

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

Michael F Scott*¹, Matthew M Osmond*², and Sarah P Otto²

* These authors contributed equally to this work

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

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

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

Contributions:

Abstract

Sex-determination systems are remarkably dynamic; many taxa display shifts in the location of sex-determining loci or the evolution of entirely new sex-determining systems. Predominant theories for why we observe such transitions generally conclude that novel sex-determining systems are favoured by selection if they equalise the sex ratio or increase linkage with a sexually-antagonistic locus. We use population genetic models to extend these theories in two ways: (1) We explicitly consider how selection on very tightly sex-linked loci influences the spread of novel sex-determiners. We find that tightly sex-linked genetic variation can favour the spread of new sex-determination systems in which the heterogametic sex changes (XY to ZW or ZW to XY) and the new sex-determining region is less closely linked (or unlinked) to the sex-linked locus under selection; a result that is not found with loose sex-linkage. (2) We also consider selection upon haploid genotypes either during gametic competition (e.g., pollen/sperm competition) or meiosis (i.e., non-Mendelian segregation); selective processes that typically occur in one sex or the other. As well as having sex-specific fitness consequences, haploid selection can cause the zygotic sex ratio to become biased because sex ratios are determined by the production and fertilization success of X- versus Y-bearing pollen/sperm (or Z- versus W-bearing ovules/eggs). Consequently, selection for XY to ZW transitions and ZW to XY transitions can be asymmetrical when linkage between the ancestral sex-determining locus and a locus under haploid selection is tight, in which case ancestral sex ratio biases can be strong. With looser linkage and haploid selection, we again find that transitions between male and female heterogamety can occur even if the new sex-determining region is less closely linked to the locus under selection. That is, favourable associations that develop between the ancestral sex-determining locus and selected loci can be broken during the spread of a new sex-determining region. Overall, our models provide new predictions for the types of selection and the genomic location of loci that can drive transitions between sex-determination systems.

32 **Introduction**

Animals and angiosperms exhibit extremely diverse sex-determination systems
34 (reviewed in Bull 1983, Charlesworth and Mank 2010, Beukeboom and Perrin
2014, Bachtrog et al. 2014). Among species with genetic sex determination of
36 diploid sexes, some taxa have heterogametic males (XY) and homogametic fe-
males (XX), including mammals and most dioecious plants (Ming et al. 2011);
38 whereas other taxa have homogametic males (ZZ) and heterogametic females (ZW),
including Lepidoptera and birds. Within several taxa, the chromosome that har-
40 bours the master sex-determining region changes. For example, transitions of the
master sex-determining gene between chromosomes or the evolution of new mas-
42 ter 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
44 addition, many gonochoric clades with genetic sex determination exhibit transi-
tions between male (XY) and female (ZW) heterogamety, including lizards (Ezaz
46 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
48 angiosperm genus *Silene* (Slancarova et al. 2013), and Coleoptera and Hemiptera
(Beukeboom and Perrin 2014, plate 2). Indeed, in some cases, both male and fe-
50 male 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
52 et al. 2007). In addition, multiple transitions have occurred between genetic and
environmental sex-determination systems, e.g., in reptiles and fishes (Conover and
54 Heins 1987, Mank et al. 2006, Pokorná and Kratochvíl 2009, Ezaz et al. 2009, Pen
et al. 2010, Holleley et al. 2015).

56 Predominant theories accounting for the spread of new sex-determination sys-
tems by selection involve fitness differences between sexes (e.g., sexually antag-
58 onistic selection) or sex-ratio selection. van Doorn and Kirkpatrick (2007; 2010)
show that new sex-determining loci can be favoured if they arise in closer link-
60 age with a locus that experiences sexual antagonism. For example, tighter link-
age allows a stronger favourable association to build up between a male-beneficial

62 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
64 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
66 loci that are more closely linked to the ancestral sex-determination locus will de-
velop similar, favourable associations and select against the spread of a new sex-
68 determination system.

The sex ratio is directly affected by the sex-determination system, and it has
70 therefore 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,
72 Chapter 7). ‘Fisherian’ sex-ratio selection favours a 1:1 zygotic sex ratio when as-
suming that males and females are equally costly to produce (Fisher 1930, Charnov
74 1982). This follows from the fact that, for an autosomal locus, half of the genetic
material is inherited from a male, and half from a female (West 2009). Thus,
76 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
78 the contribution from females (and vice versa for male-biased sex ratios). There-
fore, a mutant that increases investment in males (e.g., increases the proportion of
80 males produced) will spread via the higher per-individual contributions made by
males. In the case of sex-chromosome evolution, Kozielska et al. (2010) consider
82 systems in which the ancestral sex chromosomes experience meiotic drive (e.g.,
where driving X or Y chromosomes are inherited disproportionately often), which
84 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
86 loci) can then spread, which restore an even sex ratio.

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

92 refer to the biased (non-Mendelian) segregation of genotypes during gamete pro-
duction (from one parent) and the term ‘gametic competition’ to refer to selection
94 upon haploid genotypes within a gamete/gametophyte pool (potentially from by
multiple parents); the term ‘haploid selection’ encompasses both processes. Mei-
96 otic drive generally occurs either during the production of male or female gametes
only (Úbeda and Haig 2005, Lindholm et al. 2016). Because there are typically
98 many more pollen/sperm than required for fertilization, gametic competition is
also typically sex specific, occurring primarily among male gametes. Gametic
100 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
102 of selection than random genes (Borg et al. 2009, Arunkumar et al. 2013, Goss-
mann et al. 2014). In addition, artificial selection pressures applied to male game-
104 tophtes are known to cause a response to selection (e.g., Hormaza and Herrero
1996, Ravikumar et al. 2003, Hedhly et al. 2004, Clarke et al. 2004) and gametic
106 selection appears to occur during the creation of F2 crosses (Kumar, 2007). A
much smaller proportion of genes are thought to be expressed and selected dur-
108 ing competition in animal sperm, although precise estimates are uncertain (Zheng
et al. 2001, Joseph and Kirkpatrick 2004, Vrbánek et al. 2010, Immler et al.
110 2014).

There are various ways in which a period of haploid selection could influence
112 transitions between sex-determination systems. If we assume that haploid selec-
tion at any particular locus predominantly occurs in one sex (e.g., meiotic drive
114 during spermatogenesis), then such loci experience a form of sex-specific selec-
tion. In this respect, we might expect that haploid selection to affect transitions
116 between sex-determination systems in a similar manner to sex-specific diploid se-
lection (as explored by van Doorn and Kirkpatrick 2007; 2010). That is, new
118 masculinizing mutations (neo-Y chromosomes) could be favoured via associations
with alleles that are beneficial in the male haploid stage. On the other hand, sex
120 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

122 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
124 (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
126 systems would be influenced by the combination of sex-ratio biases and associa-
tions between haploid selected loci and sex-determining regions.

128 Our models have two important new features. Firstly, when considering loci
that are under selection and also in very tight linkage with the ancestral sex-determining
130 region we explicitly calculate equilibrium allele frequencies. This allows us to
show that transitions between male and female heterogamety can evolve even when
132 the neo-sex-determining locus is less closely linked to a locus under selection and
therefore disrupts favourable ancestral associations between sex and the alleles se-
134 lected in that sex. Secondly, we allow sex-specific haploid selection to occur on a
locus in tight or loose linkage with the ancestral sex-determining region. We find
136 that sex-ratio biases caused by haploid selection can exert Fisherian sex-ratio se-
lection upon novel sex-determiners but that their spread is also determined by the
138 fitness of the alleles that are associated with them. Indeed, it is only when haploid-
selected loci are tightly linked to the ancestral sex-determining region (and so sex-
140 ratio biases are initially large) that we see an asymmetry between selection for XY
to ZW transitions and ZW to XY transitions (e.g., because haploid selection in
142 males only causes biased zygotic sex ratios in an ancestrally XY system). It is also
possible for selection on linked alleles to drive turnover between sex-determining
144 systems despite causing transitory or even permanent increases in sex-ratio bias.

Model

146 We consider transitions between ancestral and novel sex-determining systems us-
ing a three locus model, each locus having two alleles. Locus **X** is the ancestral
148 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,

150 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, \mathbf{X} ;
 152 XX genotypes become females and XY become males (or ZW become females
 and ZZ become males). To evaluate the evolution of new sex-determination sys-
 154 tems, we consider the invasion, fixation, maintenance, and/or loss of novel sex-
 determining alleles (m) at the \mathbf{M} locus. We assume that the \mathbf{M} locus is epistatically
 156 dominant over the \mathbf{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
 158 \mathbf{X} locus genotype. With $k = 0$, the m allele is a masculinizer (i.e., a neo-Y) and
 with $k = 1$ the m allele is a feminizer (i.e., a neo-W). With intermediate k , we
 160 can interpret m as an environmental sex determination (ESD) allele, such that zy-
 gotes develop as females in a proportion (k) of the environments they (randomly)
 162 experience. We also analyze a model of maternally-controlled environmental sex-
 determination, where mothers with at least one m allele produce daughters with
 164 probability k .

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

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

Table 1: Relative fitness of different genotypes in sex $\phi \in \{\varphi, \delta\}$

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

190 Results

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

we relabel the two sexes as being ancestrally ‘heterogametic’ or ancestrally ‘homogametic’. Without loss of generality, we primarily refer to the ancestrally heterogametic sex as male and the ancestrally homogametic sex as female. That is, we describe an ancestral XY sex-determination system but our model is just as easily applied to an ancestral ZW sex-determination system.

Generic invasion by a neo-Y or neo-W

The evolution of a new sex-determination system requires that a rare mutant allele at the novel sex-determining locus, m , increases in frequency when rare. The spread of a rare mutant m at the \mathbf{M} locus is determined by the leading eigenvalue, λ , of the system of eight equations describing the next generation frequency of eggs and sperm carrying the mutation, (S.1c, S.1d, S.1g, S.1h). This system simplifies substantially in a number of cases of interest. Dominant neo-Y (when $k = 0$) or neo-W alleles (when $k = 1$) are only found in male diploids (neo-Y) or female diploids (neo-W) such that their growth rate ultimately depends only on the change in frequency of m -bearing gametes produced by males (for a neo-Y) or by females (for a neo-W). Furthermore, if the m allele is fully epistatically dominant over the ancestral sex-determining system, phenotypes are not affected by the genotype at the ancestral sex-determining region (\mathbf{X} locus). Thus, the invasion of rare dominant neo-Y or neo-W alleles is determined by the largest eigenvalue that solves a quadratic characteristic polynomial, $\lambda^2 + b\lambda + c = 0$. Here, $b = -(\lambda_{mA} + \lambda_{ma}) + (\rho_{mA} + \rho_{ma})$ and $c = (\lambda_{mA} - \rho_{mA})(\lambda_{ma} - \rho_{ma}) - \rho_{mA}\rho_{ma}$, where λ_{mi} is the multiplicative growth rate of mutant haplotypes on background $i \in \{A, a\}$, without accounting for loss due to recombination, and ρ_{mi} is the rate at which mutant haplotypes on background $i \in \{A, a\}$ recombine onto the other \mathbf{A} locus background in heterozygotes (see table 2). The λ_{mi} and ρ_{mi} , and thus the spread of the mutant m allele, depend on the frequency of alleles at the other two loci in the ancestral population. In the ancestral population, it is convenient to follow the frequency of the A allele in female gametes (eggs) from an XX female, p_X° , and in X-bearing, p_X^δ , and Y-bearing, p_Y^δ , male gametes (sperm/pollem). We

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

226

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

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

$\bar{p}^\delta = p_Y^\delta q + p_X^\delta (1 - q)$ 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**.

ζ is the zygotic sex ratio (fraction female)

\bar{w}^\varnothing is the mean fitness of diploids of sex \varnothing , see Table S.2

\bar{w}_H^\varnothing is the mean fitness of haploids from sex \varnothing , see Table S.2

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

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

236 For example, if we assume that only the mA haplotype has a positive growth rate
 ($\lambda_{ma} < 1 < \lambda_{mA}$), the second term on the left-hand side of (1) is negative and inva-
 238 sion requires that the growth rate of mA haplotypes and the rate at which they are
 produced by recombination is sufficiently large relative to that of ma haplotypes.
 240 In other words, invasion requires that the average growth rate of recombinants,
 weighted by the rates they are created, is positive.

