Evolution of Autosomal Suppression of the *Sex-Ratio* Trait in Drosophila

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ABSTRACT

The *sex-ratio* trait is the production of female-biased progenies due to X-linked meiotic drive in males of several Drosophila species. The driving X chromosome (called *SR*) is not fixed due to at least two stabilizing factors: natural selection (favoring *ST*, the nondriving *standard* X) and drive suppression by either Y-linked or autosomal genes. The evolution of autosomal suppression is explained by Fisher's principle, a mechanism of natural selection that leads to equal proportion of males and females in a sexually reproducing population. In fact, *sex-ratio* expression is partially suppressed by autosomal genes in at least three Drosophila species. The population genetics of this system is not completely understood. In this article we develop a mathematical model for the evolution of autosomal suppressors of *SR* (*sup* alleles) and show that: (i) an autosomal suppressor cannot invade when *SR* is very deleterious in males ($c < \frac{1}{3}$, where c is the fitness of *SR/Y* males); (ii) "*SR/ST, sup/+*" polymorphisms occur when *SR* is partially deleterious ($\sim 0.3 < c < 1$); while (iii) *SR* neutrality ($c = 1$) results in *sup* fixation and thus in total abolishment of drive. So, surprisingly, as long as there is any selection against *SR/Y* males, neutral autosomal suppressors will not be fixed. In that case, when a polymorphic equilibrium exists, the average female proportion in *SR/Y* males' progeny is given approximately by $(ac + 1 - a + \sqrt{a^2(c+1)^2 + 1 - 4ac})/4ac$, where a is the fitness of *SR/ST* females.

MENDEL'S first law states that heterozygotes produce equal proportions of the two gamete types. This equality results from the meiotic segregation of gene pairs during gamete formation. Yet several genetic elements have been found to violate Mendelian transmission by actively biasing segregation in their favor. The best-studied example of segregation distortion was first recorded by Gershenson (1928) and later named meiotic drive by Sandler and Novitski (1957).

The *sex-ratio* trait known in 12 Drosophila species is a case of meiotic drive in the sex chromosomes. Males carrying certain X chromosomes, called *SR*, produce female-biased progenies due to the degeneration of Y-bearing sperm. The effect of drive in sexual proportion has important evolutionary consequences. The driving X (*SR*) has a transmission advantage over nondriving X (*ST*, for *standard*) so one can expect *SR* fixation followed by population extinction due to the lack of males (Gershenson 1928; Hamilton 1967; reviewed in Carvalho and Vaz 1999; Jaenike 2001). However, *SR* frequency in natural populations is usually low and stable (Dobzhansky 1958). In *Drosophila mediopunctata*, for example, *SR* frequency remained between 13 and 20% for 10 years (A. B. Carvalho, M. D. Vibranovski and S. C. Vaz, unpublished data). At least two factors seem to be responsible for the stabilization of *SR/ST* polymorphisms in natural populations: natural selection and drive suppression by modifier genes.

Fitness measurements have been made mainly in *D. pseudoobscura*. The main findings from these experimental studies are that *SR/Y* males have lower fertility and/or viability than *ST/Y* males and that *SR/SR* female homozygosis is highly deleterious (Wallace 1948; Curtsinger and Feldman 1980; Beckenbach 1996). There are also indications of *SR/ST* female overdominance (Gebhardt and Anderson 1993). Edwards (1961) and Curtsinger and Feldman (1980) carried out mathematical studies with *sex-ratio* models showing that the stabilization of X polymorphism under meiotic drive is possible under a wide range of fitness values. Thus, experimental and theoretical investigations support the idea that *SR* drive is counterbalanced by *SR* deleterious effects on individual fitness, resulting in *SR/ST* polymorphism.

Another stabilizing mechanism may be provided by autosomal or Y-linked drive suppressors. Suppressors are genes that restore the Mendelian transmission by neutralizing the effect of genes responsible for meiotic drive (Stalker 1961; Hamilton 1967; Thomson and Feldman 1975). The spread of Y-linked suppressors of *sex-ratio* in *SR*-bearing populations can be explained by meiotic drive theory: any Y-linked gene that increases the transmission rate of the Y chromosome (as does a *sex-ratio* suppressor) is directly favored. Therefore, Y-linked suppressors are expected to run to fixation unless they are deleterious (Clark 1987; Carvalho *et al.* 1997).

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Autosomal suppressors of *sex-ratio* are expected to evolve in response to *SR* because of a notably simple mechanism known as Fisher's (1930) principle (reviewed in Bull and Charnov 1988). Fisher's argument can be put as follows. In any sexually reproducing population, half of the genes come from each sex, regardless of the population sexual proportion. If the genetic system generates excess of one sex (as does the *sex-ratio* trait), the rare sex will be effectively more fertile as a result of a greater *per capita* contribution to the next generation. So, the rare sex has a selective advantage. If sexual proportion is a hereditary trait, then alleles directing the progeny sexual proportion to the rare sex (the males, in the case of *sex-ratio*) are expected to invade the population. These alleles should spread until the equilibrium of equal number of males and females is reached. This mechanism of natural selection is the most accepted explanation for the commonness of the 1:1 sexual proportion in nature (Bull and Charnov 1988). When parental expenditure is different between sexes, Fisher (1930) suggested that the sex ratio evolves to a value such that expenditure is equalized between male and female offspring. A clear theoretical demonstration of Fisher's principle under this circumstance was provided by Uyenoyama and Bengtsson (1979). A clear experimental demonstration of Fisher's principle was carried out by Carvalho *et al.* (1998) in a study with *D. mediopunctata*. They founded populations fixed for *SR* and thus with female excess. The proportion of males rose from 16 to 32% in 49 generations due to the accumulation of *sex-ratio* autosomal suppressors. This work demonstrated that sexual proportion actually responds to natural selection as postulated by Fisher (see also Conover and Van Voorhees 1990; Basolo 1994).

As expected by theory, autosomal suppressors have been found in some *SR*-bearing Drosophila populations. In *D. mediopunctata* there are at least four suppressor genes in different chromosomes (Carvalho and Klaczko 1993). Female proportion averages 95.1% in a suppressor-free strain and 51.7% in a strain full of suppressors, while in a hybrid strain the average is 72.3% (n = 6, 5, and 7 *SR/Y* males, respectively; Carvalho and Klaczko 1993, Table 1). Hence, there seems to be no dominance in expression, although the experimental design would not detect fully recessive suppressors. In *D. simulans* suppression seems to be partially recessive in the two main chromosomes (Cazemajor *et al.* 1997). Autosomal suppression also seems to be present in *D. quinaria* (Jaenike 1999) and *D. paramelanica* (Stalker 1961).

D. pseudoobscura is an interesting exception. No Y-linked or autosomal *sex-ratio* suppressor was ever found in this species despite directed search (Policansky and Dempsey 1978; Beckenbach *et al.* 1982). Wu (1983) investigated this fact with a mathematical model for the evolution of autosomal suppressors. He showed that a neutral suppressor (*i.e.*, that suppresses meiotic drive but has no fitness effect) is not expected to invade a *SR*-bearing population if the fitness of *SR/Y* males is $< \sim 0.3$ in relation to *ST/Y* males (in that case the stabilization of a "*SR/ST*" polymorphism requires female overdominance). So, according to this model a very low viability and/or fertility of *SR/Y* males can explain the absence of suppressors in *D. pseudoobscura*. It remains to be shown what happens when fitness configurations allow the initial spread of these suppressors. Will they remain polymorphic as suggested by Varandas *et al.* (1997, Figure 5) or will they run to fixation?

In this article we develop and study a theoretical model for the evolution of *sex-ratio* autosomal suppressors. Numerical simulations show three possible outcomes for a neutral suppressor in a population with *SR/ST* polymorphism: (i) noninvasion, (ii) polymorphism, and (iii) fixation. Through mathematical analysis we define the stability conditions for the two trivial equilibria (noninvasion and fixation) whereas the polymorphic equilibrium was studied mainly with simulations. Two results can be outlined. First, meiotic drive in a polymorphic equilibrium ($\hat{t}$, defined as the average female proportion in *SR/Y* males progeny) is given by $\hat{t} \sim (ac + 1 - a + \sqrt{a^2(c+1)^2 + 1 - 4ac})/4ac$ (where a and c are the fitness of *SR/ST* females and *SR/Y* males, respectively) and, since drive is a known parameter from natural populations, estimates for fitness combinations can be made from the above formula. Second, as long as there is selection against *SR/Y* males ($\frac{1}{3} < c < 1$), neutral autosomal suppressors always remain polymorphic; this result contrasts with the dynamics of Y-linked suppressors, expected to run to fixation unless they are deleterious. These conclusions are relevant for the understanding of naturally occurring *sex-ratio* polymorphisms in Drosophila.

