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

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Contributions:

Abstract

Sex-determination systems are remarkably dynamic; many taxa display shifts in the location of sex-determining loci or the evolution of entirely new sex-determining systems. Predominant theories for why we observe such transitions generally conclude that novel sex-determining systems are favoured by selection if they equalise the sex ratio or increase linkage with a sexually-antagonistic locus. We use population genetic models to extend these theories in two ways: (1) We explicitly consider how selection on very tightly sex-linked loci influences the spread of novel sex-determiners. We find that tightly sex-linked genetic variation can favour the spread of new sex-determination systems in which the heterogametic sex changes (XY to ZW or ZW to XY) and the new sex-determining region is less closely linked (or unlinked) to the sex-linked locus under selection; a result that is not found with loose sex-linkage. (2) We also consider selection upon haploid genotypes either during gametic competition (e.g., pollen/sperm competition) or meiosis (i.e., non-Mendelian segregation); selective processes that typically occur in one sex or the other. As well as having sex-specific fitness consequences, haploid selection can cause the zygotic sex ratio to become biased because sex ratios are determined by the production and fertilization success of X- versus Y-bearing pollen/sperm (or Z- versus W-bearing ovules/eggs). Consequently, selection for XY to ZW transitions and ZW to XY transitions can be 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 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. However, 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 rate at which mA haplotypes are produced by recombination, ρ_{ma}, is sufficiently greater than the rate at which ma haplotypes are, ρ_{mA}. 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 $p_Y^{\male}$). To do so we assume that the A allele reaches a stable equilibrium frequency under the ancestral sex-determination system before the neo-sex-determining allele (m) arises. We can then analytically calculate the allele frequency of the A allele using two alternative simplifying as-

sumptions: (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 ($s^{♀}$, $t^{♀}$, $\alpha_{\Delta}^{♀}$ 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 ($p_Y^{♂} = 0$), without loss of generality . If there are two alleles maintained at the **A** locus, the X can either be fixed for the A allele ($p_X^{♀} = p_X^{♂} = 1$) or polymorphic ($0<p_X^{♀}, p_X^{♂}<1$). 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.

Neo-W alleles, on the other hand, can invade an ancestral XY system under some conditions (given in detail in the appendix). Briefly, neo-W-A and/or neo-W-a haplotypes can spread when rare in the absence of recombination ($\lambda_{ma} > 1$ and/or $\lambda_{mA} > 1$), depending on the ancestral sex-ratio and allele frequencies. Firstly, haploid selection causes the zygotic sex ratio to be male biased ($\zeta < 1/2$) when the a allele (which is fixed on the Y) is favoured during haploid 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, neo-W alleles can also be favoured via their associations with **A** locus alleles that confer a fitness advantage in females. In the main text we explore the effect of these associations under the simplifying assumption of no

haploid selection, which means that there are no zygotic sex ratio biases. Haploid selection modifies invasion by exerting direct selection on neo-W haplotypes (i.e., competition among eggs favours one neo-W haplotype at the expense of the other while female meiotic drive will affect the spread of neo-W haplotypes only when they arise in Aa heterozygotes). The full characteristic polynomials, including the effect of haploid selection, are given in the appendix (equations S.5 and S.6).

In the absence of haploid selection and with the A allele is fixed on the X, it is possible for both neo-W haplotypes can spread, and thus neo-W invasion can occur regardless of its linkage to the selected locus. Invasion does not occur with purely sexually-antagonistic selection (i.e., a directionally favoured in males and A directionally favoured in females) because the X is then already as specialized as possible on the female sex. However, if, for example, AA individuals suffer a fitness cost in females, yet A is fixed on the X due to strong overdominance in males, both neo-W-A and neo-W-a haplotypes spread because they produce fewer unfit AA females and never experience counterselection in males. This is true even for the neo-W-A haplotype because it can pair with a $Y - a$ haplotype and still be female. Because both haplotypes can spread alone, the rate of recombination between the neo-W and the selected locus, R, does not prevent invasion, and the system can thus evolve looser sex-linkage (e.g., the neo-W could arise on an autosome, $R = 1/2$). Even when only one haplotype can spread, invasion can still occur up to some positive rate of recombination, $R > 0$ (as long as equation 1 is satisfied). That looser sex-linkage can evolve is contrary to the conclusions of van Doorn and Kirkpatrick (2010), who did not explicitly calculate invasion fitness under ancestrally tight sex-linkage. Similar scenarios have been shown to select for a modifier that increases recombination between the sexes (green regions of Figure 2 in Otto 2014).

It is also possible, in the absence of haploid selection, for a neo-W to invade when there is a stable polymorphism at the **A** locus on X chromosomes. For example, overdominance in males and strong directional selection for a in females creates a scenario that favours the spread of both neo-W haplotypes at equilibrium,

as both bring more a alleles into females and never experience counterselection in males. Thus, as in the case of the A being fixed on the X, looser sex-linkage can evolve with a polymorphic X and this is expected under the same scenarios that select for a modifier that increases recombination between the sex chromosomes (blue regions of Figure 2 in Otto 2014).

