Gametic Selection, Meiotic Drive, Sex Ratio Bias, and Transitions Between sex-determination systems

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

∗ These authors contributed equally to this work

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

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

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

Contributions:

Abstract

Sex-determination systems are remarkably dynamic; many taxa display shifts in the location of sex-determining loci or the evolution of entirely new sex-determining systems. Predominant theories for why we observe such transitions generally conclude that novel sex-determining systems are favoured by selection if they equalise the sex ratio or increase linkage with a sexually-antagonistic locus. We use population genetic models to extend these theories in two ways: (1) We explicitly consider 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 assymetrical 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.

Introduction

Animals and angiosperms exhibit extremely diverse sex-determination systems (reviewed in Bull 1983, Charlesworth and Mank 2010, Beukeboom and Perrin 2014, Bachtrog et al. 2014). Among species with genetic sex determination of diploid sexes, some taxa have heterogametic males (XY) and homogametic females (XX), including mammals and most dioecious plants (Ming et al. 2011); whereas other taxa have homogametic males (ZZ) and heterogametic females (ZW), including Lepidoptera and birds. Within several taxa, the chromosome that harbours the master sex-determining region changes. For example, transitions of the master sex-determining gene between chromosomes or the evolution of new master sex-determining genes have occurred in Salmonids (Li et al. 2011, Yano et al. 2012), Diptera (Vicoso and Bachtrog 2015), and *Oryzias* (Myosho et al. 2012). In addition, many gonochoric clades with genetic sex determination exhibit transitions between male (XY) and female (ZW) heterogamety, including snakes (Gamble 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 2015), amphibians (Hillis and Green 1990), the angiosperm genus *Silene* (Slancarova et al. 2013), and Coleoptera and Hemiptera (Beukeboom and Perrin 2014, plate 2). Indeed, in some cases, both male and female heterogametic sex-determination systems can be found in the same species, as exhibited by some cichlid species (Ser 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., in reptiles and fishes (Conover and Heins 1987, Mank et al. 2006, Pokorná and Kratochvíl 2009, Ezaz et al. 2009, Pen et al. 2010, Holleley et al. 2015).

Predominant theories accounting for the spread of new sex-determination systems by selection involve fitness differences between sexes (e.g., sexually antagonistic selection) or sex-ratio selection. van Doorn and Kirkpatrick (2007; 2010) 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 allows a stronger favourable association to build up between a male-beneficial

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 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 loci that are more closely linked to the ancestral sex-determination locus will develop similar, favourable associations and select against the spread of a new sex-determination system.

The sex ratio is directly affected by the sex-determination system, and it has therefore been suggested that sex-ratio selection is a dominant force in the evolution of sex determination (e.g., Bull 1983, p66-67; Beukeboom and Perrin 2014, Chapter 7). 'Fisherian' sex-ratio selection favours a 1:1 zygotic sex ratio when assuming that males and females are equally costly to produce (Fisher 1930, Charnov 1982). This follows from the fact that, for an autosomal locus, half of the genetic material is inherited from a male, and half from a female (West 2009). Thus, if the population sex ratio is biased towards females, the average per-individual contribution of genetic material to the next generation from males is greater than the contribution from females (and vice versa for male-biased sex ratios). Therefore, a mutant that increases investment in males (e.g., increases the proportion of 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 systems in which the ancestral sex chromosomes experience meiotic drive (e.g., where driving X or Y chromosomes are inherited disproportionately often), which causes sex ratios to become biased (Hamilton 1967). They find that new, unlinked sex-determining loci (masculinizing or feminizing mutations, i.e., neo-Y or neo-W loci) can then spread, which restore an even sex ratio.

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

refer to the biased (non-Mendelian) segregation of genotypes during gamete production (from one parent) and the term 'gametic competition' to refer to selection upon haploid genotypes within a gamete/gametophyte pool (potentially from by multiple parents); the term 'haploid selection' encompasses both processes. Meiotic 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 many more pollen/sperm than required for fertilization, gametic competition is also typically sex specific, occurring primarily among male gametes. Gametic competition may be particularly common in plants, in which 60-70% of all genes are expressed in the male gametophyte and these genes exhibit stronger signatures of selection than random genes (Borg et al. 2009, Arunkumar et al. 2013, Gossmann et al. 2014). In addition, artificial selection pressures applied to male gametophytes are known to cause a response to selection (e.g., Hormaza and Herrero 1996, Ravikumar et al. 2003, Hedhly et al. 2004, Clarke et al. 2004) and gametic 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 during competition in animal sperm, although precise estimates are uncertain (Zheng et al. 2001, Joseph and Kirkpatrick 2004, Vibranovski et al. 2010, Immler et al. 2014).

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

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

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 region we explicitly calculate equilibrium allele frequencies. This allows us to show that transitions between male and female heterogamety can evolve even when 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 selected 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 that sex-ratio biases caused by haploid selection can exert Fisherian sex-ratio selection upon novel sex-determiners but that their spread is also determined by the 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-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 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 systems despite causing transitory or even permanent increases in sex-ratio bias.

Model

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

at which the null allele (M) is initially fixed in the population such that sex of zygotes is determined by the genotype at the ancestral sex-determining region, **X**; XX genotypes become females and XY become males (or ZW become females and ZZ become males). To evaluate the evolution of new sex-determination systems, we consider the invasion, fixation, maintenance, and/or loss of novel sex-determining alleles (m) at the **M** locus. We assume that the **M** locus is epistatically dominant over the **X** locus such that zygotes with at least one m allele develop as females with probability k and as males with probability $1 - k$, regardless of the **X** locus genotype. With $k = 0$, the m allele is a masculinizer (i.e., a neo-Y) and with $k = 1$ the m allele is a feminizer (i.e., a neo-W). With intermediate k, we can interpret m as an environmental sex determination (ESD) allele, such that zygotes develop as females in a proportion (k) of the environments they (randomly) experience. We also analyze a model of maternally-controlled environmental sex-determination, where mothers with at least one m allele produce daughters with probability k.

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

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

Table 1: Relative fitness of different genotypes in sex $\mathfrak{P} \in \{\mathfrak{P}, \mathfrak{F}\}$

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

Results

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

we relabel the two sexes as being ancestrally 'heterogametic' or ancestrally 'homogametic'. Without loss of generality, we primarily refer to the ancestrally heterogametic sex as male and the ancestrally homogametic sex as female. That is, we describe an ancestral XY sex-determination system but our model is 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 **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 (**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 **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, $p_X^{\female}$, and in X-bearing, $p_X^{\male}$, and Y-bearing, $p_Y^{\male}$, male gametes (sperm/pollem). We

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

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

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

$\bar{p}^{\male} = p_Y^{\male} q + p_X^{\male}(1-q)$ 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)
$\bar{w}^{\female}$ is the mean fitness of diploids of sex ♀, see Table S.2
$\bar{w}_H^{\female}$ is the mean fitness of haploids from sex ♀, see Table S.2

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

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

For example, if we assume that only the mA haplotype has a positive growth rate ($\lambda_{ma} < 1 < \lambda_{mA}$), the second term on the left-hand side of (1) is negative and invasion 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. In other words, invasion requires that the average growth rate of recombinants, weighted by the rates they are created, is positive.

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 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 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-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 $p_X^{\female}$ and $\hat{p}^{\male}$). This is because a dominant neo-Y (neo-W) is always found in males (females), and therefore the frequency of the neo-Y (neo-W) allele, m, only changes in males (females). 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 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 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 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.

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 ancestral population (i.e., $p_X^{\female}$, $p_X^{\male}$, and $p_Y^{\male}$). Since only the **A** locus experiences selection directly, any deterministic evolution requires that there is a polymorphism at the **A** locus. Polymorphisms can be transiently present during the spread of uniformly 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 ($s^{\male}_{\female}$, $t^{\male}_{\female}$, $\alpha^{\male}_{\Delta}$ of order $\epsilon << 1$).

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 ($p^{\male}_{Y} = 0$), without loss of generality . If there are two alleles maintained at the **A** locus, the X can either be fixed for the A allele ($p^{\female}_{X} = p^{\male}_{X} = 1$) or polymorphic ($0<p^{\female}_{X}, p^{\male}_{X}<1$). 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 ($s^{\text{♀}} > 0$, $0 < h^{\text{♀}} < 1$) 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 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 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 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 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 females. This is true for the neo-W-A haplotype because it can pair with a $Y - a$ haplotype and still be female.