THE MODEL

The model we describe below represents a typical *sex-ratio* system with natural selection on males and females and meiotic drive restricted to X sperm excess in *SR/Y* males. It follows the usual assumptions of population genetics modeling: random mating, large population size, nonoverlapping generations, and constant selection coefficients. Fitness is given by the egg-to-adult viability component (*sex-ratio* models including fecundity selection produce the same general results as viability models; Curtsinger and Feldman 1980). In accordance with Edwards' (1961) notation, a, b, and c refer to the fitness of *ST/SR*, *SR/SR*, and *SR/Y* genotypes, respectively, relative to the fitness of *ST/Y* and *ST/ST*, which are set to 1. *Sex-ratio* expression in *SR/Y* males depends on an autosomal locus that affects the sexual proportion only: *sup* denotes the suppressor allele and "+" is the wild-type nonsuppressor allele. We assumed absence of dominance in suppression, which is somewhat simpler to study and seems to be the case in *D.*

TABLE 1

Selection coefficients and drive values

	Females			Males			
					SR/Y		
Genotype:	*ST/ST*	*ST/SR*	*SR/SR*	*ST/Y*	+/+	+/*sup*	*sup/sup*
Viability	1	*a*	*b*	1	*c*	*c*	*c*
Meiotic drive (proportion of X sperm)	—	—	—	½	1	¾	½

mediopunctata (Carvalho and Klaczko 1993). Males with the +/+ genotype produce 100% of X-bearing sperm, +/*sup* males produce 75%, and totally suppressed *sup/sup* males produce 50% (see Table 1; numerical simulations assuming other dominance relations produced essentially the same results). The *sup* allele is not expressed in females or *ST/Y* males. Autosomal suppression in *D. mediopunctata* and *D. simulans* is known to be polygenic; however, a monogenic model simplifies the problem considerably. Besides, monogenic and polygenic models on the evolution of sexual proportion (Nur 1974; Bulmer and Bull 1982) predict the same evolutionary rate and the same sexual proportion in the equilibrium (Carvalho *et al.* 1998, pp. 729–730).

Let the frequency of *SR* chromosomes be given by p while the frequency of *ST* chromosomes is $1 - p$. The frequency of *sup* is r and that of the nonsuppressor allele (+) is $1 - r$. The p and r variables are listed in Table 2.

The complete system consists of eight recurrence equations (for p_e, p_s, p_m, r_{e1}, r_{e2}, r_{s1}, r_{s2}, and r_{sY}) deduced in appendix a.

We used these equations in the numerical simulations and stability analysis described in the next sections. Our aim is to answer if it is possible to maintain *SR/ST, sup/+* polymorphism and, in this case, verify the fitness conditions (a, b, and c parameter values, see Table 1) in which it happens.

NUMERICAL SIMULATIONS

Numerical simulations covering a biologically meaningful set of the $a \times c$ parametric space were carried out. Each value of c between 0 and 1.5 with a 0.01 interval was tested with each value of a between 0 and 3 with the same interval. Initial allele frequencies set to either 0.01 or 0.99 converged to the same equilibrium point (the system was considered to be in equilibrium when all allele frequencies varied $<10^{-5}$ in one generation). The results of the $a \times c$ scanning for two different values of b are shown in Figure 1. When there is *SR/ST* polymorphism, there are three possible fates for the autosomal suppressor depending on *SR* fitness values: *sup* does not invade ($r = 0$; *SR/ST,* + equilibrium), *sup* invades but is not fixed (r between 0 and 1; *SR/ST, sup/+* polymorphism), and *sup* invades and is fixed ($r = 1$; *SR/ST, sup* equilibrium). Some important observations can be made: (i) *sup* does not invade when c is very low ($< \sim 0.3$), as shown by Wu (1983); (ii) when *sup* invades it is not fixed when there is any selection against *SR/Y* males ($c < 1$); and (iii) *SR/ST, sup/+* polymorphisms occur when $a > 1$ only, *i.e.*, when there is overdominance. These results suggest a role for selection against *SR/Y* males and female overdominance in species that are polymorphic for X and autosomal alleles (*e.g.*, *D. mediopunctata* and *D. simulans*).

Figure 2 shows the relation between $\hat{t}$, the equilibrium value of the drive parameter t, and each of the selection coefficients: a, b, and c, the three variables of our model. Note that $\hat{t}$ is a linear function of *sup* frequency (see Equation A11).

It is clear from Figure 2 that c is the parameter with the greatest effect on the value of $\hat{t}$. Biologically, it means that suppressor frequency in the population and thus

TABLE 2

Variables definition

Variable	Definition
t	Meiotic drive[a]
	SR frequency
p_s	In X sperm
p_e	In eggs
p_m	In male adults
p_f	In female adults
	Suppressor (*sup*) frequency
r_{s1}	In *SR* sperm
r_{s2}	In *ST* sperm
r_{sY}	In Y sperm
r_{e1}	In *SR* eggs
r_{e2}	In *ST* eggs
r_{m1}	In *SR/Y* males[b]
r_{m2}	In *ST/Y* males[b]
r_{f11}	In *SR/SR* females[b]
r_{f12}	In *ST/SR* females[b]
r_{f22}	In *ST/ST* females[b]

[a] Proportion of X-bearing sperm from *SR/Y* males.
[b] Frequencies are identical in zygote and adult phases (see appendix a).

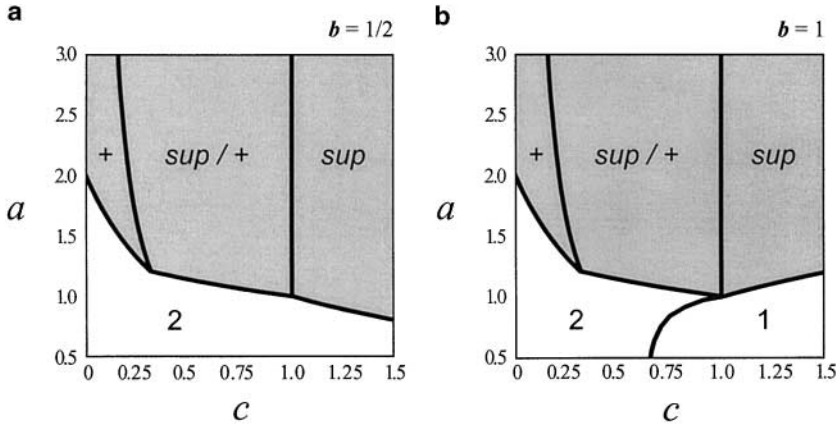

FIGURE 1.—Numerical simulations with a model for *sex-ratio* autosomal suppression. The parameters *a*, *b*, and *c* are the fitnesses of *ST/SR*, *SR/SR*, and *SR/Y* genotypes, respectively. (a) $b = \frac{1}{2}$. (b) $b = 1$. *SR/ST* polymorphisms occur for *a* and *c* values in the shaded space. An autosomal suppressor does not invade the population in the region denoted by +, remains polymorphic in the *sup*/+ region, and is fixed in the *sup* region. Region 1 is *SR* fixation (with fixed *sup*) and region 2 is *ST* fixation (with *sup*/+ neutral polymorphism).

drive intensity in *SR/Y* males are basically determined by the degree of selection against these males. As selection becomes less intense (high *c* values) *sup* frequency rises up to the point where no selection ($c = 1$) results in a totally suppressed drive (fixed *sup* and $\hat{t} = \frac{1}{2}$; see Figures 1 and 2c). It should be noted that the male proportion in the equilibrium (*Mz*, see Equation A5), is always close to 0.5 in the cases of *SR/ST, sup/+* polymorphism (it varied from ~0.46 to 0.50 in the numerical simulations). The explanation for this small variation of *Mz*, in spite of $\hat{t}$ varying from 0.5 to 1, is that when *SR* frequency is high, *sup* frequency is also high (not shown).

