COMPONENTS OF SELECTION IN *X* CHROMOSOME LINES OF *DROSOPHILA MELANOGASTER*: SEX RATIO MODIFICATION BY MEIOTIC DRIVE AND VIABILITY SELECTION

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Manuscript received May 9, 1984
Revised copy accepted August 11, 1984

ABSTRACT

Selection coefficients and segregation parameters have been estimated in 18 randomly chosen lines carrying wild *X* chromosomes on the *cn bw* genetic background. Each line was studied in replicated crosses of four types, with approximately 100 replications per line per cross. Crosses in which male *X* chromosomes differed exhibited significant sex ratio heterogeneity. Maximum likelihood estimation of segregation parameters revealed two lines in which the proportion of *X*-bearing gametes produced by males was significantly different from Mendelian expectations. These observations suggest that segregation distortion is a common feature of naturally occurring genetic variation. Non-Mendelian segregation has important evolutionary implications.

THE study of selection components, recently reviewed by HEDRICK (1983), has revealed fitness differences between genotypes in virtually all stages of the life cycle of several model species. It is usual in these studies to assume that precise Mendelian segregation ratios apply to all genotypes, except for the case of complete meiotic drive associated with the "Sex-Ratio" inversions of *Drosophila pseudoobscura* (WALLACE 1948; BECKENBACH 1978; CURTSINGER and FELDMAN 1980; WU 1983) and a special case studied by CLARK and FELDMAN (1981). Because there are many documented examples of "strong" meiotic drive (25 references are given in CURTSINGER 1984a), and because characters subject to modification by a major genetic element are also generally subject to polygenic or "continuous" variation, it is likely that "slight" modification of segregation ratio (on the order of a few percent) occurs in natural genomes. Such variation would be difficult to detect in one generation transition (MULCAHY and KAPLAN 1979) but has the potential of being a strong force relative to typical per-locus selection coefficients.

This report presents a novel design for the study of selection components including meiotic drive, associated with wild *X* chromosomes of *D. melanogaster*. The experimental design is applied to a random sample of wild chromosomes

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TABLE 1

Crosses executed with 23 X chromosome lines

Cross	Male	Female	No. of crosses	Progeny counted
I	X^iY	$X^{cn\ bw}X^{cn\ bw}$	2356	109,060
II	$X^{cn\ bw}Y$	$X^{FM7}X^i$	2196	47,147
III	X^iY	$X^{FM7}X^i$	2106	55,117
IV	X^iY	$X^{cn\ bw}X^{FM7}$	2265	59,838
		Totals	8923	271,162

X^i = one of the 23 wild X chromosomes derived from Texas and Odate isofemale lines.

not previously analyzed and not classified by any particular polymorphism. Detailed study of 18 lines reveals a rather complex picture of selective forces that include statistically significant non-Mendelian segregation in addition to line variations in viability.

The terms "meiotic drive," "segregation distortion" and "non-Mendelian segregation" are used interchangeably here to denote systematic deviation from equal representation of alleles or homologous chromosomes among the functional gametes. The mechanism is not necessarily meiotic, and no zygotic or postzygotic selection is implied.

MATERIALS AND METHODS

Experimental stocks carried X chromosomes from randomly chosen isofemale lines collected in Brownsville, Texas (18 lines), or Odate, Japan (five lines). The wild X chromosomes are symbolized X^i (i = 1–23). Immediately following the collection of isofemale lines, X chromosomes were placed on the *cn bw* genetic background by ten generations of repeated backcrossing to X^{FM7} on the same background. These crosses were executed by Y. HIRAIZUMI. The *cn bw* stock is well characterized and has been used extensively in studies of autosomal meiotic drive (HARTL and HIRAIZUMI 1976). *FM7* is an X chromosome balancer marked with Bar. Mutations and balancer chromosomes are described by LINDSLEY and GRELL (1968).

Each line was studied at 23°–24° in replicated crosses of the four types shown in Table 1. Males were collected on day 0, mated singly with three females on day 1 and cleared from vials on day 3. Emerging adult progeny were counted twice, on day 12 or 13 and again on day 19. This schedule results in the counting of all progeny with little mortality in the adult stage. Crosses were completed in a 6-month period, all lines being tested simultaneously within each type of cross.

The estimation of viability and segregation parameters is based on a numerical maximum likelihood method developed by CLARK, FELDMAN and CHRISTIANSEN (1981). The algorithm will be described. Routine statistical analyses employed the SPSS statistical package.

