Gametic Selection, Meiotic Drive, Sex Ratio Bias, and Transitions Between Sex Determination Systems

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

∗ These authors contributed equally to this work

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

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

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

Contributions:

Abstract

Sex determination systems are remarkably dynamic; many studied taxa display transitions of sex-determining genes between chromosomes or the evolution of entirely new sex-determining systems. Predominant theories in which new sex-determining systems are favoured by selection involve sex ratio selection or sex-specific selection (e.g., sexually antagonistic selection). Here, we utilize population genetic models to study the spread of novel sex-determiners when there is a period of sex-specific haploid selection. Many loci experience sex-specific selection on their haploid genotypes during gametic competition (e.g., pollen/sperm competition) or meiosis (i.e., meiotic drive); selective processes that typically occur in one sex or the other. In addition, 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. Notably, we find that the spread of new genetic sex determination systems is not affected by sex ratio biases that are caused by haploid selection. In addition, we find that, with haploid selection, transitions between male and female heterogamety (XY to ZW or ZW to XY) can occur despite breaking up favourable associations the between ancestral sex-determining locus and selected loci. These transitions occur because an unlinked neo-Y (neo-W) can have higher fitness in males (females), even if the population mean fitness is reduced. Such transitions are not possible with diploid selection alone, in which case tighter linkage increases the fitness of both males and females. Furthermore, a period of selection among haploids can favour the stable maintenance of polymorphic sex determination systems. Thus, our models offer several new insights to be explored as information about sex determination in non-model taxa accumulates.

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/dioecious 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), 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 in which new sex determination systems are favoured 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 determination loci can be favoured if they arise in close linkage with a locus that experiences sexual antagonism. For example, linkage allows favourable associations to build up between a male-beneficial allele and a neo-Y chromo-

some. 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 linked to the ancestral sex-determination locus will develop similar, favourable associations and select against the spread of a new sex-determination system.

It has been suggested that sex ratio selection could be a particularly important force driving transitions between sex-determining systems (Beukeboom and Perrin 2014, Chapter 7). The default mode of sex ratio selection is 'Fisherian' sex ratio selection, which favours equal investment in male and female offspring (i.e., a 1:1 zygotic sex ratio when assuming that males and females are equally costly to produce, Fisher 1930, Charnov 1982). Given that the sex determination system can directly affect the sex ratio, we might expect Fisherian sex ratio selection to influence the spread of new sex determination systems. For example, 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.

We note two other ways in which sex determination has been shown to relate to zygotic sex ratios. Firstly, female-biased sex ratios can be favoured when there is local mate competition, where all matings are between siblings and assuming one male can inseminate many females (Hamilton 1967). Therefore, with local mate competition, feminizing mutations can spread because they bias the sex ratio towards females (Wilson and Colwell 1981, Vuillleumier et al. 2007). Secondly, environmental conditions (e.g., maternal condition, mate quality, age, or host size) can differentially affect the fitness of males versus females such that the optimal allocation to males/females depends on the environment (Trivers and Willard 1973, Charnov and Bull 1977, Charnov 1982). In such cases, flexible sex determination systems may evolve in order to allow the zygotic sex ratio to be determined in a

way that depends on the environment (Charnov and Bull 1977, Werren and Taylor 1984, Pen et al. 2010). In this study, we do not consider environmental condition dependence or local mate competition (reviewed in Charnov 1982, Bull 1983, West 2009).

Here, we use mathematical models to find the conditions under which new sex determination systems are favoured when loci experience haploid selection. 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 and the term 'gametic competition' to refer to selection upon haploid genotypes within a gamete/gametophyte pool; 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 cause the frequency of resistant alleles to increase (e.g., Hormaza and Herrero 1996, Ravikumar et al. 2003, Hedhly et al. 2004, Clarke et al. 2004). 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).

There are various ways in which a period of haploid selection could influence transitions between sex determination systems. Firstly, 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 would affect

transitions between sex determination systems in a similar manner to sex-specific diploid selection (as explored by van Doorn and Kirkpatrick 2007; 2010). That is, new masculizing 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.

Surprisingly, our models show that haploid selection influences the evolution of new sex determination systems in a way that is distinct from both diploid sex-specific selection and Fisherian sex ratio selection. We find that the spread of new sex determination systems are independent of there being a zygotic sex ratio bias caused by associations between sex-determining regions and haploid selected loci. In addition, we find that associations that build up between an ancestral sex-determining locus and a haploid-selected locus can favour sex chromosome transitions between male and female heterogamety (e.g., a neo-W allele arising at a previously autosomal locus spreads in an ancestrally XY system), despite the fact that these ancestral associations were built up by selection. This does not occur in models that do not include haploid selection.