EQUILIBRIUM FREQUENCIES

Numerical simulations indicate that it is possible to maintain a polymorphism for a neutral autosomal suppressor in a *SR*-bearing population. The suppressor equilibrium frequency (and the intensity of drive) is a function of selection coefficients, where *c* has the strongest effect. But what function is it? A formula for $\hat{t}$ would be very useful because drive is easy to measure in natural populations. Take *D. mediopunctata* as an example: it would be interesting to predict fitness configurations that result in $\hat{t} = 0.78$, the average female proportion in the progenies of *SR/Y* males from a natural population (VARANDAS *et al.* 1997).

***SR* equilibrium frequency:** The equilibrium frequency of *SR*, as a function of constant selection coefficients and meiotic drive in the absence of suppression, was first obtained by EDWARDS (1961; see also STABILITY OF EQUILIBRIA).

The equilibrium frequencies of *SR* can be obtained in our model by equating $p'_s = p_s = \hat{p}_s$, $p'_m = p_m = \hat{p}_m$, and $p'_e = p_e = \hat{p}_e$ (see Table 2 for variables definitions). The system of equations (Equations A2, A3, A4, and A6) has two trivial solutions ($\hat{p} = 0$ and $\hat{p} = 1$) and a third one,

$$\hat{p}_e = \hat{p}_f = \frac{V_1}{2V_1 + V_2}, \quad \hat{p}_m = \frac{cV_1}{(c+1)V_1 + V_2}, \quad \hat{p}_s = \frac{2c\hat{t}V_1}{(2c\hat{t}+1)V_1 + V_2}, \tag{1}$$

where $V_1 = 2ac\hat{t} + a - 2$ and $V_2 = 2 - 4bc\hat{t}$.

Equations 1 agree with Edwards' results, where $\hat{t}$ corre-

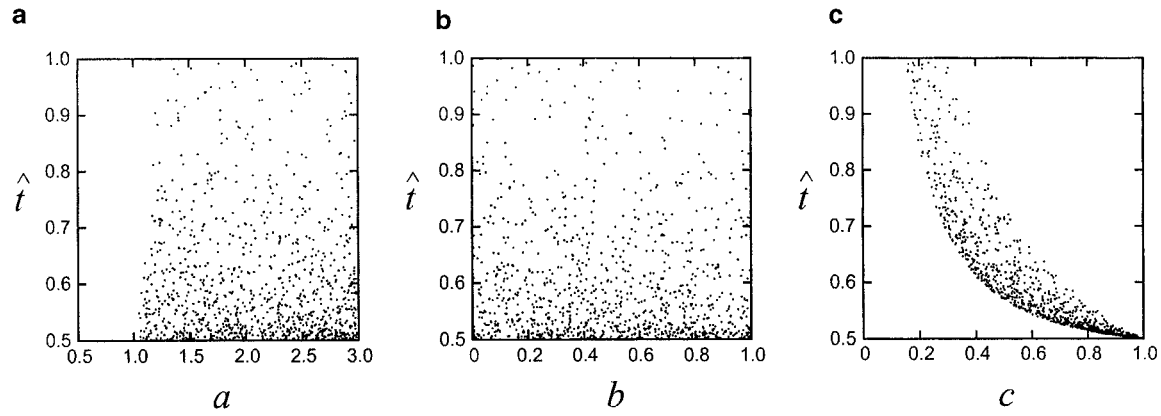

FIGURE 2.—Numerical simulations with a model for *sex-ratio* autosomal suppression. The points represent 1000 random fitness combinations that result in *SR/ST, sup/+* polymorphism. The parameters *a*, *b*, and *c* are the fitnesses of *ST/SR*, *SR/SR*, and *SR/Y* genotypes, respectively. $\hat{t}$ is the equilibrium value of the drive parameter *t* ($\hat{t} = 1 - \frac{1}{2}\hat{r}_{m1}$, see Equation A11). (a) $\hat{t}$ as a function of *a*; (b) $\hat{t}$ as a function of *b*; (c) $\hat{t}$ as a function of *c*.

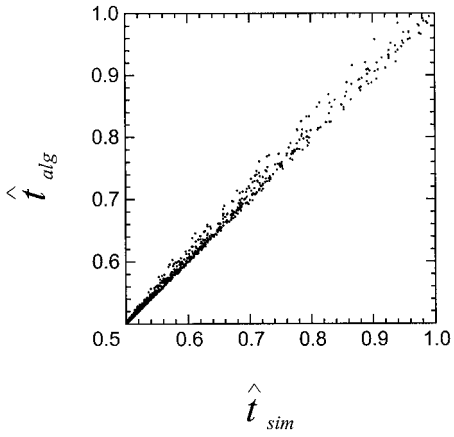

FIGURE 3.—Comparison between simulated and algebraically estimated meiotic drives under autosomal suppression ($\hat{t}_{sim}$ and $\hat{t}_{alg}$, respectively). $\hat{t}_{sim}$ was obtained by iterating the recurrence equations (A3, A4, A6, A9, A10, A12, A13, and A14) until an equilibrium was attained, with 1000 random values for the parameters a (between 0 and 3), b (0–1), and c (0–1) that resulted in *SR/ST, sup/+* polymorphism. $\hat{t}_{alg}$ is the value of $\hat{t}$ given by the formula $(ac + 1 - a + \sqrt{a^2(c+1)^2 + 1 - 4ac})/4ac$ (see Equation 2), with the same set of a and c values used in the simulations. Note that we also carried out simulations with $b = 0$ (not shown) and in this case $\hat{t}_{sim}$ matches perfectly with $\hat{t}_{alg}$, confirming that the small discrepancy between them in the figure is due solely to the assumption $b = 0$, used to obtain the formula for $\hat{t}_{alg}$.

sponds to a fixed-drive parameter. This parameter is not constant in our model but dependent on suppressor frequency (see Equation A11).

Suppressor equilibrium frequency: Numerical simulations indicate that the value of b (when between 0 and 1) has practically no influence on the equilibrium value of t ($\hat{t}$; see Figure 2b). This result suggested that we could simplify the algebraic solution assuming $b = 0$. A direct approach to obtain the equilibrium frequencies would be to solve the five-equation system (setting $r' = r = \hat{r}$ for all five recurrence equations—A9, A10, A12, A13, and A14—and substituting p with $\hat{p}$ for the four p variables given in Equations 1, where $\hat{t} = 1 - \frac{1}{4}(\hat{r}_{e1} + \hat{r}_{sY})$; see Table 2 for the variables listing). A straightforward solution was not possible so we solved the problem by reducing the system step-by-step with the help of *Maple* computer software (not shown). The solutions we found for $\hat{t}$ are ½, 1, and

$$\hat{t} = \frac{ac + 1 - a + \sqrt{a^2(c+1)^2 + 1 - 4ac}}{4ac}. \quad (2)$$

Given $\hat{r}_{m1} = 2 - 2\hat{t}$ (from Equation A11), the suppressor equilibrium frequency in *SR/Y* males is

$$\hat{r}_{m1} = \frac{3ac - 1 + a - \sqrt{a^2(c+1)^2 + 1 - 4ac}}{2ac}.$$

Figure 3 compares the algebraic value of $\hat{t}$ ($\hat{t}_{alg}$, given by the formula in Equation 2) to the true value of $\hat{t}$ (suggested by $\hat{t}_{sim}$, obtained from 1000 computer simulations with b varying from 0 to 1). The estimate given by Equation 2, which used the simplification $b = 0$, slightly overestimates the true value of $\hat{t}$ but provides an excellent approximation since $\hat{t}_{sim}$ and $\hat{t}_{alg}$ are highly correlated ($r = 0.998$; $p \ll 10^{-3}$). The accuracy of our algebraic solution was confirmed by simulations with $b = 0$ where the values of $\hat{t}_{sim}$ had a perfect match with those predicted by $\hat{t}_{alg}$ (not shown). Thus, we can safely affirm that the expression $(ac + 1 - a + \sqrt{a^2(c+1)^2 + 1 - 4ac})/4ac$ is a very good estimate of $\hat{t}$ for any value of b between 0 and 1. Note that this interval ($0 < b < 1$), implying selection against *SR/SR* females, is the biologically meaningful range for this parameter (WALLACE 1948; CURTSINGER and FELDMAN 1980; BECKENBACH 1996).

STABILITY OF EQUILIBRIA

In this section we apply a stability analysis to outline the conditions for the two trivial equilibria (+ and *sup*). Next, we deduce the conditions for the polymorphic equilibrium (*sup/+*) with the help of numerical simulations. In other words, we find the mathematical functions for the boundaries shown in Figure 1.