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 and no haploid selection (corresponding to Figure 2a in Otto 2014). Wherever both haplotypes have positive growth rates (gray region of Figure **??**), invasion 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 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 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-W. Take, for instance, selection directionally favouring A in both diploid sexes and meiotic drive in males. Figure **??**B then shows that ploidally-antagonisitic selection can allow both neo-W haplotypes to invade.

Loose linkage with the ancestral sex-determining region

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 a neo-W ($k = 1$) into an ancestrally XY system by $\lambda_{Y',XY}$ and $\lambda_{W',XY}$, respectively, which are

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

and

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

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $S_A = (D^{\male} + \alpha_\Delta^{\male} + t^{\male}) - (D^{\female} + \alpha_\Delta^{\female} + t^{\female})$ describes sex differences in selection for the A versus a across diploid selection, meiosis, and gametic competition. The diploid selection term, $D^{\sharp} = \left(\bar{p}s^{\sharp} + (1-\bar{p})h^{\sharp}s^{\sharp}\right) - \left(\bar{p}h^{\sharp}s^{\sharp} + (1-\bar{p})\right)$, is the difference in fitness between A and a alleles in diploids of sex $\sharp \in \{\female, \male\}$, where $\bar{p}$ is the leading-order probability 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) 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., 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 (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 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 section, with weak selection and no haploid selection ($t^{\sharp} = \alpha_\Delta^{\sharp} = 0$), as considered by van Doorn and Kirkpatrick (2010), the spread of a neo-W is equivalent to the 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 closely linked to a locus under selection ($R < r$). However, if there is any haploid selection, the additional term in equation (3) can be positive, which can allow, for example, neo-W invasion ($\lambda_{W',XY} > 1$) even when the neo-sex-determining region is less closely linked to the selected locus ($R > r$). These transitions are

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 weakened. Mean diploid fitness therefore decreases during heterogametic transitions that create looser sex-linkage (Figure 4B,D).

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 $\lambda_{W',XY} > 1$, we consider several special cases. Firstly, if the **A** locus is unlinked to the ancestral sex-determining region ($r = 1/2$), a more closely linked neo-W ($R < 1/2$) can always invade because there is then no association between A alleles and sex chromosomes, $\left(\hat{p}_Y^{\male} - \hat{p}_X^{\male}\right) = 0$. The second term in equation (3) then disappears 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-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 the special case where $R = 1/2$ and $r < 1/2$ (e.g., the selected locus is on the ancestral sex chromosome and the novel sex-determining locus arises on an autosome). In table 3 we give the conditions where invasion occurs when we further assume that haploid selection only occurs in one sex (e.g., during male meiosis only) and dominance coefficients are equal in the two sexes, $h^{\female} = h^{\male}$. When there is no gametic competition and meiotic drive is in one sex only, an unlinked neo-W can invade as long as the same allele is favoured during diploid selection in males and females ($s^{\female} s^{\male} > 0$, see Figure 6B). When there is no meiotic drive and gametic competition occurs in one sex only, an unlinked neo-W can invade as long as the same allele is favoured in male and female diploid selection and there are sex differences in selection of one type (e.g., $s^{\female}(s^{\male} - s^{\female}) > 0$, see Figure 6C,D). These special cases indicate that neo-W invasion can occur for a relatively large fraction of parameter space, even if the neo-W uncouples the sex-determining locus from a locus under selection.

Previous research suggests that when the ancestral sex-determining locus is linked to a locus that experiences haploid selection (e.g., meiotic drive), 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	$h^{♂} = h^{♀}$, $t^{♀} = t^{♂} = \alpha_{\Delta}^{♀} = 0$	$s^{♀}s^{♂} > 0$
female drive only	$h^{♂} = h^{♀}$, $t^{♀} = t^{♂} = \alpha_{\Delta}^{♂} = 0$	$s^{♀}s^{♂} > 0$
sperm competition only	$h^{♂} = h^{♀}$, $t^{♀} = \alpha_{\Delta}^{♀} = \alpha_{\Delta}^{♂} = 0$	$s^{♀}(s^{♂} - s^{♀}) > 0$
egg competition only	$h^{♂} = h^{♀}$, $t^{♂} = \alpha_{\Delta}^{♀} = \alpha_{\Delta}^{♂} = 0$	$s^{♂}(s^{♀} - s^{♂}) > 0$

unlinked sex-determining locus invades in order to restore equal sex ratios (Kozielska et al. 2010). Consider, for example, the case where the **A** locus is linked to the ancestral-SDR ($r < 1/2$) and experiences meiotic drive in males only (e.g., during spermatogenesis but not during oogenesis, $\alpha^{♂} \neq 1/2$, $\alpha^{♀} = 1/2$). Disregarding gametic competition ($t^{♀} = t^{♂} = 0$) such that zygotic sex ratios are only biased by meiotic drive in males. In this case, the zygotic sex ratio can be initially biased 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 transitions. 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 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 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 linkage becomes tighter), this symmetry between sex-ratio selection and haploid selection is lost, causing differences in the strength of selection favouring the two heterogametic transitions (compare red to black near -25cM and 25 cM in Figure 6).

Environmental sex determination

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

(environmental sex 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

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

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

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

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

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).

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.

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 $\lambda_{Y',XY} = \lambda_{W',ZW}$, $\lambda_{W',XY} = \lambda_{Y',ZW}$). Thus, by the same argument as above (if drive only occurs in males then the sex ratio is only biased when the ancestral 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. 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 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 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 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 $r < 1/2$).

Discussion

Two predominant theories explaining the remarkably high frequency of transitions between sex-determination systems are sexually-antagonistic selection and sex-ratio selection (reviewed in Blaser et al. 2012) (van Doorn, 2014, sexual development). 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 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 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 relative to selection or selection happens in both diploid and haploid phases.

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-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 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-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 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 that looser sex-linkage could evolve, even in the absence of haploid selection (Figure 7A), was overlooked in van Doorn and Kirkpatrick (2010), likely because they did not explicitly calculate the resident equilibria (equation S.2; Lloyd and Webb 1977, Otto 2014). Interestingly, there is substantial overlap between the parameter 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 chromosomes (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 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.

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 locus (van Doorn and Kirkpatrick 2007; 2010). Our results show that genetic variation at loci that experience haploid selection can generate selection in favour of 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. 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 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-

cestral sex-determination system and/or females (males) are the rarer sex. With sexually-antagonistic selection (between diploid sexes) only, linkage between a selected locus and the sex-determining region strengthens associations between male beneficial alleles and the male-determining allele (Y or Z) and between female beneficial 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 region. Therefore, new sex-determining alleles only invade if they are more closely linked than the ancestral sex-determining region. However, if there is haploid selection on loci linked to an XY (ZW) sex-determining region, selection can maintain polymorphisms at which the product of the frequency of females (males) and 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 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).

Sex ratio biases caused by gametic competition or meiotic drive have been shown to exert Fisherian sex-ratio selection on various autosomal (Stalker 1961, 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 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 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 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 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 3), preventing the neo-W from invading. Indeed, these additional selective effects can even favour transitions between sex-determining systems that create new sex-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

(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 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 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 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 heterogametic transitions both via sex-ratio selection and via fitness effects of alleles that are associated with the neo-sex-determining allele, and these selection pressures are often of equal magnitude.

We assume that sex-determining alleles do not experience direct selection except 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 or W) in the ancestral sex-determining region because recessive deleterious mutations and/or deletions may fix around the Y or W allele (Rice 1996, Charlesworth 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 that all individuals have YY or WW genotypes (Figure 1). Any recessive deleterious alleles linked to the Y or W will therefore be revealed to selection during a heterogametic transition. This phenomenon was studied by van Doorn and Kirkpatrick (2010), who found that degeneration can prevent fixation of a neo-W or a neo-Y allele, leading to a mixed sex-determination system where the ancestral- and neo- sex-determining loci are both polymorphic. However, they noted that very rare recombination events around the ancestral sex-determining region can allow these heterogametic transitions to complete. While not explicitly studied, we also predict that Y or W degeneration would prevent fixation of the new sex-determiners considered here.

