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 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 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 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). For example, flexible sex determination systems may be favoured in order to exploit local environmental conditions that are optimal for males or females, which creates locally biased sex ratios (Charnov and Bull 1977, Werren and Taylor 1984, Pen et al. 2010). In addition, feminizing mutations may invade when female biased sex ratios are favoured due to selection among demes (Wilson and Colwell 1981, Vuillleumier et al. 2007). In other situations, sex ratio selection may favour transitions in order to restore equal sex ratios. 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, restoring an even sex ratio.

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-medelian) 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 (Ubeda and Haig, 2005; Lindholm et al. 2016). Because there are typically 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 smaller (but non-negligible) 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 might 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 (**?**, , 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 sex ratio selection. We find that new genetic sex determination systems are not affected by any sex ratio biases 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 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 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 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 (ESD), 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 (see Sup. Mat. for recursion equations). 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 $w_A^{⚥}$ and $w_a^{⚥}$ ($⚥ \in \{♀, ♂\}$; 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 $w_g^{♂}$ in males and $w_g^{♀}$ 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 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 $⚥$ produce gametes bearing allele A with probability $\alpha^{⚥}$. Thus, the **A** locus can experience sex-specific gametic competition, diploid selection and/or meiotic drive.

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

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

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

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 $\mathbf{M}$ 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). Therefore, the invasion of rare mutant neo-Y or neo-W alleles can be simplified and given by the largest eigenvalue that solves the quadratic characteristic polynomial $\lambda^2 + b\lambda + c = 0$, where b is the average of the growth rates of the two haplotypes that carry the m allele (mA and ma), $b = (\lambda_{mA} + \lambda_{ma})/2$, and c also involves the fitness of m alleles when they recombine onto the other **A** background in a heterozygote, $c = \lambda_{mA}\lambda_{ma} + \rho_{mA}\rho_{ma}$ (see table 2).

Table 2: Parameters determining invasion for neo-Y or neo-W alleles

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

$\bar{p}^{\male} = p_Y^{\male} q + p_X^{\male}(1 - q)$ is the average frequency of the A allele among X- and Y-bearing male gametes
see Table S.2 for 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 $p_X^{\female} w_A^{\female}/\bar{w}_H^{\female}$). 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 $\bar{p}^{\male} w^{\male}_A/\bar{w}^{\male}_H$). 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 occur with probability $\bar{p}^{\male}_X w^{\male}_A/\bar{w}^{\male}_H$). If the **A** locus is initially linked to the ancestral sex-determining locus, **X**, (i.e., $r < 1/2$) 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. 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 $\lambda > 1$). 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

$$R\left[\frac{p^{\female}_X w^{\female}_A w^{\male}_a (1-\alpha^{\male})}{\bar{w}^{\female}_H \bar{w}^{\male}_H (\lambda_{mA}-1)} + \frac{(1-p^{\female}_X) w^{\female}_a w^{\male}_A \alpha^{\male}}{\bar{w}^{\female}_H \bar{w}^{\male}_H (\lambda_{ma}-1)}\right]\frac{w^{\male}_{Aa}}{\bar{w}^{\male}} < 1, \tag{1}$$

for the neo-Y, and

$$R\left[\frac{\bar{p}^{\male} w^{\male}_A w^{\female}_a (1-\alpha^{\female})}{\bar{w}^{\male}_H \bar{w}^{\female}_H (\lambda_{mA}-1)} + \frac{(1-\bar{p}^{\male}) w^{\male}_a w^{\female}_A \alpha^{\female}}{\bar{w}^{\male}_H \bar{w}^{\female}_H (\lambda_{ma}-1)}\right]\frac{w^{\male}_{Aa}}{\bar{w}^{\male}} < 1, \tag{2}$$

for the neo-W. Equations (1) and (2) show that the new sex-determining allele, m, is expected to invade for any recombination rate, R, 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 1 and 2 negative). Q: is it definitely possible to have negative square brackets for a equilibria maintained by selection? 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, R, is small enough. Q:Is it the case that sometimes the square brackets are positive and invasion occurs for $R = 1/2$? In which case it might be better to have slightly different phrasing here.

