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THE RELATIVE RATES OF EVOLUTION OF SEX CHROMOSOMES AND AUTOSOMES

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> Moreover, selection is ineffective on recessive characters when these are rare, except in the case of sex-linked characters, when selection is effective in the heterozygous sex. . . . It seems therefore very doubtful whether natural selection in random-mating organisms can cause the spread of autosomal recessive characters. (Haldane 1924)

Several workers have noted that genetic studies of species differences often show large effects of loci on the X chromosome. Such effects of the X have been reported in studies of mating behavior in interspecific crosses (Tan 1946; Ewing 1969; Grula and Taylor 1980*b*; Kawanishi and Watanabe 1981; Kyriacou and Hall 1986), morphology (Templeton 1977; Val 1977; Grula and Taylor 1980*a*), and especially sterility (Dobzhansky 1936, 1974; Sturtevant and Novitski 1941; Oshima 1949; Grula and Taylor 1980*a*; Curtis 1982; Coyne 1984, 1985*a*; Coyne and Kreitman 1986; Naveira and Fontdevila 1986). Without considering negative findings as well, it is of course dangerous to infer a special role for the X in species differences; we attempt to discuss the overall picture in the final section of this paper.

Another evolutionary phenomenon that is probably connected with the sex chromosomes is Haldane's rule, the generalization that it is nearly always the heterogametic sex that is missing, inviable, or infertile in interspecific hybrids (Haldane 1922). These abnormalities do not seem to reflect an intrinsic sensitivity of males to hybridism, because females suffer disproportionately in interspecific crosses between taxa with female heterogamety (e.g., in birds and Lepidoptera; Haldane 1922). A more likely explanation is that the asymmetry has something to do with the sex chromosomes themselves (Muller 1940, p. 203). Genetic studies have indeed implicated epistatic interactions between the X chromosome and the autosomes or Y chromosome (Dobzhansky 1936; Moran 1979; Coyne 1984, 1985*a*; Coyne and Kreitman 1986; Naveira and Fontdevila 1986) and between the Y chromosome and the autosomes (Zouros 1981*b*; Vigneault and Zouros 1986) as

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causes of hybrid sterility. Although Haldane's rule applies widely throughout the genus *Drosophila* (Patterson and Stone 1952, p. 435; Bock 1984), there are several exceptions in which female offspring of interspecies crosses are the most affected (Crow 1942; Patterson and Griffen 1944; Bock 1984).

This empirical work shows that the sex chromosomes may play a special role in evolution and speciation, but we do not know why. One explanation is simply that, because the sex chromosomes contain a disproportionate share of genes, they contribute relatively more gene substitutions if all loci evolve at similar rates (Muller 1940, pp. 203–204). The Y chromosome is, of course, for the most part, genetically inert, apart from loci concerned with sex determination and/or male fertility (e.g., Dronomraju 1965; Lindsley and Tokoyasu 1980; Pimpinelli et al. 1986). In *D. melanogaster* at least, the Y-linked male-fertility loci are extraordinarily large in physical size and therefore seem to mutate at rates 50–100 times those of X-chromosome male-fertility genes (Pimpinelli et al. 1986). This may partly account for the role of the Y in hybrid-male sterility. This explanation is unlikely to hold for the X chromosome, however, since in most species it is not disproportionately large in physical size. In *D. melanogaster*, studies of induced male-sterility mutations show that the X chromosome does not have an increased concentration per salivary chromosome band of relevant loci (Lindsley and Lifschytz 1972; Lindsley and Tokoyasu 1980).

A more likely explanation for the prominent role of X-linked effects in speciation resides in the evolutionary behavior of chromosomes that are hemizygous in one sex and only three-quarters as numerous as autosomes. Similarly, rates of change at Y-linked loci are affected by the fact that Y chromosomes are permanently hemizygous and one-quarter as numerous as autosomes. In some groups, there is also evidence for a disproportionate involvement of the X chromosome in chromosomal rearrangements that differentiate species such as Orthoptera (Hewitt 1979) and simuliid flies (Post 1982). The dynamics of selection and drift on rearrangements are strongly affected by sex linkage, as we show below.

Only a few theoretical studies since those of Haldane (1924, 1926) have compared the long-term evolutionary dynamics of sex chromosomes and autosomes. Hartl (1971, 1972) pointed out that the rate of change in mean fitness at X-linked loci experiencing equal selection in males and females would be greater than that for comparable autosomal loci. Lester and Selander (1979) commented briefly on the fact that the chance of fixation would be higher for a semi-dominant X-linked mutation increasing the fitness of both sexes equally than for a similar autosomal mutation. Avery (1984) reviewed the earlier theoretical literature and demonstrated that deleterious or advantageous alleles often rise or fall in frequency more rapidly at X-linked loci. Rice (1984) showed that the evolution of either X chromosomes or autosomes can be more rapid when selection acts in opposite directions in the two sexes, depending on the degree of dominance.

In this paper, we provide a general analysis of the rate of evolution of sex chromosomes and autosomes, taking into account both the origin of variants by mutation and their subsequent chance of fixation. We concentrate on two models: the case of evolution at a single locus, and the case of a polygenic quantitative character undergoing a change in optimum. We find that, compared with auto-

TABLE 1

PARAMETERS DESCRIBING THE POPULATION COMPOSITION AND NATURE OF SELECTIVE DIFFERENCES BETWEEN GENOTYPES AT A SINGLE LOCUS

Locus	Females			Males		
Autosomal						
Genotype	A_1A_1	A_1A_2	A_2A_2	A_1A_1	A_1A_2	A_2A_2
Fitness	1	$1 + hs_1$	$1 + s_1$	1	$1 + hs_2$	$1 + s_2$
Frequency	$x_{1f}x_{1m}$	$x_{1f}x_{2m} + x_{2f}x_{1m}$	$x_{2f}x_{2m}$	$x_{1f}x_{1m}$	$x_{1f}x_{2m} + x_{2f}x_{1m}$	$x_{2f}x_{2m}$
X-linked						
Genotype	A_1A_1	A_1A_2	A_2A_2	A_1	A_2	
Fitness	1	$1 + hs_1$	$1 + s_1$	1	$1 + s_3$	
Frequency	$x_{1f}x_{1m}$	$x_{1f}x_{2m} + x_{2f}x_{1m}$	$x_{2f}x_{2m}$	x_{1m}	x_{2m}	
Y-linked						
Genotype				A_1	A_2	
Fitness				1	$1 + s_4$	
Frequency				x_{1m}	x_{2m}	

somal loci, loci on the sex chromosomes tend to evolve more rapidly under natural selection if favorable mutations are partially or fully recessive. This conclusion also holds for changes, such as chromosome rearrangements, that reduce fitness when heterozygous (as a result of the production of aneuploid gametes) and are established by genetic drift or by other, positive selection pressures. In contrast, the substitution of slightly deleterious alleles by random drift usually proceeds more slowly for sex-linked loci. These results provide an evolutionary explanation for some patterns of karyotypic change, for Haldane's rule, and for genetic data from species crosses.

RATES OF EVOLUTION AT AUTOSOMAL AND SEX-LINKED LOCI

The Fixation of Favorable Mutations

The simplest model for the long-term rate of evolution at individual loci under natural selection and mutation is to assume that each new favorable mutation is unique, such that the rate of gene substitution equals the product of the number of mutations entering the population each generation and their probability of fixation (Kimura and Ohta 1971, p. 12). In a large, randomly mating population of constant size, the probability of fixation of a new advantageous mutation can be calculated using branching-process theory (Fisher 1922; Haldane 1927). If the species population size is N and the mutation rate per locus to advantageous alleles is v, the rates of gene substitution for autosomal, X-linked, and Y-linked loci are $K_A = 2Nvu_A$, $K_X = 1.5Nvu_X$, and $K_Y = 0.5Nvu_Y$, respectively. The quantities u_A, u_X, and u_Y are the fixation probabilities of autosomal and sex-linked genes under the assumed regimen of selection. The fixation probabilities are completely determined by the selection coefficients in males and females. A one-to-one sex ratio is assumed; minor deviations from this will not greatly affect our conclusions.

We use the notation of table 1 to represent selection at single autosomal, X-linked, and Y-linked loci. For brevity, members of the heterogametic sex will be

referred to as males, but the results apply equally well to species with female heterogamety. The original and mutant alleles are denoted by A_1 and A_2, respectively. For simplicity, the coefficient of dominance, h, for the autosomal case has been assumed to be the same in males and females. The existence of dosage compensation of the type found in *Drosophila* and eutherian mammals means that s_3 equals s_1 when selection acts in the same way on both sexes; if dosage compensation is absent (as in Lepidoptera, Johnson and Turner 1979; birds, Baverstock et al. 1982), s_3 equals $\frac{1}{2}s_1$ for this mode of selection, assuming that a single dose of the favorable allele will be only half as effective as two doses.

In general, fixation probabilities for these models must be calculated using two-type branching-process theory (e.g., Ewens 1968, chap. 7); the relevant equations for this are given in the Appendix, and can be solved numerically by Newton-Raphson iteration. With weak selection, the rates of change in gene frequency for the autosomal and X-linked cases can be well approximated by assuming $x_{if} = x_{im} = x_i$ ($i = 1, 2$) and averaging the expressions for gene-frequency change in males and females, giving females twice the weight of males with X-linkage (Haldane 1926; Nagylaki 1979; Avery 1984). This enables explicit formulas for substitution rates to be obtained, using Haldane's (1927) result that the chance of fixation of a favorable gene with a small selective advantage s (such that the change in gene frequency of a rare allele with frequency x is given by $\Delta x = sx$) is $2s$. This result can be applied directly to the case of Y linkage, substituting s_4 for s. As shown below, the approximate results obtained from these formulas agree well with the exact results displayed in figures 1–3, even if selection is strong, for the cases that we have studied. For purposes of comparison, rates of substitution are expressed in time units of $(N\nu)^{-1}$ generations in order to remove the effects of population size and mutation rate, which are of no interest here.

