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DEPARTMENT OF BIOLOGY

MEIOTIC DRIVE VIA SEX RATIO CHROMOSOME IN *DROSOPHILA PSEUDOOBSCURA*

JONATHAN GEORGE WESTLAKE
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Reviewed and approved* by the following:

Stephen Schaeffer
Professor of Biology and Associate Department Head of Graduate Education
Thesis Supervisor

James Marden
Professor of Biology and Associate Director, Huck Institutes of the Life Sciences
Honors Adviser

* Signatures are on file in the Schreyer Honors College.

ABSTRACT

Under normal circumstances in an XY sex determination system, an XY male mated to a female should produce 50% male and 50% female offspring. Selfish genetic elements can defy Mendel's law of segregation through a biased transmission of the X chromosome over the Y leading to a biased sex ratio. *Drosophila pseudoobscura* has such a selfish genetic element on its X chromosome referred to as the Sex ratio chromosome. Males with a Sex Ratio X chromosome produce 95% daughters rather than the expected 50%. Cytogenetic analysis of the Sex ratio chromosome found three nonoverlapping inversion differences between the Standard and Sex Ratio X chromosomes, basal, medial, and terminal inversions. Inversion mutations occur when a chromosome breaks in two locations and the intervening segment rejoins in reverse order. The genetic consequence of the inversion is to suppress genetic exchange between maternal and paternal chromosomes during the formation of eggs and sperm. For nonoverlapping inversions, it may be possible for genetic exchange to shuffle the three different inversions during gamete formation. Here, we test whether genetic exchange shuffles the three nonoverlapping inversions in a three-point mapping cross. We used a genetic cross of an ST/SR female crossed to an ST/Y male. Male offspring from this cross were crossed to a female strain homozygous for a multiply marked Standard X chromosome and tested for which of the three inverted segments that they carried and the sex ratio of their offspring. We found no evidence for genetic exchange among any of the nonoverlapping inversions despite a significant genetic distance between the medial and terminal inversion. Sex ratio males confirmed the strong biased transmission of the X chromosome versus the Y chromosome. We conclude that the three nonoverlapping inversions suppress genetic exchange even in regions where genetic exchange could occur.

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Chapter 1

Introduction

Segregation Distorters and Sex-Ratio biology. The principles of inheritance outlined by Gregor Mendel in the mid-1800s culminated in three laws that were widely controversial, but now are accepted as scientific law related to segregation, independent assortment, and dominance. The First Law, the Law of Segregation in diploid organisms, states that during gamete formation, the two alleles at a locus segregate from each other so that each gamete carries only one of the two alleles, or that alleles are transmitted at a 50:50 ratio (Lyttle 1991).

The 1:1 sexual proportion expected in nature can be attributed to the biological phenomenon Ronald Fisher explained in 1930, coined Fisher's Principle (Hamilton 1967). W.D. Hamilton then expanded on Fisher's Principle with a general model to explain sex-ratios that are expected in nature. He explained that if male births are less frequent than female, then newborn males have more mating prospects and can expect to have more offspring. Subsequently, the parents that have genetic dispositions to produce more males in turn have more grandchildren. The genes for producing males spread and male births are more common in the population, bringing the proportion of sexes closer to 1:1 (Hamilton 1967). The natural selection mechanism that stabilizes the proportion supports an equilibrium ratio that is observed in nearly every sexually reproducing population.

In principle, parent alleles should have an equal probability of being present in a mature gamete, but there is a mechanism where unequal transmission occurs known as a segregation distortion. Segregation distortion occurs when one of two alleles at a locus is transmitted more often than the other (Lyttle 1991). These distorters are often associated with regions in the genome with lower levels of recombination either in regions near centromeres or within chromosomal inversions (Lindsley *et al.* 1977). When a segregation distorter is associated with sex chromosomes, which this paper will investigate, they are known as Sex-Ratio distorters, which lead to skewed sex-ratios in offspring.

In natural populations of *Mus domesticus* and *Mus musculus* mice, a form of chromosome 17 has been identified as causing segregation distortion. The variant consists of several inversions and spans 20-40 megabases of DNA, approximately 1.2% of the mouse genome (Lyttle 1991). This distortion has been denoted as a t-haplotype and involves multiple transmission elements, showing evolutionary success despite male sterility.

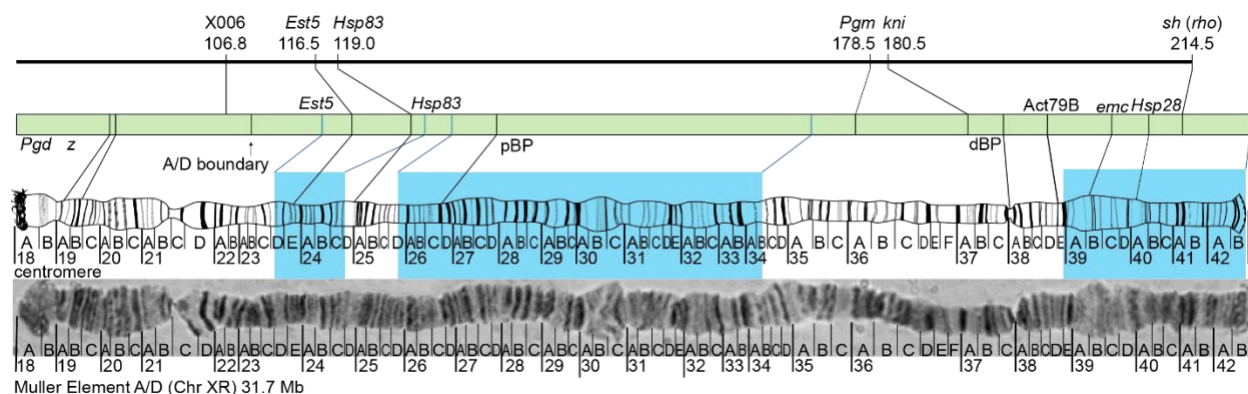


Figure 1: Genetic, physical, and cytological map of the right arm of the X chromosome (XR) in *Drosophila pseudoobscura*. The top line shows the genetic map for markers on this chromosome. The green bar indicates the physical map of XR showing the locations of genes and features mapped to the cytological map. The blue lines and boxes indicate the locations of the three nonoverlapping inversions on XR that discriminate between the Standard and Sex Ratio chromosomes (from left to right, basal, medial, and terminal inversions). The bottom image is the cytogenetic map of XR. This figure was adapted from Schaeffer *et al.* (2008) updating map positions based on PACBio long read data.