242 Table 2 illustrates a number of key points about the invasion of neo-Y and neo-
 W mutations. First, Fisherian sex-ratio selection will favour the spread of a neo-Y
 244 if the ancestral zygotic sex ratio is biased towards females, $\zeta > 1/2$, and vice versa
 for a neo-W (i.e., $\zeta > 1/2$ causes the first factor of the λ_{mi} to be greater than one
 246 for a neo-Y). However, the spread of a neo-Y (neo-W) also depends on the male
 (female) fitness of alleles that they are associated with. Second, invasion by a neo-
 248 Y (neo-W) allele does not directly depend on the fitness of female (male) diploids
 (although they indirectly affect invasion by determining the allele frequencies p_X°
 250 and \hat{p}°). This is because a dominant neo-Y (neo-W) is always found in males
 (females), and therefore the frequency of the neo-Y (neo-W) allele, m , only changes
 252 in males (females). Finally, invasions by a neo-Y and a neo-W are qualitatively
 different. This is because a gamete containing a neo-Y always pairs with the same
 254 gamete type as a male gamete without the neo-Y does (both pair with a female
 gamete containing an X), and both develop into males. Meanwhile a gamete with
 256 a neo-W can pair with an X or Y male gamete, and develop into a female, while
 female gametes without the neo-W must pair with a male gamete containing an X
 258 to remain female. This is consequential because it means that females with and
 without a neo-W differ in the frequency of A alleles they obtain from mating.

260 In order to explicitly determine the conditions under which a rare neo-sex-
 determining allele spreads, we must calculate the frequency of the A allele in the
 262 ancestral population (i.e., p_X° , p_X^δ , and p_Y^δ). Since only the A locus experiences se-
 lection directly, any deterministic evolution requires that there is a polymorphism
 264 at the A locus. Polymorphisms can be transiently present during the spread of uni-
 formly beneficial alleles but polymorphisms maintained by selection can maintain

alleles at higher allele frequencies for longer periods, during which time new sex-determining alleles can arise. Therefore, we will assume that the A allele reaches a stable intermediate equilibrium frequency under the ancestral sex-determination system before the neo-sex-determining allele (m) arises. We can analytically calculate the allele frequency of the A allele using two alternative simplifying assumptions: (1) the A locus is within (or tightly linked to) the non-recombining region around the ancestral SDR ($r \approx 0$) or (2) selection is weak relative to recombination ($s^\phi, t^\phi, \alpha_\Delta^\phi$ of order $\epsilon \ll 1$).

Tight linkage with the ancestral sex-determining region

When there is perfect linkage between the ancestral sex-determining region and the A locus ($r = 0$), either the A allele or the a allele must be fixed on the Y. Because the labelling of alleles is arbitrary, we will assume that the a locus is fixed on the Y ($p_Y^\phi = 0$), without loss of generality. If there are two alleles maintained at the A locus, the X can either be fixed for the A allele ($p_X^\phi = p_X^\circ = 1$) or polymorphic ($0 < p_X^\phi, p_X^\circ < 1$). These equilibrium allele frequencies and their stability conditions are given in the appendix.

A neo-Y will never invade an ancestral XY system that already has tight linkage with the locus under selection ($r = 0$). A neo-Y haplotype with the same allele as the ancestral Y is neutral ($\lambda_{ma} = 1$) and does not change in frequency. The other neo-Y haplotype will not spread ($\lambda_{mA} < 1$) given that the initial equilibrium is stable. Therefore, a neo-Y mutation cannot spread ($\lambda \leq 1$) in an ancestral XY system that is at equilibrium with all selected loci within the non-recombining region around the SDR. In essence, through tight linkage with the A locus, the ancestral Y becomes strongly specialized on the allele that has the highest fitness across male haploid and diploid phases. Given that the ancestral Y is at this equilibrium, it is not possible for a neo-Y to create males that have higher fitness than the ancestral Y.

Neo-W alleles, on the other hand, can invade an ancestral XY system under some conditions (the full invasion conditions are given in the appendix; equations

S.6 and S.7). Significantly, we note that it is possible for both neo-W haplotypes to spread ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$), in which case neo-W invasion can occur regardless of linkage to the selected locus. That is, selection on loci within the non-recombining region of the SDR can favour the invasion of a less closely linked neo-W (e.g., on an autosome). Although haploid selection can favour neo-W alleles because the ancestral sex ratio becomes male biased, this is not the only circumstance in which less tightly linked neo-W alleles invade. For example, unlinked neo-W alleles can invade in the absence of any haploid selection. This result is unexpected given the results of van Doorn and Kirkpatrick (2010), who did not explicitly calculate equilibrium allele frequencies under tight linkage and generally concluded that heterogametic transitions occur when neo-sex-determining alleles are in tighter linkage with loci under sex-specific diploid selection. Therefore, we focus on cases where there is no haploid selection and discuss the effects of haploid selection in the appendix.

If we categorise the a allele as being ancestrally ‘male-beneficial’ via the fact that it is fixed on the Y, then $\lambda_{mA} > 1$ indicates that the neo-W spreads when found with the ancestrally ‘female-beneficial’ allele. Intuitively, this is possible because the ancestral X chromosome is not able to specialise on the ‘female-beneficial’ allele due to the fact that X’s are sometimes found in males. For example, a polymorphism of A and a alleles can be maintained on the X despite directional selection in favour of the A allele in females ($s^{\varphi} > 0$, $0 < h^{\varphi} < 1$) because the a allele is favoured in males. W- A haplotypes will only create females with high fitness AA or Aa genotypes and can therefore have higher fitness than ancestral females, which sometimes also produce aa females. Thus, the neo-W can spread by allowing increased specialization on female beneficial alleles.

Given that the a allele can be considered ancestrally ‘male-beneficial’ because it is fixed on the Y, it might be surprising that neo-W- a haplotypes can be favoured by selection in females ($\lambda_{ma} > 1$). Again, this occurs because ancestral X’s also experience selection in males, in which they will always be paired with a Y- a . Hence, if there is overdominance in males, X- A Y- a males have high fitness and

the A allele is favoured by selection on the X in males. Therefore, the X can be
 326 polymorphic or even fixed for the A allele despite favouring the a allele during
 selection in females (Lloyd and Webb 1977, Otto 2014). In such cases, neo-W- a
 328 haplotypes, which are never found in males, can spread because they both create
 more Aa and aa females when pairing with an X from males and they bring Y- a
 330 haplotypes into females, in which case females are always aa . Indeed, it is possible
 for both W- A and W- a haplotypes to spread, as is the case when AA individuals
 332 have low fitness in females yet the A is fixed on the X due to strong overdominance
 in males. Both neo-W- A and neo-W- a haplotypes then produce fewer unfit AA
 334 females. This is true for the neo-W- A haplotype because it can pair with a Y - a
 haplotype and still be female.

336 In Figure ??A we show the region of parameter space within which both neo-W
 haplotypes invade ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$) when there is overdominance in females
 338 and no haploid selection (corresponding to Figure 2a in Otto 2014). Wherever both
 haplotypes have positive growth rates (gray region of Figure ??), invasion by a neo-
 340 W is expected regardless of its linkage with the selected locus (i.e., even unlinked
 neo-W alleles can invade). In regions where only one haplotype can spread (white
 342 region of Figure ??), a neo-W can invade as long as equation (1) is satisfied, which
 can require that the recombination rate, R , is small enough and yet still indicates
 344 that more loosely linked sex-determining regions can spread. It is also possible for
 haploid selection to drive the invasion of a loosely linked neo-W. Take for instance
 346 selection directionally favouring A in both diploid sexes and meiotic drive in males.
 Figure ??B then shows that ploidy-antagonistic selection can allow both neo-W
 348 haplotypes to invade.

Loose linkage with the ancestral sex-determining region

350 Assuming that selection is weak relative to all recombination rates (r , R and χ),
 we denote the leading eigenvalues describing the invasion of a neo-Y ($k = 0$) and
 352 a neo-W ($k = 1$) into an ancestrally XY system by $\lambda_{Y',XY}$ and $\lambda_{W',XY}$, respectively,
 which are

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

354 and

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

where $V_A = \bar{p}(1 - \bar{p})$ is the variance in the frequency of A and $S_A = (D^\delta + \alpha_\Delta^\delta +$
 356 $t^\delta) - (D^\varphi + \alpha_\Delta^\varphi + t^\varphi)$ describes sex differences in selection for the A versus a across
 diploid selection, meiosis, and gametic competition. The diploid selection term,
 358 $D^\varphi = (\bar{p}s^\varphi + (1 - \bar{p})h^\varphi s^\varphi) - (\bar{p}h^\varphi s^\varphi + (1 - \bar{p}))$, is the difference in fitness between A
 and a alleles in diploids of sex $\varphi \in \{\varphi, \delta\}$, where \bar{p} is the leading-order probability
 360 of mating with an A -bearing gamete from the opposite sex (see Appendix).

The neo-sex-determining allele, m , will spread if $\lambda_{m,XY} > 1$. Equation (2)
 362 demonstrates that under weak selection a neo-Y will invade if and only if it is more
 closely linked to the selected locus than the ancestral sex-determining region (i.e.,
 364 if $R < r$; note that V_A and S_A^2 are strictly positive as long as \mathbf{A} is polymorphic). This
 echoes our tight linkage results above and the results of van Doorn and Kirkpatrick
 366 (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
 368 locus is more closely linked to a locus under sexually-antagonistic selection.

Equation (3) shows that, in contrast to the tight linkage results of the previous
 370 section, if there is no haploid selection ($t^\varphi = \alpha_\Delta^\varphi = 0$), as considered by van Doorn
 and Kirkpatrick (2010) and weak selection, the spread of a neo-W is equivalent to
 372 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
 374 closely linked to a locus under selection ($R < r$). However, if there is any hap-
 loid selection, the additional term in equation (3) can be positive, which can allow,
 376 for example, neo-W invasion ($\lambda_{W',XY} > 1$) even when the neo-sex-determining
 region is less closely linked to the selected locus ($R > r$). These transitions are

378 unusual because, when $R > r$, associations that selection has built up between
alleles more favourable in one sex and alleles that determine sex will be weak-
380 ened. Mean diploid fitness therefore decreases during heterogametic transitions
that create looser sex-linkage (Figure 4B,D).

382 Equation (3) shows that neo-W alleles can invade an XY system for a large
number of selective regimes. To clarify the parameter space under which $\lambda_{W',XY} >$
384 1, we consider several special cases. Firstly, if the **A** locus is unlinked to the an-
cestral sex-determining region ($r = 1/2$), a more closely linked neo-W ($R < 1/2$)
386 can always invade because there is then no association between *A* alleles and sex
chromosomes, $(\hat{p}_Y^\delta - \hat{p}_X^\delta) = 0$. The second term in equation (3) then disappears
388 and invasion depends only on the sign of $(r - R)$. Indeed, invasion typically occurs
when the neo-W is more closely linked to the selected locus than the ancestral sex-
390 determining region, under a variety of selective regimes (Figure 6). Secondly, we
can simplify cases where invasion occurs despite looser sex-linkage, $R > r$, using
392 the special case where $R = 1/2$ and $r < 1/2$ (e.g., the selected locus is on the
ancestral sex chromosome and the novel sex-determining locus arises on an auto-
394 some). In table 3 we give the conditions where invasion occurs when we further
assume that haploid selection only occurs in one sex (e.g., during male meiosis
396 only) and dominance coefficients are equal in the two sexes, $h^\varnothing = h^\delta$. When there
is no gametic competition and meiotic drive is in one sex only, an unlinked neo-W
398 can invade as long as the same allele is favoured during diploid selection in males
and females ($s^\varnothing s^\delta > 0$, see Figure 6B). When there is no meiotic drive and gametic
400 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 dif-
402 ferences in selection of one type (e.g., $s^\varnothing(s^\delta - s^\varnothing) > 0$, see Figure 6C,D). These
special cases indicate that neo-W invasion can occur for a relatively large fraction
404 of parameter space, even if the neo-W uncouples the sex-determining locus from
a locus under selection.