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, $D^{\mathfrak{s}} = \left(\bar{p}s^{\mathfrak{s}} + (1-\bar{p})h^{\mathfrak{s}}s^{\mathfrak{s}}\right) - \left(\bar{p}h^{\mathfrak{s}}s^{\mathfrak{s}} + (1-\bar{p})\right)$, is the difference in fitness between A and a alleles in diploids of sex $\mathfrak{s} \in \{\female, \male\}$, 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 result echoes that 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 if there is no haploid selection ($t^{\varphi}_{\delta} = \alpha^{\varphi}_{\Delta} = 0$), as considered by van Doorn and Kirkpatrick (2010), with weak selection 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 fitness can therefore decrease with a heterogametic transition (Figure 3B,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, $\left(\hat{p}^{\delta}_{Y} - \hat{p}^{\delta}_{X}\right) = 0$. 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 4). 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, $h^{\varphi} = h^{\delta}$. 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 ($s^{♀}s^{♂} > 0$, see Figure 4B). 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., $s^{♀}(s^{♂} - s^{♀}) > 0$, see Figure 4C,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.

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	$h^{♂} = h^{♀}$, $t^{♂} = \alpha_{\Delta}^{♀} = \alpha_{\Delta}^{♂} = 0$	$s^{♂}(s^{♀} - s^{♂}) > 0$

Previous research suggests that when the ancestral sex-determining locus is linked to a locus that experiences haploid selection (e.g., meiotic drive), a new, unlinked sex-determining locus invades in order to restore equal sex ratios (Kozielska et al. 2010). Our model provides a good opportunity to determine whether Fisherian sex-ratio selection provides a useful explanation for the evolution of new sex-determining loci in other contexts. 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, $\alpha^{♂} \neq 1/2$, $\alpha^{♀} = 1/2$). We will also disregard 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). If the ancestral sex-determining system is ZW, the zygotic sex ratio will be 1:1 because diploid sex is determined by the proportion of Z-bearing versus W-bearing eggs and meiosis in females is fair (Figure 1D). Thus, if the zygotic sex ratio is crucial to the evolution of new genetic sex-determining systems,

invasion into ZW and XY systems will be distinct. However, under weak selection we find that invasion by a homogametic neo-sex-determining allele (XY to XY or ZW to ZW) or by a heterogametic neo-sex-determining allele (XY to ZW or ZW to XY) occur under the same conditions. That is, we can show that $\lambda_{Y',XY} = \lambda_{W',ZW}$ and $\lambda_{Y',ZW} = \lambda_{W',XY}$ (at least up to order ϵ^3; for a numerical example, compare Figure 1A,B to Figure 1C,D). As it turns out, under weak selection the strength of sex-ratio selection favouring, say, the invasion of a neo-W in an XY system is the same as the strength of meiotic drive favouring the invasion of a neo-Y in a ZW system. Even when these forces are not exactly the same (e.g., under tight sex-linkage; compare black and red curves near -25 and 25cM in Figure 4), it is important to remember that sex-ratio selection is only one of many potential selective forces acting to determine transitions between sex-determining systems. It is even possible for the other selective forces to overwhelm sex-ratio selection and favour sex-determination transitions that create sex-ratio biases (Figure 1A,C).

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). 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 $k = 1$.

Under Fisherian sex-ratio selection, autosomal modifiers favour equal invest-

ment in male and female offspring, i.e., a 1:1 sex ratio (Fisher 1930, Charnov 1982, West 2009). A novel environmental sex-determiner that causes half of its carriers to become female and half to become male ($k = 1/2$) will be in males half of the time and in females half of the time (like an autosome). In addition, these novel sex-determination alleles equalize the sex ratio and therefore one might expect them to be favoured by Fisherian sex-ratio selection when the resident sex ratio is biased. However, assuming weak selection, we find that the growth rate of a rare, dominant offspring-controlled neo-ESD allele that produces males or females with equal probability ($k = 1/2$) is

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

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.

Equation (5) 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 $r < 1/2$).

Fisherian sex-ratio selection is sometimes considered in terms of balancing parental investment in male versus female offspring (Charnov 1982). In addition, under environmental sex-determination, the proportion of males/females is sometimes controlled by the mother (e.g., the proportion of eggs laid in warm versus cold environments). We therefore also considered the invasion of a neo-sex-determining allele (m) in a model in which mothers that have at least one m allele produce daughters with probability k. As with offspring-controlled ESD, for all $k \in \{0, 1/2, 1\}$, we find that invasion into an ancestral XY system is the same as invasion into an ancestrally ZW system (at least up to order ϵ^3, assuming weak selection), implying that transitions between genetic sex-determination and maternally controlled environmental sex-determination are not driven by Fisherian sex-ratio selection alone. (Maternal ESD analysis still lacks meiotic drive – Mathematica can't seem to deal with the added complexity.)

Discussion

I messed with the sex-ratio selection paragraphs to tone down our "it doesn't matter" speech from before. Linkage between haploid selected loci and sex-determining regions cases biased zygotic sex ratios (Hamilton 1967, Burt and Trivers 2006, Field et al. 2012; 2013). One might then expect Fisherian sex-ratio selection to drive the spread of new sex-determining systems that bring the sex ratio closer to 50:50. Fisherian sex-ratio selection follows from the fact that, for an autosomal locus, half of the genetic material is inherited from a male, and half from a female (Fisher 1930, 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 will spread via the higher per-individual contributions made by males.

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 $(2\zeta)^{-1} > 1$, 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 detrimental to male diploids but beneficial for female diploids; Table 3), preventing the neo-W from invading. Conversely, 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. This of course generates new sex-ratio selection that may drive further turnover (Úbeda et al. 2015). What we would like to stress is that sex-ratio selection alone cannot predict when new sex-determining systems can evolve.

