamety can occur even if the new sex-determining region is less closely linked to the locus under selection. That is, favourable associations that develop between the ancestral sex-determining locus and selected loci can be broken during the spread of a new sex-determining region. Overall, our models provide new predictions for the types of selection and the genomic location of loci that can drive transitions between sex-determination systems.

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, some taxa have heterogametic males (XY) and homogametic females (XX), including mammals and most dioecious plants (Ming et al. 2011);
38 whereas other taxa have homogametic males (ZZ) and heterogametic females (ZW), including Lepidoptera and birds. Within several taxa, the chromosome that harbours the master sex-determining region changes. For example, transitions of the
40 master sex-determining gene between chromosomes or the evolution of new master sex-determining genes have occurred in Salmonids (Li et al. 2011, Yano et al. 2012),
42 Diptera (Vicoso and Bachtrog 2015), and *Oryzias* (Myosho et al. 2012). In addition, many gonochoric clades with genetic sex determination exhibit transitions between male (XY) and female (ZW) heterogamety, including snakes (Gam-
46 ble et al. 2017, *Current Biology*), lizards (Ezaz et al. 2009), eight of 26 teleost fish families (Mank et al. 2006), true fruit flies (Tephritids, Vicoso and Bachtrog
48 2015), amphibians (Hillis and Green 1990), the angiosperm genus *Silene* (Slancarova et al. 2013), and Coleoptera and Hemiptera (Beukeboom and Perrin 2014, plate
50 2). Indeed, in some cases, both male and female heterogametic sex-determination systems can be found in the same species, as exhibited by some cichlid species (Ser
52 et al. 2010) and *Rana rugosa* (Ogata et al. 2007). In addition, multiple transitions have occurred between genetic and environmental sex-determination systems, e.g.,
54 in reptiles and fishes (Conover and Heins 1987, Mank et al. 2006, Pokorná and Kratochvíl 2009, Ezaz et al. 2009, Pen et al. 2010, Holleley et al. 2015).

56 Predominant theories accounting for the spread of new sex-determination systems by selection involve fitness differences between sexes (e.g., sexually antagonistic selection) or sex-ratio selection. van Doorn and Kirkpatrick (2007; 2010)
58 show that new sex-determining loci can be favoured if they arise in closer linkage with a locus that experiences sexual antagonism. For example, tighter linkage
60 allows a stronger favourable association to build up between a male-beneficial

62 allele and a neo-Y chromosome. Such associations can favour a new master sex-
determining gene on a new chromosome (van Doorn and Kirkpatrick 2007) and can
64 also favour a transition between male and female heterogamety (e.g., a ZW to XY
transition, van Doorn and Kirkpatrick 2010). However, any sexually-antagonistic
66 loci that are more closely linked to the ancestral sex-determination locus will de-
velop similar, favourable associations and select against the spread of a new sex-
68 determination system.

The sex ratio is directly affected by the sex-determination system, and it has
70 therefore been suggested that sex-ratio selection is a dominant force in the evolu-
tion of sex determination (e.g., Bull 1983, p66-67; Beukeboom and Perrin 2014,
72 Chapter 7). ‘Fisherian’ sex-ratio selection favours a 1:1 zygotic sex ratio when as-
suming that males and females are equally costly to produce (Fisher 1930, Charnov
74 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,
76 if the population sex ratio is biased towards females, the average per-individual
contribution of genetic material to the next generation from males is greater than
78 the contribution from females (and vice versa for male-biased sex ratios). There-
fore, a mutant that increases investment in males (e.g., increases the proportion of
80 males produced) will spread via the higher per-individual contributions made by
males. In the case of sex-chromosome evolution, Kozielska et al. (2010) consider
82 systems in which the ancestral sex chromosomes experience meiotic drive (e.g.,
where driving X or Y chromosomes are inherited disproportionately often), which
84 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
86 loci) can then spread, which restore an even sex ratio.

Here we extend current theory by using mathematical models to find the con-
88 ditions under which new sex-determination systems spread when individuals ex-
perience selection at both diploid and haploid stages. Haploid genotypes at many
90 loci experience selection during gamete competition and/or meiotic drive (Mulc-
ahy et al. 1996, Joseph and Kirkpatrick 2004). We use the term ‘meiotic drive’ to

92 refer to the biased (non-Mendelian) segregation of genotypes during gamete pro-
duction (from one parent) and the term ‘gametic competition’ to refer to selection
94 upon haploid genotypes within a gamete/gametophyte pool (potentially from by
multiple parents); the term ‘haploid selection’ encompasses both processes. Mei-
96 otic drive generally occurs either during the production of male or female gametes
only (Úbeda and Haig 2005, Lindholm et al. 2016). Because there are typically
98 many more pollen/sperm than required for fertilization, gametic competition is
also typically sex specific, occurring primarily among male gametes. Gametic
100 competition may be particularly common in plants, in which 60-70% of all genes
are expressed in the male gametophyte and these genes exhibit stronger signatures
102 of selection than random genes (Borg et al. 2009, Arunkumar et al. 2013, Goss-
mann et al. 2014). In addition, artificial selection pressures applied to male game-
104 tophtes are known to cause a response to selection (e.g., Hormaza and Herrero
1996, Ravikumar et al. 2003, Hedhly et al. 2004, Clarke et al. 2004) and gametic
106 selection appears to occur during the creation of F2 crosses (Kumar, 2007). A
much smaller proportion of genes are thought to be expressed and selected dur-
108 ing competition in animal sperm, although precise estimates are uncertain (Zheng
et al. 2001, Joseph and Kirkpatrick 2004, Vibrationovski et al. 2010, Immler et al.
110 2014).

There are various ways in which a period of haploid selection could influence
112 transitions between sex-determination systems. If we assume that haploid selec-
tion at any particular locus predominantly occurs in one sex (e.g., meiotic drive
114 during spermatogenesis), then such loci experience a form of sex-specific selec-
tion. In this respect, we might expect that haploid selection to affect transitions
116 between sex-determination systems in a similar manner to sex-specific diploid se-
lection (as explored by van Doorn and Kirkpatrick 2007; 2010). That is, new
118 masculinizing mutations (neo-Y chromosomes) could be favoured via associations
with alleles that are beneficial in the male haploid stage. On the other hand, sex
120 ratios can also become biased by linkage between the sex-determining region and
a locus that harbours genetic variation in haploid fitness. For example, there are

122 several known cases of sex-ratio bias caused by sex-linked meiotic drive alleles
(Burt and Trivers 2006, Chapter 3) or selection among X- and Y-bearing pollen
124 (Lloyd 1974, Conn and Blum 1981, Stehlik and Barrett 2005; 2006, Field et al.
2012; 2013). It is not immediately clear how the spread of new sex-determination
126 systems would be influenced by the combination of sex-ratio biases and associa-
tions between haploid selected loci and sex-determining regions.

128 Our models have two important new features. Firstly, when considering loci
that are under selection and also in very tight linkage with the ancestral sex-determining
130 region we explicitly calculate equilibrium allele frequencies. This allows us to
show that transitions between male and female heterogamety can evolve even when
132 the neo-sex-determining locus is less closely linked to a locus under selection and
therefore disrupts favourable ancestral associations between sex and the alleles se-
134 lected in that sex. Secondly, we allow sex-specific haploid selection to occur on a
locus in tight or loose linkage with the ancestral sex-determining region. We find
136 that sex-ratio biases caused by haploid selection can exert Fisherian sex-ratio se-
lection upon novel sex-determiners but that their spread is also determined by the
138 fitness of the alleles that are associated with them. Indeed, it is only when haploid-
selected loci are tightly linked to the ancestral sex-determining region (and so sex-
140 ratio biases are initially large) that we see an asymmetry between selection for XY
to ZW transitions and ZW to XY transitions (e.g., because haploid selection in
142 males only causes biased zygotic sex ratios in an ancestrally XY system). It is also
possible for selection on linked alleles to drive turnover between sex-determining
144 systems despite causing transitory or even permanent increases in sex-ratio bias.

Model

146 We consider transitions between ancestral and novel sex-determining systems us-
ing a three locus model, each locus having two alleles. Locus **X** is the ancestral
148 sex-determining region, with alleles *X* and *Y* (or *Z* and *W*). Locus **A** is a locus
under selection, with alleles *A* and *a*. Locus **M** is a novel sex-determining region,

150 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} ;
 152 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-
 154 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
 156 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
 158 \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
 160 can interpret m as an environmental sex determination (ESD) allele, such that zy-
 gotes develop as females in a proportion (k) of the environments they (randomly)
 162 experience. We also analyze a model of maternally-controlled environmental sex-
 determination, where mothers with at least one m allele produce daughters with
 164 probability k .

In each generation, we census the genotype frequencies in male and female
 166 gametes/gametophytes (hereafter gametes) before gametic competition. A full de-
 scription of our model, including recursion equations, is given in the Appendix.
 168 First, competition occurs among male gametes (sperm/pollen competition) and
 among female gametes (egg/ovule competition) separately. Selection during ga-
 170 metic competition depends on the \mathbf{A} locus genotype, relative fitnesses are given
 by w_A^{ϕ} and w_a^{ϕ} ($\phi \in \{\text{♀}, \text{♂}\}$; see table 1). We assume that all gametes compete for
 172 fertilization during gametic competition, which is not the case for monogamous
 mating systems where gametes from only one mating partner are present. Gametic
 174 competition in monogamous mating systems is equivalent to meiotic drive in our
 model (described below), which only alters the frequency of gametes produced by
 176 heterozygotes. After gametic competition, random mating occurs between male
 and female gametes. The resulting zygotes develop as males or females, depend-
 178 ing on their genotypes at the \mathbf{X} and \mathbf{M} loci (and the \mathbf{M} genotype of their mother
 in the case of maternal control) as described above. Diploid males and females

180 then experience selection, with relative fitnesses w_{AA}^{ϕ} , w_{Aa}^{ϕ} , and w_{aa}^{ϕ} . The next
 182 generation of gametes is produced by meiosis, during which recombination and
 sex-specific meiotic drive can occur. Recombination (i.e., an odd number of cross-
 overs) occurs between loci **X** and **A** with probability r , between loci **A** and **M** with
 184 probability R , and between loci **X** and **M** with probability χ . Any linear order of
 the loci can be modelled with appropriate choices of r , R , and χ (see Table S.1).
 186 Individuals that are heterozygous at the **A** locus may experience meiotic drive; a
 gamete produced by Aa heterozygotes of sex ϕ bear allele A with probability α^{ϕ} .
 188 Thus, the **A** locus can experience sex-specific gametic competition, diploid selec-
 tion, and/or meiotic drive.

Table 1: Relative fitness of different genotypes in sex $\phi \in \{\varphi, \delta\}$

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	$1 - \alpha^{\phi} = 1/2 - \alpha_{\Delta}^{\phi}/2$

190 Results

The only asymmetry between males and females in our model is that, under the
 192 ancestral sex-determination system, males develop with genotype XY (or ZZ)
 and females with genotype XX (or ZW). Therefore, the model outlined above
 194 describes both ancestrally- XY and ancestrally- ZW sex-determination systems if

we relabel the two sexes as being ancestrally ‘heterogametic’ or ancestrally ‘homogametic’. Without loss of generality, we primarily refer to the ancestrally heterogametic sex as male and the ancestrally homogametic sex as female. That is, we describe an ancestral XY sex-determination system but our model is just as easily applied to an ancestral ZW sex-determination system.