Selection acting equally on the two sexes, with dosage compensation.—In this case, with weak selection and $s_1 = s_2 = s_3 = s_4$, we obtain

$$K_A \approx 4s_1h, \tag{1a}$$

$$K_X \approx s_1(2h + 1), \tag{1b}$$

$$K_Y \approx s_1. \tag{1c}$$

The ratio of the rate of evolution at an autosomal locus to that at an equivalent X-linked locus is thus

$$R_X \approx 4h/(2h + 1), \tag{2a}$$

and the ratio to that at an equivalent Y-linked locus is

$$R_Y \approx 4h. \tag{2b}$$

It is easily seen that R_X equals $\frac{4}{3}$ for $h = 1$ (complete dominance), decreases as h declines, equals 1 for $h = 0.5$, and approaches zero as h approaches zero, reflecting the low probability of survival of a recessive autosomal allele in a large population (Haldane 1927; Kimura 1962). Similarly, R_Y equals 4 for $h = 1$, equals 1 for $h = 0.25$, and approaches zero as h tends to zero. Figure 1 shows the results

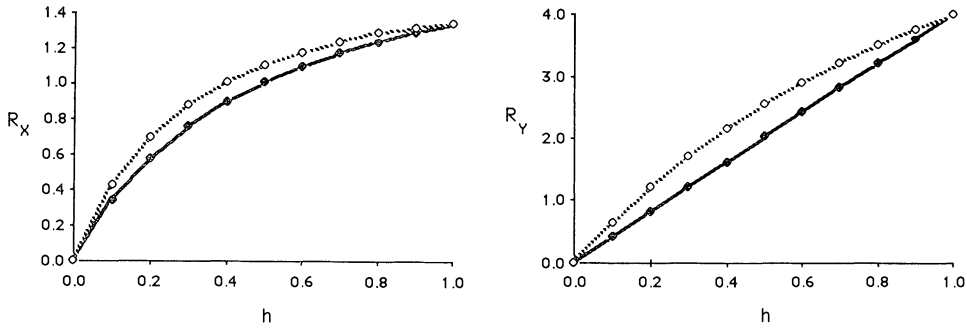

FIG. 1.—Ratios of the rate of evolution of autosomal loci to the rate of evolution of X-linked loci (R_X) and Y-linked loci (R_Y), plotted against the coefficient of dominance (h), for two different values of the selection coefficient (s) for mutant homozygotes. Favorable mutations, equal selection on the two sexes, and dosage compensation are assumed. *Solid*, $s = 0.01$; *open*, $s = 0.5$.

of branching-process calculations, which confirm these patterns. The lines for $s_1 = 0.01$ are very close to those predicted by equations (2), and the lines for $s_1 = 0.5$ differ only slightly.

Selection acting on males only, with dosage compensation.—In this case, $s_1 = 0$ and the rates of substitution with weak selection and $s_4 = s_3 = s_2$ are

$$K_A \approx 2s_2h\,,$$
$$K_X \approx s_2\,, \tag{3}$$
$$K_Y \approx s_2\,,$$

and we have

$$R_X \approx R_Y \approx 2h\,. \tag{4}$$

In this case, R_X and R_Y equal 2 when h equals 1, become 1 when h equals 0.5, and fall off faster than in the preceding case as h tends to zero. The differences between the two cases are attributable to the fact that the selection on a sex-linked gene is in this case confined to the hemizygous sex. Examples of the exact branching-process results are shown in figure 2.

Selection acting on females only.—We now have $s_2 = s_3 = 0$; and with weak selection

$$K_A \approx K_X \approx 2s_1h\,, \tag{5}$$

and K_Y must equal zero. Expression (5) results because selection acts on females with equal strength on X chromosomes and autosomes. Calculations of the exact branching-process results show that R_X is indeed close to 1 for weak selection, but for strong selection, the X-linked rate tends to be slightly lower than the autosomal rate.

Selection acting equally on the two sexes, with no dosage compensation.—We

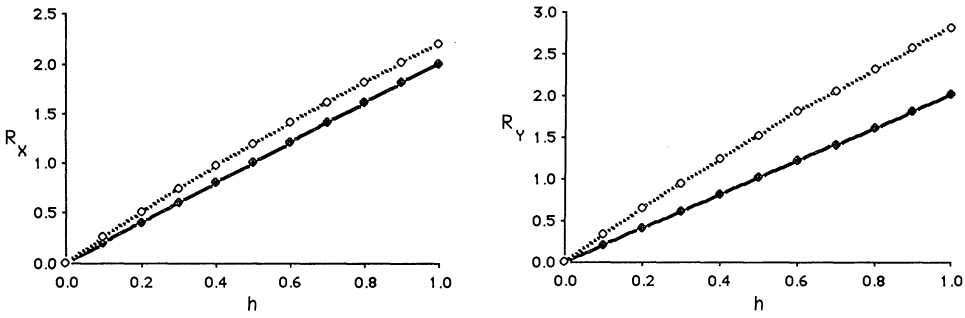

FIG. 2.—Ratios of the rate of evolution of autosomal loci to the rate of evolution of X-linked loci (R_X) and Y-linked loci (R_Y), plotted against the coefficient of dominance (h), for two different values of the selection coefficient (s) for mutant homozygotes. Favorable mutations, selection acting on males only, and dosage compensation are assumed. *Solid*, s = 0.01; *open*, s = 0.5.

have $s_3 = \frac{1}{2}s_1$, and find with weak selection that K_A is given by equation (1a), whereas

$$K_X \approx s_1(2h + \tfrac{1}{2}); \tag{6}$$

therefore,

$$R_X \approx 8h/(4h + 1). \tag{7}$$

The rate for Y-linked genes is unchanged by the absence of dosage compensation for X-linked loci (eq. 2b), assuming that their activity has been adjusted to a level similar to that of autosomal loci with equivalent functions.

The ratio of autosomal to X-linked rates now has a maximum of $\frac{8}{5}$, which is intermediate between the values for the first two cases. The ratio is one when h = 0.25, and decreases toward zero more slowly than in the first two cases. This pattern is seen in the exact results shown in figure 3.

Selection acting on males only, with no dosage compensation.—When selection acts only on males and there is no dosage compensation, one would expect s_3 to equal $\frac{1}{2}s_2$ for genes with comparable primary effects; thus, the rate of evolution for X-linked genes is one-half the rate with dosage compensation. Accordingly, the rate for X-linked genes will exceed that for autosomes only when h is less than 0.25. This is seen in the exact branching-process calculations (fig. 3).

Antagonistic effects in the two sexes.—The case of opposing selection pressures on the two sexes has been studied in detail by Rice (1984), who showed that there is a wide range of parameter values under which the spread of an X-linked mutation is possible when an autosomal mutation cannot invade. We merely note here that, with weak selection, a gene with a selective advantage in males but a disadvantage in females can spread when $s_2 > |s_1|$ (the autosomal case) or when $s_3 > 2h|s_1|$ (the X-linked case). With fitness effects of similar sizes in the two sexes, this situation thus favors a faster rate of evolution for sex-linked genes when $h <$ 0.5. The reverse is true for mutations that are favored in females but not favored in males.

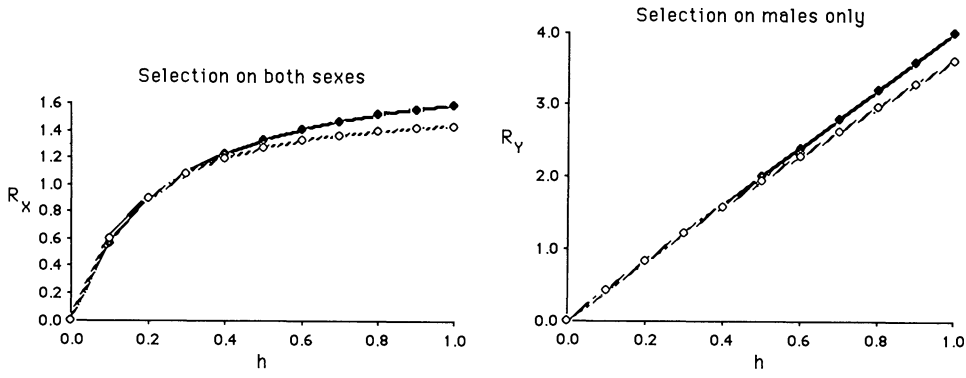

FIG. 3.—Ratios of the rate of evolution of autosomal loci to the rate of evolution of X-linked loci (R_X), plotted against the coefficient of dominance (h), for two different values of the selection coefficient (s) for mutant homozygotes. Favorable mutations and no dosage compensation are assumed. *Solid*, $s = 0.01$; *open*, $s = 0.5$.

The Fixation of Slightly Deleterious Mutations

An important factor of evolution at the level of DNA and protein sequences is represented by the fixation of neutral or nearly neutral mutations, the majority of which are probably slightly deleterious (Kimura 1983, chap. 3). Models of speciation can be constructed that involve this process (Bengtsson and Christiansen 1983; Nei et al. 1983; Wu 1985); thus, it cannot necessarily be assumed that alleles contributing to reproductive isolation between species have been fixed by selection acting on favorable mutations with relatively large effects on fitness, implying that $Ns \gg 1$, as assumed above. In this section, we shall consider the rates of stochastic substitution of alleles with small effects on fitness, such that $|Ns| \ll 1$. Because the rate of substitution of deleterious mutations is very small when this condition is violated (Kimura 1983, p. 44), detectable differences between closely related species are unlikely to develop by this mechanism unless the condition holds.

The method used here for calculating the rates of substitution is the same one used before, except that the probabilities of fixation of new mutations are now calculated from Kimura's (1962) general diffusion-equation formula for a finite population of effective size N. The calculations are outlined in the Appendix, and the results for the various cases analyzed are listed below, expressed as ratios of the rates for sex-linked and autosomal loci, using the same notation as before.

Selection acting equally on the two sexes, with dosage compensation.—When selections acts equally on both sexes and there is dosage compensation, then

$$R_X \approx 1 + \tfrac{1}{3}Ns_1(h - \tfrac{1}{2}), \tag{8a}$$

$$R_Y \approx 1 + \tfrac{1}{3}Ns_1(2h + \tfrac{1}{2}). \tag{8b}$$

When s_1 is less than zero, the rate of evolution of X-linked loci is faster when $h > 0.5$ and slower when $h < 0.5$, in contrast to the earlier finding for the case with $s_1 > 0$. The rate for Y-linked loci is always greater than for autosomal loci when $s_1 <$

0, and vice versa. Since $|Ns_1| \ll 1$ is assumed, the differences in rate are small, but larger effects in the same direction will be seen with larger values of $|Ns_1|$.

Selection acting on males only, with dosage compensation.—For selection acting on males only and with dosage compensation, we find that

$$R_X \approx R_Y \approx 1 + \tfrac{1}{3}Ns_3(h - \tfrac{1}{2}). \quad (9)$$

The relative rates of evolution of X-linked and autosomal loci behave as before with respect to the effect of h (eq. 4), but the relative rates for Y-linked and autosomal loci are now the same as for X-linked and autosomal loci.

