

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

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Contributions:

Abstract

2 Sex determination systems are remarkably dynamic; many studied taxa
display transitions of sex-determining genes between chromosomes or the
4 evolution of entirely new sex-determining systems. Predominant theories
in which new sex-determining systems are favoured by selection involve
6 sex ratio selection or sex-specific selection (e.g., sexually antagonistic se-
lection). Here, we utilize population genetic models to study the spread of
8 novel sex-determiners when there is a period of sex-specific haploid selec-
tion. Many loci experience sex-specific selection on their haploid genotypes
10 during gametic competition (e.g., pollen/sperm competition) or meiosis (i.e.,
non-Mendelian segregation); selective processes that typically occur in one
12 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
14 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
16 sex ratio biases that are caused by haploid selection. A surprising result given
that other determinants of sex allocation typically experience strong Fische-
18 rian sex ratio selection to equalize sex ratios. In addition, we find that, with
haploid selection, transitions between male and female heterogamety (XY
20 to ZW or ZW to XY) can occur despite breaking up favourable associations
that build up between the ancestral sex-determining locus and selected loci.
22 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.
24 Such transitions are not possible with diploid selection alone, in which case
tighter linkage increases the fitness of both males and females. Thus, our
26 models offer several new insights to be explored as information about sex
determination in non-model taxa accumulates.

28 **Introduction**

Animals and angiosperms exhibit extremely diverse sex determination systems (reviewed in Bull 1983, Charlesworth and Mank 2010, Beukeboom and Perrin 2014, Bachtrog et al. 2014). Among species with genetic sex determination of diploid sexes, some taxa have heterogametic males (XY) and homogametic females (XX), including mammals and most dioecious plants (Ming et al. 2011); whereas other taxa have homogametic males (ZZ) and heterogametic females (ZW), including Lepidoptera and birds. Within several taxa, the chromosome that harbours the master sex-determining region changes. For example, transitions of the master sex-determining gene between chromosomes or the evolution of new master sex-determining genes have occurred in Salmonids (Li et al. 2011, Yano et al. 2012), Diptera (Vicoso and Bachtrog 2015), and *Oryzias* (Myosho et al. 2012). In addition, many gonochoric clades with genetic sex determination exhibit transitions between male (XY) and female (ZW) heterogamety, including lizards (Ezaz et al. 2009), eight of 26 teleost fish families (Mank et al. 2006), true fruit flies (Tephritids, Vicoso and Bachtrog 2015), amphibians (Hillis and Green 1990), the angiosperm genus *Silene* (Slancarova et al. 2013), 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 accounting for the spread of new sex determination systems by selection involve fitness differences between sexes (e.g., sexually antagonistic selection) or sex ratio selection. van Doorn and Kirkpatrick (2007; 2010) show that new sex 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

58 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 tran-
60 sition between male and female heterogamety (e.g., a ZW to XY transition, van
Doorn and Kirkpatrick 2010). However, any sexually-antagonistic loci that are
62 linked to the ancestral sex-determination locus will develop similar, favourable
associations and select against the spread of a new sex-determination system.

64 It has been suggested that sex ratio selection is a dominant force in the evolu-
tion of sex determination (e.g., Bull 1983, p66-67; Beukeboom and Perrin 2014,
66 Chapter 7). The default mode of sex ratio selection is ‘Fisherian’ sex ratio se-
lection, which favours equal investment in male and female offspring (i.e., a 1:1
68 zygotic sex ratio when assuming that males and females are equally costly to pro-
duce, Fisher 1930, Charnov 1982). Given that the sex determination system can
70 directly affect the sex ratio, we might expect Fisherian sex ratio selection to influ-
ence the spread of new sex determination systems. For example, Kozielska et al.
72 (2010) consider systems in which the ancestral sex chromosomes experience mei-
otic drive (e.g., where driving X or Y chromosomes are inherited disproportion-
74 ately often), which causes sex ratios to become biased (Hamilton 1967). They find
that new, unlinked sex-determining loci (masculinizing or feminizing mutations,
76 i.e., neo-Y or neo-W loci) can then spread, which restore an even sex ratio.

Here, we use mathematical models to find the conditions under which new
78 sex determination systems are favoured when loci experience haploid selection.
Haploid genotypes at many loci experience selection during gamete competition
80 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
82 genotypes during gamete production (from one parent) and the term ‘gametic com-
petition’ to refer to selection upon haploid genotypes within a gamete/gametophyte
84 pool (potentially from by multiple parents); the term ‘haploid selection’ encom-
passes both processes. Meiotic drive generally occurs either during the production
86 of male or female gametes only (Úbeda and Haig 2005, Lindholm et al. 2016). Be-
cause there are typically many more pollen/sperm than required for fertilization,

88 gametic competition is also typically sex specific, occurring primarily among male
gametes. Gametic competition may be particularly common in plants, in which 60-
90 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, Arunku-
92 mar et al. 2013, Gossmann et al. 2014). In addition, artificial selection pressures
applied to male gametophytes are known to cause a response to selection (e.g.,
94 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
96 selected during competition in animal sperm, although precise estimates are un-
certain (Zheng et al. 2001, Joseph and Kirkpatrick 2004, Vibranovski et al. 2010,
98 Immler et al. 2014).

There are various ways in which a period of haploid selection could influence
100 transitions between sex determination systems. Firstly, if we assume that haploid
selection at any particular locus predominantly occurs in one sex (e.g., meiotic
102 drive during spermatogenesis), then such loci experience a form of sex-specific
selection. In this respect, we might expect that haploid selection would affect
104 transitions between sex determination systems in a similar manner to sex-specific
diploid selection (as explored by van Doorn and Kirkpatrick 2007; 2010). That
106 is, new masculinizing mutations (neo-Y chromosomes) could be favoured via asso-
ciations with alleles that are beneficial in the male haploid stage. However, sex
108 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
110 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
112 (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
114 systems would be influenced by the combination of sex ratio biases and associa-
tions between haploid selected loci and sex-determining regions.