The *SR/ST* polymorphism: EDWARDS' (1961) theoretical studies showed that the ratio between *SR* and *ST* equilibrium frequencies in adult females in the case of polymorphism is equal to $[a(2ct + 1) - 2]/[a(2ct + 1) - 4bct]$ and that stable *SR/ST* polymorphisms occur when both numerator and denominator of the expression are greater than zero:

$$a > 2/(2ct + 1) \quad (3)$$

$$a > 4bct/(2ct + 1). \quad (4)$$

Note that if $bct > \frac{1}{2}$ the determining condition is (4). If $bct < \frac{1}{2}$ the determining condition is (3) and in this case the polymorphism stability does not depend on b.

Suppressor noninvasion: The equilibrium corresponding to a population bearing X polymorphism with no *sex-ratio* suppression (*i.e.*, full drive expression) is referred to as *SR/ST, +*. A natural example could be *D. pseudoobscura*.

Numerical simulations suggested that there is no difference between the boundaries of the *SR/ST, +* equilibrium in the cases where $b = 1$ and $b = \frac{1}{2}$ (see Figure 1). Besides, since c has a very low value in this equilibrium ($c < \sim 0.3$) and since $\hat{t} = 1$ and b is between 0 and 1, we know that $bc\hat{t} < \frac{1}{2}$. Consequently, the stability condition of *SR/ST* polymorphisms is given by (3), which does not depend on b. Then, to simplify the problem, we could assume $b = 0$ in the analysis detailed in APPENDIX B. In short, the analysis consisted in applying the *Perron-Frobenius* theorem (ORTEGA 1987) for nonnegative matrices, which allows one to set the eigenvalue equal to 1 ($\lambda = 1$) to find the stability boundaries. By setting $\lambda = 1$ in the characteristic equation of

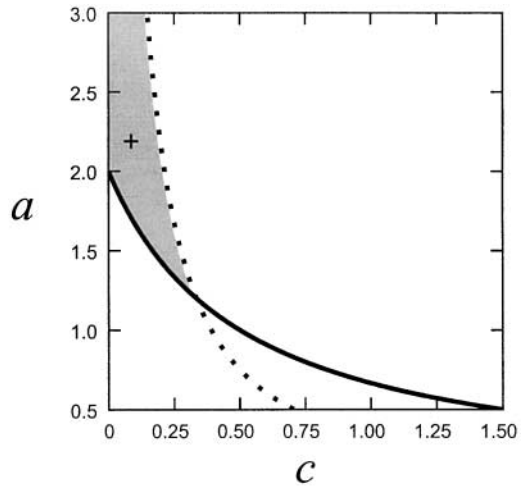

FIGURE 4.—Stability analysis of a model for *sex-ratio* autosomal suppression: suppressor noninvasion (*SR/ST,* + equilibrium). The parameters a and c are the fitnesses of *ST/SR* and *SR/Y* genotypes, respectively. The *SR/ST,* + equilibrium is stable when $a > 2/(2c + 1)$ (solid line) and $a < (c + 1)/[2c(2c + 1)]$ (dotted line).

the *SR/ST,* + Jacobian matrix we find the following solutions: $c = 0$, $a = 2/(2c + 1)$, and $a = (c + 1)/[2c(2c + 1)]$.

Figure 1 indicates the boundaries of *SR/ST,* + equilibria according to numerical simulations. In fact, the curves limiting this equilibrium are the two nontrivial solutions obtained with $\lambda = 1$ (see Figure 4). Thus, the *SR/ST,* + equilibrium is predicted when

$$a > \frac{2}{2c + 1} \tag{5}$$

and

$$a < \frac{c + 1}{2c(2c + 1)}. \tag{6}$$

Regarding the condition in (5), note that $a > 2/(2c + 1)$ is the *SR/ST* polymorphism stability condition when $bct < \frac{1}{2}$ [see (3) for $t = 1$]. In fact, $bct < \frac{1}{2}$ always holds for *SR/ST,* + equilibria since here $t = 1$, $b < 1$, and c is very low ($< \sim 0.3$). In short, *SR/ST,* + equilibria depend on two basic conditions: stability of the *SR/ST* polymorphism [in (5)] and stability of the + allele fixation [in (6)].

Wu's (1983) studies showed that the noninvasion of a suppressor allele requires strong selection against *SR/Y* males and *SR/ST* female overdominance ($c < \sim 0.3$ and $a > 1$). Our findings agree with and extend those previous results. The above analysis allows the formal deduction of Wu's conditions, as follows. In accordance with (5) and (6) (and knowing that a and c are positive) we have $2/(2c + 1) < (c + 1)/[2c(2c + 1)] \Rightarrow c < \frac{1}{3}$. Therefore, the upper limit of c is $c_{max} = \frac{1}{3}$. And, since $a > 2/(2c + 1)$, the lower limit of a can be calculated: $a_{min} = 2/(2c_{max} + 1) = 1.2$.

Suppressor fixation: The *SR/ST, sup* equilibrium corresponds to a *SR/ST* population with a totally suppressed *SR* ($\hat{t} = \frac{1}{2}$). CARVALHO and VAZ (1999) suggest that Y-linked suppressors are in fact fixed in some populations and, therefore, *SR* remains undetectable (no *sex-ratio* phenotype). It is possible that the same happens with autosomal suppressors. As we can see in Figure 1, suppressor fixation occurs when $c \geq 1$ (when $c = 1$ *sup* frequency reaches 100% very slowly).

The analysis for this equilibrium also consisted in setting the eigenvalue equal to 1 ($\lambda = 1$) as allowed by Perron-Frobenius theorem for all-positive matrices (APPENDIX B). In addition to four nonrelevant solutions there are three from which we find the stability boundary conditions:

$$c = 1 \tag{7}$$

$$a = \frac{2bc}{c + 1} \tag{8}$$

$$a = \frac{2}{c + 1}. \tag{9}$$

The solutions obtained in Equations 8 and 9 represent the *SR/ST* polymorphism stability boundaries, which can be demonstrated as follows. In this equilibrium *sex-ratio* is totally suppressed so $\hat{t} = \frac{1}{2}$. We know that if $bct > \frac{1}{2}$ (*i.e.*, $bc > 1$), the condition determining the *SR/ST* polymorphism is given by (4). It can be simplified to $a > 2bc/(c + 1)$ for $t = \frac{1}{2}$. If $bct < \frac{1}{2}$ (*i.e.*, $bc < 1$) stability is determined by (3) that (given $t = \frac{1}{2}$) simplifies to $a > 2/(c + 1)$.

We assumed $bc < 1$, which seems compatible with biological values for b. The equations limiting the *SR/ST, sup* parametric space are (7) and (9) (Figure 5). Therefore, the *SR/ST, sup* equilibrium is stable provided that $c > 1$ and $a > 2/(c + 1)$.

In short, the *SR/ST, sup* equilibrium depends on two basic conditions: the stability of the *SR/ST* polymorphism [$a > 2/(c + 1)$, for $bc < 1$] and the stability of the *sup* allele fixation ($c > 1$).

Polymorphism: This equilibrium may represent *D. mediopunctata*, *D. simulans*, and other species known to be polymorphic for *sex-ratio* autosomal suppressors. We can observe from Figure 1 that the double polymorphism occurs when there is overdominance ($a > 1$) and selection against *SR/Y* males (c between ~ 0.3 and 1).

The Jacobian elements for the *SR/ST, sup/+* equilibrium are functions of suppressor equilibrium frequencies (the $\hat{r}$ variables) and these happen to be quite extended polynomials in a and c (not shown). Therefore, we could not solve the characteristic equation and perform a formal stability analysis for this equilibrium. However, the boundaries for a preserved polymorphism can be inferred from our previous analysis on *sup* noninva-

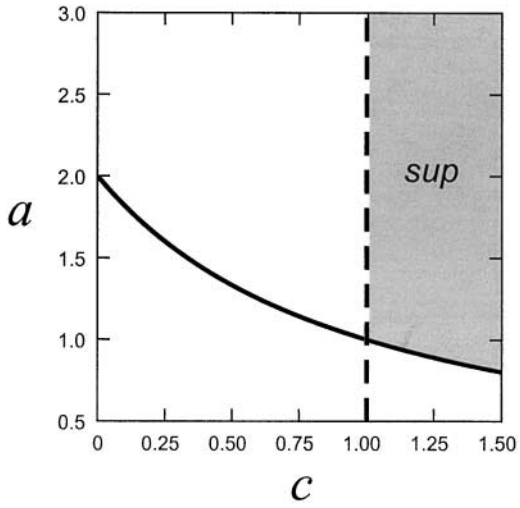

FIGURE 5.—Stability analysis of a model for *sex-ratio* autosomal suppression: suppressor fixation (*SR/ST, sup* equilibrium) for $bc < 1$. The parameters *a*, *b*, and *c* are the fitnesses of *ST/SR*, *SR/SR*, and *SR/Y* genotypes, respectively. The *SR/ST, sup* equilibrium is stable when $c > 1$ (dashed line) and $a > 2/(c + 1)$ (solid line).