Generic invasion by a neo-Y or neo-W

The evolution of a new sex-determination system requires that a rare mutant allele at the novel sex-determining locus, m , increases in frequency when rare. The spread of a rare mutant m at the \mathbf{M} locus is determined by the leading eigenvalue, λ , of the system of eight equations describing the next generation frequency of eggs and sperm carrying the mutation, (S.1c, S.1d, S.1g, S.1h). This system simplifies substantially in a number of cases of interest. Dominant neo-Y (when $k = 0$) or neo-W alleles (when $k = 1$) are only found in male diploids (neo-Y) or female diploids (neo-W) such that their growth rate ultimately depends only on the change in frequency of m -bearing gametes produced by males (for a neo-Y) or by females (for a neo-W). Furthermore, if the m allele is fully epistatically dominant over the ancestral sex-determining system, phenotypes are not affected by the genotype at the ancestral sex-determining region (\mathbf{X} locus). Thus, the invasion of rare dominant neo-Y or neo-W alleles is determined by the largest eigenvalue that solves a quadratic characteristic polynomial, $\lambda^2 + b\lambda + c = 0$. Here, $b = -(\lambda_{mA} + \lambda_{ma}) + (\rho_{mA} + \rho_{ma})$ and $c = (\lambda_{mA} - \rho_{mA})(\lambda_{ma} - \rho_{ma}) - \rho_{mA}\rho_{ma}$, where λ_{mi} is the multiplicative growth rate of mutant haplotypes on background $i \in \{A, a\}$, without accounting for loss due to recombination, and ρ_{mi} is the rate at which mutant haplotypes on background $i \in \{A, a\}$ recombine onto the other \mathbf{A} locus background in heterozygotes (see table 2). The λ_{mi} and ρ_{mi} , and thus the spread of the mutant m allele, depend on the frequency of alleles at the other two loci in the ancestral population. In the ancestral population, it is convenient to follow the frequency of the A allele in female gametes (eggs) from an XX female, p_X° , and in X-bearing, p_X^δ , and Y-bearing, p_Y^δ , male gametes (sperm/pollem). We

224 also track the fraction of male gametes that are Y-bearing, q , which may deviate
 225 from 1/2 due to meiotic drive in males.

226

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

neo-Y ($k = 0$)
$\lambda_{mA} = [2(1 - \zeta)]^{-1} [p_X^{\varnothing} w_A^{\varnothing} w_A^{\delta} w_{AA}^{\delta} + 2(1 - p_X^{\varnothing}) w_a^{\varnothing} w_A^{\delta} w_{Aa}^{\delta} \alpha^{\delta}] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\delta})$ $\lambda_{ma} = [2(1 - \zeta)]^{-1} [(1 - p_X^{\varnothing}) w_a^{\varnothing} w_a^{\delta} w_{aa}^{\delta} + 2p_X^{\varnothing} w_A^{\delta} w_a^{\delta} w_{Aa}^{\delta} (1 - \alpha^{\delta})] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\delta})$ $\rho_{mA} = R [2(1 - \zeta)]^{-1} [2(1 - p_X^{\varnothing}) w_a^{\varnothing} w_A^{\delta} w_{Aa}^{\delta} \alpha^{\delta}] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\delta})$ $\rho_{ma} = R [2(1 - \zeta)]^{-1} [2p_X^{\varnothing} w_A^{\delta} w_a^{\delta} w_{Aa}^{\delta} (1 - \alpha^{\delta})] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\delta})$
neo-W ($k = 1$)
$\lambda_{mA} = (2\zeta)^{-1} [\bar{p}^{\delta} w_A^{\delta} w_A^{\varnothing} w_{AA}^{\varnothing} + 2(1 - \bar{p}^{\delta}) w_a^{\delta} w_A^{\varnothing} w_{Aa}^{\varnothing} \alpha^{\varnothing}] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\varnothing})$ $\lambda_{ma} = (2\zeta)^{-1} [(1 - \bar{p}^{\delta}) w_a^{\delta} w_a^{\varnothing} w_{aa}^{\varnothing} + 2\bar{p}^{\delta} w_A^{\delta} w_a^{\varnothing} w_{Aa}^{\varnothing} (1 - \alpha^{\varnothing})] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\varnothing})$ $\rho_{mA} = R (2\zeta)^{-1} [2(1 - \bar{p}^{\delta}) w_a^{\delta} w_A^{\varnothing} w_{Aa}^{\varnothing} \alpha^{\varnothing}] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\varnothing})$ $\rho_{ma} = R (2\zeta)^{-1} [2\bar{p}^{\delta} w_A^{\delta} w_a^{\varnothing} w_{Aa}^{\varnothing} (1 - \alpha^{\varnothing})] / (\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \bar{w}^{\varnothing})$

$\bar{p}^{\delta} = p_Y^{\delta} q + p_X^{\delta} (1 - q)$ is the average frequency of the A allele among X- and Y-bearing male gametes.

R is the probability of recombination between loci **A** and **M**.

ζ is the zygotic sex ratio (fraction female)

\bar{w}^{δ} is the mean fitness of diploids of sex ♂, see Table S.2

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

228 We are particularly concerned with the conditions under which a rare neo-sex-
 229 determining allele increases in frequency, which occurs when the largest eigen-
 230 value, λ , is greater than one. If the average change in frequency of the two haplo-
 231 types that carry the m allele (Am and am) is positive, invasion will always occur,
 232 i.e., if $(\lambda_{mA} + \lambda_{ma})/2 > 1$ then $\lambda > 1$. If neither haplotype increases in frequency
 233 ($\lambda_{mA}, \lambda_{ma} < 1$), the m allele will not invade. Otherwise, the new sex-determining
 234 allele increases in frequency on one **A** background and declines on the other, and
 invasion requires

$$\rho_{ma} (\lambda_{mA} - 1) + \rho_{mA} (\lambda_{ma} - 1) > 0. \quad (1)$$

236 For example, if we assume that only the mA haplotype has a positive growth rate
 (238 $\lambda_{ma} < 1 < \lambda_{mA}$), the second term on the left-hand side of (1) is negative and inva-
 sion requires that the growth rate of mA haplotypes and the rate at which they are
 produced by recombination is sufficiently large relative to that of ma haplotypes.
 240 In other words, invasion requires that the average growth rate of recombinants,
 weighted by the rates they are created, is positive.

242 Table 2 illustrates a number of key points about the invasion of neo-Y and neo-
 W mutations. First, Fisherian sex-ratio selection will favour the spread of a neo-Y
 244 if the ancestral zygotic sex ratio is biased towards females, $\zeta > 1/2$, and vice versa
 for a neo-W (i.e., $\zeta > 1/2$ causes the first factor of the λ_{mi} to be greater than one
 246 for a neo-Y). However, the spread of a neo-Y (neo-W) also depends on the male
 (female) fitness of alleles that they are associated with. Second, invasion by a neo-
 248 Y (neo-W) allele does not directly depend on the fitness of female (male) diploids
 (although they indirectly affect invasion by determining the allele frequencies p_X°
 250 and \hat{p}°). 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
 252 in males (females). Finally, invasions by a neo-Y and a neo-W are qualitatively
 different. This is because a gamete containing a neo-Y always pairs with the same
 254 gamete type as a male gamete without the neo-Y does (both pair with a female
 gamete containing an X), and both develop into males. Meanwhile a gamete with
 256 a neo-W can pair with an X or Y male gamete, and develop into a female, while
 female gametes without the neo-W must pair with a male gamete containing an X
 258 to remain female. This is consequential because it means that females with and
 without a neo-W differ in the frequency of A alleles they obtain from mating.

260 In order to explicitly determine the conditions under which a rare neo-sex-
 determining allele spreads, we must calculate the frequency of the A allele in the
 262 ancestral population (i.e., p_X° , p_X^δ , and p_Y^δ). Since only the A locus experiences se-
 lection directly, any deterministic evolution requires that there is a polymorphism
 264 at the A locus. Polymorphisms can be transiently present during the spread of uni-
 formly beneficial alleles but polymorphisms maintained by selection can maintain

alleles at higher allele frequencies for longer periods, during which time new sex-determining alleles can arise. Therefore, we will assume that the A allele reaches a stable intermediate equilibrium frequency under the ancestral sex-determination system before the neo-sex-determining allele (m) arises. We can analytically calculate the allele frequency of the A allele using two alternative simplifying assumptions: (1) the A locus is within (or tightly linked to) the non-recombining region around the ancestral SDR ($r \approx 0$) or (2) selection is weak relative to recombination ($s^\phi, t^\phi, \alpha_\Delta^\phi$ of order $\epsilon \ll 1$).

Tight linkage with the ancestral sex-determining region

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

A neo-Y will never invade an ancestral XY system that already has tight linkage with the locus under selection ($r = 0$). A neo-Y haplotype with the same allele as the ancestral Y is neutral ($\lambda_{ma} = 1$) and does not change in frequency. The other neo-Y haplotype will not spread ($\lambda_{mA} < 1$) given that the initial equilibrium is stable. Therefore, a neo-Y mutation cannot spread ($\lambda \leq 1$) in an ancestral XY system that is at equilibrium with all selected loci within the non-recombining region around the SDR. In essence, through tight linkage with the A locus, the ancestral Y becomes strongly specialized on the allele that has the highest fitness across male haploid and diploid phases. Given that the ancestral Y is at this equilibrium, it is not possible for a neo-Y to create males that have higher fitness than the ancestral Y.

Neo-W alleles, on the other hand, can invade an ancestral XY system under some conditions (the full invasion conditions are given in the appendix; equations

S.6 and S.7). Significantly, we note that it is possible for both neo-W haplotypes to spread ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$), in which case neo-W invasion can occur regardless of linkage to the selected locus. That is, selection on loci within the non-recombining region of the SDR can favour the invasion of a less closely linked neo-W (e.g., on an autosome). Although haploid selection can favour neo-W alleles because the ancestral sex ratio becomes male biased, this is not the only circumstance in which less tightly linked neo-W alleles invade. For example, unlinked neo-W alleles can invade in the absence of any haploid selection. This result is unexpected given the results of van Doorn and Kirkpatrick (2010), who did not explicitly calculate equilibrium allele frequencies under tight linkage and generally concluded that heterogametic transitions occur when neo-sex-determining alleles are in tighter linkage with loci under sex-specific diploid selection. Therefore, we focus on cases where there is no haploid selection and discuss the effects of haploid selection in the appendix.

If we categorise the a allele as being ancestrally ‘male-beneficial’ via the fact that it is fixed on the Y, then $\lambda_{mA} > 1$ indicates that the neo-W spreads when found with the ancestrally ‘female-beneficial’ allele. Intuitively, this is possible because the ancestral X chromosome is not able to specialise on the ‘female-beneficial’ allele due to the fact that X’s are sometimes found in males. For example, a polymorphism of A and a alleles can be maintained on the X despite directional selection in favour of the A allele in females ($s^{\varphi} > 0$, $0 < h^{\varphi} < 1$) because the a allele is favoured in males. W- A haplotypes will only create females with high fitness AA or Aa genotypes and can therefore have higher fitness than ancestral females, which sometimes also produce aa females. Thus, the neo-W can spread by allowing increased specialization on female beneficial alleles.

Given that the a allele can be considered ancestrally ‘male-beneficial’ because it is fixed on the Y, it might be surprising that neo-W- a haplotypes can be favoured by selection in females ($\lambda_{ma} > 1$). Again, this occurs because ancestral X’s also experience selection in males, in which they will always be paired with a Y- a . Hence, 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
 326 polymorphic or even fixed for the A allele despite favouring the a allele during
 selection in females (Lloyd and Webb 1977, Otto 2014). In such cases, neo-W- a
 328 haplotypes, which are never found in males, can spread because they both create
 more Aa and aa females when pairing with an X from males and they bring Y- a
 330 haplotypes into females, in which case females are always aa . Indeed, it is possible
 for both W- A and W- a haplotypes to spread, as is the case when AA individuals
 332 have low fitness in females yet the A is fixed on the X due to strong overdominance
 in males. Both neo-W- A and neo-W- a haplotypes then produce fewer unfit AA
 334 females. This is true for the neo-W- A haplotype because it can pair with a Y - a
 haplotype and still be female.

336 In Figure ??A we show the region of parameter space within which both neo-W
 haplotypes invade ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$) when there is overdominance in females
 338 and no haploid selection (corresponding to Figure 2a in Otto 2014). Wherever
 both haplotypes have positive growth rates (gray region of Figure ??), invasion
 340 by a neo-W is expected regardless of its linkage with the selected locus (i.e., even
 unlinked neo-W alleles can invade). In regions where only one haplotype can
 342 spread (white region of Figure ??), a neo-W can invade as long as equation (1) is
 satisfied, which can require that the recombination rate, R , is small enough and
 344 yet still indicates that more loosely linked sex-determining regions can spread. It
 is also possible for haploid selection to drive the invasion of a loosely linked neo-
 346 W. Take, for instance, selection directionally favouring A in both diploid sexes
 and meiotic drive in males. Figure ??B then shows that ploidy-antagonistic
 348 selection can allow both neo-W haplotypes to invade.