116 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-

118 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
 120 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-
 122 determining locus and a haploid-selected locus can favour sex chromosome trans-
 transitions between male and female heterogamety (e.g., a neo-W allele arising at a
 124 previously autosomal locus spreads in an ancestrally XY system), despite the fact
 that these ancestral associations were built up by selection. Such transitions are
 126 not favoured in models lacking haploid selection.

Model

128 We consider the transition between an ancestral and novel sex determination sys-
 tems using a three locus model. Locus **X** is the ancestral sex-determining region,
 130 with alleles X and Y (or Z and W). Locus **A** is a locus under selection, with al-
 leles A and a . Locus **M** is a novel sex-determining region, at which the null allele
 132 (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
 134 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 in-
 136 vasion, 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**
 138 locus such that zygotes with at least one m allele develop as females with proba-
 bility k and as males with probability $1 - k$, regardless of the **X** locus genotype.
 140 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
 142 environmental sex determination (ESD) such that zygotes develop as females in
 a proportion (k) of the environments they experience. Finally, we also analyze a
 144 model of maternally-controlled environmental sex-determination, where mothers
 with at least one m allele produce daughters with probability k .

146 In each generation, we census the genotype frequencies in male and female
 gametes/gametophytes (hereafter gametes) before gametic competition. A full de-
 148 scription of our model, including recursion equations, is given in the Appendix.
 First, competition occurs among male gametes (sperm/pollen competition) and
 150 among female gametes (egg/ovule competition) separately. Selection during ga-
 metic competition depends on the **A** locus genotype, relative fitnesses are given
 152 by w_A^{\varnothing} and w_a^{\varnothing} ($\varnothing \in \{\varnothing, \sigma\}$; see table 1). We assume that all gametes compete for
 fertilization during gametic competition, which is not the case for monogamous
 154 mating systems where gametes from only one mating partner are present. Ga-
 metic competition in monogamous mating systems is equivalent to meiotic drive
 156 in our model, which only alters the frequency of gametes produced by heterozy-
 gotes. After gametic competition, random mating occurs between male and female
 158 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
 160 of maternal control) as described above. Diploid males and females then expe-
 rience selection, relative fitnesses are given by w_g^{σ} in males and w_g^{\varnothing} in females,
 162 where g is the diploid genotype at the **A** locus ($g \in \{AA, Aa, aa\}$). The next gen-
 eration of gametes is then produced by meiosis, during which recombination and
 164 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
 166 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
 168 S.1). Males/females that are heterozygous at the **A** locus may experience meiotic
 drive; Aa heterozgotes of sex \varnothing produce gametes bearing allele A with probability
 170 α^{\varnothing} . 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 $\varnothing \in \{\varnothing, \delta\}$

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

172 Results

The only asymmetry between males and females in our model is that, under the
174 ancestral sex determination system, males develop with genotype XY (or ZZ) and
females with genotype XX (or ZW). Therefore, without loss of generality, we
176 primarily present results for an ancestral XY sex determination system. Ancestral
 ZW sex determination can be considered by changing the notation such that X
178 becomes Z , Y becomes W and the labelling of male and female selection terms
are reversed.

180 Turnover between sex-determination systems

The evolution of a new sex determination system requires that a rare mutant al-
182 lele, 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,
184 λ , of the system of eight equations describing the next generation frequency of
eggs and sperm carrying the mutation, (S.1c), (S.1d), (S.1g), (S.1h). This system
186 simplifies substantially in a number of cases of interest. Dominant neo-Y (when

$k = 0$) or neo-W alleles (when $k = 1$) are only found in male diploids (neo-Y)
 188 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
 190 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
 192 the ancestral sex-determining region (\mathbf{X} locus). Thus, the invasion of rare domi-
 nant neo-Y or neo-W alleles is determined by the largest eigenvalue that solves the
 194 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
 196 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 $i \in \{A, a\}$
 198 due to recombination, see table 2. The spread of the mutant m allele depends on
 the frequency of alleles at the other loci in the ancestral population. In the ances-
 200 tral population, it is convenient to follow the frequency of the A allele in female
 gametes (eggs) from an XX female, p_X^φ , and in X-bearing, p_X^δ , and Y-bearing,
 202 p_Y^δ , male gametes (sperm). We also track the fraction of male gametes that are
 Y-bearing, q , which may deviate from $1/2$ due to meiotic drive in males.

204 I have now put the q 's in the lamdbas (i.e., removed them from \bar{w}^δ and \bar{w}^φ).
 Let's wait until we have more results before deciding on a consistent system for \bar{w} .