We can explicitly determine the conditions under which invasion occurs if we assume 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 ($\hat{p}_Y^{♂}$, $\hat{p}_X^{♂}$, and $\hat{p}_X^{♀}$) is given by equations (S.3) and (S.4) where we assume selection and meiotic drive are weak relative to recombination ($s^{⚥}$, $t^{⚥}$, $\alpha_\Delta^{⚥}$ of order ϵ). Under weak selection, we denote the leading eigenvalue describing the invasion of a neo-Y ($k = 0$) and a neo-W ($k = 0$) into an ancestrally XY system by $\lambda_{Y',XY}$ and $\lambda_{W',XY}$, respectively, which are given by

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

and

$$\lambda_{W',XY} = \lambda_{Y',XY} + \left(2\alpha_\Delta^{♂} - 2\alpha_\Delta^{♀} + t^{♂} - t^{♀}\right)\left(\hat{p}_Y^{♂} - \hat{p}_X^{♂}\right) + O\left(\epsilon^3\right) \tag{4}$$

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $S_A = (D^{♂} + \alpha_\Delta^{♂} + t^{♂}) - (D^{♀} + \alpha_\Delta^{♀} + t^{♀})$ 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 (3) 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.

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 (4) can be positive, which can allow 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 S.1B,D.

We find that neo-W alleles can invade 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 (4) disappears and invasion depends 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 2). Secondly, we can simplify cases where $R > r$ 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 equal dominance, $h^{♀} = h^{♂}$. 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 2B), 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 ($s^{♀}(s^{♂} - s^{♀}) > 0$, see Figure 2C,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 $R > r$.

Previous research suggests, when the ancestral sex-determining locus is linked

Table 3: Invasion conditions for unlinked neo-W ($R = 1/2$, $r < 1/2$) with one form of haploid selection only

Assumptions	neo-W spreads ($\lambda_{W',XY} > 1$) if
$h^{\male} = h^{\female}, t^{\female} = t^{\male} = \alpha_{\Delta}^{\female} = 0$	$s^{\female} s^{\male} > 0$
$h^{\male} = h^{\female}, t^{\female} = t^{\male} = \alpha_{\Delta}^{\male} = 0$	$s^{\female} s^{\male} > 0$
$h^{\male} = h^{\female}, t^{\female} = \alpha_{\Delta}^{\female} = \alpha_{\Delta}^{\male} = 0$	$s^{\female}(s^{\male} - s^{\female}) > 0$
$h^{\male} = h^{\female}, t^{\male} = \alpha_{\Delta}^{\female} = \alpha_{\Delta}^{\male} = 0$	$s^{\male}(s^{\female} - s^{\male}) > 0$

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, $\alpha^{\male} \neq 1/2$, $\alpha^{\female} = 1/2$). We will also disregard gametic competition ($t^{\female} = t^{\male} = 0$) 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 $\lambda_{Y',ZW} = \lambda_{W',XY}$ (for a numerical example, compare Figure 1A,B to Figure 1C,D).

Offspring-controlled neo-ESD

Perhaps sex ratio selection can be invoked only when the invading mutation arises half the time in males and half the time in females, like an autosomal locus. If so, then we should see sex ratio influence the invasion of a novel sex-determining region that causes half of its carries to become female and half to become male. However, we find that the growth rate of a rare, dominant offspring-controlled neo-ESD region that produces males or females with equal probability ($k = 1/2$) is

$$\lambda_{ESD} \approx 1 + \frac{1}{2}\frac{(\lambda_{Y,XY} - 1) + (\lambda_{W,XY} - 1)}{2}\Big|_{R=1/2}, \tag{5}$$

which is the same for invasion into 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 in males only then sex ratio only biased when ancestrally XY), sex ratio selection does not drive the turnover to a perfect ($k = 1/2$), offspring-controlled neo-ESD. Also note that with $k = 1/2$ the neo-ESD gets half of the advantages of a neo-W and half that of a 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). 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.

Maternally-controlled neo-ESD

One might think that when the sex of zygotes is under the control of mothers, there would be strong selection to balance the sex ratio among zygotes. However, we find that, as with offspring control, under weak selection the invasion fitness of a sex-determiner that is maternally controlled can be written

$$\lambda_{k,XY} \approx 1 + V_A S_A C_k, \tag{6}$$

where C_k is a term that depends on k. Of particular interest is $k = 1/2$ (i.e., when the mother perfectly balances the sex ratio of her offspring). When both recombination rates are small we have $C_{1/2} \approx R(s^{\male} - s^{\female})/8 = \lim_{r \to 0} C_1/4$. This implies that, at least under tight linkage, the invasion of maternally-controlled ESD is independent of R (because $S_A \propto R^{-1}$) and can invade whenever a neo-W can (which can invade even when it biases the sex ratio further; Figures **??** – **??**).