Loose linkage with the ancestral sex-determining region

350 Assuming that selection is weak relative to all recombination rates (r , R and χ),
 we denote the leading eigenvalues describing the invasion of a neo-Y ($k = 0$) and
 352 a neo-W ($k = 1$) into an ancestrally XY system by $\lambda_{Y',XY}$ and $\lambda_{W',XY}$, respectively,
 which are

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

354 and

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

where $V_A = \bar{p}(1 - \bar{p})$ is the variance in the frequency of A and $S_A = (D^\delta + \alpha_\Delta^\delta +$
 356 $t^\delta) - (D^\varphi + \alpha_\Delta^\varphi + t^\varphi)$ describes sex differences in selection for the A versus a across
 diploid selection, meiosis, and gametic competition. The diploid selection term,
 358 $D^\varphi = (\bar{p}s^\varphi + (1 - \bar{p})h^\varphi s^\varphi) - (\bar{p}h^\varphi s^\varphi + (1 - \bar{p}))$, is the difference in fitness between A
 and a alleles in diploids of sex $\varphi \in \{\varphi, \delta\}$, where \bar{p} is the leading-order probability
 360 of mating with an A -bearing gamete from the opposite sex (see Appendix).

The neo-sex-determining allele, m , will spread if $\lambda_{m,XY} > 1$. Equation (2)
 362 demonstrates that under weak selection a neo-Y will invade if and only if it is more
 closely linked to the selected locus than the ancestral sex-determining region (i.e.,
 364 if $R < r$; note that V_A and S_A^2 are strictly positive as long as \mathbf{A} is polymorphic). This
 echoes our tight linkage results above and the results of van Doorn and Kirkpatrick
 366 (2007), who considered diploid selection only and also found that homogametic
 transitions (XY to XY or ZW to ZW) can occur when the neo-sex-determining
 368 locus is more closely linked to a locus under sexually-antagonistic selection.

Equation (3) shows that, in contrast to the tight linkage results of the previous
 370 section, with weak selection and no haploid selection ($t^\varphi = \alpha_\Delta^\varphi = 0$), as considered
 by van Doorn and Kirkpatrick (2010), the spread of a neo-W is equivalent to the
 372 spread of a neo-Y ($\lambda_{W',XY} = \lambda_{Y',XY}$), such that heterogametic transitions (XY to
 ZW or ZW to XY) can also occur only if the neo-sex-determining region is more
 374 closely linked to a locus under selection ($R < r$). However, if there is any hap-
 loid selection, the additional term in equation (3) can be positive, which can allow,
 376 for example, neo-W invasion ($\lambda_{W',XY} > 1$) even when the neo-sex-determining
 region is less closely linked to the selected locus ($R > r$). These transitions are

378 unusual because, when $R > r$, associations that selection has built up between
alleles more favourable in one sex and alleles that determine sex will be weak-
380 ened. Mean diploid fitness therefore decreases during heterogametic transitions
that create looser sex-linkage (Figure 4B,D).

382 Equation (3) shows that neo-W alleles can invade an XY system for a large
number of selective regimes. To clarify the parameter space under which $\lambda_{W',XY} >$
384 1, we consider several special cases. Firstly, if the **A** locus is unlinked to the an-
cestral sex-determining region ($r = 1/2$), a more closely linked neo-W ($R < 1/2$)
386 can always invade because there is then no association between *A* alleles and sex
chromosomes, $(\hat{p}_Y^\delta - \hat{p}_X^\delta) = 0$. The second term in equation (3) then disappears
388 and invasion depends only on the sign of $(r - R)$. Indeed, invasion typically occurs
when the neo-W is more closely linked to the selected locus than the ancestral sex-
390 determining region, under a variety of selective regimes (Figure 6). Secondly, we
can simplify cases where invasion occurs despite looser sex-linkage, $R > r$, using
392 the special case where $R = 1/2$ and $r < 1/2$ (e.g., the selected locus is on the
ancestral sex chromosome and the novel sex-determining locus arises on an auto-
394 some). In table 3 we give the conditions where invasion occurs when we further
assume that haploid selection only occurs in one sex (e.g., during male meiosis
396 only) and dominance coefficients are equal in the two sexes, $h^\varnothing = h^\delta$. When there
is no gametic competition and meiotic drive is in one sex only, an unlinked neo-W
398 can invade as long as the same allele is favoured during diploid selection in males
and females ($s^\varnothing s^\delta > 0$, see Figure 6B). When there is no meiotic drive and gametic
400 competition occurs in one sex only, an unlinked neo-W can invade as long as the
same allele is favoured in male and female diploid selection and there are sex dif-
402 ferences in selection of one type (e.g., $s^\varnothing(s^\delta - s^\varnothing) > 0$, see Figure 6C,D). These
special cases indicate that neo-W invasion can occur for a relatively large fraction
404 of parameter space, even if the neo-W uncouples the sex-determining locus from
a locus under selection.

406 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,

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	$h^\delta = h^\varphi, t^\delta = \alpha_\Delta^\varphi = \alpha_\Delta^\delta = 0$	$s^\delta(s^\varphi - s^\delta) > 0$

408 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
410 ancestral-SDR ($r < 1/2$) and experiences meiotic drive in males only (e.g., during
spermatogenesis but not during oogenesis, $\alpha^\delta \neq 1/2$, $\alpha^\varphi = 1/2$). Disregarding
412 gametic competition ($t^\varphi = t^\delta = 0$) such that zygotic sex ratios are only biased
by meiotic drive in males. In this case, the zygotic sex ratio can be initially bi-
414 ased only if the ancestral sex-determining system is XY (Figure 1B). We might
therefore expect a difference in the potential for XY to ZW and ZW to XY tran-
416 sitions. However, to leading order with selection weak relative to recombination,
we find that sex ratio selection (first terms in table 2) is equal in magnitude to
418 the fitness effects of alleles associated with new sex-determining alleles (second
terms in table 2). Thus, invasion by a neo-W into an XY system and invasion by
420 a neo-Y into a ZW system occur under the same conditions ($\lambda_{Y',XY} = \lambda_{W',ZW}$
and $\lambda_{Y',ZW} = \lambda_{W',XY}$, at least up to order ϵ^2). As selection becomes stronger (or
422 linkage becomes tighter), this symmetry between sex-ratio selection and haploid
selection is lost, causing differences in the strength of selection favouring the two
424 heterogametic transitions (compare red to black near -25cM and 25 cM in Figure
6).

426 Environmental sex determination

We next consider the case where the new sex-determining mutation, m , causes sex
428 to be determined probabilistically or by heterogeneous environmental conditions

(environmental sex determiner, ESD). We assume that individuals carrying the m allele develop as females with probability k (e.g., in a fraction k of the environments they randomly experience). The characteristic polynomial determining the eigenvalues of the 8 equation system (equations S.1) does not reduce for ESD mutants as it does for $k = 0$ or $k = 1$. We therefore focus on weak selection here. Assuming weak selection, the spread of these mutations is given by

$$\lambda_{ESD',XY} = 1 + (1 - 2k)^2 V_A S_A^2 \frac{r - R}{rR} + \frac{k(\hat{p}_Y^\phi - \hat{p}_X^\phi)}{2} (k(2\alpha_\Delta^\phi - 2\alpha_\Delta^\phi + t^\phi - t^\phi) - 4(1 - k)S_A) + O(\epsilon^3), \quad (4)$$

which reduces to $\lambda_{Y',XY}$ when $k = 0$ and $\lambda_{W',XY}$ when $k = 1$.

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

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

where we have indicated that $\lambda_{Y',XY}$ and $\lambda_{W',XY}$ are evaluated at $R = 1/2$. 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. An important result from equation (5) is that ESD can invade if there is haploid selection. When evaluated at $R = 1/2$, $\lambda_{Y',XY} \leq 1$ but $\lambda_{W',XY}$ can be greater than one if there is haploid selection, as discussed above. Previous studies where ESD is favoured have typically assumed that environmental conditions (e.g., maternal condition, mate quality, age, or host size) can differentially affect the fitness of males versus females such that ESD invades because it allows sex determination to depend on the environment (reviewed in Charnov 1982, Bull 1983, West 2009).

450 Here, ESD mutations can spread because they generate females that are either rare or have high fitness, in the same manner as a neo-W.

452 Equation (5) also shows that invasion by a novel ‘perfect’ ESD (equal sex ratio, $k = 1/2$) mutation is the same for an ancestrally XY or ZW system (since
454 $\lambda_{Y',XY} = \lambda_{W',ZW}$, $\lambda_{W',XY} = \lambda_{Y',ZW}$). Thus, by the same argument as above (if drive only occurs in males then the sex ratio is only biased when the ancestral
456 sex-determination system is XY), Fisherian sex-ratio selection alone does not explain the invasion of an offspring-controlled neo-ESD allele under weak selection.
458 Rather, 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
460 half of the time (the other half of the time it produces the same sex as the ancestral system would have, to leading order). The net result can be that perfect ESD will
462 not invade, even if current sex ratios are biased. For example, if there is haploid selection in males (either drive or pollen/sperm competition) but the conditions in
464 table 3 are not met, perfect ESD will not invade, even though it would equalize the zygotic sex ratio from an initially biased case (assuming $r < 1/2$).

466 Discussion

Two predominant theories explaining the remarkably high frequency of transitions
468 between sex-determination systems are sexually-antagonistic selection and sex-ratio selection (reviewed in Blaser et al. 2012) (van Doorn, 2014, sexual develop-
470 ment). 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). The latter predicts that neo-W alleles will invade an XY
472 system when there is a male bias caused by haploid selection in males, and vice-versa, a neo-Y will invade a ZW system when there is a female bias caused by
474 haploid selection in females (Kozielska et al. 2010, Úbeda et al. 2015). Here we have shown that both predictions must be amended when recombination is weak
476 relative to selection or selection happens in both diploid and haploid phases.

478 When the rate of recombination between the ancestral sex-determining locus
 and a locus under selection is small relative to the strength of selection (i.e., sex-
 480 linkage is tight, or selection is strong), heterogametic transitions (XY to ZW or
 ZW to XY) that reduce sex-linkage are possible, with or without haploid selection
 482 or sexually-antagonistic selection (Figure 7). The likelihoods of these transitions
 are driven by sex-ratio selection, direct selection on alleles linked to the neo-sex-
 484 determining allele, the ability of the neo-sex-determining allele to avoid selection
 in one sex, and the ability of the neo-sex-determining allele to bring alleles on the
 486 sex-specific chromosome in the ancestor into the other sex (given that the neo-sex
 determining allele is epistatically dominant to its predecessor). This possibility
 488 that looser sex-linkage could evolve, even in the absence of haploid selection (Fig-
 ure 7A), was overlooked in van Doorn and Kirkpatrick (2010), likely because they
 490 did not explicitly calculate the resident equilibria (equation S.2; Lloyd and Webb
 1977, Otto 2014). Interestingly, there is substantial overlap between the parame-
 492 ter space that allows both neo-W-A and neo-W-a haplotypes to spread in an XY
 system and that which selects for increased recombination between X and Y chro-
 494 mosomes (e.g., compare gray region of Figure 7A with coloured regions of Figure
 2(a) in Otto 2014). This makes sense, as when both neo-W haplotypes can spread
 496 the neo-W can invade despite reducing sex-linkage, i.e., the rate of recombination
 between the sex-determining allele and the selected locus increases.

498 Under weak selection (or loose sex-linkage), transitions to new sex-determining
 systems can occur when they arise more closely linked to a sexually-antagonistic
 500 locus (van Doorn and Kirkpatrick 2007; 2010). Our results show that genetic vari-
 ation at loci that experience haploid selection can generate selection in favour of
 502 new sex-determining systems in a similar way. New sex-determining alleles are
 again favoured if they are more closely linked to a locus under haploid selection.
 504 However, with haploid selection, heterogametic transitions (XY to ZW or ZW to
 XY) can also occur when the new sex-determining region is less closely linked
 506 to the locus under selection. Neo-W (neo-Y) alleles invade when their fitness in
 females (males) is greater than the mean fitness of females (males) under the an-

508 cestral sex-determination system and/or females (males) are the rarer sex. With
sexually-antagonistic selection (between diploid sexes) only, linkage between a se-
510 lected locus and the sex-determining region strengthens associations between male
beneficial alleles and the male-determining allele (Y or Z) and between female ben-
512 eficial alleles and the female-determining allele (X or W). Thus, the mean fitness
of both males and females increases with closer linkage to the sex-determining re-
514 gion. Therefore, new sex-determining alleles only invade if they are more closely
linked than the ancestral sex-determining region. However, if there is haploid se-
516 lection on loci linked to an XY (ZW) sex-determining region, selection can main-
tain polymorphisms at which the product of the frequency of females (males) and
518 the mean fitness of females (males) is lower than it would be without sex-linkage.
In these cases, unlinked neo-W (neo-Y) alleles can increase the frequency and/or
520 fitness of the only sex they are found in, at a cost to the other sex, and invade despite
lowering population mean fitness (Figure 4).