206

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

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

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

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

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 is driven by the fitness of male gametes and diploids, where the latter is weighted by the chance that a female egg will give rise to that diploid. For example, matings with A -bearing female gametes occur with probability $p_X^\varnothing w_A^\varnothing / \bar{w}_H^\varnothing$. Since a neo-Y is always found in males, the allele frequencies at the neo-Y (**M**) locus only change in males. Therefore, invasion by a neo-Y allele does not involve any female diploid selection terms (w_g^\varnothing). Similarly, invasion by a neo-W is driven by the fitness of female gametes and diploids and does not involve any direct selection in male diploids. However, in the case of a neo-W, female diploids can result from matings with either an X-bearing or a Y-bearing sperm. In either case, the zygote will develop as a female due to the presence of a neo-W. For example, neo-W females will therefore inherit an A from a male

gamete with probability $\bar{p}^\delta w_A^\delta / \bar{w}_H^\delta$, where $\bar{p}^\delta = p_Y^\delta q + p_X^\delta (1 - q)$. By contrast, females that do not carry the neo-W only result from matings with X-bearing sperm. They will therefore inherit an A from a male gamete with probability probability $(1 - q) \bar{p}_X^\delta w_A^\delta / \bar{w}_H^\delta$. 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^δ , \hat{p}_X^δ , and \hat{p}_X^\varnothing) is given by equations (S.3) and (S.4) where we assume selection and meiotic drive are weak relative to recombination (s^δ , t^δ , α_Δ^δ of order ϵ). Under weak selection, we denote the leading eigenvalues describing the invasion of a neo-Y ($k = 0$) and a neo-W ($k = 1$) into an ancestrally XY system by $\lambda_{Y',XY}$ and $\lambda_{W',XY}$, respectively, which are given by

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

and

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

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

246 A and a alleles in diploids of sex $\phi \in \{\varphi, \sigma\}$; \bar{p} is the leading-order probability of mating with an A -bearing gamete from the opposite sex, see appendix.

248 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 250 that V_A and S_A^2 are strictly positive as long as \mathbf{A} is polymorphic). This result echoes that of van Doorn and Kirkpatrick (2007), who considered diploid selection only 252 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 254 sexually-antagonistic selection.

Equation (2) shows that if there is no selection upon haploid genotypes ($t^\phi =$ 256 $\alpha_\Delta^\phi = 0$), 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 ($R < r$). 258 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 260 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 have built up 262 between alleles more favourable in one sex and that sex will be weakened. Therefore, mean fitness can decrease (Figure 2B,D).

266 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 268 consider several special cases. Firstly, if the \mathbf{A} locus is unlinked to the ancestral sex-determining region ($r = 1/2$), a more closely linked neo-W ($R < 1/2$) can 270 always invade because $(\hat{p}_Y^\phi - \hat{p}_X^\phi) = 0$ such that the second term in equation (2) disappears and invasion depends only on the sign of $(r - R)$. Indeed, invasion 272 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 274 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
 276 assume that haploid selection only occurs in one sex (e.g., during male meiosis
 only) and dominance coefficients are equal in the two sexes, $h^{\varphi} = h^{\delta}$. Where
 278 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 during diploid selection in
 280 males and females ($s^{\varphi}s^{\delta} > 0$, see Figure 3B). Where there is no meiotic drive and
 gametic competition occurs in one sex only, an unlinked neo-W can invade as long
 282 as the same allele is favoured in male and female diploid selection and there are sex
 differences in selection of one type (e.g., $s^{\varphi}(s^{\delta} - s^{\varphi}) > 0$, see Figure 3C,D). These
 284 special cases indicate that neo-W invasion can occur for a relatively large fraction
 of parameter space, even if the neo-W uncouples the sex-determining locus from
 286 a locus under selection.

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

Scenario	Assumptions	neo-W spreads ($\lambda_{W',XY} > 1$) if
male drive only	$h^{\delta} = h^{\varphi}, t^{\varphi} = t^{\delta} = \alpha_{\Delta}^{\varphi} = 0$	$s^{\varphi}s^{\delta} > 0$
female drive only	$h^{\delta} = h^{\varphi}, t^{\varphi} = t^{\delta} = \alpha_{\Delta}^{\delta} = 0$	$s^{\varphi}s^{\delta} > 0$
sperm competition only	$h^{\delta} = h^{\varphi}, t^{\varphi} = \alpha_{\Delta}^{\varphi} = \alpha_{\Delta}^{\delta} = 0$	$s^{\varphi}(s^{\delta} - s^{\varphi}) > 0$
egg competition only	$h^{\delta} = h^{\varphi}, t^{\delta} = \alpha_{\Delta}^{\varphi} = \alpha_{\Delta}^{\delta} = 0$	$s^{\delta}(s^{\varphi} - s^{\delta}) > 0$

Previous research suggests, when the ancestral sex-determining locus is linked
 288 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.
 290 2010). Our model provides a good opportunity to determine whether Fisherian
 sex ratio selection provides a useful explanation for the evolution of new sex-
 292 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
 294 males only (e.g., during spermatogenesis but not during oogenesis, $\alpha^{\delta} \neq 1/2$,
 $\alpha^{\varphi} = 1/2$). We will also disregard gametic competition ($t^{\varphi} = t^{\delta} = 0$) such that
 296 zygotic sex ratios are only biased by meiotic drive in males. In this case, the zy-
 gotic 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 stochastically or 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

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

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). In addition, these novel sex-determination alleles equalize the sex ratio and so one might expect them to be favoured by Fisherian sex ratio selection when the resident sex ratio is biased. However, we find that the growth rate of a rare, dominant offspring-

322 controlled neo-ESD allele that produces males or females with equal probability
 (k = 1/2) is

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

324 where we have indicated that $\lambda_{Y',XY}$ and $\lambda_{W',XY}$ are evaluated at $R = 1/2$. Re-
 combination between the selected locus and the novel sex-determining locus, R ,
 326 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.

328 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 $\lambda_{Y',XY} =$
 330 $\lambda_{W',ZW}$, $\lambda_{W',XY} = \lambda_{Y',ZW}$). 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
 332 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 femi-
 334 nizing mutation (neo- W) and half of the fitness of a masculinizing mutation (neo- Y),
 but only has an effect one half of the time (the other half of the time it produces
 336 the same sex as the ancestral system would have, to leading order). The net result
 can be that perfect ESD will not invade, even if current sex ratios are biased. For
 338 example, if there is haploid selection in males (either drive or pollen/sperm com-
 petition) but the conditions in table 3 are not met, perfect ESD will not invade,
 340 even though it would equalize the zygotic sex ratio from an initially biased case
 (assuming $r < 1/2$).