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-

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 can be heavily dependent on the interaction between two loci and the recombination rate between them, which in turn can be affected by sex-linkage if there is reduced recombination between sex chromosomes (Hurst and Pomiankowski 1991). Furthermore, in some cases, a driving allele may act by killing any gametes that carry a 'target' allele at another locus, in which case there is a two-locus drive system and the total number of gametes produced can be reduced by meiotic drive. 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 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 donate 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, the evolution of new sex-determination system could by influenced by these dynamics. How the evolution of new sex-determining mechanisms could be influenced by two-locus meiotic drive and/or by ecological feedbacks under different mating systems remains to be studied.

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

selection to maintain polymorphisms under a different and larger parameter space (Rice 1987, Jordan and Charlesworth 2011). As with sexually-antagonistic selection, the presence of haploid selected loci around ancestral- or novel-sex-determining regions could support their role in sex chromosome turnover. A recent transcriptome 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 pollen but not in male diploids, indicating variation currently or previously maintained by haploid selection; over-expression also occurs on the autosome that is orthologous to the sex chromosomes in closely related species (Sandler et al., 2017, Personal Communication).

Taken at face value, our results indicate that transitions in heterogametey (XY to ZW or vice versa) are more likely than transitions in homogamety when genetic conflict is predominately between the haploids of each sex (e.g., with $|D^{\male} - D^{\female}| << |\alpha_{\Delta}^{\male} - \alpha_{\Delta}^{\female} + t^{\male} - t^{\female}|$ we have $\lambda_{W',XY} > \lambda_{Y',XY}$; equations 3 and S.5). In addition, because 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-determination systems (e.g., the final state in Figure 1C is the starting state in Figure 1B). Potentially, successive heterogametic transitions between master regulators of sex-determination could be inferred from careful examination of the molecular pathways by which sex is determined. Our predictions could also be examined 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 competition. Furthermore, assuming that transitions from dioecy to hermaphroditism (equal parental investment in male and female gametes) are favoured in a similar manner to the ESD examined here (equal probability of zygotes developing as males or females), our results suggest that haploid competition during the multicellular haploid stage could drive transitions between dioecy and hermaphroditism in plants (Käfer et al., 2017, Sabath et al., 2017). In animals, one might expect gametic 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.

References

Arunkumar, R., E. B. Josephs, R. J. Williamson, and S. I. Wright. 2013. Pollen-specific, but not sperm-specific, genes show stronger purifying selection and higher rates of positive selection than sporophytic genes in *Capsella grandiflora*. Molecular biology and evolution 30:2475–2486.

Bachtrog, D. 2006. A dynamic view of sex chromosome evolution. Current opinion in genetics & development 16:578–585.

Bachtrog, D., J. E. Mank, C. L. Peichel, M. Kirkpatrick, S. P. Otto, T.-L. Ashman, M. W. Hahn, J. Kitano, I. Mayrose, R. Ming, N. Perrin, L. Ross, N. Valenzuela,

J. C. Vamosi, and Tree of Sex Consortium. 2014. Sex determination: why so many ways of doing it? PLoS Biol 12:e1001899.

Beukeboom, L. W., and N. Perrin. 2014. The evolution of sex determination. Oxford University Press, Oxford, UK.

Blaser, O., C. Grossen, S. Neuenschwander, and N. Perrin. 2012. Sex-chromosome turnovers induced by deleterious mutation load. Evolution 67:635–645.

Borg, M., L. Brownfield, and D. Twell. 2009. Male gametophyte development: a molecular perspective. Journal of Experimental Botany 60:1465–1478.

Bull, J. J. 1983. Evolution of sex determining mechanisms. The Benjamin Cummings Publishing Company.

Burt, A., and R. Trivers. 2006. Genes in conflict: the biology of selfish genetic elements. Belknap Press, Cambridge, MA.

Charlesworth, B., and D. Charlesworth. 2000. The degeneration of Y chromosomes. Philosophical transactions of the Royal Society of London. Series B, Biological sciences 355:1563–1572.

Charlesworth, D., and J. E. Mank. 2010. The birds and the bees and the flowers and the trees: lessons from genetic mapping of sex determination in plants and animals. Genetics 186:9–31.

Charnov, E. L. 1982. The theory of sex allocation. Monographs in population biology.

Clarke, H. J., T. N. Khan, and K. H. M. Siddique. 2004. Pollen selection for chilling tolerance at hybridisation leads to improved chickpea cultivars. Euphytica 139:65–74.

Conn, J. S., and U. Blum. 1981. Sex ratio of *Rumex hastatulus*: the effect of environmental factors and certation. Evolution 35:1108–1116.

Conover, D. O., and S. W. Heins. 1987. Adaptive variation in environmental and genetic sex determination in a fish. Nature 326:496–498.

Ezaz, T., S. D. Sarre, and D. O'Meally. 2009. Sex chromosome evolution in lizards: independent origins and rapid transitions. Cytogenetic and Genome Research 127:249–260.

Field, D. L., M. Pickup, and S. C. H. Barrett. 2012. The influence of pollination intensity on fertilization success, progeny sex ratio, and fitness in a wind-pollinated, dioecious plant. International Journal of Plant Sciences 173:184–191.

———. 2013. Comparative analyses of sex-ratio variation in dioecious flowering plants. Evolution 67:661–672.

Fisher, R. 1930. The genetical theory of natural selection. Clarendon Press, London.

Frank, S. A. 1989. The Evolutionary Dynamics of Cytoplasmic Male Sterility. American Naturalist 133:345–376.

Gossmann, T. I., M. W. Schmid, U. Grossniklaus, and K. J. Schmid. 2014. Selection-driven evolution of sex-biased genes Is consistent with sexual selection in *Arabidopsis thaliana*. Molecular biology and evolution 31:574–583.

Haldane, J. B. S. 1919. The combination of linkage values and the calculation of distances between the loci of linked factors. Journal of Genetics 8:299–309.

Hamilton, W. D. 1967. Extraordinary sex ratios. Science 156:477–488.

Hedhly, A., J. I. Hormaza, and M. Herrero. 2004. Effect of temperature on pollen tube kinetics and dynamics in sweet cherry, *Prunus avium* (Rosaceae). American journal of botany 91:558–564.

Hillis, D. M., and D. M. Green. 1990. Evolutionary changes of heterogametic sex in the phylogenetic history of amphibians. Journal of Evolutionary Biology 3:49–64.

Holleley, C. E., D. O'Meally, S. D. Sarre, J. A. Marshall Graves, T. Ezaz, K. Matsubara, B. Azad, X. Zhang, and A. Georges. 2015. Sex reversal triggers the rapid transition from genetic to temperature-dependent sex. Nature 523:79–82.

Holman, L., T. A. R. Price, N. Wedell, and H. Kokko. 2015. Coevolutionary dynamics of polyandry and sex-linked meiotic drive. Evolution 69:709–720.

Hormaza, J. I., and M. Herrero. 1996. Male gametophytic selection as a plant breeding tool. Scientia horticulturae 65:321–333.

Hough, J., S. Immler, S. Barrett, and S. P. Otto. 2013. Evolutionarily stable sex ratios and mutation load. Evolution 7:1915–1925.

Hurst, L. D., and A. Pomiankowski. 1991. Causes of sex ratio bias may account for unisexual sterility in hybrids: a new explanation of Haldane's rule and related phenomena. Genetics 128:841–858.

Immler, S., G. Arnqvist, and S. P. Otto. 2012. Ploidally antagonistic selection maintains stable genetic polymorphism. Evolution 66:55–65.

Immler, S., C. Hotzy, G. Alavioon, E. Petersson, and G. Arnqvist. 2014. Sperm variation within a single ejaculate affects offspring development in Atlantic salmon. Biology letters 10:20131040.

Jordan, C. Y., and D. Charlesworth. 2011. The potential for sexually antagonistic polymorphism in different genome regions. Evolution 66:505–516.

Joseph, S., and M. Kirkpatrick. 2004. Haploid selection in animals. Trends in Ecology & Evolution 19:592–597.

Karlin, S., and J. McGregor. 1972*a*. Application of method of small parameters to multi-niche population genetic models. Theoretical Population Biology 3:186–209.

———. 1972*b*. Polymorphisms for genetic and ecological systems with weak coupling. Theoretical Population Biology 3:210–238.

Kozielska, M., F. J. Weissing, L. W. Beukeboom, and I. Pen. 2010. Segregation distortion and the evolution of sex-determining mechanisms. Heredity 104:100–112.

Lenormand, T., and J. Dutheil. 2005. Recombination difference between sexes: a role for haploid selection. PLoS Biol 3:e63.