522 Sex ratio biases caused by gametic competition or meiotic drive have been
shown to exert Fisherian sex-ratio selection on various autosomal (Stalker 1961,
524 Smith 1975, Frank 1989, Hough et al. 2013, Úbeda et al. 2015, Otto et al. 2015)
and sex-linked (Úbeda et al. 2015) modifiers. We find that sex-ratio biases caused
526 by haploid selection can also affect transitions between sex-determining systems
(e.g., see ζ terms in Table 2). For instance, when an allele that drives in males
528 is linked to an XY locus it will often become associated with the Y and therefore
produce a male bias ($\zeta < 1/2$). This male bias increases the potential for a neo-W
530 to invade (as we then have $(2\zeta)^{-1} > 1$ in Table 2), which can equalize the sex-ratio
(for a related example see Úbeda et al. 2015). However, this sex-ratio selection
532 can be overwhelmed when the driving allele has additional selective effects (e.g.,
when it is beneficial for male diploids but detrimental for female diploids; Table
534 3), preventing the neo-W from invading. Indeed, these additional selective effects
can even favour transitions between sex-determining systems that create new sex-
536 ratio biases. For example, in an ancestral ZW system, an allele that drives only
in males can allow a linked neo-Y to invade, despite the fact it creates a male bias

538 (Figure 1C). Furthermore, with weak selection, there is no asymmetry between
XY to ZW and ZW to XY transitions, indicating that sex-ratio selection does not
540 dominate (i.e., the sex-ratio bias created by haploid selection impacts the spread
of a neo-W into an XY system the same way it impacts the spread of a neo-Y into
542 a ZW system with a 1:1 sex ratio). An asymmetry can develop when sex-linkage
is tight (e.g., Figure 6 near -25cM and 25cM) but under most circumstances we
544 do not predict asymmetry between XY to ZW and ZW to XY transitions despite
the presence/absence of sex ratio selection. Thus, haploid selection can favour
546 heterogametic transitions both via sex-ratio selection and via fitness effects of al-
leles that are associated with the neo-sex-determining allele, and these selection
548 pressures are often of equal magnitude.

We assume that sex-determining alleles do not experience direct selection ex-
550 cept via their associations with sex and alleles at a selected locus. However, in
some cases, there may be significant degeneration around the sex-limited allele (Y
552 or W) in the ancestral sex-determining region because recessive deleterious muta-
tions and/or deletions may fix around the Y or W allele (Rice 1996, Charlesworth
554 and Charlesworth 2000, Bachtrog 2006, Marais et al. 2008). During heterogametic
transitions (XY to ZW or ZW to XY), the formally sex-limited allele fixes such
556 that all individuals have YY or WW genotypes (Figure 1). Any recessive delete-
rious alleles linked to the Y or W will therefore be revealed to selection during a
558 heterogametic transition. This phenomenon was studied by van Doorn and Kirk-
patrick (2010), who found that degeneration can prevent fixation of a neo-W or
560 a neo-Y allele, leading to a mixed sex-determination system where the ancestral-
and neo- sex-determining loci are both polymorphic. However, they noted that
562 very rare recombination events around the ancestral sex-determining region can
allow these heterogametic transitions to complete. While not explicitly studied,
564 we also predict that Y or W degeneration would prevent fixation of the new sex-
determiners considered here.

566 In addition, our model of meiotic drive is simple, involving a single locus with
two alleles. However, many meiotic drive systems involve an interaction with an-

568 other locus at which alleles may ‘suppress’ the action of meiotic drive (Burt and
Trivers 2006, Lindholm et al. 2016). Thus, the dynamics of meiotic drive alleles
570 can be heavily dependent on the interaction between two loci and the recombina-
tion rate between them, which in turn can be affected by sex-linkage if there is re-
572 duced recombination between sex chromosomes (Hurst and Pomiankowski 1991).
Furthermore, in some cases, a driving allele may act by killing any gametes that
574 carry a ‘target’ allele at another locus, in which case there is a two-locus drive sys-
tem and the total number of gametes produced can be reduced by meiotic drive.
576 Where gamete number is reduced by meiotic drive, the number of mates competing
for fertilization (mating system) can affect the equilibrium frequency of a meiotic
578 drive allele (Holman et al. 2015). In polygamous mating systems, the intensity
of pollen/sperm competition can depend on the density of males available to do-
580 nate pollen/sperm, which can itself depend on the sex ratio (Taylor and Jaenike
2002). Since the sex ratio is partly determined by the sex-determination system,
582 the evolution of new sex-determination system could be influenced by these dy-
namics. How the evolution of new sex-determining mechanisms could be influ-
584 enced by two-locus meiotic drive and/or by ecological feedbacks under different
mating systems remains to be studied.

586 The hypotheses presented here can be empirically investigated in a similar
manner to the idea that transitions between sex-determining systems are favoured
588 by linkage to sexually-antagonistic variation. In the case of sexually-antagonistic
variation, one supporting observation is that genes expected to be under sexually-
590 antagonistic selection (e.g., those causing bright male colouration) have been found
on recently derived sex chromosomes (Lindholm and Breden 2002, Tripathi et al.
592 2009, Ser et al. 2010). Our results suggest that polymorphic loci that are ancestrally
sex-linked and under sex-specific selection could also drive heterogametic transi-
594 tions between sex-determination systems. As noted by van Doorn and Kirkpatrick
(2010), it would be prudent to compare closely related clades in order to deter-
596 mine whether observed polymorphisms pre-dates a transition in sex-determination
or arose afterwards, particularly because sex-linkage allows sexually-antagonistic

598 selection to maintain polymorphisms under a different and larger parameter space
 (Rice 1987, Jordan and Charlesworth 2011). As with sexually-antagonistic selec-
 600 tion, the presence of haploid selected loci around ancestral- or novel-sex-determining
 regions could support their role in sex chromosome turnover. A recent transcrip-
 602 tome analysis in *Rumex*, suggests a role for haploid competition in the evolution
 of sex-determination systems by showing that Y-linked genes are overexpressed in
 604 pollen but not in male diploids, indicating variation currently or previously main-
 tained by haploid selection; over-expression also occurs on the autosome that is or-
 606 thologous to the sex chromosomes in closely related species (Sandler et al., 2017,
 Personal Communication).

608 Taken at face value, our results indicate that transitions in heterogamete (XY
 to ZW or vice versa) are more likely than transitions in homogamete when genetic
 610 conflict is predominately between the haploids of each sex (e.g., with $|D^\delta - D^\varphi| \ll$
 $|\alpha_\Delta^\delta - \alpha_\Delta^\varphi + t^\delta - t^\varphi|$ we have $\lambda_{W',XY} > \lambda_{Y',XY}$; equations 3 and S.5). In addition, be-
 612 cause haploid selection can cause transitions that increase or decrease sex-linkage,
 haploid selection may lead to less stability, and greater potential for cycling, in sex-
 614 determination systems (e.g., the final state in Figure 1C is the starting state in Fig-
 ure 1B). Potentially, successive heterogametic transitions between master regula-
 616 tors of sex-determination could be inferred from careful examination of the molec-
 ular pathways by which sex is determined. Our predictions could also be examined
 618 using a suitable proxy for haploid selection, for example, Lenormand and Dutheil
 (2005) use the outcrossing rate in plants as a proxy for the strength of pollen com-
 620 petition. Furthermore, assuming that transitions from dioecy to hermaphroditism
 (equal parental investment in male and female gametes) are favoured in a simi-
 622 lar manner to the ESD examined here (equal probability of zygotes developing as
 males or females), our results suggest that haploid competition during the multi-
 624 cellular haploid stage could drive transitions between dioecy and hermaphroditism
 in plants (Käfer et al., 2017, Sabath et al., 2017). In animals, one might expect ga-
 626 metic competition to be stronger in species where sperm is required to live for a
 long time after spermatogenesis because transcripts shared during spermatogene-

sis may become depleted, revealing the haploid phenotype of the sperm (Immler et al. 2014). Given the caveats mentioned above about the form of meiotic drive modelled, we would also expect that heterogametic transitions in sex determination would be more common in clades where there is meiotic drive.

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 alone can cause transitions analogous to those caused by purely sexually-antagonistic selection, eliminating the need for differences in selection between male and female diploids. Perhaps counterintuitively, transitions involving haploid selection can be driven by sex-ratio selection, or cause sex-ratio biases to evolve. We therefore argue that haploid selection should be considered, alongside sexually-antagonistic and sex-ratio selection, as a potentially pivotal factor in the evolution of many sex-determination systems. Overall, our results suggest several new scenarios under which new sex-determination systems are favoured, including sex-specific selection on ancestrally sex-linked loci, which could help to explain why the evolution of sex-determination systems is so dynamic.

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Figures

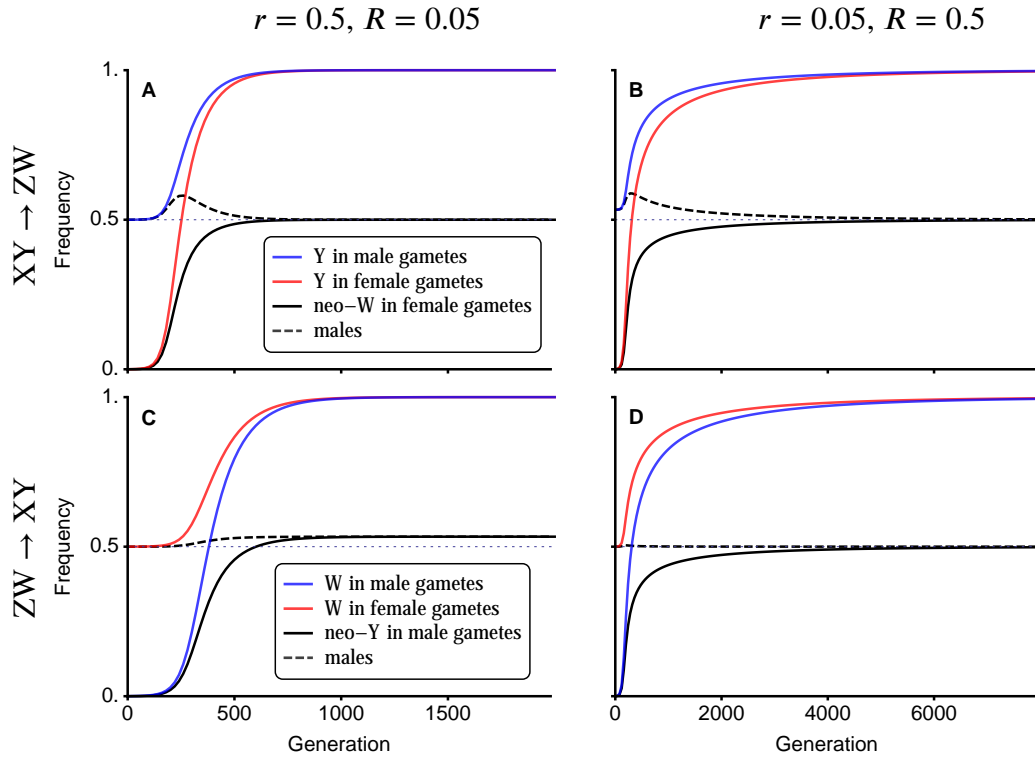


Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occur similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines show male frequency). During invasion by a neo-ZW sex-determination system (A and B), the ancestral Y fixes in both males and females (blue and red lines). Similarly, the ancestral W allele fixes in males and females (blue and red lines) during a ZW to XY transition. In this plot, there is no gametic competition ($t^{\text{f}} = r^{\text{f}} = 0$) and meiotic drive occurs during male meiosis only ($\alpha_{\Delta}^{\text{f}} = 0, \alpha_{\Delta}^{\text{m}} = -1/5$). Therefore, sex ratio biases can only arise when the A locus is linked to an XY sex-determining locus. In panels A and C, the neo-sex-determining locus is more closely linked to the A locus than the ancestral sex-determining region ($r = 1/2, R = 1/20$) such that a neo-Y can cause biased sex ratios (panel C). In panels B and D, the ancestral sex-determining locus is more closely linked to the A locus than the neo-sex-determining locus ($r = 1/20, R = 1/2$). Therefore, an ancestral XY sex determination can have a biased zygotic sex ratio that becomes unbiased after an unlinked neo-W invades (B). However, in panel D, a unlinked neo-Y invades an ancestral ZW sex-determination system in a similar manner but no biases to the zygotic sex ratio occur. With diploid selection alone, neo-sex-determining loci do not spread if they are less closely linked to the A locus than the ancestral sex-determining locus (see equation (3) and Figure 6A). In this plot there are no sex differences in selection and an equilibrium is maintained because selection in diploids opposes meiotic drive, $s^{\text{f}} = s^{\text{m}} = 1/5, h^{\text{f}} = h^{\text{m}} = 7/10$.