Selection acting on females only.—As for favorable mutations with $Ns_1 \gg 1$, when selection acts only on females, the rates of evolution of X-linked and autosomal loci are approximately equal.

Selection acting equally on the two sexes, with no dosage compensation.—When selection acts equally on both sexes and there is no dosage compensation,

$$R_X \approx 1 + \tfrac{1}{3}Ns_1(h + \tfrac{1}{4}). \quad (10)$$

Therefore, when s_1 is less than zero, the rate of evolution of X-linked loci is always higher than that of autosomal loci. A similar result holds for the case of selection acting only on males only in the absence of dosage compensation, when s_3 is substituted for s_1. As before, the result for selection acting on females only is unaffected by the absence of dosage compensation (eq. 5). As expected, the formulas in the Appendix show that the rate of evolution for strictly neutral substitutions in each case equals the mutation rate (Hartl 1971), such that R_X and R_Y always equal unity for neutral mutations.

RATES OF EVOLUTION OF POLYGENIC CHARACTERS

Long-Term Rates of Evolution

For most morphological characteristics, a model of polygenic inheritance, with approximately additive effects across loci, seems appropriate. The above theory can readily be extended to this case, if we assume that species differences largely reflect the fixation of polygenic mutations accumulated by directional selection. (According to Hill [1982], data on rates of polygenic mutation suggest that new mutations will start to contribute to selection responses within a relatively short time after the initiation of directional selection.) The contribution of variability existing in the population before the application of directional selection will be examined below. Only autosomal and X-linked loci are considered because there is little evidence for effects of Y-linked genes on morphological traits.

Following Bulmer (1980, chap. 10), we assume that directional selection changes the mean phenotypic value of the character by ΔM, within each generation. If selection is applied to both sexes, the same change in mean is assumed to apply to each sex; if selection is applied to only one sex, then ΔM is the change in mean for this sex. Let V be the phenotypic variance for the character, and ΔV be the change in variance within a generation resulting from selection. When rates of substitution at autosomal and X-linked loci are compared, it is not necessary to

assume constancy of ΔM, V, and ΔV from generation to generation. It will be assumed, however, that these quantities are the same for males and females when selection is exerted on both sexes. This assumption requires the contribution of sex-linked loci to the phenotypic variance to be small in relation to the contribution of autosomal loci and environment, because the additive genetic variance in males caused by X-linked genes is twice that in females if there is dosage compensation (Bulmer 1980, p. 98). The intensity of directional selection is determined by $A = \Delta M/V$, and the effect of stabilizing selection is measured by $B = [\Delta V + (\Delta M)^2]/V^2$.

Consider the case of equal selection on both sexes with dosage compensation. Let the ith autosomal locus affecting the character be associated with values $-a_i$, d_i, and a_i for the three genotypes A_1A_1, A_1A_2, and A_2A_2. A similar representation can be used for the female genotypic values for an X-linked locus j, substituting j for i. The values of the male genotypes A_1 and A_2 are then $-a_j$ and a_j. The equations for change in gene frequency for these cases are given in the Appendix, using the method of Bulmer (1980, chap. 10) and neglecting the effects of linkage disequilibrium. With directional selection, such that the optimum is far from the mean, the contribution of the terms involving B can be neglected. Treating the allele A_2 as a new mutation, these equations imply that the terms s_1h and $s_1(2h + 1)$ in equations (1) are proportional to $(a_i + d_i)$ and $2(2a_j + d_j)$, respectively. Writing a and d for the mean values over all loci of the a's and d's, and assuming these to be the same for autosomal and X-linked loci, we obtain the ratio of the rates of substitution as

$$R_X = 2(a + d)/(2a + d). \tag{11}$$

This may be more conveniently expressed as

$$R_X = 2(1 + \delta)/(2 + \delta), \tag{12}$$

where $\delta = d/a$.

Complete dominance of all mutations implies that δ equals 1, and consequently, R_X equals ⅔, as before. Intermediate dominance on the average implies that δ equals zero, such that R_X equals 1, and complete recessivity implies that δ equals -1, such that R_X equals zero.

As one would expect intuitively, the mean degree of dominance at the level of phenotype, relative to the effect of the locus, maps onto the degree of dominance at the level of fitness effect. The same is true for the other fitness models considered above; the details will be omitted. If dominance is intermediate, we expect, on the average, no difference in rate between X-linked and autosomal loci, except for cases with no dosage compensation. Here, intermediate dominance leads to a slower rate of fixation for X-linked genes; a faster rate is attained with X linkage only if genes are, on the average, partially recessive.

Short-Term Rates of Evolution

It is harder to make clear-cut predictions about the rates of substitution for genes present in equilibrium frequencies before directional selection begins, because we do not know how variability in quantitative characters is maintained.

Such predictions are especially relevant in interpreting the results of artificial-selection experiments. The model of such mechanisms that is most amenable to quantitative study in this context is the mutation-selection-balance model originally proposed by Fisher (1930, chap. 5) and elaborated by many later authors (e.g., Kimura 1965, 1981; Latter 1970; Bulmer 1972, 1980; Lande 1975; Turelli 1984). We use Bulmer's (1972, 1980, chap. 10) version of this model, which postulates the existence of two alleles at each locus affecting a quantitative character under stabilizing selection, with mutation at rate μ in each direction. Because the more elaborate multi-allelic model of Turelli (1984) has very similar general properties, our general conclusions will probably be valid for this model.

We first discuss the properties of equilibria for both autosomal and X-linked loci, assuming that the mean of the character has been adjusted by selection to coincide with the selective optimum under stabilizing selection, such that $A = 0$ and $B = \Delta V/V^2$. This assumption requires some justification. Under stabilizing selection with a Gaussian fitness function, equation (A5) allows several stable equilibria, under which the mean may differ slightly from the optimum and the allele frequencies and genetic variances may differ substantially (Bulmer 1980, p. 168; Barton 1986). However, because equilibria that deviate substantially from the optimum are much less stable than equilibria near the optimum, either genetic drift or fluctuations in selection pressures may keep populations close to equilibria with $A = 0$. With this assumption, we apply the equilibrium results to the prediction of the short-term response to directional selection resulting from a shift in optimum. We consider in detail only the case of equal selection in both sexes with dosage compensation.

Equilibria under stabilizing selection.—Applying Bulmer's (1980, p. 180) argument to the equations in the Appendix, we obtain the following equation for equilibrium at the ith autosomal locus:

$$x_{1i}x_{2i}[a_i^2(x_{1i} - x_{2i}) + 2a_id_i(1 - 6x_{1i}x_{2i}) + d_i^2(x_{1i} - x_{2i})^3] = 2\mu/B. \quad (13)$$

The corresponding formula for the jth X-linked locus is

$$x_{1i}x_{2i}[6a_i^2(x_{1i} - x_{2i}) + 4a_id_i(1 - 6x_{1i}x_{2i}) + 2d_i^2(x_{1i} - x_{2i})^3] = 6\mu/B. \quad (14)$$

These relations are subject to the constraint

$$\sum_i [a_i(x_{1i} - x_{2i}) + d_ix_{1i}x_{2i}] + \sum_j [a_j(x_{1j} - x_{2j}) + \tfrac{1}{2}d_jx_{1j}x_{2j}] = 0, \quad (15)$$

which follows from the assumption that the population mean for the sexes combined is adjusted to the optimum, here arbitrarily taken to be zero.

With intermediate dominance and an even number of loci, and assuming some expression of the effects of each allele when heterozygous, such that $d_i \ll a_i$, equations (13)–(15) yield the following approximate solutions for autosomal and X-linked loci, respectively,

$$x_{1i} = -2\mu/B(a_i - d_i)^2 \quad \text{or} \quad x_{2i} = -2\mu/B(a_i + d_i)^2, \quad (16)$$

$$x_{1j} = -3\mu/B[(a_j - d_j)^2 + 2a_j^2]$$
$$\text{or} \qquad x_{2j} = -3\mu/B[(a_j + d_j)^2 + 2a_j^2]. \tag{17}$$

Completely recessive rare autosomal alleles have the equilibrium frequency $(\mu/2Ba_i^2)^{1/2}$.

With intermediate dominance, such that the d's equal zero, the above formulas show that X-linked loci come to equilibrium with rare alleles at one-half the frequency of alleles at autosomal loci. Rare-allele frequencies for any dominance level are always higher for autosomal than for X-linked loci, consistent with the classical results for mutation-selection balance (Haldane 1927). This suggests that relatively fewer X-linked than autosomal polygenes will be fixed during an initial selection response in this case.

Short-term responses to selection.—Short-term responses to selection can be examined as follows. For a natural population or for an artificial-selection experiment with a large foundation population, we can assume that the initial allele frequencies equal the equilibrium frequencies under mutation-selection balance. The probability of fixation of a favorable allele at an autosomal locus present at the start of directional selection approximately equals $4Ns$ times its initial frequency (A. Robertson 1960), where s is the selection coefficient on the heterozygote. Here, $4Ns$ equals $4NA(a + d)x_{2i}$, assuming that selection is in the positive direction. The corresponding formula for a sex-linked locus is $2NA(2a + d)x_{2j}$. If Q_r is the fraction of autosomal loci at which recessive favorable alleles are at the above equilibrium frequency and if recessive autosomal alleles have a negligible probability of fixation, the products of these fixation probabilities with the equilibrium allele frequencies yield the following expression for the ratio of the mean rate of fixation of autosomal alleles to the rate for X-linked alleles:

$$R_X \approx 4(1 - Q_r)[2 + (1 + \delta')^2]/3(2 + \delta')(1 + \delta'), \tag{18}$$

where δ' is the mean of d/a for nonrecessive favorable alleles in the equilibrium population. (It has been assumed that the variance in the d/a values is sufficiently small that the mean of quantities such as $a_i/[a_i + d_i]$ can be approximated by $1/[1 + \delta']$.) This formula underestimates R_X because, in practice, recessive autosomal alleles have a nonzero chance of fixation in a small population (Haldane 1927; Kimura 1962).

If there are no recessives, this ratio decreases with increasing δ', from near infinity for δ' close to -1, through 2 for δ' equal to zero, to $\frac{4}{3}$ for δ' equal to one. A ratio less than one requires a large proportion of loci possessing rare recessive alleles at equilibrium.