406 Previous research suggests that when the ancestral sex-determining locus is
linked to a locus that experiences haploid selection (e.g., meiotic drive), a new,

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

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

408 unlinked sex-determining locus invades in order to restore equal sex ratios (Koziel-
ska et al. 2010). Consider, for example, the case where the **A** locus is linked to the
410 ancestral-SDR ($r < 1/2$) and experiences meiotic drive in males only (e.g., dur-
ing spermatogenesis but not during oogenesis, $\alpha^\delta \neq 1/2$, $\alpha^\varphi = 1/2$). Disregard
412 gametic competition ($t^\varphi = t^\delta = 0$) such that zygotic sex ratios are only biased by
meiotic drive in males. In this case, the zygotic sex ratio can be initially biased
414 only if the ancestral sex-determining system is XY (Figure 1B). We might there-
fore expect a difference in the potential for XY to ZW and ZW to XY transitions.
416 However, with weak selection we find that invasion by a neo-W into an XY system
and invasion by a neo-Y into a ZW system occur under the same conditions. As
418 it turns out, with weak selection, the strength of a male biased zygotic sex ratio
favouring the invasion of a neo-W is equal to the strength of meiotic drive favour-
420 ing the invasion of a driving neo-Y are equal (at least up to order ϵ^2). As selection
becomes stronger (or linkage becomes tighter), this symmetry between sex-ratio
422 selection and drive is lost, causing differences in the strength of selection favour-
ing the two heterogametic transitions (compare red to black near -25cM and 25 cM
424 in Figure 6).

Environmental sex determination

426 We next consider the case where the new sex-determining mutation, m , causes sex
to be determined probabilistically or by heterogeneous environmental conditions
428 (environmental sex determiner, ESD). We assume that individuals carrying the m

allele develop as females with probability k (e.g., in a fraction k of the environments they randomly experience). The characteristic polynomial determining the eigenvalues of the 8 equation system (equations S.1) does not reduce for ESD mutants as it does for $k = 0$ or $k = 1$. We therefore focus on weak selection here. Assuming weak selection, the spread of these mutations is given by

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

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

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

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

where we have indicated that $\lambda_{Y',XY}$ and $\lambda_{W',XY}$ are evaluated at $R = 1/2$. That is, recombination between the selected locus and the novel sex-determining locus, R , doesn't enter into the $k = 1/2$ results. This is because sex is essentially randomized each generation, preventing associations from building up between allele A and sex.

Equation (5) shows that invasion by a novel ‘perfect’ ESD (equal sex ratio, $k = 1/2$) mutation is the same for an ancestrally XY or ZW system (since $\lambda_{Y',XY} = \lambda_{W',ZW}$, $\lambda_{W',XY} = \lambda_{Y',ZW}$). Thus, by the same argument as above (if drive only occurs in males then the sex ratio is only biased when the ancestral sex-determination system is XY), Fisherian sex-ratio selection alone does not explain the invasion of an offspring-controlled neo-ESD allele under weak selection. Rather, the neo-ESD gets half of the fitness of a feminizing mutation (neo- W) and half of the fitness of a masculinizing mutation (neo- Y), but only has an effect one half of the time (the other half of the time it produces the same sex as the ancestral system would have, to leading order). The net result can be that perfect ESD will not invade, even if current sex ratios are biased. For example, if there is haploid selection in males (either drive or pollen/sperm competition) but the conditions in table 3 are not met, perfect ESD will not invade, even though it would equalize the zygotic sex ratio from an initially biased case (assuming $r < 1/2$).

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

Discussion

Two predominant theories explaining the remarkably high frequency of transitions between sex-determination systems are sexually-antagonistic selection and sex-ratio selection (reviewed in Blaser et al. 2012). The former predicts that neo-sex-determining alleles can invade when they arise in closer linkage with a sexually-antagonistic locus (van Doorn and Kirkpatrick 2007; 2010). The latter predicts that neo-W alleles will invade an XY system when there is a male bias caused by haploid selection in males, and vice-versa, a neo-Y will invade a ZW system when there is a female bias caused by haploid selection in females (Kozielska et al. 2010, Úbeda et al. 2015). Here we have shown that both predictions must be amended when recombination is weak relative to selection or selection happens in both diploid and haploid phases.

When the rate of recombination between the ancestral sex-determining locus and a locus under selection is small relative to the strength of selection (i.e., sex-linkage is tight), heterogametic transitions (XY to ZW or ZW to XY) that reduce sex-linkage are possible, with or without haploid selection (Figure 7A) or sexually-antagonistic selection (Figure 7B). The likelihood of these transitions are driven by sex-ratio selection, direct selection on alleles linked to the neo-sex-determining allele, the ability of the neo-sex-determining allele to avoid selection in one sex, and the ability of the neo-sex-determining allele to bring alleles on the sex-specific chromosome in the ancestor into the other sex (given that the neo-sex determining allele is epistatically dominant to its predecessor). This possibility was overlooked in van Doorn and Kirkpatrick (2010), possibly because they did not explicitly calculate the resident equilibria (equation S.2; Lloyd and Webb 1977, Otto 2014). Interestingly, there is substantial overlap between the parameter space that allows both neo-W-*A* and neo-W-*a* haplotypes to spread in an XY system and that which selects for increased recombination between X and Y chromosomes (e.g., compare gray region in Figure 7A with coloured regions of Figure 2(a) in Otto 2014). This makes sense as when both neo-W haplotypes can spread the neo-W can invade despite reducing sex-linkage, i.e., the rate of recombination between the sex-

determining allele and the selected locus increases. explain difference too? also
508 explain why a neo-Y doesn't invade to reduce linkage despite selection for more
recombination? mention something about haploid selection (Fig7B)?

510 Under weak selection (i.e., loose sex-linkage), transitions to new sex-determining
systems can occur when new sex-determining regions are more closely linked to a
512 sexually-antagonistic locus (van Doorn and Kirkpatrick 2007; 2010). Our results
show that genetic variation at loci that experience haploid selection can also gen-
514 erate selection in favour of new sex-determining systems. New sex-determining
alleles are again favoured if they are more closely linked to a locus under hap-
516 loid 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
518 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)
520 under the ancestral sex-determination system. With sexually-antagonistic selec-
tion (between diploid sexes) only, linkage between a selected locus and the sex-
522 determining region strengthens associations between male beneficial alleles and
the male-determining allele (Y or Z) and between female beneficial alleles and the
524 female-determining allele (X or W). Thus, the mean fitness of both males and fe-
males increases with closer linkage to the sex-determining region. Therefore, new
526 sex-determining alleles only invade if they are more closely linked than the ances-
tral sex-determining region. However, if there is haploid selection on loci linked
528 to an XY (ZW) sex-determining region, selection can maintain polymorphisms at
which the mean fitness of females (males) is lower than it would be without sex-
530 linkage. In these cases, unlinked neo-W (neo-Y) alleles can increase female (male)
fitness, at a cost to the other sex, and invade despite lowering mean fitness (Figure
532 4).

Sex ratio biases caused by gametic competition or meiotic drive have been
534 shown to exert Fisherian sex-ratio selection on various autosomal (Stalker 1961,
Smith 1975, Frank 1989, Hough et al. 2013, Úbeda et al. 2015, Otto et al. 2015)
536 and sex-linked (Úbeda et al. 2015) modifiers. We find that sex-ratio biases caused

by haploid selection can also affect transitions between sex-determining systems (e.g., see ζ terms in Table 2). For instance, when an allele that drives in males is linked to an XY locus it will often become associated with the Y and therefore produce a male bias ($\zeta < 1/2$). This male bias increases the potential for a neo-W to invade (as we then have $(2\zeta)^{-1} > 1$, Table 2), which can equalize the sex-ratio (for a related example see Úbeda et al. 2015). However, this sex-ratio selection can be overwhelmed when the driving allele has additional selective effects (e.g., when it is detrimental to male diploids but beneficial for female diploids; Table 3), preventing the neo-W from invading. Conversely, these additional selective effects can even favour transitions between sex-determining systems that create new sex-ratio biases. For example, in an ancestral ZW system, an allele that drives only in males can allow a linked neo-Y to invade, despite the fact it creates a male bias. This of course generates new sex-ratio selection that may drive further turnover (Úbeda et al. 2015). Furthermore, with weak selection/loose sex-linkage, there is no asymmetry between XY to ZW and ZW to XY transitions, indicating that sex-ratio selection does not dominate (i.e., the sex-ratio bias created by haploid selection impacts the spread of a neo-W into an XY system the same way it impacts the spread of a neo-Y into an unbiased ZW system). An asymmetry can develop when sex-linkage is tight (e.g., Figure 6 near -25cM and 25cM) but under most circumstances we do not predict asymmetry between XY to ZW and ZW to XY transitions despite the presence/absence of sex ratio selection. Thus, haploid selection can favour heterogametic transitions both via sex-ratio selection and via the fitness of alleles that are associated with the neo-sex-determining allele; and these selection pressures are often of equal magnitude.

We assume that sex-determining alleles do not experience direct selection except via their associations with sex and alleles at a selected locus. However, in some cases, there may be significant degeneration around the sex-limited allele (Y or W) in the ancestral sex-determining region because recessive deleterious mutations and/or deletions may fix around the Y or W allele (Rice 1996, Charlesworth and Charlesworth 2000, Bachtrog 2006, Marais et al. 2008). During heterogametic

transitions (XY to ZW or ZW to XY), the formally sex-limited allele fixes such
568 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
570 heterogametic transition. This phenomenon was studied by van Doorn and Kirkpatrick (2010), who found that degeneration can prevent fixation of a neo-W or
572 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
574 very rare recombination events around the ancestral sex-determining region can allow these heterogametic transitions to complete. While not explicitly studied,
576 we also predict that Y or W degeneration would prevent fixation of the new sex-determiners considered here.

578 In addition, our model of meiotic drive is simple, involving a single locus with two alleles. However, many meiotic drive systems involve an interaction with another locus at which alleles may ‘suppress’ the action of meiotic drive (Burt and
580 Trivers 2006, Lindholm et al. 2016). Thus, the dynamics of meiotic drive alleles can be heavily dependent on the interaction between two loci and the recombination rate between them, which in turn can be affected by sex-linkage if there is reduced recombination between sex chromosomes (Hurst and Pomiankowski 1991).
582 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.
586 Where gamete number is reduced by meiotic drive, the number of mates competing for fertilization (mating system) can affect the equilibrium frequency of a meiotic drive allele (Holman et al. 2015). In polygamous mating systems, the intensity
590 of pollen/sperm competition can depend on the density of males available to donate pollen/sperm, which can itself depend on the sex ratio (Taylor and Jaenike 2002). Since the sex ratio is partly determined by the sex-determination system,
594 the evolution of new sex-determination system could be influenced by these dynamics. How the evolution of new sex-determining mechanisms could be influenced by two-locus meiotic drive and/or by ecological feedbacks under different
596

mating systems remains to be studied.

598 The hypotheses presented here can be empirically investigated in a similar
manner to the idea that transitions between sex-determining systems are favoured
600 by linkage to sexually-antagonistic variation. In the case of sexually-antagonistic
variation, one supporting observation is that genes expected to be under sexually-
602 antagonistic selection (e.g., those causing bright male colouration) have been found
on recently derived sex chromosomes (Lindholm and Breden 2002, Tripathi et al.
604 2009, Ser et al. 2010). However, it is possible that sexually-antagonistic varia-
tion accumulated after sex chromosome transitions because linkage with the sex-
606 determining regions allows sexually-antagonistic selection to maintain polymor-
phisms under a larger parameter space (Rice 1987, Jordan and Charlesworth 2011).
608 We note that linkage with sex chromosomes is not, a priori, more permissive to the
maintainence of ploidally antagonistic variation (Immler et al. 2012). However, as
610 with sexually-antagonistic variation, a comparison between closely related clades
could indicate whether a polymorphism pre-dates a transition in sex-determination
612 or arose afterwards (George Sandler, an undergrad in the Wright and Barrett labs,
has done some yet-to-be-published work on *Rumex* that we should cite here. We
614 can send him this draft and get his permission to cite him as personal commu-
nication or something. I think he has basically found that genes retained on the
616 Y are overexpressed in pollen but not in male diploids, suggesting they are being
maintained by haploid selection, not sexual antagonism. I guess this is a follow
618 up to Crowson et al 2017 *Mol Biol Evol* 34:1140, which we could potentially cite
as well.). Secondly, we have shown that new sex-determination systems can be
620 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 hap-
622 loid selected loci around ancestral- or novel-sex-determining regions could support
their role in sex chromosome turnover.

