SEX CHROMOSOME MEIOTIC DRIVE

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Key Words  intragenomic conflict, levels of selection, evolutionary genetics,
segregation distortion, sex ratio

Abstract  Sex chromosome drive refers to the unequal transmission of X and Y chromosomes from individuals of the heterogametic sex, resulting in biased sex ratios among progeny and within populations. The presence of driving sex chromosomes can reduce mean fitness within a population, bring about intragenomic conflict between the X chromosome, the Y, and the autosomes, and alter the intensity or mode of sexual selection within species. Sex chromosome drive, or its genetic equivalent, is known in plants, mammals, and flies. Many species harboring driving X chromosomes have evolved Y-linked and autosomal suppressors of drive. If a drive polymorphism is not stable, then driving chromosomes may spread to fixation and cause the extinction of a species. Certain characteristics of species, such as population density and female mating rate, may affect the probability of fixation of driving chromosomes. Thus, sex chromosome drive could be an agent of species-level selection.

INTRODUCTION

In most species, individuals of the heterogametic sex produce equal numbers of X- and Y-bearing gametes, thus resulting in approximately equal numbers of male and female offspring. The general tendency to produce 1:1 sex ratio, as well as many deviations from it, can often be explained in terms of adaptive sex ratio theory, with individuals producing a sex ratio that maximizes the transmission of autosomal alleles to future generations (Fisher 1930, Hamilton 1967, Trivers & Willard 1973, Charnov 1982).

In some species, however, a fraction of the individuals produce highly unequal and, for autosomal genes, nonadaptive offspring sex ratios. For instance, some maternally inherited microorganisms enhance their own transmission by killing male offspring, inducing parthenogenesis, or causing feminization of males (Stouthamer 1997, Rigaud 1997, Hurst & Jiggins 2000). This review focuses on a different non-adaptive mechanism of sex-ratio distortion: unequal transmission of functional X- and Y-bearing gametes by individuals of the heterogametic sex. The genes responsible are typically linked to one of the sex chromosomes and act by preventing or interfering with the production of functional gametes bearing the other sex chromosome. In most cases, the sex-ratio distortion results in the production...
of an excess of female offspring and depends only on the genotype of the male parent. Because sex-ratio genes usually act during spermatogenesis, the unequal production of X- and Y-bearing gametes is due to meiotic drive, or segregation distortion (Lytte 1991).

The presence of driving sex chromosomes can be of considerable ecological and evolutionary importance in those groups where it occurs. For simplicity, the following discussion focuses on X drive, which is much more common than Y drive, but the arguments presented apply similarly. The most important ecological consequences of sex chromosome drive stem from the biased sex ratio that arises at the population level. The presence of a driving X chromosome within a population is expected to lead to a female-biased population (Hamilton 1967), and this has been found to be the case in natural populations (Bryant et al. 1982, James & Jaenike 1990). At moderate frequencies of $X^D$ (the driving X chromosome), there may be enough males to inseminate all the females in a population. In such cases, a population harboring $X^D$ chromosomes may have a greater intrinsic rate of increase and thus be capable of rebounding more quickly from population declines. However, if an $X^D$ chromosome reaches a very high frequency, which is expected to occur in the absence of countervailing selection, the female bias will become so great that many females will go unmated and the population may go extinct (Hamilton 1967; see also Hatcher et al. 1999). Thus, the effect of $X^D$ on population persistence probably depends on the frequency of these chromosomes.

Driving X chromosomes can also affect mating behavior and sexual selection in several ways. Because populations harboring $X^D$ chromosomes are more female biased, this will affect the operational sex ratio among sexually active individuals, and one might expect the intensity of sexual selection on males to be less in such species, perhaps even selecting for male mate choice, as Randerson et al. (2000) have suggested for sex-ratio distortion brought about by male-killing bacteria. The female bias at the population level imposes selection on females to mate in a way that maximizes the proportion of sons among their offspring (Fisher 1930), and there are several ways this might be achieved. Lande & Wilkinson (1999) have shown that the presence of X drive could lead to the evolution of female preference for male traits encoded by genes linked to wild-type allele at the sex-ratio locus. Thus, linkage between genes for the male trait and the drive locus provides the basis for a “good genes” type of sexual selection.

Multiple mating by females may also result in the production of less female-biased offspring sex ratios. As discussed below, sperm competition can adversely affect offspring production by Sex-ratio males relative to Standard males. Consequently, females that mate randomly with several males will produce, on average, more male offspring than females that mate infrequently and for which there is no sperm competition. Thus, the presence of a meiotic drive gene can favor the evolution of multiple mating by females (Haig & Bergstrom 1995). Similarly, selection might favor females that are not susceptible to an “insemination reaction,” a phenomenon known in many species of Drosophila (Patterson 1946). The insemination reaction, which is caused by some substance transmitted with a male's ejaculate, renders females less capable of remating for some period of time. Thus,
susceptibility to the insemination reaction lowers the level of sperm competition within females and could result in their producing a lower percentage of male offspring. These possibilities remain to be tested within a comparative phylogenetic context.

The broader evolutionary consequences of sex chromosome drive are equally profound, as many general principles of population genetic theory are violated by non-Mendelian segregation (Charlesworth & Hartl 1978). For example, meiotic drive at any genetic locus reduces the mean fitness of the population, because variation is maintained by a balance between meiotic drive and countervailing natural selection (Hiraizumi et al. 1960). X drive also sets the stage for intense intragenomic conflicts. This topic has recently been reviewed by Hurst et al. (1996) and Werren & Beukeboom (1998), and I highlight only some salient points here. Because enhanced transmission of driving X chromosomes depends on preventing the production of functional Y-bearing sperm, there is strong selection on the Y to resist this effect. The presence of driving X chromosomes is a plausible explanation for the maintenance of a Y chromosome polymorphism in natural populations (Clark 1987, Carvalho et al. 1997, Jaenike 1999). The autosomes are also selected to suppress the X-linked drive, for two reasons. First, because the presence of X^D chromosomes results in a female-biased population, males have a higher mean fitness than females (Fisher 1930). Autosomal genes that suppress X drive will be passed more frequently to male offspring and thus will experience enhanced transmission to subsequent generations. Furthermore, because polymorphism at a drive locus requires countervailing selection against carriers of the drive allele, autosomal suppressors are less likely than nonsuppressors to be associated with low-fitness individuals carrying the drive allele in future generations.

Meiotic drive has also been hypothesized to have major effects on the structure of the genome. In all cases that have been well characterized, drive involves interactions between a drive locus on one chromosome and a sensitive responder locus on the homologous chromosome (Lyttle 1991). For a newly arisen drive allele to spread, it is necessary that there be little or no recombination between the drive and responder loci. Haig & Grafen (1991) therefore suggested that genome-wide recombination between homologous chromosomes is an evolutionary response to the threat of meiotic drive genes.