RESULTS

The completed crosses shown in Table 1 consist of approximately 100 replicated matings per line per cross I–IV. Because of line variation in fertility, the number of usable replications per line per cross varied from 76 to 109. The number of pair matings set up was doubled for line 16, which showed a lower fertility. Overall productivity averaged 30 adult progeny per vial.

TABLE 2

Sex ratio variation among Texas X *chromosome lines*

	Cross			
	I	II	III	IV
Sex ratio (% female)				
High line mean ± SD	51.0 ± 9.8	65.0 ± 17.0	61.9 ± 14.9	55.4 ± 12.8
Low line mean ± SD	42.0 ± 9.5	52.6 ± 14.6	51.3 ± 11.7	49.4 ± 14.0
Grand mean ± SE	48.1 ± 2.2	55.1 ± 2.9	54.6 ± 2.7	53.0 ± 1.5
Line heterogeneity				
F ratio	6.34	1.12	1.62	1.81
Probability	<0.001	>0.30	0.05	0.02

SE = standard error of line means.

As shown in Table 2, there is statistically significant sex ratio heterogeneity among lines in crosses I, III and IV, in which the paternal genotype varies among lines, but not in cross II, in which paternal genotype is constant across lines. Percentages were arc-sine transformed for normality. This observation is consistent with a prezygotic modification of gamete ratios in males but is not sufficient to rule out variation in viability parameters as the sole cause of the sex ratio heterogeneity. Because of the construction of the lines, the heterogeneity can be attributed to variation among wild *X* chromosomes, regardless of mechanism.

Three classes of factors could generate the observed sex ratio heterogeneity: prezygotic selection (including meiotic drive), viability selection dependent on the zygotic genotype and interactions between larval genotypes that influence egg-to-adult viability. Because the number of interaction parameters is potentially large, a parsimonious approach will be adopted, invoking interactions only where viability and segregation parameter estimates cannot account for the observations. It will further be assumed that segregation is precisely Mendelian in both sexes for laboratory stocks.

A parameterization of viability and segregation effects is shown in Table 3. Note that chromosomes are superscripted and variables are subscripted. Because crosses involved balancer chromosomes, segregation parameters refer to whole-chromosome segregation in both males and females. To obtain parameter estimates for each *X* chromosome line, a numerical maximum likelihood method based on the algorithm of CLARK, FELDMAN and CHRISTIANSEN (1981) has been adopted. A brief description of the computer program follows. Expected frequencies of progeny genotypes in crosses I–IV are functions of the underlying viability and segregation parameters, as shown in Table 4. For each line, the data consist of observed numbers N_1–N_{14}. Following the input of initial parameter estimates, the program sequentially and repeatedly modifies the parameters V_1–V_7, k_i and l_i by a prescribed increment and decrement. At each modification, the fit between observed and expected frequencies is tested by the log likelihood ratio statistic *G* (SOKAL and ROHLF 1969). Maximum

TABLE 3

Viability and segregation parameters

Genotype	Relative viability	Gametes produced	Ratios
$X^{cn\ bw}Y$	V_1	$X^{cn\ bw}$:Y	k_{cb}:1 − k_{cb}
$X^{FM7}Y$	V_2	X^{FM7}:Y	k_{FM7}:1 − k_{FM7}
X^iY	V_3	X^i:Y	k_i:1 − k_i
$X^{cn\ bw}X^{FM7}$	V_4	$X^{cn\ bw}$:X^{FM7}	l_{cb}:1 − l_{cb}
$X^{cn\ bw}X^i$	V_5	Recombinant	Not estimated
$X^{FM7}X^i$	V_6	X^i:X^{FM7}	l_i:1 − l_i
X^iX^i	V_7	X^i	1