Aesthetic adjustments: Add chromosome cartoons to depict recombination rates?

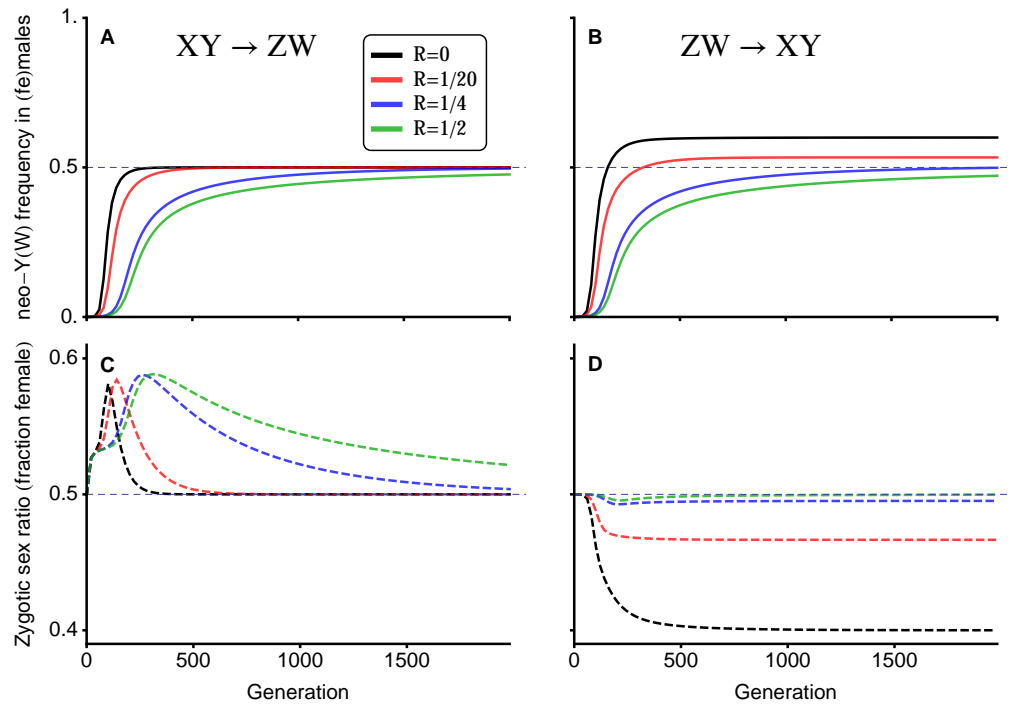


Figure 2: Is this what Sally was thinking? I think this works but I'm confused as to why the speed of spread should be so much different for XY and ZW here. Figure 1 and 6 suggests that there's not much difference between XY→ZW and ZW→XY. Maybe we should just stick with the 4 cases in figure 1. i messed up and had $r = 0.5$ instead of $r = 0.05$ for B and D. haven't fixed fitness plot below.

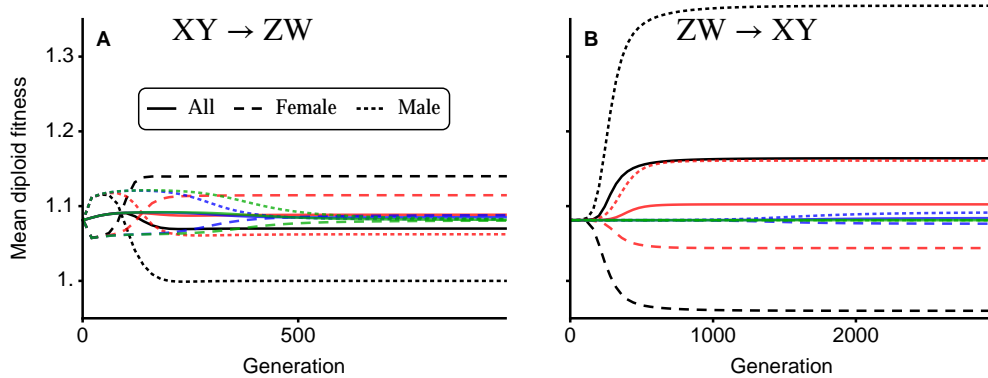


Figure 3: This complicated thing matches the plot above. I don't think we want to include it...?

Appendix

834 Recursion Equations

Should we adjust the subscripts throughout this subsection? Right now we end up re-defining i and j (when switching from haploid to diploid; this might have been my doing!) and then introduce three new subscripts b , c , and l , all of which can be derived from i and j . Might be more straightforward to just use $p_{x_1, x_2, a_1, a_2, m_1, m_2}^{\phi}$ where 1 is maternal and 2 is paternal? We then no longer have to switch indices from haploid to diploid and the connection to other variables is clear: $b = m_1 m_2$, $c = x_1 x_2$, and $l = a_1 a_2$. I guess the downside will be re-writing the recursion equations... which is why I haven't gone ahead and tried this.

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_{ij}^{ϕ} and y_{ij}^{ϕ} , where $\phi \in \{\sigma, \phi\}$ specifies the sex of the diploid that the gamete came from, $i \in \{A, a\}$ specifies the allele at the selected locus **A**, and $j \in \{M, m\}$ specifies the allele at the novel sex-determining locus **M**. The gamete frequencies from each sex sum to one,

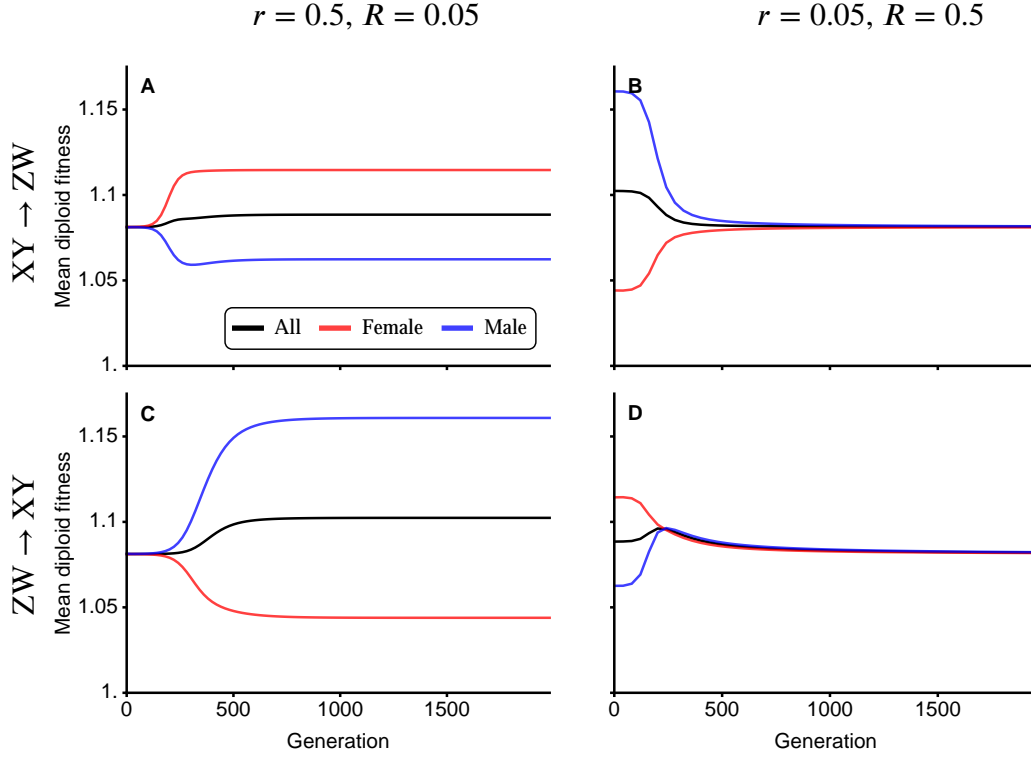


Figure 4: Changes in mean diploid fitness of males (blue lines), females (red lines), and the entire population (black lines) during the transitions between sex-determination systems shown in Figure 1. Here mean diploid fitness of a particular sex is its mean diploid viability fitness times twice its frequency in the population, to capture the fact that epistatically dominant sex-determining alleles can also invade because they selfishly make more of the sex they are in. The mean fitness of females increases during the spread of neo-W alleles (A and B) and the mean fitness of males increases during the spread of neo-Y alleles (C and D). However, when a neo-sex determining system evolves that is less closely linked to a locus under selection (B and D), population mean fitness decreases. *I think we should give this plot showing (male mean fitness * freq males) and (female mean fitness * freq females), without multiplying by 2 (leave off black lines, population mean fitness). We could also re-plot the sex ratios on this same scale. The plot below, 'adjusted for sex ratio', could then go in the appendix. The point is that neo-W (neo-Y) can invade when the frequency of females (males) multiplied by their mean fitness increases.*

$$\sum_{i,j} x_{ij}^{\phi} + y_{ij}^{\phi} = 1.$$

Competition then occurs among gametes of the same sex (e.g., among eggs and among sperm separately) according to the **A** locus allele, i (see Table 1). The genotype frequencies after gametic competition are $x_{ij}^{\phi,s} = w_i x_{ij}^{\phi} / \bar{w}_H^{\phi}$ and $y_{ij}^{\phi,s} = w_i y_{ij}^{\phi} / \bar{w}_H^{\phi}$, where $\bar{w}_H^{\phi} = \sum_{i,j} w_i x_{ij}^{\phi} + w_i y_{ij}^{\phi}$ is the mean fitness of male ($\phi = \sigma$) or female ($\phi = \varphi$) gametes.

Random mating then occurs between gametes to produce diploid zygotes. To

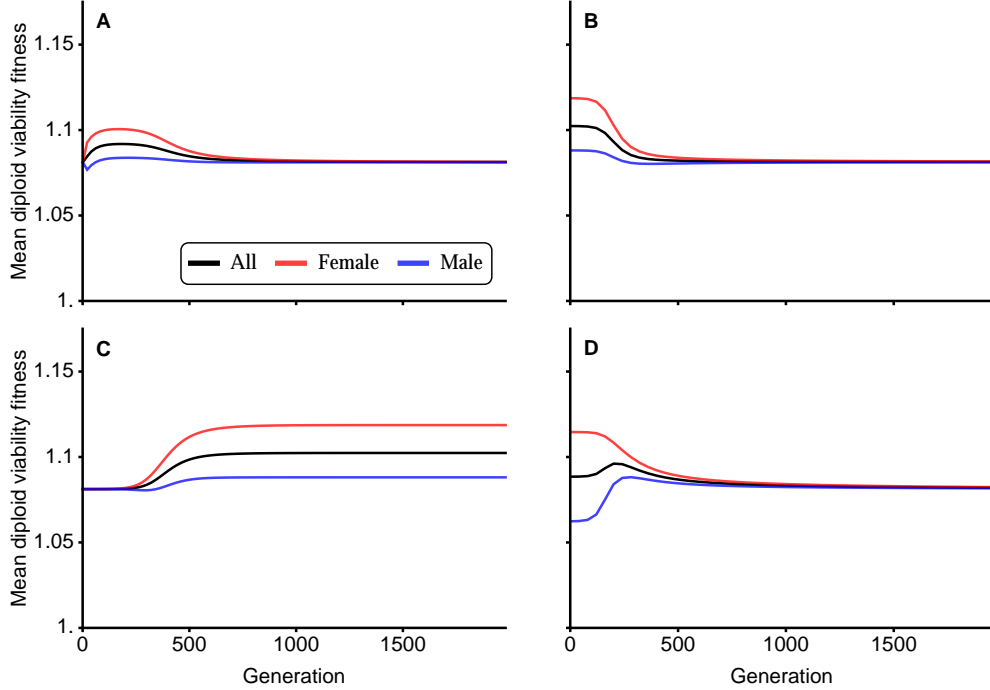


Figure 5: Last plot with mean fitness of sexes corrected for sex ratio. Could add to previous plot with dashed lines?

shorten notation we now use index i (and j) to denote the alleles at both the **A** and **M** loci and label $MA = 1$, $Ma = 2$, $mA = 3$, and $ma = 4$, such that $i, j \in \{1, 2, 3, 4\}$. The frequencies of XX zygotes are then denoted as xx_{ij} , XY zygotes as xy_{ij} , and YY zygotes as yy_{ij} . 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, $xx_{ij} = (x_i^{\varphi,s} x_j^{\delta,s} + x_j^{\varphi,s} x_i^{\delta,s})/2$ and $yy_{ij} = (y_i^{\varphi,s} y_j^{\delta,s} + y_j^{\varphi,s} y_i^{\delta,s})/2$.