Discussion

One might expect Fisherian sex ratio selection to influence the spread of new sex-determining systems because linkage between haploid selected loci and sex-determining regions cause biased zygotic sex ratios (Hamilton 1967, **?**, 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. 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. That is, under Fisherian sex ratio selection, the success of a mutant relative to the non-mutant depends, in equal parts, on the contributions made by males and females to the next generation. 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 mutations depends only on the number of alleles contributed by males (equation **??** and Table 2). Even mutants that are equally likely to be found in males or females, such as an environmental sex determination mutation (equation 5), 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 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 upon 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 allleles 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, polymorphisms can be maintained at which the mean fitness of females (males) or males is lower than it would be without sex-linkage, allowing unlinked neo-W (neo-Y) alleles to invade, see figure S.1.

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.

Our model of meiotic drive is very 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 (**?**) (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 (here, we assume that the total gamete number is not affected by drive). Thus, the number of mates competing for fertilization (mating system) can further affect the frequency of a meiotic drive allele Holman et al., 2015). Finally, the intensity of pollen/sperm competition under a particular mating system can depend on the density of males available to donate pollen/sperm, which can depend on the sex ratio and population size (Taylor and Jaenike, 2002). Here, we do not consider feedbacks between sex ratios and the intensity of haploid selection. It remains to be investigated how the evolution of new sex-determining mechanisms could be influenced by ecological feedbacks under different mating systems and by two-locus meiotic drive.

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 CHECK (Kallman 1973; Wada et al. 1998; Lande et al. 2001; Lindholm and Breden 2002; Streelman et al. 2003; Fernandez and Morris 2008; Kitano et al. 2009; Roberts et al. 2009). 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, 2010-ish). We note that linkage with sex chromosomes is not, a priori, more permissive to the maintainence of ploidally antagonistic variation (Immler et al. 2012). Secondly, we note 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.

Do we have any cool examples? Meiotic drive alleles certainly more common on the sex chromosomes - although there are other explanations: (1) Divergence between X and Y provides a ready supply of target alleles for meiotic drive. (2) sex-linked meiotic drive has a more obvious phenotype to detect, sex ratio bias.

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. Thus,

In broadcast spawning animal species (e.g., corals, many fish) and species where sperm typically requires greater longevity, haploid selection may be stronger because transcripts shared during spermatogenesis may become depleted (Immler et al. 2014). also, mating systems (e.g., fewer alleles are available during gametic competition in monogamous species), selfing rates, and estimates of pollen limitation could be used as indicators of the intensity of haploid selection

We have results where polygenic sex determination is sometimes stable, may be worth mentioning:

"Polygenic sex determination has been reported in many plants (e.g. Shannon & Holsinger 2007), fishes (Vandeputte et al. 2007; Ser et al. 2010; Liew et al. 2012), crustaceans (e.g. Battaglia 1958; Battaglia & Malesani 1959; Voordouw & Anholt 2002), bivalves (Haley 1977; Saavedra et al. 1997), gastropods (Yusa 2007a,b), and polychaetes (Bacci 1965, 1978; Premoli et al. 1996)." From Vuilleumier et al. 2007: "Polymorphism for sex-determining genes within or among populations has been reported in many species including houseflies, midges, woodlice, platyfish, cichlid fish, and frogs (Gordon, 1944; Kallman, 1970; Thomp-son, 1971; Macdonald, 1978; Bull, 1983; Rigaud et al., 1997; Caubet et al., 2000; Lande et al., 2001; Ogataet al., 2003; Lee et al., 2004; Mank et al., 2006)." Also check Kallman (1984) -from vD&K, 2010.

vD&K also suggest that this build up of sex-antagonistic polymorphisms may help to stabilize the ancestral sex-determining system, which would not be the case with haploid selection.

