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The Segregation Distorter (*SD*) complex and the accumulation of deleterious genes in laboratory strains of *Drosophila melanogaster*

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Abstract. Segregation Distorter (*SD*) associated with the second chromosome of *D. melanogaster* is found in nature at equilibrium frequencies lower than 5%. We report extremely high frequencies of *SD* (30–50%) in two selected strains, established in 1976, and show it to be responsible for the accumulation of deleterious genes in chromosome II. Samples of chromosomes extracted over a 4-year period were characterized with respect to distortion, sensitivity, lethality, sterility, and inversions. *SD* chromosomes were inversion-free as they have been shown to be in the Mediterranean area. The cosmopolitan inversion In(2*L*)*t* was found associated with SD^+ chromosomes. Lines polymorphic for *SD* have accumulated linked lethal and female-sterile genes approaching a near balanced system. It is proposed that deleterious genes linked in coupling to *SD* were accumulated by the balancing effect of distortion, while drift and restricted recombination account for the accumulation of deleterious genes linked in repulsion by a mechanism similar to Muller's ratchet. Our results should not be viewed as a particular case as *SD* chromosomes associated with detrimental genes and inversions are present in almost all populations around the world. The system could evolve in the way we describe whenever equilibrium conditions are broken down in small populations and lead to an increase in *SD* frequency.

Key words: Population genetics – Segregation distortion – Lethals – *Drosophila melanogaster* – Muller's ratchet

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Introduction

The accumulation of lethal genes in selected lines is a rather common phenomenon (Clayton and Robertson 1957; Yoo 1980) which is explained as a consequence of artificial selection. When a lethal has an effect on the selected trait, or is closely linked to another gene with such an effect, selection will change its frequency until an equilibrium is reached. An additional consequence of selecting lethal heterozygotes at a given locus is the lower probability of losing lethal alleles at other loci that are linked in disequilibrium to the given locus and thus protected from natural selection (Madalena and Robertson 1975). This will occur whether or not the alleles in question affect the selected trait. A progressive accumulation of lethals at high frequencies in the selected line will then ensue.

In a previous study (Domínguez et al. 1987) we have reported the accumulation of lethal genes in lines selected for increasing dorsocentral bristle number over a long-term period. Artificial selection could not explain the accumulation of lethals in our lines since none of them had any effect on the selected trait. In one of the lines, it was shown that the more frequent lethal on chromosome II (frequency of 36%) was associated with preferential transmission in heterozygous males. It was suggested that self-selection of that lethal would lead to the accumulation of other lethals linked to it in disequilibrium, in a way similar to that proposed by Madalena and Robertson (1975) for the case of an artificially-selected lethal.

The present paper demonstrates that preferential transmission was in fact due to the well-known Segregation Distorter system (for recent reviews see Lyttle 1991; Temin et al. 1991).

Segregation Distortion (*SD*) is a naturally-occurring meiotic drive system on the second chromosome

of *Drosophila melanogaster*. Males heterozygous for an *SD* chromosome and a sensitive SD^+ homologue transmit the *SD* chromosome in an excess over the theoretical 50%. The *SD* complex has two major components: Segregation Distorter (*Sd*), the locus responsible for producing distortion located at 37D5 in the euchromatin of the left arm, and Responder (*Rsp*) which behaves as the target for the action of *Sd* and is located in the proximal centromeric heterochromatin of the right arm. The normal allele of *Sd* is referred to as Sd^+. *Rsp* alleles fall into at least two major classes: sensitive (Rsp^s) and insensitive (Rsp^i). In these terms the *SD* chromosome in nature is *Sd Rsp*^{i} while a sensitive SD^+ chromosome is Sd^+ Rsp^s. Segregation distortion, taking place in SD/SD^+ males, is the consequence of interactions between the two loci of the complex. *Sd* on the *SD* chromosome is assumed to interact with Rsp^s on the sensitive SD^+ homologue to cause dysfunction of the sperm that receive the sensitive SD^+ chromosome. In addition to these major loci, there are also a number of modifiers of *SD* action.

SD chromosomes have been found at low stable polymorphic frequencies, about 1–5%, in almost all populations screened for them. They are frequently associated with inversions which give an advantage to the *SD* chromosome because they keep the components of the complex together (Charlesworth and Hartl 1978). *SD* is also frequently associated with lethal mutations and most *SD* chromosomes that are homozygous-viable cause male sterility (Hartl and Hiraizumi 1976).

We provide here a full description of the selected lines, after a period of relaxation, with regard to *SD*, *Rsp*, lethals, sterility genes, and iversions and show that *SD* may lead to the accumulation of recessive lethal and sterile genes in small populations.

