Autosomal suppression of meiotic drive can prevent sex chromosome cycling

Anjali Gupta[1*] and Robert L. Unckless[2*]

[1]Department of Ecology and Evolutionary Biology, University of Kansas, Lawrence, KS, USA

[2]Department of Molecular Biosciences, University of Kansas, Lawrence, KS, USA

[*]Corresponding authors

Email: anjaligupta@ku.edu, unckless@ku.edu

Running title: Autosomal and Y-linked suppression of X chromosome meiotic drive

Keywords: Sex-ratio meiotic drive, X-linked drive, autosomal suppressors, Y-linked suppressors, sex-chromosome cycling, invasion.

Data accessibility: Data and code will be archived in DRYAD upon acceptance.

Abstract:

Sex-ratio meiotic drivers are selfish genes or gene complexes that bias the transmission of chromosomes resulting in skewed sex ratios. While existing theoretical models have suggested the maintenance of a four-chromosome equilibrium (X, X^{SR}, Y, Y^{SUP}; SR: sex-ratio driver, SUP: suppressor) in a cyclic dynamic, studies of natural populations have failed to capture this pattern. Although there are several plausible explanations for this lack of cycling, interference from autosomal suppressors has not been studied using a population genetic framework even though autosomal suppressors and Y-linked suppressors both exist in populations of some species. In this study, we use a simulations-based approach to investigate the influence of autosomal suppressors on the cycling of sex chromosomes. Our findings demonstrate that the presence of an autosomal suppressor can hinder the invasion of a Y-linked suppressor under some parameter space, thereby impeding the cyclic dynamics. Even when a Y-linked suppressor invades, the presence of an autosomal suppressor can prevent cycling. Our study demonstrates the potential role of autosomal suppressors in preventing sex chromosome cycling and provides insights into the conditions and consequences of the maintenance of both Y-linked and autosomal suppressors.

Introduction:

Meiotic drivers are selfish genetic elements that manipulate transmission during gametogenesis to cheat Mendelian segregation and bias transmission in their favor. When these drivers are present on sex chromosomes in the heterogametic sex, the unequal transmission of sex chromosomes results in biased sex ratios among progeny and within populations. This phenomenon is known as sex-ratio meiotic drive. As with other selfish genetic elements, genomes have also evolved both Y-linked and autosomal strategies to suppress such drivers. The ecological and evolutionary importance of sex-ratio meiotic drive and its suppression has been discussed in detail previously (Dyer & Hall, 2019; Fuller et al., 2020; Jaenike, 2001; Lindholm et al., 2016; Mackintosh et al., 2021; Unckless & Clark, 2014). However, given that X-linked drivers are often associated with reduced recombination across large swaths of the X chromosome and Y-linked suppressors are, by definition, linked to the entire Y chromosome, both stable equilibria of driver and suppressor and cycling dynamics carry important implications for segregating genetic variation in populations.

How genomes fight back against meiotic drive is varied (Babcock & Anderson, 1996; Beckenbach, 1978, 1996; Beckenbach et al., 1982; Bircher et al., 1995; Capillon & Atlan, 1999; Carvalho et al., 1997, 1998; Carvalho & Vaz, 1999; Cazemajor et al., 1997, 2000; Curtsinger & Feldman, 1980; de Carvalho et al., 1989; de Carvalho & Klaczko, 1993; Dermitzakis et al., 2000; Faulhaber, 1967; Hauschteck-Jungen, 1990; Hauschteck-Jungen & Maurer, 1976; Jaenike, 1996a, 1999; James & Jaenike, 1990; Mercot et al., 1995; Montchamp□Moreau et al., 2001; Policansky, 1974, 1979; Policansky & Ellison, 1970; Prakash & Merritt, 1972; Presgraves et al., 1997; Stalker, 1961; Taylor, 1994a, 1994b, 1996, 1999; Taylor et al., 1999; Varandas et al., 1997;

Voelker, 1972; Wallace, 1948; Wilkinson, Kahler, et al., 1998; Wilkinson, Presgraves, et al., 1998; Wilkinson & Sanchez, 2001) [Table 1]. Suppression often is on the homologous chromosome either evolving away from a drive target site (often referred to as resistance) or through a specific suppression mechanism that interferes with the drive machinery. In the case of X-linked sex-ratio meiotic drive, this homologous suppression is encoded on the Y chromosome. Suppression also sometimes occurs on the autosomes through loci that somehow interfere with expression of the drive machinery (Tao, Araripe, et al., 2007; Tao, Masly, et al., 2007). In several systems, no suppressors have been identified even with significant searching (Babcock & Anderson, 1996; Beckenbach, 1978, 1996; Beckenbach et al., 1982; Curtsinger & Feldman, 1980; Dyer et al., 2007; Gershenson, 1928; Jaenike, 1996b; James & Jaenike, 1990; Policansky, 1974, 1979; Policansky & Ellison, 1970; Prakash & Merritt, 1972; Wallace, 1948; Wu & Beckenbach, 1983).

The selective benefits of suppression depend on the chromosome on which it resides. Any X-linked driver that is strong and/or at high frequency will result in a population that is female-biased because males carrying the driver produce an excess of daughters and a dearth of sons. Classic sex-ratio theory predicts that any mutation (whether autosomal or Y-linked) that suppresses drive and is therefore found at higher frequencies in the rarer males will have a selective advantage since offspring always have exactly one mother and one father, meaning the expected number of offspring produced by rare males is greater than that for common females. Thus, suppressors that restore a one-to-one sex-ratio are selected for regardless of the chromosome on which they find themselves. Y-linked suppressors have an additional selective advantage since they are associated with higher average fitness than their susceptible Y-linked

counterparts. For example, imagine an X-linked driver segregating at 20% frequency in males that is perfect (produces all daughters) in the absence of a Y-linked suppressor. Also imagine that Y-linked suppression is perfect (males carrying the driver and Y-linked suppressor have 50% daughters). In such a case, the average fitness of the susceptible Y chromosome is 0.4 (80% of the time, half of the offspring carry the Y chromosome, 20% of the time, none of the offspring carry the Y chromosome). However, the average fitness of the resistant Y chromosome is 0.5 (regardless of the frequency of the driver, half of the offspring carry the driving Y chromosome. Thus, while autosomal suppressors benefit by finding themselves in the rarer sex, Y-linked suppressors benefit from both being in the rarer sex *and* having a fitness advantage over the susceptible Y chromosome. Note, these arguments are somewhat different when meiotic drive threatens populations with extinction (Veller and Unckless in prep).

The maintenance and stability of X-linked meiotic drivers has been thoroughly studied using theoretical population genetics (Clark, 1987; Curtsinger & Feldman, 1980; Edwards, 1961; Hall, 2004; Vaz & Carvalho, 2004; Wu, 1983). Some of these models focused on Y-linked suppression of drive (Clark, 1987; Hall, 2004), and a few others discussed autosomal suppression of drive (Vaz & Carvalho, 2004; Wu, 1983). Hall 2004 predicted the maintenance of a stable four-chromosome equilibrium (X, X^{SR}, Y, Y^{SUP}; SR: sex-ratio driver, SUP: suppressor) when a driving X chromosome and Y-linked suppressor are segregating in a population, and costs associated with the driving X and suppressor are small. Hall also predicted that X/X^{SR} and Y/Y^{SUP} might undergo stable cycling under some parameter sets. Field surveys focused on sex-ratio meiotic drive have failed to capture cycling in real populations prompting Hall to question why cycling dynamics have not been observed in nature. While there are several possible explanations

(including the lack of an appropriate timeframe for observations of cycling or migration), Hall suggested possibility is that autosomal suppressors of X-linked drivers might impede cycling of the sex chromosomes (Hall, 2004).