Model

We consider the transition between an ancestral and novel sex determination systems using a three locus model. 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, the m allele confers environmental sex determination (ESD) such that zygotes develop as females in a proportion (k) of the environments they experience. Finally, 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 $w_A^{\male\female}$ and $w_a^{\male\female}$ ($\male\female \in \{\female, \male\}$; 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, 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, relative fitnesses are given by $w_g^{\male}$ in males and $w_g^{\female}$ in females,

where g is the diploid genotype at the **A** locus ($g \in \{AA, Aa, aa\}$). The next generation of gametes are then produced by meiosis, during which recombination and sex-specific meiotic drive can occur. Recombination (i.e., an odd number of cross-overs) occurs between loci **X** and **A** with probability r, between loci **A** and **M** with probability R, and between loci **X** and **M** with probability χ. Therefore, any order of the loci can be modelled with appropriate choices of r, R, and χ (see Table S.1). Males/females that are heterozygous at the **A** locus experience meiotic drive; Aa heterozgotes of sex $\mathfrak{s}$ produce gametes bearing allele A with probability $\alpha^{\mathfrak{s}}$. 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 $\mathfrak{s} \in \{♀, ♂\}$

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

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, without loss of generality, we primarily present results for ancestral XY sex determination. Ancestral ZW sex

determination can be considered by changing the notation such that X becomes Z, Y becomes W and the labelling of male and female selection terms are reversed.

Turnover between sex-determination systems

The evolution of a new sex determination system requires that a rare mutant allele, m, at the novel sex-determining locus 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 described by the next generation frequency of eggs and sperm carrying the mutation, (S.1c), (S.1d), (S.1g), (S.1h), which is an eight equation system. 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 dominant over the ancestral sex-determining system, phenotypes are not affected by the genotype at the ancestral sex-determining region (**X** locus). Thus, the invasion of rare dominant neo-Y or neo-W alleles is determined by the largest eigenvalue that solves the quadratic characteristic polynomial $\lambda^2 + b\lambda + c = 0$. In this case $b = -(\lambda_{mA} + \lambda_{ma})$ and $c = \lambda_{mA}\lambda_{ma} - \rho_{mA}\rho_{ma}$, where λ_{mi} is the (discrete time) growth rate of mutant haplotypes on background $i \in \{A, a\}$, accounting for loss due to recombination, and ρ_{mi} is the rate of addition of mutant haplotypes onto background $i \in \{A, a\}$ due to recombination (see table 2). check these interpretations (note the 2s in the lambdas of table 2). the λs are certainly related to true growth rates because we get them by looking at the case where $R = 0$ so that you only have the haplotypes growing/declining.

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

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

$\bar{p}^{\sigma} = p_Y^{\sigma} q + p_X^{\sigma} (1 - q)$ 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**.
See Table S.2 for expressions of mean fitnesses.

Table 2 illustrates a number of key points about the invasion of neo-Y and neo-W mutations. For a neo-Y, invasion depends on the relative lifetime fitness of A-bearing and a-bearing male gametes (i.e., sperm only). The lifetime fitness of male gametes partly depends on the allele carried by the female gamete that they mate with (e.g., A with probability $p_X^{\varphi} w_A^{\varphi} / \bar{w}_H^{\varphi}$). Similarly, invasion of a neo-W depends on the relative lifetime fitness of A-bearing and a-bearing female gametes (i.e., eggs only). However, in the case of a neo-W, the allele carried by the male gamete that they mate with can come from either an X-bearing or a Y-bearing sperm (e.g., A with probability $\bar{p}^{\sigma} w_A^{\sigma} / \bar{w}_H^{\sigma}$, where $\bar{p}^{\sigma} = p_Y^{\sigma} q + p_X^{\sigma} (1 - q)$). In either case, the zygote will then develop as a female due to the presence of a neo-W. By contrast, females that do not carry the neo-W only result from matings with X-bearing sperm (e.g., matings with A-bearing sperm that result in females occur

with probability $(1-q)\bar{p}_X^{\male} w_A^{\male}/\bar{w}_H^{\male}$). If the **A** locus is initially linked to the ancestral sex-determining locus, **X**, the frequency of the A allele among X- and Y-bearing sperm can differ (equation S.4). Thus, eggs with and without a neo-W differ in the frequency of A alleles they obtain from mating with male gametes.

We are particularly concerned with whether or not a rare neo-sex-determining allele increases in frequency, which occurs when the largest eigenvalue, λ, is greater than one. In the Appendix, we derive these conditions without assuming that selection is weak relative to recombination. Here, we explicitly determine the conditions under which invasion occurs by assuming that the A allele reaches an equilibrium frequency under the ancestral sex-determination system before the neo-sex-determination system (m) arises. The equilibrium frequency of A on different ancestral backgrounds ($\hat{p}_Y^{\male}$, $\hat{p}_X^{\male}$, and $\hat{p}_X^{\female}$) is given by equations (S.3) and (S.4) where we assume selection and meiotic drive are weak relative to recombination ($s^{\female}$, $t^{\female}$, $\alpha_\Delta^{\female}$ of order ϵ). Under weak selection, we denote the leading eigenvalue 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 given by

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

and

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

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $S_A = (D^{\male} + \alpha_\Delta^{\male} + t^{\male}) - (D^{\female} + \alpha_\Delta^{\female} + t^{\female})$ is the difference in fitness in males versus females for the A allele against the a allele across diploid selection, gametic competition, and meiosis.