624 I think Sally was sceptical of this idea. i.e., if the second term in 3 is nega-
tive, then get less transitions with haploid selection included, right? Yeah, and
626 given that only 1/2 the discovered plant sex chromosomes are heteromorphic and

there are so few plant sex chromosomes to begin with (Charlesworth 2016 Annual
 628 Review Plant Biology), might it be the case that haploid selection is constraining
 things? perhaps we could think of some particular forms of haploid selection that
 630 might be common and give their predicted effects, or just say some things that
 are possible with haploid selection that are not without it – if there are any. just
 632 looking at eq 3 though, its gonna be hard to get a low freq of A on the Y if hap-
 loid selection in males favours A, i.e., it should often be positive when there is no
 634 female haploid selection, right? Taken at face value, our results indicate that trans-
 transitions in heterogametey (XY to ZW or vice versa) are more likely to be favoured
 636 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
 638 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 ani-
 640 mals, 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
 642 during spermatogenesis may become depleted, revealing the haploid phenotype of
 the sperm (Immler et al. 2014). Given the caveats mentioned above about the form
 644 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.
 646 similarly, this part doesn't discuss our new tight linkage results or our new
 perspective on sex ratios. We have shown that haploid selection can drive transi-
 648 tions between sex-determination systems. We therefore argue that haploid selec-
 tion should be considered, alongside sex-ratio selection and sexually-antagonistic
 650 selection, as an important factor influencing the evolution of sex determination.
 Further, we have shown the way in which transitions are affected by haploid se-
 652 lection is not intuitively obvious. Firstly, sex-specific haploid selection affects
 turnovers between sex-determination systems in a manner that is qualitatively dif-
 654 ferent from diploid sex-specific selection. In particular, closer linkage between a
 sex-determining locus and a selected locus is not always favoured during heteroga-
 656 metic transitions when there is haploid selection. Secondly, even though haploid

selection is a source of zygotic sex-ratio biases, in our models Fisherian sex-ratio
658 selection does not have good explanatory power in determining whether various
sex-determination systems evolve. This result is surprising given that sex ratios
660 are ultimately determined via the sex-determination system, and leads us to the
conclusion that three selective forces – haploid, diploid, and sex-ratio selection
662 – should all be considered when exploring transitions between sex-determination
systems.

664 **References**

- Arunkumar, R., E. B. Josephs, R. J. Williamson, and S. I. Wright. 2013. Pollen-
666 specific, but not sperm-specific, genes show stronger purifying selection and
higher rates of positive selection than sporophytic genes in *Capsella grandiflora*.
668 *Molecular biology and evolution* 30:2475–2486.
- Bachtrog, D. 2006. A dynamic view of sex chromosome evolution. *Current opin-*
670 *ion in genetics & development* 16:578–585.
- Bachtrog, D., J. E. Mank, C. L. Peichel, M. Kirkpatrick, S. P. Otto, T.-L. Ashman,
672 M. W. Hahn, J. Kitano, I. Mayrose, R. Ming, N. Perrin, L. Ross, N. Valenzuela,
J. C. Vamosi, and Tree of Sex Consortium. 2014. Sex determination: why so
674 many ways of doing it? *PLoS Biol* 12:e1001899.
- Beukeboom, L. W., and N. Perrin. 2014. *The evolution of sex determination*.
676 Oxford University Press, Oxford, UK.
- Blaser, O., C. Grossen, S. Neuenschwander, and N. Perrin. 2012. Sex-chromosome
678 turnovers induced by deleterious mutation load. *Evolution* 67:635–645.
- Borg, M., L. Brownfield, and D. Twell. 2009. Male gametophyte development: a
680 molecular perspective. *Journal of Experimental Botany* 60:1465–1478.

- 682 Bull, J. J. 1983. Evolution of sex determining mechanisms. The Benjamin Cum-
mings Publishing Company.
- 684 Burt, A., and R. Trivers. 2006. Genes in conflict: the biology of selfish genetic
elements. Belknap Press, Cambridge, MA.
- 686 Charlesworth, B., and D. Charlesworth. 2000. The degeneration of Y chromo-
somes. Philosophical transactions of the Royal Society of London. Series B,
Biological sciences 355:1563–1572.
- 688 Charlesworth, D., and J. E. Mank. 2010. The birds and the bees and the flowers
and the trees: lessons from genetic mapping of sex determination in plants and
690 animals. Genetics 186:9–31.
- 692 Charnov, E. L. 1982. The theory of sex allocation. Monographs in population
biology.
- 694 Clarke, H. J., T. N. Khan, and K. H. M. Siddique. 2004. Pollen selection for chill-
ing tolerance at hybridisation leads to improved chickpea cultivars. Euphytica
139:65–74.
- 696 Conn, J. S., and U. Blum. 1981. Sex ratio of *Rumex hastatulus*: the effect of
environmental factors and certation. Evolution 35:1108–1116.
- 698 Conover, D. O., and S. W. Heins. 1987. Adaptive variation in environmental and
genetic sex determination in a fish. Nature 326:496–498.
- 700 Ezaz, T., S. D. Sarre, and D. O’Meally. 2009. Sex chromosome evolution in lizards:
independent origins and rapid transitions. Cytogenetic and Genome Research
702 127:249–260.
- 704 Field, D. L., M. Pickup, and S. C. H. Barrett. 2012. The influence of pollina-
tion intensity on fertilization success, progeny sex ratio, and fitness in a wind-
pollinated, dioecious plant. International Journal of Plant Sciences 173:184–
706 191.

- . 2013. Comparative analyses of sex-ratio variation in dioecious flowering
708 plants. *Evolution* 67:661–672.
- Fisher, R. 1930. The genetical theory of natural selection. Clarendon Press, Lon-
710 don.
- Frank, S. A. 1989. The Evolutionary Dynamics of Cytoplasmic Male Sterility.
712 *American Naturalist* 133:345–376.
- Gossmann, T. I., M. W. Schmid, U. Grossniklaus, and K. J. Schmid. 2014.
714 Selection-driven evolution of sex-biased genes Is consistent with sexual selec-
tion in *Arabidopsis thaliana*. *Molecular biology and evolution* 31:574–583.
- 716 Haldane, J. B. S. 1919. The combination of linkage values and the calculation of
distances between the loci of linked factors. *Journal of Genetics* 8:299–309.
- 718 Hamilton, W. D. 1967. Extraordinary sex ratios. *Science* 156:477–488.
- Hedhly, A., J. I. Hormaza, and M. Herrero. 2004. Effect of temperature on pollen
720 tube kinetics and dynamics in sweet cherry, *Prunus avium* (Rosaceae). *Ameri-
can journal of botany* 91:558–564.
- 722 Hillis, D. M., and D. M. Green. 1990. Evolutionary changes of heterogametic
sex in the phylogenetic history of amphibians. *Journal of Evolutionary Biology*
724 3:49–64.
- Holleley, C. E., D. O’Meally, S. D. Sarre, J. A. Marshall Graves, T. Ezaz, K. Mat-
726 subara, B. Azad, X. Zhang, and A. Georges. 2015. Sex reversal triggers the
rapid transition from genetic to temperature-dependent sex. *Nature* 523:79–82.
- 728 Holman, L., T. A. R. Price, N. Wedell, and H. Kokko. 2015. Coevolutionary
dynamics of polyandry and sex-linked meiotic drive. *Evolution* 69:709–720.
- 730 Hormaza, J. I., and M. Herrero. 1996. Male gametophytic selection as a plant
breeding tool. *Scientia horticultrae* 65:321–333.

- 732 Hough, J., S. Immler, S. Barrett, and S. P. Otto. 2013. Evolutionarily stable sex
ratios and mutation load. *Evolution* 7:1915–1925.
- 734 Hurst, L. D., and A. Pomiankowski. 1991. Causes of sex ratio bias may account for
unisexual sterility in hybrids: a new explanation of Haldane’s rule and related
736 phenomena. *Genetics* 128:841–858.
- Immler, S., G. Arnqvist, and S. P. Otto. 2012. Ploidally antagonistic selection
738 maintains stable genetic polymorphism. *Evolution* 66:55–65.
- Immler, S., C. Hotzy, G. Alavioun, E. Petersson, and G. Arnqvist. 2014. Sperm
740 variation within a single ejaculate affects offspring development in Atlantic
salmon. *Biology letters* 10:20131040.
- 742 Jordan, C. Y., and D. Charlesworth. 2011. The potential for sexually antagonistic
polymorphism in different genome regions. *Evolution* 66:505–516.
- 744 Joseph, S., and M. Kirkpatrick. 2004. Haploid selection in animals. *Trends in
Ecology & Evolution* 19:592–597.
- 746 Karlin, S., and J. McGregor. 1972*a*. Application of method of small parameters to
multi-niche population genetic models. *Theoretical Population Biology* 3:186–
748 209.
- . 1972*b*. Polymorphisms for genetic and ecological systems with weak
750 coupling. *Theoretical Population Biology* 3:210–238.
- Kozielska, M., F. J. Weissing, L. W. Beukeboom, and I. Pen. 2010. Segregation
752 distortion and the evolution of sex-determining mechanisms. *Heredity* 104:100–
112.
- 754 Lenormand, T., and J. Dutheil. 2005. Recombination difference between sexes: a
role for haploid selection. *PLoS Biol* 3:e63.

- 756 Li, J., R. B. Phillips, A. S. Harwood, B. F. Koop, and W. S. Davidson. 2011. Identification of the Sex Chromosomes of Brown Trout (*Salmo trutta*) and Their
758 Comparison with the Corresponding Chromosomes in Atlantic Salmon (*Salmo salar*) and Rainbow Trout (*Oncorhynchus mykiss*). Cytogenetic and Genome
760 Research 133:25–33.
- Lindholm, A., and F. Breden. 2002. Sex chromosomes and sexual selection in
762 poeciliid fishes. The American Naturalist 160 Suppl 6:S214–24.
- Lindholm, A. K., K. A. Dyer, R. C. Firman, L. Fishman, W. Forstmeier, L. Holman, H. Johannesson, U. Knief, H. Kokko, A. M. Larracuenta, A. Manser, C. Montchamp-Moreau, V. G. Petrosyan, A. Pomiankowski, D. C. Presgraves,
764 L. D. Safronova, A. Sutter, R. L. Unckless, R. L. Verspoor, N. Wedell, G. S. Wilkinson, and T. A. R. Price. 2016. The Ecology and Evolutionary Dynamics
766 of Meiotic Drive. Trends in Ecology & Evolution 31:315–326.
768
- Lloyd, D. G. 1974. Female-predominant sex ratios in angiosperms. Heredity
770 32:35–44.
- Lloyd, D. G., and C. Webb. 1977. Secondary sex characters in plants. Botanical
772 Review 43:177–216.
- Mank, J. E., D. E. L. Promislow, and J. C. Avise. 2006. Evolution of alternative sex-determining mechanisms in teleost fishes. Biological Journal of the
774 Linnean Society 87:83–93.
- 776 Marais, G. A. B., M. Nicolas, R. Bergero, P. Chambrier, E. Kejnovsky, F. Monéger, R. Hobza, A. Widmer, and D. Charlesworth. 2008. Evidence for degeneration
778 of the Y chromosome in the dioecious plant *Silene latifolia*. Current Biology 18:545–549.
- 780 Ming, R., A. Bendahmane, and S. S. Renner. 2011. Sex chromosomes in land plants. Annu. Rev. Plant Biol. 62:485–514.