Similar to the t-haplotype in mice, *Drosophila pseudoobscura* has a segregation distortion system on the X chromosome. The sex-ratio polymorphism mechanism found in *Drosophila pseudoobscura* is a naturally occurring meiotic-drive system where males sire 95% female offspring. This mechanism is driven by the degeneration of half of the spermatids during spermatogenesis (Novitski *et al.* 1965), which results in almost completely eliminating any Y-bearing spermatid. The Sex Ratio chromosome is associated with three nonoverlapping inversions on the X chromosome, from the centromere to the telomere, basal, medial, and terminal positions (Beckenbach 1991) (Figure 2).

Both the t-haplotype and the SR system are evolutionary successes as they appear to be ubiquitous in their species (Lyttle 1991). While the difference in autosomal and sexual systems is apparent, there still is a common feature of these two systems which is dysfunctional sperm carrying the target of the distorter allele.

Sexual Conflict and Genetic Variation. All living organisms have some form of selfish genetics that can cause a reduction in fertility and sperm competition in males (Dawkins 1976). For *Drosophila pseudoobscura*, the presence of sex-ratio was found to create sexual conflict regarding female remating rates between noncarrier males and females (Price *et al.* 2010). Despite usually being extremely rare in populations, the sex-ratio polymorphism has tangible meiotic drive and promotes coevolution of males' ability to suppress female remating (Wallace 1948). This study investigates the recombinant patterns of these inversions.



Figure 2: *Drosophila pseudoobscura* chromosome showing three nonoverlapping inversions indicating presence of sex-ratio

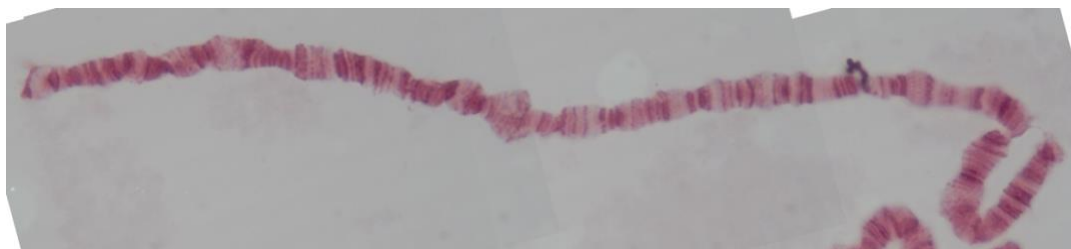


Figure 3: *Drosophila pseudoobscura* chromosome showing no chromosomal inversions or effect of segregation distorter

Population Genetics. The geographic distribution of the sex-ratio gene in *Drosophila pseudoobscura* spans the Southwestern United States (Sturtevant *et al.* 1936). The highest frequency of sex-ratio is near the Mexican border at almost 30% and it is known that the frequency decreases with an increase of altitude and latitude.

Beckenbach (1996) observed several unusual sex-ratio arrangements and recombination patterns. In one population, he saw chromosomes that only had a terminal inversion. He noted that this

arrangement is phenotypically wild-type, meaning that males sired equal number of males and females. He also saw an arrangement that had only the basal and medial inversions, but this arrangement resulted in Sex Ratio phenotype (Wallace 1948). These aberrant SR karyotypes are rare in populations raising the question about how the three nonoverlapping inversions remain linked together despite sufficient distance between the medial and terminal inversion for crossing over to dissociate them. *D. subobscura* and *D. robusta* also have nonoverlapping inversions that are in linkage disequilibrium with each other (Carson 1958; Krimbas 1992; Levitan 1958; Levitan 1992).

It is an open question how the associations of these nonoverlapping inversions are maintained especially when the distances among the inverted segments is sufficient to allow recombinants to occur. Here, we perform a genetic mapping experiment with the Sex Ratio system to determine if one can generate recombinants among the three nonoverlapping inversions. We will test the resulting chromosomes from the mapping experiment for their sex ratios. We are especially interested in the sex ratios of recombinant karyotypes to see if we can attribute which of the basal, medial, and terminal inversions are critical to the Sex Ratio phenotype.

Chapter 2

Methods

***Drosophila* Strain.** A *Drosophila pseudoobscura* isofemale line AO4 was collected from a dumpster behind the Allred Orchard fruit market in Provo, Utah (2109 N University) (Latitude 40° 15' 43" N Longitude 111° 39' 32" W) on September 23, 2017. On January 22nd, 2018, the

AO4 was found to produce all female offspring suggesting that these females had been sired by an SR male and were heterozygous for the SR chromosome. These heterozygous ST/SR females provided an opportunity to test whether recombination occurred between the three non-overlapping inversions.