In this study, we explore whether autosomal suppressors can inhibit the invasion of Y-linked suppressors and prevent the cycling of sex chromosomes. While there has been extensive modeling of meiotic driver systems, we are unaware of models that combine the maintenance of sex-ratio driver chromosomes, Y-linked suppressors, and autosomal suppressors. Importantly, both Y-linked suppressors and autosomal suppressors of sex-ratio meiotic drive have been found co-segregating in multiple species making their interactions a compelling subject of study. Some examples of species where autosomal and Y-linked suppressors for X-linked drive have been studied are presented in Table 1.

Table 1: Examples of species with X-linked sex-ratio meiotic drive and its suppressors.

Observation	**Cases**
X-linked drivers without suppressors	• *D. pseudoobscura* (Babcock & Anderson, 1996; Beckenbach, 1978, 1996; Beckenbach et al., 1982; Curtsinger & Feldman, 1980; Policansky, 1974, 1979; Policansky & Ellison, 1970; Prakash & Merritt, 1972; Wallace, 1948), • *D. neotestacea* (James & Jaenike, 1990) • *D. obscura* (Gershenson, 1928) • *D. persimilis* (Wu & Beckenbach, 1983) • *D. recens* (Dyer et al., 2007; Jaenike, 1996b)
X-linked drivers with only Y-linked suppressors	• *D. affinis* (Voelker, 1972), • *Silene alba* (Taylor, 1994a, 1994b, 1996, 1999; Taylor et al., 1999)

X-linked drivers with only autosomal suppressors	• None known
X-linked drivers with both Y-linked and autosomal suppressors	• *Drosophila subobscura* (Bircher et al., 1995; Hauschteck-Jungen, 1990; Hauschteck-Jungen & Maurer, 1976), • *D. simulans* (Atlan et al., 1997; Capillon & Atlan, 1999; Cazemajor et al., 1997, 2000; Dermitzakis et al., 2000; Faulhaber, 1967; Mercot et al., 1995; Montchamp□Moreau et al., 2001), • *D. quinaria* (Jaenike, 1996a, 1999), • *D. paramelanica* (Stalker, 1961), • *D. mediopunctata* (Carvalho et al., 1997, 1998; de Carvalho et al., 1989; de Carvalho & Klaczko, 1993; Varandas et al., 1997) and • *Cyrtodiopsis dalmanni* (Presgraves et al., 1997; Wilkinson, Kahler, et al., 1998; Wilkinson, Presgraves, et al., 1998; Wilkinson & Sanchez, 2001)

We develop a mathematical model to consider the population genetics of an X-linked driver, a Y-linked suppressor, and an autosomal suppressor. Using numerical simulations for our model, we address whether autosomal suppressors can prevent sex chromosome cycling or even the initial invasion of the Y-linked suppressor. By comparisons between populations where an autosomal suppressor was initially absent along with a driving X-chromosome, we ask whether the presence of an autosomal suppressor influences the ability of a Y-linked suppressor to invade the population. If a Y-linked suppressor cannot invade the population, the cyclic dynamic equilibrium as predicted by Hall 2004 is impossible. We also broadly investigate how a Y-linked suppressor influences the population equilibrium upon invasion. Further, we corroborate our results by testing for invasion of an autosomal suppressor in populations at equilibrium for a Y-linked suppressor and the driving X. We also specifically examine cases where the initial populations exhibited stable cycling for the driving X and Y-linked suppressor and tested

whether an autosomal suppressor could invade these cycling population and impede the cycling. Finally, we explore parameter space where Y-linked suppressors exhibit stable cycling with the driving X but start our initial populations at equilibrium for the driving X and autosomal suppressor instead, and then test whether a Y-linked suppressor can invade the population and if cycling could occur in the presence of the autosomal suppressor. We also discuss other potential factors which could be a possible reason for why this cycling dynamics is not seen in natural populations.

Methods:

The Model:

We model this meiotic drive system by assuming a bi-allelic tri-locus system combining elements of models proposed by Wu (Wu, 1983), Clark (Clark, 1987) and Hall (Hall, 2004). An X chromosome can be either X (standard X) or X^{SR} (SR: sex-ratio meiotic drive), a Y chromosome can be either Y (standard Y) or Y^{SUP} (SUP: suppressor), and an autosome can be either A (standard autosome) or A^{SUP} (SUP: suppressor). A single copy of a suppressor (either A^{SUP} or Y^{SUP}) is sufficient for complete suppression of the drive locus, in other words, resistance is complete and dominant. In the absence of a suppressor, an $X^{SR}Y$ male produces (1/2 + d) X^{SR} sperm (d represents the strength of drive) and (1/2 - d) Y sperm ($0 < d \leq 1/2$). We assume viability cost for carrying a driving X or suppressors. We denote these costs as s_M^{SR} and s_F^{SR} for the cost of carrying a driving X in males and females respectively. We denote the cost of carrying a Y-linked suppressor as s^Y and an autosomal suppressor as s^A which is the same regardless of sex. These costs can range between 0 to 1. Furthermore, the dominance of X^{SR} on viability in

females is denoted as h^{SR} and the dominance of A^{SUP} on viability is denoted as h^{A}, where $0 \leq h \leq 1$, however, we restrict our analysis to the three simple cases where costs are recessive (h=0), additive (h=1/2), or dominant (h=1). Following Wu, 1983, we denote the frequencies of genotypes for females as p_i and for males as q_i and each genotype is associated with a mean fitness ($\underline{u}_i$ for females and v_i for males, Table S1).

Table 2: Variables and parameters used in the model.

Variable / Parameter	**Description**
X	Standard X chromosome
X^{SR}	X chromosome carrying a sex-ratio driver gene
Y	Standard Y chromosome
Y^{SUP}	Y chromosome carrying a suppressor gene
A	Standard autosome
A^{SUP}	Autosome carrying a suppressor gene
p_i	Genotypic frequencies in females (see Table S1 for more information)
q_i	Genotypic frequencies in males (see Table S1 for more information)
h^{A}	Dominance of A^{SUP} on viability
h^{SR}	Dominance of X^{SR} on viability in females
s_M^{SR}	Cost of carrying a sex-ratio driving X in males
s_F^{SR}	Cost of carrying a sex-ratio driving X in females
s^{A}	Cost of carrying an autosome-linked suppressor
s^{Y}	Cost of carrying a Y-linked suppressor
d	Strength of drive ($0 < d \leq 1/2$)

We tracked the genotypic frequencies across generations using recursion equations in a standard Wright-Fisher model (see Supplementary Information). The frequencies of driving X and suppressors in males and females can be estimated at any time point using the associated genotypic frequencies.

$$X_M^{SR} = \frac{q4+q5+q6+q10+q11+q12}{q1+q2+q3+q4+q5+q6+q7+q8+q9+q10+q11+q12} \quad [1]$$

$$X_F^{SR} = \frac{p4+p5+p6+2(p7+p8+p9)}{2(p1+p2+p3+p4+p5+p6+p7+p8+p9)} \quad [2]$$

$$A_M^{SUP} = \frac{q2+q5+q8+q11+2(q3+q6+q9+q12)}{2(q1+q2+q3+q4+q5+q6+q7+q8+q9+q10+q11+q12)} \quad [3]$$

$$A_F^{SUP} = \frac{p2+p5+p8+2(p3+p6+p9)}{2(p1+p2+p3+p4+p5+p6+p7+p8+p9)} \quad [4]$$

$$Y^{SUP} = \frac{q7+q8+q9+q10+q11+q12}{q1+q2+q3+q4+q5+q6+q7+q8+q9+q10+q11+q12} \quad [5]$$

Due to the complex nature of the model, we were unable to find analytical solutions for equilibrium. Instead, we took a deterministic simulation approach to explore the parameter space.