- 782 Mulcahy, D. L., M. Sari-Gorla, and G. B. Mulcahy. 1996. Pollen selection - past,
present and future. *Sexual Plant Reproduction* 9:353–356.
- 784 Myosho, T., H. Otake, H. Masuyama, M. Matsuda, Y. Kuroki, A. Fujiyama,
K. Naruse, S. Hamaguchi, and M. Sakaizumi. 2012. Tracing the Emergence
786 of a Novel Sex-Determining Gene in Medaka, *Oryzias luzonensis*. *Genetics*
191:163–170.
- 788 Ogata, M., Y. Hasegawa, H. Ohtani, M. Mineyama, and I. Miura. 2007. The
ZZ/ZW sex-determining mechanism originated twice and independently during
790 evolution of the frog, *Rana rugosa*. *Heredity* 100:92–99.
- Otto, S. P. 2014. Selective maintenance of recombination between the sex chro-
792 mosomes. *Journal of Evolutionary Biology* 27:1431–1442.
- Otto, S. P., M. F. Scott, and S. Immler. 2015. Evolution of haploid selection in
794 predominantly diploid organisms. *Proc Natl Acad Sci* 112:15952–15957.
- Pen, I., T. Uller, B. Feldmeyer, A. Harts, G. M. While, and E. Wapstra. 2010.
796 Climate-driven population divergence in sex-determining systems. *Nature*
468:436–438.
- 798 Pokorná, M., and L. Kratochvíl. 2009. Phylogeny of sex-determining mecha-
nisms in squamate reptiles: are sex chromosomes an evolutionary trap? *Zoo-*
800 *logical Journal of the ...* 156:168–183.
- Ravikumar, R. L., B. S. Patil, and P. M. Salimath. 2003. Drought tolerance in
802 sorghum by pollen selection using osmotic stress. *Euphytica* 133:371–376.
- Rice, W. R. 1987. The accumulation of sexually antagonistic genes as a selective
804 agent promoting the evolution of reduced recombination between primitive sex
chromosomes. *Evolution* 41:911.
- 806 ———. 1996. Evolution of the Y Sex Chromosome in Animals. *BioScience*
46:331–343.

- 808 Ser, J. R., R. B. Roberts, and T. D. Kocher. 2010. Multiple interacting loci control sex determination in lake Malawi cichlid fish. *Evolution* 64:486–501.
- 810 Slancarova, V., J. Zdanska, B. Janousek, M. Talianova, C. Zschach, J. Zluvova, J. Siroky, V. Kovacova, H. Blavet, J. Danihelka, B. Oxelman, A. Widmer, and
812 B. Vyskot. 2013. Evolution of sex determination systems with heterogametic males and females in *Silene*. *Evolution* 67:3669–3677.
- 814 Smith, D. A. S. 1975. All-female broods in the polymorphic butterfly *Danaus chrysippus* L. and their ecological significance. *Heredity* 34:363–371.
- 816 Stalker, H. D. 1961. The Genetic Systems Modifying Meiotic Drive in *Drosophila Paramelanica*. *Genetics* 46:177–202.
- 818 Stehlik, I., and S. Barrett. 2005. Mechanisms governing sex-ratio variation in dioecious *Rumex nivalis*. *Evolution* 59:814–825.
- 820 Stehlik, I., and S. C. H. Barrett. 2006. Pollination intensity influences sex ratios in dioecious *Rumex nivalis*, a wind-pollinated plant. *Evolution* 60:1207–1214.
- 822 Taylor, J. E., and J. Jaenike. 2002. Sperm competition and the dynamics of X chromosome drive: stability and extinction. *Genetics* 160:1721–1731.
- 824 Tripathi, N., M. Hoffmann, E.-M. Willing, C. Lanz, D. Weigel, and C. Dreyer. 2009. Genetic linkage map of the guppy, *Poecilia reticulata*, and quantitative
826 trait loci analysis of male size and colour variation. *Proceedings. Biological sciences / The Royal Society* 276:2195–2208.
- 828 Úbeda, F., and D. Haig. 2005. On the evolutionary stability of Mendelian segregation. *Genetics* 170:1345–1357.
- 830 Úbeda, F., M. M. Patten, and G. Wild. 2015. On the origin of sex chromosomes from meiotic drive. *Proceedings of the Royal Society B: Biological Sciences*
832 282:20141932.

- van Doorn, G. S., and M. Kirkpatrick. 2007. Turnover of sex chromosomes induced by sexual conflict. *Nature* 449:909–912.
- . 2010. Transitions Between Male and Female Heterogamety Caused by Sex-Antagonistic Selection. *Genetics* 186:629–645.
- Vibranovski, M. D., D. S. Chalopin, H. F. Lopes, M. Long, and T. L. Karr. 2010. Direct evidence for postmeiotic transcription during *Drosophila melanogaster* spermatogenesis. *Genetics* 186:431–433.
- Vicoso, B., and D. Bachtrog. 2015. Numerous transitions of sex chromosomes in Diptera. *PLoS Biol* 13:e1002078.
- West, S. 2009. Sex allocation. Princeton University Pres.
- Yano, A., B. Nicol, E. Jouanno, E. Quillet, A. Fostier, R. Guyomard, and Y. Guiguen. 2012. The sexually dimorphic on the Y-chromosome gene (sdY) is a conserved male-specific Y-chromosome sequence in many salmonids. *Evolutionary Applications* 6:486–496.
- Zheng, Y., X. Deng, and P. A. Martin-DeLeon. 2001. Lack of sharing of Spam1 (Ph-20) among mouse spermatids and transmission ratio distortion. *Biology of Reproduction* 64:1730–1738.

Figures

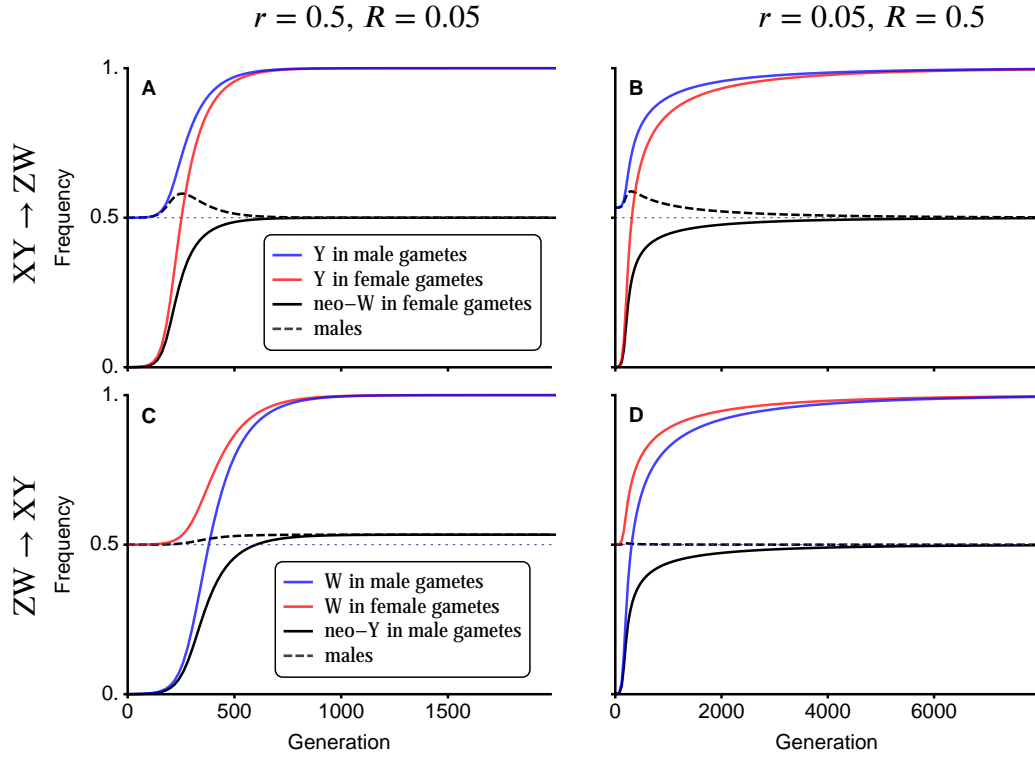


Figure 1: Heterogametic transitions from XY to ZW sex determination (neo-W frequency shown by black lines, panels A and B) or from ZW to XY (neo-Y frequency shown by black lines, panels C and D) occur similarly regardless of sex ratio biases present before (B versus D) or after (C versus A, dashed lines show male frequency). During invasion by a neo-ZW sex-determination system (A and B), the ancestral Y fixes in both males and females (blue and red lines). Similarly, the ancestral W allele fixes in males and females (blue and red lines) during a ZW to XY transition. In this plot, there is no gametic competition ($t^{\text{f}} = t^{\text{m}} = 0$) and meiotic drive occurs during male meiosis only ($\alpha_{\Delta}^{\text{f}} = 0$, $\alpha_{\Delta}^{\text{m}} = -1/5$). 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, a unlinked neo-Y invades an ancestral ZW sex-determination system in a similar manner but no biases to the zygotic sex ratio occur. With diploid selection alone, neo-sex-determining loci do not spread if they are less closely linked to the A locus than the ancestral sex-determining locus (see equation (3) and Figure 6A). In this plot there are no sex differences in selection and an equilibrium is maintained because selection in diploids opposes meiotic drive, $s^{\text{f}} = s^{\text{m}} = 1/5$, $h^{\text{f}} = h^{\text{m}} = 7/10$.

Aesthetic adjustments: Add chromosome cartoons to depict recombination rates?

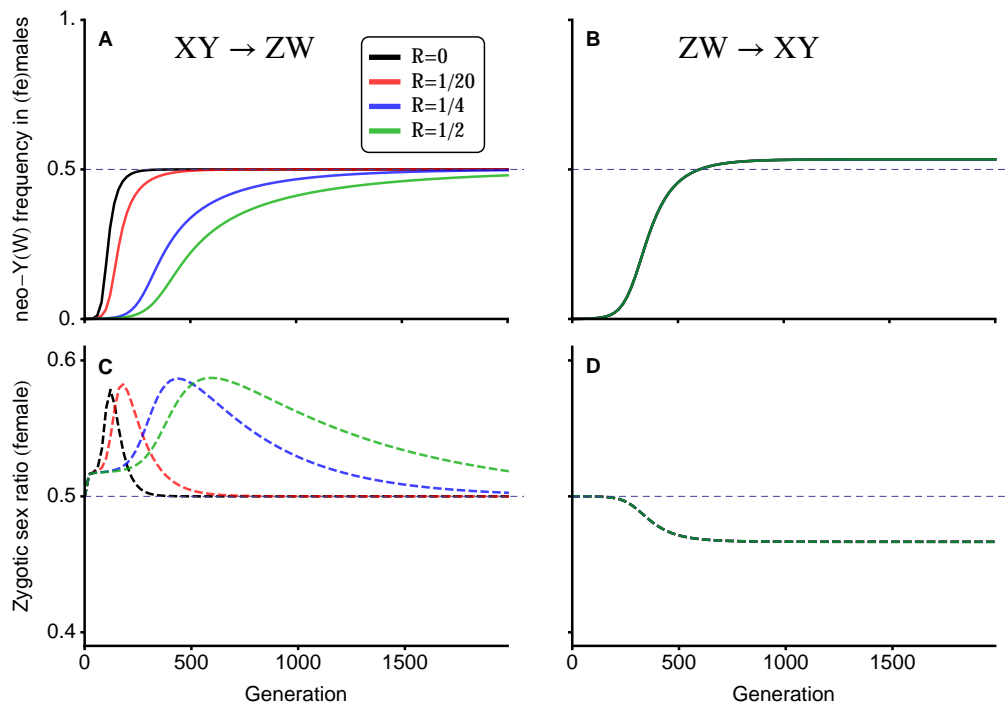


Figure 2: Is this what Sally was thinking? I guess the right panel is pretty boring

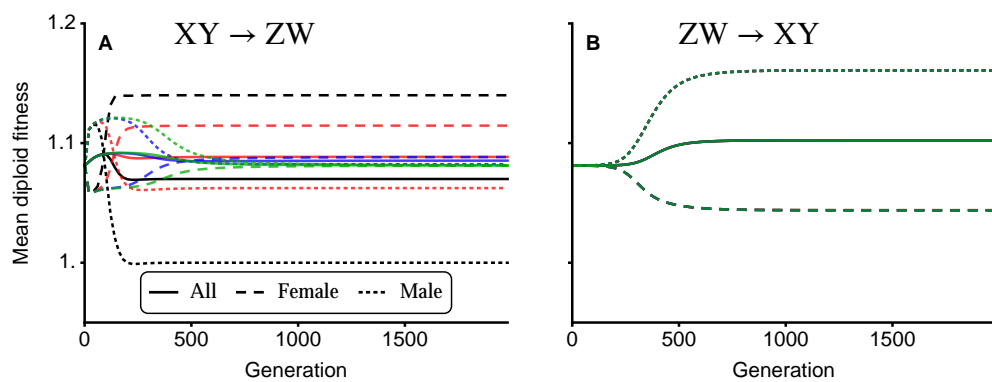


Figure 3: This complicated thing matches the plot above. We could combine this with that to make a 6 panel-er?