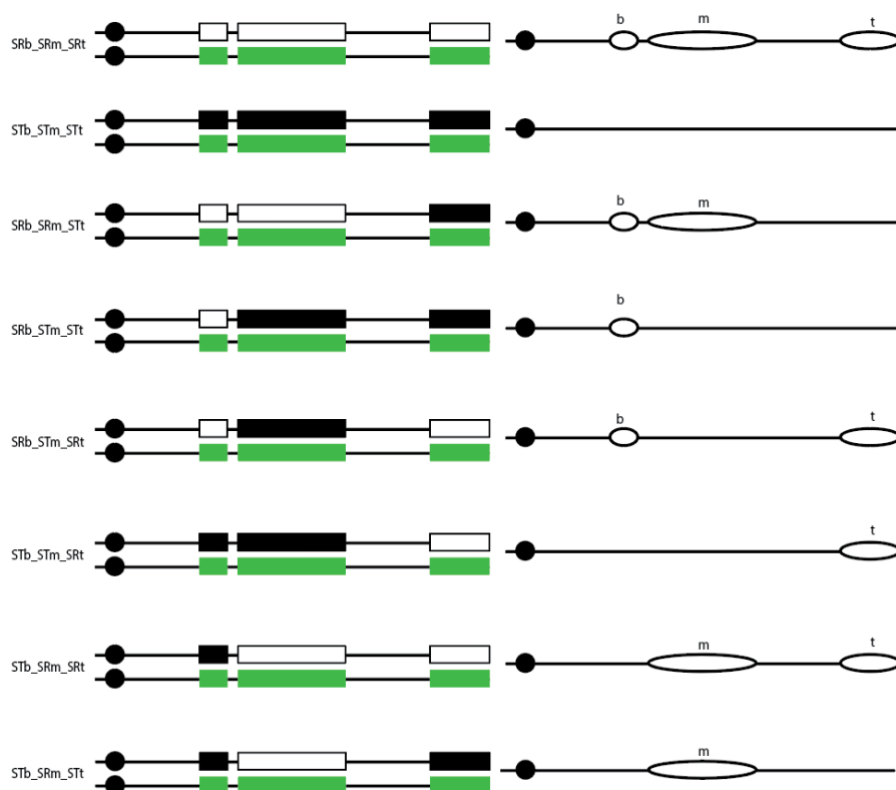


Figure 4: Possible outcomes of recombination between the cross of standard marked and SR genotypes. The green chromosome was donated by the ST (ct sd y se) female parent and the possible male parental X chromosome configurations. Open box indicates the SR arrangement and the close box indicates the ST arrangement.

Genetic Crosses. The females that were isolated from this strain were crossed to males that carried a multiply marked ST X chromosome (cut scalloped yellow sepia; abbreviated as ct sd y se) on January 29th 2018. F1 males from this cross were crossed to ST (ct sd y se)/ST (ct sd y se)

females. These F1 males carried parental or recombinant X chromosomes, which could be directly traced in the subsequent generations and visualized. The female larva resulting from the F1 male cross and the ST/ST female cross would have a ST chromosome from the female and theoretically any of the possibilities of recombinant chromosomes from the male. The possible recombinants that could result from the heterozygous females are shown in Figure 4.

Recombination Estimates. ST/SR females from the A04 *D. Pseudoobscura* line were crossed to ST standard males and one-hundred of the resulting male offspring, whose genotypes were unknown, were collected and crossed to ST marked females and labeled in vials G1 M1 – G1 M100 (Figure 5). Four of the vials were lost due to contamination and mold, while the remainder were able to be used in the rest of the experiment and analysis.

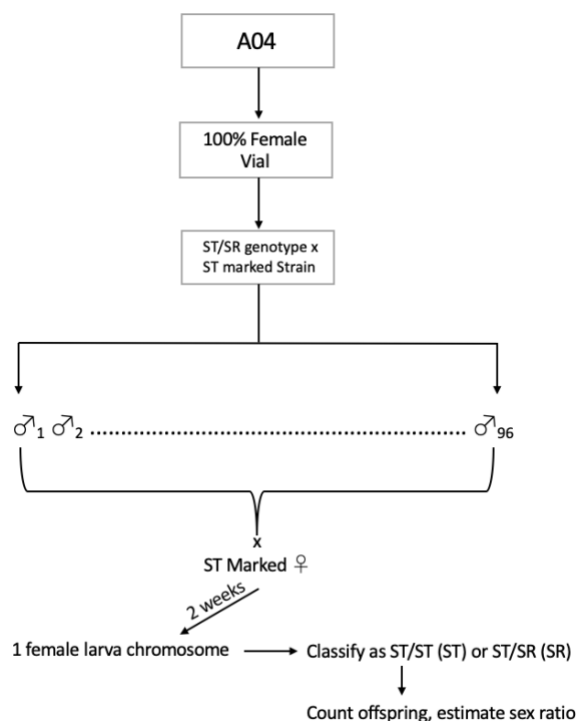


Figure 5: Experimental design for recombination estimates

After a two-week incubation period, one female larva from each cross was collected from each vial to prepare polytene chromosomes with a salivary squash (Painter 1934). Female larvae were distinguished from male larvae based on the absence of the male gonad (Figure 6).

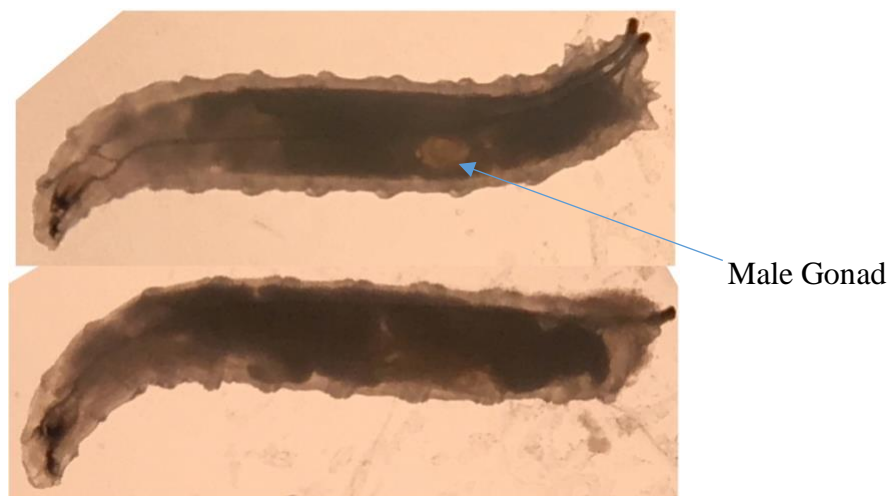


Figure 6: *Drosophila pseudoobscura* larvae showing the presence and absence of the male gonad male (top image) and female (bottom image).