342 Fisherian sex ratio selection is sometimes considered in terms of balancing
 parental investment in male versus female offspring (Charnov 1982). In addition,
 344 under environmental sex-determination, the proportion of males/females is some-
 times controlled by the mother, e.g., the proportion of eggs laid in warm versus
 346 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
 348 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
 350 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
 352 maternally controlled environmental sex determination are not driven by Fisherian
 sex ratio selection on biased zygotic sex ratios.

354 Discussion

Because linkage between haploid selected loci and sex-determining regions causes
 356 biased zygotic sex ratios (Hamilton 1967, Burt and Trivers 2006, Field et al. 2012;
 2013), one might expect Fisherian sex ratio selection to drive the spread of new
 358 sex-determining systems that bring the sex ratio closer to 50:50. Fisherian sex
 ratio selection follows from the fact that, for an autosomal locus, half of the ge-
 360 netic 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
 362 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
 364 ratios). Therefore, a mutant that increases investment in males will spread via
 the higher per-individual contributions made by males. An implicit assumption
 366 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
 368 here, neo-sex-determining alleles, break this assumption. For example, the suc-
 cess of neo-Y/neo-W mutations depends only on the number of alleles contributed
 370 by males/females (Table 2). In this respect, a neo-W is similar to a cytoplasmic el-
 ement, which also does not experience selection to balance sex ratios (Frank 1989,
 372 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 mu-
 374 tation (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
 376 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
378 et al. 2015), we do not find evidence of Fisherian sex ratio selection acting dur-
ing invasion by neo-sex-determination systems (e.g., see Figure 1 and Úbeda et al.
380 2015, in which a neo-Y invades despite biasing sex ratios).

We note two other ways in which sex determination has been shown to relate
382 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
384 one male can inseminate many females (Hamilton 1967). Therefore, with local
mate competition, feminizing mutations can spread because they bias the sex ratio
386 towards females (Wilson and Colwell 1981, Vuilleumier et al. 2007). Secondly,
environmental conditions (e.g., maternal condition, mate quality, age, or host size)
388 can differentially affect the fitness of males versus females such that the optimal al-
location to males/females depends on the environment (Trivers and Willard 1973,
390 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
392 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 condi-
394 tion dependence or local mate competition (reviewed in Charnov 1982, Bull 1983,
West 2009).

It has previously been demonstrated that new sex-determining systems can
396 evolve if there is genetic variation maintained by sexually-antagonistic selection
(van Doorn and Kirkpatrick 2007; 2010). In particular, transitions to new sex-
398 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
400 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
402 are linked with a locus under haploid selection and the ancestral sex-determination
locus is not. However, with haploid selection, heterogametic transitions (XY to
404 ZW or ZW to XY) can also occur when the new sex-determining region is less
406 closely linked to the locus under selection.

Neo-W (neo-Y) alleles invade when their fitness in females (males) is greater
408 than the mean fitness of females (males) under the ancestral sex determination
system. With sexually antagonistic selection (between diploid sexes) only, linkage
410 between a selected locus and the sex-determining region strengthens associations
between male beneficial alleles and the male-determining allele (Y or Z) and be-
412 tween 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-
414 determining region. Therefore, new sex-determining alleles only invade if they are
more closely linked than the ancestral sex-determining region. However, if there
416 is haploid selection on loci linked to an XY (ZW) sex-determining region, selec-
tion can maintain polymorphisms at which the mean fitness of females (males)
418 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.

420 We assume that sex-determining alleles do not experience direct selection ex-
cept via their associations with sex and alleles at a selected locus. However, in
422 some cases, there may be significant degeneration around the sex-limited allele (Y
or W) in the ancestral sex determining region because recessive deleterious muta-
424 tions 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
426 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 delete-
428 rious 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 Kirk-
430 patrick (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-
432 and neo- sex-determining loci are both polymorphic. However, they noted that
very rare recombination events around the ancestral sex-determining region can
434 allow these heterogametic transitions to complete. While not explicitly studied,
we also predict that Y or W degeneration would prevent fixation of the new sex-
436 determiners considered here.

In addition, our model of meiotic drive is simple, involving a single locus with
438 two alleles. However, many meiotic drive systems involve an interaction with an-
other locus at which alleles may ‘suppress’ the action of meiotic drive (Burt and
440 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 recombina-
442 tion rate between them, which in turn can be affected by sex-linkage if there is re-
duced recombination between sex chromosomes (Hurst and Pomiankowski 1991).
444 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 sys-
446 tem 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 com-
448 peting for fertilization (mating system) can affect the equilibrium frequency of a
meiotic drive allele (Holman et al. 2015). In polygamous mating systems, the in-
450 tensity 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
452 2002). Since the sex ratio is partly determined by the sex determination system, the
evolution of new sex determination system could be influenced by these dynam-
454 ics. How the evolution of new sex-determining mechanisms could be influenced
by two-locus meiotic drive and/or by ecological feedbacks under different mating
456 systems remains to be studied.