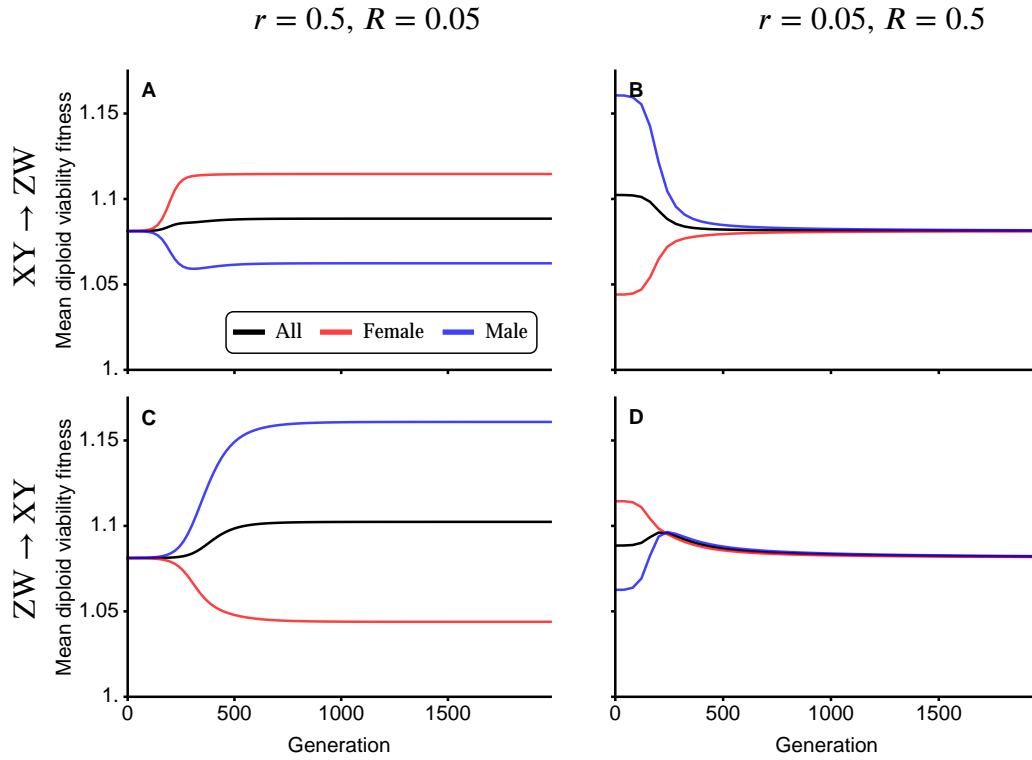


Figure 4: Changes in mean diploid fitness of males (blue lines), females (red lines), and the entire population (male mean fitness plus female mean fitness, black lines) during the transitions between sex-determination systems shown in Figure 1. Here we multiply male and female mean fitnesses by two so that we can show them on the same scale as population mean fitness. The mean fitness of females increases during the spread of neo-W alleles (A and B) and the mean fitness of males increases during the spread of neo-Y alleles (C and D). However, when a neo-sex determining system evolves that is less closely linked to a locus under selection (B and D), population mean fitness decreases. *I'm still confused why male and female mean fitnesses aren't normalized by their frequency. I'm not sure we should be calling them means without this normalization step. Or we should justify this by saying that mean fitness also has something to do with the number of a sex, i.e., multiply *real* mean fitness in females by $\text{freqfemale}/(1/2)$? See the next figure for what happens when we do normalize.*

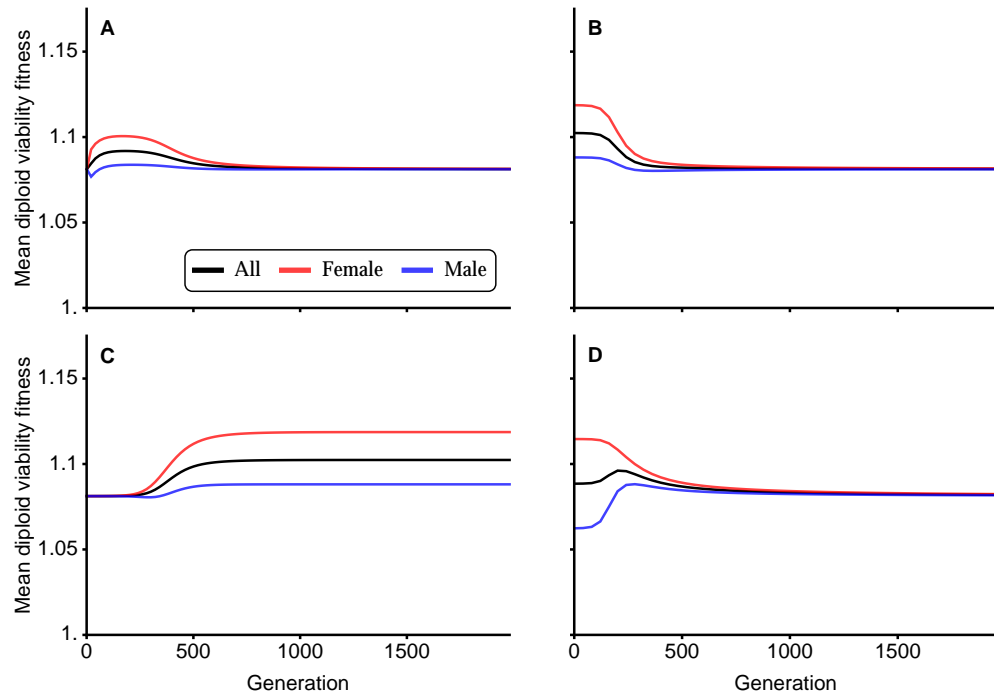


Figure 5: Last plot with mean fitness of sexes corrected for sex ratio.

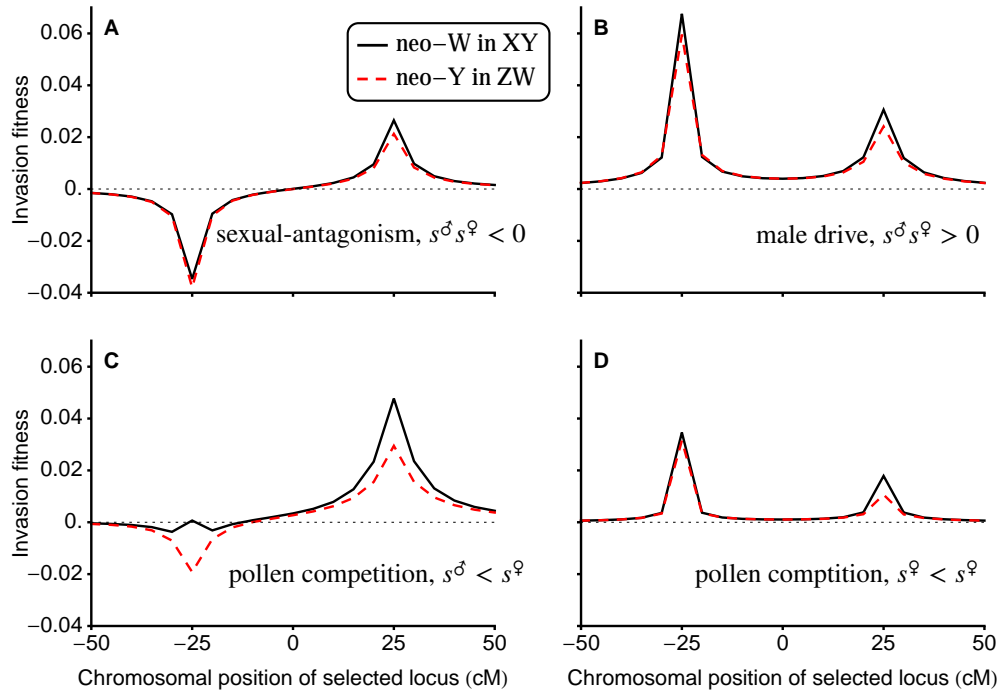


Figure 6: Invasion fitness of a neo-W allele plotted against the relative genomic location of a locus under direct selection, **A**, for various selective regimes. The ancestral sex-determining locus is located at -25 and the novel sex-determining locus is located at 25. We use Haldane's map function (Equation 3 in Haldane 1919) to convert from map distance (centiMorgans) to the probability of a cross-over event. In **A**, there is no haploid selection ($r^\delta = \alpha_\Delta^\delta = 0$) 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 ($s^\delta = 1/10$, $h^\delta = 7/10$, $s^\delta = -1/10$, $h^\delta = 3/10$). In **B-D** we include haploid selection and assume that selection in diploids is not sexually-antagonistic ($s^\delta s^\delta > 0$). 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 ($\alpha_\Delta^\delta = -1/20$), no female meiotic drive or gametic competition, $r^\delta = \alpha_\Delta^\delta = 0$, and equal selection in diploid sexes ($s^\delta = s^\delta = 1/10$, $h^\delta = h^\delta = 7/10$). 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 ($r^\delta = \alpha_\Delta^\delta = 0$). In this case, the neo-W does not invade if $s^\delta > s^\delta$ (panel **C**: $s^\delta = 3/20$, $s^\delta = 1/20$) but does if $s^\delta < s^\delta$ (panel **D**: $s^\delta = 1/20$, $s^\delta = 3/20$), see Table 3.

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

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

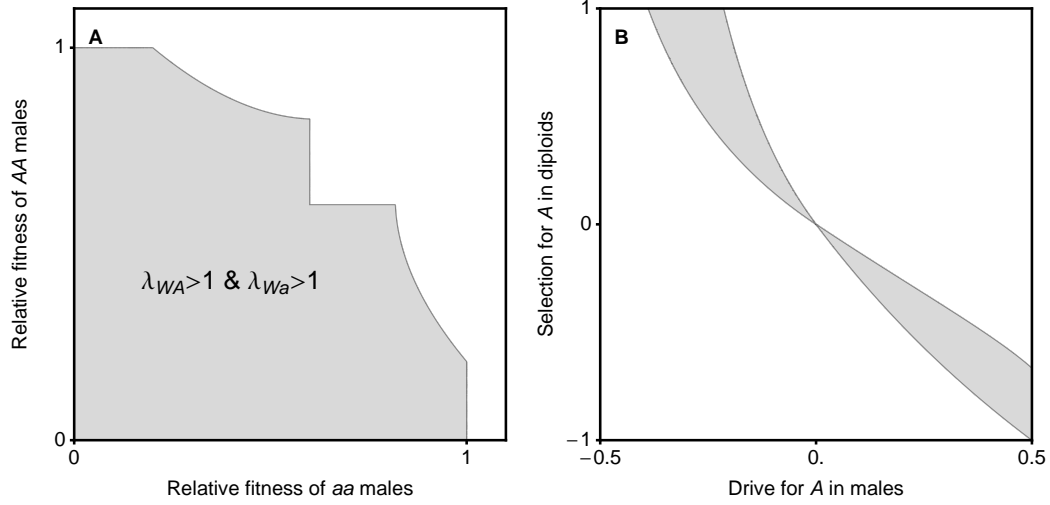


Figure 7: Parameter space (gray) where both neo-W haplotypes can invade from the same stable resident $r = 0$ equilibria (equations S.2), and therefore where an unlinked neo-W can invade an XY system with perfect sex-linkage. **A**, In the absence of haploid selection, both neo-W haplotypes can invade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

Appendix

852 Recursion Equations

Should we adjust the subscripts throughout this subsection? Right now we end up
 854 re-defining i and j (when switching from haploid to diploid; this might have been
 my doing!) and then introduce three new subscripts b , c , and l , all of which can
 856 be derived from i and j . Might be more straightforward to just use $p_{x_1, x_2, a_1, a_2, m_1, m_2}^{\phi}$
 where 1 is maternal and 2 is paternal? We then no longer have to switch indices
 858 from haploid to diploid and the connection to other variables is clear: $b = m_1 m_2$,
 $c = x_1 x_2$, and $l = a_1 a_2$. I guess the downside will be re-writing the recursion
 860 equations... which is why I haven't gone ahead and tried this.