It has previously been demonstrated that new sex-determining systems can evolve if there is genetic variation maintained by sexually-antagonistic selection (van Doorn and Kirkpatrick 2007; 2010). In particular, transitions to new sex-determining systems can occur when new sex-determining regions are more closely linked to a sexually-antagonistic locus. Our results show that genetic variation at loci that experience haploid selection can also generate selection in favour of new sex-determining systems. New sex-determining alleles are again favoured if they are linked with a locus under haploid selection and the ancestral sex-determination locus is not. 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 ancestral sex-determination system. 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 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 female (male) fitness, at a cost to the other sex, and invade despite lowering mean fitness (Figure 3).

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 another 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). However, it is possible that sexually-antagonistic variation accumulated after sex chromosome transitions because linkage with the sex-determining regions allows sexually-antagonistic selection to maintain polymorphisms under a larger parameter space (Rice 1987, Jordan and Charlesworth 2011).

We note that linkage with sex chromosomes is not, a priori, more permissive to the maintainence of ploidally antagonistic variation (Immler et al. 2012). However, as with sexually-antagonistic variation, a comparison between closely related clades could indicate whether a polymorphism pre-dates a transition in sex-determination or arose afterwards (George Sandler, an undergrad in the Wright and Barrett labs, has done some yet-to-be-published work on Rumex that we should cite here. We can send him this draft and get his permission to cite him as personal communication or something. I think he has basically found that genes retained on the Y are overexpressed in pollen but not in male diploids, suggesting they are being maintained by haploid selection, not sexual antagonism. I guess this is a follow up to Crowson et al 2017 Mol Biol Evol 34:1140, which we could potentially cite as well.). Secondly, we have shown that new sex-determination systems can be favoured if either the ancestral sex-determining region or the new sex-determining region are linked to loci under haploid selection. Therefore, the presence of haploid selected loci around ancestral- or novel-sex-determining regions could support their role in sex chromosome turnover.

Taken at face value, our results indicate that transitions in heterogametey (XY to ZW or vice versa) are more likely to be favoured by selection if there is selection upon both haploid and diploid genotypes rather than diploid selection alone. This prediction could 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. 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 spermatogenesis 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 haploid selection can drive transitions between sex-determination systems. We therefore argue that haploid selection should be considered, along-

side sex-ratio selection and sexually-antagonistic selection, as an important factor influencing the evolution of sex determination. Further, we have shown the way in which transitions are affected by haploid selection is not intuitively obvious. Firstly, sex-specific haploid selection affects turnovers between sex-determination systems in a manner that is qualitatively different from diploid sex-specific selection. In particular, closer linkage between a sex-determining locus and a selected locus is not always favoured during heterogametic transitions when there is haploid selection. Secondly, even though haploid selection is a source of zygotic sex-ratio biases, in our models Fisherian sex-ratio selection does not have good explanatory power in determining whether various sex-determination systems evolve. This result is surprising given that sex ratios are ultimately determined via the sex-determination system, and leads us to the conclusion that three selective forces – haploid, diploid, and sex-ratio selection – should all be considered when exploring transitions between sex-determination systems.

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Figures

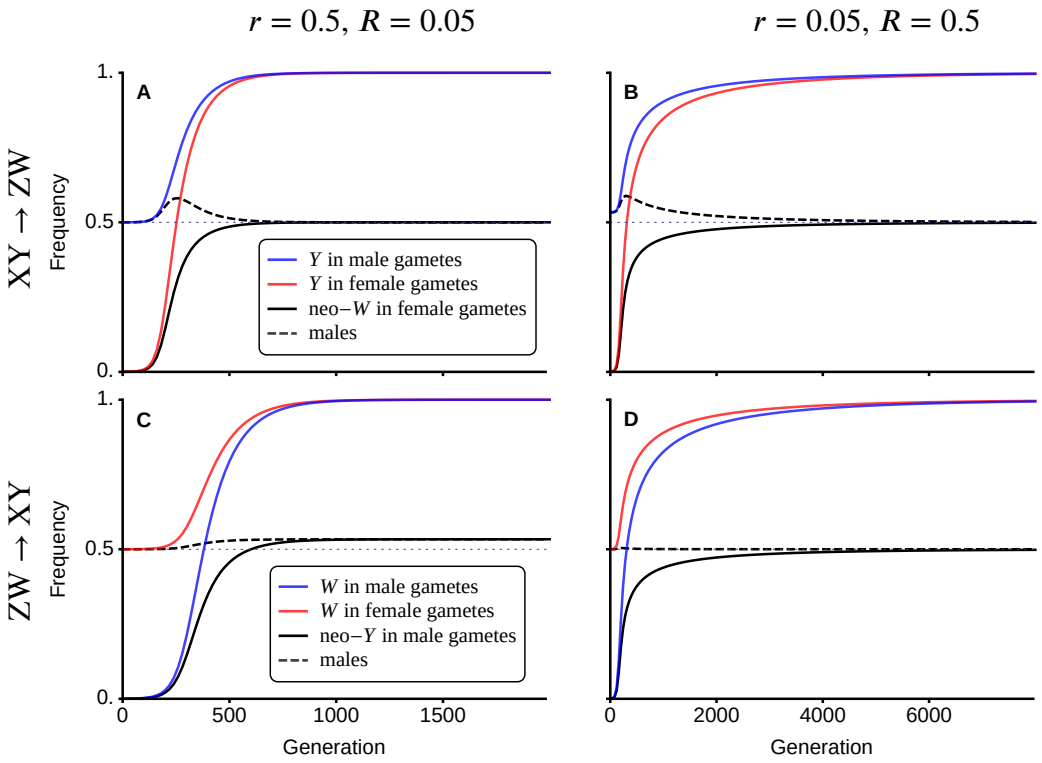

Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occur similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines show male frequency). During invasion by a neo-ZW sex-determination system (A and B), the ancestral Y fixes in both males and females (blue and red lines). Similarly, the ancestral W allele fixes in males and females (blue and red lines) during a ZW to XY transition. In this plot, there is no gametic competition ($t^{\varphi} = t^{\sigma} = 0$) 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 4A). 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?