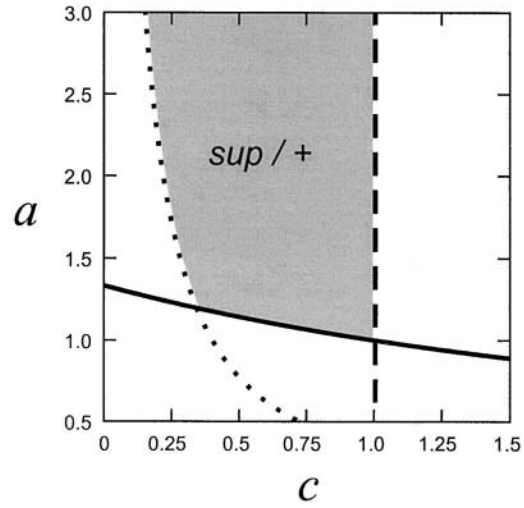

FIGURE 6.—Stability analysis of a model for *sex-ratio* autosomal suppression: polymorphism (*SR/ST, sup/+* equilibrium). The parameters *a* and *c* are the fitnesses of *ST/SR* and *SR/Y* genotypes, respectively. The *SR/ST, sup/+* equilibrium is stable when $c < 1$ (dashed line), $a > (c + 1)/[2c(2c + 1)]$ (dotted line), and $a > 4/(c + 3)$ (solid line).

sion and *sup* fixation (where $\hat{r}$ could be set to 0 or 1) and from our simulation results (Figure 1). The *SR/ST, sup/+* equilibrium is found between + and *sup* trivial equilibria. The first boundary of the polymorphism is that of the suppressor invasion: $a > (c + 1)/[2c(2c + 1)]$ [obtained from the noninvasion condition in (6) with the simplification $b = 0$]. The second boundary ($c < 1$) is obtained from the suppressor fixation condition [in (7)]. The third and last boundary should be the stability condition of *SR/ST* polymorphisms. In fact, it can be obtained as follows. First, we verified by simulations that *SR/ST, sup/+* polymorphisms occur in the space where $bct < \frac{1}{2}$ (when *b* ranges between 0 and 1; not shown). Therefore, the stability condition for the X polymorphism is given by (3): $a > 2/(2ct + 1)$. If we substitute *t* for the formula we found for $\hat{t}$ in Equation 2 and solve $a > 2/(2c\hat{t} + 1)$ for *a*, we obtain the surprisingly simple expression: $a > 4/(c + 3)$.

Figure 6 summarizes the results for the *SR/ST, sup/+* equilibrium. Note that conditions $c < 1$ and $a > 4/(c + 3)$ imply $a > 1$, *i.e.*, *SR/ST* female overdominance. Table 3 outlines the analysis results for all equilibria.

TABLE 3

Stability analysis of a *sex-ratio* model with autosomal suppression

Equilibrium	Stability conditions
Suppressor noninvasion (+)	$a < \dfrac{c + 1}{2c(2c + 1)}$ and $a > \dfrac{2}{2c + 1}$*
Polymorphism (*sup/+*)	$c < 1$, $a > \dfrac{c + 1}{2c(2c + 1)}$, $a > \dfrac{4}{c + 3}$*
Suppressor fixation (*sup*)	$c > 1$, $a > \dfrac{2bc}{c + 1}$**, $a > \dfrac{2}{c + 1}$*

The parameters *a*, *b*, and *c* are the fitnesses of *ST/SR*, *SR/SR*, and *SR/Y* individuals, respectively. *Stability of the *SR/ST* polymorphism; **stability of the *SR/ST* polymorphism for $bc > 1$.

DISCUSSION

Autosomal suppressors of *sex-ratio* were first investigated in theory by WU (1983) who demonstrated that they are not expected to spread under some fitness configurations. He aimed to explain the absence of suppression in *D. pseudoobscura*. In this work we developed a different model to study the evolution of these suppressors in Drosophila. We showed that an invading suppressor either remains polymorphic or runs to fixation. Essentially, a preserved polymorphism occurs when *SR* is deleterious in males ($c < 1$) and suppressor fixation occurs when *SR* is neutral or positively selected ($c \geq 1$). Our main conclusions are (i) a polymorphism for suppression can be preserved even if the suppressor allele is neutral in fitness; (ii) the conditions for this preserved polymorphism (*SR/ST, sup/+* equilibrium) are $a > (c + 1)/[2c(2c + 1)]$, $a > 4/(c + 3)$, and $c < 1$, where *a* and *c* are the *ST/SR* female and *SR/Y* male selection coefficients, respectively; and (iii) the meiotic drive in the equilibrium (*i.e.*, the average female proportion in *SR/Y* males progeny) is given by $\hat{t} \sim (ac + 1 - a + \sqrt{a^2(c + 1)^2 + 1 - 4ac})/4ac$.

Experimental *vs.* theoretical data: Three species bear sufficient data to weigh against our theoretical results:

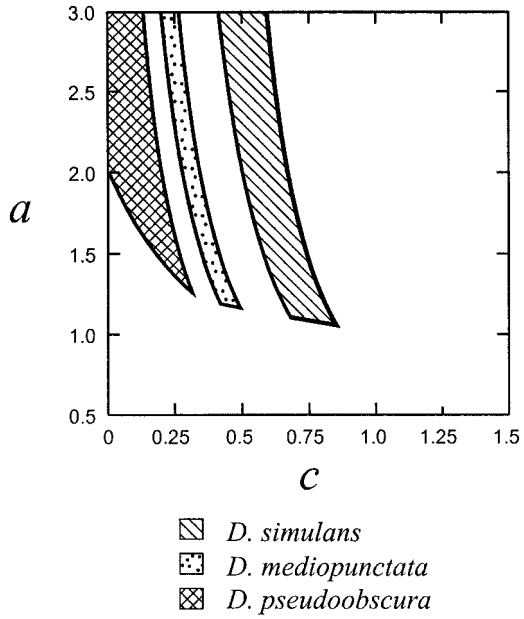

FIGURE 7.—Fitness configurations compatible with meiotic drive data for natural populations of Drosophila. The parameters a and c are the fitnesses of *ST/SR* and *SR/Y* genotypes, respectively. Simulations were carried out with the formula $\hat{t} = (ac + 1 - a + \sqrt{a^2(c+1)^2 + 1 - 4ac})/4ac$ (Equation 2), selecting a and c values that resulted in a given range of $\hat{t}$. In *D. simulans*, $0.55 < \hat{t} < 0.60$. For this range, the frequency of *SR* in male adults ($\hat{p}_m$; see Equation 1) is between 1 and 30% in the simulations. In *D. mediopunctata* $0.75 < \hat{t} < 0.80$. For this range, $\hat{p}_m$ is between 3 and 13%. In *D. pseudoobscura*, $\hat{t} = 1$ and $\hat{p}_m$ varied from 1 to 8%.

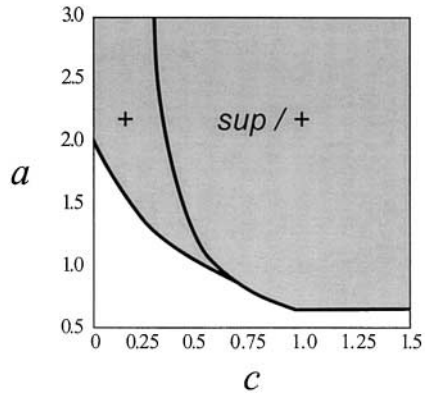

FIGURE 8.—Numerical simulations with a model for deleterious autosomal suppressors. This figure should be compared to Figure 1a. Recurrence equations different from those used to produce Figure 1 were developed to include selection against *sup*. The fitness parameters a, b (set to ½), and c are defined in Table 1 with the difference that the fitness of males with the *sup/+* and *sup/sup* genotypes was multiplied by 0.99 and 0.98, respectively. *SR/ST* polymorphisms occur for a and c values in the shaded space. Autosomal suppressors do not invade the population in the region denoted by + and there is polymorphism in the *sup/+* region. The open region represents *SR* or *ST* fixation.