The neo-sex-determining allele m will spread if $\lambda_{m,XY} > 1$. Equation (1) demonstrates that 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). 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 (2) shows that if there is no selection upon haploid genotypes ($t^{♀♂} = \alpha_{\Delta}^{♀♂} = 0$), as considered by van Doorn and Kirkpatrick (2010), the spread of a neo-W is equivalent to the spread of a neo-Y ($\lambda_{W',XY} = \lambda_{Y',XY}$) such that heterogametic transitions (XY to ZW or ZW to XY) can also occur only if the neo-sex-determining region is more closely linked to a locus under selection ($R < r$). However, if there is any haploid selection, the additional term in equation (2) 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 build up by selection between sex and selected alleles will be weakened. Therefore, mean fitness can decrease, see Figure 2B,D.

We find 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 $\left(\hat{p}_Y^{♂} - \hat{p}_X^{♂}\right) = 0$ such that the second term in equation (2) 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 (Figure 3). Secondly, we can simplify cases where invasion occurs despite $R > r$ using the special case where $R = 1/2$ and $r < 1/2$. In table 3 we give the conditions where invasion occurs where we further assume that haploid selection only occurs during one phase in one sex (e.g., during male meiosis only) and dominance coefficients are equal in the two sexes, $h^{♀} = h^{♂}$. Where there is no gametic competition and meiotic drive in one sex only, an unlinked neo-W can invade as long as the same allele is favoured in male and female diploid selection ($s^{♀}s^{♂} > 0$, see Figure 3B), which is 50% of the parameter space. Where 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 3C,D), which is 25% of the parameter space. These special cases indicate that neo-W invasion can occur for a relatively large fraction of parameter space, even if the neo-W is less tightly linked to the selected locus, $R > r$.

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, 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 can only be 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, 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).

We next consider the case where the new sex-determining mutation, m, causes sex to be determined by environmental conditions (environmental sex determiner, ESD). We assume that individuals carrying the m allele develop as females in a fraction, k, of the environments they experience. The spread of these mutations is given by

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

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 investment in male and female offspring, i.e., a 1:1 sex ratio (Fisher 1930, Charnov 1982, West 2009). Therefore, 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), and so should be favoured by sex ratio selection. However, 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

$$\lambda_{ESD',XY} = 1 + \frac{1}{2}\frac{(\lambda_{Y',XY} - 1) + (\lambda_{W',XY} - 1)}{2}\Big|_{R=1/2} + O\left(\epsilon^3\right), \tag{4}$$

We note that recombination between the selected locus and the novel sex-determining locus, R, doesn't enter into the $k = 1/2$ results because sex is essentially randomized each generation, preventing associations from building up between allele A

and sex.

Equation (4) 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 occurs in males only then the sex ratio is only biased when the ancestral sex-determination system is XY), Fisherian sex ratio selection does not explain invasion by an offspring-controlled neo-ESD locus. Rather, the neo-ESD gets half of the fitness of a feminizing mutation (neo-W) and half of the fitness of a masculizing 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 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 could determine the sex ratio of offspring. 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 ancestrally XY system is the same as invasion into an ancestrally ZW system (at least up to order ϵ^3), implying transitions between genetic sex determination and maternally controlled environmental sex determination are not driven by Fisherian sex ratio selection on biased zygotic sex ratios.

Discussion

One might expect Fisherian sex ratio selection to influence the spread of new sex-determining systems in our models because linkage between haploid selected loci and sex-determining regions causes biased zygotic sex ratios (Hamilton 1967, Burt and Trivers 2006, Field et al. 2012; 2013). 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. An implicit assumption of Fisherian sex ratio selection is that the mutant allele is autosomal and has the same inheritance pattern as the non-mutant allele. The mutations we consider here, neo-sex-determining alleles, break this assumption. For example, the success of neo-Y/neo-W mutations depends only on the number of alleles contributed by males/females (Table 2). In this respect, a neo-W is similar to a cytoplasmic element, which also do not experience selection to balance sex ratios (Frank 1989, Werren and Beukeboom 1998, Chase 2007). Even mutants that are equally likely to be found in males or females, such as an environmental sex determination mutation (equation 4), are not strictly autosomal if they determine sex. Thus, despite the fact that sex ratio biases caused by gametic competition or meiotic drive have been shown to exert Fisherian sex ratio selection on various autosomal modifiers (Stalker 1961, Smith 1975, Frank 1989, Hough et al. 2013, Úbeda et al. 2015, Otto et al. 2015), we do not find evidence of Fisherian sex ratio selection acting during invasion by neo-sex-determination systems (e.g., see Figure 1 and Úbeda et al. 2015, in which a neo-Y invades despite biasing sex ratios).

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 more closely linked with a locus under haploid selection. However, with haploid selection, heterogametic transitions (XY to ZW or ZW to XY) can also occur when the new sex-determining region is less closely linked to the locus under selection.

Neo-W (neo-Y) alleles invade when their fitness in females (males) is greater than the mean fitness of females (males) under the 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) or males is lower than it would be without sex-linkage. In these cases, unlinked neo-W (neo-Y) alleles can invade, see figure 2.

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.

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 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 that appear to experience sexually-antagonistic

selection 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. 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 new- 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 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, such that haploid selection is should be incorporated into the factors that influence the evolution of sex determination. However, the particular

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, Fisherian sex ratio selection does not have good explanatory power in our models in determining whether various sex-determination systems evolve; this result is surprising given that sex ratios are ultimately determined via the sex-determination system.