Once female larvae were distinguished from male, the salivary glands of each larva were extracted by slowly pulling the anterior end of the larva behind the food hooks away from the body with a needle and forceps. This allows the two salivary glands to be dissected away from the carcass. The glands were transferred to a clean microscope slide and stained with lacto-orcein-acetic acid. A cover slip was placed on the stained glands and subsequently squashed between absorbance paper with a roller dowel to disrupt the nuclei and spread the polytene chromosomes. After slides were prepared and dried, they were analyzed and imaged under a microscope to cytogenetically determine the chromosome type based on the recombination possibilities of the basal, medial, and terminal inversions (Figure 4).

The three nonoverlapping inversions were scored in the salivary squashes (Figure 4). ST/ST combinations were recorded as a ST marking while ST/SR were labeled with SR designation. Following cytogenetic analysis, the resulting adult offspring were counted over a two-week period from the initial emergence of the F2 generation and the numbers of males and females was counted for each vial. All experimental data was entered into an Excel spreadsheet and percent female was estimated for all viable crosses. Data were then visualized using Tableau and Excel to show the frequency of different arrangements in F1 males. Median frequency of females, average frequency of females, and the ranges of frequency of female for each tested F1 male were estimated. A binomial test was run to ascertain whether the percent female differed from the expected Mendelian ratio was significantly different from 50:50.

Chapter 3

Results: Recombination

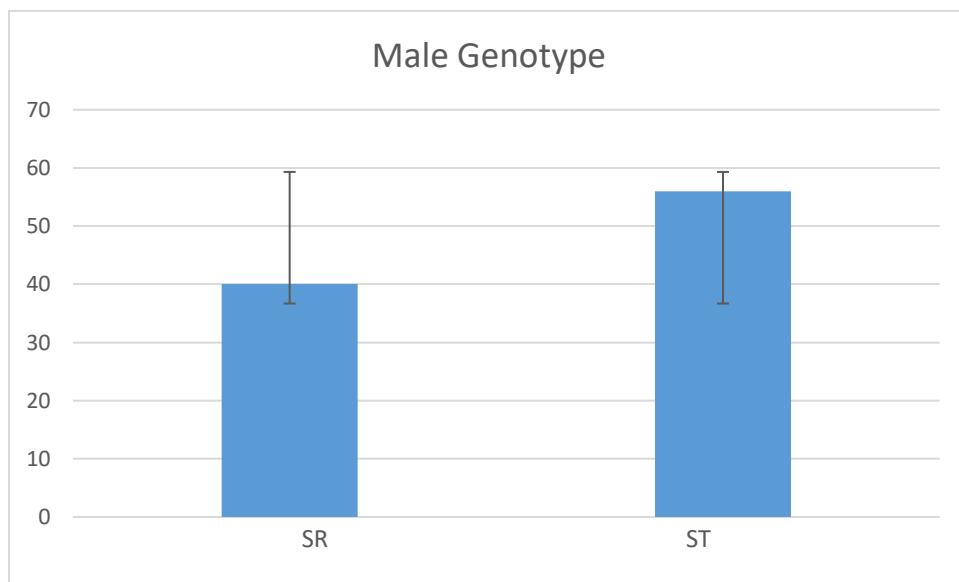


Figure 7: Incidence of recombination types for the first experiment.

Experimental Observations. In the recombination experiment, I only observed the two parental chromosomal arrangements: STb_STm_STt/STb_STm_STt or STb_STm_STt/SRb_SRm_SRt derived from the tested F1 male offspring. There was no evidence of crossing over among the basal, medial, and terminal inversions in the original heterozygous female parent. There was no detected crossing over between the medial and terminal inversion despite there being sufficient nucleotide distance between these two inversions.

Transmission of SR. The cytogenetic analysis of this experiment found that 40 of the 96 (42%) tested males obtained the SRb_SRm_SRt arrangement from their mothers while 56 of the 96 (58%) tested males carried the STb_STm_STt arrangement (Figure 7). The one-tailed probability that exactly, or fewer than 40 out of the 96 had the SRb_SRm_SRt arrangement is $p = 0.063$ with a Z-score of -1.53. The near 50:50 transmission of the SRb_SRm_SRt and STb_STm_STt in the original AO4 heterozygous female demonstrates no transmission bias. I will refer to SRb_SRm_SRt and STb_STm_STt as SR and ST, respectively, from here on. The error bars represent one standard deviation and show that the difference between the two genotypes is not statistically significant from 50% in this population.

Sex ratios of F1 male offspring. After scoring the male and female offspring of each cytogenetically analyzed male genotype, clear differences emerged in the median percent female offspring. The median percent female for SR males was 98.15%, whereas the median percent female for the ST males was 55.32%. The error bars represent a 95% confidence interval and illustrate that even within the confidence interval, the two medians are drastically different.

While the percent female offspring in ST males was slightly skewed past the expected 50:50 ratio, SR males clearly and overwhelmingly produced female offspring.