The hypotheses presented here can be empirically investigated in a similar
458 manner to the idea that transitions between sex-determining systems are favoured
by linkage to sexually antagonistic variation. In the case of sexually antagonis-
460 tic variation, one supporting observation is that genes that appear to experience
sexually-antagonistic selection have been found on recently derived sex chromo-
462 somes (Lindholm and Breden 2002, Tripathi et al. 2009, Ser et al. 2010). However,
it is possible that sexually antagonistic variation accumulated after sex chromo-
464 some transitions because linkage with the sex-determining regions allows sexu-
ally antagonistic selection to maintain polymorphisms under a larger parameter
466 space (Rice 1987, Jordan and Charlesworth 2011). We note that linkage with sex

chromosomes is not, a priori, more permissive to the maintenance of ploidy 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 heterogamety (XY to ZW or vice versa) are more likely to be favoured by selection if there is selection upon both haploid and diploid genotypes rather than diploid selection alone. This prediction could be examined using a suitable proxy for haploid selection, for example, Lenormand and Dutheil (2005) use the outcrossing rate in plants as a proxy for the strength of pollen competition. In animals, one might expect gametic competition to be stronger in species where sperm is required to live for a long time after spermatogenesis because transcripts shared during spermatogenesis may become depleted, revealing the haploid phenotype of the sperm (Immler et al. 2014). Given the caveats mentioned above about the form of meiotic drive modelled, we would also expect that heterogametic transitions in sex determination would be more common in clades where there is meiotic drive.

We have shown that haploid selection can drive transitions between sex determination systems, such that haploid selection 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
498 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-
500 determination system.

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Figures

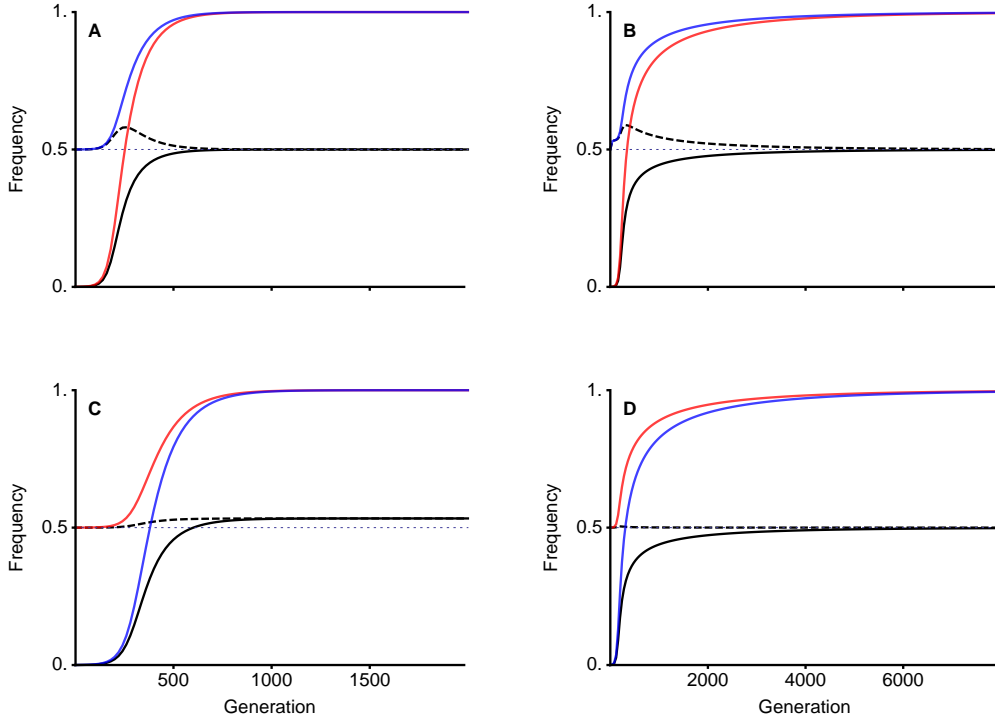


Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occur similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines show male frequency). During invasion by a neo-ZW sex determination system (A and B), the ancestral Y fixes in both males and females (blue and red lines). Similarly, the ancestral W allele fixes in males and females (blue and red lines) during a ZW to XY transition. In this plot, there is no gametic competition ($r^{\varnothing} = r^{\sigma} = 0$) and meiotic drive occurs during male meiosis only ($\alpha_{\Delta}^{\varnothing} = 0$, $\alpha_{\Delta}^{\sigma} = -1/5$). 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-determining region ($r = 1/2$, $R = 1/20$) such that a neo-Y can cause biased sex ratios (panel C). In panels B and D, the ancestral sex-determining locus is more closely linked to the **A** locus than the neo-sex-determining locus ($r = 1/20$, $R = 1/2$). Therefore, an ancestral XY sex determination can have a biased zygotic sex ratio that becomes unbiased after an unlinked neo-W invades (B). However, in panel D, an 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, $s^{\varnothing} = s^{\sigma} = 1/5$, $h^{\varnothing} = h^{\sigma} = 7/10$.
Aesthetic 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).