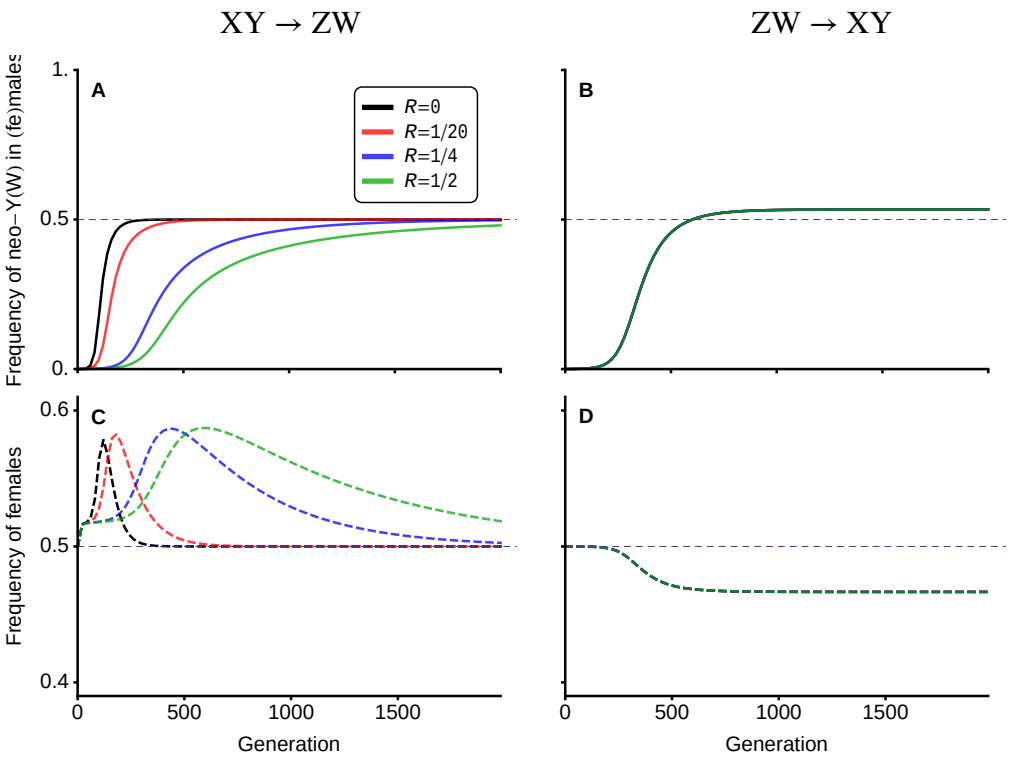

Figure 2: Is this what Sally was thinking?

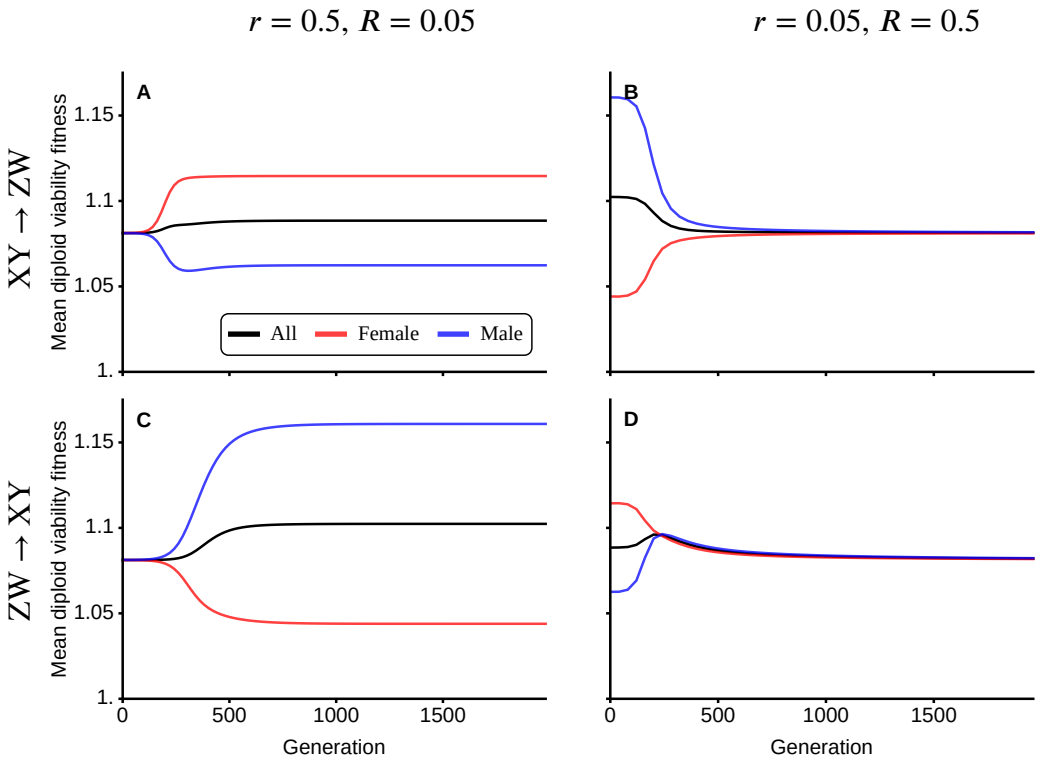

Figure 3: Changes in mean diploid fitness of males (blue lines), females (red lines), and the entire population (male mean fitness plus female mean fitness, black lines) during the transitions between sex-determination systems shown in Figure 1. Here we multiply male and female mean fitnesses by two so that we can show them on the same scale as population mean fitness. 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'm still confused why male and female mean fitnesses aren't normalized by their frequency. I'm not sure we should be calling them means without this normalization step.