Li, J., R. B. Phillips, A. S. Harwood, B. F. Koop, and W. S. Davidson. 2011. Identification of the Sex Chromosomes of Brown Trout *(Salmo trutta)* and Their Comparison with the Corresponding Chromosomes in Atlantic Salmon *(Salmo salar)* and Rainbow Trout *(Oncorhynchus mykiss)*. Cytogenetic and Genome Research 133:25–33.

Lindholm, A., and F. Breden. 2002. Sex chromosomes and sexual selection in poeciliid fishes. The American Naturalist 160 Suppl 6:S214–24.

Lindholm, A. K., K. A. Dyer, R. C. Firman, L. Fishman, W. Forstmeier, L. Holman, H. Johannesson, U. Knief, H. Kokko, A. M. Larracuente, A. Manser, C. Montchamp-Moreau, V. G. Petrosyan, A. Pomiankowski, D. C. Presgraves, L. D. Safronova, A. Sutter, R. L. Unckless, R. L. Verspoor, N. Wedell, G. S. Wilkinson, and T. A. R. Price. 2016. The Ecology and Evolutionary Dynamics of Meiotic Drive. Trends in Ecology & Evolution 31:315–326.

Lloyd, D. G. 1974. Female-predominant sex ratios in angiosperms. Heredity 32:35–44.

Lloyd, D. G., and C. Webb. 1977. Secondary sex characters in plants. Botanical Review 43:177–216.

Mank, J. E., D. E. L. Promislow, and J. C. Avise. 2006. Evolution of alternative sexâĂŘdetermining mechanisms in teleost fishes. Biological Journal of the Linnean Society 87:83–93.

Marais, G. A. B., M. Nicolas, R. Bergero, P. Chambrier, E. Kejnovsky, F. Monéger, R. Hobza, A. Widmer, and D. Charlesworth. 2008. Evidence for degeneration of the Y chromosome in the dioecious plant *Silene latifolia*. Current Biology 18:545–549.

Ming, R., A. Bendahmane, and S. S. Renner. 2011. Sex chromosomes in land plants. Annu. Rev. Plant Biol. 62:485–514.

Mulcahy, D. L., M. Sari-Gorla, and G. B. Mulcahy. 1996. Pollen selection - past, present and future. Sexual Plant Reproduction 9:353–356.

Myosho, T., H. Otake, H. Masuyama, M. Matsuda, Y. Kuroki, A. Fujiyama, K. Naruse, S. Hamaguchi, and M. Sakaizumi. 2012. Tracing the Emergence of a Novel Sex-Determining Gene in Medaka, Oryzias luzonensis. Genetics 191:163–170.

Ogata, M., Y. Hasegawa, H. Ohtani, M. Mineyama, and I. Miura. 2007. The ZZ/ZW sex-determining mechanism originated twice and independently during evolution of the frog, Rana rugosa. Heredity 100:92–99.

Otto, S. P. 2014. Selective maintenance of recombination between the sex chromosomes. Journal of Evolutionary Biology 27:1431–1442.

Otto, S. P., M. F. Scott, and S. Immler. 2015. Evolution of haploid selection in predominantly diploid organisms. Proc Natl Acad Sci 112:15952–15957.

Pen, I., T. Uller, B. Feldmeyer, A. Harts, G. M. While, and E. Wapstra. 2010. Climate-driven population divergence in sex-determining systems. Nature 468:436–438.

Pokorná, M., and L. Kratochvíl. 2009. Phylogeny of sexâĂŘdetermining mechanisms in squamate reptiles: are sex chromosomes an evolutionary trap? Zoological Journal of the … 156:168–183.

Ravikumar, R. L., B. S. Patil, and P. M. Salimath. 2003. Drought tolerance in sorghum by pollen selection using osmotic stress. Euphytica 133:371–376.

Rice, W. R. 1987. The accumulation of sexually antagonistic genes as a selective agent promoting the evolution of reduced recombination between primitive sex chromosomes. Evolution 41:911.

———. 1996. Evolution of the Y Sex Chromosome in Animals. BioScience 46:331–343.

Ser, J. R., R. B. Roberts, and T. D. Kocher. 2010. Multiple interacting loci control sex determination in lake Malawi cichlid fish. Evolution 64:486–501.

Slancarova, V., J. Zdanska, B. Janousek, M. Talianova, C. Zschach, J. Zluvova, J. Siroky, V. Kovacova, H. Blavet, J. Danihelka, B. Oxelman, A. Widmer, and B. Vyskot. 2013. Evolution of sex determination systems with heterogametic males and females in *Silene*. Evolution 67:3669–3677.

Smith, D. A. S. 1975. All-female broods in the polymorphic butterfly Danaus chrysippus L. and their ecological significance. Heredity 34:363–371.

Stalker, H. D. 1961. The Genetic Systems Modifying Meiotic Drive in Drosophila Paramelanica. Genetics 46:177–202.

Stehlik, I., and S. Barrett. 2005. Mechanisms governing sex-ratio variation in dioecious *Rumex nivalis*. Evolution 59:814–825.

Stehlik, I., and S. C. H. Barrett. 2006. Pollination intensity influences sex ratios in dioecious Rumex nivalis, a wind-pollinated plant. Evolution 60:1207–1214.

Taylor, J. E., and J. Jaenike. 2002. Sperm competition and the dynamics of X chromosome drive: stability and extinction. Genetics 160:1721–1731.

Tripathi, N., M. Hoffmann, E.-M. Willing, C. Lanz, D. Weigel, and C. Dreyer. 2009. Genetic linkage map of the guppy, Poecilia reticulata, and quantitative trait loci analysis of male size and colour variation. Proceedings. Biological sciences / The Royal Society 276:2195–2208.

Úbeda, F., and D. Haig. 2005. On the evolutionary stability of Mendelian segregation. Genetics 170:1345–1357.

Úbeda, F., M. M. Patten, and G. Wild. 2015. On the origin of sex chromosomes from meiotic drive. Proceedings of the Royal Society B: Biological Sciences 282:20141932.

van Doorn, G. S., and M. Kirkpatrick. 2007. Turnover of sex chromosomes induced by sexual conflict. Nature 449:909–912.

———. 2010. Transitions Between Male and Female Heterogamety Caused by Sex-Antagonistic Selection. Genetics 186:629–645.

Vibranovski, M. D., D. S. Chalopin, H. F. Lopes, M. Long, and T. L. Karr. 2010. Direct evidence for postmeiotic transcription during *Drosophila melanogaster* spermatogenesis. Genetics 186:431–433.

Vicoso, B., and D. Bachtrog. 2015. Numerous transitions of sex chromosomes in Diptera. PLoS Biol 13:e1002078.

West, S. 2009. Sex allocation. Princeton University Pres.

Yano, A., B. Nicol, E. Jouanno, E. Quillet, A. Fostier, R. Guyomard, and Y. Guiguen. 2012. The sexually dimorphic on the Y-chromosome gene (sdY) is a conserved male-specific Y-chromosome sequence in many salmonids. Evolutionary Applications 6:486–496.

Zheng, Y., X. Deng, and P. A. Martin-DeLeon. 2001. Lack of sharing of Spam1 (Ph-20) among mouse spermatids and transmission ratio distortion. Biology of Reproduction 64:1730–1738.