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Figures

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 $X_i^{\text{⚥},s} = w_g X_i^{\text{⚥}} / \bar{w}_H^{\text{⚥}}$ and $Y_i^{\text{⚥},s} = w_g Y_i^{\text{⚥}} / \bar{w}_H^{\text{⚥}}$, where $\bar{w}_H^{\text{⚥}} = \sum_{i=1}^{4} w_g X_i^{\text{⚥}} + w_g Y_i^{\text{⚥}}$ is the mean fitness of male ($\text{⚥} = \male$) or female ($\text{⚥} = \female$) 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

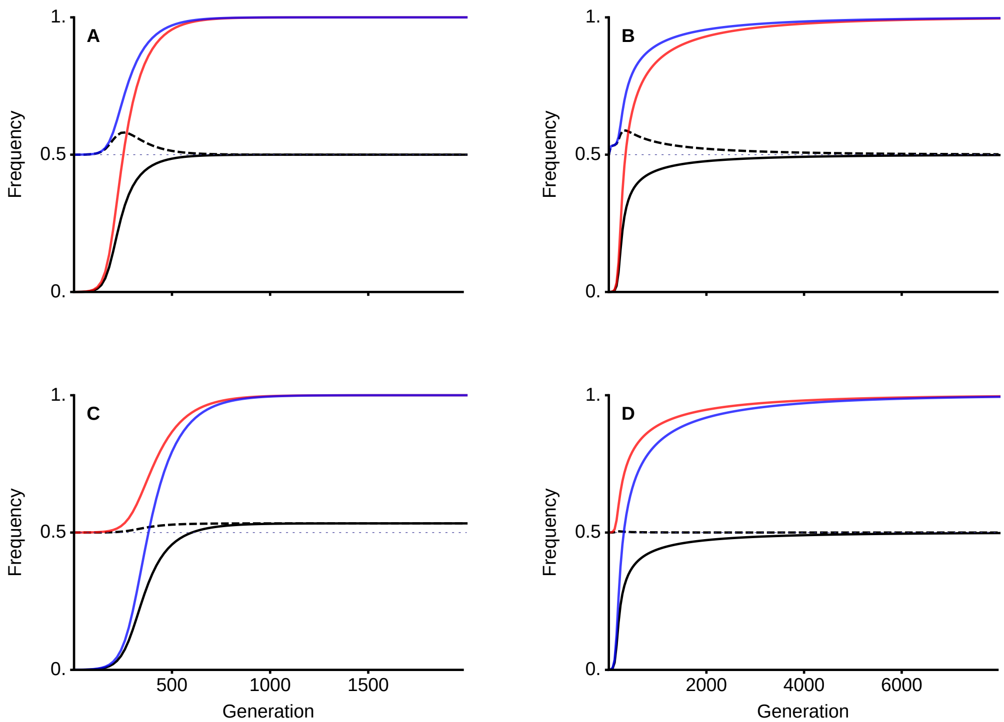

Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occurs similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines show male frequency). During the invasion of 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 ($t^{♀} = t^{♂} = 0$) and meiotic drive occurs during male meiosis only ($\alpha^{♀}_{\Delta} = 0$, $\alpha^{♂}_{\Delta} = -1/5$). 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-deteming region ($r = 1/2$, $R = 1/20$) such that a neo-Y can caused biased sex ratios (panel C). Unlike with diploid selection alone, when there is haploid selection (in this case meiotic drive), neo-sex-determining loci that are less closely linked to the **A** locus can also spread (panels B and D, $r = 1/20$, $R = 1/2$), see equation (4) and Figure 2B. These transitions are unusual because linkage generally allows favourable associations to arise via selection and the new sex determination systems in B and D have looser linkage. Thus, diploid mean fitness decreases over the course of the transitions in B and D, see Figure S.1. However, the mean fitness of females increases during the spread of dominant neo-W alleles and the mean fitness of males increases during the spread of dominant neo-Y alleles, Figure S.1. In this plot there are no sex differences in selection and an equilirbium is maintained because selection in diploids opposes meiotic drive, $s^{♀} = s^{♂} = 1/5$, $h^{♀} = h^{♂} = 7/10$. 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. Could make sex ratio biases more extreme by reducing the r in A and C and reducing R in B and D. Matt - could you uncomment the line legends in the Mathematica file (function not included in my Mathematica version).