Simulations:

We started each simulation realization with an initial effectively infinite population at a 50:50 sex ratio where the driving X (X^{SR}) and autosomal suppressor (A^{SUP}) are segregating at a low frequency, and Y-linked suppressor (Y^{SUP}) was absent in the population (frequency of X^{SR}=0.015, Y^{SUP}=0, A^{SUP}=0.005). Assuming a Wright-Fisher model, we ran the simulation by

calculating frequencies based on recursions (Supplementary Information, Equations 1-5) and tracked genotypic frequencies for 5000 generations. After 5000 generations, we asked whether the population reached equilibrium, and if it did, we introduced a Y-linked suppressor (Y^{SUP}) into the population at a very low frequency (such that the frequency of Y^{SUP}=0.0005).We then ran the simulation for another 5000 generations after introduction of the Y-linked suppressor (Y^{SUP}) and tracked genotypic frequencies as before. At the end of 10,000 generations, we assessed whether the Y-linked suppressor (Y^{SUP}) invaded the population, and when it invaded, how invasion affected the population equilibrium. We repeated this process over a finite range of parameter space spanning combinations of variable fitness costs for the driving X and suppressors (incrementing s_M^{SR}, s_F^{SR}, s^Y, s^A by 0.1 each time between 0 and 1), variable strength of drive (incrementing drive strength (d) by 0.05 each time within 0 to 0.5), and variable dominance (recessive, additive, or dominant).

We first determined whether segregating autosomal suppression influences the behavior (invasion ability and equilibrium frequency) of a suppressor on the Y chromosome. We compared the simulations described above to those where the autosomal suppressor was *never* introduced, and the X-linked driver and Y-linked suppressor interacted alone.

To determine whether a Y suppressor influences the behavior of an autosomal suppressor, we repeated the simulations but with a different initial population where an autosomal suppressor (A^{SUP}) was initially absent (A^{SUP}=0) and tested for the invasion of an autosomal suppressor in a population at equilibrium for the Y-linked suppressor and driving X. We again examined the

parameter spaces where an autosomal suppressor could invade the population, and what happened to the population equilibrium upon invasion.

Further, we explored cases where our initial population was in stable cycling for the driving X and Y-linked suppressor, and tested if an autosomal suppressor could invade stable cycling populations and what happened to the cycling upon invasion. Finally, we confirmed our predictions by specifically choosing cases illustrated in Hall, 2004 for stable cycling of driving X and Y-linked suppressor but our initial populations were at equilibrium for the driving X and autosomal suppressor instead. We tested for invasion of a Y-linked suppressor for these cycling parameter regions, and whether cycling persisted upon invasion of Y-linked suppressor in the presence of an autosomal suppressor. For simplicity, the methods for the four different simulation scenarios have been summarized in Table 3.

The simulations were written and run in R version 4.2.2 (R Core Team, 2013). Data was analyzed and plotted in R using the following packages: ggplot2 (Wickham, 2011), ggpubr (Kassambara & Kassambara, 2020), and wesanderson (Ram & Wickham, 2018).

Table 3: Summary of the different simulation scenarios.

	Initial population	**Test for invasion of**	**Questions**
A.	Equilibrium for X^{SR}/A^{SUP} *(Y^{SUP} absent)* & X^{SR} *(both Y^{SUP} & A^{SUP} absent)*	Y^{SUP}	1) When can Y^{SUP} invade? 2) Effect of Y^{SUP} on equilibrium of X^{SR} and A^{SUP}?

B.	Equilibrium for X^{SR}/Y^{SUP} *(A^{SUP} absent)*	A^{SUP}	1) When can A^{SUP} invade? 2) Effect of A^{SUP} on equilibrium of X^{SR} and Y^{SUP}?
C.	Stable cycling for X^{SR}/Y^{SUP} *(A^{SUP} absent)*	A^{SUP}	1) Can A^{SUP} invade? 2) What happens to cycling upon invasion?
D.	Equilibrium for X^{SR}/A^{SUP} *(Y^{SUP} absent)* [only specific parameter spaces X^{SR}/Y^{SUP} would be in stable cycling]	Y^{SUP}	1) Does Y^{SUP} invade? 2) Does cycling occur in presence of A^{SUP}?

Results:

Scenario A: Autosomal suppressors can prevent the invasion of Y-linked suppressors in a restricted set of parameters.

We first considered whether a Y-linked suppressor could invade a population at equilibrium for both X-linked driver and autosomal suppression. We compared the dynamics for the invasion of a Y-linked suppressor between populations where an autosomal suppressor was initially absent or present and at stable equilibrium to determine whether the presence of the autosomal suppressor influenced invasion of the Y-linked suppressor. When the fitness costs of the driving X and autosomal suppressor were recessive, and there was no cost of carrying a driving X in males, a Y-linked suppressor could not invade a population where an autosomal suppressor was segregating unless the cost of Y-linked suppression was small [Figure 1]. We also found that a Y-linked suppressor could not invade when:

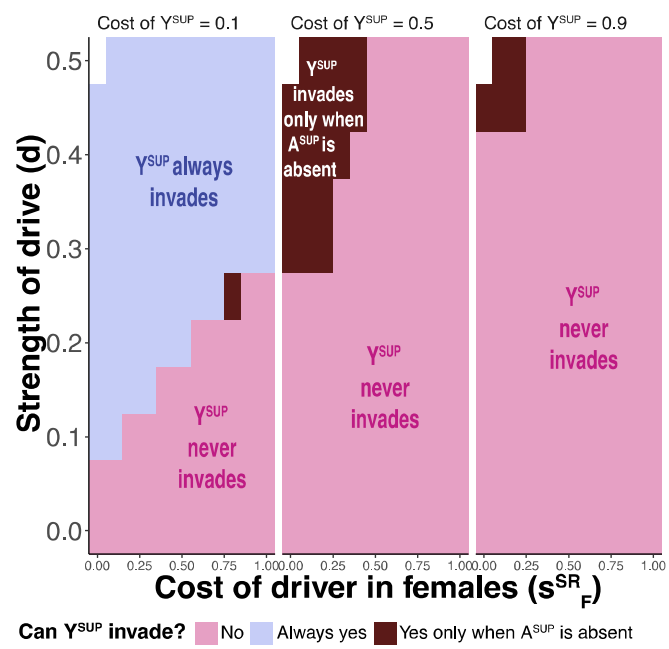

Figure 1: Y-linked suppressors invade a population at equilibrium for driving X and an autosomal suppressor [h^A=0, h^{SR}=0 (recessive costs), s_M^{SR}=0, s^A=0.5, s^Y=0.1 (low), 0.5 (moderate), 0.9 (high)] Parameter space representing whether Y-linked suppressor can invade into the population. (Note that the white boxes on the top right are the spaces where X^{SR} fixes into the population in the absence of a suppressor due to strong drive with no fitness cost, hence the population becomes extinct).

$$s^Y > s_F^{SR} \geq 2 \times d \qquad [6]$$

However, this condition was sufficient but not necessary to prevent the invasion of a Y-linked suppressor. There were other cases where this condition is not met, but the Y-linked suppressor still could not invade the population.