Frank (1991) and Hurst & Pomiankowski (1991) postulated that sex chromosome drive could be responsible for Haldane’s rule, the greater inviability or sterility of heterogametic-sex hybrids. There is, however, little empirical support for this idea (Coyne et al. 1991, Coyne & Orr 1993). It has also been suggested that the presence of X chromosome drive could lead to evolutionary changes in sex determination mechanisms to restore a more equal sex ratio (Lyttle 1981, Haig 1993a,b, Werren & Beukeboom 1998). As seen below, there are several species groups in which a change in the genetics of sex determination is at least correlated with the presence of sex chromosome drive. These considerations highlight the potential ecological and evolutionary ramifications of sex chromosome drive, from intragenomic conflict to species-level extinction.
EMPIRICAL PATTERNS

Table 1 lists species in which sex chromosome drive has been documented, or for which there is strongly suggestive evidence. Although several species exhibit Y drive, X drive is far more common. Sex chromosome drive has a spotty taxonomic distribution, having been found so far in insects, mammals, and angiosperms. The vast majority of known cases are from insects, within which sex chromosome drive is phylogenetically concentrated, being known with certainty only from Diptera, although there is one possible example in butterflies. Within flies, most examples are from the acalyprate families, and within these families, certain clades (e.g., the *Drosophila obscura* group, stalk-eyed flies) seem particularly prone to *sex-ratio* polymorphisms. Among flies, sex chromosome drive has been discovered serendipitously in a number of species that are studied because of their medical (mosquitoes, tsetse flies), agricultural (medflies), or genetic importance (*Drosophila*). This suggests that sex chromosome drive is probably very common, at least within certain taxonomic groups. A more detailed discussion of the individual species can be obtained elsewhere (http://www.annualreviews.org/supmat/supmat.asp).

There is considerable variability among species in the specifics of sex chromosome drive. The following discussion is aimed at determining whether any patterns apply broadly across these systems, as such patterns would facilitate an understanding of the evolution and dynamics of sex chromosome drive in general. A consistent system of nomenclature has not been applied to sex chromosome drive, resulting in confusion and misunderstanding. For instance, the term sex-ratio has been variously applied to the phenomenon of X chromosome drive, the driving X chromosome itself, males that carry such chromosomes, and the loci responsible for the drive. In Table 2, I suggest terms that could be used to more clearly distinguish among the different aspects of X chromosome drive.

MECHANISMS OF DRIVE

Cytological studies of several species of flies with strong X drive reveal that Sex-ratio males are characterized by abnormal Y chromosome behavior in meiosis II. These males typically produce about half as many functional sperm as do Standard males, with the remaining sperm failing to individualize properly. Such patterns have been found in *Drosophila pseudoobscura* (see Novitsky et al. 1965, Policansky & Ellison 1970, Cobbs et al. 1991), *Drosophila subobscura* (see Hauschteck-Jungen & Maurer 1976), *Drosophila simulans* (see Montchamp-Moreau & Joly 1997, Cazemajor et al. 2000), *Drosophila neotestacea* (K. Dyer, personal communication), and *Cyrtodiopsis whitei* (see Wilkinson & Sanchez 2001, unpublished manuscript). Using fluorescence in situ hybridization with a Y-specific marker, Cazemajor et al. (2000) demonstrated that Y-bearing spermatids do not elongate properly.

Males of the *D. obscura* group produce both long and short sperm. Bircher et al. (1995) found that Sex-ratio males actually produce more short sperm than
do Standard males and suggested that the excess short sperm compensates for the reduction in numbers of long sperm produced by these males. This is unlikely, because only the long sperm in this species are involved in fertilization (Snook & Karr 1998). Bircher et al. (1995) also hypothesized that sperm dimorphism is a necessary prerequisite for the evolution of a sex-ratio polymorphism, but this cannot be a general prerequisite, as sperm are not dimorphic in the sex-ratio polymorphic D. simulans (see Joly et al. 1989).

Although the mechanism outlined above appears to be the most common, several other mechanisms of sex chromosome drive have been uncovered. In Drosophila melanogaster, males carrying large deletions of the X heterochromatic region (denoted Xh−) sire a significant excess of female offspring (McKee 1991). X drive in this species is due to mispairing of the X and Y chromosomes in meiosis I (McKee et al. 1998). Because spermatid viability is inversely related to the amount of chromatin a spermatid contains and because Xh− males produce spermatids carrying smaller X chromosomes, they sire relatively more female offspring than do Xh males (McKee 1991).

In Aedes aegypti, the target of the driving D allele is thought to be the m allele of the sex-determining locus, with drive brought about by preferential breakage of the m-bearing chromosome during male meiosis. This effectively Y drive in Aedes is also associated with abnormal spermiogenesis and premature senescence of spermatozoa (Newton et al. 1976, Owusu-Daaka et al. 1997).

Cytological studies of wood lemmings reveal that although the somatic cells of X∗Y females carry both the X* and Y chromosomes, their oocytes are X*X*, presumably as a result of selective nondisjunction and elimination of the Y chromosome from the germ line (Fregda et al. 1976, 1977). Thus, these females produce only X∗-bearing ova. Because all males are XY, X∗Y females produce X*X and X∗Y progeny, all of which will develop as females. Thus, the sex-ratio distortion in this species, which leads to production of all-female progeny, results from germline selection (Hastings 1991).

In the plant Silene alba, biased offspring sex ratios are produced even at low pollen densities, with distorter and nondistorter males siring equal numbers of progeny (Taylor et al. 1999), indicating that distorter males produce a greater proportion of X-bearing pollen, and that differential fertilization success of X- and Y-bearing pollen cannot alone be responsible for the sex-ratio bias. The fraction of female progeny sired by distorter males increases with pollen density, indicating that Y-bearing pollen do poorly in pollen competition (Taylor et al. 1999). Furthermore, the genotype of a female crossed to a distorter male affects offspring sex ratio (Taylor 1994, 1999, Taylor et al. 1999). These observations indicate that sex-ratio distortion in this species is due to both meiotic and postmeiotic events.