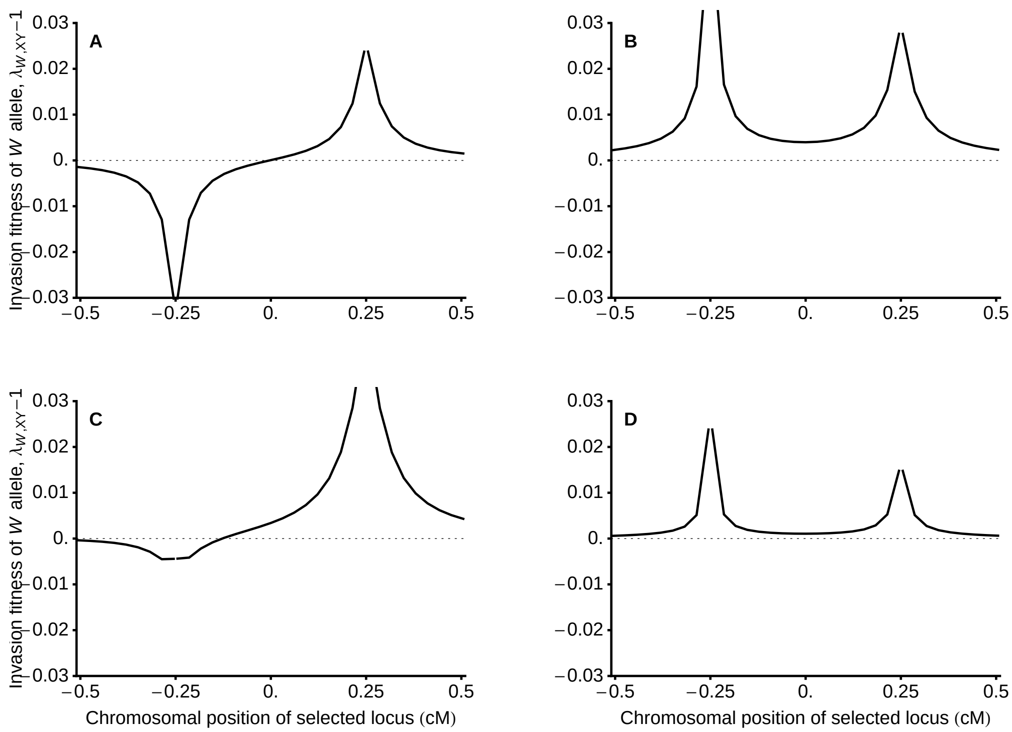

Figure 2: A sexual antagonism (no haploid selection), B drive (no gametic competition), equal selection in sexes ($s^{♀} = s^{♂}$), C & D Pollen/Sperm competition only (no drive). C allele favoured in pollen/sperm competition selected against less in males ($t < 0$, $s^{♀}, s^{♂} > 0$, $s^{♀} < s^{♀}$). D allele favoured in pollen/sperm competition selected against more in males than females ($t < 0$, $s^{♀}, s^{♂} > 0$, $s^{♀} > s^{♀}$). I suspect that panel C has a region where no equilibrium is maintained (CHECK! Maybe include different parameters here). Currently use different parameters for B than using in figure 1 (selection/drive twice as strong in turnover figure)

$k_{MMXY} = k_{MMYY} = 0$) 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 $xx_{ij}^{⚥,s} = w_h^{⚥} xx_{ij}/\bar{w}^{⚥}$, $xy_{ij}^{⚥,s} = w_h^{⚥} xy_{ij}/\bar{w}^{⚥}$, and $yy_{ij}^{⚥,s} = w_h^{⚥} yy_{ij}/\bar{w}^{⚥}$, where $\bar{w}^{⚥} = \sum_{i=1}^{4}\sum_{j=1}^{4} w_h^{⚥} xx_{ij} + w_h^{⚥} xy_{ij} + w_h^{⚥} yy_{ij}$ is the mean fitness of individuals of sex d.