The same ratio of mean fixation rates is obtained for the case in which the initial population exposed to directional selection forms a relatively small sample from an equilibrium population, such that rare alleles are either lost during the foundation of the population or are present at an initial frequency of $1/2N$(autosomal loci) or $2/3N$(X-linked loci), with no change in expected frequencies. The numbers of initially segregating loci are then proportional to the equilibrium frequencies divided by these quantities, and the fixation probabilities for nonrecessive alleles may be taken as twice the selection coefficients on rare alleles, as in the calcula-

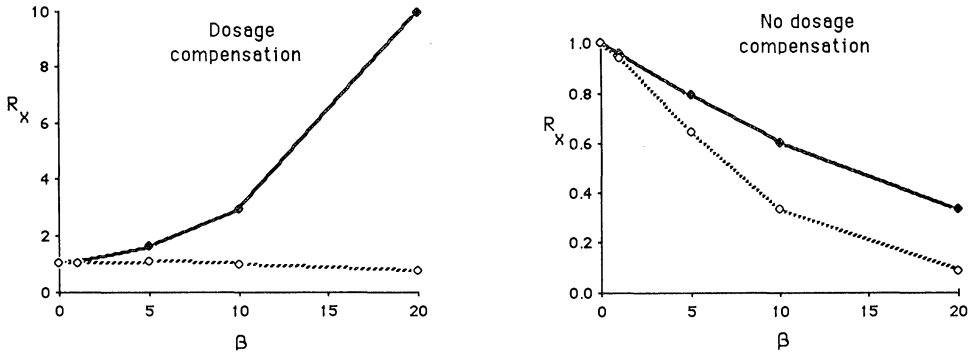

FIG. 4.—Ratios of the rate of evolution of autosomal loci to the rate of evolution of X-linked loci (R_X), plotted against $\beta = 2Na^2$, under the stochastic turnover of alleles at polygenic loci subject to stabilizing selection. Equal selection acting on the two sexes is assumed. The cases of semidominance and complete dominance or recessivity of mutant alleles on the scale of the polygenic trait are shown. *Solid*, semidominance; *open*, dominance.

tion of long-term rates above. Multiplying the numbers of segregating loci by the fixation probabilities yields the stated conclusion.

Parallel results can be obtained for cases in which selection acts differently on the sexes, with some differences in the numerical values of the ratios of rates, but we will omit the details. These calculations suggest that the short-term responses to selection nearly always involve the fixation of relatively more autosomal than X-linked genes, unless a high fraction of loci harbor rare, recessive favorable alleles.

Stochastic Turnover of Alleles under Stabilizing Selection

Kimura (1981, 1983, chap. 6) has suggested that because of the low intensity of selection acting on alleles at individual loci when a large number of loci affect the same trait, extensive stochastic turnover in allele frequencies may occur at loci controlling a highly polygenic trait under stabilizing selection balanced by mutation. This process of turnover may be studied by methods similar to those used for the random fixation of deleterious alleles at single loci. Using the above results for the equilibrium frequencies of alleles at polygenic loci, we can assume that most loci have allele frequencies close to zero or one in an infinite population. If the population size is sufficiently small in relation to the mutation rate, most loci will be fixed; occasionally, drift causes a new allele to replace the one prevailing at a locus. As before, the probability of such a turnover event at a locus equals the number of new mutations entering the population each generation times the probability of fixation of each mutation. The latter can be evaluated using the method described in the Appendix, substituting the gene-frequency equations (A5) and (A6) into the fixation probability formulas (A4).

The relative values of the rates of turnover for autosomal and X-linked loci with equal selection on both sexes, assuming either recessivity, no dominance, or complete dominance of the rare alleles, are shown in figure 4. The parameter $\beta =$

TABLE 2

PARAMETERS DESCRIBING THE SELECTIVE DIFFERENCES BETWEEN GENOTYPES AT A SINGLE LOCUS WITH UNDERDOMINANCE

	AUTOSOMAL LOCUS						X-LINKED LOCUS				
	Females			Males			Females			Males	
Genotype	A_1A_1	A_1A_2	A_2A_2	A_1A_1	A_1A_2	A_2A_2	A_1A_1	A_1A_2	A_2A_2	A_1	A_2
Fitness	1	$1-s$	$1+\alpha s$	1	$1-s$	$1+\alpha s$	1	$1-s$	$1+\alpha s$	1	$1+\alpha s$

$2Na_f^2$ measures the effect of an individual locus in relation to population size. With conventional dosage compensation and no dominance, the rate of turnover is higher at autosomal loci. With dominance or recessivity, the rate for X-linked loci is slightly higher. With no dosage compensation, the rate is higher for X-linked loci. Similar results are obtained for selection acting on males only. Selection acting only on females yields equal rates for sex-linked and autosomal loci.

If the population size is so large that most loci, rather than being fixed, are close to their equilibrium frequencies, the problem of calculating the rates of stochastic transition becomes much more complicated, and no general solution is yet available (Barton and S. Rouhani, MS). Qualitatively, it seems likely that, relative to alleles at X-linked loci, alleles at autosomal loci usually have rates of turnover higher than those given by the above method. Autosomal alleles usually reach higher equilibrium frequencies (except when strongly dominant), and hence have a greater opportunity to increase in frequency by drift.

THE FIXATION OF CHROMOSOMAL REARRANGEMENTS

In this section, we calculate the expected rate of fixation of chromosomal rearrangements, subject to heterozygous disadvantage because of improper meiotic disjunction (see Wright 1941; Lande 1979, 1985). The rate for X-linked rearrangements is compared with that for autosomal loci, taking into account both the rate of origin of new arrangements by mutation, and their chance of fixation by drift.

The model of selection used is shown in table 2. Here, s represents the reduction in fitness of heterozygotes and is kept constant. The term αs represents an advantage of A_2 over A_1, which might be caused by meiotic drive, a change in recombination between loci under selection, or a direct effect of karyotype on fitness. In general, both s and α may differ between the sexes and also for autosomal and sex-linked rearrangements. We ignore such complications here (see the Discussion and Appendix).

The probability of fixation of a newly arisen rearrangement can be calculated by substituting into equations (A4) the equations for change in gene frequency derived from Table 2, as was done for the case of stochastic turnover under stabilizing selection. If μ is the rate of origin of new arrangements per chromosome per generation, the rate of substitution of new arrangements on an autosome

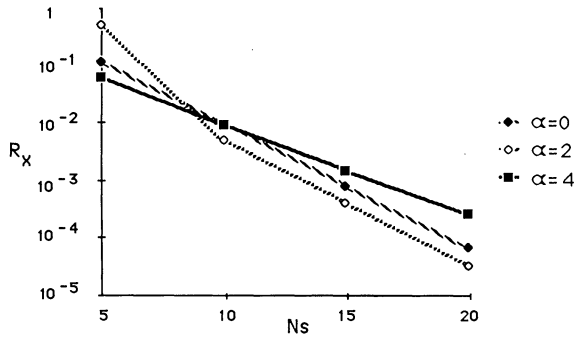

FIG. 5.—Ratios of the rate of evolution of autosomal chromosome rearrangements to the rate of evolution of X-linked rearrangements (R_X), plotted against Ns, for various values of α (s is the selection coefficient against chromosomal heterozygotes and $s\alpha$ is their advantage when homozygous).

in a single population of effective size N (in time units of μ^{-1}) is

$$K_A = (2Ns\alpha/\pi)^{1/2}\exp(-2Ns/\alpha)/\{P(2[Ns/\alpha]^{1/2}) - P(2[1 - \alpha][Ns/\alpha]^{1/2})\}, \quad (19)$$

where $P(x) = \int_{-\infty}^{x}\exp - \frac{1}{2}t^2dt/[(2)^{1/2}\pi]$.

Lande (1979) has shown that the same expression holds for the rate of substitution for a species divided into partially isolated demes subject to random extinction and recolonization; the population sizes in question are still those for individual demes.

A similar calculation for the case of sex-linked rearrangements yields the formula

$$K_X = \frac{(Ns\alpha/\pi)^{1/2}\exp[-Ns(4 - \alpha)^2/4\alpha]}{P([3\alpha - 4][2Ns\alpha]^{1/2}/2\alpha) - P([\alpha - 4][2Ns\alpha]^{1/2}/2\alpha)}. \quad (20)$$

Two factors make this rate higher than that for comparable autosomal rearrangements. First, the effective population size is smaller with sex linkage. Second, selection can act only against heterozygotes in females. This means that the new arrangement can increase even when rare, if its homozygous advantage is sufficiently high ($\alpha > 3$); this is never possible for an autosomal arrangement. When Ns is large, the above formula simplifies to one of two forms:

$$K_X = (Ns\alpha/\pi)^{1/2}\exp[-(4 - \alpha)^2Ns/4\alpha], \qquad \alpha < 2; \quad (21a)$$

$$K_X = Ns(\alpha - 4), \qquad \alpha > 4. \quad (21b)$$

The ratio of the rates of autosomal and sex-linked evolution given by equations (19) and (20) is shown in figure 5, for a range of values of α and Ns. The range of values of Ns used corresponds to that suggested by Lande's (1979) analysis of rates of chromosomal evolution. It is evident that the rate of evolution can be much faster for X-linked rearrangements, when Ns is large and the overall rate of change is slow.

DISCUSSION

Long-Term Evolution: Theoretical Considerations

Fixation of selectively favorable alleles.—Our theoretical results show that selection in individual loci, acting either in the heterogametic sex alone or equally in both sexes, will lead to a faster long-term rate of accumulation per locus of partially recessive alleles for the X and Y chromosomes than for the autosomes, if there is dosage compensation (when $h < 0.5$ and $h < 0.25$, respectively). This makes intuitive sense, because partially recessive alleles are somewhat shielded from selection when heterozygous but are completely exposed to selection in the hemizygous sex (Haldane 1924). In the absence of dosage compensation, the rate for X-linked loci exceeds that for autosomes only when h is less than 0.25, since the hemizygotes now enjoy only half the advantage of homozygotes. When selection is restricted to the homogametic sex, dosage compensation is largely irrelevant, and favorable mutations accumulate at approximately equal rates on the X chromosome and autosomes.

Similar results hold for the long-term evolution of loci affecting characters under polygenic control that is additive across loci, since the evolution of an additive polygenic character is merely the summation of events occurring at single loci. The sex chromosomes evolve faster than the autosomes only when, on the average, there is partial recessivity of mutations affecting the character in the direction of selection. We would thus expect a differential in favor of the sex chromosomes in this case only if selection is in the same direction as the effect of inbreeding on the phenotypic mean (which depends on the existence of directional dominance; Falconer 1981, chap. 14). Because there is no firm evidence of directional dominance for new mutations affecting such classical polygenic characters as *Drosophila* bristle numbers (reviewed in Hill 1982), we would usually expect little or no differential in favor of the X for these characters.