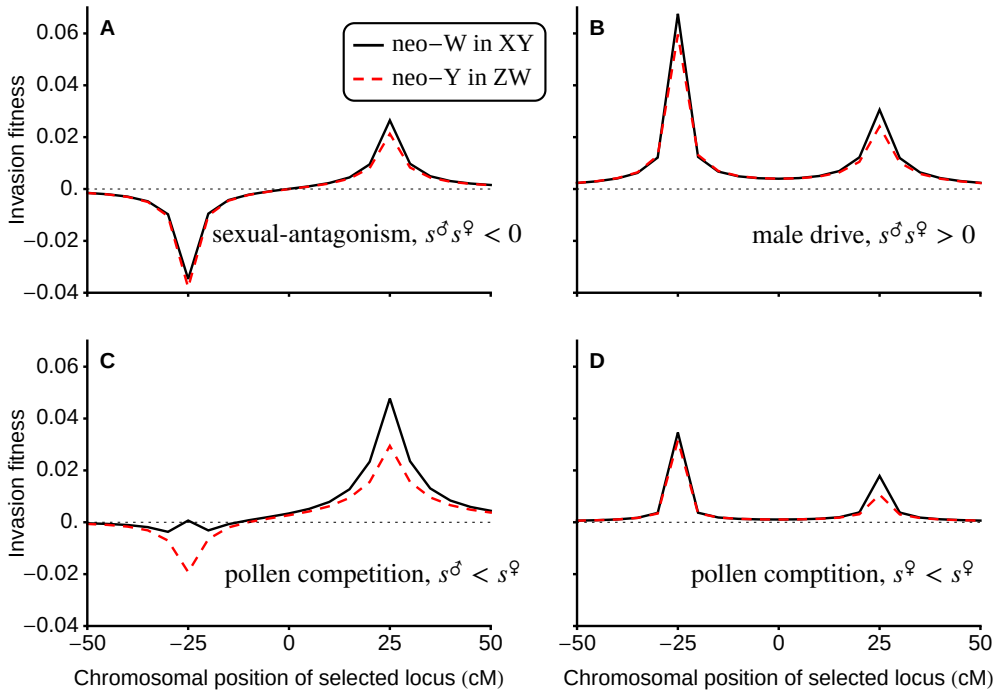

Figure 4: Invasion fitness of a neo-W allele plotted against the relative genomic location of a locus under direct selection, **A**, for various selective regimes. The ancestral sex-determining locus is located at -25 and the novel sex-determining locus is located at 25. We use Haldane's map function (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.

1. I suspect that panel C has a region where no equilibrium is maintained (CHECK! Maybe include different parameters here or remove the part when no equilibrium). MMO: If you trust the sieve function there are stable equilibria across the entire range, although this differ greatly between XY and ZW systems near -25cM.

2. Currently use different parameters for B than using in figure 1 (selection/drive twice as strong in turnover figure). MMO: this is to keep it within the bounds of the plot – using the same parameters makes the peak at -25 reach roughly 0.1, and then it is difficult to see the details of A,C, and D.

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) 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 $p^{\male\female}_{x_1,x_2,a_1,a_2,m_1,m_2}$ where 1 is maternal and 2 is paternal? We then no longer have to switch indices from haploid to diploid and $b = m_1 m_2$, $c = x_1 x_2$, and $l = a_1 a_2$. I guess the downside will be writing the recursion equations...

In each generation we census the genotype frequencies in male and female gametes/gametophytes (hereafter, gametes) between meiosis (and any meiotic drive) and gametic competition. At this stage we denote the frequencies of X- and Y-bearing gametes from males and females $x^{\male\female}_{ij}$ and $y^{\male\female}_{ij}$, where $\male\female \in \{\male, \female\}$ 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, $\sum_{i,j} x^{\male\female}_{ij} + y^{\male\female}_{ij} = 1$.

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 $x^{\male\female,s}_{ij} = w_i x^{\male\female}_{ij} / \bar{w}^{\male\female}_H$ and $y^{\male\female,s}_{ij} = w_i y^{\male\female}_{ij} / \bar{w}^{\male\female}_H$, where $\bar{w}^{\male\female}_H = \sum_{i,j} w_i x^{\male\female}_{ij} + w_i y^{\male\female}_{ij}$ is the mean fitness of male ($\male\female = \male$) or female ($\male\female = \female$) 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 $♀$ are given by $xx_{ij}^{♀,s} = w_l^{♀}xx_{ij}/\bar{w}^{♀}$, $xy_{ij}^{♀,s} = w_l^{♀}xy_{ij}/\bar{w}^{♀}$, and $yy_{ij}^{♀,s} = w_l^{♀}yy_{ij}/\bar{w}^{♀}$, where $\bar{w}^{♀} = \sum_{i=1}^{4}\sum_{j=1}^{4} w_l^{♀}xx_{ij} + w_l^{♀}xy_{ij} + w_l^{♀}yy_{ij}$ is the mean fitness of individuals of sex $♀$.