Figures

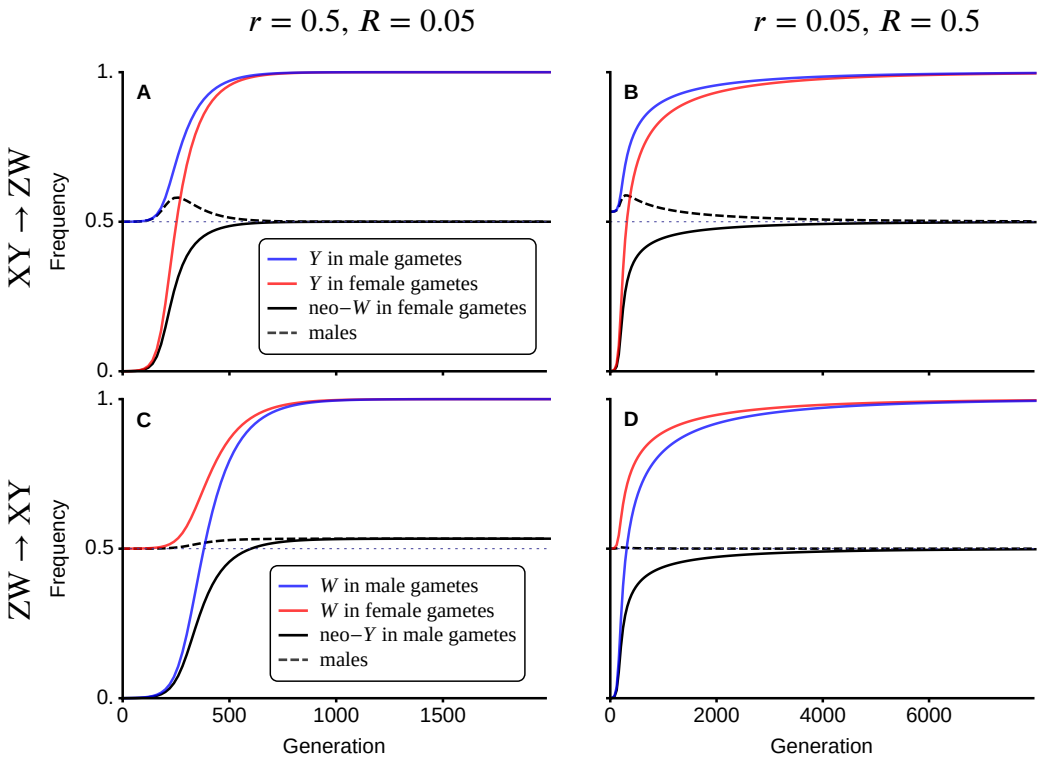

Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occur similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines 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 ($t^{\varphi} = t^{\sigma} = 0$) and meiotic drive occurs during male meiosis only ($\alpha_{\Delta}^{\varphi} = 0$, $\alpha_{\Delta}^{\sigma} = -1/5$). 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-detemining region ($r = 1/2$, $R = 1/20$) such that a neo-Y can caused 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-detemining 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, $s^{\varphi} = s^{\sigma} = 1/5$, $h^{\varphi} = h^{\sigma} = 7/10$. Aesthetic adjustments: Add chromosome cartoons to depict recombination rates?

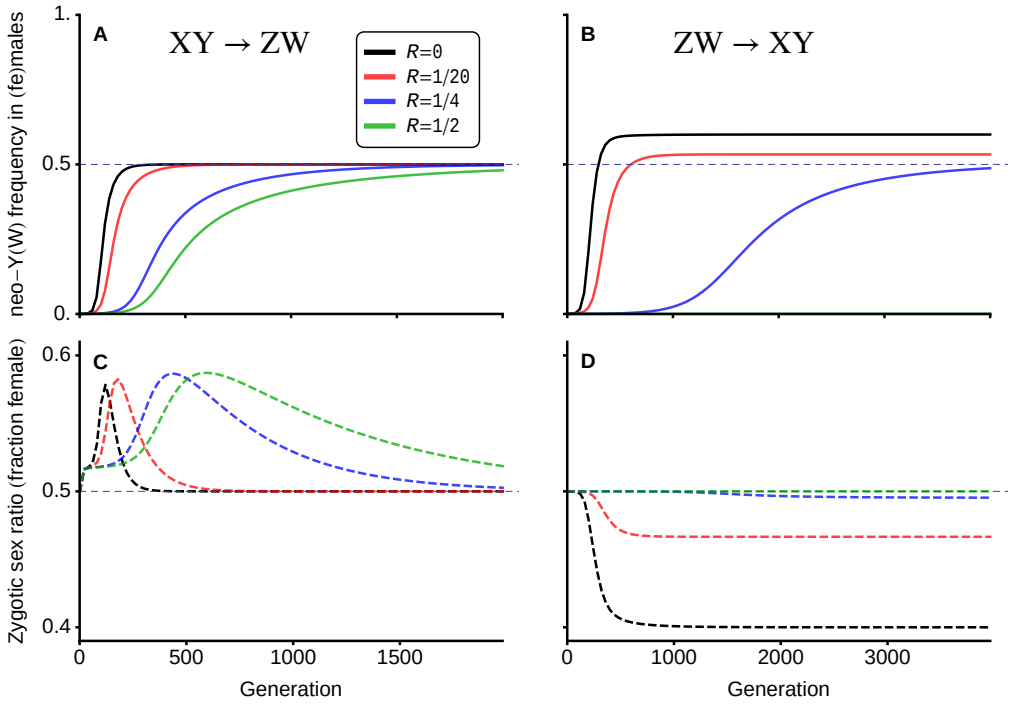

Figure 2: Is this what Sally was thinking? I think this works but I'm confused as to why the speed of spread should be so much different for XY and ZW here. Figure 1 and 6 suggests that there's not much difference between XY->ZW and ZW->XY. Maybe we should just stick with the 4 cases in figure 1.

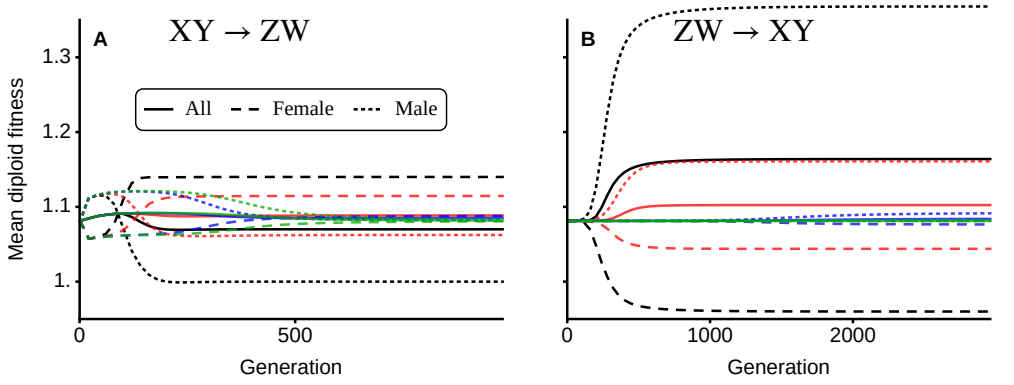

Figure 3: This complicated thing matches the plot above. I don't think we want to include it...?

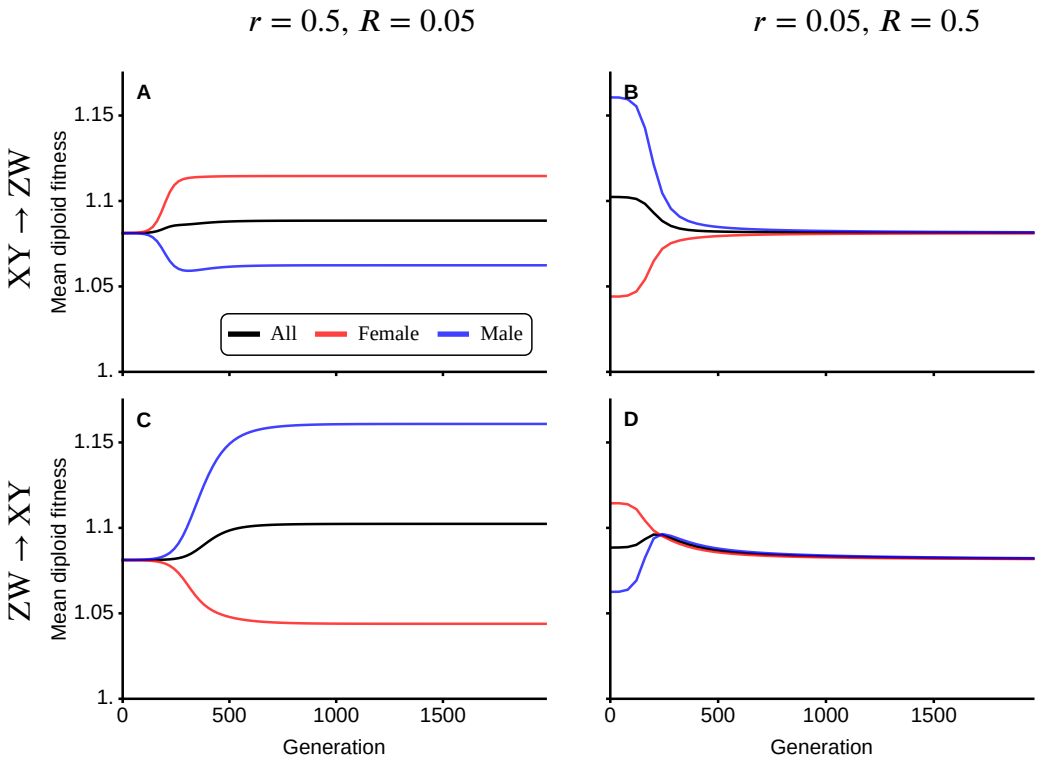

Figure 4: Changes in mean diploid fitness of males (blue lines), females (red lines), and the entire population (black lines) during the transitions between sex-determination systems shown in Figure 1. Here mean diploid fitness of a particular sex is its mean diploid viability fitness times twice its 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.