Numerical results suggest that polygenic sex determination can be stable with gametic competition. i.e., feminizers/masculinizers sometimes invade but don't fix. We have not discussed this. Might be interesting because it appears that polygenic sex determination exists (possibly stably, rather than transitionally) but previous models don't show any advantage to polygenic sex determination. There are two other ways that polygenic sex determination could be observed. (1) Direct selection against WW or YY genotypes during heterogametic transitions, mentioned above. (2) Loss of variation at the selected locus: The conditions under which polymorphism is maintained can depend on linkage to the SDR, and when a neo-SDR evolves you can move into a region where A or a fixes, at which point there is no longer any selection.

References

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

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

Bachtrog, D., J. E. Mank, C. L. Peichel, M. Kirkpatrick, S. P. Otto, T.-L. Ashman, M. W. Hahn, J. Kitano, I. Mayrose, R. Ming, N. Perrin, L. Ross, N. Valenzuela, J. C. Vamosi, and Tree of Sex Consortium. 2014. Sex determination: why so many ways of doing it? PLoS Biol 12:e1001899.

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

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

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

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

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

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

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

Charnov, E. L., and J. Bull. 1977. When is sex environmentally determined? Nature 266:828–830.

Chase, C. D. 2007. Cytoplasmic male sterility: a window to the world of plant mitochondrial-nuclear interactions. Trends in Genetics 23:81–90.

524 Clarke, H. J., T. N. Khan, and K. H. M. Siddique. 2004. Pollen selection for chilling tolerance at hybridisation leads to improved chickpea cultivars. Euphytica
526 139:65–74.

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

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

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

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

538 ———. 2013. Comparative analyses of sex-ratio variation in dioecious flowering plants. Evolution 67:661–672.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Marais, G. A. B., M. Nicolas, R. Bergero, P. Chambrier, E. Kejnovsky, F. Monéger, R. Hobza, A. Widmer, and D. Charlesworth. 2008. Evidence for degeneration

of the Y chromosome in the dioecious plant *Silene latifolia*. Current Biology 18:545–549.

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

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

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

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

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

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

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

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

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

628 ———. 1996. Evolution of the Y Sex Chromosome in Animals. BioScience 46:331–343.

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

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

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

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

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

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

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

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

650 Trivers, R. L., and D. E. Willard. 1973. Natural selection of parental ability to vary the sex ratio of offspring. Science 179:90–92.

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

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

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

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

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

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

Vuillleumier, S., R. Lande, J. J. M. van Alphen, and O. Seehausen. 2007. Invasion and fixation of sex-reversal genes. Journal of Evolutionary Biology 20:913–920.

Werren, J. H., and L. W. Beukeboom. 1998. SEX DETERMINATION, SEX RATIOS, AND GENETIC CONFLICT. Annual Review of Ecology and Systematics 29:233–261.

Werren, J. H., and P. D. Taylor. 1984. The effects of population recruitment on sex ratio selection. The American Naturalist 124:143–148.

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

Wilson, D. S., and R. K. Colwell. 1981. Evolution of sex ratio in structured demes. Evolution 35:882–897.