It is reasonable to assume that the ability of any suppressor to invade a population would be dependent on the equilibrium of frequency of the driving X in the absence of Y-linked suppression. We therefore looked at whether the ability of a Y-linked suppressor to invade is associated with the equilibrium frequency of driving X (X^{SR}) in males before introduction of the Y-linked suppressor. Overall, when the driving X is not at a high frequency, the Y linked suppressor is likely to invade, but other factors including the cost of suppression, the cost of the driving X and the strength of drive are also important. While the presence of a driving X was necessary for a Y-linked suppressor to increase in frequency, the presence of an autosomal suppressor in the population prevented a moderate or high-cost Y-linked suppressor to increase in frequency even when the driving X frequency was close to fixation [Figure S1].

Since the equilibrium frequency of the driving X alone did not adequately explain the pattern of invasion of a Y-linked suppressor, we visualized the invasion ability against both the equilibrium frequency of the driving X and of the autosomal suppressor. We found that Y-linked suppressor could invade when the equilibrium frequency of driving X was high, and the equilibrium frequency of autosomal suppressor was low [Figure S2]. When there is no cost of autosomal suppressor in the population, the autosomal suppressor rises in frequency and keeps the driving X in check, inhibiting the invasion of a Y-linked suppressor. However, the autosomal suppressor

did not reach fixation, instead it stayed at an equilibrium once the sex-ratio was restored to 50% females.

When the cost of the driving X was dominant, the ability of invasion of a Y-linked suppressor was low, but that would be true for any population since the fitness cost prevents the driving X from reaching high frequency [Figure S3]. When the fitness cost of an autosomal suppressor was moderate-high and additive or dominant, a Y-linked suppressor with a low to moderate fitness cost could invade the population because of its fitness advantage over the autosomal suppressor [Figure S4].

Y-linked suppressors reduce the equilibrium frequencies of the driving X and autosomal suppressor.

For cases where a Y-linked suppressor (small fitness cost of Y^{SUP}) could invade a population where an autosomal suppressor was initially present, we explored how this affects the equilibrium frequencies of both driving X and autosomal resistance. We looked at the relative reduction in the equilibrium frequencies of X^{SR} and A^{SUP} in males (defined as ΔX_m^{SR} and ΔA_m^{SUP} respectively) upon invasion of a Y-linked suppressor (Y^{SUP}).

$$\Delta X_m^{SR} = \frac{eqbm\,\mathbf{X}^{SR}_{males_before\,Y^{SUP}invasion} - eqbm\,\mathbf{X}^{SR}_{males_after\,Y^{SUP}invasion}}{eqbm\,\mathbf{X}^{SR}_{males_before\,Y^{SUP}invasion}} \quad [7]$$

$$\Delta A_m^{SUP} = \frac{eqbm\,\mathbf{A}^{SUP}_{males_before\,Y^{SUP}invasion} - eqbm\,\mathbf{A}^{SUP}_{males_after\,Y^{SUP}invasion}}{eqbm\,\mathbf{A}^{SUP}_{males_before\,Y^{SUP}invasion}} \quad [8]$$

In cases of a strong driving X with no cost, Y^{SUP} was not effective at reducing the X^{SR} frequency in the population. While for all other cases, Y^{SUP} invasion led to a decline in the equilibrium

frequency of X^{SR} [Figure 2A]. Due to the advantage in fitness cost of the Y-linked suppressor over the autosomal suppressor, when a low-cost Y-linked suppressor invaded the population, the equilibrium frequency of the autosomal suppressor declined to nearly zero [Figure 2B]. We also looked at whether the dominance of costs of the autosomal suppressor have an influence on the relative reduction in the equilibrium frequency of the driving X and the autosomal suppressor [Figure S5]. When costs of autosomal suppressor were additive or dominant, invasion of a Y-linked suppressor caused a sharp decline in the equilibrium frequency of the autosomal suppressor, such that it falls to almost zero, even when the fitness cost of autosomal suppression is small (s^A = 0.1) [Figure S5-B]. As expected, a low-cost Y-linked suppressor was able to effectively replace a high-cost autosomal suppressor.

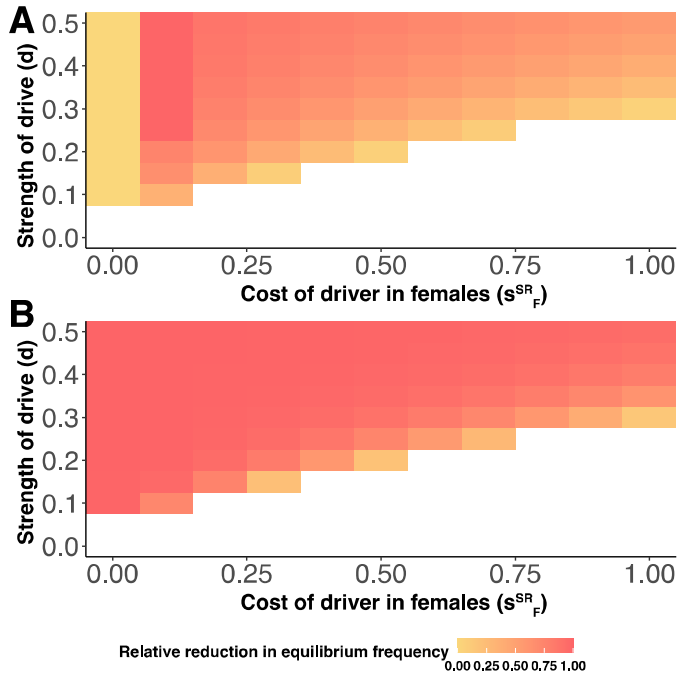

Figure 2: Relative reduction in equilibrium frequencies upon invasion of a Y-linked suppressor [h^A=0, h^{SR}=0 (recessive costs), s_M^{SR}=0, s^A=0.5, s^Y=0.1] **A**. Relative reduction in equilibrium frequency of X^{SR} in males. **B**. Relative reduction in equilibrium frequency of A^{SUP} in males. The white space represents the space where Y^{SUP} cannot invade into the population.