D. mediopunctata, *D. simulans*, and *D. pseudoobscura*. Such comparison is based on the assumption that our model is valid for them, in particular that autosomal suppressors are neutral (see *Limitations of the model*). The first two species harbor *SR/ST, sup/+* polymorphisms (CARVALHO and KLACZKO 1993; CAZEMAJOR *et al.* 1997), while *D. pseudoobscura* lacks suppression (POLICANSKY and DEMPSEY 1978; BECKENBACH *et al.* 1982). *D. mediopunctata SR/Y* males sire progenies with 78% of females on average ($t \sim 0.78$; VARANDAS *et al.* 1997). Figure 7 presents fitness combinations from simulations resulting in $\hat{t}$ values compatible with this species (dotted region). The polymorphism in this case occurs when $\sim 0.2 < c < \sim 0.5$ and $a > \sim 1.2$. Regarding *D. simulans*, *SR*-bearing populations differ in *SR* frequency but drive expression is usually highly suppressed. The hatched region in Figure 7 presents fitness combinations that explain $\hat{t}$ values compatible with this species (0.55–0.60; ATLAN *et al.* 1997). Two natural examples could be the population of Nairobi, Kenya, where $\hat{p}_m \sim 15\%$ and $t \sim 0.58$ and the population of St. Martin where $\hat{p}_m \sim 22\%$ and $t \sim 0.57$ (ATLAN *et al.* 1997). According to our model, the *SR/ST, sup/+* polymorphism for such populations requires overdominance ($a > 1$) and c between ~0.4 and ~0.8. The example of *D. simulans* illustrates that even when $c < 1$ we might be dealing with undetectable *sex-ratio* due to high suppressor frequency. In fact, despite more than 70 years of research with this species, only recently MERÇOT *et al.* (1995) crossed distant populations revealing a high frequency of masked *SR*, almost totally neutralized by population-specific Y-linked and autosomal suppressors. Heterospecific crosses with *D. sechellia* and *D. mauritiana* also suggest cryptic *sex-ratio* in *D. simulans* (DERMITZAKIS *et al.* 2000; TAO *et al.* 2001). If this phenomenon is common, known *sex-ratio* populations of Drosophila could be just a biased sample of what actually exists in nature: "known" populations (where $c \ll 1$) plus "hidden" populations (where c is close to 1). A similar observation was made by CARVALHO and VAZ (1999).

In spite of direct search efforts, no suppression has ever been found in natural populations of *D. pseudoobscura*. A possible explanation is that suppressors are not expected to invade when there is strong selection against *SR/Y* males, *i.e.*, a very low value of c (WU 1983). An alternative though unlikely explanation is that suppression has not yet arisen by mutation in that species. Here we showed that the stability conditions for suppressor noninvasion are overdominance—a is always >1.2—and strong selection against *SR/Y* males—c is always <⅓ (Figure 7, cross-hatched area). These results confirm and extend those obtained by WU (1983).

What holds *sup* in check? Our model indicates that as long as there is any selection against *SR/Y* males an autosomal suppressor (even with no deleterious effect) will not run to fixation. This result contrasts with Y-linked

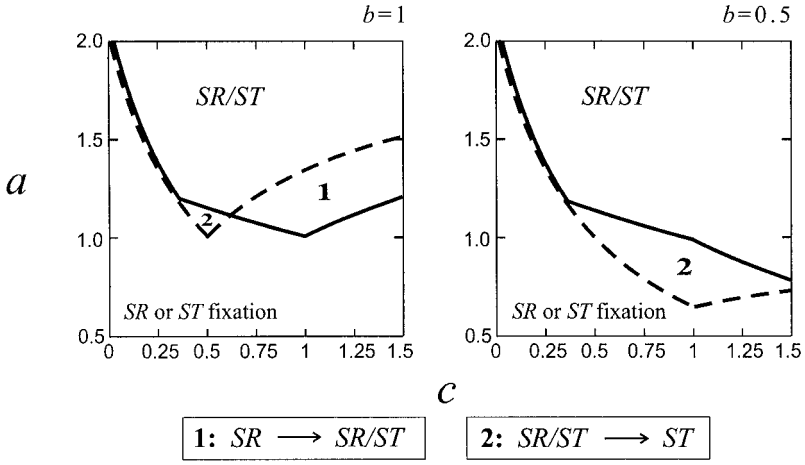

FIGURE 9.—Role of autosomal suppression in the stability of *SR/ST* polymorphisms. The parameters *a*, *b*, and *c* are the fitnesses of *ST/SR*, *SR/SR*, and *SR/Y* genotypes, respectively. All regions above the dashed line represent a *SR/ST* population *before sup* invasion (conditions set by Equations 3 and 4 for $t = 1$). All regions above the solid line represent a *SR/ST* population *after sup* invasion (see conditions marked * and ** in Table 3). Depending on fitness values suppression can convert *SR* fixation to *SR/ST* polymorphism (increasing the polymorphism's parametric space; region 1) or convert *SR/ST* polymorphism to *ST* fixation (reducing the polymorphism's parametric space; region 2). Note that the region denoted by *SR/ST* means polymorphism if suppressor is either present or absent.

suppressors: in the presence of *SR* chromosomes a neutral suppressor allele will always run to fixation. For this reason naturally occurring polymorphisms for Y-linked suppression can be explained only by a deleterious effect of the suppressor allele (CARVALHO *et al.* 1997). If a neutral autosomal suppressor (*sup*) is not fixed then there is at least some female bias; this means that Fisher's principle should be favoring *sup*. Thus, what holds *sup* in check? In the meiosis of *SR/Y* males, autosomal suppression decreases the proportion of *SR* gametes, increasing the proportion of Y gametes. Therefore *sup* is associated with Y gametes while + is associated with *SR* gametes. Because of this linkage disequilibrium, *sup* and + frequencies are different not only between sexes but also between *ST/ST*, *ST/SR*, *SR/SR*, *ST/Y*, and *SR/Y* individuals (which explains why eight recurrence equations were required to follow *SR* and *sup* frequencies!). Since *sup* and + are associated with different genotypes with different fitnesses (*a*, *b*, and *c* parameters), they are indirectly selected. This indirect selection most likely holds *sup* in check. We have done some preliminary calculations on the marginal fitness of *sup* and + alleles, which indicate that the + alleles are associated with best-fit genotypes (*ST/SR* females, for example). A complete investigation of this issue is beyond the scope of this article and should be considered elsewhere.

Limitations of the model: We have focused our investigation on the case of neutral suppressors, and it will be interesting to explore the consequences of selection. A suggestion of selection against autosomal suppressors appeared in CARVALHO *et al.* (1998). They followed the sexual proportion in experimental populations of *D. mediopunctata* fixed for *SR* and the frequency of males rose from 16 to 32% in 49 generations due to the accumulation of *sex-ratio* autosomal suppressors. However, this rate of change was slower than that expected by Fisherian selection (CARVALHO *et al.* 1998, p. 726). A possible explanation for this difference is that autosomal suppressors are slightly deleterious. If suppression does have a cost then suppressor equilibrium frequency may be quite different from what a neutral model predicts. We carried out numerical simulations assuming a 1% fitness loss in all males with the *+/sup* genotype and a 2% loss in all males with the *sup/sup* genotype. The essence of our previous findings remains: suppressors will not invade when selection against *SR* is strong and will remain polymorphic when *SR* is moderately deleterious ($c \geq \sim 0.6$; Figure 8). However, there are some significant changes: *ST/SR* female overdominance is no longer obligatory for the stability of *SR/ST*, *sup/+* polymorphisms and suppressor equilibrium frequency is drastically decreased even by weak selection (for example, *sup* does not run to fixation when *SR* is not deleterious, *i.e.*, $c \geq 1$). It should be noted that a 1% selection is very hard to detect experimentally.