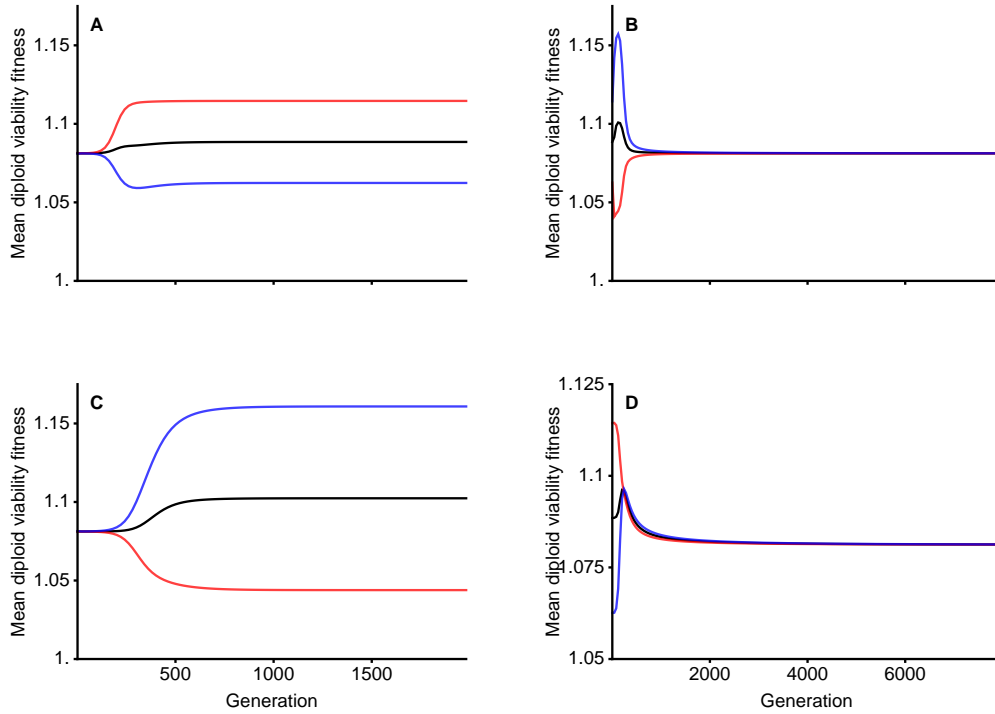


Figure 2: Here, we plot how male mean fitness (blue lines), female mean fitness (red lines), and population mean fitness (male mean fitness plus female mean fitness, black lines) changes during the transitions between sex-determination systems shown in Figure 1. Here we multiply male mean fitness and 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).**

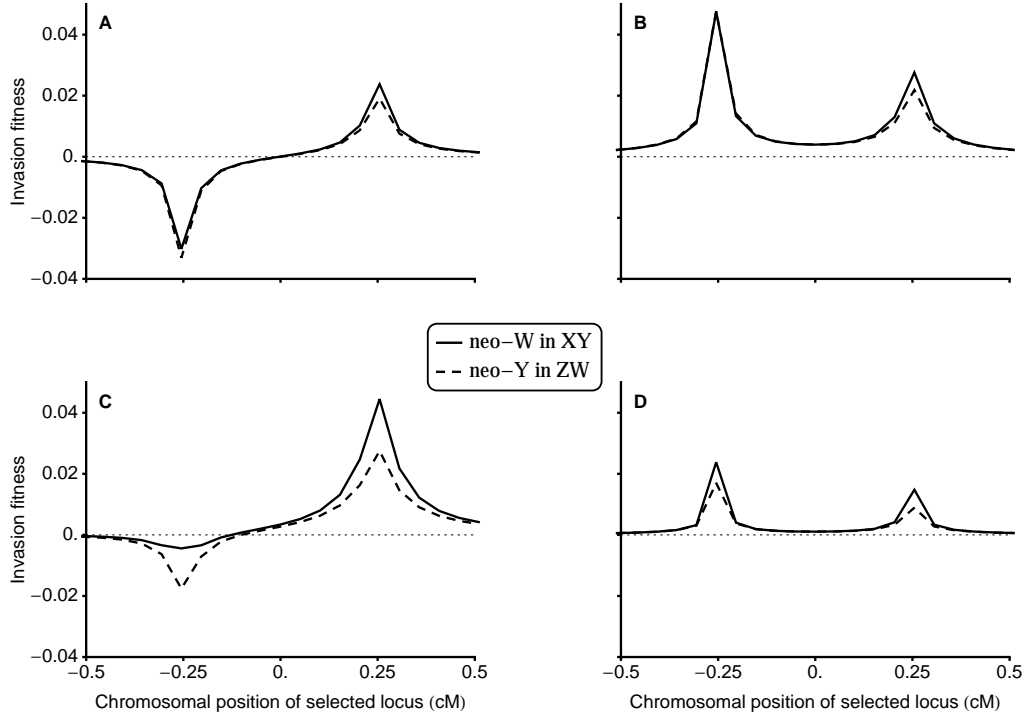


Figure 3: The invasion fitness of a neo-W allele plotted against the relative location of a locus under direct selection, **A**, for various selective regimes. We assume that the ancestral sex-determining locus is located at -0.25, the novel sex-determining locus is located at 0.25 and that there is 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 ($r^\delta = \alpha_\Delta^\delta = 0$) and selection in diploids is sexually antagonistic (following van Doorn and Kirkpatrick 2010), in which case a neo-W can only invade if it is more closely linked to the selected locus ($s^\varnothing = 1/10$, $h^\varnothing = 7/10$, $s^\delta = -1/10$, $h^\delta = 3/10$). In **B-D** we include haploid selection and assume that selection in diploids is not sexually-antagonistic ($s^\varnothing s^\delta > 0$). A polymorphism can then be maintained by opposing selection between the haploid and diploid phases. In **B**, there is drive in favour of the a allele in males ($\alpha_\Delta^\delta = -1/10$), no female meiotic drive or gametic competition, $r^\delta = \alpha_\Delta^\delta = 0$, and equal selection in diploid sexes ($s^\varnothing = s^\delta = 1/10$, $h^\varnothing = h^\delta = 7/10$). In this case, a neo-W can invade even when the selected locus is more closely linked to the ancestral sex determining locus (see Table 3 and Figure 1). In **C** and **D**, there is gametic competition among male gametes only (favouring a , $r^\delta = -1/10$) and no meiotic drive or gametic competition in females ($r^\varnothing = \alpha_\Delta^\varnothing = 0$). In this case, the neo-W does not invade if $s^\varnothing > s^\delta$ (panel **C**: $s^\varnothing = 3/20$, $s^\delta = 1/20$) but does if $s^\varnothing < s^\delta$ (panel **D**: $s^\varnothing = 1/20$, $s^\delta = 3/20$), see Table 3. **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, $s^\varnothing s^\delta < 0$ ” for **A**, “male meiotic drive, $s^\varnothing s^\delta > 0$ ” for **B**