Finally, these diploids undergo meiosis to produce the next generation of gametes. Recombination and sex-specific meiotic drive occur during meiosis. Here, we allow any relative locations for the 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 $♀$, meiotic drive occurs such that, in Aa heterozygotes, a fraction $\alpha^{♀}$ of gametes produced carry the A allele and $(1-\alpha^{♀})$ carry the a allele.

Among gametes from sex $♀$ (sperm/pollen when $♀ = ♂$, eggs/ovules when $♀ = ♀$), the frequencies of haplotypes (before gametic competition) in the next

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

generation are given by

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

$$
\begin{aligned}
x_{mA}^{\male\prime} =& 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 \\
x_{ma}^{\male\prime} =& 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 \\
y_{MA}^{\male\prime} =& 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 \\
y_{Ma}^{\male\prime} =& 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.1c}
\tag{S.1d}
\tag{S.1e}
\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 ($x x_{11}^{\male} = x x_{12}^{\male} = x x_{22}^{\male} = x y_{11}^{\female} = x y_{12}^{\female} = x y_{21}^{\female} = x y_{22}^{\female} = y y_{11}^{\female} = y y_{12}^{\female} = y y_{22}^{\female} = 0$). In this case, the system only involves six recursion equations, which yields equilibrium (S.3).

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 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:

$$
\begin{aligned}
(A)\quad & \hat{p}_Y^{\male} = 0,\ \hat{q} = \frac{1}{2} - \frac{(\alpha^{\male} - 1/2) w_{Aa}^{\male} \phi}{w_{Aa}^{\male}\phi + w_{aa}^{\male}\psi}, \\
& \hat{p}_X^{\female} = \frac{w_a^{\female}\phi}{w_a^{\female}\phi + w_A^{\female}\psi},\ \hat{p}_X^{\male} = \frac{2\alpha^{\male} w_{Aa}^{\male}\phi}{2\alpha^{\male} w_{Aa}^{\male}\phi + w_{AA}^{\male}\psi} \\
(A')\quad & \hat{p}_Y^{\male} = 1,\ \hat{q} = \frac{1}{2} + \frac{(\alpha^{\male} - 1/2) w_{Aa}^{\male} \phi'}{w_{Aa}^{\male}\phi' + w_{AA}^{\male}\psi'}, \\
& \hat{p}_X^{\female} = 1 - \frac{w_A^{\female}\phi'}{w_A^{\female}\phi' + w_a^{\female}\psi'},\ \hat{p}_X^{\male} = 1 - \frac{2(1-\alpha^{\male}) w_{Aa}^{\male}\phi'}{2(1-\alpha^{\male}) w_{Aa}^{\male}\phi' + w_{aa}^{\male}\psi'} \\
(B)\quad & \hat{p}_Y^{\male} = 0,\ \hat{p}_X^{\female} = 1,\ \hat{p}_X^{\male} = 1,\ \hat{q} = 1 - \alpha^{\male} \\
(B')\quad & \hat{p}_Y^{\male} = 1,\ \hat{p}_X^{\female} = 0,\ \hat{p}_X^{\male} = 0,\ \hat{q} = \alpha^{\male}
\end{aligned}
$$

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

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 ($\alpha^{\mathfrak{P}} = 1/2$, $w_A^{\mathfrak{P}} = w_a^{\mathfrak{P}} = 1$), 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 $\bar{w}_{Ya}^{\mathfrak{F}} > \bar{w}_{YA}^{\mathfrak{F}}$ where $\bar{w}_{Ya}^{\mathfrak{F}} = w_a^{\mathfrak{F}}(2p_X^{\mathfrak{P}}(1-\alpha^{\mathfrak{F}})w_A^{\mathfrak{P}}w_{Aa}^{\mathfrak{F}} + (1-p_X^{\mathfrak{P}})w_a^{\mathfrak{P}}w_{aa}^{\mathfrak{F}})$ and $\bar{w}_{YA}^{\mathfrak{F}} = w_A^{\mathfrak{F}}(p_X^{\mathfrak{P}}w_A^{\mathfrak{P}}w_{AA}^{\mathfrak{F}} + 2(1-p_X^{\mathfrak{P}})\alpha^{\mathfrak{F}}w_a^{\mathfrak{P}}w_{Aa}^{\mathfrak{F}})$. That is, Ya haplotypes must have higher fitness than YA haplotypes. Substituting in $p_X^{\mathfrak{P}} = \hat{p}_X^{\mathfrak{P}}$ from above, fixation of the a allele on the Y requires that $\gamma_i > 0$ where $\gamma_{(A)} = w_a^{\mathfrak{F}}(2(1-\alpha^{\mathfrak{F}})w_{Aa}^{\mathfrak{F}}\phi + w_{aa}^{\mathfrak{F}}\psi) - w_A^{\mathfrak{F}}(w_{AA}^{\mathfrak{F}}\phi + 2\alpha^{\mathfrak{F}}w_{Aa}^{\mathfrak{F}}\psi)$ for equilibrium (A) and $\gamma_{(B)} = 2(1-\alpha^{\mathfrak{F}})w_a^{\mathfrak{F}}w_{Aa}^{\mathfrak{F}} - w_A^{\mathfrak{F}}w_{AA}^{\mathfrak{F}}$ 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 $w_A^{\mathfrak{P}}w_{AA}^{\mathfrak{P}} > (1-\alpha^{\mathfrak{P}})w_a^{\mathfrak{P}}w_{Aa}^{\mathfrak{P}}$.