In each generation we census the genotype frequencies in male and female ga-
 862 metes/gametophytes (hereafter, gametes) between meiosis (and any meiotic drive)
 and gametic competition. At this stage we denote the frequencies of X- and Y-
 864 bearing gametes from males and females x_{ij}^{ϕ} and y_{ij}^{ϕ} , where $\phi \in \{\delta, \varphi\}$ speci-
 fies the sex of the diploid that the gamete came from, $i \in \{A, a\}$ specifies the
 866 allele at the selected locus **A**, and $j \in \{M, m\}$ specifies the allele at the novel
 sex-determining locus **M**. The gamete frequencies from each sex sum to one,
 868 $\sum_{i,j} x_{ij}^{\phi} + y_{ij}^{\phi} = 1$.

Competition then occurs among gametes of the same sex (e.g., among eggs
 870 and among sperm separately) according to the **A** locus allele, i (see Table 1). The
 genotype frequencies after gametic competition are $x_{ij}^{\phi, s} = w_i x_{ij}^{\phi} / \bar{w}_H^{\phi}$ and $y_{ij}^{\phi, s} =$
 872 $w_i y_{ij}^{\phi} / \bar{w}_H^{\phi}$, where $\bar{w}_H^{\phi} = \sum_{i,j} w_i x_{ij}^{\phi} + w_i y_{ij}^{\phi}$ is the mean fitness of male ($\phi = \delta$) or
 female ($\phi = \varphi$) gametes.

874 Random mating then occurs between gametes to produce diploid zygotes. To
 shorten notation we now use index i (and j) to denote the alleles at both the **A**
 and **M** loci and label $MA = 1$, $Ma = 2$, $mA = 3$, and $ma = 4$, such that
 876 $i, j \in \{1, 2, 3, 4\}$. The frequencies of XX zygotes are then denoted as xx_{ij} , XY
 zygotes as xy_{ij} , and YY zygotes as yy_{ij} . In XX and YY zygotes, individuals with
 878 diploid genotype ij are equivalent to those with diploid genotype ji ; for simplicity,

we use xx_{ij} and yy_{ij} with $i \neq j$ to denote the average of these frequencies, $xx_{ij} = (x_i^{\varphi,s} x_j^{\delta,s} + x_j^{\varphi,s} x_i^{\delta,s})/2$ 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 $b \in \{MM, Mm, mm\}$ and the **X** locus genotype by $c \in \{XX, XY, YY\}$, zygotes develop as females with probability k_{bc} . Therefore, the frequencies of XX females are given by $xx_{ij}^{\varphi} = k_{bc}xx_{ij}$, XY 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 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 determine zygotic sex according to an XY system, a ZW system, or an environmental sex-determining system. In addition, we can consider any epistatic dominance relationship between the two sex-determining loci. For example, here we assume that the ancestral sex-determining system (**X** locus) is XY ($k_{MMXX} = 1$ and $k_{MMXY} = k_{MMYY} = 0$) or ZW ($k_{MMZZ} = 0$ and $k_{MMZW} = k_{MMWW} = 1$) and epistatically recessive to a dominant novel sex-determining locus, **M** ($k_{Mmc} = k_{mmc} = k$).

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

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

Among gametes from sex φ (sperm/pollen when $\varphi = \delta$, eggs/ovules when

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

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

910 $\phi = \varphi$), the frequencies of haplotypes (before gametic competition) in the next generation are given by

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

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

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

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

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

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

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

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

912

The full system is therefore described by 16 recurrence equations (three diallelic
914 loci in two sexes, $2^3 \times 2 = 16$). However, some diploid types are not produced
under a given sex-determination system. For example, with the M allele fixed and
916 ancestral XY sex determination, there are no m alleles, XX males, XY females,
or YY females ($xx_{11}^{\phi} = xx_{12}^{\phi} = xx_{22}^{\phi} = xy_{11}^{\phi} = xy_{12}^{\phi} = xy_{21}^{\phi} = xy_{22}^{\phi} = yy_{11}^{\phi} =$
918 $yy_{12}^{\phi} = yy_{22}^{\phi} = 0$). In this case, the system only involves six recursion equations,
which yields equilibrium (S.4).

920 Resident equilibrium and stability

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

926 types: $x_{MA}^{\varnothing} = p_X^{\varnothing}$, $x_{Ma}^{\varnothing} = 1 - p_X^{\varnothing}$, $x_{MA}^{\sigma} = (1 - q)p_X^{\sigma}$, $x_{Ma}^{\sigma} = (1 - q)(1 - p_X^{\sigma})$,
 $y_{MA}^{\sigma} = qp_Y^{\sigma}$, and $y_{Ma}^{\sigma} = q(1 - p_Y^{\sigma})$. Mean fitnesses in the resident population are
 928 given in table S.2.

Various forms of selection can maintain a polymorphism at the **A** locus, including sexually antagonistic selection, overdominance, conflicts between diploid
 930 selection and selection upon haploid genotypes (ploiddally antagonistic selection, Immler et al. 2012), and a combination of these selective regimes.

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

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

In particular special cases, e.g., no sex-differences in selection or meiotic drive
 934 ($s^{\sigma} = s^{\varnothing}$, $h^{\sigma} = h^{\varnothing}$, and $\alpha^{\sigma} = \alpha^{\varnothing} = 1/2$), the equilibrium allele frequency and stability can be calculated analytically without assuming anything about the relative
 936 strengths of selection and recombination. However, here, we focus on two regimes (tight linkage and weak selection) in order to make fewer assumptions about fitnesses.
 938

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

940 We first calculate the equilibrium frequency of the **Y** and **A** alleles in the ancestral
population when the recombination rate between the **X** and **A** loci is small (r of
942 order ϵ). The **A** locus will not affect evolution at the novel sex-determining locus,
M, if one **A** allele is fixed on all backgrounds. We therefore focus on the five
944 equilibria that maintain both **A** and **a** alleles, four of which are given to leading
order by:

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

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

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

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

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

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

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

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

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

We next calculate when (A) and (B) are locally stable for $r = 0$. According to the ‘small parameter theory’ (Karlin and McGregor 1972a;b), these stability properties are unaffected by small amounts of recombination between the SDR and A locus, although equilibrium frequencies may be slightly altered. For the a allele to be stably fixed on the Y requires that $\bar{w}_{Ya}^\delta > \bar{w}_{YA}^\delta$ where $\bar{w}_{Ya}^\delta = w_a^\delta(2p_X^\varphi(1 - \alpha^\delta)w_A^\varphi w_{Aa}^\delta + (1 - p_X^\varphi)w_a^\varphi w_{aa}^\delta)$ and $\bar{w}_{YA}^\delta = w_A^\delta(p_X^\varphi w_A^\varphi w_{AA}^\delta + 2(1 - p_X^\varphi)\alpha^\delta w_a^\varphi w_{Aa}^\delta)$. That is, Ya haplotypes must have higher fitness than YA haplotypes. Substituting in $p_X^\varphi = \hat{p}_X^\varphi$ from above, fixation of the a allele on the Y requires that $\gamma_i > 0$ where $\gamma_{(A)} = w_a^\delta(2(1 - \alpha^\delta)w_{Aa}^\delta \phi + w_{aa}^\delta \psi) - w_A^\delta(w_{AA}^\delta \phi + 2\alpha^\delta w_{Aa}^\delta \psi)$ for equilibrium (A) and $\gamma_{(B)} = 2(1 - \alpha^\delta)w_a^\delta w_{Aa}^\delta - w_A^\delta w_{AA}^\delta$ for equilibrium (B) . Stability of a polymorphism on the X chromosome (equilibrium A) further requires that $\phi > 0$ and $\psi > 0$. Fixation of the a allele on the X (equilibrium B) is mutually exclusive with equilibrium (A) and requires $\psi < 0$ and $w_A^\varphi w_{AA}^\varphi > (1 - \alpha^\varphi)w_a^\varphi w_{Aa}^\varphi$.

Selection weak relative to recombination (weak selection)

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

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

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

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

976 $(\hat{p}_X^\varnothing = \hat{p}_X^\delta = \hat{p}_Y^\delta = \bar{p})$ and given, to leading order, by

$$\bar{p} = \frac{h^\varnothing s^\varnothing + h^\delta s^\delta + t^\varnothing + t^\delta + \alpha_\Delta^\varnothing + \alpha_\Delta^\delta}{(2h^\varnothing - 1)s^\varnothing + (2h^\delta - 1)s^\delta} + O(\epsilon). \quad (\text{S.4})$$

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

$$\begin{aligned} \hat{p}_X^\delta - \hat{p}_X^\varnothing &= V_A (D^\delta - D^\varnothing + \alpha_\Delta^\delta - \alpha_\Delta^\varnothing) + O(\epsilon^2) \\ \hat{p}_Y^\delta - \hat{p}_X^\varnothing &= V_A (D^\delta - D^\varnothing + \alpha_\Delta^\delta - \alpha_\Delta^\varnothing + (1 - 2r)(t^\delta - t^\varnothing)) / 2r + O(\epsilon^2) \\ \hat{p}_Y^\delta - \hat{p}_X^\delta &= V_A (D^\delta - D^\varnothing + \alpha_\Delta^\delta - \alpha_\Delta^\varnothing + t^\delta - t^\varnothing)(1 - 2r) / 2r + O(\epsilon^2) \end{aligned} \quad (\text{S.5})$$

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

988 **Invasion conditions**

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

the largest solution to a quadratic characteristic polynomial $\lambda^2 + b\lambda + c = 0$. It can be shown (see supplementary Mathematica file) that the coefficients are $b = -(\lambda_{mA} + \lambda_{ma}) + (\rho_{mA} + \rho_{ma})$ and $c = (\lambda_{mA} - \rho_{mA})(\lambda_{ma} - \rho_{ma}) - \rho_{mA}\rho_{ma}$, where λ_{mi} is the multiplicative growth rate of the frequency of mutants on background $i \in \{A, a\}$, without accounting for loss due to recombination, and ρ_{mi} is the rate at which mutants on background $i \in \{A, a\}$ recombine onto the other **A** locus background in heterozygotes. The leading eigenvalue is then greater than one whenever $\lambda_{mA} > 1$ and $\lambda_{ma} > 1$, less than one whenever $\lambda_{mA} < 1$ and $\lambda_{ma} < 1$, and greater than one whenever $\lambda_{mA} > 1$ or $\lambda_{ma} > 1$ and $\rho_{ma}(\lambda_{mA} - 1) + \rho_{mA}(\lambda_{ma} - 1) > 0$.

For tight linkage between the ancestral sex-determining locus and the selected locus we can calculate each of these terms exactly, while for weak selection we take a Taylor series of the leading eigenvalue.

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

Here, we explore the conditions under which a neo-W invades an XY system assuming that the **A** locus is initially in close linkage with the ancestral sex-determining region ($r \approx 0$). We disregard neo-Y mutations, which never spread given that the ancestral population is at a stable equilibrium.