These conclusions assume that the population size and rate of mutation to favorable alleles are sufficiently small that each new mutation that becomes established is unique. With this assumption, the rate of allelic substitution is controlled jointly by the total number of genes at a locus in the population, the mutation rate to favorable alleles, and their probability of fixation by selection (Kimura and Ohta 1971, p. 12). As pointed out by Maynard Smith (1974, 1978, p. 21), the same favorable mutation will appear many times at a locus if the product of population size and mutation rate is sufficiently large, and the formulas we have used for the long-term rate of evolution will be invalid. Although alternative models have been proposed (Maynard Smith 1974, 1978; Gillespie 1984), no simple analytic predictions seem possible.

A rough idea of the consequences of this situation can be obtained as follows. Suppose that the environment is constantly changing, and the fixation of an allele at a locus is quickly followed by an increase in frequency of another one, such that the latest allele favored by selection can only arise by mutation from the preceding allele that was favored. Alternatively, imagine that a new allele can be favored at one locus only after selection has fixed a new allele at another locus, because of

epistatic interactions in fitness. In these cases, one gene substitution must become nearly fixed before the next can be initiated. If an abundant pool of mutations is available at the loci concerned, the number of substitutions in a given period of evolutionary time will be controlled by the time occupied by each substitution. In a large population, this is inversely related to the strength of selection (Haldane 1924; Ewens 1968, p. 62), and hence to the fixation probabilities we have used here.

Because the rate of evolution is now no longer affected by the number of mutations entering the population each generation, it is irrelevant that the number of genes at an X-linked locus is only ¾ of that at an autosomal locus. This implies that a higher rate of evolution at X-linked loci is expected under less restrictive conditions with respect to dominance than those derived earlier; for example, equal selection on both sexes results in faster evolution of the X, except with complete dominance. The effect for the Y chromosome is similar. If this model is applicable, somewhat faster rates of evolution for sex chromosomes would frequently be expected for all types of characters. Presumably, in nature the true situation is somewhere between this situation and the one assumed earlier. In any event, a large discrepancy in rate is only found if favorable mutations are nearly recessive on the average. We examine the biological plausibility of this case below.

Random fixation of alleles.—The results for the rates of fixation of alleles with small effects on fitness, relative to the reciprocal of the species' population size, show that the rate of substitution of strictly neutral mutations is identical for sex-linked and autosomal loci, as previously pointed out by Hartl (1971). As can be seen from equations (8)–(11), the rate of substitution of slightly deleterious alleles at X-linked loci is always somewhat lower or the same as at autosomal loci when h is less than 0.5, except for the case of selection in both sexes in the absence of dosage compensation. A slower rate of substitution of deleterious alleles, relative to the autosomes, is expected for Y-linked loci with selection only in males when h is less than 0.5; there is a higher rate of evolution for Y-linked loci compared with autosomal loci exposed to selection in both sexes. As we discuss below, since alleles with small deleterious effects on fitness are nearly always partially recessive, the condition that h is less than 0.5 is likely to be satisfied; we therefore predict that at sex-linked loci the rate of evolution by this mechanism will be slower than or equal to that at autosomal loci.

Similarly, the process of stochastic turnover of alleles at loci affecting polygenic traits under stabilizing selection is usually faster for autosomal than for X-linked loci, unless the mutant alleles are predominantly dominant in their effects on the character (fig. 4). Combining these conclusions, we infer that the evidence for a disproportionate involvement of sex-linked genes in the control of reproductive isolation (see the introduction) suggests that these effects are the result of the substitution of selectively favorable alleles, rather than from fixation by random drift in opposition to selection. The loss of hybrid fitness occurs because alleles that have been substituted in one of two separate populations are not selected to produce high fitness when combined with genes from the other population (Muller 1940).

Long-Term Evolution: Empirical Evidence

Genetics of species crosses.—For additive polygenic characters, the above reasoning leads us to expect little evidence for involvement of the X chromosome disproportionate to its size in relation to the rest of the genome, in interpopulation or interspecies differences. It is hard to test this expectation, since there are few cases in animals in which such differences have been analyzed genetically. The results of Coyne (1983, 1985*b*) and Coyne and Kreitman (1986) on the *melanogaster* subgroup of *Drosophila* did not yield any evidence for disproportionate X effects on three morphological characteristics, in contrast to the very pronounced effects of the X and Y chromosomes on male fertility (Coyne 1984, 1985*a*; Coyne and Kreitman 1986). There is evidence for a strong X-chromosome effect on one of five morphological characters examined in the other well-studied *Drosophila* hybrid, *D. silvestris* × *D. heteroneura* (Templeton 1977; Val 1977). Carson and Lande (1984) found that the X chromosome contributed about 30% (somewhat more than the expected 20%) of the difference in tibial bristles between two populations of *D. silvestris*. Similarly, strong effects of the X on ethological isolation have been observed for crosses of *D. pseudoobscura* with *D. persimilis* (Tan 1946; Ewing 1969) and of *D. melanogaster* with *D. simulans* (Kawanishi and Watanabe 1981; Kyriacou and Hall 1986) but not for semispecies of *D. paulistorum* (Ehrman 1961) or for crosses of *D. mojavensis* with *D. arizonensis* (Zouros 1981*b*). Similarly, Zouros (1981*a*) found no evidence for a substantial X effect on viability in crosses of *D. mojavensis* with *D. arizonensis*. Bentley and Hoy (1979) reported a reciprocal effect in the F_1 of the kind expected from an X-chromosome effect for one of five characters studied in cricket hybrids (a group in which dosage compensation exists; Hebbert 1984). Henry (1985) found no evidence for sex-linked effects in 13 song characteristics of hybrids of the lacewing *Chrysoperla*.

Birds and butterflies are known to lack dosage compensation in the heterogametic sex (Johnson and Turner 1979; Baverstock et al. 1982). One might therefore expect fewer disproportionately large X-chromosome effects in interpopulation and interspecific crosses in birds and butterflies than in groups with dosage compensation. One study of butterflies (Grula and Taylor 1980*a*,*b*) has shown large X-linked effects on several morphological and behavioral characters, but evolutionary studies of other butterflies have failed to show any evidence for effects of sex-linked genes on morphology (Clarke and Sheppard 1955, 1960; Clarke et al. 1977). An exception is Y linkage of the female-limited mimetic polymorphism of *Papilio glaucus* (Clarke and Sheppard 1962), in which maintaining female limitation by Y linkage presumably results in a sexual selective advantage (Turner 1978). The evidence is particularly clear for the Müllerian mimics *Heliconius erato* and *H. melpomene*, in which genetic analysis of 8 and 11 major mimicry loci has failed to reveal any sex linkage of alleles distinguishing the numerous geographical races (Sheppard et al. 1985).

Overall, the evidence suggests that usually the X chromosome does not disproportionately affect morphology in hybrids, whereas fertility or viability frequently exhibit strong effects of the X and/or Y chromosome (see the introduction for further references). The evidence for behavioral characteristics is equivocal, with

some indication that the X may have a disproportionate effect. A possible difficulty concerning the conclusion with respect to hybrid fitness traits is that loss of fitness in hybrids can be studied genetically only if F_1 individuals possess some degree of viability and fertility (H. Orr, pers. comm.). Genetic studies are therefore inevitably biased toward cases in which only one sex, rather than both, is sterile or inviable. It might be that no disproportionate effects of the sex chromosomes would be found in the unanalyzable cases where both sexes are sterile or inviable, especially since sex bias is not expected from incompatibilities between autosomal alleles of different species. The apparently large role of the sex chromosomes might reflect a chance accumulation of a large number of substitutions on the sex chromosomes in individual cases, resulting in a greater fitness loss to the heterogametic sex (see below), rather than a real difference in underlying rate between the sex chromosomes and autosomes. But if this were so, it is hard to understand the high frequency with which the sex asymmetry expressed in Haldane's rule is found, especially in crosses between close relatives in *Drosophila* (Coyne and Orr, MS) and in groups like the Lepidoptera and birds (Haldane 1922; Grula and Taylor 1980*a*; Clarke and Ford 1982) in which the sex chromosomes make up a very small proportion of the genome (White 1973). These facts suggest a real disproportionality between the sex chromosomes and autosomes with respect to hybrid fitness loss.

If our calculations of evolutionary rate are relevant, these considerations suggest that the genetic control of hybrid breakdown may reflect a history of selection on recessive or partially recessive, favorable mutant alleles. These alleles are presumably selected for because of their individual effects on specific phenotypes, rather than their effects on a phenotype controlled by a number of loci with approximately additive, interchangeable effects, in which lack of dominance would, on the average, be expected (Hill 1982). In other words, they are selected for essentially as major genes, contributing the bulk of the genetic variance in the characters that they affect during the period of their spread and fixation, in the same way as the color and pattern genes of *Heliconius* (Sheppard et al. 1985). This does not necessarily imply, of course, that the fitness or phenotypic effects of the genes were large in an absolute sense during the course of the gene substitutions involved. However, a recent mapping study has demonstrated a major effect of an allele at an X-chromosome locus in determining male sterility in the *D. mauritiana* $\times$ *D. simulans* hybrid when placed on the appropriate autosomal background (Coyne and Charlesworth 1986).

Haldane's rule.—As mentioned above, the model of more-rapid substitution of recessive or partially recessive sex-linked alleles provides an explanation for Haldane's rule (Haldane 1922), provided that there is epistasis between them and autosomal loci (see Muller 1940, p. 203). A simple two-locus model of such epistasis involves an ancestral population homozygous for an autosomal and an X-linked locus, with genotype X_1/X_1 (or X_1/Y) A_1/A_1. Assume that one descendant population becomes X_2/X_2 A_1/A_1 and the other X_1/X_1 A_2/A_2, as a result of the substitutions of a favorable recessive allele on the X and of a dominant allele on the autosome, respectively. Assume also that X_2 has a damaging effect on fertility

or viability in combination with A_1. On the basis of these assumptions, matings between X_2/X_2 A_1/A_1 females and X_1/Y A_2/A_2 males will produce X_2/X_1 A_1/A_2 female hybrids and X_2/Y A_1/A_2 male hybrids. Male hybrids will suffer the deleterious consequences of the interaction between the alleles at the two loci. In this model, the other reciprocal cross produces offspring of high fitness of both sexes; but with the substitution of an additional X-linked or autosomal locus, one can obtain males that suffer deleterious effects in both reciprocal crosses. Given sufficient time for the accumulation of many autosomal substitutions with incompatibilities between alleles derived from different populations, effects on both sexes in the F_1 will appear. A similar scenario can be devised for interactions between X- and Y-linked genes or between Y-linked genes and autosomes, except that in the second case only the heterogametic sex is affected (cf. Zouros 1981*c*; Coyne 1985*a*; Vigneault and Zouros 1986).