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 $xx_{ij}^{\delta} = (1 - k_{bc})xx_{ij}$, XY male frequencies are $xy_{ij}^{\delta} = (1 - k_{bc})xy_{ij}$, and YY males frequencies are $yy_{ij}^{\delta} = (1 - k_{bc})yy_{ij}$. This

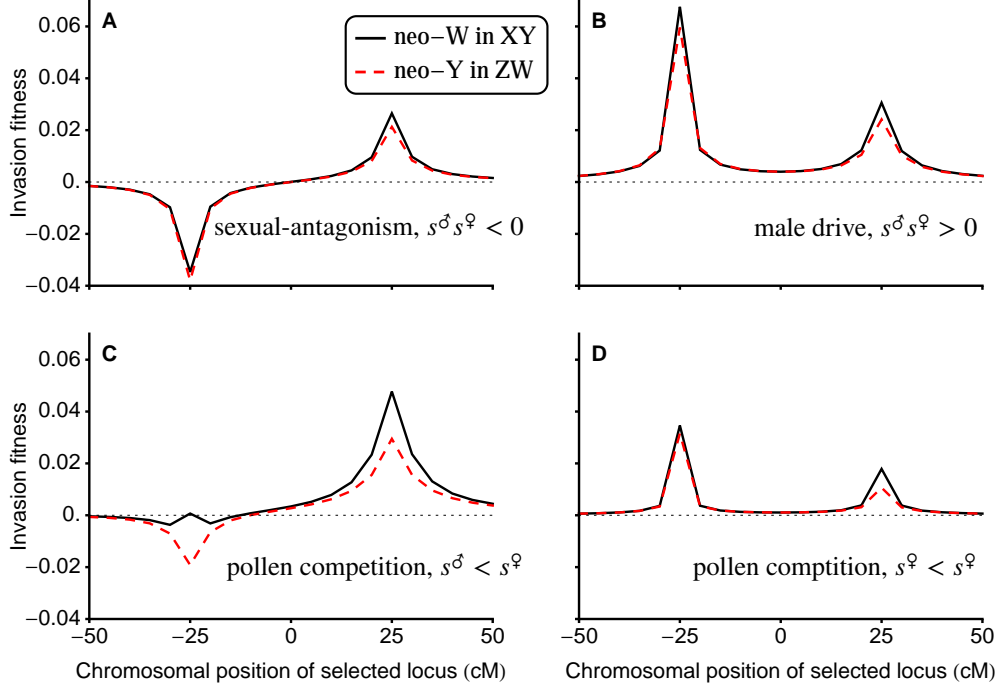


Figure 6: Invasion fitness of a neo-W allele plotted against the relative genomic location of a locus under direct selection, **A**, for various selective regimes. The ancestral sex-determining locus is located at -25 and the novel sex-determining locus is located at 25. We use Haldane’s map function (Equation 3 in Haldane 1919) to convert from map distance (centiMorgans) to the probability of a cross-over event. In **A**, there is no haploid selection ($r^\delta = \alpha_\Delta^\delta = 0$) and selection in diploids is sexually antagonistic (following van Doorn and Kirkpatrick 2010), in which case a neo-W can only invade if it is more closely linked to the selected locus ($s^\omega = 1/10$, $h^\omega = 7/10$, $s^\delta = -1/10$, $h^\delta = 3/10$). In **B-D** we include haploid selection and assume that selection in diploids is not sexually-antagonistic ($s^\delta s^\omega > 0$). A polymorphism can then be maintained by opposing selection between the haploid and diploid phases. In **B**, there is drive in favour of the a allele in males ($\alpha_\Delta^\delta = -1/20$), no female meiotic drive or gametic competition, $r^\omega = \alpha_\Delta^\omega = 0$, and equal selection in diploid sexes ($s^\omega = s^\delta = 1/10$, $h^\omega = h^\delta = 7/10$). In this case, a neo-W can invade even when the selected locus is more closely linked to the ancestral sex determining locus (see Table 3 and Figure 1). In **C** and **D**, there is gametic competition among male gametes only (favouring a , $r^\delta = -1/10$) and no meiotic drive or gametic competition in females ($r^\omega = \alpha_\Delta^\omega = 0$). In this case, the neo-W does not invade if $s^\omega > s^\delta$ (panel **C**: $s^\omega = 3/20$, $s^\delta = 1/20$) but does if $s^\omega < s^\delta$ (panel **D**: $s^\omega = 1/20$, $s^\delta = 3/20$), see Table 3.

870 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-
872 determining system. In addition, we can consider any epistatic dominance rela-
tionship between the two sex-determining loci. For example, here we assume that
874 the ancestral sex-determining system (**X** locus) is XY ($k_{MMXX} = 1$ and $k_{MMXY} =$

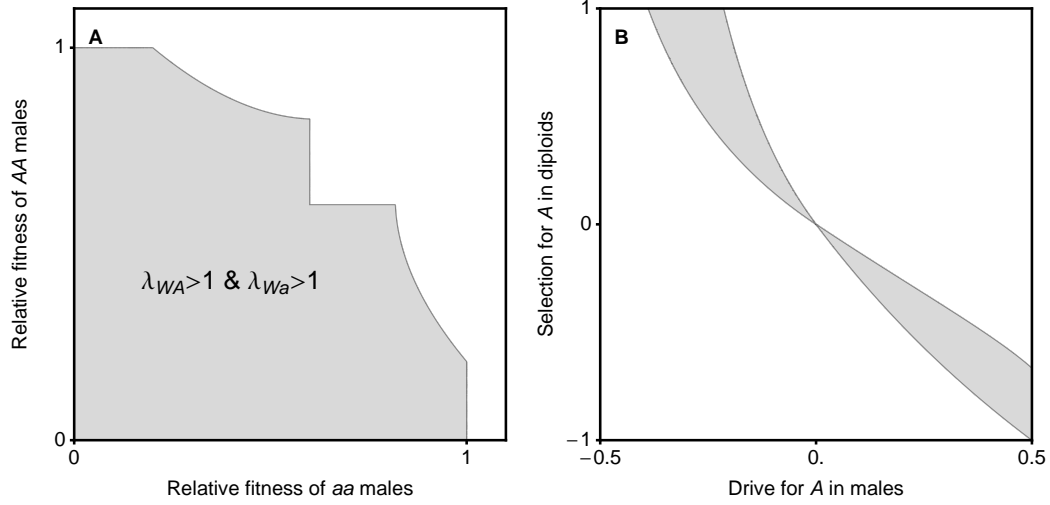


Figure 7: Parameter space (gray) where both neo-W haplotypes can invade from the same stable resident $r = 0$ equilibria (equations S.2), and therefore where an unlinked neo-W can invade an XY system with perfect sex-linkage. **A**, In the absence of haploid selection, both neo-W haplotypes can invade for much of the parameter space where the relative fitnesses of male homozygotes, w_{AA}^ϕ and w_{aa}^ϕ , are both less than that of the heterozygote, $w_{Aa}^\phi = 1$. In the white region neo-W haplotypes paired with the allele fixed on the Y cannot invade. Parameters as in Otto (2014) Figure 2a: $w_A^\phi = w_a^\phi = 1/2$, $w_A a^\phi = 1$, and $w_A A^\phi = w_a a^\phi = 0.75$. **B**, When selection is the same in both diploid sexes ($w_{aa}^\phi = 1$, $w_{Aa}^\phi = 1 + hs$, $w_{AA}^\phi = 1 + s$), both neo-W haplotypes can invade over a portion of the parameter space where selection in diploids (s) opposes the force of drive during meiosis in males (α_A^ϕ). Parameters: $w_A^\phi = w_a^\phi$, $\alpha^\phi = 1/2$, $h = 1/2$.

876 $k_{MMYY} = 0$) or ZW ($k_{MMZZ} = 0$ and $k_{MMZW} = k_{MMWW} = 1$) and epistatically recessive to a dominant novel sex-determining locus, **M** ($k_{Mmc} = k_{mmc} = k$).

878 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 .

882 Finally, these diploids undergo meiosis to produce the next generation of gametes. Recombination and sex-specific meiotic drive occur during meiosis. Here, 884 we allow any relative locations for the SDR, **A**, and **M** loci by using three parameters to describe the recombination rates between them. R is the recombination rate between the **A** locus and the **M** locus, χ is the recombination rate between the 886

888 **M** locus and the **X** locus, and r is the recombination rate between the **A** locus and
the **X** locus. Table S.1 shows how χ can be substituted to give any linear order of
890 loci. 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: χ substitutions for different loci orders (assuming no interference)

Order of loci	
SDR-A-M	$\chi = R(1 - r) + r(1 - R)$
SDR-M-A	$\chi = (r - R)/(1 - 2R)$
A-SDR-M	$\chi = (R - r)/(1 - 2r)$

Among gametes from sex ϕ (sperm/pollen when $\phi = \delta$, eggs/ovules when
892 $\phi = \eta$), the frequencies of haplotypes (before gametic competition) in the next
generation are given by

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

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

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

$$\begin{aligned}
x_{ma}^{\tilde{\phi}'} = & xx_{44}^{\tilde{\phi},s} + xx_{34}^{\tilde{\phi},s}/2 + (xx_{14}^{\tilde{\phi},s} + xx_{24}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& - R(xx_{14}^{\tilde{\phi},s} - xx_{23}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& (xy_{44}^{\tilde{\phi},s} + xy_{42}^{\tilde{\phi},s})/2 + (xy_{41}^{\tilde{\phi},s} + xy_{43}^{\tilde{\phi},s})(1-\alpha^{\tilde{\phi}}) \\
& - r(xy_{43}^{\tilde{\phi},s} - xy_{34}^{\tilde{\phi},s})(1-\alpha^{\tilde{\phi}}) - \chi(xy_{42}^{\tilde{\phi},s} - xy_{24}^{\tilde{\phi},s})/2 \\
& + \{ -(R+r+\chi)xy_{41}^{\tilde{\phi},s} + (r+\chi-R)xy_{14}^{\tilde{\phi},s} \\
& + (R+r-\chi)xy_{32}^{\tilde{\phi},s} + (R+\chi-r)xy_{23}^{\tilde{\phi},s} \}(1-\alpha^{\tilde{\phi}})/2
\end{aligned} \tag{S.1d}$$

$$\begin{aligned}
y_{MA}^{\tilde{\phi}'} = & yy_{11}^{\tilde{\phi},s} + yy_{13}^{\tilde{\phi},s}/2 + (yy_{12}^{\tilde{\phi},s} + yy_{14}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& - R(yy_{14}^{\tilde{\phi},s} - yy_{23}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& (xy_{11}^{\tilde{\phi},s} + xy_{31}^{\tilde{\phi},s})/2 + (xy_{21}^{\tilde{\phi},s} + xy_{41}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& - r(xy_{21}^{\tilde{\phi},s} - xy_{12}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} - \chi(xy_{31}^{\tilde{\phi},s} - xy_{13}^{\tilde{\phi},s})/2 \\
& + \{ -(R+r+\chi)xy_{41}^{\tilde{\phi},s} + (r+\chi-R)xy_{14}^{\tilde{\phi},s} \\
& + (R+r-\chi)xy_{32}^{\tilde{\phi},s} + (R+\chi-r)xy_{23}^{\tilde{\phi},s} \}\alpha^{\tilde{\phi}}/2
\end{aligned} \tag{S.1e}$$