Scenario B: An autosomal suppressor can invade a population at equilibrium for the driving X and Y-linked suppressor when the sex-ratios are female-biased

In general, autosomal suppressors of sex-ratio meiotic drive are selected for because of Fisherian selection for equal sex-ratios, not because they gain a direct benefit from suppressing drive (Crow, 1991). We therefore suspected that autosomal suppressors would be able to invade systems where the driving X and the Y-linked suppressor were both at equilibrium *if* the population sex-ratio was still female-biased. To test this, we ran another set of simulations starting with an initial population (50:50 sex-ratio) with frequencies X^{SR}=0.015, Y^{SUP}=0.005, A^{SUP}=0, and tracked the genotypic frequencies for 5000 generations and asked if the system reached equilibrium. When the population was at equilibrium for the driver X and Y-linked suppressor, we introduced autosomal suppressor into the population at a very low frequency (A^{SUP}=0.0005) and ran the model for another 5000 generations to see if the autosomal suppressor could invade the population in the presence of a Y-linked suppressor. We confirmed that an autosomal suppressor

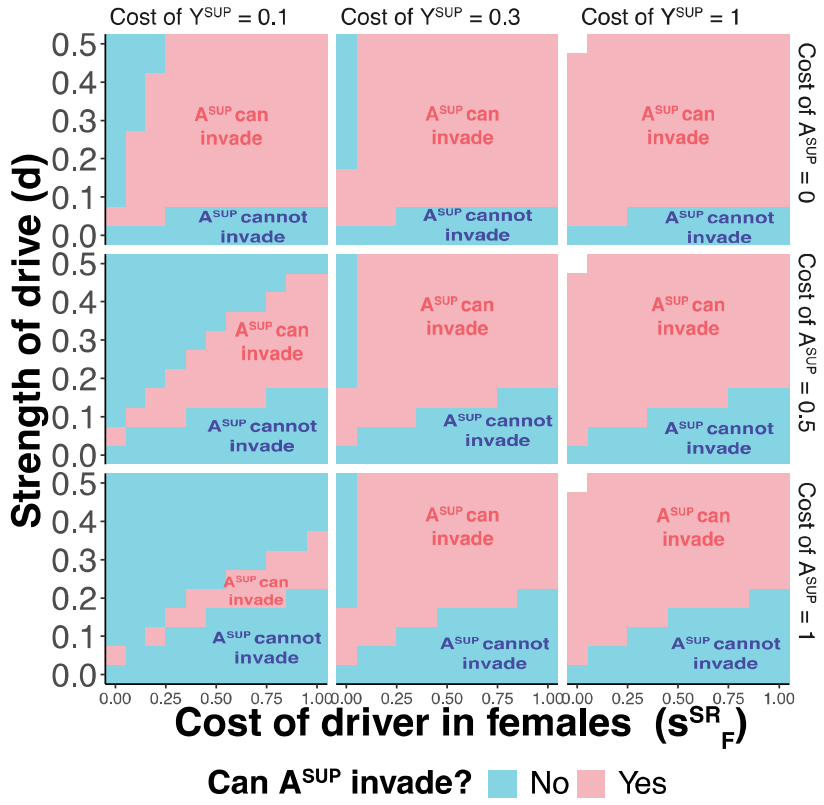

Figure 3: Can an autosomal suppressor invade into a population at equilibrium for a Y-linked suppressor and driving X? [h^A=0, h^{SR}=0 (recessive costs), s_M^{SR}=0, s^A=0 (no cost), 0.5 (moderate), 1 (high), s^Y=0.1 (low), 0.3 (intermediate), 1 (high)]. (Note that the white boxes on the top right are the spaces where X^{SR} fixes into the population due to strong drive with no fitness cost, hence the population becomes

could invade the population in the presence of a Y-linked suppressor for some of the parameter space when the sex-ratio was imbalanced [Figure S6], and the cost of autosomal suppressor was comparably small [Figure 3]. For cases where the sex-ratio was balanced by the Y-linked suppressor at equilibrium, the autosomal suppressor couldn't invade the population. We further explored whether the invasion of autosomal suppressor depends on the equilibrium frequency of the X-linked driver and Y-linked suppressor. The equilibrium frequency of the X-linked driver and Y-linked suppressor, combined with the fitness advantage of the autosomal suppressor over the Y-linked suppressor explained the pattern of whether an autosomal suppressor could invade the population [Figure S7]. The autosomal suppressor couldn't invade the population when (i) the frequency of driver was very low, and (ii) the Y-linked suppressor was at a high frequency.

Next, we looked at the relative reduction in the equilibrium frequencies of the Y-linked suppressor and driving X (defined as ΔX_m^{SR} and ΔY_m^{SUP} respectively) upon invasion of the autosomal suppressor.

$$\Delta X_m^{SR} = \frac{eqbm\,\mathbf{X}^{SR}_{males_before\,A^{SUP}invasion} - eqbm\,\mathbf{X}^{SR}_{males_after\,A^{SUP}invasion}}{eqbm\,\mathbf{X}^{SR}_{males_before\,A^{SUP}invasion}} \quad [9]$$

$$\Delta Y_m^{SUP} = \frac{eqbm\,\mathbf{Y}^{SUP}_{males_before\,A^{SUP}invasion} - eqbm\,\mathbf{Y}^{SUP}_{males_after\,A^{SUP}invasion}}{eqbm\,\mathbf{Y}^{SUP}_{males_before\,A^{SUP}invasion}} \quad [10]$$

Unlike our previous case where we looked at the relative reduction in the equilibrium frequencies upon invasion of a Y-linked suppressor, when an autosomal suppressor invaded the population, it did not eliminate the Y-linked suppressor completely from the population, but only caused a small decline in its equilibrium frequency that restored the sex-ratio back to 50-50. The patterns for the relative reduction in the equilibrium frequencies of the driving X showed a

significant decline only when the autosomal suppressor had a zero cost and Y-linked suppression was quite costly. For all other cases, the decline in driving X was small such that the sex-ratio restored to 50-50 [Figure S8]. There were some cases where the driving X increased in frequency upon the invasion of the autosomal suppressor because it was at a low frequency in equilibrium with the Y-linked suppressor initially, but due to the skewed sex-ratio in the population, the autosomal suppressor could invade even in the presence of Y-linked suppressor and this led to a reduction in the frequency of Y-linked suppressor in the population. This, in turn, allowed a small increase in the driving X frequency until the point where the sex-ratio was balanced. These results make a strong case in favor of the argument how autosomal suppressors evolve only due to selection towards a 50-50 sex-ratio while a Y-linked suppressor persists to eliminate the driver from the population.

Scenario C: Autosomal suppressors can invade populations undergoing stable cycles for X-linked driver and Y-linked suppressor and this impedes the cycling

In simulations where we aimed to test the invasion of an autosomal suppressor in populations at equilibrium for X-linked driver and Y-linked suppressor, we had a small subset of parameter space where the driving X and Y-linked suppressor cycles in the absence of an autosomal suppressor as predicted by Hall, 2004. We explored this subset of parameters on a case-by-case basis, and looked at how the introduction of an autosomal suppressor affected the cycling dynamics in these scenarios. The autosomal suppressor always invaded these cycling populations, though it gets lost in certain cases after invasion if it is at a fitness disadvantage over the Y-linked suppressor. We observed some interesting patterns of alternative cycling of the autosomal and Y-linked suppressor with the driver in populations when the fitness of autosomal

and Y-linked suppressor was comparable [e.g.: Figure S9-C, D, E]. Often these cycles were extreme and resulted in long spans of time when the driver or Y-linked suppressor were at very low frequency. In these cases, the autosomal suppressor was not really tested against the presence of the Y-linked suppressor until the Y-linked suppressor's frequency began to increase.