692 Appendix

Recursion Equations

694 In each generation we census the genotype frequencies in male and female gametes/gametophytes (hereafter, gametes) after meiosis (and any meiotic drive)
 696 and immediately before gametic competition. At this stage, the frequencies of X-bearing male and female gametes are given by X_i^δ and X_i^φ and the frequen-
 698 cies of Y-bearing gametes are given by Y_i^δ and Y_i^φ where the index i specifies genotypes $MA = 1$, $Ma = 2$, $mA = 3$, and $ma = 4$ ($\sum_{i=1}^4 Y_i^\delta + X_i^\delta = 1$ and
 700 $\sum_{i=1}^4 Y_i^\varphi + X_i^\varphi = 1$). Competition then occurs among gametes of the same sex (e.g., among eggs and among sperm separately) according to the **A** locus allele, g
 702 ($g \in A, a$, see Table 1), carried by individuals with genotype i . The genotype frequencies after gametic competition are $X_i^{\delta,s} = w_g X_i^\delta / \bar{w}_H^\delta$ and $Y_i^{\delta,s} = w_g Y_i^\delta / \bar{w}_H^\delta$,
 704 where $\bar{w}_H^\delta = \sum_{i=1}^4 w_g X_i^\delta + w_g Y_i^\delta$ is the mean fitness of male ($\delta = \delta$) or female ($\delta = \varphi$) gametes. Random mating then occurs between gametes to produce diploid
 706 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,
 708 individuals with genotype ij are equivalent to those with genotype ji ; for simplicity, we denote the frequency of genotype ij to the average of these frequencies,
 710 $xx_{ij} = (X_i^{\varphi,s} X_j^{\delta,s} + X_j^{\varphi,s} X_i^{\delta,s})/2$ and $yy_{ij} = (Y_i^{\varphi,s} Y_j^{\delta,s} + Y_j^{\varphi,s} Y_i^{\delta,s})/2$.

Denoting the **M** locus genotype by b ($b \in MM, Mm, mm$) and the **X** locus
 712 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 $xx_{ij}^\varphi = k_{bc} xx_{ij}$, XY
 714 females are given by $xy_{ij}^\varphi = k_{bc} xy_{ij}$, and YY females are given by $yy_{ij}^\varphi = k_{bc} yy_{ij}$. Similarly, XX male frequencies are $xx_{ij}^\delta = (1 - k_{bc})xx_{ij}$, XY male frequencies
 716 are $xy_{ij}^\delta = (1 - k_{bc})xy_{ij}$, and YY males frequencies are $yy_{ij}^\delta = (1 - k_{bc})yy_{ij}$. This notation allows both the ancestral and novel sex-determining regions to de-
 718 termine zygotic sex according to an XY system, a ZW system, or an environ-
 mental sex-determining system. In addition, we can consider any epistatic domi-
 720 nance relationship between the two sex-determining loci. Typically, we assume

that the ancestral sex-determining system (**X** locus) is XY ($k_{MMXX} = 1$ and
722 $k_{MMXY} = k_{MYY} = 0$) and epistatically recessive to a dominant novel sex-
determining locus, **M** ($k_{Mmc} = k_{mmc} = k$).

724 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
726 diploid frequencies after selection in sex ϕ are given by $xx_{ij}^{\phi,s} = w_h^{\phi}xx_{ij}/\bar{w}^{\phi}$,
 $xy_{ij}^{\phi,s} = w_h^{\phi}xy_{ij}/\bar{w}^{\phi}$, and $yy_{ij}^{\phi,s} = w_h^{\phi}yy_{ij}/\bar{w}^{\phi}$, where $\bar{w}^{\phi} = \sum_{i=1}^4 \sum_{j=1}^4 w_h^{\phi}xx_{ij} +$
728 $w_h^{\phi}xy_{ij} + w_h^{\phi}yy_{ij}$ is the mean fitness of individuals of sex ϕ .

Finally, these diploids undergo meiosis to produce the next generation of ga-
730 metes. 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
732 three parameters to describe the recombination rates between them. R is the re-
combination rate between the **A** locus and the **M** locus, χ is the recombination rate
734 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
736 locations of these loci. During meiosis in sex ϕ , meiotic drive occurs such that, in
 Aa heterozygotes, a fraction α^{ϕ} of gametes produced carry the A allele and $(1 - \alpha^{\phi})$
738 carry the a allele.

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

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

Among gametes from sex ϕ (sperm/pollen when $\phi = \sigma$, eggs/ovules when
740 $\phi = \varphi$), the frequencies of haplotypes (before gametic competition) in the next
generation are given by

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

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

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

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

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

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

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

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

$$\tag{S.1i}$$

742 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
 744 diploid types are not produced under a given sex determination system. For exam-
 ple, with the M allele fixed and ancestral XY sex determination, there are no XX
 746 males, XY females, or YY females (xx_{11}^{ϕ} , xx_{12}^{ϕ} , xx_{22}^{ϕ} , xy_{11}^{ϕ} , xy_{12}^{ϕ} , xy_{22}^{ϕ} , yy_{11}^{ϕ} , yy_{12}^{ϕ} ,
 and yy_{22}^{ϕ} are all 0). In this case, the system only involves six recursion equations
 748 because there is only one M locus allele and no Y-bearing female gametes. This
 six-equation system yields equilibrium (S.3).