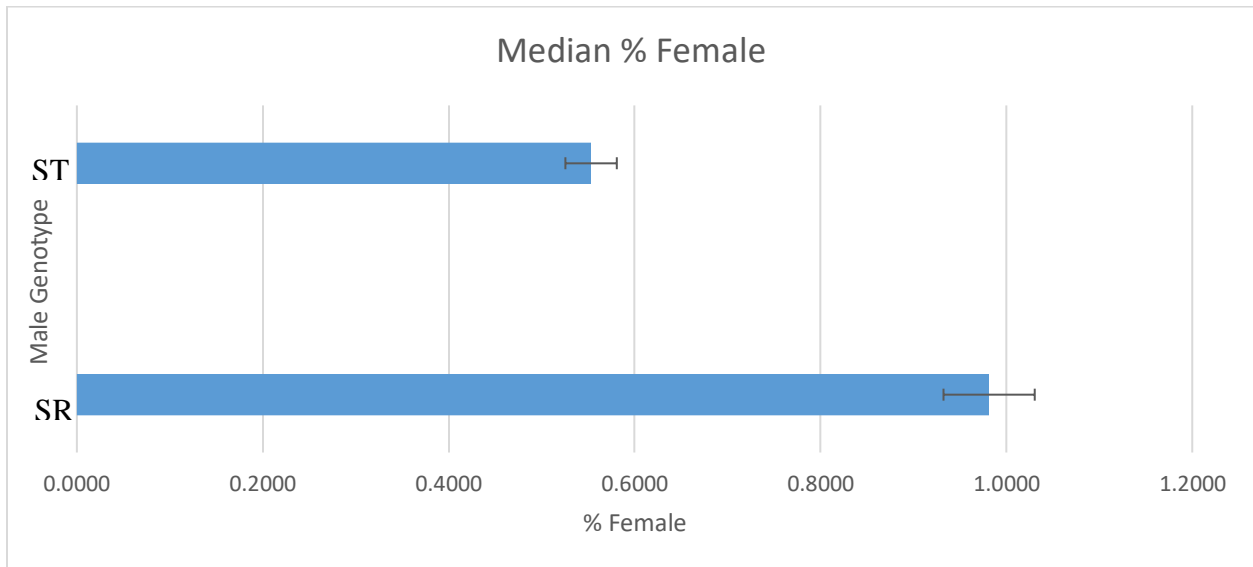


Figure 8: Median percent female for each observed genotype.

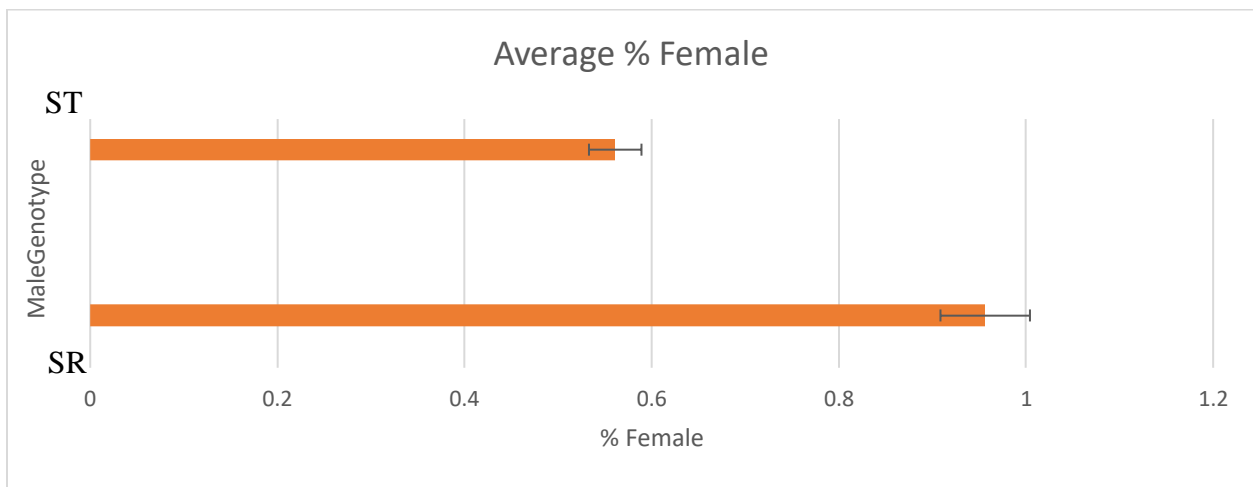


Figure 9: Average percent female offspring for each observed genotype.

Similar to the median percent female statistic, the average percent female for SR males is extremely skewed toward female offspring, with an average percent of 95.64%. The average percent female for ST males was 56.11%, again slightly above expected values. Similar to

median percent female, the average percent female also has error bars showing 95% confidence interval and that SR males produce significantly more females than ST males.

For each male genotype, there were ranges of percent females. The ST genotype had a broad range from 47.1% female all the way to 84.1% female. The SR genotype, however, had a more concentrated range between 80.0% and 100%. This range and the density around 100% female illustrates how prominently females are favored in this genotype.

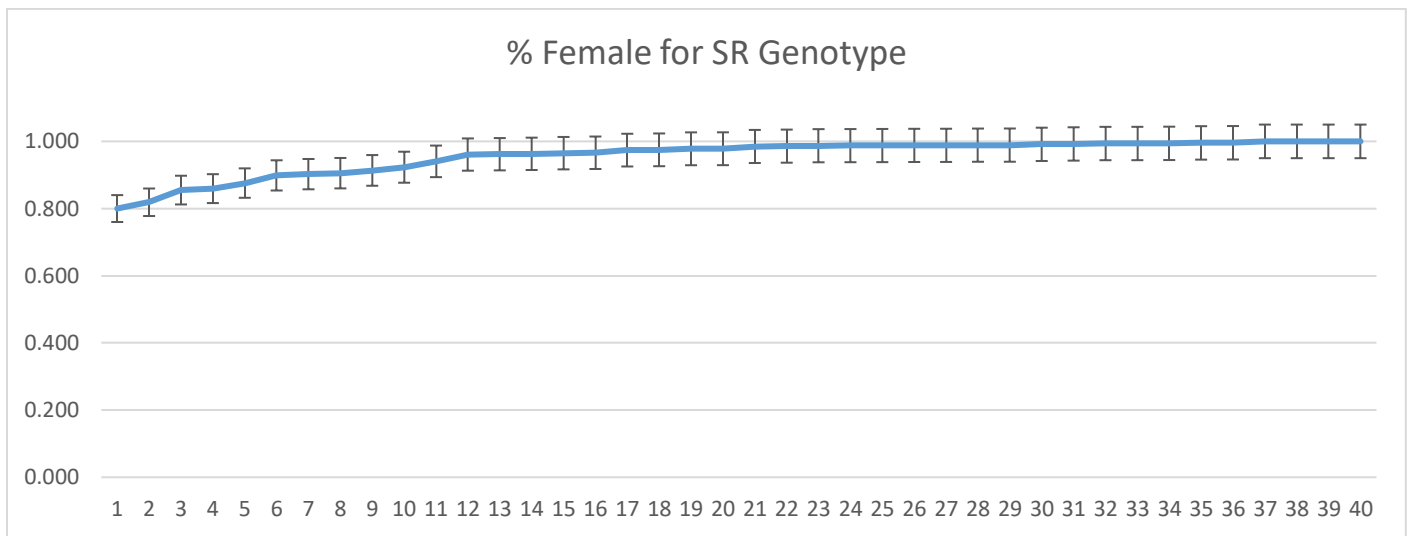


Figure 10: Range of percent female offspring for all observed SR strains.