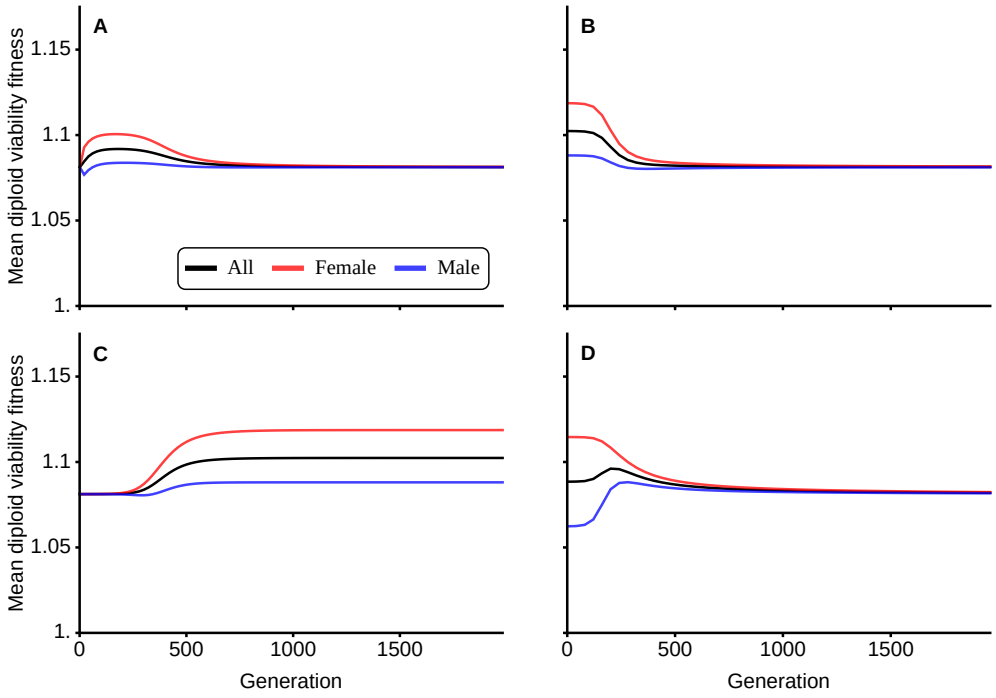

Figure 5: Last plot with mean fitness of sexes corrected for sex ratio. Could add to previous plot with dashed lines?

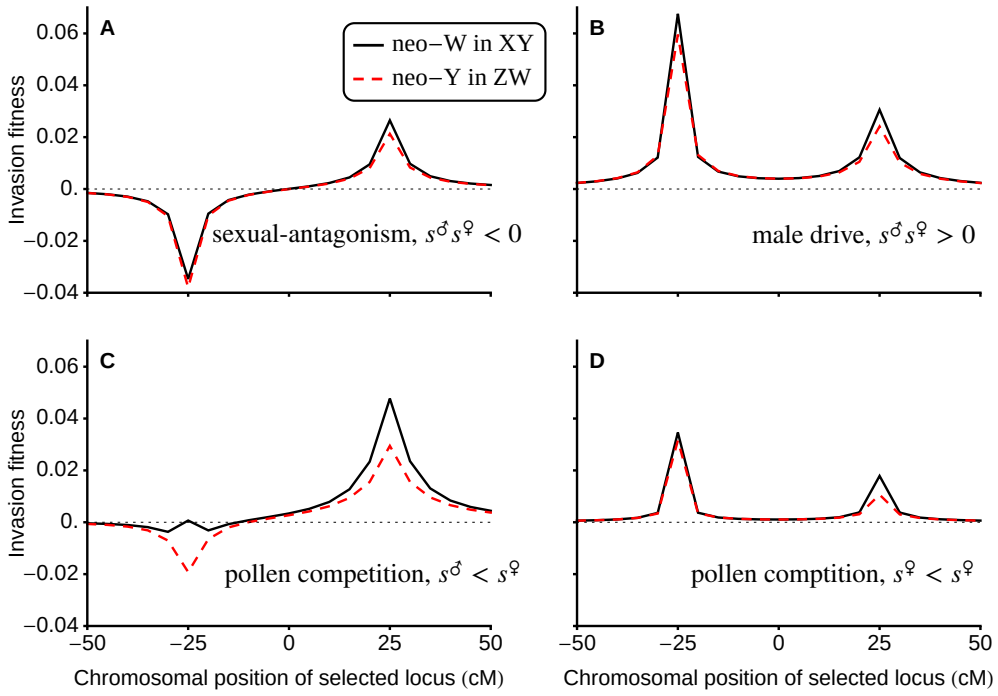

Figure 6: Invasion fitness of a neo-W allele plotted against the relative genomic location of a locus under direct selection, **A**, for various selective regimes. The ancestral sex-determining locus is located at -25 and the novel sex-determining locus is located at 25. We use Haldane's map function (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 ($t^{♀}_{♂} = \alpha^{♀}_{\Delta} = 0$) 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 ($s^{♀} = 1/10$, $h^{♀} = 7/10$ $s^{♂} = -1/10$, $h^{♂} = 3/10$). In B-D we include haploid selection and assume that selection in diploids is not sexually-antagonistic ($s^{♀}s^{♂} > 0$). 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 ($\alpha^{♂}_{\Delta} = -1/20$), no female meiotic drive or gametic competition, $t^{♀}_{♂} = \alpha^{♀}_{\Delta} = 0$), and equal selection in diploid sexes ($s^{♀} = s^{♂} = 1/10$, $h^{♀} = h^{♂} = 7/10$). 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, $t^{♂} = -1/10$) and no meiotic drive or gametic competition in females ($t^{♀} = \alpha^{♀}_{\Delta} = 0$). In this case, the neo-W does not invade if $s^{♀} > s^{♂}$ (panel C: $s^{♀} = 3/20$, $s^{♂} = 1/20$) but does if $s^{♀} < s^{♂}$ (panel D: $s^{♀} = 1/20$, $s^{♂} = 3/20$), see Table 3.

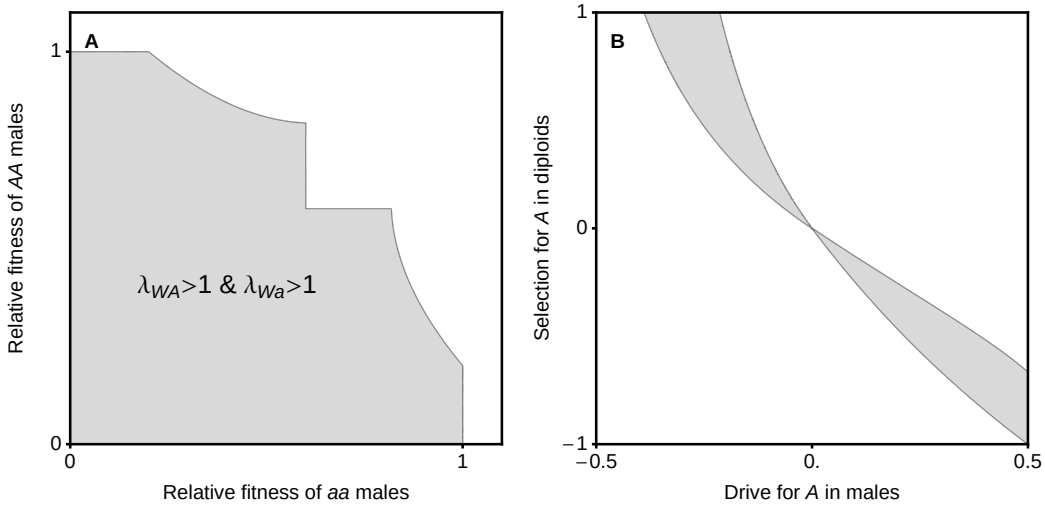

Figure 7: Parameter space (gray) where both neo-W haplotypes can invade from the same stable resident $r = 0$ equilibria (equations S.2), and therefore where an unlinked neo-W can invade an XY system with perfect sex-linkage. **A**, In the absence of haploid selection, both neo-W haplotypes can invade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

Appendix

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 $p^{\female}_{x_1,x_2,a_1,a_2,m_1,m_2}$ 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 $x^{\female}_{ij}$ and $y^{\female}_{ij}$, where $\female \in \{\male, \female\}$ 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, $\sum_{i,j} x^{\female}_{ij} + y^{\female}_{ij} = 1$.