750 Resident equilibrium and stability

In the resident population (allele M fixed), we follow the frequency of A in female
 752 gametes (eggs) from an XX female, p_X^{ϕ} , and in X-bearing, p_X^{ϕ} , and Y-bearing,
 p_Y^{ϕ} , male gametes (sperm). We also track the total frequency of Y among male
 754 gametes, q , which may deviate from 1/2 due to meiotic drive in males. Within this
 resident population (when m is absent) we can then describe frequencies among
 756 different gamete types, which are given by $X_{MA}^{\phi} = p_{Xf}$, $X_{Ma}^{\phi} = (1 - p_{Xf})$, $X_{MA}^{\phi} =$
 $(1 - q)p_{Xm}$, $X_{Ma}^{\phi} = (1 - q)(1 - p_{Xm})$, $Y_{MA}^{\phi} = qp_{Ym}$, and $Y_{Ma}^{\phi} = q(1 - p_{Ym})$. Mean
 758 fitnesses in this resident population are given in table S.2.

Various forms of selection can maintain a polymorphism at the A locus, includ-
 760 ing sexually antagonistic selection, overdominance and conflicts between diploid

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

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

selection and selection upon haploid genotypes (ploidal antagonistic selection,
 762 Immler et al. 2012) or a combination of these selective regimes. Here, we assume
 that selection and meiotic drive are weak relative to recombination ($s^\varphi, t^\varphi, \alpha_\Delta^\varphi$ of
 764 order ϵ). The maintenance of a polymorphism at the **A** locus then requires that

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

which indicates that a polymorphism is maintained under various selective regimes.
 766 In particular special cases, e.g., no sex-differences in selection or meiotic drive
 ($s^\delta = s^\varphi, h^\delta = h^\varphi$, and $\alpha^\delta = \alpha^\varphi = 1/2$), the equilibrium allele frequency and
 768 stability can be calculated analytically without assuming weak selection. How-
 ever, here, we focus on weak selection in order to make fewer assumptions about
 770 fitnesses.

Given that a polymorphism is maintained at the **A** locus by selection, with
 772 weak selection and drive, to leading order, the frequencies of A in each type of

gamete are the same ($\hat{p}_X^\varnothing = \hat{p}_X^\delta = \hat{p}_Y^\delta = \bar{p}$) and given by

$$\bar{p} = \frac{h^\varnothing s^\varnothing + h^\delta s^\delta + t^\varnothing + t^\delta + \alpha_\Delta^\varnothing + \alpha_\Delta^\delta}{(2h^\varnothing - 1)s^\varnothing + (2h^\delta - 1)s^\delta} + O(\epsilon). \quad (\text{S.3})$$

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

$$\begin{aligned} \hat{p}_X^\delta - \hat{p}_X^\varnothing &= V_A (D^\delta - D^\varnothing + \alpha_\Delta^\delta - \alpha_\Delta^\varnothing) + O(\epsilon^2) \\ \hat{p}_Y^\delta - \hat{p}_X^\varnothing &= V_A (D^\delta - D^\varnothing + \alpha_\Delta^\delta - \alpha_\Delta^\varnothing + (1 - 2r)(t^\delta - t^\varnothing)) / 2r + O(\epsilon^2) \\ \hat{p}_Y^\delta - \hat{p}_X^\delta &= V_A (D^\delta - D^\varnothing + \alpha_\Delta^\delta - \alpha_\Delta^\varnothing + t^\delta - t^\varnothing)(1 - 2r) / 2r + O(\epsilon^2) \end{aligned} \quad (\text{S.4})$$

776 where $V_A = \bar{p}(1 - \bar{p})$ is the variance in the frequency of A and $D^\varnothing = (\bar{p}s^\varnothing + (1 - \bar{p})h^\varnothing s^\varnothing) - (\bar{p}h^\varnothing s^\varnothing + (1 - \bar{p}))$ corresponds to the difference in fitness between A and
778 a alleles in diploids of sex $\varnothing \in \{\varnothing, \delta\}$ (\bar{p} is the leading-order probability of mating
with an A -bearing gamete from the opposite sex). The frequency of Y among male
780 gametes depends upon the difference in the frequency of the A allele between X -
and Y -bearing male gametes and the strength of meiotic drive in favour of the A
782 allele in males, $q = 1/2 + \alpha_\Delta^\delta(\hat{p}_Y^\delta - \hat{p}_X^\delta)/2 + O(\epsilon^3)$. Without gametic competition
or drive ($\alpha_\Delta^\varnothing = t^\varnothing = 0$), these results reduce to those of van Doorn and Kirkpatrick
784 (2007).

Invasion without assuming weak selection

786 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
788 carry the m allele (Am and am) is positive, invasion will always occur (i.e., if
 $\{(\lambda_{mA} - 1) + (\lambda_{ma} - 1)\} / 2 > 0$ then $\lambda > 1$, see table 2 for λ_{mi}). If neither haplo-
790 type 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

$$R \left[\frac{p_X^\varnothing w_A^\varnothing w_a^\delta (1 - \alpha^\delta)}{\bar{w}_H^\varnothing \bar{w}_H^\delta (\lambda_{mA} - 1)} + \frac{(1 - p_X^\varnothing) w_a^\varnothing w_A^\delta \alpha^\delta}{\bar{w}_H^\varnothing \bar{w}_H^\delta (\lambda_{ma} - 1)} \right] \frac{w_{Aa}^\delta}{q \bar{w}^\delta} < 1, \quad (\text{S.5})$$

for the neo- Y , and

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

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 , 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.