**IS SEX CHROMOSOME MEIOTIC DRIVE COMMON?**

In addition to the examples shown in Table 1, female-biased offspring sex ratios have been found in several genera of dioecious angiosperms in which males are the heterogametic sex (Lloyd 1974). Other than Silene, it is not known whether these
### TABLE 1  Examples of sex chromosome drive. Detailed discussion of individual case studies available at http://www.annualreviews.org/supmat/supmat.asp

<table>
<thead>
<tr>
<th>Species</th>
<th>Drive Type</th>
<th>Known Suppressors</th>
<th>Notes</th>
<th>Selected References</th>
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<tbody>
<tr>
<td><em>Drosophila obscura</em> (Drosophilidae)</td>
<td>X m</td>
<td></td>
<td>First example of X drive.</td>
<td>Gershenson 1928</td>
</tr>
<tr>
<td><em>D. pseudoobscura</em></td>
<td>X m</td>
<td>Note found, despite extensive search</td>
<td>Polymorphism depends on effect on females, as well as males. Sperm competition in multiply-mated females reduces transmission of X&lt;sup&gt;B&lt;/sup&gt;. Loci associated with SR inversions are genetically depauperate compared to ST-associated alleles. Cryptic sex-ratio system uncovered in crosses between mainland and Bogota subspecies.</td>
<td>Wallace 1948; Curtisinger &amp; Feldman 1980; Policansky 1974, 1979; Beckenbach 1978, 1981, 1983, 1996; Policansky &amp; Ellison 1970; Wu 1983a,b; Prakash &amp; Merritt 1972; Babcock &amp; Anderson 1996; Beckenbach et al. 1982</td>
</tr>
<tr>
<td><em>D. persimilis</em></td>
<td>X m</td>
<td></td>
<td>Drive requires presence of several X-linked loci</td>
<td>Wu &amp; Beckenbach 1983</td>
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<tr>
<td><em>D. azteca</em></td>
<td>X m</td>
<td></td>
<td></td>
<td>Sturtevant &amp; Dobzhansky 1936</td>
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<tr>
<td><em>D. subobscura</em></td>
<td>X m</td>
<td>Y and/or autosomal</td>
<td>X&lt;sup&gt;D&lt;/sup&gt; present in North African, but not European populations. Drive is stronger in normal genetic background. Interpopulation crosses result in hybrid male sterility if male carries X&lt;sup&gt;D&lt;/sup&gt;.</td>
<td>Hauschteck-Jungen &amp; Maurer 1976; Hauschteck-Jungen 1990; Bircher et al. 1995</td>
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<tr>
<td><em>D. affinis</em></td>
<td>X m</td>
<td>Y</td>
<td>X&lt;sup&gt;0&lt;/sup&gt;O males produce only sons. Y chromosome types differ in susceptibility to the different X&lt;sup&gt;D&lt;/sup&gt;’s</td>
<td>Voelker 1972</td>
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<tr>
<td><em>D. athabasca</em></td>
<td>X m</td>
<td></td>
<td>X drive occurs in two eastern semispecies, but not in western-northern semispecies. Its presence in the closely related <em>D. affinis</em> and <em>D. azteca</em> suggests that X&lt;sup&gt;D&lt;/sup&gt; has been lost from the western-northern semispecies.</td>
<td>Miller &amp; Voelker 1969</td>
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<tr>
<td><em>D. melanogaster</em></td>
<td>X m</td>
<td></td>
<td><em>Stellite</em> hypothesized to be relic X-linked drive locus. Males carrying large deletions from heterochromatic region sire excess of females → abnormal behavior of Y during meiosis I.</td>
<td>Hurst 1992, 1996; McKee 1991</td>
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<tr>
<td>Species</td>
<td>Sex</td>
<td>Chromosome</td>
<td>Drive</td>
<td>Description</td>
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<tr>
<td><em>D. simulans</em></td>
<td>X m</td>
<td>Y, autosomes</td>
<td></td>
<td>Populations carrying $X^D$ also carry suppressors, so drive is rarely expressed. A different and completely suppressed X drive system uncovered in interspecific crosses with <em>D. sechellia</em>.</td>
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<tr>
<td><em>D. quinaria</em></td>
<td>X m</td>
<td>Y, autosomes</td>
<td></td>
<td>Local polymorphism for susceptible and partially resistant Y chromosome types.</td>
</tr>
<tr>
<td><em>D. recens</em></td>
<td>X m</td>
<td>Y, autosomes</td>
<td></td>
<td>For both <em>D. recens</em> and <em>D. quinaria</em>, multiple mating by males reduces fertility of SR males more than that of ST males.</td>
</tr>
<tr>
<td><em>D. paramelanica</em></td>
<td>X m</td>
<td>Y, autosomes</td>
<td></td>
<td>Geographic variation in frequencies of two types of $X^D$ and two types of Y. $X^D$’s drive best the Y’ with which they are usually associated locally.</td>
</tr>
<tr>
<td><em>D. mediopunctata</em></td>
<td>X m</td>
<td>Y, autosomes</td>
<td></td>
<td>X drive due to at least two loci, one of which may be primary drive locus, and the 2nd is an enhancer. Little geographic variation in frequencies of suppressor and non-suppressor Y chromosome types.</td>
</tr>
<tr>
<td><em>D. neotestacea</em></td>
<td>X m</td>
<td>none found</td>
<td></td>
<td>Unlike most other <em>Drosophila</em> species, SR not associated with inversions. $X^D$ occurs at 20% to 30% frequency in all sampled populations in eastern United States.</td>
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<tr>
<td><em>Cyrtodiopsis dalmanni</em></td>
<td>X m</td>
<td>Y and/or autosomes</td>
<td></td>
<td>Sex-ratio males carrying $X^D$ and suppressors sire significant excess of sons. Sperm competition in multiply-mated females reduces transmission of $X^D$.</td>
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<td></td>
<td>Presgraves et al. 1997; Wilkinson et al. 1998a,b, Wilkinson &amp; Sanchez 2000</td>
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<tr>
<td><em>C. whitei</em></td>
<td>X m</td>
<td></td>
<td></td>
<td>In both <em>C. whitei</em> and <em>C. dalmanni</em>, males may mate many times per day. Females in these species remate much more rapidly than congeneric species that lacks X drive. For both species, interpopulation crosses yield hybrid males with defects in spermatogenesis similar to that seen in sex-ratio males.</td>
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<td>Presgraves et al. 1997</td>
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### TABLE 1  (Continued)