An F_1 fitness differential in favor of the homogametic sex will always be produced by X-linked loci, provided that the deleterious effects of their interaction with the autosomes are less than completely dominant (in the presence of dosage compensation). The disproportionately large role for the sex chromosomes in those cases of Haldane's rule that have been analyzed genetically (see above) suggests that there must have been partial recessivity of the favorable fitness effects of the relevant loci in order that a sufficient number of genes could have accumulated on the X chromosome, relative to the autosomes, to cause such disproportionality. The dominance coefficients during the gene substitutions need not, of course, be the same as those for the interspecies hybrids. Furthermore, the evidence for a strong role of the X in the two cases of the reverse of Haldane's rule in *Drosophila* that have been genetically analyzed (Crow 1942; Patterson and Griffen 1944) is not necessarily inconsistent with our theory, which predicts no disproportionality in favor of the X chromosome for loci that affect only females; it is conceivable that the genes concerned have been selected by virtue of their favorable effects on both sexes.

The above model suggests that there could be an intermediate stage of evolution in which heterogametic sterility or inviability appears in only one reciprocal cross. We therefore predict the following sequence of events in speciation: (1) hybrids of both sexes are fertile and viable; (2) the heterogametic sex is sterile or inviable in one reciprocal cross; (3) the heterogametic sex is sterile or inviable in both reciprocal crosses; (4) both sexes are sterile or inviable in both reciprocal crosses. We are testing this scenario by correlating the stage of divergence among species pairs with respect to hybrid sterility or viability with an independent measure of time since divergence, such as electrophoresis or DNA sequence data (Coyne and Orr, MS). Zouros (1986) has proposed an alternative model for the evolution of asymmetrical male sterility caused by sex chromosome–autosome interactions. In his model, a new allele at one locus increases in frequency only if the frequency of the old allele at another locus is sufficiently low, because the new-old allelic combinations are male-sterile. This model produces consequences similar to ours, but requires a delicate balance of the relevant fitness parameters in order to work. Our model, however, requires only the existence of selectively favorable genes

with adverse effects on fertility on an inappropriate genetic background. Furthermore, this model provides no general explanation for Haldane's rule, since it arbitrarily assumes that male sterility is the affected trait.

Dominance of mutant-gene effects.—There is some evidence about the dominance relations of favorable mutations with major effects. "Haldane's sieve" (Haldane 1924, 1927; Turner 1981) means that fully recessive, autosomal mutations have a near-zero chance of fixation in a large, random-mating population (Kimura 1962). When the direction of evolution is known for a character that has undergone evolution by selection of major autosomal genes, it has been found that dominant and semidominant rather than recessive alleles have been fixed (Kettlewell 1973; Wood 1981). In sharp contrast, for all species that have been examined, mutations with major effects on the external phenotype are overwhelmingly recessive (Fisher 1930, 1958; Haldane 1939). In *Drosophila*, homozygous lethal or deleterious viability mutations are somewhat recessive on the average, and mutations with the smallest homozygous fitness effects are the least recessive (Simmons and Crow 1977; Mukai and Nagano 1983; Eanes et al. 1985). Such a pattern is expected if most deleterious mutations exert their effects by inactivating or partially inactivating enzymes for which their loci code (Wright 1934; Kacser and Burns 1981). Experimental evidence supporting the model of Kacser and Burns has been reviewed by Hartl et al. (1985).

It is therefore reasonable to believe that most mutations with relatively large deleterious effects on fitness are nearly recessive, whereas mutations with small fitness effects are nearer to semidominance. This is not equivalent to saying that most new favorable mutations will be partially recessive, because such alleles may not usually work by reducing the catalytic activity of enzymes; they might be regulatory mutations that alter the timing or tissue specificity of gene activity, for example. It is therefore desirable to seek direct evidence concerning the dominance coefficients of favorable mutations. One source of information is strains or populations of self-compatible plants that have acquired metal or herbicide tolerance. If some self-fertilization is taking place, selecting for recessive favorable mutations is not difficult. What little is known about these cases suggests that recessive alleles for tolerance are sometimes selected for (Macnair 1979, 1981; Hayes 1959); in contrast, pesticide resistance in insects always involves dominant or semidominant genes (Wood 1981). These considerations suggest some empirical basis for thinking that the conditions for a rate of long-term evolution that is faster at X- or Y-linked loci than at autosomal loci will often be met for genes with relatively major positive effects on fitness. There is considerable scope, however, for further studies of the dominance relationships of newly established favorable mutations in inbreeding or haplodiploid species, in order to test properly the hypothesis of partial recessivity.

Chromosome rearrangements.—The theory developed earlier shows that, compared with autosomal mutations having similar effects on fitness, X-linked underdominant mutations will more often be fixed by drift or by selection for favorable homozygous effects. The differential in favor of sex-linked changes may be substantial when the overall rate of evolution is low (fig. 5). This theory is most

likely to apply to chromosome rearrangements, which, when heterozygous, frequently cause the production of duplication/deficient or aneuploid gametes (Wright 1941; Lande 1979, 1985). In groups with Y chromosomes, the model is probably most appropriate for inversions; the properties of translocations or centric fusions involving the X chromosome will be affected in the heterogametic sex by the frequency of improper disjunction of the X-A chromosome from the Y-A homologous pair, which is arbitrarily assumed to be zero here.

If this mode of karyotypic evolution were common, we would expect a disproportionate incidence of rearrangements involving the X chromosome when comparing related species. A similar effect would be expected for rearrangements that have positive effects on fitness both when they are heterozygous and when they are homozygous, because sex-linked rearrangements in the heterogametic sex would not suffer any negative effects of aneuploidy (eq. 21b). Another possible contributing factor arises when polymorphic autosomal alleles exert different selective effects on the two sexes, generating a selective advantage to rearrangements linking the alleles to the sex chromosomes (Charlesworth and Charlesworth 1980). Unfortunately, the operation of these processes may be obscured by various other factors. For example, the X chromosome often differs from the autosomes in condensation and meiotic behavior (White 1973); nondisjunction of the X (whose frequency can be increased even by heterozygosity for paracentric inversions; Sturtevant and Beadle 1936) can result in viable offspring in groups with a *Drosophila* type of sex determination, whereas autosomal nondisjunction is normally lethal. Similarly, X-autosome translocations frequently cause male sterility (Lindsley and Lifschytz 1972). Caution is therefore necessary in interpreting the comparative data.

A second problem is that sufficiently detailed information is only available for a few groups. In order to compare the rates of sex-linked and autosomal karyotypic evolution, we need to examine groups with well-understood phylogenies, in which the sex chromosomes are reliably identifiable. Adequate information is only available for three groups: Mammalia, Orthoptera, and Diptera. We present an analysis of the available data for these groups in the Appendix.

This analysis suggests that the sterility effects of translocations involving X chromosomes and autosomes outweigh any differential rate of evolution in favor of the sex chromosomes for this class of rearrangement in mammals and *Drosophila*. There is, however, evidence for a weak effect in the expected direction in Orthoptera and *Didymuria*. In marsupials, Orthoptera, and *Drosophila*, there is an excess of fixed inversions on the X, probably caused by the process we have modeled. Despite this qualitative agreement, however, the ratio between sex-linked and autosomal rates is much smaller than would be expected from a model of simple underdominance, given the Ns values needed to explain observed autosomal rates of evolution (in the range 10–20; Lande 1979). Thus, chromosomal rearrangements may often be established as a result of a selective advantage that is expressed when they are heterozygous. Similarly, the predominance of X-linked inversions in simuliids (see the Appendix) is probably a consequence of sex-specific selection.

Short-Term Responses to Selection

We have shown that the equilibrium frequencies of X-linked alleles affecting a polygenic character exposed to mutation and stabilizing selection will be lower than those at equivalent autosomal loci. In addition, a short-term response to directional selection will accordingly involve a lower rate of fixation of alleles at X-linked loci, unless a large fraction of loci carry low-frequency recessive alleles that affect the character in the direction of selection. We would therefore expect that changes observed in short-term artificial-selection experiments would be disproportionately likely to result from autosomal genes. Relevant data from a number of selection experiments on *D. melanogaster* are reviewed in the Appendix (table A3).

Overall, the evidence from the characters for which several replicate lines have been studied suggests that the average X-chromosome contribution to a selection response does not differ greatly from the fraction of the genome contributed by the X. For several of these characters, factors of the type discussed in the Appendix must have inflated the contribution of the X compared with the theoretical expectation of 10%, one-half of its genomic contribution (the expectation is based on the hypothesis of semidominance of individual-locus effects; see the earlier section on the theory of short-term responses). There is certainly no evidence at all for dramatic effects of the X comparable to those found with interspecific sterility and inviability. A major feature of the results is the disproportionate contribution by chromosome 3 to the responses, compared with that by chromosome 2 or by the X. We can offer no explanation for this finding, which does not appear to have been noticed previously.

SUMMARY

We develop models of the rates of evolution at sex-linked and autosomal loci and of the rates of fixation of chromosomal rearrangements involving sex chromosomes and autosomes. We show that the substitution of selectively favorable mutations often proceeds more rapidly for X- or Y-linked loci than for the autosomes, provided that mutations are recessive or partially recessive on the average. Selection acting on a quantitative character is expected to result in similar long-term rates of gene substitution for X-linked and autosomal loci, unless there is strong directional dominance. Short-term responses to such selection often preferentially fix alleles at autosomal loci. The fixation of slightly deleterious alleles by random drift and the stochastic turnover of alleles at loci controlling quantitative characters under stabilizing selection usually proceed somewhat more slowly at sex-linked loci. In contrast, the fixation of underdominant chromosomal rearrangements by random genetic drift is faster with sex linkage. Sex-specific selection may also differentially favor the fixation of sex-linked rearrangements.