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

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

Figures

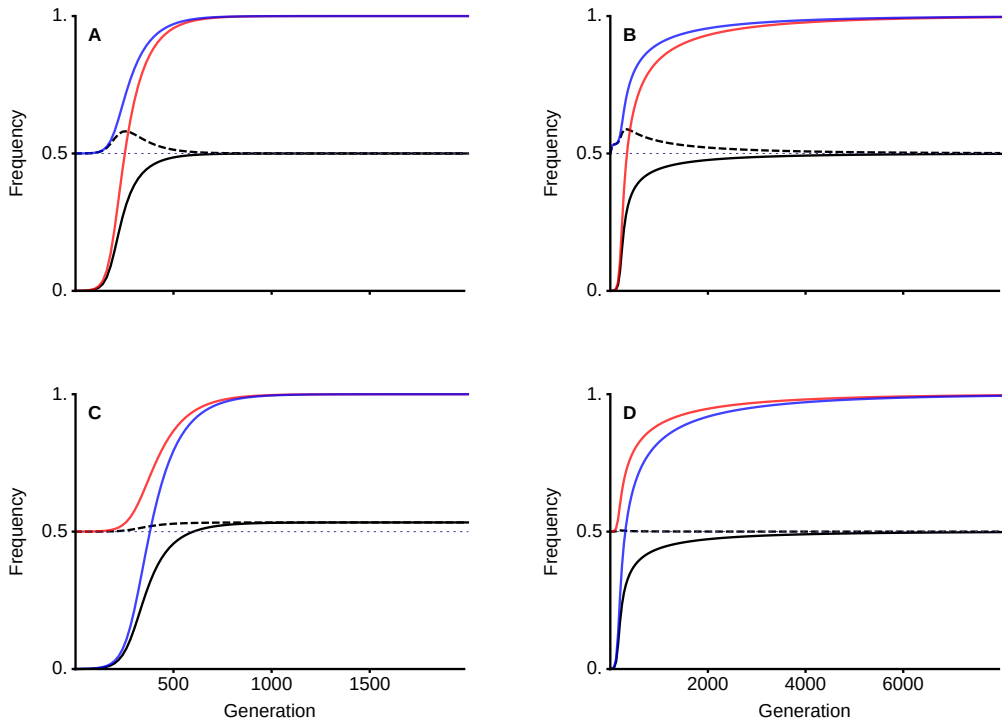

Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occur similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines show male frequency). During invasion by a neo-ZW sex determination system (A and B), the ancestral Y fixes in both males and females (blue and red lines). Similarly, the ancestral W allele fixes in males and females (blue and red lines) during a ZW to XY transition. In this plot, there is no gametic competition ($t^{\varphi} = t^{\sigma} = 0$) and meiotic drive occurs during male meiosis only ($\alpha_{\Delta}^{\varphi} = 0$, $\alpha_{\Delta}^{\sigma} = -1/5$). Therefore, sex ratio biases can only arise when the **A** locus is linked to an XY sex-determining locus. In panels A and C, the neo-sex-determining locus is more closely linked to the **A** locus than the ancestral sex-detemining region ($r = 1/2$, $R = 1/20$) such that a neo-Y can caused biased sex ratios (panel C). In panels B and D, the ancestral sex-determining locus is more closely linked to the **A** locus than the neo-sex-detemining locus ($r = 1/20$, $R = 1/2$). Therefore, an ancestral XY sex determination can have a biased zygotic sex ratio that becomes unbiased after an unlinked neo-W invades (B). However, in panel D, a unlinked neo-Y invades an ancestral ZW sex determination system in a similar manner but no biases to the zygotic sex ratio occur. With diploid selection alone, neo-sex-determining loci do not spread if they are less closely linked to the **A** locus than the ancestral sex-determining locus (see equation (2) and Figure 3A). In this plot there are no sex differences in selection and an equilibrium is maintained because selection in diploids opposes meiotic drive, $s^{\varphi} = s^{\sigma} = 1/5$, $h^{\varphi} = h^{\sigma} = 7/10$. Aethetic adjustments: Could add titles to the columns/rows: neo-W for row 1, neo-Y for row 3, $r = 0.5$, $R = 0.05$ for column 1 and $r = 0.05$, $R = 0.5$ for column 2. Could adjust padding (too much whitespace where there is no axis label). It also seems could increase ratio of font size relative to plot size to make figure more compact. Matt - could you uncomment the line legends in the Mathematica file (function not included in my Mathematica version).

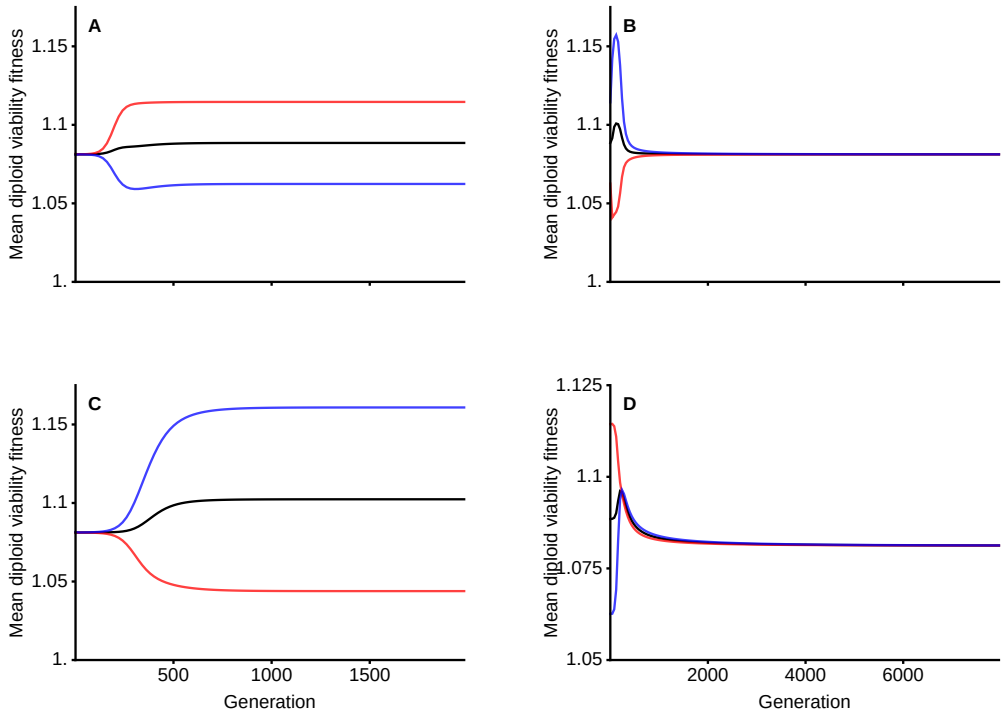

Figure 2: Here, we plot how male mean fitness (blue lines), female mean fitness (red lines), and population mean fitness (male mean fitness plus female mean fitness, black lines) changes during the transitions between sex-determination systems shown in Figure 1. Here we multiply male mean fitness and female mean fitness by two so that we can show it 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. Could add titles to the columns/rows: neo-W for row 1, neo-Y for row 3, $r = 0.5$, $R = 0.05$ for column 1 and $r = 0.05$, $R = 0.5$ for column 2. & possibly adjust padding (too much whitespace?). Matt - could you uncomment the line legends in the Mathematica file (function not included in my Mathematica version).