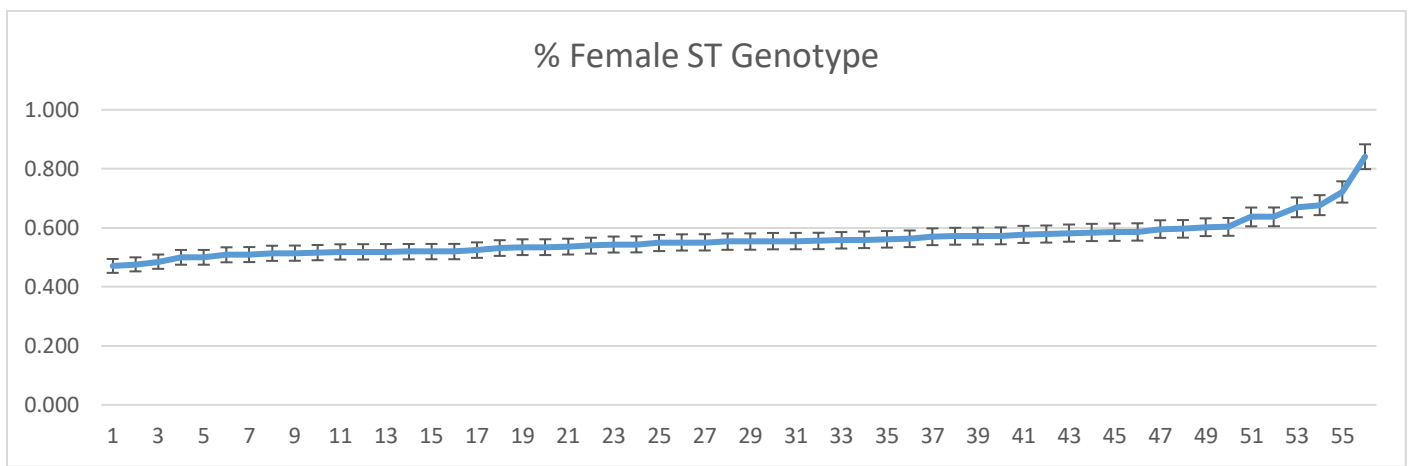


Figure 11: Range of percent female offspring for all observed ST strains.

Chapter 4

Discussion

Previous studies detail the cytological SR karyotype and its effects on offspring sex ratios in *Drosophila pseudoobscura* (Beckenbach 1996). Beckenbach (1996) found two aberrant karyotypes on the right arm of the X chromosome, one that carried only the SR terminal inversion found in two strains and one that carried both the basal and medial SR inversions. The strains with the terminal inversion only produced sex ratios similar to the ST males, while the basal and medial inversions only produced sex ratios similar to SR males. This study tested whether recombination occurred between the non-overlapping inversions SR and ST arrangements. The crosses were set up to not only to observe whether there was recombination in intervals that such overlapping is expected based on distance, but also what haplotypes (Figure 4) were experimentally observed or suppressed. It is still unclear as to why the sex-ratio polymorphism is not selected against over the course of generations as it would theoretically lead to the extinction of a strain (Price *et al.* 2012).

Is there any recombination among the three non-overlapping inversions in SR and ST females? The experiment yielded only the two parental genotypes: the SR and ST arrangements. There was no recombination among the three non-overlapping inversions on the chromosome, as either all three inversions occurred together or none of the three were found. Ortiz-Barrientos *et al.* (2006) mapped several microsatellite loci to the third chromosome. The genetic distance

between the DPSX023 and DPSX037N loci is 137.3 cM and the physical distance between these loci is 25.08 Mb (Schaeffer, unpublished data from PACBIO sequencing). This is equivalent to a genetic to physical distance of 5.48 cM/Mb. The physical distance between the medial and terminal inversions is 7 Mb or 38.3 cM. Thus, I would expect 38% of F1 male offspring to have recombination in the seven megabase distance between the medial and terminal inversions. In this experiment of 96 males, zero had recombination in this region. The presence of the three nonoverlapping inversions appears to suppress recombination even in the regions where crossing over can theoretically occur.

When considering SR recombinants in nature, Sturtevant (1936) described the incidence of SR presence geographically in *D. pseudoobscura*. There is a clear geographic distribution of this distorter and the highest prevalence is seen in the Southwest United States bordering Mexico. In such areas, SR is commonly seen at near 30%, but in some areas, can be as high as 38%. More North, in areas like Oregon, Washington, and Idaho, SR occurs less often in nature. In these areas, Sturtevant (1936) found the prevalence of sex-ratio factors to be between 0% and 10%.

These data suggest that the presence of the three inversions is a strong recombination suppressor. While each genotype results in drastically different offspring female ratios as illustrated in Figure 10 and 11, the incidence of SR and ST was not significantly different from the expected 50:50 ratio. These data are important as they illustrate a clear and documented vulnerability in Mendelian genetics.