TABLE 4

Expected and observed genotype distributions among progeny of crosses I–IV

Cross	Progeny genotypes	Expected relative frequencies	Observed nos.
I	$X^{cn\ bw}X^i$	k_iV_5	N_1
	$X^{cn\ bw}Y$	$(1 - k_i)V_1$	N_2
II	$X^{cn\ bw}X^{FM7}$	$(1 - l_i)k_{cb}V_4$	N_3
	$X^{cn\ bw}X^i$	$l_ik_{cb}V_5$	N_4
	$X^{FM7}Y$	$(1 - l_i)(1 - k_{cb})V_2$	N_5
	X^iY	$l_i(1 - k_{cb})V_3$	N_6
III	$X^{FM7}X^i$	$(1 - l_i)k_iV_6$	N_7
	X^iX^i	$l_ik_iV_7$	N_8
	$X^{FM7}Y$	$(1 - l_i)(1 - k_i)V_2$	N_9
	X^iY	$l_i(1 - k_i)V_3$	N_{10}
IV	$X^{FM7}X^i$	$(1 - l_{cb})k_iV_6$	N_{11}
	$X^{cn\ bw}X^i$	$l_{cb}k_iV_5$	N_{12}
	$X^{FM7}Y$	$(1 - l_{cb})(1 - k_i)V_2$	N_{13}
	$X^{cn\ bw}Y$	$l_{cb}(1 - k_i)V_1$	N_{14}

likelihood corresponds to minimum G, which is asymptotically distributed as chi-square. If neither the increment nor the decrement of a parameter improves the fit, then the program retains the initial estimate and reduces the increment in subsequent cycles of parameter modifications. Otherwise, the modified estimate is retained. This algorithm converges more slowly than those that seek the maximum local slope of the likelihood surface (*e.g.*, Fisher's method) but has the advantage of not diverging from local maxima. For the data analzyed here, initial parameter values were set to equal viability and Mendelian segregation in all genotypes. No problems with failure of convergence or negative parameter estimates arose.

Maximum likelihood estimates of viability and segregation parameters for 18 Texas lines are shown in Table 5. Viability parameters are scaled within each line relative to $V_1 = 100$. In five lines, the estimate of the male segregation parameter is $k_i = 0.46$, with the remainder being precisely Mendelian.

TABLE 5

Maximum likelihood estimates of viability and segregation parameters

Line (i)	V_2	V_3	V_4	V_5	V_6	V_7	k_i	l_i	G
1	61	115	78	109	98	125	0.46	0.50	5.4
2	57	101	86	101	76	99	0.50	0.50	19.1***
3	40	82	69	80	72	86	0.50	0.50	126.7***
4	52	94	83	91	86	101	0.50	0.50	24.0***
5	66	64	83	96	85	85	0.50	0.50	31.7***
6	54	99	81	95	89	98	0.50	0.50	5.2
7	54	102	88	98	79	110	0.50	0.50	11.2***
8	57	68	73	86	72	77	0.50	0.50	3.8
9	60	93	83	99	78	89	0.50	0.50	24.6***
10	60	85	77	100	80	83	0.50	0.50	14.1***
11	59	83	70	90	81	91	0.50	0.50	8.3**
12	62	88	85	94	80	89	0.50	0.50	13.7***
13	58	102	90	114	96	126	0.46	0.50	4.7
14	67	106	89	112	100	125	0.46	0.50	2.4
15	58	95	81	97	80	96	0.50	0.50	4.4
16	50	66	89	108	91	80	0.46	0.50	17.8***
17	56	93	76	98	79	102	0.50	0.51	6.1*
18	51	98	81	103	101	113	0.46	0.50	9.9***

Viability parameters are scaled to $V_1 = 100$.
* $P < 0.05$.
** $P < 0.025$.
*** $P < 0.01$.

The last column of Table 5 shows the log likelihood ratio G statistic associated with the parameter estimates for each line. Because replications were pooled in order to obtain line estimates, there is 1 d.f. arising from cross I and 3 d.f. arising from each of the other three crosses, giving a total of 10 d.f. With six free viability parameters, two free segregation parameters and $k_{cb} = l_{cb} = 0.50$, there remain 2 d.f. for the G statistic. The viability and segregation parameter estimates adequately account for the observed progeny distributions in six lines, three of which have $k_i = 0.46$.

To test the non-Mendelian k_i estimates for lines 1, 13 and 14, we compare the G statistic for a strictly Mendelian model (six free viability parameters and 4 d.f.) with a model that allows non-Mendelian segregation in males (seven parameters and 3 d.f.). The difference is another G statistic with 1 d.f. As shown in Table 6, the non-Mendelian model significantly improves the fit between observed and expected progeny distributions in two cases, causing us to reject the null hypothesis $k_i = 0.50$ for lines 1 and 14.