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 $(1-\alpha^{⚥})$ 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 ⚥ (sperm/pollen when ⚥ = ♂, eggs/ovules when ⚥ = ♀), the frequency of haplotypes (before gametic competition) in the next generation are given by

$$
\begin{aligned}
X^{\text{⚥}\prime}_{MA} =& xx^{\text{⚥},s}_{11} + xx^{\text{⚥},s}_{13}/2 + (xx^{\text{⚥},s}_{12} + xx^{\text{⚥},s}_{14})\alpha^{\text{⚥}} \\
&- R(xx^{\text{⚥},s}_{14} - xx^{\text{⚥},s}_{23})\alpha^{\text{⚥}} \\
&+ (xy^{\text{⚥},s}_{11} + xy^{\text{⚥},s}_{13})/2 + (xy^{\text{⚥},s}_{12} + xy^{\text{⚥},s}_{14})\alpha^{\text{⚥}} \\
&- r(xy^{\text{⚥},s}_{12} - xy^{\text{⚥},s}_{21})\alpha^{\text{⚥}} - \chi(xy^{\text{⚥},s}_{13} - xy^{\text{⚥},s}_{31})/2 \\
&+ \Big\{ -(R + r + \chi)xy^{\text{⚥},s}_{14} + (r + \chi - R)xy^{\text{⚥},s}_{41} \\
&+ (R + r - \chi)xy^{\text{⚥},s}_{23} + (R + \chi - r)xy^{\text{⚥},s}_{32} \Big\}\alpha^{\text{⚥}}/2
\end{aligned}
\tag{S.1a}
$$

$$
\begin{aligned}
X^{\text{⚥}\prime}_{Ma} =& xx^{\text{⚥},s}_{22} + xx^{\text{⚥},s}_{24}/2 + (xx^{\text{⚥},s}_{12} + xx^{\text{⚥},s}_{23})\alpha^{\text{⚥}} \\
&- R(xx^{\text{⚥},s}_{23} - xx^{\text{⚥},s}_{14})\alpha^{\text{⚥}} \\
&(xy^{\text{⚥},s}_{22} + xy^{\text{⚥},s}_{24})/2 + (xy^{\text{⚥},s}_{21} + xy^{\text{⚥},s}_{23})(1 - \alpha^{\text{⚥}}) \\
&- r(xy^{\text{⚥},s}_{21} - xy^{\text{⚥},s}_{12})(1 - \alpha^{\text{⚥}}) - \chi(xy^{\text{⚥},s}_{24} - xy^{\text{⚥},s}_{42})/2 \\
&+ \Big\{ -(R + r + \chi)xy^{\text{⚥},s}_{23} + (r + \chi - R)xy^{\text{⚥},s}_{32} \\
&+ (R + r - \chi)xy^{\text{⚥},s}_{14} + (R + \chi - r)xy^{\text{⚥},s}_{41} \Big\}(1 - \alpha^{\text{⚥}})/2
\end{aligned}
\tag{S.1b}
$$

$$
\begin{aligned}
X^{\text{⚥}\prime}_{mA} =& xx^{\text{⚥},s}_{33} + xx^{\text{⚥},s}_{13}/2 + (xx^{\text{⚥},s}_{23} + xx^{\text{⚥},s}_{34})\alpha^{\text{⚥}} \\
&- R(xx^{\text{⚥},s}_{23} - xx^{\text{⚥},s}_{14})\alpha^{\text{⚥}} \\
&(xy^{\text{⚥},s}_{33} + xy^{\text{⚥},s}_{31})/2 + (xy^{\text{⚥},s}_{32} + xy^{\text{⚥},s}_{34})\alpha^{\text{⚥}} \\
&- r(xy^{\text{⚥},s}_{34} - xy^{\text{⚥},s}_{43})\alpha^{\text{⚥}} - \chi(xy^{\text{⚥},s}_{31} - xy^{\text{⚥},s}_{13})/2 \\
&+ \Big\{ -(R + r + \chi)xy^{\text{⚥},s}_{32} + (r + \chi - R)xy^{\text{⚥},s}_{23} \\
&+ (R + r - \chi)xy^{\text{⚥},s}_{41} + (R + \chi - r)xy^{\text{⚥},s}_{14} \Big\}\alpha^{\text{⚥}}/2
\end{aligned}
\tag{S.1c}
$$