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 $x^{\female,s}_{ij} = w_i x^{\female}_{ij} / \bar{w}^{\female}_H$ and $y^{\female,s}_{ij} = w_i y^{\female}_{ij} / \bar{w}^{\female}_H$, where $\bar{w}^{\female}_H = \sum_{i,j} w_i x^{\female}_{ij} + w_i y^{\female}_{ij}$ is the mean fitness of male ($\female = \male$) or female ($\female = \female$) gametes.

Random mating then occurs between gametes to produce diploid zygotes. To 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, $xx_{ij} = (x_i^{♀,s} x_j^{♂,s} + x_j^{♀,s} x_i^{♂,s})/2$ and $yy_{ij} = (y_i^{♀,s} y_j^{♂,s} + y_j^{♀,s} y_i^{♂,s})/2$.

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

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

Finally, these diploids undergo meiosis to produce the next generation of gametes. Recombination and sex-specific meiotic drive occur during meiosis. Here, we allow any relative locations for the SDR, **A**, and **M** loci by using three parameters to describe the recombination rates between them. R is the recombination rate between the **A** locus and the **M** locus, χ is the recombination rate between the **M** locus and the **X** locus, and r is the recombination rate between the **A** locus and the **X** locus. Table S.1 shows how χ can be substituted to give any linear order of loci. During meiosis in sex $\mathfrak{♂}$, meiotic drive occurs such that, in Aa heterozygotes, a fraction $\alpha^{\mathfrak{♂}}$ of gametes produced carry the A allele and $(1 - \alpha^{\mathfrak{♂}})$ carry the a allele.

Among gametes from sex $\mathfrak{♀}$ (sperm/pollen when $\mathfrak{♀} = ♂$, eggs/ovules when

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	$\chi = (R-r)/(1-2r)$

892 $\male = \female$), the frequencies of haplotypes (before gametic competition) in the next generation are given by

$$
\begin{aligned}
x_{MA}^{\male'} =& x x_{11}^{\male,s} + x x_{13}^{\male,s}/2 + (x x_{12}^{\male,s} + x x_{14}^{\male,s})\alpha^{\female} \\
&- R(x x_{14}^{\male,s} - x x_{23}^{\male,s})\alpha^{\female} \\
&+ (x y_{11}^{\male,s} + x y_{13}^{\male,s})/2 + (x y_{12}^{\male,s} + x y_{14}^{\male,s})\alpha^{\female} \\
&- r(x y_{12}^{\male,s} - x y_{21}^{\male,s})\alpha^{\female} - \chi(x y_{13}^{\male,s} - x y_{31}^{\male,s})/2 \\
&+ \big\{ -(R+r+\chi) x y_{14}^{\male,s} + (r+\chi-R) x y_{41}^{\male,s} \\
&+ (R+r-\chi) x y_{23}^{\male,s} + (R+\chi-r) x y_{32}^{\male,s} \big\}\alpha^{\female}/2 \\
x_{Ma}^{\female'} =& x x_{22}^{\female,s} + x x_{24}^{\female,s}/2 + (x x_{12}^{\female,s} + x x_{23}^{\female,s})\alpha^{\female} \\
&- R(x x_{23}^{\female,s} - x x_{14}^{\female,s})\alpha^{\female} \\
&(x y_{22}^{\female,s} + x y_{24}^{\female,s})/2 + (x y_{21}^{\female,s} + x y_{23}^{\female,s})(1-\alpha^{\female}) \\
&- r(x y_{21}^{\female,s} - x y_{12}^{\female,s})(1-\alpha^{\female}) - \chi(x y_{24}^{\female,s} - x y_{42}^{\female,s})/2 \\
&+ \big\{ -(R+r+\chi) x y_{23}^{\female,s} + (r+\chi-R) x y_{32}^{\female,s} \\
&+ (R+r-\chi) x y_{14}^{\female,s} + (R+\chi-r) x y_{41}^{\female,s} \big\}(1-\alpha^{\female})/2
\end{aligned}
\tag{S.1a}
\tag{S.1b}
$$

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

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

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

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

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

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

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

Resident equilibrium and stability

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

types: $x^{\varphi}_{MA} = p^{\varphi}_X$, $x^{\varphi}_{Ma} = 1 - p^{\varphi}_X$, $x^{\delta}_{MA} = (1-q)p^{\delta}_X$, $x^{\delta}_{Ma} = (1-q)(1-p^{\delta}_X)$, $y^{\delta}_{MA} = qp^{\delta}_Y$, and $y^{\delta}_{Ma} = q(1-p^{\delta}_Y)$. Mean fitnesses in the resident population are given in table S.2.

Various forms of selection can maintain a polymorphism at the **A** locus, including sexually antagonistic selection, overdominance, conflicts between diploid selection and selection upon haploid genotypes (ploidally antagonistic selection, Immler et al. 2012), 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 ($\bar{w}^{\varphi}_H$)	$p^{\varphi}_X w^{\varphi}_A + (1-p^{\varphi}_X)w^{\varphi}_a$
male gametes ($\bar{w}^{\delta}_H$)	$\bar{p}^{\delta} w^{\delta}_A + (1-\bar{p}^{\delta})w^{\delta}_a$
females ($\bar{w}^{\varphi}$)	$\{p^{\varphi}_X w^{\varphi}_A p^{\delta}_X w^{\delta}_A w^{\varphi}_{AA} +$ $(1-p^{\varphi}_X)w^{\varphi}_a p^{\delta}_X w^{\delta}_A w^{\varphi}_{Aa} +$ $p^{\varphi}_X w^{\varphi}_A (1-p^{\delta}_X) w^{\delta}_a w^{\varphi}_{Aa} +$ $(1-p^{\varphi}_X)w^{\varphi}_a(1-p^{\delta}_X)w^{\delta}_a w^{\varphi}_{aa}\}/\{\bar{w}^{\varphi}_H \bar{w}^{\delta}_H \zeta\}$
males ($\bar{w}^{\delta}$)	$\{p^{\varphi}_X w^{\varphi}_A p^{\delta}_Y w^{\delta}_A w^{\delta}_{AA} +$ $(1-p^{\varphi}_X)w^{\varphi}_a p^{\delta}_Y w^{\delta}_A w^{\delta}_{Aa} +$ $p^{\varphi}_X w^{\varphi}_A (1-p^{\delta}_Y) w^{\delta}_a w^{\delta}_{Aa} +$ $(1-p^{\varphi}_X)w^{\varphi}_a(1-p^{\delta}_Y)w^{\delta}_a w^{\delta}_{aa}\}/\{\bar{w}^{\varphi}_H \bar{w}^{\delta}_H (1-\zeta)\}$
zygotic sex ratio ζ	$\{(1-q)(p^{\delta}_X w^{\delta}_A + (1-p^{\delta}_X)w^{\delta}_a)\}/\bar{w}^{\delta}_H$

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

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

We first calculate the equilibrium frequency of the Y and A alleles in the ancestral population when the recombination rate between the **X** and **A** loci is small (r of order ϵ). 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 equilibria that maintain both A and a alleles, four of which are given to leading order by:

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

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

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

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

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

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

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

A fifth equilibrium (C) also exists where A is present at an intermediate frequency on the Y chromosome ($0 < \hat{p}_Y^{\male} < 1$). However, equilibrium (C) is never locally stable when $r \approx 0$ and is therefore not considered further. Thus, the Y can either be fixed for the a allele (equilibria A and B) or the A allele (equilibria A' and B'). The X chromosome can then either be polymorphic (equilibria A and A')