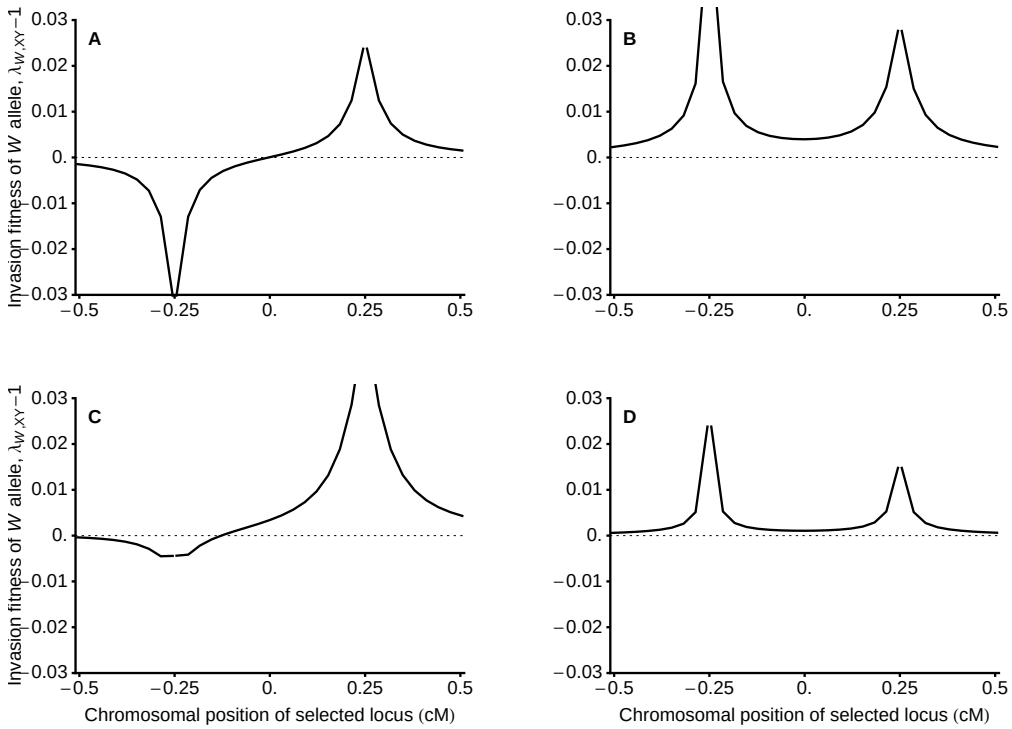

Figure 3: The invasion fitness of a neo-W allele plotted against the relative location of a locus under direct selection, **A**, for various selective regimes. We assume that the ancestral sex-determining locus is located at -0.25, the novel sex-determining locus is located at 0.25 and that there is a polymorphism at the **A** locus maintained by selection. We used 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 ($t^{\male} = \alpha_{\Delta}^{\male} = 0$) 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 ($s^{\female} = 1/10$, $h^{\female} = 7/10$ $s^{\male} = -1/10$, $h^{\male} = 3/10$). In B-D we include haploid selection and assume that selection in diploids is not sexually-antagonistic ($s^{\female}s^{\male} > 0$). 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 ($\alpha_{\Delta}^{\male} = -1/10$), no female meiotic drive or gametic competition, $t^{\female} = \alpha_{\Delta}^{\female} = 0$), and equal selection in diploid sexes ($s^{\female} = s^{\male} = 1/10$, $h^{\female} = h^{\male} = 7/10$). 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, $t^{\male} = -1/10$) and no meiotic drive or gametic competition in females ($t^{\female} = \alpha_{\Delta}^{\female} = 0$). In this case, if the selected locus is closely linked to the ancestral sex-determining locus, the neo-W only invades when the allele favoured in pollen/sperm competition selected against more in males than females (D versus C, see Table 3). In C, $s^{\female} = 3/20$, and $s^{\male} = 1/20$, whereas in D, $s^{\female} = 1/20$, and $s^{\male} = 3/20$. In both C and D, $h^{\female} = h^{\male} = 7/10$. 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). Currently use different parameters for B than using in figure 1 (selection/drive twice as strong in turnover figure). This plot would also benefit from titles giving, e.g., "sexually-antagonistic selection, $s^{\female}s^{\male} < 0$" for A, "male meiotic drive, $s^{\female}s^{\male} > 0$" for B