Another limitation of our model is the existence of Y-linked suppressors of *sex-ratio* in natural populations (CARVALHO *et al.* 1997; JAENIKE 1999; MONTCHAMP-MOREAU *et al.* 2001). Since Y-linked suppressors are directly favored by meiotic drive, their evolution is expected to be faster than that caused by Fisher's principle. In fact, the frequency of a Y-linked suppressor, even being deleterious, will rapidly run to equilibrium in simulations (~1000 generations; not shown). In our simulations, an autosomal suppressor might take ~2500 generations to attain the equilibrium. In that sense, autosomal suppressors might be less important than Y-linked ones. A model including both types of suppression may be useful, if it does not call for too many arbitrary assumptions.

Suppression and the stability of *SR/ST* polymorphisms: At least two factors have a role in the stabilization of *SR/ST* polymorphisms: natural selection and suppression. Both effects can be measured by the conditions determined by EDWARDS (1961) for the stability of the X polymorphism [see (3) and (4)]. Selection is given by the *a*, *b*, and *c* parameters while suppression affects *t*, the drive parameter. Figure 9 shows the effect of autosomal suppression on the stability of *SR/ST* polymorphisms.

Suppression reduces the value of $\hat{t}$ and so can (i) avoid

SR fixation, increasing the *SR/ST* parametric space (region 1), or (ii) eliminate *SR*, decreasing the *SR/ST* parametric space (region 2). The first situation corresponds to the idea that suppression stabilizes the polymorphism because it avoids *SR* fixation. Polymorphism stabilization due to suppression happens when selection against *SR* is weaker (b and c close to 1) and, hence, *SR* frequency is higher (in this case when $c \geq 1$ *sup* is fixed and when $c < 1$ there is *sup*/+ polymorphism). It is possible that some suppressor-bearing present populations have suffered the risk of extinction in the past due to a high *SR* frequency in the absence of suppression (*D. simulans* and *D. mediopunctata* are candidate species; Varandas *et al.* 1997; Carvalho and Vaz 1999). The second situation (*SR* is eliminated; region 2 in Figure 9) occurs when selection against *SR* is stronger. In this case the equilibrium resulting from *sup* invasion is *ST* fixation and a neutral +/*sup* polymorphism. Thus, perhaps some populations devoid of *SR* chromosomes were once balanced *SR/ST* polymorphisms but *SR* was eliminated by natural selection when suppressors spread and diminished drive. Note that this evolutionary scenario is a very likely outcome if *SR* is deleterious ($b = 0.5$; Figure 9). Should we question the common idea that suppression stabilizes *SR/ST* polymorphisms? Atlan *et al.* (1997) studied several *D. simulans* populations from America, Europe, Asia, and Africa that lacked *SR* but exhibited resistance (suppression) to the *SR* of a different population. Maybe *SR* chromosomes were once present but were eliminated due to suppression.

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APPENDIX A: RECURRENCE EQUATIONS

Consider a generation cycle starting with the production of gametes. Union of gametes in G_0 results in zygotes that grow to adults of G_0. These adults produce the gametes of G_1 and so on. Let p be *SR* frequency in G_0 (as defined in Table 2) while p' is *SR* frequency in the next generation (G_1).

***SR* frequency:** Assuming random mating and random union of gametes, the frequency of *ST/ST* female zygotes, for example, is the product of *ST* frequency in eggs and sperm, *i.e.*, $(1 - p_e) \times (1 - p_s)$. The frequencies of *SR/SR*, *ST/SR*, and *ST/ST* female adults (F_{11}, F_{12}, and F_{22}) can be calculated from the respective zygotic frequencies by applying the selection coefficients (see Table 1),

$$\begin{aligned} F_{11} &= bp_e p_s / w_F \\ F_{12} &= a[(1 - p_e)p_s + p_e(1 - p_s)]/w_F \\ F_{22} &= (1 - p_e)(1 - p_s)/w_F, \end{aligned} \tag{A1}$$

where $w_F = bp_e p_s + a[(1 - p_e)p_s + p_e(1 - p_s)] + (1 - p_e)(1 - p_s)$.

SR frequency in G_0 female adults will be $F_{11} + \frac{1}{2} F_{12}$:

$$p_f = \frac{\frac{1}{2}a[(1 - p_e)p_s + p_e(1 - p_s)] + bp_e p_s}{w_F}. \tag{A2}$$

Since we assume no drive in females and no selection on fecundity, *SR* frequency in eggs from G_1 is equal to *SR* frequency in female adults from G_0:

$$p'_e = p_f. \tag{A3}$$

Let t be the proportion of X-bearing sperm resulting from *SR/Y* male meiosis (and $1 - t$ is the proportion of Y-bearing sperm). Since this proportion is ½ for *ST/Y* males, the proportion of *SR* among X sperm from G_1 is

$$p'_s = \frac{tp_m}{tp_m + \frac{1}{2}(1 - p_m)}. \tag{A4}$$

Similarly, the proportion of Y-bearing sperm in the population sperm pool, *i.e.*, the zygotic male proportion in G_1, is

$$M'_z = (1 - t)p_m + \tfrac{1}{2}(1 - p_m). \tag{A5}$$

SR frequency in male zygotes is equal to *SR* frequency in eggs (p_e). *SR* frequency in male adults from G_0 can then be calculated by applying the selection coefficient c (see Table 1): $p_m = cp_e/[cp_e + (1 - p_e)]$. It suffices to substitute $p'_e = p_f$ (from Equation A3) to obtain *SR* frequency in male adults from G_1:

$$p'_m = \frac{cp_f}{cp_f + (1 - p_f)}. \tag{A6}$$

Suppressor frequency: As we assumed that autosomal suppression is selectively neutral (Table 1), the frequency of *sup* in *SR/Y* adults, for example, is equal to its frequency in *SR/Y* zygotes from the same generation (r_{m1}, see Table 2). The same holds true for any other genotype (*ST/Y*, *SR/SR*, *ST/SR*, and *ST/ST*). In this way, *sup* frequency in adults can be calculated directly from *sup* frequency in the gametes that originated these adults (instead of separately modeling the gamete-to-zygote and zygote-to-adult transitions). It is worth stating that this approach was essential to bring forward the analytical and algebraic solutions of the model.

The frequency of *sup* in *SR/SR*, *ST/SR*, and *ST/ST* female zygotes and adults (r_{f11}, r_{f12}, and r_{f22}, respectively) is the average between *sup* frequency in eggs and in X sperm:

$$r_{f11} = \tfrac{1}{2}(r_{e1} + r_{s1}),\ r_{f22} = \tfrac{1}{2}(r_{e2} + r_{s2}),$$

and

$$r_{f12} = \frac{\frac{1}{2}(r_{e2} + r_{s1})(1 - p_e)p_s + \frac{1}{2}(r_{e1} + r_{s2})p_e(1 - p_s)}{(1 - p_e)p_s + p_e(1 - p_s)}.$$

Similarly, *sup* frequency in *SR/Y* and *ST/Y* male zygotes and adults (r_{m1} and r_{m2}, respectively) is the average between *sup* frequency in eggs and in Y sperm:

$$r_{m1} = \tfrac{1}{2}(r_{e1} + r_{sY}) \tag{A7}$$

TABLE A1

Meiosis of *SR/Y* males under autosomal suppression

Genotype	Genotype frequency	Sperm haplotypes proportion			
		*SR*_+	Y_+	*SR_sup*	Y_*sup*
+/+	$(1 - r_{e1})(1 - r_{sY})$	1	0	—	—
+/*sup*	$r_{e1}(1 - r_{sY}) + (1 - r_{e1})r_{sY}$	$\frac{3}{8}$	$\frac{1}{8}$	$\frac{3}{8}$	$\frac{1}{8}$
sup/*sup*	$r_{e1}r_{sY}$	—	—	$\frac{1}{2}$	$\frac{1}{2}$

Individuals that are +/+ produce 100% *SR*-bearing sperm, +/*sup* males produce 75%, and totally suppressed *sup/sup* males produce 50%. r_{e1} and r_{sY} are *sup* frequencies in *SR* eggs and Y sperm, respectively.