Appendix A

SR Recombination Raw Data

Table 1: Raw Data for Recombination scoring

Cross	Setup Date	End Adult Count	Male Genotype	Female	Male	% Female
G1 M.59	2/2/18	3/16/18	SR1_SR2_SR3	132	33	0.800
G1 M.69	2/2/18	3/16/18	SR1_SR2_SR3	131	29	0.819
G1 M.77	2/5/18	3/19/18	SR1_SR2_SR3	112	19	0.855
G1 M.50	2/1/18	3/15/18	SR1_SR2_SR3	110	18	0.859
G1 M.48	2/1/18	3/15/18	SR1_SR2_SR3	127	18	0.876
G1 M.40	2/1/18	3/15/18	SR1_SR2_SR3	142	16	0.899
G1 M.62	2/2/18	3/16/18	SR1_SR2_SR3	185	20	0.902
G1 M.58	2/2/18	3/16/18	SR1_SR2_SR3	153	16	0.905
G1 M.55	2/2/18	3/16/18	SR1_SR2_SR3	148	14	0.914
G1 M.10	1/29/18	3/12/18	SR1_SR2_SR3	72	6	0.923
G1 M.42	2/1/18	3/15/18	SR1_SR2_SR3	174	11	0.941
G1 M.3	1/29/18	3/12/18	SR1_SR2_SR3	98	4	0.961
G1 M.98	2/5/18	3/19/18	SR1_SR2_SR3	151	6	0.962
G1 M.19	1/31/18	3/14/18	SR1_SR2_SR3	156	6	0.963
G1 M.81	2/5/18	3/19/18	SR1_SR2_SR3	165	6	0.965
G1 M.4	1/29/18	3/12/18	SR1_SR2_SR3	114	4	0.966
G1 M.7	1/29/18	3/12/18	SR1_SR2_SR3	150	4	0.974
G1 M.36	2/1/18	3/15/18	SR1_SR2_SR3	155	4	0.975
G1 M.72	2/5/18	3/19/18	SR1_SR2_SR3	133	3	0.978
G1 M.37	2/1/18	3/15/18	SR1_SR2_SR3	134	3	0.978
G1 M.9	1/29/18	3/12/18	SR1_SR2_SR3	130	2	0.985
G1 M.21	1/31/18	3/14/18	SR1_SR2_SR3	139	2	0.986
G1 M.86	2/5/18	3/19/18	SR1_SR2_SR3	153	2	0.987
G1 M.56	2/2/18	3/16/18	SR1_SR2_SR3	156	2	0.987
G1 M.85	2/5/18	3/19/18	SR1_SR2_SR3	159	2	0.988
G1 M.39	2/1/18	3/15/18	SR1_SR2_SR3	165	2	0.988
G1 M.87	2/5/18	3/19/18	SR1_SR2_SR3	168	2	0.988
G1 M.57	2/2/18	3/16/18	SR1_SR2_SR3	176	2	0.989
G1 M.76	2/5/18	3/19/18	SR1_SR2_SR3	178	2	0.989
G1 M.63	2/2/18	3/16/18	SR1_SR2_SR3	226	2	0.991

G1 M.90	2/5/18	3/19/18	SR1_SR2_SR3	130	1	0.992
G1 M.71	2/5/18	3/19/18	SR1_SR2_SR3	155	1	0.994
G1 M.30	2/1/18	3/15/18	SR1_SR2_SR3	157	1	0.994
G1 M.31	2/1/18	3/15/18	SR1_SR2_SR3	169	1	0.994
G1 M.65	2/2/18	3/16/18	SR1_SR2_SR3	220	1	0.995
G1 M.73	2/5/18	3/19/18	SR1_SR2_SR3	242	1	0.996
G1 M.12	1/29/18	3/12/18	SR1_SR2_SR3	103	0	1.000
G1 M.6	1/29/18	3/12/18	SR1_SR2_SR3	136	0	1.000
G1 M.8	1/29/18	3/12/18	SR1_SR2_SR3	167	0	1.000
G1 M.47	2/1/18	3/15/18	SR1_SR2_SR3	126	0	1.000
G1 M.23	1/31/18	3/14/18	ST1_ST2_ST3	81	91	0.471
G1 M.16	1/30/18	3/13/18	ST1_ST2_ST3	60	66	0.476
G1 M.91	2/5/18	3/19/18	ST1_ST2_ST3	82	87	0.485
G1 M.41	2/1/18	3/15/18	ST1_ST2_ST3	68	68	0.500
G1 M.52	2/1/18	3/15/18	ST1_ST2_ST3	25	25	0.500
G1 M.66	2/2/18	3/16/18	ST1_ST2_ST3	119	115	0.509
G1 M.46	2/1/18	3/15/18	ST1_ST2_ST3	109	105	0.509
G1 M.83	2/5/18	3/19/18	ST1_ST2_ST3	75	71	0.514
G1 M.34	2/1/18	3/15/18	ST1_ST2_ST3	91	86	0.514
G1 M.49	2/1/18	3/15/18	ST1_ST2_ST3	97	91	0.516
G1 M.27	2/1/18	3/15/18	ST1_ST2_ST3	85	79	0.518
G1 M.95	2/5/18	3/19/18	ST1_ST2_ST3	56	52	0.519
G1 M.93	2/5/18	3/19/18	ST1_ST2_ST3	82	76	0.519
G1 M.70	2/5/18	3/19/18	ST1_ST2_ST3	108	100	0.519
G1 M.18	1/30/18	3/13/18	ST1_ST2_ST3	67	62	0.519
G1 M.100	2/5/18	3/19/18	ST1_ST2_ST3	53	49	0.520
G1 M.1	1/29/18	3/12/18	ST1_ST2_ST3	75	68	0.524
G1 M.92	2/5/18	3/19/18	ST1_ST2_ST3	76	67	0.531
G1 M.25	2/1/18	3/15/18	ST1_ST2_ST3	101	88	0.534
G1 M.35	2/1/18	3/15/18	ST1_ST2_ST3	101	88	0.534
G1 M.82	2/5/18	3/19/18	ST1_ST2_ST3	96	83	0.536
G1 M.13	1/30/18	3/13/18	ST1_ST2_ST3	75	64	0.540
G1 M.28	2/1/18	3/15/18	ST1_ST2_ST3	69	58	0.543
G1 M.43	2/1/18	3/15/18	ST1_ST2_ST3	99	83	0.544
G1 M.14	1/30/18	3/13/18	ST1_ST2_ST3	79	65	0.549
G1 M.5	1/29/18	3/12/18	ST1_ST2_ST3	60	49	0.550
G1 M.94	2/5/18	3/19/18	ST1_ST2_ST3	76	62	0.551
G1 M.45	2/1/18	3/15/18	ST1_ST2_ST3	125	101	0.553
G1 M.38	2/1/18	3/15/18	ST1_ST2_ST3	114	92	0.553