Appendix

Recursion Equations

In each generation we census the genotype frequencies in male and female gametes/gametophytes (hereafter, gametes) before gametic competition. Before gametic competition, the frequencies of X-bearing male and female gametes are given by $X_i^{\male}$ and $X_i^{\female}$ and the frequencies of Y-bearing gametes are given by $Y_i^{\male}$ and $Y_i^{\female}$ where the index i specifies genotypes $MA = 1$, $Ma = 2$, $mA = 3$, and $ma = 4$. Competition then occurs among gametes of the same sex (e.g., among eggs and among sperm separately) according to the **A** locus allele, g ($g \in A$, a, see Table 1), carried by individuals with genotype i. The genotype frequencies after gametic competition are $X_i^{\male,s} = w_g X_i^{\male} / \bar{w}_H^{\male}$ and $Y_i^{\male,s} = w_g Y_i^{\male} / \bar{w}_H^{\male}$, where $\bar{w}_H^{\male} = \sum_{i=1}^{4} w_g X_i^{\male} + w_g Y_i^{\male}$ is the mean fitness of male ($\male = \male$) or female ($\male = \female$) gametes. Random mating then occurs between gametes to produce diploid zygotes with genotype ij at the **A** and **M** loci, such that XX zygotes are denoted xx_{ij}, XY zygotes are xy_{ij}, and YY zygotes are yy_{ij}. In XX and YY zygotes, individuals with genotype ij are equivalent to those with genotype ji. For simplicity, we denote the frequency of genotype ij in XX and YY zygotes to the average of these frequencies, $xx_{ij} = (X_i^{\female,s} X_j^{\male,s} + X_j^{\female,s} X_i^{\male,s})/2$ and $yy_{ij} = (Y_i^{\female,s} Y_j^{\male,s} + Y_j^{\female,s} Y_i^{\male,s})/2$.

Denoting the **M** locus genotype by b ($b \in MM$, Mm, mm) and the **X** locus genotype by c ($c \in XX$, XY, YY), zygotes develop as females with probability k_{bc}. Therefore, the frequencies of XX females are given by $xx_{ij}^{\female} = k_{bc} xx_{ij}$, XY females are given by $xy_{ij}^{\female} = k_{bc} xy_{ij}$, and YY females are given by $yy_{ij}^{\female} = k_{bc} xy_{ij}$. Similarly, XX male frequencies are $xx_{ij}^{\male} = (1 - k_{bc}) xx_{ij}$, XY male frequencies are $xy_{ij}^{\male} = (1 - k_{bc}) xy_{ij}$, and YY males frequencies are $yy_{ij}^{\male} = (1 - k_{bc}) xy_{ij}$. 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. Typically, we assume that the ancestral sex-determining system (**X** locus) is XY ($k_{MMXX} = 1$ and

$k_{MMXY} = k_{MMYY} = 0$) 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, h, for an individual of type ij ($h \in AA$, Aa, aa, see Table 1). The diploid frequencies after selection in sex d are given by $xx_{ij}^{\female,s} = w_h^{\female} xx_{ij} / \bar{w}^{\female}$, $xy_{ij}^{\female,s} = w_h^{\female} xy_{ij} / \bar{w}^{\female}$, and $yy_{ij}^{\female,s} = w_h^{\female} yy_{ij} / \bar{w}^{\female}$, where $\bar{w}^{\female} = \sum_{i=1}^{4} \sum_{j=1}^{4} w_h^{\female} xx_{ij} + w_h^{\female} xy_{ij} + w_h^{\female} yy_{ij}$ is the mean fitness of individuals of sex $\female$.

Finally, these diploids undergo meiosis to produce the next generation of gametes. Recombination and sex-specific meiotic drive occur during meiosis. Here, we allow the relative locations of the SDR, **A**, and **M** loci to be generic 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 gives substitutions for χ for defined relative locations of these loci. During meiosis in sex d, meiotic drive occurs such that, in Aa heterozygotes, a fraction α_d of gametes produced carry the A allele and $(1-\alpha^{\female})$ carry the a allele.

Table S.1: χ substitutions for different loci orders (assuming no interference)

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

Among gametes from sex $\female$ (sperm/pollen when $\female = \male$, eggs/ovules when $\female = \female$), the frequency of haplotypes (before gametic competition) in the next generation are given by

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

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

734

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

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

736

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

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

738

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

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

740

The full system is therefore described by 16 recurrence equations (three loci, each
742 with two alleles, and two gamete sexes yields 16 combinations). However, some diploid types are not produced under a given sex determination system. For exam-
744 ple, with the M allele fixed and ancestral XY sex determination, there are no XX males, XY females, or YY females ($xx_{11}^{\male}$, $xx_{12}^{\male}$, $xx_{22}^{\male}$, $xy_{11}^{\female}$, $xy_{12}^{\female}$, $xy_{22}^{\female}$, $yy_{11}^{\female}$, $yy_{12}^{\female}$,
746 and $yy_{22}^{\female}$ are all 0). In this case, the system only involves six recursion equations because there is only one **M** locus allele and no Y-bearing female gametes. This six-
748 equation system yields equilibrium (S.3). Within this resident population (when m is absent) we describe frequencies among different gamete types, which are given
750 by $X_{MA}^{\female} = p_{Xf}$, $X_{Ma}^{\female} = (1-p_{Xf})$, $X_{MA}^{\male} = (1-q)p_{Xm}$, $X_{Ma}^{\male} = (1-q)(1-p_{Xm})$, $Y_{MA}^{\male} = qp_{Ym}$, and $Y_{Ma}^{\male} = q(1-p_{Ym})$. In this resident population, the mean fitnesses
752 are given in table S.2.