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<thead>
<tr>
<th>Species</th>
<th>Drive Type</th>
<th>Known Suppressors</th>
<th>Notes</th>
<th>Selected References</th>
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<tbody>
<tr>
<td><em>Diasemopsis sylvestra</em></td>
<td>X m</td>
<td></td>
<td></td>
<td>Lande &amp; Wilkinson 1999</td>
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<tr>
<td>(Diopsidae)</td>
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<tr>
<td><em>Sphyropsophala beccarii</em></td>
<td>X m</td>
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<td>Lande &amp; Wilkinson 1999</td>
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<tr>
<td>(Diosidae)</td>
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<tr>
<td><em>Ceratitis capitata</em></td>
<td>Y m</td>
<td></td>
<td>Driving Y arose in laboratory population after X irradiation treatment.</td>
<td>Wood 1995</td>
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<td>(Tephritidae: medfly)</td>
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<tr>
<td><em>Musca domestica</em></td>
<td>Y m</td>
<td></td>
<td>Drive associated with neo-Y chromosome, which arose following translocation of part of Y to the 3rd chromosome.</td>
<td>M. Clark, personal communication</td>
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<tr>
<td>(Muscidae: housefly)</td>
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<tr>
<td><em>Glossina morsitans</em></td>
<td>X m</td>
<td></td>
<td>Sex-ratio males known from several areas in Africa; associated with female-biased emergence sex ratios.</td>
<td>Rawlings &amp; Maudlin 1984;</td>
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<tr>
<td>(Muscidae: tsetse fly)</td>
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<td>Gooding 1986; Gooding et al. 1989</td>
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<tr>
<td><em>Aedes aegypti</em></td>
<td>Y m</td>
<td>X</td>
<td>Drive locus (D) closely linked to sex determining locus. Responder thought to be m allele at the sex-determining locus. Drive associated with breakage of m-bearing chromosome. Drive allele (D) tends to be geographically associated with resistant X chromosomes resistant to drive.</td>
<td>Hickey &amp; Craig 1966;</td>
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<td>(Culicidae)</td>
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<td>Hickey 1970; Newton et al. 1976;</td>
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<td>Hastings &amp; Wood 1978;</td>
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<td>Wood &amp; Newton 1991;</td>
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<td>Owusu-Daaku et al. 1997</td>
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<tr>
<td><em>Culex pipiens</em></td>
<td>Y m</td>
<td></td>
<td>Sex ratio distortion occurs only in individuals homozygous for drive allele <em>d</em>. Drive allele therefore gains no obvious transmission advantage.</td>
<td>Sweeny &amp; Barr 1978</td>
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<td>(Culicidae)</td>
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<tr>
<td><em>Eucinera socialis</em></td>
<td>X f</td>
<td></td>
<td>Strongly male-biased primary sex ratios in some egg masses. Bias toward males indicates that distortion is not caused by a cytoplasmic factor such as Wolbachia.</td>
<td>Underwood &amp; Shapiro 1999</td>
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<td>(Lepidoptera: Pieridae)</td>
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<td>Species</td>
<td>Chromosome</td>
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<tr>
<td>Dicrostonyx torquatus</td>
<td>Y m</td>
<td>Includes both XX and X*Y females. Weak Y drive in males.</td>
<td>Bull &amp; Bulmer 1981; Gileva et al. 1982; Gileva 1987</td>
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<td>(Cricetidae: varying lemming)</td>
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<tr>
<td>Myopus schisticolor</td>
<td>X f</td>
<td>Includes XX, XX*, and X<em>Y females. Drive results from germine selection in X</em>Y females, yielding only X*-bearing ova.</td>
<td>Frega et al. 1976, 1977</td>
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<td>(Cricetidae: wood lemming)</td>
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<tr>
<td>Akodon azarae</td>
<td>Y m and Y f</td>
<td>Includes both XX and XY* females. Weak Y drive occurs in males, and weak Y* drive occurs in XY* females.</td>
<td>Hoekstra &amp; Edwards 2000, Hoekstra &amp; Hoekstra 2000</td>
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<tr>
<td>(Muridae: field mouse)</td>
<td>Y m and Y f</td>
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<tr>
<td>Silene alba</td>
<td>X m Y</td>
<td>Dioecious plant. Female-biased sex ratios appear due to both meiotic drive and pollen competition. Maternal genotype can affect success of X- and Y-pollen. Considerable variation among local populations in sex-ratio frequencies. Although X chromosome enjoys transmission advantage, it is the Y chromosome that determines this. Y may be polymorphic for resistance to fixed X drive in this species. Pollen competition reduces fertilization success of pollen from distorter males.</td>
<td>Taylor 1993, 1994, 1996; Taylor et al. 1999</td>
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<td>(Caryophyllaceae: white campion)</td>
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<tr>
<td>Datisca cannabina</td>
<td>X m</td>
<td>Dioecious plant. X drive may have been a factor in the evolution to androecy in the sister species D. glomerata.</td>
<td>Wolf &amp; Rieseberg 2000</td>
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</table>

*X and Y indicate driving chromosome; m and f indicate whether drive occurs in males or females.
species harbor driving sex chromosomes. Among insects, sex chromosome drive has been unequivocally demonstrated only in Diptera, although within this group, drive has evolved repeatedly. In other insects, sex-ratio distortion is often due to maternally inherited endosymbionts, which can act by killing male offspring, feminizing them, or inducing parthenogenesis. Jiggins et al. (1999) have argued that, statistically at least, such endosymbionts are a more important cause of sex-ratio bias than meiotic drive outside the Diptera. However, it remains to be seen how taxonomically widespread sex chromosome drive is; only a tiny, and taxonomically nonrandom, sample of species has been examined in a way that could reveal such drive. In species that have them, driving sex chromosomes are often present at low frequency and their expression can be masked by suppressors. Therefore, ruling out their existence within a species may require large sample sizes of wild-caught males bred individually to virgin females, perhaps from different populations that may lack suppressors.

IS X CHROMOSOME DRIVE MORE COMMON THAN AUTOSOMAL DRIVE?

Whereas numerous examples of sex chromosome drive have been documented, far fewer examples of autosomal drive are known, with the best-studied examples being Segregation Distorter in D. melanogaster, the t locus in mice, and spore killer in Neurospora (reviewed in Lyttle 1991). One obvious reason for the discrepancy is that X (or Y) drive leads to distorted offspring sex ratios, which are easily detected. In contrast, autosomal drive is evident only when one can follow the unequal segregation of genetic markers that happen to be linked to the drive locus. Thus, autosomal drive had previously been discovered only in species that served as model organisms for genetic research. Ongoing Quantitative Trait Loci (QTL)
studies should provide a basis for detection of autosomal drive, although if the drive alleles occur at low frequency, then numerous crosses may have to be carried out. More recently, QTL analyses using molecular markers have revealed that what appears to be autosomal segregation distortion may be more common than previously thought (reviewed in Doebley & Stec 1991). However, because many of these cases involve plant hybrids, the apparent segregation distortion might actually be due to differential pollen inviability or fertilization success. The increasing number of QTL studies in animals should provide data with which to assess the relative frequency of autosomal and sex-linked meiotic drive.

There are two reasons why sex chromosome drive may be more common than autosomal drive. First, in all cases that have been examined in detail, drive entails linkage between the driving allele (e.g., SD of D. melanogaster) and an insensitive allele at a responder locus (e.g., Rsp1 of D. melanogaster). Such linkage disequilibrium can occur if the drive and responder loci are located near the centromere and/or are associated with inversions, as is the case for SD, the t complex of Mus, and spore killer of Neurospora (Temin et al. 1991, Lyon et al. 1988, Turner & Perkins 1991). As Lyttle (1991) and Hurst & Pomiankowski (1991) have pointed out, the lack of recombination between the X and Y chromosomes means that, in terms of linkage relationships, any gene on the X (or Y) can drive against any responder site on the Y (or X). Thus, there may be fewer genetic constraints for the evolution of a driving sex chromosome. If low levels of recombination are the limiting factor for the evolution of drive, then one might expect inversion-rich species, such as D. pseudoobscura and many other drosophilids, to exhibit autosomal drive. Yet, aside from SD drive of D. melanogaster, no cases of autosomal drive have been discovered in Drosophila. It is possible that autosomal inversions do harbor loci that drive, but the lack of genetic markers has precluded their discovery.