When the Y-linked suppressor had a fitness advantage over the autosomal suppressor, the autosomal suppressor was eventually lost from the population even after the invasion, and the cycling of driving X and Y-linked suppressor was impeded only for a short timespan [e.g.: Figure S9-A, B]. But for cases where Y-linked suppression was costly and an autosomal suppressor had zero cost, the autosomal suppressor eliminated the Y-linked suppressor from the population, thus obstructing the cycling [e.g.: Figure S9-F]. In all these cases when an autosomal suppressor invaded a cycling population, the invasion impeded

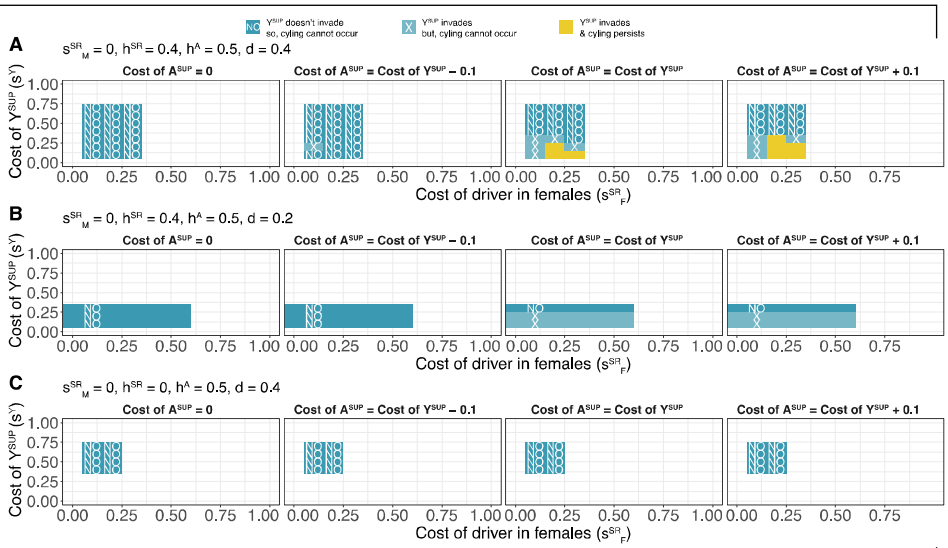

Figure 4: Can cycling persist in presence of an autosomal suppressor? Examples of regions of parameter spaces of stable cycling from Hall 2004, where we tested whether a Y-linked suppressor could invade populations at equilibrium for an autosomal suppressor and the driving X. The blue boxes labelled 'NO' represents the cases where a Y-linked suppressor couldn't invade the population and thus, cycling couldn't occur. The light blue boxes labelled 'X' represents the cases where a Y-linked suppressor invades the population, but cycling still couldn't occur due to the presence of an autosomal suppressor. The yellow boxes represent the cases where the cycling could persist in the presence of an autosomal suppressor.

cycling of Y-linked suppressor and the driving X for certain timespans depending upon the fitness of both suppressors [Figure S9]. These results suggest that the introduction of a low-cost autosomal suppressor may inhibit sex chromosome cycling due to meiotic drive.

Scenario D: Autosomal suppressors prevent the stable cycling of Y-linked suppressors and driving X

We examined specific examples presented in Hall 2004 as cases where stable cycling of a driving X and a Y-linked suppressor was expected. These regions of stable cycling were restricted to a small subset of the parameter space. First, we tested whether a Y-linked suppressor could invade populations at equilibrium for an autosomal suppressor and the driving X in this subset of parameter space where otherwise a driving X and a Y-linked suppressor would be under stable cycling. Next, we examined whether cycling persisted upon invasion of the Y-linked suppressor in these populations which were initially at equilibrium for an autosomal suppressor. For most of the parameter space, the Y-linked suppressor could not invade the population and hence, cycling did not occur. There were some cases where the Y-linked suppressor could invade the population but cycling still didn't occur in the presence of the autosomal suppressor. The parameter space where the cycling could occur shrank to a very small region in the presence of an autosomal suppressor [Figure 4]. Therefore, the presence of autosomal suppressors winnowed Hall's predicted parameter space for stable cycling considerably.

Discussion:

Our study highlights that autosomal suppressors can interfere with stable cycling in populations harboring X-linked meiotic drivers and Y-linked suppressors. Stable cycling can theoretically persist in populations harboring X, X^{SR}, Y, Y^{SUP} in certain restricted parameter spaces (Carvalho & Vaz, 1999; Clark, 1987; Hall, 2004). But studies of natural populations have failed to capture this cycling of sex chromosomes in nature. Hall 2004 modeled how migration between populations might prevent this cycling. He also suggested that evolution at autosomal loci may prevent driving sex chromosomes from cycling but did not explore the possibility. Using a simulations-based approach, we explored how autosomal suppressors interfere with sex chromosome cycling and meiotic drive.

We first investigated the conditions for the invasion of a Y-linked suppressor in the presence of an autosomal suppressor, considering factors such as the fitness costs of Y-linked suppression (s^Y), X-linked driver in females (s_F^{SR}), and drive strength (d). The equilibrium frequency of the driving X and the autosomal suppressor also played a crucial role. Our analysis compared populations with and without an autosomal suppressor, revealing that a Y-linked suppressor could only invade when the cost of Y-linked suppression is minimal, consistent with Hall's 2004 conditions for stable cycling with low fitness costs of X^{SR} and Y^{SUP}. The autosomal suppressor acted as a barrier against the invasion of Y-linked suppressor. We derived a general inequality [Equation 6] to describe this condition. We further examined the relationship between the equilibrium frequency of the driving X in males and Y-linked suppressor invasion, finding no strong association. The invasion of a low-cost Y-linked suppressor led to a decline in the equilibrium frequency of the driving X and a significant decrease in the autosomal suppressor's frequency due to the Y-linked suppressor's relative fitness advantage. We also studied the

influence of autosomal suppressor dominance on equilibrium frequencies, finding that when the autosomal suppressor's costs are additive or dominant, the Y-linked suppressor's invasion led to a sharp decline in the autosomal suppressor's frequency, potentially eliminating it from the population.

Next, we examined the potential for invasion of an autosomal suppressor into a population at equilibrium with a driving X and a Y-linked suppressor. Our simulations revealed that an autosomal suppressor could invade when the sex ratio favored females. The success of this invasion hinged on the equilibrium frequencies of the X-linked driver and Y-linked suppressor, as well as the autosomal suppressor's fitness advantage over the Y-linked suppressor. Invasion didn't occur when: (i) the sex ratio was balanced, (ii) the driver had a low frequency, (iii) the Y-linked suppressor had a high frequency, or (iv) the Y-linked suppressor had a fitness advantage over the autosomal suppressor. The finding that autosomal suppressors could invade populations with skewed sex ratios even if Y suppressors were also segregating makes sense – as long as the population is female-biased and fitness costs of suppression don’t outweigh the benefit of being in the rarer sex, the classic Fisherian sex-ratio selection should apply and autosomal suppressors should invade.

Furthermore, in some parameter spaces, the X-linked driver and Y-linked suppressor exhibited cyclic equilibrium without an autosomal suppressor, aligning with Hall's (2004) predictions. We analyzed the impact of introducing an autosomal suppressor in these cases, usually finding invasion, although the autosomal suppressor occasionally failed to invade if it had lower fitness

than the Y-linked suppressor. We observed alternating cycling between the autosomal and Y-linked suppressor when their fitness was similar. However, if the Y-linked suppressor held a fitness advantage, it eventually displaced the autosomal suppressor, temporarily interrupting cycling. Remarkably, when Y-linked suppression was costly and the autosomal suppressor had no cost, the autosomal suppressor eliminated the Y-linked suppressor, disrupting cycling. Overall, our findings demonstrate that the invasion of an autosomal suppressor disrupts cycling in a population for varying durations depending on the suppressor fitness. Thus, even if the population eventually regains the sex chromosome cycling dynamics, these occasional perturbations may be enough to throw off cycling long enough to preclude any observation of stable cycling.