These results are discussed in relation to genetic and cytological data on species differences. We show that the frequently disproportionate effects of the sex

chromosomes on interspecific inviability or sterility are consistent with the hypothesis that the gene differences concerned involve recessive or partially recessive alleles fixed by selection. Haldane's rule is readily interpreted in this light. There is little evidence for strong effects of the sex chromosomes on quantitative characters in interspecific crosses, in accordance with our theoretical results. Thus, the evolution of reproductive isolation may not be the byproduct of selective change in additively inherited, polygenic traits. Rather, it may be due mainly to the fixation of favorable mutations whose effects on fitness reflect locus-specific effects on the phenotype. These mutations behave as major genes in the sense of contributing the bulk of the genetic variance in the characters that they control during the course of the mutations' substitution. The data on the genetics of short-term responses to selection in *Drosophila* are hard to interpret, but, in accordance with theory, these responses do not usually seem to involve the X chromosome disproportionately.

In some groups, there is evidence for a disproportionate role of the sex chromosomes in chromosomal changes, but others show no clear pattern. Factors that may distort the expectations of the simple models of chromosomal evolution are discussed.

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APPENDIX

BRANCHING-PROCESS RESULTS

Consider first an autosomal locus obeying the fitness scheme of table 1 of the text, with a low-frequency x_{2f} and x_{2m} of allele A_2 in females and males, respectively. This generates the linearized recurrence relations

$$\begin{aligned} x'_{2f} &= \tfrac{1}{2}x_{2f}(1 + hs_1) + \tfrac{1}{2}x_{2m}(1 + hs_2) \\ x'_{2m} &= \tfrac{1}{2}x_{2f}(1 + hs_1) + \tfrac{1}{2}x_{2m}(1 + hs_2). \end{aligned} \tag{A1}$$

The fixation probabilities u_{Af} and u_{Am} for mutations to A_2 arising in a female or male, assuming stationary population size and Poisson offspring distributions, satisfy the following equations (Ewens 1968, chap. 7):

$$\begin{aligned} \ln(1 - u_{Af}) &= \tfrac{1}{2}u_{Af}(1 + hs_1) + \tfrac{1}{2}u_{Am}(1 + hs_1) \\ \ln(1 - u_{Am}) &= \tfrac{1}{2}u_{Af}(1 + hs_2) + \tfrac{1}{2}u_{Am}(1 + hs_2). \end{aligned} \tag{A2}$$

The unconditional probability of fixation of a single mutation to A_2 is $u_A = \tfrac{1}{2}(u_{Af} + u_{Am})$.

Similarly, the probabilities of fixation of mutations at an X-linked locus arising in females and males (u_{Xf} and u_{Xm}, respectively) are given by

$$\begin{aligned} \ln(1 - u_{Xf}) &= \tfrac{1}{2}u_{Xf}(1 + hs_1) + \tfrac{1}{2}u_{Xm}(1 + hs_1) \\ \ln(1 - u_{Xm}) &= u_{Xf}(1 + s_3)\,. \end{aligned} \tag{A3}$$

The unconditional probability of fixation of a single X-linked mutation is $u_X = \tfrac{1}{3}(2u_{Xf} + u_{Xm})$.

FIXATION PROBABILITIES OF MUTATIONS WITH SMALL EFFECTS ON FITNESS

The frequency of the mutant gene, averaged over the two sexes, is denoted by x. The mean and variance of gene-frequency change in a population of size N are $M_{\delta x}$ and $V_{\delta x}$, respectively. Kimura's (1962) general diffusion formula for the probability of fixation of a gene with initial frequency p is

$$u(p) = \int_0^p G(x)\,dx \Big/ \int_0^1 G(x)\,dx\,, \tag{A4a}$$

where

$$G(x) = \exp[-2\textstyle\int(M_{\delta x}/V_{\delta x})\,dx]\,. \tag{A4b}$$

With weak selection, such that $M_{\delta x}/V_{\delta x} \ll 1$, the numerator of equation (A4a) is approximated adequately by p, and only the denominator need be evaluated. In this case, $G(x) \approx 1 - 2\int(M_{\delta x}/V_{\delta x})\,dx$, and the integral of $G(x)$ can be obtained approximately by neglecting second-order and higher-order terms in $M_{\delta x}/V_{\delta x}$ in this equation.

These results may be used as follows to obtain approximate expressions for the probabilities of fixation of mutations with small effects on fitness. Consider, for example, the case of equal selection on the two sexes with dosage compensation. Using the notation of table 1, $M_{\delta x}$ and $V_{\delta x}$ for an autosomal locus equal $x(1 - x)s_1[h + x(1 - 2h)]$ and $x(1 - x)/2N$, with $p = 1/2N$. The values of $M_{\delta x}$ and $V_{\delta x}$ for an X-linked locus are then $\tfrac{1}{3}x(1 - x)s_1\{2[h + x(1 - 2h)] + 1\}$ and $2x(1 - x)/3N$, with $p = 2/3N$. The respective fixation probabilities are approximately $[1 + 2Ns_1(1 + h)/3]/2N$ (autosome) and $2[1 + Ns_1(5 + 2h)/6]/3N$ (X chromosome), assuming that $Ns_1 \ll 1$.

Noting that the numbers of new mutations entering the population each generation are proportional to $2N$ and $1.5N$ for autosomal and X-linked loci, respectively, the ratio of the rates of evolution at equivalent autosomal and X-linked loci is given by the ratio of the above terms in brackets, which is approximately $1 + \tfrac{1}{3}Ns_1(h - \tfrac{1}{2})$.

GENE-FREQUENCY EQUATIONS FOR POLYGENIC LOCI

Using the method of Bulmer (1980, pp. 164–165), the gene-frequency equation for an autosomal locus i, writing x_{1i} and x_{2i} for the average frequencies of A_1 and A_2 over the two sexes, is

$$\begin{aligned} \Delta x_{2i} \approx{}& \tfrac{1}{2}x_{1i}x_{2i}A[a_i + d_i(x_{1i} - x_{2i})] \\ &+ \tfrac{1}{2}[a_i^2(x_{1i} - x_{2i}) + 2a_id_i(1 - 6x_{1i}x_{2i}) + d_i^2(x_{1i} - x_{2i})]\,. \end{aligned} \tag{A5}$$

The corresponding equation for the jth X-linked locus is

$$\begin{aligned} \Delta x_{2j} \approx{}& \tfrac{1}{3}x_{1i}x_{2i}A[4a_i + 2d_i(x_{1i} - x_{2i})] \\ &+ \tfrac{1}{3}x_{1i}x_{2i}B[3a_i^2(x_{1i} - x_{2i}) + 2a_id_i(1 - 6x_{1i}x_{2i}) + d_i^2(x_{1i} - x_{2i})^3]\,. \end{aligned} \tag{A6}$$

In order to incorporate the effect of reversible mutation between A_1 and A_2, terms of the form $\mu(x_1 - x_2)$ must be added to these equations.

COMPARATIVE DATA ON CHROMOSOME REARRANGEMENTS

Mammalia

Comparisons of both karyotypes and linkage maps between species show that the mammalian X chromosome rarely becomes involved with the autosomes. Fredga (1970, 1983) listed 27 species in which fusions between the autosomes and a sex chromosome have been established (12 with the X, 15 with the Y). Egozcue (1975) noted another Y-autosome fusion in two marmoset colonies (*Callimico goeldii*). These fusions can be accounted for by 18 independent events (9 for the X, and 9 for the Y). All but 2 seem to have occurred after the origin of the genera concerned and are thus represented in one or two species. In some cases, the X is much larger than usual, possibly because of X-A fusions (Fredga 1970). A rough measure of the rate of establishment of sex-chromosome fusions can be obtained by dividing the number of events by the product of the total number of species examined (about 1500) and the average duration of a mammalian genus (about 6.5 million yr; Bush et al. 1977). This gives a rate of roughly 0.0016 million yr^{-1}, an order of magnitude smaller than the average rate of change of chromosome number in mammals (0.13 million yr^{-1}; Bush et al. 1977; Wilson et al. 1977), even after allowing, on the average, for about 20 pairs of autosomes (White 1973, fig. 12.18).

This evidence is supported by comparisons of linkage relationships between homologous genes. Although the autosomes of man and mouse are generally homologous, Nadeau and Taylor (1984) estimated that 178 ± 39 breaks in the linkage map must have occurred during the 140-million-yr divergence time, yielding a rate of fixation of breaks of 1.3 million yr^{-1}. Thus, a considerable number of rearrangements that did not affect chromosome number must have occurred. In contrast, comparisons involving 15 genes and more than 22 species show complete conservation of sex linkage, with one possible exception (Roderick et al. 1984; Lalley and McKusick 1985).

The rarity of X-autosome rearrangements in mammalian evolution probably reflects the fact that spontaneous X-autosome translocations are usually male-sterile, apparently because they interfere with the normal process of inactivation of the X chromosome in male meiosis (Lindsley and Lifschytz 1972). Furthermore, the process of X inactivation in females may be disturbed by such rearrangements (Lyon 1974). There is, however, no obvious reason why rearrangements internal to the X chromosome should suffer a disadvantage of this kind, and our population-genetics theory leads us to expect an excess rate of fixation of X-chromosome inversions. Too few loci are available at present for comparison of X-chromosome and autosomal gene orders. In marsupials, however, the X chromosomes vary in morphology considerably more than the autosomes, and there is evidence that this is at least partly due to rearrangements rather than changes in heterochromatin (Hayman and Martin 1974, sect. 5.4).

Orthoptera

The Orthoptera have a predominantly acrocentric karyotype, with XO males, and centric fusions are a relatively frequent type of rearrangement (White 1973; Hewitt 1979). There is a clear excess of fusions involving the X chromosome; for combined information from the Morabinae, Acrididae, and Tettigoniidae, the number of X-A fusions roughly equals the number of A-A fusions, even though the primitive and most frequent karyotype has a haploid set of 1X + 11A (table A1). Similarly, there is a clear excess of fixed inversions on the X and a deficit of polymorphic inversions, as would be expected with underdominance. Although the data are sparse, there is no evidence that the rate of spontaneous rearrangements involving the X differs from the expected (table A1).