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

We next calculate when (A) and (B) are locally stable for $r = 0$. According to the 'small parameter theory' (Karlin and McGregor 1972*a*;*b*), these stability 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 $\bar{w}_{Ya}^{\male} > \bar{w}_{YA}^{\male}$ where $\bar{w}_{Ya}^{\male} = w_a^{\male}(2p_X^{\female}(1-\alpha^{\male})w_A^{\female}w_{Aa}^{\male} + (1-p_X^{\female})w_a^{\female}w_{aa}^{\male})$ and $\bar{w}_{YA}^{\male} = w_A^{\male}(p_X^{\female}w_A^{\female}w_{AA}^{\male} + 2(1-p_X^{\female})\alpha^{\male}w_a^{\female}w_{Aa}^{\male})$. That is, Ya haplotypes must have higher fitness than YA haplotypes. Substituting in $p_X^{\female} = \hat{p}_X^{\female}$ from above, fixation of the a allele on the Y requires that $\gamma_i > 0$ where $\gamma_{(A)} = w_a^{\male}(2(1-\alpha^{\male})w_{Aa}^{\male}\phi + w_{aa}^{\male}\psi) - w_A^{\male}(w_{AA}^{\male}\phi + 2\alpha^{\male}w_{Aa}^{\male}\psi)$ for equilibrium (A) and $\gamma_{(B)} = 2(1-\alpha^{\male})w_a^{\male}w_{Aa}^{\male} - w_A^{\male}w_{AA}^{\male}$ 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 $w_A^{\female}w_{AA}^{\female} > (1-\alpha^{\female})w_a^{\female}w_{Aa}^{\female}$.

Selection weak relative to recombination (weak selection)

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

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

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

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

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

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

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

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

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

Invasion conditions

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

the largest solution to a quadratic characteristic polynomial $\lambda^2 + b\lambda + c = 0$. It can be shown (see supplementary Mathematica file) that the coefficients are $b = -(\lambda_{mA} + \lambda_{ma}) + (\rho_{mA} + \rho_{ma})$ 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 $i \in \{A, a\}$, 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 background 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 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 locus we can calculate each of these terms exactly, while for weak selection we take a Taylor series of the leading eigenvalue.

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 assuming 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 ancestral population is at a stable equilibrium.

Starting with the simpler equilibrium (B), the terms of the characteristic polynomial are

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

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

$$\rho_{mA} = (2\alpha^{\male})^{-1} \frac{R w_a^{\male} w_A^{\female} w_{Aa}^{\female} \alpha^{\female} (1 - \alpha^{\male})}{w_A^{\male} w_A^{\female} w_{AA}^{\female}} \tag{S.6c}$$

$$\rho_{ma} = (2\alpha^{\male})^{-1} \frac{R w_A^{\male} w_a^{\female} w_{Aa}^{\female} (1 - \alpha^{\female}) \alpha^{\male}}{w_A^{\male} w_A^{\female} w_{AA}^{\female}} \tag{S.6d}$$

Haploid selection impacts the spread of neo-W haplotypes in three ways. Firstly, the zygotic sex ratio becomes male biased ($\zeta < 1/2$; at equilibrium (B) the sex ratio is $\zeta = \alpha^{\male} w_A^{\male} / [(1-\alpha^{\male}) w_a^{\male} + \alpha^{\male} w_A^{\male}]$) when the a allele (which is fixed on 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 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 frequencies in the male gametes that female gametes pair with. For instance, because an epistatically dominant neo-W always causes its carrier to become female, it creates females who carry either Y-a or X genotypes from their father. Thus, because when there is a polymorphism the X carries some non-zero frequency of A, 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 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 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 often XX and neo-W females are heterozygous. Competition among female gametes acts similarly, and depends on the frequency of A on resident X chromosomes (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 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 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.

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 $w_{Aa}^{\female} > w_{AA}^{\female}$ and $\lambda_{ma} > 1$ when $(w_{Aa}^{\female} + w_{aa}^{\female})/2 > w_{AA}^{\female}$. These conditions cannot be met under purely sexually-antagonistic selection, where a is directionally favoured in males ($w_{AA}^{\male} > w_{Aa}^{\male} > w_{aa}^{\male}$) and A is directionally favoured in females ($w_{AA}^{\female} >$

$w^{\varphi}_{Aa} > w^{\varphi}_{aa}$). 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 of those females.

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

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

When both haplotypes can spread on their own ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$), the 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 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 larger than the rate of recombination off this background (i.e., equation1 is satisfied).

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

$$\lambda_{mA} = \frac{a}{b}\left[w^{\varphi}_{AA} w^{\sigma}_{Aa} w^{\sigma}_{A} \alpha^{\sigma} \phi + 2 w^{\varphi}_{Aa} \alpha^{\varphi} w^{\sigma}_{a} \frac{c}{d}\right] / w^{\varphi}_{a} \tag{S.7a}$$

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

$$\rho_{mA} = \frac{a}{b} R\left[2 w^{\varphi}_{Aa} \alpha^{\varphi} w^{\sigma}_{a} \frac{c}{d}\right] / w^{\varphi}_{a} \tag{S.7c}$$

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

where

$$a = w^{\varphi}_{a} \phi + w^{\varphi}_{A} \psi \tag{S.8a}$$

$$b = w^{\varphi}_{AA} \phi (2 w^{\sigma}_{Aa} w^{\sigma}_{A} \alpha_{\sigma} \phi) + w^{\varphi}_{Aa} \psi (2 w^{\sigma}_{Aa} w^{\sigma}_{A} \alpha_{\sigma} \phi + w^{\sigma}_{AA} w^{\sigma}_{a} \psi) + w^{\varphi}_{aa} \psi (w^{\sigma}_{AA} w^{\sigma}_{a} \psi) \tag{S.8b}$$

$$c = 2(w^{\sigma}_{Aa} \phi)^2 (1-\alpha^{\sigma}) \alpha_{\sigma} + w^{\sigma}_{Aa} \phi (w^{\sigma}_{AA} \psi + w^{\sigma}_{aa} \psi \alpha^{\sigma}) + w^{\sigma}_{aa} \psi w^{\sigma}_{AA} \psi \tag{S.8c}$$

$$d = 2 w^{\sigma}_{Aa} \alpha^{\sigma} \phi + w^{\sigma}_{aa} \psi \tag{S.8d}$$

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.

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

$$2(w^{\varphi}_{Aa} - w^{\varphi}_{aa}) w^{\sigma}_{AA} \psi^2 > (w^{\varphi}_{AA} - w^{\varphi}_{Aa}) w^{\sigma}_{Aa} \phi (\phi - \psi) \tag{S.9}$$

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

(A) is stable. In contrast to equilibrium (B), a neo-W haplotype can spread under purely sexually-antagonistic selection ($w^{\male}_{AA} > w^{\male}_{Aa} > w^{\male}_{aa}$ and $w^{\female}_{AA} > w^{\female}_{Aa} > w^{\female}_{aa}$). 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-W-A never makes, are strongly selected against. This can be intuited from the fact that (S.9) will be more easily met when $w^{\female}_{Aa} - w^{\female}_{aa} \approx w^{\female}_{Aa}$ and $w^{\female}_{AA} - w^{\female}_{Aa} \approx 0$, implying $w^{\female}_{aa} \approx 0$ and $w^{\female}_{Aa} \approx w^{\female}_{AA}$ (although this is complicated by the fact that $w^{\female}_{aa}$ and $w^{\female}_{Aa}$ affect ϕ and ψ too, the intuition holds).

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

$$(w^{\female}_{aa} + w^{\female}_{Aa} - 2w^{\female}_{AA})w^{\male}_{Aa}\phi^2 + (w^{\female}_{aa} - w^{\female}_{Aa})(w^{\male}_{Aa} + 2w^{\male}_{AA})\phi\psi > 0 \qquad \text{(S.10)}$$

This condition cannot be met with purely sexually antagonistic selection (as both terms on the left-hand side would then be negative), but it can be met under other circumstances. For example, with overdominance in males there is selection for increased A frequencies on X chromosomes in males, which are always paired with Y-a haplotypes. Then, directional selection for a in females maintains a polymorphism at the **A** locus on the X and by creating selection for decreased A frequencies 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 Otto 2014) and facilitates the spread of neo-W-a haplotypes, which create more heterozygote and aa females than ancestral X chromosomes do.

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, $R \geq 0$. 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 occur under modest rates of recombination between the novel sex-determining and selected loci.

Selection weak relative to recombination (weak selection)

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