Finally, we focused on instances where stable cycling is predicted by Hall 2004. Such stable cycling phenomenon is limited to a specific subset of parameter space. We assessed the potential invasion of a Y-linked suppressor into populations initially at equilibrium with autosomal suppressors and a driving X chromosome within this subset. In most cases, the Y-linked suppressor failed to invade, preventing cycling. Even when invasion occurred, cycling did not resume in the presence of autosomal suppressors. Consequently, the parameter space where cycling could occur is greatly reduced in presence of autosomal suppressors. These findings suggest that the dynamics of stable cycling of the driving X and a Y-linked suppressor are highly sensitive to specific parameters, and the presence of autosomal suppressors may significantly constrain the occurrence of stable cycling. Additionally, we considered realistic scenarios of finite population sizes for populations under stable cycling and find that cycling disappeared in most cases with moderate (1,000,000) population sizes [Figure S10].

Stable cycling of driving X chromosomes and Y-linked suppressors is a rare phenomenon in surveys of natural populations. Using theoretical models, it occurs only within a narrow parameter range, which further shrinks in the presence of autosomal suppressors. Realistic scenarios, including finite population sizes, make the occurrence of stable cycling negligible, rendering it exceptionally rare in nature. Furthermore, capturing temporal variations in these frequencies in natural populations is challenging due to time lags between sampling and resampling populations, making it exceptionally rare to encounter the cycling of driving X chromosomes in nature. Stable sex chromosome cycling due to meiotic drive may therefore be an elegant theoretical result that requires too many constraints to ever exist in real populations.

Acknowledgements:

We thank members of the Unckless lab for helpful comments and suggestions on early drafts. We would like to thank Dr. Maria Orive for motivating AG and teaching a course on population genetics that equipped her with the necessary knowledge to pursue this research. This work was supported by the National Science Foundation Career Award #2047052 to RLU. Computational work was performed at the HPC facilities operated by the Center for Research Computing at the University of Kansas supported in part through the National Science Foundation MRI Award #2117449.

References:

Atlan, A., Merçot, H., Landre, C., & Montchamp□Moreau, C. (1997). The sex□ratio trait in Drosophila simulans: geographical distribution of distortion and resistance. *Evolution*, *51*(6), 1886–1895.

Babcock, C. S., & Anderson, W. W. (1996). Molecular evolution of the Sex-Ratio inversion complex in Drosophila pseudoobscura: analysis of the Esterase-5 gene region. *Molecular Biology and Evolution*, *13*(2), 297–308.

Beckenbach, A. T. (1978). The" sex-ratio" trait in Drosophila pseudoobscura: fertility relations of males and meiotic drive. *The American Naturalist*, *112*(983), 97–117.

Beckenbach, A. T. (1996). Selection and the “sex□ratio” polymorphism in natural populations of Drosophila pseudoobscura. *Evolution*, *50*(2), 787–794.

Beckenbach, A. T., Curtsinger, J. W., & Policansky, D. (1982). Fruitless experiments with fruit flies: the ‘sex ratio’chromosomes of D. pseudoobscura. *Drosophila Information Service*, *58*(22).

Bircher, U., Jungen, H., Burch, R., & Hauschteck□Jungen, E. (1995). Multiple morphs of sperm were required for the evolution of the sex ratio trait in Drosophila. *Journal of Evolutionary Biology*, *8*(5), 575–588.

Bull, J. J., & Charnov, E. (1988). *How fundamental are Fisherian sex ratios?*

Capillon, C., & Atlan, A. (1999). Evolution of driving X chromosomes and resistance factors in experimental populations of Drosophila simulans. *Evolution*, *53*(2), 506–517.

Carvalho, A. B., Sampaio, M. C., Varandas, F. R., & Klaczko, L. B. (1998). An experimental demonstration of Fisher's principle: evolution of sexual proportion by natural selection. *Genetics*, *148*(2), 719–731.

Carvalho, A. B., & Vaz, S. C. (1999). Are Drosophila SR drive chromosomes always balanced? *Heredity*, *83*(3), 221–228.

Carvalho, A. B., Vaz, S. C., & Klaczko, L. B. (1997). Polymorphism for Y-linked suppressors of sex-ratio in two natural populations of Drosophila mediopunctata. *Genetics*, *146*(3), 891–902.

Cazemajor, M., Joly, D., & Montchamp-Moreau, C. (2000). Sex-ratio meiotic drive in Drosophila simulans is related to equational nondisjunction of the Y chromosome. *Genetics*, *154*(1), 229–236.

Cazemajor, M., Landre, C., & Montchamp-Moreau, C. (1997). The sex-ratio trait in Drosophila simulans: genetic analysis of distortion and suppression. *Genetics*, *147*(2), 635–642.

Charnov, E. L., Los-den Hartogh, R. L., Jones, W. T., & Van den Assem, J. (1981). Sex ratio evolution in a variable environment. *Nature*, *289*(5793), 27–33.

Clark, A. G. (1987). Natural selection and Y-linked polymorphism. *Genetics*, *115*(3), 569–577.

Crow, J. F. (1991). Why is Mendelian segregation so exact? *BioEssays*, *13*(6), 305–312.

Curtsinger, J. W., & Feldman, M. W. (1980). Experimental and theoretical analysis of the" sex-ratio" polymorphism in Drosophila pseudoobscura. *Genetics*, *94*(2), 445–466.

de Carvalho, A. B., & Klaczko, L. B. (1993). Autosomal suppressors of sex-ratio in Drosophila mediopunctata. *Heredity*, *71*(5), 546–551.

de Carvalho, A. B., Peixoto, A. A., & Klaczko, L. B. (1989). Sex-ratio in Drosophila mediopunctata. *Heredity*, *62*(3), 425–428.

Dermitzakis, E. T., Masly, J. P., Waldrip, H. M., & Clark, A. G. (2000). Non-Mendelian segregation of sex chromosomes in heterospecific Drosophila males. *Genetics*, *154*(2), 687–694.

Dyer, K. A., Charlesworth, B., & Jaenike, J. (2007). Chromosome-wide linkage disequilibrium as a consequence of meiotic drive. *Proceedings of the National Academy of Sciences*, *104*(5), 1587–1592.

Dyer, K. A., & Hall, D. W. (2019). Fitness consequences of a non-recombining sex-ratio drive chromosome can explain its prevalence in the wild. *Proceedings of the Royal Society B*, *286*(1917), 20192529.

Edwards, A. W. F. (1961). The population genetics of “sex-ratio” in Drosophila pseudoobscura. *Heredity*, *16*(3), 291–304.

Faulhaber, S. H. (1967). An abnormal sex ratio in Drosophila simulans. *Genetics*, *56*(1), 189.

Fisher, R. A. (1930). *The genetical theory of natural selection. Clarendon*. Oxford.

Fuller, Z. L., Koury, S. A., Leonard, C. J., Young, R. E., Ikegami, K., Westlake, J., Richards, S., Schaeffer, S. W., & Phadnis, N. (2020). Extensive recombination suppression and epistatic selection causes chromosome-wide differentiation of a selfish sex chromosome in Drosophila pseudoobscura. *Genetics*, *216*(1), 205–226.

Gershenson, S. (1928). A new sex-ratio abnormality in Drosophila obscura. *Genetics*, *13*(6), 488.

Hall, D. W. (2004). Meiotic drive and sex chromosome cycling. *Evolution*, *58*(5), 925–931.