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

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

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

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

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

The full system is therefore described by 16 recurrence equations (three loci, each with two alleles, and two gamete sexes yields 16 combinations). 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 XX males, XY females, or YY females ($xx_{11}^{\text{♂}}$, $xx_{12}^{\text{♂}}$, $xx_{22}^{\text{♂}}$, $xy_{11}^{\text{♀}}$, $xy_{12}^{\text{♀}}$, $xy_{22}^{\text{♀}}$, $yy_{11}^{\text{♀}}$, $yy_{12}^{\text{♀}}$, and $yy_{22}^{\text{♀}}$ 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-equation system yields equilibrium (S.3). Within this resident population (when m is absent) we describe frequencies among different gamete types, which are given by $X_{MA}^{\text{♀}} = p_{Xf}$, $X_{Ma}^{\text{♀}} = (1 - p_{Xf})$, $X_{MA}^{\text{♂}} = (1 - q)p_{Xm}$, $X_{Ma}^{\text{♂}} = (1 - q)(1 - p_{Xm})$, $Y_{MA}^{\text{♂}} = qp_{Ym}$, and $Y_{Ma}^{\text{♂}} = q(1 - p_{Ym})$. In this resident population, the mean fitnesses 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 ($s^{\female\male}$, $t^{\female\male}$, $\alpha_\Delta^{\female\male}$ of order ϵ). The maintenance of a polymorphism at the **A** locus then requires that

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

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

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

where $V_A = \bar{p}(1-\bar{p})$ is the variance in the frequency of A and $D^{⚥} = \big(\bar{p}s^{⚥} + (1-\bar{p})h^{⚥}s^{⚥}\big) - \big(\bar{p}h^{⚥}s^{⚥} + (1-\bar{p})\big)$ 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).

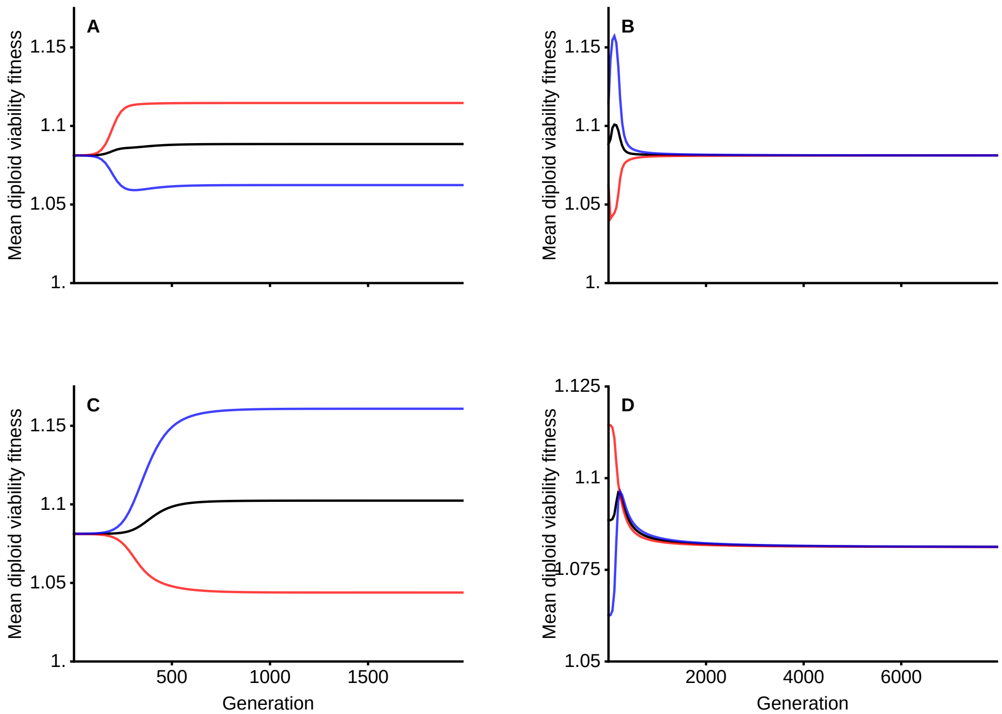

Figure S.1: Could add titles to the columns/rows: neo-W for row 1, neo-Y for row 3, $r = 0.5$, $R = 0.05$ for column 1 and $r = 0.05$, $R = 0.5$ for column 2. & possibly adjust padding (too much whitespace?). Matt - could you uncomment the line legends in the Mathematica file (function not included in my Mathematica version).

708 # Supplementary Figures