Table S.2: mean fitnesses in resident (M fixed, XY sex determination)

Sex & Life Cycle Stage	Mean Fitness
female gametes ($\bar{w}_H^{\female}$)	$p_X^{\female} w_A^{\female} + (1 - p_X^{\female}) w_a^{\female}$
male gametes ($\bar{w}_H^{\male}$)	$\bar{p}^{\male} w_A^{\male} + (1 - \bar{p}^{\male}) w_a^{\male}$
females ($\bar{w}^{\female}$)	$\{p_X^{\female} w_A^{\female} (1-q) p_X^{\male} w_A^{\male} w_{AA}^{\female} +$ $(1 - p_X^{\female}) w_a^{\female} (1-q) p_X^{\male} w_A^{\male} w_{Aa}^{\female} +$ $p_X^{\female} w_A^{\female} (1-q)(1 - p_X^{\male}) w_a^{\male} w_{Aa}^{\female} +$ $(1 - p_X^{\female}) w_a^{\female} (1-q)(1 - p_X^{\male}) w_a^{\male} w_{aa}^{\female}\} / \{\bar{w}_H^{\female} \bar{w}_H^{\male}\}$
males ($\bar{w}^{\male}$)	$\{p_X^{\female} w_A^{\female} q p_Y^{\male} w_A^{\male} w_{AA}^{\male} +$ $(1 - p_X^{\female}) w_a^{\female} q p_Y^{\male} w_A^{\male} w_{Aa}^{\male} +$ $p_X^{\female} w_A^{\female} q (1 - p_Y^{\male}) w_a^{\male} w_{Aa}^{\male} +$ $(1 - p_X^{\female}) w_a^{\female} q (1 - p_Y^{\male}) w_a^{\male} w_{aa}^{\male}\} / \{\bar{w}_H^{\male} \bar{w}_H^{\male}\}$

Resident equilibrium and stability

In the resident population (allele M fixed), we 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-bearing male gametes, q, which may deviate from $1/2$ due to meiotic drive in males.

Various forms of selection can maintain a polymorphism at the **A** locus, including sexually antagonistic selection, overdominance and conflicts between diploid selection and selection upon haploid genotypes (ploidally antagonistic selection, Immler et al. 2012) or a combination of these selective regimes. Here, we assume that selection and meiotic drive are weak relative to recombination ($s^{\female}$, $t^{\female}$, $\alpha_\Delta^{\female}$ of order ϵ). The maintenance of a polymorphism at the **A** locus then requires that

$$\begin{aligned} 0 &< -((1 - h^{\female}) s^{\female} + (1 - h^{\male}) s^{\male} + t^{\female} + t^{\male} + \alpha_\Delta^{\female} + \alpha_\Delta^{\male}) \\ 0 &< (h^{\female} s^{\female} + h^{\male} s^{\male} + t^{\female} + t^{\male} + \alpha_\Delta^{\female} + \alpha_\Delta^{\male}). \end{aligned} \tag{S.2}$$

which indicates that a polymorphism is maintained under various selective regimes.

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

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

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

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

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

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 $♀ \in \{♀, ♂\}$ ($\bar{p}$ 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 A allele frequency on 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 ($\alpha_{\Delta}^{♀} = t^{♀} = 0$), these results reduce to those of van Doorn and Kirkpatrick (2007).

Invasion without assuming weak selection

Here, we determine whether a rare neo-Y or neo-W allele spreads when rare, which occurs when $\lambda > 1$. 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 $\left\{(\lambda_{mA} - 1) + (\lambda_{ma} - 1)\right\}/2 > 0$ then $\lambda > 1$, see table 2 for λ_{mi}). 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

$$r_{AM}\left[\frac{p_X^{\female} w_A^{\female} w_a^{\male}(1-\alpha^{\male})}{\bar{w}_H^{\female}\bar{w}_H^{\male}(\lambda_{mA}-1)} + \frac{(1-p_X^{\female}) w_a^{\female} w_A^{\male}\alpha^{\male}}{\bar{w}_H^{\female}\bar{w}_H^{\male}(\lambda_{ma}-1)}\right]\frac{w_{Aa}^{\male}}{\bar{w}^{\male}} < 1, \tag{S.5}$$

for the neo-Y, and

$$R\left[\frac{\bar{p}^{\male} w_A^{\male} w_a^{\female}(1-\alpha^{\female})}{\bar{w}_H^{\male}\bar{w}_H^{\female}(\lambda_{mA}-1)} + \frac{(1-\bar{p}^{\male}) w_a^{\male} w_A^{\female}\alpha^{\female}}{\bar{w}_H^{\male}\bar{w}_H^{\female}(\lambda_{ma}-1)}\right]\frac{w_{Aa}^{\male}}{\bar{w}^{\male}} < 1, \tag{S.6}$$

for the neo-W. Equations (S.5) and (S.6) show that the new sex-determining allele, m, is expected to invade for any probability of recombination between loci **A** and **M**, r_{AM}, when the net flow of recombinants is from the less fit (smaller λ_{mi}) to the more fit **A** background (making the terms inside the square brackets in Equations S.5 and S.6 negative). When the net flow of recombinants is from the more fit to the less fit haplotype, the new sex-determining allele can still invade when the rate of recombination between it and the selected locus is small enough.