Another reason X chromosome drive may be more common than autosomal drive concerns the nature of the responder sites. Responder, the target of drive by the SD locus in D. melanogaster, is a repetitive sequence located within the centromeric heterochromatin (Wu et al. 1988). Similarly, the X-linked m allele of Aedes aegypti is thought to be the target of the drive (D) locus and it is completely linked to the centromere (Wood & Newton 1991). In both cases, therefore, the responder locus occurs within a heterochromatic region. Because the Y chromosome of many species appears to be composed entirely of heterochromatin (White 1973), it may offer a much larger array of targets for various X-linked drive loci. If target sites are the limiting factor, then X drive may be particularly common in species with heterochromatic Y chromosomes.

Y CHROMOSOME DRIVE

Several species exhibit what is effectively Y drive, leading to male-biased offspring sex ratios. The Y drive appears to be of two types, which may be termed primary and redirected drive. The mosquitoes A. aegypti and Culex pipiens exhibit primary drive. In these species, drive of the Y-linked D allele requires that the X
chromosome have a sensitive allele at the responder locus (Hickey 1970). If the X chromosome has an insensitive responder, then males sire unbiased offspring sex ratios, whether they carry the D allele or not. Genetically, the situation is somewhat similar to the autosomal SD drive of D. melanogaster, in which drives occurs when the SD allele on one chromosome drives against a sensitive responder allele on the homologous chromosome.

The only known examples of primary Y chromosome drive among insects occur in mosquitoes. Because sex is determined by a single locus or chromosomal region, the X and Y chromosomes are largely homomorphic. In this sense, the X and Y chromosomes are similar to autosomes and would seem equally likely to evolve drive. Why then has Y, but not X, chromosome drive arisen in these species? One reason could be that there is stronger selection for Y drive, as such a chromosome is passed only to sons and can therefore express drive every generation, whereas a driving X is carried by both males and females but is expressed only in males (Hamilton 1967).

Male-biased offspring sex ratios can also result from what I would call redirected drive. In the stalk-eyed fly Cyrtodiopsis dalmanni, males that carry particular Y chromosomes exhibit what is effectively Y drive, but this occurs only if that male also carries a driving XD chromosome. Males that carry the same Y chromosomes in conjunction with standard Xs chromosomes sire normal offspring sex ratios (Presgraves et al. 1997). Drosophila affinis exhibits a similar phenomenon: Whereas XDY males sire only daughters,XD0 males sire only sons (Voelker 1972). In males that carry the nondriving Xs chromosome, both XsY and XsO males sire normal offspring sex ratios. In both C. dalmanni and D. affinis, therefore, Y (or O) drive requires the presence of an XD chromosome. One possible explanation for the type of male bias seen in XD males of C. dalmanni and D. affinis is the following. Suppose the driving XD encodes a product that can bind to certain target sites. If a typical Y chromosome has many such target sites and the X chromosome has a few, then the Y chromosome will suffer disproportionately and thus be driven against. However, if there are Y chromosome variants that have fewer target sites than the X—and XO males would have no Y chromosome targets at all—then the X chromosome would be the target of its own drive, resulting in an underproduction of X-bearing sperm and few female offspring. The fact that XD0 males of D. affinis sire all male offspring indicates that a Y chromosome is not required to bring about reduced transmission of XD.

MECHANISMS TO EXPLAIN THE POLYMORPHISM

Any X- or Y-linked factor that exhibits complete drive will cause the extinction of a population or species if it spreads to fixation. The persistence of a species with a driving sex chromosome could thus depend on the action of countervailing selection against these elements. Thus, there has been considerable effort devoted to understanding the selective factors that lead to stable sex-ratio polymorphisms.
Wallace (1968) proposed a group selection mechanism that requires a metapopulation structure. He argued that if \( \text{X}^D \) chromosomes spread rapidly to fixation within individual populations, these populations will exhibit higher extinction rates and send out fewer colonists than populations founded by individuals lacking \( \text{X}^D \). Wallace did not present a formal analysis of his hypothesis, and it is not clear that such a group selection process could result in a stable metapopulation-wide polymorphism. Empirically, patterns of \( \text{X}^D \) frequencies in nature provide little support for this hypothesis. In \( \text{D. pseudoobscura}, \text{D. subobscura}, \) and \( \text{D. neote-} \\
\text{racea,} \) long-term studies reveal (a) no directional changes in the frequency of \( \text{X}^D \) and (b) either uniform or clinal changes in gene frequency across the range of a species, rather than a checkerboard pattern of presence and absence (Sturtevant & Dobzhansky 1936, Dobzhansky & Epling 1944, Hauschteck-Jungen 1990, James & Jaenike 1990, Beckenbach 1996). Thus, for \( \text{Drosophila} \) at least, there is no evidence that population-level selection facilitates the maintenance of sex-ratio polymorphisms.

Based on the cytological finding that Sex-ratio males produce only half as many sperm as do Standard males in \( \text{D. pseudoobscura} \) (see Policansky & Ellison 1970), Policansky (1974) argued that the 50% reduction in the number of sperm produced by Sex-ratio males exactly balanced the twofold meiotic drive advantage of the \( \text{X}^D \) chromosome in these males. Consequently, he suggested that \( \text{X}^D \) chromosomes would not experience greater transmission than nondriving \( \text{X}^S \) chromosomes and should therefore show no tendency to increase. This hypothesis assumes that offspring production is limited by sperm rather than egg production, an assumption at variance with most life history and sexual selection theory. Furthermore, the polymorphism thus brought about would be neutrally stable (Thomson & Feldman 1975), and the frequency of \( \text{X}^D \) would drift to fixation or loss.

Edwards (1961) and Curtsinger & Feldman (1980) derived the conditions for maintenance of a stable polymorphism of an X-linked drive locus. In their formulations, the fitnesses of all genotypes were constant, i.e., independent of the frequency of \( \text{X}^D \). Their models assumed that there was no Y-linked or autosomal variation for suppression of drive. An important result of their models was that a stable polymorphism at the drive locus could be maintained only if the fitness of females were affected by the sex-ratio loci or genes linked to these loci. For instance, a polymorphism could be maintained via heterozygote superiority in females or by a balance between drive in males and adverse fitness effects in females.