$$\begin{aligned}
y_{Ma}^{\tilde{\phi}'} = & yy_{22}^{\tilde{\phi},s} + yy_{24}^{\tilde{\phi},s}/2 + (yy_{12}^{\tilde{\phi},s} + yy_{23}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& - R(yy_{23}^{\tilde{\phi},s} - yy_{14}^{\tilde{\phi},s})\alpha^{\tilde{\phi}} \\
& (xy_{22}^{\tilde{\phi},s} + xy_{42}^{\tilde{\phi},s})/2 + (xy_{12}^{\tilde{\phi},s} + xy_{32}^{\tilde{\phi},s})(1-\alpha^{\tilde{\phi}}) \\
& - r(xy_{12}^{\tilde{\phi},s} - xy_{21}^{\tilde{\phi},s})(1-\alpha^{\tilde{\phi}}) - \chi(xy_{42}^{\tilde{\phi},s} - xy_{24}^{\tilde{\phi},s})/2 \\
& + \{ -(R+r+\chi)xy_{32}^{\tilde{\phi},s} + (r+\chi-R)xy_{23}^{\tilde{\phi},s} \\
& + (R+r-\chi)xy_{41}^{\tilde{\phi},s} + (R+\chi-r)xy_{14}^{\tilde{\phi},s} \}(1-\alpha^{\tilde{\phi}})/2
\end{aligned} \tag{S.1f}$$

$$\begin{aligned}
y_{mA}^{\phi'} = & yy_{33}^{\phi,s} + yy_{13}^{\phi,s}/2 + (yy_{23}^{\phi,s} + yy_{34}^{\phi,s})\alpha^{\phi} \\
& - R(yy_{23}^{\phi,s} - yy_{14}^{\phi,s})\alpha^{\phi} \\
& (xy_{33}^{\phi,s} + xy_{13}^{\phi,s})/2 + (xy_{23}^{\phi,s} + xy_{43}^{\phi,s})\alpha^{\phi} \\
& - r(xy_{43}^{\phi,s} - xy_{34}^{\phi,s})\alpha^{\phi} - \chi(xy_{13}^{\phi,s} - xy_{31}^{\phi,s})/2 \\
& + \{ -(R + r + \chi)xy_{23}^{\phi,s} + (r + \chi - R)xy_{32}^{\phi,s} \\
& + (R + r - \chi)xy_{14}^{\phi,s} + (R + \chi - r)xy_{41}^{\phi,s} \}\alpha^{\phi}/2
\end{aligned} \tag{S.1g}$$

$$\begin{aligned}
y_{ma}^{\phi'} = & yy_{44}^{\phi,s} + yy_{34}^{\phi,s}/2 + (yy_{14}^{\phi,s} + yy_{24}^{\phi,s})\alpha^{\phi} \\
& - R(yy_{14}^{\phi,s} - yy_{23}^{\phi,s})\alpha^{\phi} \\
& (xy_{44}^{\phi,s} + xy_{24}^{\phi,s})/2 + (xy_{14}^{\phi,s} + xy_{34}^{\phi,s})(1 - \alpha^{\phi}) \\
& - r(xy_{34}^{\phi,s} - xy_{43}^{\phi,s})(1 - \alpha^{\phi}) - \chi(xy_{24}^{\phi,s} - xy_{42}^{\phi,s})/2 \\
& + \{ -(R + r + \chi)xy_{14}^{\phi,s} + (r + \chi - R)xy_{41}^{\phi,s} \\
& + (R + r - \chi)xy_{23}^{\phi,s} + (R + \chi - r)xy_{32}^{\phi,s} \}(1 - \alpha^{\phi})/2
\end{aligned} \tag{S.1h}$$

894

The full system is therefore described by 16 recurrence equations (three diallelic
896 loci in two sexes, $2^3 \times 2 = 16$). However, some diploid types are not produced
under a given sex-determination system. For example, with the M allele fixed and
898 ancestral XY sex determination, there are no m alleles, XX males, XY females,
or YY females ($xx_{11}^{\phi} = xx_{12}^{\phi} = xx_{22}^{\phi} = xy_{11}^{\phi} = xy_{12}^{\phi} = xy_{21}^{\phi} = xy_{22}^{\phi} = yy_{11}^{\phi} =$
900 $yy_{12}^{\phi} = yy_{22}^{\phi} = 0$). In this case, the system only involves six recursion equations,
which yields equilibrium (S.4).

902 Resident equilibrium and stability

In the resident population (allele M fixed), we choose to follow the frequency
904 of A in female gametes (eggs) from an XX female, p_X^{ϕ} , and in X -bearing, p_X^{ϕ} ,
and Y -bearing, p_Y^{ϕ} , male gametes (sperm). We also track the total frequency of
906 Y among male gametes, q , which may deviate from $1/2$ due to meiotic drive in
males. These four variables determine the frequencies of the six resident gamete

908 types: $x_{MA}^{\varnothing} = p_X^{\varnothing}$, $x_{Ma}^{\varnothing} = 1 - p_X^{\varnothing}$, $x_{MA}^{\delta} = (1 - q)p_X^{\delta}$, $x_{Ma}^{\delta} = (1 - q)(1 - p_X^{\delta})$,
 $y_{MA}^{\delta} = qp_Y^{\delta}$, and $y_{Ma}^{\delta} = q(1 - p_Y^{\delta})$. Mean fitnesses in the resident population are
910 given in table S.2.

Various forms of selection can maintain a polymorphism at the **A** locus, in-
912 cluding sexually antagonistic selection, overdominance, conflicts between diploid
selection and selection upon haploid genotypes (ploiddally antagonistic selection,
914 Immler et al. 2012), and a combination of these selective regimes.

Table S.2: mean fitnesses 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})	$\{p_X^{\varnothing} w_A^{\varnothing} p_X^{\delta} w_A^{\delta} w_{AA}^{\varnothing} + (1 - p_X^{\varnothing}) w_a^{\varnothing} p_X^{\delta} w_A^{\delta} w_{Aa}^{\varnothing} + p_X^{\varnothing} w_A^{\varnothing} (1 - p_X^{\delta}) w_a^{\delta} w_{Aa}^{\varnothing} + (1 - p_X^{\varnothing}) w_a^{\varnothing} (1 - p_X^{\delta}) w_a^{\delta} w_{aa}^{\varnothing}\} / \{\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} \zeta\}$
males (\bar{w}^{δ})	$\{p_X^{\varnothing} w_A^{\varnothing} p_Y^{\delta} w_A^{\delta} w_{AA}^{\delta} + (1 - p_X^{\varnothing}) w_a^{\varnothing} p_Y^{\delta} w_A^{\delta} w_{Aa}^{\delta} + p_X^{\varnothing} w_A^{\varnothing} (1 - p_Y^{\delta}) w_a^{\delta} w_{Aa}^{\delta} + (1 - p_X^{\varnothing}) w_a^{\varnothing} (1 - p_Y^{\delta}) w_a^{\delta} w_{aa}^{\delta}\} / \{\bar{w}_H^{\varnothing} \bar{w}_H^{\delta} (1 - \zeta)\}$
zygotic sex ratio ζ	$\{(1 - q)(p_X^{\delta} w_A^{\delta} + (1 - p_X^{\delta}) w_a^{\delta})\} / \bar{w}_H^{\delta}$

In particular special cases, e.g., no sex-differences in selection or meiotic drive
916 ($s^{\delta} = s^{\varnothing}$, $h^{\delta} = h^{\varnothing}$, and $\alpha^{\delta} = \alpha^{\varnothing} = 1/2$), the equilibrium allele frequency and sta-
bility can be calculated analytically without assuming anything about the relative
918 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-
920 nesses.

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

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

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

$$\hat{p}_X^\varnothing = \frac{w_a^\varnothing \phi}{w_a^\varnothing \phi + w_A^\varnothing \psi}, \quad \hat{p}_X^\delta = \frac{2\alpha^\delta w_{Aa}^\delta \phi}{2\alpha^\delta w_{Aa}^\delta \phi + w_{AA}^\delta \psi}$$

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

$$\hat{p}_X^\varnothing = 1 - \frac{w_A^\varnothing \phi'}{w_A^\varnothing \phi' + w_a^\varnothing \psi'}, \quad \hat{p}_X^\delta = 1 - \frac{2(1 - \alpha^\delta)w_{Aa}^\delta \phi'}{2(1 - \alpha^\delta)w_{Aa}^\delta \phi' + w_{aa}^\delta \psi'}$$

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

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

$$\begin{aligned} \phi &= \alpha^\varnothing w_A^\varnothing w_{Aa}^\varnothing (w_a^\delta w_{aa}^\delta + 2\alpha^\delta w_A^\delta w_{Aa}^\delta) - w_a^\delta w_a^\varnothing w_{aa}^\delta w_{aa}^\varnothing \\ \psi &= (1 - \alpha^\varnothing) w_a^\varnothing w_{Aa}^\varnothing (w_a^\delta w_{aa}^\delta + 2\alpha^\delta w_A^\delta w_{Aa}^\delta) - 2\alpha^\delta w_A^\delta w_A^\varnothing w_{Aa}^\delta w_{AA}^\varnothing \\ \phi' &= (1 - \alpha^\varnothing) w_a^\varnothing w_{Aa}^\varnothing (w_A^\delta w_{AA}^\delta + 2(1 - \alpha^\delta) w_a^\delta w_{Aa}^\delta) - w_A^\delta w_A^\varnothing w_{AA}^\delta w_{AA}^\varnothing \\ \psi' &= \alpha^\varnothing w_A^\varnothing w_{Aa}^\varnothing (w_A^\delta w_{AA}^\delta + 2(1 - \alpha^\delta) w_a^\delta w_{Aa}^\delta) - 2(1 - \alpha^\delta) w_a^\delta w_a^\varnothing w_{Aa}^\delta w_{aa}^\varnothing \end{aligned}$$

928 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
 930 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
 932 **B'**). The **X** chromosome can then either be polymorphic (equilibria **A** and **A'**)

or fixed for the alternative allele (equilibria B and B'). Since equilibria (A) and (B) are equivalent to equilibria (A') and (B') with the labelling of A and a alleles interchanged, we discuss only equilibria (A) and (B) , in which the Y is fixed for the a allele. If there is no haploid selection ($\alpha^\delta = 1/2$, $w_A^\delta = w_a^\delta = 1$), these equilibria are equivalent to those found by Lloyd and Webb (1977) and Otto (2014).

We next calculate when (A) and (B) are locally stable for $r = 0$. According to the ‘small parameter theory’ (Karlin and McGregor 1972a;b), these stability properties are unaffected by small amounts of recombination between the SDR and A locus, although equilibrium frequencies may be slightly altered. For the a allele to be stably fixed on the Y requires that $\bar{w}_{Ya}^\delta > \bar{w}_{YA}^\delta$ where $\bar{w}_{Ya}^\delta = w_a^\delta(2p_X^\varphi(1 - \alpha^\delta)w_A^\varphi w_{Aa}^\delta + (1 - p_X^\varphi)w_a^\varphi w_{aa}^\delta)$ and $\bar{w}_{YA}^\delta = w_A^\delta(p_X^\varphi w_A^\varphi w_{AA}^\delta + 2(1 - p_X^\varphi)\alpha^\delta w_a^\varphi w_{Aa}^\delta)$. That is, Ya haplotypes must have higher fitness than YA haplotypes. Substituting in $p_X^\varphi = \hat{p}_X^\varphi$ from above, fixation of the a allele on the Y requires that $\gamma_i > 0$ where $\gamma_{(A)} = w_a^\delta(2(1 - \alpha^\delta)w_{Aa}^\delta \phi + w_{aa}^\delta \psi) - w_A^\delta(w_{AA}^\delta \phi + 2\alpha^\delta w_{Aa}^\delta \psi)$ for equilibrium (A) and $\gamma_{(B)} = 2(1 - \alpha^\delta)w_a^\delta w_{Aa}^\delta - w_A^\delta w_{AA}^\delta$ for equilibrium (B) . Stability of a polymorphism on the X chromosome (equilibrium A) further requires that $\phi > 0$ and $\psi > 0$. Fixation of the a allele on the X (equilibrium B) is mutually exclusive with equilibrium (A) and requires $\psi < 0$ and $w_A^\varphi w_{AA}^\varphi > (1 - \alpha^\varphi)w_a^\varphi w_{Aa}^\varphi$.