G1 M.29	2/1/18	3/15/18	ST1_ST2_ST3	86	69	0.555
G1 M.74	2/5/18	3/19/18	ST1_ST2_ST3	111	89	0.555
G1 M.32	2/1/18	3/15/18	ST1_ST2_ST3	80	64	0.556
G1 M.44	2/1/18	3/15/18	ST1_ST2_ST3	87	69	0.558
G1 M.17	1/30/18	3/13/18	ST1_ST2_ST3	99	78	0.559
G1 M.54	2/2/18	3/16/18	ST1_ST2_ST3	124	97	0.561
G1 M.64	2/2/18	3/16/18	ST1_ST2_ST3	94	73	0.563
G1 M.80	2/5/18	3/19/18	ST1_ST2_ST3	98	74	0.570
G1 M.84	2/5/18	3/19/18	ST1_ST2_ST3	104	78	0.571
G1 M.53	2/1/18	3/15/18	ST1_ST2_ST3	107	80	0.572
G1 M.88	2/5/18	3/19/18	ST1_ST2_ST3	59	44	0.573
G1 M.75	2/5/18	3/19/18	ST1_ST2_ST3	104	76	0.578
G1 M.89	2/5/18	3/19/18	ST1_ST2_ST3	77	56	0.579
G1 M.26	2/1/18	3/15/18	ST1_ST2_ST3	78	56	0.582
G1 M.2	1/29/18	3/12/18	ST1_ST2_ST3	52	37	0.584
G1 M.61	2/2/18	3/16/18	ST1_ST2_ST3	134	95	0.585
G1 M.15	1/30/18	3/13/18	ST1_ST2_ST3	92	65	0.586
G1 M.99	2/5/18	3/19/18	ST1_ST2_ST3	56	38	0.596
G1 M.33	2/1/18	3/15/18	ST1_ST2_ST3	102	69	0.596
G1 M.97	2/5/18	3/19/18	ST1_ST2_ST3	118	78	0.602
G1 M.22	1/31/18	3/14/18	ST1_ST2_ST3	76	50	0.603
G1 M.51	2/1/18	3/15/18	ST1_ST2_ST3	121	69	0.637
G1 M.11	1/29/18	3/12/18	ST1_ST2_ST3	72	41	0.637
G1 M.67	2/2/18	3/16/18	ST1_ST2_ST3	83	41	0.669
G1 M.68	2/2/18	3/16/18	ST1_ST2_ST3	111	53	0.677
G1 M.20	1/31/18	3/14/18	ST1_ST2_ST3	57	22	0.722
G1 M.60	2/2/18	3/16/18	ST1_ST2_ST3	111	21	0.841
G1 M.24	2/1/18	-	-	-	-	-
G1 M.78	2/5/18	-	-	-	-	-
G1 M.79	2/5/18	-	-	-	-	-
G1 M.96	2/5/18	-	-	-	-	-

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ACADEMIC VITA — JON WESTLAKE

EDUCATION	Penn State Smeal College of Business <i>Master of Business Administration</i> <ul style="list-style-type: none">• Concentrations: Supply Chain and Consulting	University Park, PA 5/21
	Schreyer Honors College at The Pennsylvania State University <i>Bachelor of Science concentrated in Biology/Chemistry</i> <ul style="list-style-type: none">• magna cum laude	University Park, PA 5/19
EXPERIENCE	Evidation Health <i>Product Operations Intern</i> <ul style="list-style-type: none">• Triaging product development for healthcare application between engineering, data science, external partners, and medical teams through Jira.• Writing product specs for the largest digital health program ever run.	San Francisco, CA 8/19 - present
	<i>Commercial Analyst</i> <ul style="list-style-type: none">• Decreased average onboarding time for new employees from 10 weeks to 4 weeks through process improvement.• Built custom CRM and account plan to increase account revenue 320% QoQ for top 3 pharma client.• Saved 35 FTE hours per week by creating case study database & slide deck for client RFPs.	5/19 – 8/19
	KCF Technologies <i>Business Development Intern</i> <ul style="list-style-type: none">• Collaborated with CEO and CTO on new product introduction for IOT human activity sensors funded by the DoD.• Reported directly to CEO on scaling & strategy for doubling company size in four months.	State College, PA 1/19 - 5/19
	Reflexion <i>Lead Business Developer</i> <ul style="list-style-type: none">• Co-invented a patented device to quantify neural cognitions indicative of concussions.• Raised \$1.5M in high-growth startup environment• Implemented CRM software and Google Analytics that led to 250% increase in ARR.	Lancaster, PA 4/17 - 9/18
RESEARCH	Schaeffer Lab <i>Independent Undergraduate Researcher</i> <ul style="list-style-type: none">• Research efforts culminating in an Honors Thesis and publication in PLOS Genetics.	University Park, PA 1/18-present
SKILLS	Leadership, problem solving, market development, teamwork, SQL, Tableau, Excel, R, Jira.	
ACTIVITIES	Farm Hand, Westlake Tree Farms	2005 - present
AWARDS	CES Startup of the Year Eagle Scout and Eagle Scout Service Project of the Year Schreyer Honors College Academic Excellence Scholarship	