One difficulty with maintenance of an \( \text{X}^D \) polymorphism based on effects in females is that the primary effect of sex-ratio genes is on male spermatogenesis. In \( \text{D. melanogaster} \), the vast majority of genes that affect male fertility have no discernible effect on female fertility or viability (Lindsley & Zimm 1992). It is therefore unlikely that effects of sex-ratio genes in females can serve as a general mechanism for the maintenance of \( \text{X}^D \) polymorphisms. It is more likely that any fitness effects in females, as documented in \( \text{D. pseudoobscura} \), are due to other loci tied up within inversions associated with the SR gene arrangement (i.e., that characteristic of the \( \text{X}^D \) chromosome).
Before such inversions evolve, the dynamics of driving X^D chromosomes is probably governed primarily through their effects on male fitness. Because males are hemizygous for the X, maintenance of a drive polymorphism via heterosis in males is not possible. An alternative possibility is negative frequency-dependent selection. One such mechanism involves the increased proportion of females in a population, and consequently an increased rate of male mating and greater sperm depletion, that results from the spread of X^D chromosomes (Jaenike 1996). It has been shown in several species that Sex-ratio males produce about half as many sperm as do Standard males (D. pseudoobscura, Policansky & Ellison 1970; D. simulans, Montchamp-Moreau & Joly 1997; D. subobscura, Hauschteck-Jungen & Maurer 1976; Cyrtodiopsis dalmanni, Presgraves et al. 1997); thus, a high rate of male mating is likely to cause greater sperm depletion in Sex-ratio males than in Standard males. For several species, including D. pseudoobscura, D. neotestacea, D. recens, D. quinaria, and Aedes aegypti, laboratory studies have shown that virgin Sex-ratio and Standard males are about equally fertile but that multiple mating by these males results in a proportionately greater reduction in the fertility of Sex-ratio males (Wu 1983a,b, James 1992, Jaenike 1996, Hickey & Craig 1966).

Wu (1983a) has shown that Sex-ratio males suffer the greatest reduction in relative fertility when both they and their mates have mated several times. How will female multiple mating and the resulting sperm competition among males affect the dynamics of X^D? Suppose that the female mating rate is simply proportional to the male-female encounter rate. When the frequency of X^D is low, there are relatively many males per female, resulting in more frequent female remating. Thus, as a result of sperm competition, Sex-ratio males will suffer the greatest reduction in relative fertility at low frequencies of X^D, which will impede the initial spread of X^D within a population. At high frequencies, however, females will remate less often, thus reducing the intensity of selection against X^D. Consequently, if sperm competition plays a role in preventing the spread of X^D at low frequencies, there may be an unstable equilibrium frequency above which X^D spreads to fixation.

Alternatively, a female’s propensity to remate may depend on the fertility of the last male with which she mated. Suppose a female remates sooner if the last male she mated with was sperm depleted, as shown experimentally in D. pseudoobscura (see Beckenbach 1981). Under these conditions, when the frequency of X^D and the rate of male mating are high, most females will have mated with a sperm-depleted male. As a result, these females will remate more often than when X^D is at low frequency, thus intensifying selection against Sex-ratio males when X^D is common. In this manner, multiple mating by females and the resulting sperm competition could serve to stabilize X^D frequencies. However, there is still likely to be a frequency of X^D above which (and/or a population density below which) the ratio of females to males in a population is so high that multiple mating by females becomes improbable. This possibility remains to be explored both theoretically and empirically.

With respect to stabilization of a driving Y, Maffi & Jayakar (1981) examined the conditions under which a polymorphism at a Y-linked drive locus can be maintained.
in species where sex is determined by a single locus, rather than by separate X and Y chromosomes. They considered a situation, as in *Aedes aegypti*, in which the drive locus is linked to, but separate from, the sex determining locus (Newton et al. 1978). They assumed that neither locus affects male or female fertility and viability. The analysis showed that some recombination between the two loci is necessary to bring about a protected polymorphism. This analysis revealed that for species in which there is no recombination between the X and Y chromosomes, a driving Y polymorphism cannot be maintained with frequency-independent fitnesses.

**EVOLUTION OF SUPPRESSORS**

An X<sup>D</sup> chromosome spreads at the expense of the nondriving X<sup>S</sup> chromosomes in a population. However, because such drive is typically expressed only in males, X drive necessarily entails a reduction in Y chromosome transmission by Sex-ratio males. If X<sup>D</sup> exhibits complete drive, the selective difference between Y chromosomes that are completely susceptible versus completely resistant is proportional to the frequency of X<sup>D</sup>. The female-biased population-level sex ratio resulting from X drive favors the evolution of autosomal suppressors. In the absence of other fitness effects, the mean fitness of females relative to males is \( W_f = (1 - P)/(1 + P) \), where \( P \) is the frequency of X<sup>D</sup>. In Sex-ratio males, nonsuppressor alleles at autosomal loci are passed exclusively to females, whereas suppressor alleles can be transmitted to males at a rate dependent on the degree of suppression. The selective difference between autosomal suppressor and nonsuppressor alleles can be shown to be proportional to \( P^2 \). Thus, when X<sup>D</sup> is at high frequency, selection on Y-linked and autosomal suppressors of drive will be of comparable magnitude, but at low to moderate frequencies of X<sup>D</sup>, selection will be considerably stronger on the Y.

In an attempt to understand the conditions under which an autosomal suppressor of drive may or may not evolve, Wu (1983c) considered the population genetics of an autosomal locus that suppresses X<sup>D</sup> drive but otherwise has no effect on the fitness of its carriers. Wu assumed that a population is at a stable equilibrium frequency of X<sup>D</sup> and that all males are completely sensitive to drive. His model focuses on the conditions under which an autosomal suppressor can spread within a population, not the conditions for a stable polymorphism at a suppressor locus or fixation of a suppressor allele. Although one might intuitively expect that a cost-free suppressor would always be favored, Wu showed that under some conditions such a suppressor does not invade. Specifically, if Sex-ratio males have very low fitness and if there is heterozygote superiority at the drive locus in females, the suppressor will not spread. The reason for this appears to be twofold. First, if there is strong selection against Sex-ratio males, then the equilibrium frequency of X<sup>D</sup> will be low (Edwards 1961). As a result, the population will be only slightly female biased, and selection in favor of the suppressor will be correspondingly weak. Second, when \( P \) is low, most of the offspring of Sex-ratio males with unsuppressed drive
will be heterozygous females, which exhibit above-average fitness. Suppression of drive in these males would result in their siring fewer daughters, which would be heterozygous at the drive locus, resulting in reduced mean fitness of a Sex-ratio male’s offspring.