Hamilton, W. D. (1967). Extraordinary Sex Ratios: A sex-ratio theory for sex linkage and inbreeding has new implications in cytogenetics and entomology. *Science*, *156*(3774), 477–488.

Hauschteck-Jungen, E. (1990). Postmating reproductive isolation and modification of the ‘sex ratio’trait in Drosophila subobscura induced by the sex chromosome gene arrangement A 2+ 3+ 5+ 7. *Genetica*, *83*, 31–44.

Hauschteck-Jungen, E., & Maurer, B. (1976). Sperm dysfunction in sex ratio males of Drosophila subobscura. *Genetica*, *46*(4), 459–477.

Jaenike, J. (1996a). Sex-ratio meiotic drive in the Drosophila quinaria group. *The American Naturalist*, *148*(2), 237–254.

Jaenike, J. (1996b). Sex-ratio meiotic drive in the Drosophila quinaria group. *The American Naturalist*, *148*(2), 237–254.

Jaenike, J. (1999). Suppression of sex□ratio meiotic drive and the maintenance of Y□chromosome polymorphism in Drosophila. *Evolution*, *53*(1), 164–174.

Jaenike, J. (2001). Sex chromosome meiotic drive. *Annual Review of Ecology and Systematics*, *32*(1), 25–49.

James, A. C., & Jaenike, J. (1990). “ Sex ratio” meiotic drive in Drosophila testacea. *Genetics*, *126*(3), 651–656.

Kassambara, A., & Kassambara, M. A. (2020). Package ‘ggpubr.’ *R Package Version 0.1*, *6*(0).

Lindholm, A. K., Dyer, K. A., Firman, R. C., Fishman, L., Forstmeier, W., Holman, L., Johannesson, H., Knief, U., Kokko, H., & Larracuente, A. M. (2016). The ecology and evolutionary dynamics of meiotic drive. *Trends in Ecology & Evolution*, *31*(4), 315–326.

Mackintosh, C., Pomiankowski, A., & Scott, M. F. (2021). X-linked meiotic drive can boost population size and persistence. *Genetics*, *217*(1), iyaa018.

Mercot, H., Atlan, A., Jacques, M., & Montchamp□Moreau, C. (1995). Sex□ratio distortion in Drosophila simulans: co□occurence of a meiotic drive and a suppressor of drive. *Journal of Evolutionary Biology*, *8*(3), 283–300.

Montchamp□Moreau, C., Ginhoux, V., & Atlan, A. (2001). The Y chromosomes of Drosophila simulans are highly polymorphic for their ability to suppress sex□ratio drive. *Evolution*, *55*(4), 728–737.

Policansky, D. (1974). “ Sex Ratio,” Meiotic Drive, and Group Selection in Drosophila pseudoobscura. *The American Naturalist*, *108*(959), 75–90.

Policansky, D. (1979). Fertility differences as a factor in the maintenance of the" sex ratio" polymorphism in Drosophila pseudoobscura. *The American Naturalist*, *114*(5), 672–680.

Policansky, D., & Ellison, J. (1970). “ Sex Ratio” in Drosophila pseudoobscura: Spermiogenic Failure. *Science*, *169*(3948), 888–889.

Prakash, S., & Merritt, R. B. (1972). Direct evidence of genic differentiation between sex ratio and standard gene arrangements of X chromosome in Drosophila pseudoobscura. *Genetics*, *72*(1), 169–175.

Presgraves, D. C., Severance, E., & Wilkinson, G. S. (1997). Sex chromosome meiotic drive in stalk-eyed flies. *Genetics*, *147*(3), 1169–1180.

R Core Team, R. (2013). *R: A language and environment for statistical computing*.

Ram, K., & Wickham, H. (2018). wesanderson: a Wes Anderson palette generator. *R Package Version 0.3*, *6*, 2018.

Stalker, H. D. (1961). The genetic systems modifying meiotic drive in Drosophila paramelanica. *Genetics*, *46*(2), 177.

Tao, Y., Araripe, L., Kingan, S. B., Ke, Y., Xiao, H., & Hartl, D. L. (2007). A sex-ratio meiotic drive system in Drosophila simulans. II: an X-linked distorter. *PLoS Biology*, *5*(11), e293.

Tao, Y., Masly, J. P., Araripe, L., Ke, Y., & Hartl, D. L. (2007). A sex-ratio meiotic drive system in Drosophila simulans. I: an autosomal suppressor. *PLoS Biology*, *5*(11), e292.

Taylor, D. R. (1994a). Sex ratio in hybrids between Silene alba and Silene dioica: evidence for Y-linked restorers. *Heredity*, *73*(5), 518–526.

Taylor, D. R. (1994b). The genetic basis of sex ratio in Silene alba (= S. latifolia). *Genetics*, *136*(2), 641–651.

Taylor, D. R. (1996). Parental expenditure and offspring sex ratios in the dioecious plant Silene alba (= Silene latifolia). *The American Naturalist*, *147*(5), 870–879.

Taylor, D. R. (1999). Genetics of sex ratio variation among natural populations of a dioecious plant. *Evolution*, *53*(1), 55–62.

Taylor, D. R., Saur, M. J., & Adams, E. (1999). Pollen performance and sex□ratio evolution in a dioecious plant. *Evolution*, *53*(4), 1028–1036.

Unckless, R. L., & Clark, A. G. (2014). Sex□ratio meiotic drive and interspecific competition. *Journal of Evolutionary Biology*, *27*(8), 1513–1521.

Varandas, F. R., Sampaio, M. C., & Carvalho, A. B. (1997). Heritability of sexual proportion in experimental sex-ratio populations of Drosophila mediopunctata. *Heredity*, *79*(1), 104–112.

Vaz, S. C., & Carvalho, A. B. (2004). Evolution of autosomal suppression of the sex-ratio trait in Drosophila. *Genetics*, *166*(1), 265–277.

Voelker, R. A. (1972). Preliminary characterization of" sex ratio" and rediscovery and reinterpretation of" male sex ratio" in Drosophila affinis. *Genetics*, *71*(4), 597–606.

Wallace, B. (1948). Studies on'sex-ratio'in Drosophila pseudoobscura. I. Selection and'sex-ratio'. *Evolution*, 189–217.

Wickham, H. (2011). ggplot2. *Wiley Interdisciplinary Reviews: Computational Statistics*, *3*(2), 180–185.

Wilkinson, G. S., Kahler, H., & Baker, R. H. (1998). Evolution of female mating preferences in stalk-eyed flies. *Behavioral Ecology*, *9*(5), 525–533.

Wilkinson, G. S., Presgraves, D. C., & Crymes, L. (1998). Male eye span in stalk-eyed flies indicates genetic quality by meiotic drive suppression. *Nature*, *391*(6664), 276–279.

Wilkinson, G. S., & Sanchez, M. I. (2001). Sperm development, age and sex chromosome meiotic drive in the stalk-eyed fly, Cyrtodiopsis whitei. *Heredity*, *87*(1), 17–24.

Wu, C.-I. (1983). The fate of autosomal modifiers of the sex-ratio trait in Drosophila and other sex-linked meiotic drive systems. *Theoretical Population Biology*, *24*(2), 107–120.

Wu, C.-I., & Beckenbach, A. T. (1983). Evidence for extensive genetic differentiation between the sex-ratio and the standard arrangement of Drosophila pseudoobscura and D. persimilis and identification of hybrid sterility factors. *Genetics*, *105*(1), 71–86.