Selection weak relative to recombination (weak selection)

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

$$\begin{aligned} & 0 < -((1-h^{\mathfrak{P}})s^{\mathfrak{P}} + (1-h^{\mathfrak{F}})s^{\mathfrak{F}} + t^{\mathfrak{P}} + t^{\mathfrak{F}} + \alpha_\Delta^{\mathfrak{P}} + \alpha_\Delta^{\mathfrak{F}}) \\ \text{and} \quad & 0 < (h^{\mathfrak{P}}s^{\mathfrak{P}} + h^{\mathfrak{F}}s^{\mathfrak{F}} + t^{\mathfrak{P}} + t^{\mathfrak{F}} + \alpha_\Delta^{\mathfrak{P}} + \alpha_\Delta^{\mathfrak{F}}). \end{aligned} \tag{S.2}$$

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

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

$$\bar{p} = \frac{h^{\varphi}s^{\varphi} + h^{♂}s^{♂} + t^{\varphi} + t^{♂} + \alpha_{\Delta}^{\varphi} + \alpha_{\Delta}^{♂}}{(2h^{\varphi} - 1)s^{\varphi} + (2h^{♂} - 1)s^{♂}} + O(\epsilon). \tag{S.3}$$

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

$$\begin{aligned}
\hat{p}_X^{♂} - \hat{p}_X^{\varphi} &= V_A\left(D^{♂} - D^{\varphi} + \alpha_{\Delta}^{♂} - \alpha_{\Delta}^{\varphi}\right) + O(\epsilon^2) \\
\hat{p}_Y^{♂} - \hat{p}_X^{\varphi} &= V_A\left(D^{♂} - D^{\varphi} + \alpha_{\Delta}^{♂} - \alpha_{\Delta}^{\varphi} + (1-2r)(t^{♂} - t^{\varphi})\right)/2r + O(\epsilon^2) \\
\hat{p}_Y^{♂} - \hat{p}_X^{♂} &= V_A\left(D^{♂} - D^{\varphi} + \alpha_{\Delta}^{♂} - \alpha_{\Delta}^{\varphi} + t^{♂} - t^{\varphi}\right)(1-2r)/2r + O(\epsilon^2)
\end{aligned} \tag{S.4}$$

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $D^{⚥} = \left(\bar{p}s^{⚥} + (1-\bar{p})h^{⚥}s^{⚥}\right) - \left(\bar{p}h^{⚥}s^{⚥} + (1-\bar{p})\right)$ corresponds to the difference in fitness between A and a alleles in diploids of sex $⚥ \in \{\varphi, ♂\}$ ($\bar{p}$ 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, $q = 1/2 + \alpha_{\Delta}^{♂}(\hat{p}_Y^{♂} - \hat{p}_X^{♂})/2 + O(\epsilon^3)$. Without gametic competition or drive ($\alpha_{\Delta}^{⚥} = t^{⚥} = 0$) 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

$$\lambda_{mA} = (2\alpha^{\male})^{-1} \frac{w_A^{\female} \left[w_A^{\male} w_{AA}^{\female} \alpha^{\male} + 2 w_a^{\male} w_{Aa}^{\female} \alpha^{\female} (1 - \alpha^{\male}) \right]}{w_A^{\male} w_A^{\female} w_{AA}^{\female}} \tag{S.5a}$$

$$\lambda_{ma} = (2\alpha^{\male})^{-1} \frac{w_a^{\female} \left[w_a^{\male} w_{aa}^{\female} (1 - \alpha^{\male}) + 2 w_A^{\male} w_{Aa}^{\female} (1 - \alpha^{\female}) \alpha^{\male} \right]}{w_A^{\male} w_A^{\female} w_{AA}^{\female}} \tag{S.5b}$$

$$\rho_{mA} = (2\alpha^{\male})^{-1} \frac{R w_a^{\male} w_A^{\female} w_{Aa}^{\female} \alpha^{\female} (1 - \alpha^{\male})}{w_A^{\male} w_A^{\female} w_{AA}^{\female}} \tag{S.5c}$$

$$\rho_{ma} = (2\alpha^{\male})^{-1} \frac{R w_A^{\male} w_a^{\female} w_{Aa}^{\female} (1 - \alpha^{\female}) \alpha^{\male}}{w_A^{\male} w_A^{\female} w_{AA}^{\female}} \tag{S.5d}$$

In this case, the zygotic sex ratio (ζ) is given by the difference in haploid selection in males on a (fixed on the Y) and A (fixed on the X) alleles, i.e., there are more males than females if $\zeta = 2\alpha^{\male} w_A^{\male}/(w_a^{\male} + w_A^{\male}) < 1/2$. Populations with a male biased zygotic sex ratio are more permissive to invasion by a neo-W (λ_{mA} and λ_{ma} larger). In addition, the spread rate of neo-W haplotypes is determined by their fitness in females. Zygotes carrying dominant neo-W alleles will develop as females regardless of their genotype at the XY locus. Therefore, females result from matings with either X-A or Y-a male gametes. The relative proportion of these male gametes is also determined by haploid selection in males; mating with a Y-a male gamete is more likely if the a allele is favoured during male gamete production or competition ($\zeta < 1/2$).

Furthermore, haploid selection in females can directly select upon neo-W-A or neo-W-a haplotypes. A neo-W-A female gamete has the same fitness during haploid competition as resident A-bearing female gametes. On the other hand, neo-W-a female gametes can be favoured or disfavoured during female haploid competition (favoured if $w_a^{\female} > w_A^{\female}$). Meiotic drive in females ($\alpha^{\female}$) similarly affects the fitness of these haplotypes, except that meiotic drive only occurs in heterozygotes.