With respect to Y-linked suppressors of drive, Thomson & Feldman (1975) showed that if a population is polymorphic for driving and non-driving X chromosomes, then a Y chromosome that is less susceptible to drive will replace a more susceptible Y, as long as males carrying the two Y chromosome types are equally fertile. Carvalho et al. (1997) relaxed the assumption that the Y chromosome type does not affect male fitness and showed by computer simulation that the presence of a sex-ratio polymorphism can often lead to the maintenance of a stable Y chromosome polymorphism. Their models assume that X<sup>D</sup> is equally deleterious in males and homozygous females. Jaenike (1999) obtained similar results analytically and found that if there is a stable Y chromosome polymorphism, then the equilibrium frequency of the X<sup>D</sup> chromosome depends primarily on Y chromosome parameters.

Y-linked and/or autosomal suppressors of X drive are common, having been documented in *Drosophila subobscura*, *D. affinis*, *D. simulans*, *D. paramelanica*, *D. mediopunctata*, *D. quinaria*, *Cyrtoidiopsis dalmanni*, *Aedes aegypti*, and *Silene alba*. Species lacking suppressors, such as *D. pseudoobscura* and *D. neotestacea*, appear to be the exception. Population cage experiments with *D. simulans* and *D. mediopunctata* clearly show the selective advantage of suppressors when a population harbors driving X<sup>D</sup> chromosomes (Capillon & Atlan 1999, Carvalho et al. 1998). Nothing is yet known about the molecular mechanism of suppression, although Cazemajor et al. (1997) speculate that variation among Y chromosomes in sensitivity to X drive in *D. simulans* could be related to the size of a heterochromatic responder region. It is known that in *D. melanogaster*, the size of the responder locus, a tandemly repeated array, determines sensitivity to drive at the SD locus (Wu et al. 1988).

Because a driving X favors the evolution of Y-linked and autosomal suppressors, one might expect there to be a positive association among populations between the frequency of X<sup>D</sup> and these suppressors. In *D. mediopunctata*, two widely separated natural populations that have been examined are both polymorphic for X<sup>D</sup> and suppressors of drive (Carvalho et al. 1997). For *D. simulans* and *A. aegypti*, populations where driving sex chromosomes are present also have high levels of drive suppression (Atlan et al. 1997, Wood & Newton 1991). In *Drosophila paramelanica*, each of the two X<sup>D</sup> chromosome types (Northern and Southern) exhibits strong drive against the Y with which it is normally associated in natural populations (Stalker 1961). However, the Southern-type Y chromosome is capable of suppressing drive by the Northern-type X<sup>D</sup>, with which it rarely co-occurs. This pattern could have arisen as a result of the Southern-type Y excluding the Northern-type X<sup>D</sup> in areas where the Southern Y occurs. This raises the question of why the Southern Y does not spread into areas where the Northern X<sup>D</sup> and the drive-susceptible Northern Y occur. In *D. subobscura*, drive by the North African X<sup>D</sup> chromosome is stronger
when the Y and autosomes are also from North Africa than when they are from European populations (Hauschteck-Jungen 1990). Thus, it is not yet clear whether drive and suppressors of drive tend to be positively or negatively associated across populations. Such patterns may yield insights into the dynamics of these genetic arms races. The various species harboring resistant Y chromosomes provide excellent models for the study of Y chromosome polymorphism, which is generally expected to be rare (Clark 1987).

**EVOLUTION OF SEX-RATIO INVERSIONS**

In most species examined, \(X^D\) chromosomes differ from their standard, nondriving counterparts by one or more inversions. Drive is not due to a position effect, since the \(X^D\) chromosome of *D. persimilis* and the nondriving \(X^S\) of *D. pseudoobscura* have the same gene arrangement (Sturtevant & Dobzhansky 1936). Furthermore, in both *D. neotestacea* and *D. simulans*, the \(X^D\) and \(X^S\) chromosomes appear to be homosequential (James & Jaenike 1990, Cazemajor et al. 1997).

Unlike the situation for autosomal drive, association of an X-linked *sex-ratio* locus with an inversion is not necessary for the maintenance of linkage disequilibrium between the drive and responder loci. With the exception of *Aedes* and *Culex*, the X and Y chromosomes of the insect species considered here do not undergo recombination. Thus, inversions probably tie up several loci that together yield the drive characteristic of \(X^D\) chromosomes. Wu & Beckenbach (1983) clearly demonstrated that several loci are required for the expression of drive in *Drosophila persimilis*.

The evolution of SR inversions may have occurred via two selective paths. Thomson & Feldman (1975) showed that if fertility and viability are unaffected, an X chromosome with stronger drive will replace one with weaker drive. Suppose there exist several freely recombining X-linked *sex-ratio* loci, each with an allele exhibiting weak drive. If the drive effects are more or less additive across loci, then a chromosome in which two or more of these loci are tied up within a newly arisen inversion will be favored. Thus, a strongly driving \(X^D\) chromosome can evolve through the gradual recruitment of \(sr\) alleles that exhibit only weak drive individually. Similar ideas have been put forward by Sturtevant & Dobzhansky (1936) and Babcock & Anderson (1996). Cazemajor et al. (1997) have shown that X chromosome drive in *D. simulans* is probably due to the additive effects of two (or more) closely linked loci, which individually exhibit only partial drive.

Although this scenario may apply in some cases, several observations indicate that strong X drive is not always due to the additive effects of several weakly driving loci. First, the existence of strong drive in *D. neotestacea* and *D. simulans*, which lack SR inversions, indicates that one or a few closely linked loci are sufficient to achieve drive equivalent to that seen in other species with as many as five SR inversions. Second, in their genetic dissection of the sex-ratio trait in *D. persimilis*, Wu & Beckenbach (1983) found that all of the genetically marked chromosome regions were required for expression of drive: Individual chromosome
regions did not express even partial drive. This finding suggests that the different sex-ratio loci interact epistatically, rather than additively. In *D. pseudoobscura*, the SR gene arrangement of X<sup>D</sup> chromosomes differs from the ST gene arrangement of X<sup>S</sup> chromosomes by three inversions. Beckenbach (1996) discovered a very rare X chromosome type that carries only the terminal sex-ratio inversion, lacking the medial and subbasal inversions, and males carrying this X chromosome type sired normal offspring sex ratios. Another rare X chromosome type in this species lacks the terminal inversion but carries the other two. Males carrying this X chromosome type sire strongly female-biased progeny (Wallace 1948, Beckenbach 1996), indicating that a full complement of the SR inversions is not required for drive. Thus, in both *D. persimilis* and *D. pseudoobscura*, X chromosome drive results from something other than the additive effects of weak drive at individual loci.