The non-Mendelian segregation estimates for lines 1 and 14 could arise as artifacts from some special combination of genotypic viability interactions that are peculiar to those lines, but this possibility can be excluded by examining certain genotype ratios. In the absence of interactions, the following equalities are expected to be satisfied for each line, irrespective of viability or segregation parameters:

$$N_7/N_9 = N_{11}/N_{13};\ N_6/N_5 = N_{14}/N_{13};\ N_1/N_2 = N_8/N_{10}$$

TABLE 6

Tests of non-Mendelian segregation estimates

Line (i)	G Statistics		
	H_o (d.f. = 4)	$k_i \neq 0.50$ (d.f. = 3)	Difference (d.f. = 1)
1	13.1	5.4	7.7***
13	7.2	4.7	2.5
14	10.0	2.4	7.6***

H_o:$k_i = 0.50$.
*** $P < 0.01$.

For line 1, the corresponding ratios are 1.3 and 1.4; 2.1 and 1.8; 1.1 and 1.0, respectively. For line 14, the ratios are 1.3 and 1.2; 1.6 and 1.5; 1.0 and 1.1, respectively. The expected equalities are as closely satisfied for lines 1 and 14 as for any of the 18 lines. In contrast, line 3 shows evidence of marked interaction, with ratios of 1.2 and 3.0; 1.5 and 2.7; 1.4 and 1.2, respectively. It may be concluded that lines 1 and 14 are not unusually susceptible to viability interactions.

The other lines having non-Mendelian segregation estimates, numbers 16, 17 and 18, are among the 12 lines for which no statistically acceptable parameter estimates are known. One possibility is that the highest likelihood peaks were not located by the numerical methods. To search for noncontiguous likelihood peaks, 10^5 random points in the eight-dimensional parameter space were tested for each line, and the area in the vicinity of the overall average parameter values was searched extensively. No improved fit was found. A second possibility is that there are significant viability interactions. Acceptable estimates can be found for six of the 12 lines by introducing a viability interaction parameter into the underlying model, but the choice of interaction parameters is somewhat arbitrary. Furthermore, it is not possible to test more than one interaction parameter, because there remain only 2 d.f. to test the basic viability-segregation model. For these reasons, an analysis of the various possible interaction models will not be detailed here.

Returning to the lines that have been satisfactorily "explained," it is desirable to evaluate the parameter estimates and assumptions by three additional criteria: (1) In the absence of viability interactions, V_2 and V_4 are expected to show relatively low variation across lines, because the relevant genotypes are unchanging, whereas the X^i vary. Among the appropriate lines, $V_2 = 59.2 \pm 4.4$, and $V_4 = 82.0 \pm 6.5$. In contrast, other viability parameters show larger standard errors of line means, ranging from 11.1 to 20.5. (2) Independent estimates of the parameters V_2 and V_4 were obtained by the additional cross $X^{cn\ bw}X^{FM7} \times X^{cn\ bw}Y$. Four hundred and forty-seven matings were analyzed, yielding 17,494 progeny. New estimates $V_2 = 45.0$ and $V_4 = 89.3$ are not significantly different from the maximum likelihood estimates. (3) The validity of the assumption $k_{cb} = 0.50$ is supported by the observation of an additional mating of $X^{cn\ bw}X^{cn\ bw} \times X^{cn\ bw}Y$. Two hundred and three matings yielded 8585

progeny. The observed sex ratio (percent females) was 50.7 ± 7.8, which is indistinguishable from Mendelian segregation with binomial sampling error.

Although our primary interest is further investigation of the Texas *X* chromosome lines, data have been acquired demonstrating that the basic observation of sex ratio heterogeneity is not peculiar to those lines. Five *X* chromosomes from isofemale lines collected in Odate, Japan, were placed on the *cn bw* genetic background and tested in crosses I–IV with approximately 100 replicated matings per line per cross. Significant sex ratio heterogeneity among lines was again observed, based on 1726 matings analyzed.

DISCUSSION

Eighteen Texas lines carrying wild *X* chromosomes on a standard genetic background exhibit statistically significant sex ratio heterogeneity in crosses that involve males carrying the wild *X* chromosome. The range of variation is shown in Table 2. Crosses designed to show the causes of the sex ratio heterogeneity reveal three classes of lines: (1) In three lines, the distribution of progeny genotypes is accounted for by line variation in viability parameters associated with wild chromosomes. Estimates of segregation parameters in these lines conform to Mendelian expectations in both sexes. (2) In three lines, parameter estimates involve non-Mendelian segregation in males in addition to line variation in viability. For all three lines, the maximum likelihood estimate of the proportion of *X*-bearing gametes transmitted by males is 46%. In two of the three lines, numbers 1 and 14, the non-Mendelian model gives a significantly better fit to observed progeny distributions than the competing Mendelian model (see Table 6). (3) For the remaining 12 lines, no combination of viability and segregation parameters adequately accounts for the observed progeny distributions, possibly because of genotypic interactions affecting viability.