$$r_{m2} = \tfrac{1}{2}(r_{e2} + r_{sY}). \tag{A8}$$

Now, let r_e and r_s be the frequency of the *sup* allele in eggs and sperm (as defined in Table 2) while r'_e and r'_s are these same frequencies in the next generation (G_1). The frequency of *sup* in *SR* and *ST* eggs from G_1 can be obtained by

$$r'_{e1} = (F_{11}r_{f11} + \tfrac{1}{2}F_{12}r_{f12})/(F_{11} + \tfrac{1}{2}F_{12})$$

and

$$r'_{e2} = (F_{22}r_{f22} + \tfrac{1}{2}F_{12}r_{f12})/(F_{22} + \tfrac{1}{2}F_{12}),$$

where F_{11}, F_{12}, and F_{22} are defined in Equation A1. These frequencies can be simplified as

$$r'_{e1} = \frac{\frac{1}{2}a[(r_{e2} + r_{s1})(1 - p_e)p_s + (r_{e1} + r_{s2})p_e(1 - p_s)] + b(r_{e1} + r_{s1})p_ep_s}{a[(1 - p_e)p_s + p_e(1 - p_s)] + 2bp_ep_s} \tag{A9}$$

$$r'_{e2} = \frac{\frac{1}{2}a[(r_{e2} + r_{s1})(1 - p_e)p_s + (r_{e1} + r_{s2})p_e(1 - p_s)] + (r_{e2} + r_{s2})(1 - p_e)(1 - p_s)}{a[(1 - p_e)p_s + p_e(1 - p_s)] + 2(1 - p_e)(1 - p_s)}. \tag{A10}$$

The frequencies of *sup* in each of the three sperm types in G_1 (*SR*, *ST*, and Y) can be calculated if we follow G_0 male meiosis. Table A1 shows the proportion of each sperm haplotype produced by every *SR/Y* and *ST/Y* male considering the autosomal genotype (see also the meiotic drive pattern defined in Table 1).

The frequency of X-bearing sperm resulting from *SR/Y* male meiosis in G_0 is $t = [SR\_sup] + [SR\_+]$, where $[SR\_sup] = \frac{3}{8}(r_{e1} + r_{sY}) - \frac{1}{4}r_{e1}r_{sY}$ and $[SR\_+] = 1 - \frac{5}{8}(r_{e1} + r_{sY}) + \frac{1}{4}r_{e1}r_{sY}$. Therefore, t can be simplified as $1 - \frac{1}{4}(r_{e1} + r_{sY})$, which, given Equation A7, equals

$$t = 1 - \tfrac{1}{4}(r_{e1} + r_{sY}) = 1 - \tfrac{1}{2}r_{m1}. \tag{A11}$$

We can now calculate *sup* frequency in *SR* and Y sperm in G_1 (r'_s). The frequency of *sup* in *SR* sperm equals $[SR\_sup]/([SR\_sup] + [SR\_+])$:

$$r'_{s1} = \frac{\frac{3}{8}(r_{e1} + r_{sY}) - \frac{1}{4}r_{e1}r_{sY}}{1 - \frac{1}{4}(r_{e1} + r_{sY})}. \tag{A12}$$

As for *ST/Y* male meiosis the reasoning is straightforward. Because of Mendelian segregation, the frequency of *sup* in either *ST* or Y sperm equals to r_{m2}. Therefore, given Equation A8, *sup* frequency in *ST* sperm in G_1 equals

$$r'_{s2} = \tfrac{1}{2}(r_{e2} + r_{sY}). \tag{A13}$$

Similarly, the frequency of Y_*sup* haplotype in total sperm produced by *ST/Y* males will be $[Y\_sup]_2 = \frac{1}{2}r_{m2} = \frac{1}{4}(r_{e2} + r_{sY})$. And the frequency of Y_*sup* haplotype in sperm produced by *SR/Y* males can be simplified to $[Y\_sup]_1 = \frac{1}{8}(r_{e1} + r_{sY}) + \frac{1}{4}r_{e1}r_{sY}$ (see Table A1). Finally, the frequency of Y_*sup* sperm in the population sperm pool in G_1, given by r'_{sY}, is the weighted average of what came from *SR/Y* and *ST/Y* meiosis: $r'_{sY} = ([Y\_sup]_1p_m + [Y\_sup]_2(1 - p_m))/Mz'$, where Mz' is defined in Equation A5. Appropriate substitutions lead to

$$r'_{sY} = \frac{[\frac{1}{2}(r_{e1} + r_{sY}) + r_{e1}r_{sY}]p_m + (r_{e2} + r_{sY})(1 - p_m)}{(r_{e1} + r_{sY})p_m + 2(1 - p_m)}. \tag{A14}$$

The complete system consists of eight recurrence equations (for p_e, p_s, p_m, r_{e1}, r_{e2}, r_{s1}, r_{s2}, and r_{sY}): (A3), (A4), (A6), (A9), (A10), (A12), (A13), and (A14), where p_f and t are defined in Equations A2 and A11, respectively.

APPENDIX B: JACOBIANS AND EIGENVALUES

The general Jacobian of the system is a five-by-five matrix with the system's partial derivatives:

$$J = \begin{bmatrix} \partial r'_{e1}/\partial r_{e1} & \partial r'_{e1}/\partial r_{e2} & \partial r'_{e1}/\partial r_{s1} & \partial r'_{e1}/\partial r_{s2} & \partial r'_{e1}/\partial r_{sY} \\ \cdots & & & & \cdots \\ \partial r'_{sY}/\partial r_{e1} & \cdots & & & \partial r'_{sY}/\partial r_{sY} \end{bmatrix}. \tag{B1}$$

Suppressor noninvasion: Matrix J_1, the Jacobian for the *SR/ST,* + equilibrium, can be obtained from B1 by substituting $b = 0$, $\hat{r} = 0$, and $p = \hat{p}$, where $\hat{t} = 1$ in Equations 1,

$$J_1 = \begin{bmatrix} \frac{1}{2Q_1} & \frac{c}{Q_1} & \frac{c}{Q_1} & \frac{1}{2Q_1} & 0 \\ \frac{Q_2}{2aQ_1^2} & \frac{Q_1 + cQ_2}{aQ_1^2} & \frac{cQ_2}{aQ_1^2} & \frac{2Q_1 + Q_2}{2aQ_1^2} & 0 \\ \frac{3}{8} & 0 & 0 & 0 & \frac{3}{8} \\ 0 & \frac{1}{2} & 0 & 0 & \frac{1}{2} \\ \frac{cQ_2}{4aQ_1} & \frac{1}{2} & 0 & 0 & \frac{1}{2} + \frac{cQ_2}{4aQ_1} \end{bmatrix}, \tag{B2}$$

where $Q_1 = 2c + 1$ and $Q_2 = 2ac + a - 2$.

The characteristic equation can be obtained by setting the determinant of the $J_1 - \lambda I$ matrix equal to 0, where I is the five-by-five identity matrix. The roots of this equation are the eigenvalues (λ) of J_1: 0 and the roots of a 4° polynomial for λ (with extensive coefficients on a and c; not shown). Now we can check if J_1 contains only positive (or null) elements so that the Perron-Frobenius theorem can be applied (Ortega 1987). We know that Q_1 is always positive since $c \geq 0$. Thus, all elements of J_1 are positive simply when $Q_2 > 0$: $2ac + a - 2 > 0 \Rightarrow a > 2/(2c + 1)$, which is precisely one of the stability conditions we will find for this equilibrium (see Table 3). So, J_1 is always positive and the Perron-Frobenius theorem validates the procedure $\lambda = 1$ to get the stability boundaries of the equilibrium. Given $\lambda = 1$, the 4° polynomial is reduced to $c(4ac^2 + 2ac - c - 1)(2ac + a - 2) = 0$ whose solutions are $c = 0$, $a = 2/(2c + 1)$ and $a = (c + 1)/[2c(2c + 1)]$.

Suppressor fixation: The Jacobian matrix for the *SR/ST, sup* equilibrium, J_2 (not shown), can be obtained from B1 by substituting $\hat{r} = 1$ and $p = \hat{p}$, where $\hat{t} = \frac{1}{2}$ in Equations 1.

The eigenvalues (λ) of J_2 are 0 and the roots of a 4° polynomial for λ (with extensive coefficients on a, b, and c; not shown). We did not find a general condition that assured positive elements for J_2. Therefore, we checked 1000 random simulations that resulted in *SR/ST, sup* equilibria. A short *Maple* algorithm was developed to verify each element from the 1000 *SR/ST, sup* matrices. J_2 was always positive and the Perron-Frobenius theorem could also be applied. By setting $\lambda = 1$ the polynomial is reduced to $ac(c - 1)(c + 1)(ab + a - 2b)(ac + a - 2)(ac + a - 2bc) = 0$ whose solutions are four nonrelevant ones, $a = 0$, $c = 0$, $c = -1$, and $a = 2b/(b + 1)$, and three from which we will find the stability boundary conditions $c = 1$, $a = 2bc/(c + 1)$, and $2/(c + 1)$.