Inversions might also be favored as a result of interactions between autosomal or Y-linked suppressors of drive and X-linked loci that counteract the effect of those suppressors (Jaenike 1996). According to this hypothesis, SR inversions would include one locus that drives against the Y plus other loci that prevent suppression of drive. Thus, drive would be expressed only if the primary drive locus as well as the suppressors-of-suppressors were present on an X<sup>D</sup> chromosome. This would account for the all-or-none drive of partial X<sup>D</sup> chromosomes of *D. persimilis* and *D. pseudoobscura* (Wu & Beckenbach 1983, Beckenbach 1996). This hypothesis is also consistent with the observation that the strength of drive is not correlated across species with the number of SR inversions. For instance, within the obscura group of *Drosophila*, effectively complete drive is associated with as few as one (*D. persimilis,* *D. affinis*) to as many as five (*D. athabasca*) inversions.

Regardless of how inversions evolved, once large blocks of the X<sup>D</sup> chromosome became tied up within inversions, the ST and SR gene arrangements would differ at numerous loci besides those affecting X chromosome drive. Some of these are likely to affect the fertility and viability of females, thus allowing maintenance of a sex-ratio polymorphism via the frequency-independent mechanism modeled by Edwards (1961) and Curtsinger & Feldman (1980). Thus, the maintenance of the polymorphism through this frequency-independent mechanism may be a derived condition, possibly requiring coevolution between the driving X<sup>D</sup> and the suppressors in the rest of the genome (Jaenike 1996).

**MACROEVOLUTION AND EXTINCTION**

The sporadic taxonomic distribution of X chromosome drive indicates that it has evolved on numerous occasions, although the phylogenetic limits of its occurrence remain to be determined. Within the genus *Drosophila*, the loci responsible for X chromosome drive probably differ among species. Chromosomal evolution in *Drosophila* has proceeded largely through fusions and inversions among six chromosomal elements (Patterson & Stone 1952). In *D. simulans* and many species of the subgenus *Drosophila*, including *D. neotestacea*, *D. quinaria*, and *D. medio-punctata*, any X-linked drive loci would be part of element A. In contrast, the SR
inversions of *D. pseudoobscura* and *D. persimilis* are located on the right arm of the X, which in these species is equivalent to element D (Patterson & Stone 1952). In *D. affinis* and *D. paramelanica*, the X^D^ chromosomes differ from X^S^ by inversions in both the right and left arms of the X, i.e., elements A and D (Stalker 1961). Thus, at least two distinct loci, or sets of loci, appear capable of causing X chromosome drive in *Drosophila*. Although a molecular analysis of X chromosome drive has not yet been conducted in any species, such studies could shed light on the number of genetically independent pathways by which such drive can evolve.

Once a driving X has evolved, it can persist for extended evolutionary periods. For instance, the sequence difference between ST- and SR-associated alleles of *Esterase-5* in *D. pseudoobscura*, which is located within one of the SR inversions, indicate a divergence time of about 1 million years (Babcock & Anderson 1996, Kovacevic & Schaeffer 2000). Based on mtDNA sequence data, Spicer & Jaenike (1996) estimate that *Drosophila quinaria* and *D. recens* split about 1.5 million years ago. The presence of X^D^ chromosomes in both of these species suggests that the sex-ratio polymorphism may be at least this old in the quinaria species group. Similarly, X^D^ chromosomes are present in two species of stalk-eyed flies, *Cyrtodiopsis dalmanni* and *C. whitei* (Presgraves et al. 1997), which molecular evidence indicates are sister species (Wilkinson et al. 1998a). Finally, the Eastern A and Eastern B semispecies of *Drosophila athabasca* share only one X chromosome gene arrangement, the multiple-inversion SR chromosome, showing that this driving X^D^ arose before these semispecies diverged (Yoon & Aquadro 1994). All of these findings indicate that once an X^D^ chromosome has invaded a species, it has the potential to persist for extended evolutionary periods. Because X drive can bring about intense intragenomic conflict, X^D^ chromosomes may impose major long-term selective pressures of the sort discussed in the introduction.

Although X^D^ chromosomes can persist for long periods, they may be much more ephemeral in many cases. An X^D^ chromosome could fail evolutionarily either because it did not spread within a population, or because it spread to fixation and caused population- or species-level extinction. Suppose the dynamics of X^D^ is initially governed by sperm depletion in multiply mated males and sperm competition within multiply mated females. If so, then some species may be more susceptible to invasion and spread of an X^D^ chromosome than others. For example, in a high-density species with frequent male and female mating, there could be strong selection against X^D^ from the outset, whereas a low-density species would be more susceptible to invasion by X^D^ (Jaenike 1996). Alternatively, consider the insemination reaction of *Drosophila*, whose effect is to prevent a female from remating for various lengths of time (Patterson 1946). If the insemination reaction reduces the average intensity of sperm competition within females, this could facilitate the spread of a driving X^D^ chromosome. These considerations suggest that species-level characteristics could influence the fate of a newly arisen sr allele.

At the other extreme, an X^D^ chromosome could fail to persist by spreading to high frequency, bringing about a critical deficiency of males and causing extinction. Carvalho & Vaz (1999) have argued that newly arisen X^D^ chromosomes
often will not have selection coefficients that lead to a stable polymorphism and, as a result, may spread to such a high frequency that population extinction is likely. Consequently, extant sex-ratio polymorphisms might represent only a select subset of all those that have arisen. In particular, only those $X^D$ chromosomes having substantial deleterious effects on their carriers will fail to spread to fixation. A sex-ratio polymorphism could also be stabilized by the evolution of suppressors. Thus, whether $X^D$ spreads to fixation or exists at a stable equilibrium could depend on how rapidly suppressors evolve. Carvalho & Vaz (1999) conclude that if $X^D$ chromosomes have fitness effects comparable to random X chromosomes in *Drosophila*, then it is likely that hundreds of *Drosophila* species have been driven extinct by the spread of $X^D$ chromosomes whose deleterious effects were too weak to stabilize the polymorphism.

Such extinction could bring about species-level selection for traits related to susceptibility to $sr$ invasion. Alternatively, an $sr$ allele may be stabilized at an intermediate frequency, resulting in an unequal population-level sex ratio and instigating a prolonged genetics arms race between the driving $X^D$ chromosome, the Y, and the autosomes. Because of these considerable effects—species-level selection and extended intragenomic conflicts—it is important to determine the range of taxa susceptible to sex chromosome drive and the factors that determine the dynamics of these chromosomes in natural populations.

ACKNOWLEDGMENTS

I would like to thank Anne Atlan, Bernardo Carvalho, Michael Clark, Jerry Coyne, Kelly Dyer, Hopi Hoekstra, Catherine Montchamp-Moreau, Allen Orr, Daven Presgraves, Doug Taylor, Jack Werren, Jerry Wilkinson, Diana Wolf, and Roger Wood for helpful comments. This work was supported by the National Science Foundation (grant DEB 9615065), the Underwood Fund (UK), and the NERC Centre for Population Biology, Imperial College at Silwood Park.

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