There exist a large number of reports of the fitness effects of wild chromosomes sampled from natural populations of Drosophila. This study is related to the earlier studies but offers a refinement. Instead of assuming precise Mendelian segregation and then measuring viability effects by deviations from Mendelian expectations, the design employed here allows independent estimation of viability and segregation parameters. The success of this design is indicated by the detection of variation in segregation parameters that would have been otherwise overlooked.

The sex ratio heterogeneity, observed among 18 Texas lines and five Odate lines, is not unexpected. Extreme *X*-linked meiotic drive has been observed in a number of Drosophila of the *obscura* group (STURTEVANT and DOBZHANSKY 1936) and in *D. simulans*, a sibling species of *D. melanogaster* (FAULHABER 1967). It is reasonable to expect that a character subject to discontinuous variation under the influence of a major gene or complex of genes may also be subject to modification by factors of less extreme effect. "Slight" meiotic drive has been reported several times in *D. melanogaster* (HANKS 1965, 1969; HANKS and TORGERSON 1969; KATZ 1979). LYTTLE (1979) has shown that laboratory populations of this species with psuedo-*Y* meiotic drive rapidly ac-

cumulate modifiers, suggesting that many loci can modify segregation. Furthermore, artificial selection on the sex ratio in Drosophila and other experimental systems has been occasionally successful (MAYNARD SMITH 1976; CURTSINGER 1981). In the latter study, a male-limited segregation effect causing decreased transmission of *X* chromosomes was detected in *D. pseudoobscura.* The sex limitation and the direction of segregation distortion were the same as in the present study.

There is certainly no lack of feasible mechanisms for the modification of segregation ratios in male Drosophila. Gamete dysfunction in spermiogenesis is well documented (HARTL, HIRAIZUMI and CROW 1967; POLICANSKY and ELLISON 1970; MATTHEWS 1981). Heterochromatic deficiencies of the *X* chromosome can cause nondisjunction and segregation modification (MCKEE 1984). EMS-induced meiotic mutants are generally male limited and alter *X–Y* disjunction (BAKER and CARPENTER 1972). Transposable genetic elements cause chromosome breakage "hotspots" (ENGELS and PRESTON 1981), which may lead to altered segregation ratios. The observation of age- and temperature-dependent segregation (SANDLER and HIRAIZUMI 1961; HIRAIZUMI and GROVE 1969; HIRAIZUMI and WATANABE 1969) suggests that the process is subject to various physiological variables. A possible molecular mechanism for altered spermiogenesis in *SD* has been described (KETTANEH and HARTL 1976). The mechanism of the segregation modification reported here is not known but is under investigation.

The classification of the lines is entirely dependent on a maximum likelihood method of parameter estimation. Statistical feasibility is, of course, not proof, but there are additional arguments that support the estimates. Two viability parameters that are expected to exhibit low heterogeneity over lines do in fact show the lowest levels of variation (see RESULTS). Additional crosses produce progeny distributions that are consistent with certain parameter estimates (see RESULTS). The segregation distortion lines are not particularly susceptible to viability interactions (see RESULTS). The maximum likelihood estimates suggest sex-limited segregation modification, which is consistent with known segregation distorters in Drosophila. If one were to argue that the segregation distortion is a statistical artifact, then it would be difficult to account for the non-Mendelian estimates in males and simultaneous Mendelian estimates in females.

Although the detection of segregation distortion is the most important aspect of these data, several other features of the viability estimates shown in Table 5 merit discussion. There is no evidence of a bimodal distribution of viabilities, as is often observed in studies of the homozygous fitness effects of the autosomes (*e.g.*, LEWONTIN 1974). This is because lines carrying deleterious recessive alleles would have been eliminated during the inbreeding process in the construction of the lines and because of elimination in the hemizygous condition. There is a general lack of chromosomal heterosis seen in the comparison of V_6 and V_7, which can be attributed to the dominant deleterious effects of Bar. The *X* chromosomes that suffer a disadvantage in segregation have a general advantage in viability; in particular, lines 1, 13 and 14 exhibit the highest values for V_3 and V_7. This is consistent with the maintenance of vari-

ation by a balance between segregation distortion and viability selection (see also CURTSINGER and FELDMAN 1980; CURTSINGER 1981). There is a very high correlation between homozygous and hemizygous fitness effects for the wild X chromosomes among "explained" lines; the product-moment correlation coefficient between V_3 and V_7 is 0.88 ($P \approx 0.01$). The relationship between selective effects in males and females is the critical factor in determining the degree of selectively maintained genetic polymorphism for X-linked or haplo-diploid genetic systems (CURTSINGER 1980). These observations argue against the maintenance of polymorphisms by differential selection in the sexes, although the inference of single-locus effects from whole-chromosome observations must be treated cautiously (see also DRESCHER 1964; WILTON and SVED 1979).