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

$$\lambda_{mA} = (2\alpha^\delta)^{-1} \frac{w_A^\varnothing [w_A^\delta w_{AA}^\varnothing \alpha^\delta + 2w_a^\delta w_{Aa}^\varnothing \alpha^\varnothing (1 - \alpha^\delta)]}{w_A^\delta w_A^\varnothing w_{AA}^\varnothing} \quad (\text{S.6a})$$

$$\lambda_{ma} = (2\alpha^\delta)^{-1} \frac{w_a^\varnothing [w_a^\delta w_{aa}^\varnothing (1 - \alpha^\delta) + 2w_A^\delta w_{Aa}^\varnothing (1 - \alpha^\varnothing) \alpha^\delta]}{w_A^\delta w_A^\varnothing w_{AA}^\varnothing} \quad (\text{S.6b})$$

$$\rho_{mA} = (2\alpha^\delta)^{-1} \frac{Rw_a^\delta w_A^\varnothing w_{Aa}^\varnothing \alpha^\varnothing (1 - \alpha^\delta)}{w_A^\delta w_A^\varnothing w_{AA}^\varnothing} \quad (\text{S.6c})$$

$$\rho_{ma} = (2\alpha^\delta)^{-1} \frac{Rw_A^\delta w_a^\varnothing w_{Aa}^\varnothing (1 - \alpha^\varnothing) \alpha^\delta}{w_A^\delta w_A^\varnothing w_{AA}^\varnothing} \quad (\text{S.6d})$$

Haploid selection impacts the spread of neo-W haplotypes in three ways. Firstly,
 1016 the zygotic sex ratio becomes male biased ($\zeta < 1/2$; at equilibrium (B) the sex
 ratio is $\zeta = \alpha^\delta w_A^\delta / [(1 - \alpha^\delta)w_a^\delta + \alpha^\delta w_A^\delta]$) when the a allele (which is fixed on
 1018 the Y) is favoured during competition among male gametes or by meiotic drive
 in males. This facilitates the spread of a neo-W because neo-W alleles cause the
 1020 zygotes that carry them to develop as the rarer, female, sex. Secondly, haploid
 selection in males affects the diploid genotypes of females by altering the allele
 1022 frequencies in the male gametes that female gametes pair with. For instance, be-
 cause an epistatically dominant neo-W always causes its carrier to become female,
 1024 it creates females who carry either Y- a or X genotypes from their father. Thus, be-
 cause when there is a polymorphism the X carries some non-zero frequency of A ,
 1026 haploid selection in males impacts the diploid genotypes of females (e.g., creating
 more Aa females when drive in males favours Y- a). How this affects the spread
 1028 of the neo-W then depends on diploid and haploid selection in females. Thirdly,
 female drive and gamete competition directly select on neo-W haplotypes. Drive
 1030 for A in females favours neo-W- A haplotypes, at a cost to neo-W- a haplotypes, and
 vice-versa when there is drive for a . The impact of this drive depends on how of-
 1032 ten XX and neo-W females are heterozygous. Competition among female gametes
 acts similarly, and depends on the frequency of A on resident X chromosomes
 1034 (e.g., competition among eggs has no affect on the initial spread of the neo-W- A
 haplotype when A is fixed on the X). Because haploid selection in females favours
 1036 one neo-W haplotype at the expense of the other, recombination off the favoured
 background becomes more detrimental as it becomes more favoured. Thus higher
 1038 rates of recombination between the neo-W and the selected locus, R , can lead to
 smaller leading eigenvalues when there is haploid selection in females.

1040 The other terms in equations (S.6) are more easily interpreted if we assume
 that there is no haploid selection in either sex, in which case $\lambda_{mA} > 1$ when $w_{Aa}^\varnothing >$
 1042 w_{AA}^\varnothing and $\lambda_{ma} > 1$ when $(w_{Aa}^\varnothing + w_{aa}^\varnothing)/2 > w_{AA}^\varnothing$. These conditions cannot be met
 under purely sexually-antagonistic selection, where a is directionally favoured in
 1044 males ($w_{AA}^\delta > w_{Aa}^\delta > w_{aa}^\delta$) and A is directionally favoured in females ($w_{AA}^\varnothing >$

1046 $w_{Aa}^{\varphi} > w_{aa}^{\varphi}$). Essentially, the X is already as specialized as possible for the female
beneficial allele (XA is fixed), and the neo-W often makes daughters with the Y-a
1048 haplotype, increasing the flow of *a* alleles into females, which reduces the fitness
of those females.

If selection doesn't uniformly favour *A* in females, however, neo-W-*A* haplo-
1050 types and/or neo-W-*a* haplotypes can spread ($\lambda_{mA} > 1$ and/or $\lambda_{ma} > 1$) at this
equilibrium. A neo-W can spread alongside the *A* allele ($\lambda_{mA} > 1$), despite the
1052 fact that a neo-W brings *Ya* haplotypes into females, when $w_{Aa}^{\varphi} > w_{AA}^{\varphi}$. In this
case the *a* allele is favoured by selection in females despite *A* being fixed on the
1054 X. For this equilibrium to be stable, X-*A* must be sufficiently favoured in males
to keep the frequency of XA at one (specifically, from the stability conditions, we
1056 must have $w_{Aa}^{\delta} / ((w_{aa}^{\delta} + w_{Aa}^{\delta}) / 2) > w_{Aa}^{\varphi} / w_{AA}^{\varphi}$).

Under this same condition, $w_{Aa}^{\varphi} > w_{AA}^{\varphi}$, the neo-W can also spread alongside
1058 the *a* allele ($\lambda_{ma} > 1$) if there is sufficiently strong underdominance in females
($w_{aa}^{\varphi} > w_{Aa}^{\varphi}$), such that $(w_{Aa}^{\varphi} + w_{aa}^{\varphi}) / 2 > w_{AA}^{\varphi}$. In this case, *a* is not favored in
1060 females near the equilibrium where females are *AA* (comparing *Aa* to *AA* geno-
types) and yet the neo-W can spread with *a* because it produces female *aa* individ-
1062 uals by capturing *Y-a* haplotypes.

When both haplotypes can spread on their own ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$), the
1064 neo-W invades regardless the recombination rate between it and the selected locus,
R. When neither haplotype can spread ($\lambda_{mA} < 1$ and $\lambda_{ma} < 1$) the neo-W can never
1066 invade. And when only one haplotype can spread on its own the neo-W invades
only when the rate of recombination onto the favourable background is sufficiently
1068 larger than the rate of recombination off this background (i.e., equation 1 is satis-
fied).

1070 Similar equations can be derived for equilibrium (A) by subbing the equilib-
rium allele frequencies into Table 2.

$$\lambda_{mA} = \frac{a}{b} \left[w_{AA}^{\varphi} w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi + 2w_{Aa}^{\varphi} \alpha^{\varphi} w_a^{\delta} \frac{c}{d} \right] / w_a^{\varphi} \quad (\text{S.7a})$$

$$\lambda_{ma} = \frac{a}{b} \left[2w_{Aa}^{\varphi} (1 - \alpha^{\varphi}) w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi + w_{aa}^{\varphi} w_a^{\delta} \frac{c}{d} \right] / w_A^{\varphi} \quad (\text{S.7b})$$

$$\rho_{mA} = \frac{a}{b} R \left[2w_{Aa}^{\varphi} \alpha^{\varphi} w_a^{\delta} \frac{c}{d} \right] / w_a^{\varphi} \quad (\text{S.7c})$$

$$\rho_{ma} = \frac{a}{b} R \left[2w_{Aa}^{\varphi} (1 - \alpha^{\varphi}) w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi \right] / w_A^{\varphi} \quad (\text{S.7d})$$

1072 where

$$a = w_a^{\varphi} \phi + w_A^{\varphi} \psi \quad (\text{S.8a})$$

$$b = w_{AA}^{\varphi} \phi (2w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi) + w_{Aa}^{\varphi} \psi (2w_{Aa}^{\delta} w_A^{\delta} \alpha^{\delta} \phi + w_{AA}^{\delta} w_a^{\delta} \psi) + w_{aa}^{\varphi} \psi (w_{AA}^{\delta} w_a^{\delta} \psi) \quad (\text{S.8b})$$

$$c = 2(w_{Aa}^{\delta} \phi)^2 (1 - \alpha^{\delta}) \alpha^{\delta} + w_{Aa}^{\delta} \phi (w_{AA}^{\delta} \psi + w_{aa}^{\delta} \psi \alpha^{\delta}) + w_{aa}^{\delta} \psi w_{AA}^{\delta} \psi \quad (\text{S.8c})$$

$$d = 2w_{Aa}^{\delta} \alpha^{\delta} \phi + w_{aa}^{\delta} \psi \quad (\text{S.8d})$$

As with equilibrium (B), haploid selection again modifies invasion fitnesses by altering the sex-ratio and the diploid genotypes of females and directly selecting upon female gametes. The only difference is that resident XX females are no longer always homozygote AA and males are no longer always heterozygote Aa. Thus the effect of haploid selection in males is reduced, as is the difference in fitness between neo-W haplotypes and resident X haplotypes, as both can be on any diploid or haploid background.

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

$$2(w_{Aa}^{\varphi} - w_{aa}^{\varphi}) w_{AA}^{\delta} \psi^2 > (w_{AA}^{\varphi} - w_{Aa}^{\varphi}) w_{Aa}^{\delta} \phi (\phi - \psi) \quad (\text{S.9})$$

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

1084 (A) is stable. In contrast to equilibrium (B), a neo-W haplotype can spread under
 purely sexually-antagonistic selection ($w_{AA}^\delta > w_{Aa}^\delta > w_{aa}^\delta$ and $w_{AA}^\varphi > w_{Aa}^\varphi > w_{aa}^\varphi$).
 1086 In this case, the neo-W-A haplotype can spread, despite producing a lot of *Aa*
 daughters by obtaining the *a* from Y-gametes, when *aa* females, which the neo-
 1088 W-A never makes, are strongly selected against. This can be intuited from the fact
 that (S.9) will be more easily met when $w_{Aa}^\varphi - w_{aa}^\varphi \approx w_{Aa}^\varphi$ and $w_{AA}^\varphi - w_{Aa}^\varphi \approx 0$,
 1090 implying $w_{aa}^\varphi \approx 0$ and $w_{Aa}^\varphi \approx w_{AA}^\varphi$ (although this is complicated by the fact that
 w_{aa}^φ and w_{Aa}^φ affect ϕ and ψ too, the intuition holds).
 1092 Without haploid selection, the neo-W-*a* haplotype spreads ($\lambda_{ma} > 1$) if and
 only if

$$(w_{aa}^\varphi + w_{Aa}^\varphi - 2w_{AA}^\varphi)w_{Aa}^\delta \phi^2 + (w_{aa}^\varphi - w_{Aa}^\varphi)(w_{Aa}^\delta + 2w_{AA}^\delta)\phi\psi > 0 \quad (\text{S.10})$$

1094 This condition cannot be met with purely sexually antagonistic selection (as both
 terms on the left-hand side would then be negative), but it can be met under other
 1096 circumstances. For example, with overdominance in males there is selection for
 increased *A* frequencies on X chromosomes in males, which are always paired with
 1098 Y-*a* haplotypes. Then, directional selection for *a* in females maintains a polymor-
 phism at the **A** locus on the X and by creating selection for decreased *A* frequencies
 1100 on X chromosomes in females. This scenario selects for a modifier that increases
 recombination between the sex chromosomes (e.g., blue region of Figure 2d in
 1102 Otto 2014) and facilitates the spread of neo-W-*a* haplotypes, which create more
 heterozygote and *aa* females than ancestral X chromosomes do.

1104 As with equilibrium (B), if both haplotypes can spread ($\lambda_{mA} > 1$ and $\lambda_{ma} > 1$)
 then the neo-W invades under any rate of recombination with the selected locus,
 1106 $R \geq 0$. In addition, even when only one haplotype can spread (e.g., under purely
 sexually-antagonistic selection $\lambda_{mA} > 1$ and $\lambda_{ma} < 1$), neo-W invasion can still
 1108 occur under modest rates of recombination between the novel sex-determining and
 selected loci.

¹¹¹⁰ **Selection weak relative to recombination (weak selection)**

With weak selection the leading eigenvalue, λ , for any k , is given up to order ϵ^2
¹¹¹² by equation 4. Scenarios leading to $\lambda > 1$ are discussed in the main text.