Drosophila

The relevant data for *Drosophila* are reviewed in table A2. There does not seem to be any evidence for an excess of X-linked pericentric inversions or fusions over what would be

TABLE A1

CHROMOSOMAL EVOLUTION IN THE ORTHOPTERA AND PHASMATODEA

TAXON*	CENTRIC FUSIONS		PERICENTRIC INVERSIONS			RATIO
	X-A	A-A	X	A	X + A	
Morabinae	11	27	—	—	—	
Acrididae	33	23	—	—	—	
Tettigoniidae	6–7	6	—	—	—	
Total Orthoptera *F*	50–51	56	5	8	4	11.54
P			1	29	3	
Spontaneous rearrangements	1	12	0	5		
Didymuria violescens (10 races)	3	7	1	12		

NOTE.—*F* and *P* denote fixed and polymorphic rearrangements, respectively. "Ratio" gives the ratio of the proportion of fixed inversions to the proportion of polymorphic inversions, for the X chromosome. Pericentric inversions cannot be distinguished easily from transpositions of the centromere; however, White (1973) argued that most changes in centromere position are due to inversions. The number of spontaneous fusions includes spontaneous fissions as well; the distribution of fissions and fusions is essentially the same (Hewitt 1979, table 1). Figures for centric fusions give the number of rearrangements established in the phylogeny; figures for pericentric inversions in Orthoptera give the number of cases where related taxa differ (*F*) or are polymorphic (*P*) (from Hewitt 1979, tables 2 and 3). Figures for *Didymuria* may be underestimates (White 1976).

* SOURCES.—Hewitt (1979) for Orthoptera; White (1976) for *D. violescens*.

TABLE A2

CHROMOSOMAL EVOLUTION IN *Drosophila*

TAXON*	FIXED OR POLYMORPHIC	CENTRIC FUSIONS			PERICENTRIC INVERSIONS		PARACENTRIC INVERSIONS		RATIO
		Y-A	X-A	A-A	X	A	X	A	
Picture-wing Hawaiians (103 spp.)[1]	*F*	0	0	0	0	0	59	68	3.07
	P	0	0	0	0	0	13	73	
Repleta group (62 spp.)[2]	*F*	0	0	4	0	0	12	105	1.73
	P	0	0	0	0	0	7	111	
Robusta group (6 spp.)[3]	*F*	0	1	1	0	3	22	50	2.09
	P	0	0	0	0	2	6	35	
Virilis group (12 spp.)[4]	*F*	0	1	2	0	1	8	36	1.73
	P	0	0	0	0	0	6	51	
Melanica group (6 spp.)[3]	*F*	0	0	0	0	0	9	37	0.82
	P	0	0	0	0	0	19	61	
Whole genus (30 species groups)[5]	*F*	1	15	38	3	27	—	—	
Totals for paracentric inversions†	*F*						110	296	2.03
	P						51	331	

* SOURCES.—1, Carson and Yoon 1982; 2, Wasserman 1982; 3, Levitan 1982; 4, Throckmorton 1982; 5, Patterson and Stone 1952.

† Of the inversions of the X, 68% are fixed and 32% polymorphic. The numbers of fixed paracentric inversions may be underestimates.

expected by chance, in agreement with the conclusions of Charlesworth and Charlesworth (1980) for the case of fusions. Spontaneous translocations involving the X chromosome frequently cause male sterility (Lindsley and Lifschytz 1972), and this may well influence the rate of evolution of X-linked rearrangements. There seem, however, to be about twice as many fixed X-linked paracentric inversions as polymorphic ones, reflecting in part a deficit of polymorphisms on the X, as would be expected on theoretical grounds if selection is responsible for maintaining inversion polymorphism (Curtsinger 1980; Avery 1984). If only fixed paracentric inversions are compared, there are slightly more X-linked inversions than the 20% expected from the contribution of the X chromosome to the euchromatin.

Simuliidae

Closely related species of blackflies often differ only by paracentric inversions on the sex chromosomes (Rothfels 1979; Post 1982). Most blackflies have undifferentiated sex chromosomes with chiasmate male meiosis, although inversion heterozygotes do not produce aneuploid gametes. Sex-chromosome inversions in this group have probably evolved because they reduce recombination between the sex-determining locus and loci under sex-specific selection (Post 1982; Bull 1983, chap. 18). This view is supported by the occurrence of inversion polymorphisms that do not include the sex-determining locus, but that show different frequencies in males and females (Post 1982, 1985); inversions causing tighter linkage to the sex locus would be strongly favored in this situation (Charlesworth and Charlesworth 1980).

Other Groups

Although cytological information is available for many other groups, it is difficult to make useful comparisons of evolutionary rates, for the reasons mentioned above. It seems that the only well-understood example in which the numbers of rearrangements can be traced through a phylogeny, outside the mammals, Orthoptera, or Diptera, is the phasmatid *Didymuria violescens*. Here the ancestral karyotype consists of a haploid set of 20 autosomes (10 acrocentric) and an XO sex-determining system. Ten parapatric races are distinguished by centric fusions and pericentric inversions; there is an excess of fusions involving the X, and the inversion data are equivocal (see table A1).

DROSOPHILA ARTIFICIAL-SELECTION EXPERIMENTS

Table A3 summarizes data on the proportional contributions of the three major chromosomes (X ≡ 1) of *Drosophila melanogaster* to selection responses for a number of characters. Because different workers have used different experimental and statistical techniques to measure chromosome effects, it is hard to compare the results for different characters. The "dominant-marker backcross" technique (see Mather and Harrison 1949) contrasts individuals heterozygous for different combinations of selection-line chromosomes and balancer chromosomes marked with dominant genes against individuals homozygous for line chromosomes; the "homozygous-chromosome substitution" technique compares individuals homozygous for different combinations of selected and unselected chromosomes. The first method is biased toward the detection of recessive or partially recessive effects of the selected alleles; on the basis of our theoretical considerations, this method probably exaggerates the contribution of the X chromosome. This should be borne in mind when interpreting these results. In some cases, workers have reported only the effects of a given chromosome from a selection line on a background of chromosomes from an unselected stock, but others give estimates of the effect of a given chromosome averaged over all possible combinations of selected and unselected background chromosomes. In each case, the entries in the table give the effect of the chromosome in question (1, 2, or 3) expressed as a percentage of the sum of the individual effects of each chromosome in causing a difference between the selected line and unselected stock. In many cases, replicate selection lines and lines selected in opposite directions were analyzed; these are, for the most part, shown separately in order to give an impression of the great heterogeneity of chromosome effects that is usually found for the same character.

TABLE A3

CONTRIBUTIONS OF INDIVIDUAL CHROMOSOMES TO ARTIFICIAL-SELECTION RESPONSES IN *Drosophila melanogaster*

Chr.	Homozygous Chromosome Substitutions			Dominant Marker Backcross									
	Down	Up	Mean	Down				Up					Mean
				CONTRIBUTION MEASURED AS AVERAGE EFFECT OVER ALL BACKGROUND GENOTYPES									
		Wing Length[1]						Abdominal Bristles[2]					
1	67.4	(0)	33.7	17.4	55.5	40.0	30.6	43.6	26.0	21.1	15.5	17.4	29.7
2	4.2	13.2	8.7	51.1	30.0	(0)	(0)	0.0	32.8	31.0	35.7	17.8	22.0
3	28.4	86.8	57.6	31.5	14.5	59.9	69.4	56.4	41.2	47.9	48.8	64.8	48.3
		Scutellar Bristles[3]						Scutellar Bristles*[4]					
1		33.1	14.0	23.6				30					
2		10.5	65.0	37.7				28					
3		56.4	21.0	38.7				38					
		Geotaxis[5]											
1	20.3	57.9	39.1										
2	51.1	6.1	28.6										
3	28.6	36.0	32.3										
		DDT Resistance[6]											
1		24.3	40.7	32.5									
2		43.2	31.6	37.4									
3		32.5	27.7	30.1									
				CONTRIBUTION MEASURED AS EFFECT ON UNSELECTED BACKGROUND GENOTYPE									
		Abdominal Bristles[7]						Wing Length[8]					
1	(0)	38.9	19.4					12.1	15.9	19.7			15.9
2	27.1	2.8	15.0					34.9	21.2	22.0			26.0
3	72.9	58.3	65.6					53.0	62.9	58.3			58.1
		Sternopleural Bristles[7]											
1		18.5											
2		7.1											
3		74.4											
		Sternopleural Bristles[9]											
1		0.0	27.0	13.5									
2		21.8	15.7	18.8									
3		78.2	57.3	67.8									

NOTE.—Down and up indicate the direction of selection on the lines analyzed. (0) indicates a contribution in the direction opposite to that of selection; this was treated as zero in the calculations.

SOURCES.—1, F. Robertson 1954; 2, Mather and Harrison 1949; 3, Whittle 1969; 4, Scowcroft 1966; 5, Hirsch and Erlenmeyer-Kimling 1962; 6, King and Somme 1957; 7, Davies and Workman 1971; 8, F. Robertson and Reeve 1953; 9, Spickett and Thoday 1966.

* Mean over 11 replicate selection lines.

There are several difficulties in interpreting the data of table A3. First, it seems likely that new mutations contribute significantly to selection for polygenic traits if more than 20 or so generations of selection have been practiced (Frankham 1980; Hill 1982). Because most of these cases involve substantially longer periods of selection, it cannot safely be assumed that the genes concerned were all present in the base population. In the first case, down selection for wing length, it is known that the large contribution of the X chromosome was due to a major recessive mutation that appeared around generation 16 (F. Robertson and Reeve 1952). Second, not all the characters are controlled by semidominant alleles: wing length shows considerable inbreeding depression, and increased scutellar-bristle number is almost completely recessive. Increased abdominal-bristle number may also be partially recessive (Davies 1971; Frankham 1974). As we have seen, the X is expected to make a large contribution to a selection response in the direction of recessive-gene action in this case. Third, when localization of polygenes within chromosomes has been attempted, it seems that a relatively small number of genes (two or three, at most) per chromosome contribute much of the effects (Spickett and Thoday 1966; Whittle 1969; Davies 1971). There is thus a good deal of scope for chance variations in the contributions of individual chromosomes. Fourth, there is a puzzling discrepancy between the contributions of chromosomes 2 and 3 to selection responses: chromosome 2 frequently contributes much less than 3, especially for sternopleural- and abdominal-bristle numbers and wing length. This is true in 9 of the 10 experiments cited and is thus highly significant on a sign test. The physical lengths of the two chromosomes as measured by salivary chromosome-band numbers (Lefevre 1976) are similar, and their genetic contents as measured by rates of lethal mutation do not differ (Wallace 1968). A count of the number of mutant loci per unit of map length from Lindsley and Grell (1968) similarly yields figures of 2.58 and 2.03 for chromosomes 2 and 3, respectively. Furthermore, measured rates of mutation for abdominal and sternopleural bristles for the second chromosome (Durrant and Mather 1954; Paxman 1957) agree reasonably well with estimates for the whole genome (Hill 1982). In view of this discrepancy between the two autosomes, it is unclear whether an X-chromosome contribution can be meaningfully compared with its relative size in the whole genome (20%).

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