The major limitation of these studies is that the wild chromosomes are analyzed on a standardized, and, therefore, artificial, genetic background. Modification of major meiotic drive elements by unlinked genes has been documented in several species of Drosophila (HIRAIZUMI and GERSTENBERG 1981; VOELKER 1972; STALKER 1961). It is possible that natural genomes carry integrated systems of segregation modifiers that would be destroyed by the process of isolating chromosomes. The variation in viability and segregation parameters is cryptic, in the sense that several types of crosses must be replicated in order to obtain parameter estimates. Hence, there is an experimental dilemma: How can one achieve sufficient genetic control of the makeup of the experimental crosses to obtain independent estimates of viability and segregation parameters without destroying the possible natural genetic integration? HIRAIZUMI and GERSTENBERG (1981) present one solution, but the method is probably not applicable to the study of slight meiotic drive. This problem is not limited to segregation studies; selection components analyses reveal that a multiplicity of selective factors are common and generally confounded (HEDRICK 1983; SIMMONS, PRESTON and ENGELS 1980; CLARK, FELDMAN and CHRISTIANSEN 1981). The issue of fitness estimation without observer-induced distortion must be considered a major impediment to further progress in the study of natural fitness variation. Sampling mother-offspring combinations or related designs might contribute to the ultimate resolution of this fundamental problem (CHRISTIANSEN and FRYDENBERG 1973).

It is not possible to predict evolutionary trajectories from these data, primarily because the fitness components measured are only part (perhaps a small part) of total fitness. Nevertheless, the analyses produce several conclusions that are of general interest. First, the observation that 12 of 18 lines are not adequately accounted for by viability and segregation parameters suggests significant viability interactions. If this result is generally valid, then microevolutionary theory will have to discard the oversimplified notion of constant fitness parameters associated with particular genotypes. Fitness may have to be viewed as largely frequency and density dependent. Second, although sex ratio evolution is among the most widely discussed phenomena in evolutionary biology, there is limited information available about the genetic variation upon which selection is presumed to act. This study reveals two classes of selective factors that modify sex ratios in quite different ways. The mechanism of sex ratio

modification is likely to be significant for understanding sex ratio evolution. Third, the detection of non-Mendelian segregation in two of 18 otherwise "wild type" lines is significant for understanding the limits of adaptation. When segregation distortion is introduced into classical deterministic models of population genetics, the principle of maximized mean zygotic fitness is violated (HIRAIZUMI, SANDLER and CROW 1960). From the zygotic point of view, evolution can appear nonadaptive.

Several developments make it clear that segregation distortion must be incorporated into mainstream evolutionary thinking. Mechanisms of molecular turnover, including conversion bias and transposition, have recently become subjects of intense interest from an evolutionary point of view. It is apparent that these phenomena are formally equivalent in many respects to meiotic drive (HICKEY 1982; WALSH 1983). Recent theoretical work makes it possible to define analogs of the classical mean fitness for models that incorporate meiotic drive and some other frequency-dependent modes of selection (CURTSINGER 1984a,b). Like the potential function in physics, these functions are nondecreasing and maximized at equilibrium, providing dynamic evolutionary principles for general non-Mendelian systems. The detection of non-Mendelian segregation in a random sample of chromosomes suggests that such variation is a common feature of natural genetic variation. Thus, the study of meiotic drive and related modes of prezygotic selection is progressing rapidly and is likely to undergo considerable development in the near future.

This research was supported by National Science Foundation grant BSR 8211667 to J.C. and by National Institutes of Health grant GM-19770 to YUICHIRO HIRAIZUMI. I am very grateful to Y. HIRAIZUMI for the opportunity to work in his laboratory and for his support throughout this work. ANDREW CLARK (Pennsylvania State University) made helpful suggestions throughout the data analysis.

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