The other terms in equations (S.5) 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 ($w_{AA}^{\female} > w_{Aa}^{\female} > w_{aa}^{\female}$). Essentially, the X is already as specialized as possible for the female beneficial allele (X-A 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 $Y-a$ haplotypes into females, when $w^{\female}_{Aa} > w^{\female}_{AA}$. 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 X-A at one (specifically, from the stability conditions, we must have $w^{\male}_{Aa}/((w^{\male}_{aa}+w^{\male}_{Aa})/2) > w^{\female}_{Aa}/w^{\female}_{AA}$).

Under this same condition, $w^{\female}_{Aa} > w^{\female}_{AA}$, the neo-W can also spread alongside the a allele ($\lambda_{ma} > 1$) if there is sufficiently strong underdominance in females ($w^{\female}_{aa} > w^{\female}_{Aa}$), such that $(w^{\female}_{Aa}+w^{\female}_{aa})/2 > w^{\female}_{AA}$. 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. This gives

$$\lambda_{mA} = \frac{a}{b}\left[w^{\female}_{AA}w^{\male}_{Aa}w^{\male}_{A}\alpha^{\male}\phi + 2w^{\female}_{Aa}\alpha^{\female}w^{\male}_{a}\frac{c}{d}\right]/w^{\female}_{a} \tag{S.6a}$$

$$\lambda_{ma} = \frac{a}{b}\left[2w^{\female}_{Aa}(1-\alpha^{\female})w^{\male}_{Aa}w^{\male}_{A}\alpha^{\male}\phi + w^{\female}_{aa}w^{\male}_{a}\frac{c}{d}\right]/w^{\female}_{A} \tag{S.6b}$$

$$\rho_{mA} = \frac{a}{b}R\left[2w^{\female}_{Aa}\alpha^{\female}w^{\male}_{a}\frac{c}{d}\right]/w^{\female}_{a} \tag{S.6c}$$

$$\rho_{ma} = \frac{a}{b}R\left[2w^{\female}_{Aa}(1-\alpha^{\female})w^{\male}_{Aa}w^{\male}_{A}\alpha^{\male}\phi\right]/w^{\female}_{A} \tag{S.6d}$$

where

$$a = w_a^{\varphi}\phi + w_A^{\varphi}\psi \tag{S.7a}$$

$$b = w_{AA}^{\varphi}\phi(2w_{Aa}^{\sigma}w_A^{\sigma}\alpha_{\sigma}\phi) + w_{Aa}^{\varphi}\psi(2w_{Aa}^{\sigma}w_A^{\sigma}\alpha_{\sigma}\phi + w_{AA}^{\sigma}w_a^{\sigma}\psi) + w_{aa}^{\varphi}\psi(w_{AA}^{\sigma}w_a^{\sigma}\psi) \tag{S.7b}$$

$$c = 2(w_{Aa}^{\sigma}\phi)^2(1-\alpha^{\sigma})\alpha_{\sigma} + w_{Aa}^{\sigma}\phi(w_{AA}^{\sigma}\psi + w_{aa}^{\sigma}\psi\alpha^{\sigma}) + w_{aa}^{\sigma}\psi w_{AA}^{\sigma}\psi \tag{S.7c}$$

$$d = 2w_{Aa}^{\sigma}\alpha^{\sigma}\phi + w_{aa}^{\sigma}\psi \tag{S.7d}$$

As with equilibrium (B), the conditions for invasion are easier to interpret in the absence of haploid selection, which again modifies invasion fitnesses by directly selecting upon neo-W haplotypes. For instance, without haploid selection, the neo-W-A haplotype spreads ($\lambda_{mA} > 1$) if and only if

$$2(w_{Aa}^{\varphi} - w_{aa}^{\varphi})w_{AA}^{\sigma}\psi^2 > (w_{AA}^{\varphi} - w_{Aa}^{\varphi})w_{Aa}^{\sigma}\phi(\phi - \psi) \tag{S.8}$$

where $\phi - \psi = w_{AA}^{\varphi}w_{Aa}^{\sigma} - w_{aa}^{\varphi}w_{aa}^{\sigma}$ and both ϕ and ψ are positive when equilibrium (A) is stable. In contrast to equilibrium (B), a neo-W haplotype can spread under purely sexually-antagonistic selection ($w_{AA}^{\sigma} > w_{Aa}^{\sigma} > w_{aa}^{\sigma}$ and $w_{AA}^{\varphi} > w_{Aa}^{\varphi} > w_{aa}^{\varphi}$). 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.8) will be more easily met when $w_{Aa}^{\varphi} - w_{aa}^{\varphi} \approx w_{Aa}^{\varphi}$ and $w_{AA}^{\varphi} - w_{Aa}^{\varphi} \approx 0$, implying $w_{aa}^{\varphi} \approx 0$ and $w_{Aa}^{\varphi} \approx w_{AA}^{\varphi}$ (although this is complicated by the fact that w_{aa}^{φ} and w_{Aa}^{φ} affect ϕ and ψ too, the intuition holds).

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

$$(w_{aa}^{\varphi} + w_{Aa}^{\varphi} - 2w_{AA}^{\varphi})w_{Aa}^{\sigma}\phi^2 + (w_{aa}^{\varphi} - w_{Aa}^{\varphi})(w_{Aa}^{\sigma} + 2w_{AA}^{\sigma})\phi\psi > 0 \tag{S.9}$$

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.