Selection weak relative to recombination (weak selection)

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

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

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

Given that a polymorphism is maintained at the A locus by selection, with weak selection and drive the frequencies of A in each type of gamete are the same

958 $(\hat{p}_X^\varnothing = \hat{p}_X^\delta = \hat{p}_Y^\delta = \bar{p})$ and given, to leading order, by

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

Differences in frequency between gamete types are of order ϵ and given, to leading
960 order, by

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

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

970 **Invasion conditions**

A rare neo- Y or neo- W will spread from a given ancestral equilibrium when the
972 leading eigenvalue, λ , of the Jacobian matrix derived from the eight mutant re-
cursion equations (given by S.1c,d,g,h), evaluated at the ancestral equilibrium,
974 is greater than one. However, because a neo- Y (neo- W) is always in males (fe-
males) and is epistatically dominant to the ancestral sex-determining locus, we
976 need only two recursion equations (e.g., tracking the change in the frequency of
neo- Y - A and neo- Y - a gametes from males) and thus the leading eigenvalue is

978 the largest solution to a quadratic characteristic polynomial $\lambda^2 + b\lambda + c = 0$.
 It can be shown (see supplementary Mathematica file) that the coefficients are
 980 $b = -(\lambda_{mA} + \lambda_{ma}) + (\rho_{mA} + \rho_{ma})$ and $c = (\lambda_{mA} - \rho_{mA})(\lambda_{ma} - \rho_{ma}) - \rho_{mA}\rho_{ma}$, where
 λ_{mi} is the multiplicative growth rate of the frequency of mutants on background
 982 $i \in \{A, a\}$, without accounting for loss due to recombination, and ρ_{mi} is the rate at
 which mutants on background $i \in \{A, a\}$ recombine onto the other **A** locus back-
 984 ground in heterozygotes. The leading eigenvalue is then greater than one whenever
 $\lambda_{mA} > 1$ and $\lambda_{ma} > 1$, less than one whenever $\lambda_{mA} < 1$ and $\lambda_{ma} < 1$, and greater
 986 than one whenever $\lambda_{mA} > 1$ or $\lambda_{ma} > 1$ and $\rho_{ma}(\lambda_{mA} - 1) + \rho_{mA}(\lambda_{ma} - 1) > 0$.

For tight linkage between the ancestral sex-determining locus and the selected
 988 locus we can calculate each of these terms exactly, while for weak selection we
 take a Taylor series of the leading eigenvalue.

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

Here, we explore the conditions under which a neo-W invades an XY system as-
 992 suming that the **A** locus is initially in close linkage with the ancestral sex-determining
 region ($r \approx 0$). We disregard neo-Y mutations, which never spread given that the
 994 ancestral population is at a stable equilibrium.

Starting with the simpler equilibrium (**B**), the terms of the characteristic poly-
 996 nomial are

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

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

$$\rho_{mA} = (2\alpha^\delta)^{-1} \frac{Rw_a^\delta w_A^\delta w_{Aa}^\delta \alpha^\delta (1 - \alpha^\delta)}{w_A^\delta w_A^\delta w_{AA}^\delta} \quad (\text{S.6c})$$

$$\rho_{ma} = (2\alpha^\delta)^{-1} \frac{Rw_A^\delta w_a^\delta w_{Aa}^\delta (1 - \alpha^\delta) \alpha^\delta}{w_A^\delta w_A^\delta w_{AA}^\delta} \quad (\text{S.6d})$$

Haploid selection impacts the spread of neo-W haplotypes in three ways. Firstly,
 998 the zygotic sex ratio becomes male biased ($\zeta < 1/2$; at equilibrium (B) the sex
 ratio is $\zeta = \alpha^\delta w_A^\delta / [(1 - \alpha^\delta)w_a^\delta + \alpha^\delta w_A^\delta]$) when the a allele (which is fixed on
 1000 the Y) is favoured during competition among male gametes or by meiotic drive
 in males. This facilitates the spread of a neo-W because neo-W alleles cause the
 1002 zygotes that carry them to develop as the rarer, female, sex. Secondly, haploid
 selection in males affects the diploid genotypes of females by altering the allele
 1004 frequencies in the male gametes that female gametes pair with. For instance, be-
 cause an epistatically dominant neo-W always causes its carrier to become female,
 1006 it creates females who carry either Y- a or X genotypes from their father. Thus, be-
 cause when there is a polymorphism the X carries some non-zero frequency of A ,
 1008 haploid selection in males impacts the diploid genotypes of females (e.g., creating
 more Aa females when drive in males favours Y- a). How this affects the spread
 1010 of the neo-W then depends on diploid and haploid selection in females. Thirdly,
 female drive and gamete competition directly select on neo-W haplotypes. Drive
 1012 for A in females favours neo-W- A haplotypes, at a cost to neo-W- a haplotypes, and
 vice-versa when there is drive for a . The impact of this drive depends on how of-
 1014 ten XX and neo-W females are heterozygous. Competition among female gametes
 acts similarly, and depends on the frequency of A on resident X chromosomes
 1016 (e.g., competition among eggs has no affect on the initial spread of the neo-W- A
 haplotype when A is fixed on the X). Because haploid selection in females favours
 1018 one neo-W haplotype at the expense of the other, recombination off the favoured
 background becomes more detrimental as it becomes more favoured. Thus higher
 1020 rates of recombination between the neo-W and the selected locus, R , can lead to
 smaller leading eigenvalues when there is haploid selection in females.

1022 The other terms in equations (S.6) are more easily interpreted if we assume
 that there is no haploid selection in either sex, in which case $\lambda_{mA} > 1$ when $w_{Aa}^\varnothing >$
 1024 w_{AA}^\varnothing and $\lambda_{ma} > 1$ when $(w_{Aa}^\varnothing + w_{aa}^\varnothing)/2 > w_{AA}^\varnothing$. These conditions cannot be met
 under purely sexually-antagonistic selection, where a is directionally favoured in
 1026 males ($w_{AA}^\delta > w_{Aa}^\delta > w_{aa}^\delta$) and A is directionally favoured in females ($w_{AA}^\varnothing >$

1028 $w_{Aa}^{\varphi} > w_{aa}^{\varphi}$). Essentially, the X is already as specialized as possible for the female
beneficial allele (XA is fixed), and the neo-W often makes daughters with the Y-a
haplotype, increasing the flow of a alleles into females, which reduces the fitness
1030 of those females.

If selection doesn't uniformly favour A in females, however, neo-W- A haplo-
1032 types and/or neo-W- a haplotypes can spread ($\lambda_{mA} > 1$ and/or $\lambda_{ma} > 1$) at this
equilibrium. A neo-W can spread alongside the A allele ($\lambda_{mA} > 1$), despite the
1034 fact that a neo-W brings Ya haplotypes into females, when $w_{Aa}^{\varphi} > w_{AA}^{\varphi}$. In this
case the a allele is favoured by selection in females despite A being fixed on the
1036 X. For this equilibrium to be stable, X- A must be sufficiently favoured in males
to keep the frequency of XA at one (specifically, from the stability conditions, we
1038 must have $w_{Aa}^{\delta}/((w_{aa}^{\delta} + w_{Aa}^{\delta})/2) > w_{Aa}^{\varphi}/w_{AA}^{\varphi}$).

Under this same condition, $w_{Aa}^{\varphi} > w_{AA}^{\varphi}$, the neo-W can also spread alongside
1040 the a allele ($\lambda_{ma} > 1$) if there is sufficiently strong underdominance in females
($w_{aa}^{\varphi} > w_{Aa}^{\varphi}$), such that $(w_{Aa}^{\varphi} + w_{aa}^{\varphi})/2 > w_{AA}^{\varphi}$. In this case, a is not favored in
1042 females near the equilibrium where females are AA (comparing Aa to AA geno-
types) and yet the neo-W can spread with a because it produces female aa individ-
1044 uals by capturing Y- a haplotypes.

When both haplotypes can spread on their own ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$), the
1046 neo-W invades regardless the recombination rate between it and the selected locus,
 R . When neither haplotype can spread ($\lambda_{mA} < 1$ and $\lambda_{ma} < 1$) the neo-W can never
1048 invade. And when only one haplotype can spread on its own the neo-W invades
only when the rate of recombination onto the favourable background is sufficiently
1050 larger than the rate of recombination off this background (i.e., equation 1 is satis-
fied).

1052 Similar equations can be derived for equilibrium (A) by subbing the equilib-
rium allele frequencies into Table 2.

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

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

$$\rho_{mA} = \frac{a}{b} R \left[2w_{Aa}^{\varphi} \alpha^{\varphi} w_a^{\delta} \frac{c}{d} \right] / w_a^{\varphi} \quad (\text{S.7c})$$

$$\rho_{ma} = \frac{a}{b} R \left[2w_{Aa}^{\varphi} (1 - \alpha^{\varphi}) w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi \right] / w_A^{\varphi} \quad (\text{S.7d})$$

1054 where

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

$$b = w_{AA}^{\varphi} \phi (2w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi) + w_{Aa}^{\varphi} \psi (2w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi + w_{AA}^{\delta} w_a^{\delta} \psi) + w_{aa}^{\varphi} \psi (w_{AA}^{\delta} w_a^{\delta} \psi) \quad (\text{S.8b})$$

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

$$d = 2w_{Aa}^{\delta} \alpha^{\delta} \phi + w_{aa}^{\delta} \psi \quad (\text{S.8d})$$

As with equilibrium (B), haploid selection again modifies invasion fitnesses by altering the sex-ratio and the diploid genotypes of females and directly selecting upon female gametes. The only difference is that resident XX females are no longer always homozygote AA and males are no longer always heterozygote Aa. Thus the effect of haploid selection in males is reduced, as is the difference in fitness between neo-W haplotypes and resident X haplotypes, as both can be on any diploid or haploid background.

1062 The other terms are easier to interpret in the absence of haploid selection. For instance, without haploid selection, the neo-W-A haplotype spreads ($\lambda_{mA} > 1$) if
1064 and only if

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

where $\phi - \psi = w_{AA}^{\varphi} w_{Aa}^{\delta} - w_{aa}^{\varphi} w_{aa}^{\delta}$ and both ϕ and ψ are positive when equilibrium

1066 (A) is stable. In contrast to equilibrium (B), a neo-W haplotype can spread under
 purely sexually-antagonistic selection ($w_{AA}^\delta > w_{Aa}^\delta > w_{aa}^\delta$ and $w_{AA}^\varphi > w_{Aa}^\varphi > w_{aa}^\varphi$).
 1068 In this case, the neo-W-A haplotype can spread, despite producing a lot of *Aa*
 daughters by obtaining the *a* from Y-gametes, when *aa* females, which the neo-
 1070 W-A never makes, are strongly selected against. This can be intuited from the fact
 that (S.9) will be more easily met when $w_{Aa}^\varphi - w_{aa}^\varphi \approx w_{Aa}^\varphi$ and $w_{AA}^\varphi - w_{Aa}^\varphi \approx 0$,
 1072 implying $w_{aa}^\varphi \approx 0$ and $w_{Aa}^\varphi \approx w_{AA}^\varphi$ (although this is complicated by the fact that
 w_{aa}^φ and w_{Aa}^φ affect ϕ and ψ too, the intuition holds).
 1074 Without haploid selection, the neo-W-*a* haplotype spreads ($\lambda_{ma} > 1$) if and
 only if

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

1076 This condition cannot be met with purely sexually antagonistic selection (as both
 terms on the left-hand side would then be negative), but it can be met under other
 1078 circumstances. For example, with overdominance in males there is selection for
 increased *A* frequencies on X chromosomes in males, which are always paired with
 1080 Y-*a* haplotypes. Then, directional selection for *a* in females maintains a polymor-
 phism at the **A** locus on the X and by creating selection for decreased *A* frequencies
 1082 on X chromosomes in females. This scenario selects for a modifier that increases
 recombination between the sex chromosomes (e.g., blue region of Figure 2d in
 1084 Otto 2014) and facilitates the spread of neo-W-*a* haplotypes, which create more
 heterozygote and *aa* females than ancestral X chromosomes do.

1086 As with equilibrium (B), if both haplotypes can spread ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$)
 then the neo-W invades under any rate of recombination with the selected locus,
 1088 $R \geq 0$. In addition, even when only one haplotype can spread (e.g., under purely
 sexually-antagonistic selection $\lambda_{mA} > 1$ and $\lambda_{ma} < 1$), neo-W invasion can still
 1090 occur under modest rates of recombination between the novel sex-determining and
 selected loci.

1092 Selection weak relative to recombination (weak selection)

With weak selection the leading eigenvalue, λ , for any k , is given up to order ϵ^2
1094 by equation 4. Scenarios leading to $\lambda > 1$ are discussed in the main text.