Materials and methods

Strains

Ac-27P, Ac-27S, S-27P, S-27S and N-21 are five selected lines derived from a population captured in a wine cellar in Valencia (Spain) in 1976. They were long-term selected, during more than 100 generations, for increasing dorsocentral bristle number. At first, three lines were established: N-21, Ac-27 and S-27. Lines Ac-27S and Ac-27P were derived from the single selected line (Ac-27) at generation 16. In the same way, lines S-27P and S-27S were derived from the single line S-27 at generation 17 (for more details see Domínguez et al. 1987). Since generation 112, lines have been maintained without selection in three bottles with ten pairs per bottle per generation.

Strains $II_1/SM5$, $II_2/SM5$, $II_3/SM5$, $II_4/SM5$, $II_5/SM5$ and $II_6/SM5$ contain representative copies of the lethal chromosomes previously found in the lines, balanced with the *SM5* chromosome. Lethals II_1 and II_2 were extracted from line S-27P, while II_3, II_4, II_5, and II_6 were lethals from the line Ac-27P. Lethal II_3 showed preferential transmission within the line. These lethal chromosomes were used in complementation tests.

The following laboratory strains were used. For a more detailed description see Lindsley and Zimm (1992):

Cy/Pm; *D/Sb* and *SM5/Sp*, two strains containing dominant markers and balancer chromosomes; used to extract chromosomes from the selected lines.
cinnabar brown (*cn bw*, Sd^+ Rsp^s), an inbred laboratory strain (provided by R. Temin); used routinely to screen for *SD* since it is sensitive to distortion.
SDR-1 bw (*Sd Rsp*^{i}), an *SD-5* type of chromosome with the recessive marker *bw* isolated as a recombinant by Hartl (provided by R. Temin); used to measure sensitivity to distortion.
all, a strain bearing the recessive genes *aristaless* (*al* 2-0.01), *dumpy* (*dp* 2-13.0), *blace* (*b* 2-48.5), *purple* (*pr* 2-54.5), *curved* (*c* 2-75.5), *plexus* (*px* 2-100.5) and *speck* (*sp* 2-107.0) on chromosome II.
all Bl/SM1, containing a chromosome with the same recessive genes as *all* plus the dominant marker Bristle (*Bl* 2-54.8) and the balancer *SM1* chromosome.
Canton-S, a standard laboratory strain used for cytological analyses.

Methods

Samples of second chromosomes were extracted in 1987, at generation 135, and in 1989, between generations 165 and 175. Chromosomes were tested either for all or part of the following characteristics: *SD*, *Rsp*, lethality, sterility, and inversions. The crossing scheme for the complete test is given in Fig. 1. Crosses in G0 were carried out between males of the problem line and *Cy/Pm*; *D/Sb* females. In those cases where we wanted to avoid preferential transmission for obtaining unbiased gene frequencies, reciprocal crosses were performed.

Chromosomes were tested for *SD* with *cn bw* and for *Rsp* sensitivity with *SDR 1-bw*. The statistic k (proportion of cn^+ bw^+-bearing sperm recovered from heterozygous males) is used as a measured of drive strength against the standard SD^+ chromosome *cn bw* or, conversely (k = proportion of cn^+ *bw*), as a measure of the *Rsp* sensitivity to the standard *SD* chromosome *SDR 1-bw*. These k values were not viability-adjusted. The classification of chromosomes as *SD* or SD^+ is straight-forward since there is a clear discontinuity in the distribution of k values (Fig. 2). Chromosomes with a $k > 0.8$ were classified as *SD*. Chromosomes were classified with respect to *Rsp* as insensitive when $k < 0.69$ or sensitive when $k > 0.7$ based upon the observed discontinuity in k values (Fig. 3). Different degrees of sensitivity were not considered. *SDR 1-bw*, used as tester in the sensitivity test, has a k of 0.85 with *cn bw* and allows classification of responders as sensitive or insensitive. Screening with a stronger distorter would not in general alter the classification although some chromosomes insensitive to *SDR 1-bw* could be weakly sensitive to it (Temin and Marthas 1984).

A chromosome was classified as a lethal carrier when no wild-type homozygotes were recovered among at least 50 progeny from the appropriate mating (Fig. 1) Sterility data are based on ten individuals, each of them crossed separately with two individuals of the opposite sex from the standard Canton-S strain. Only complete sterility was considered.

Figure 4 outlines the matings used to evaluate the intensity of distortion in SD/SD^+ males within line Ac-27S. In essence, eight chromosomes were extracted from each individual and classified as *SD* or SD^+ by their distorting ability with *cn bw*. Hence, each individual genotype was known. Distortion within the line was measured by comparing *SD* sampling frequency in heterozygous males with that in heterozygous females.

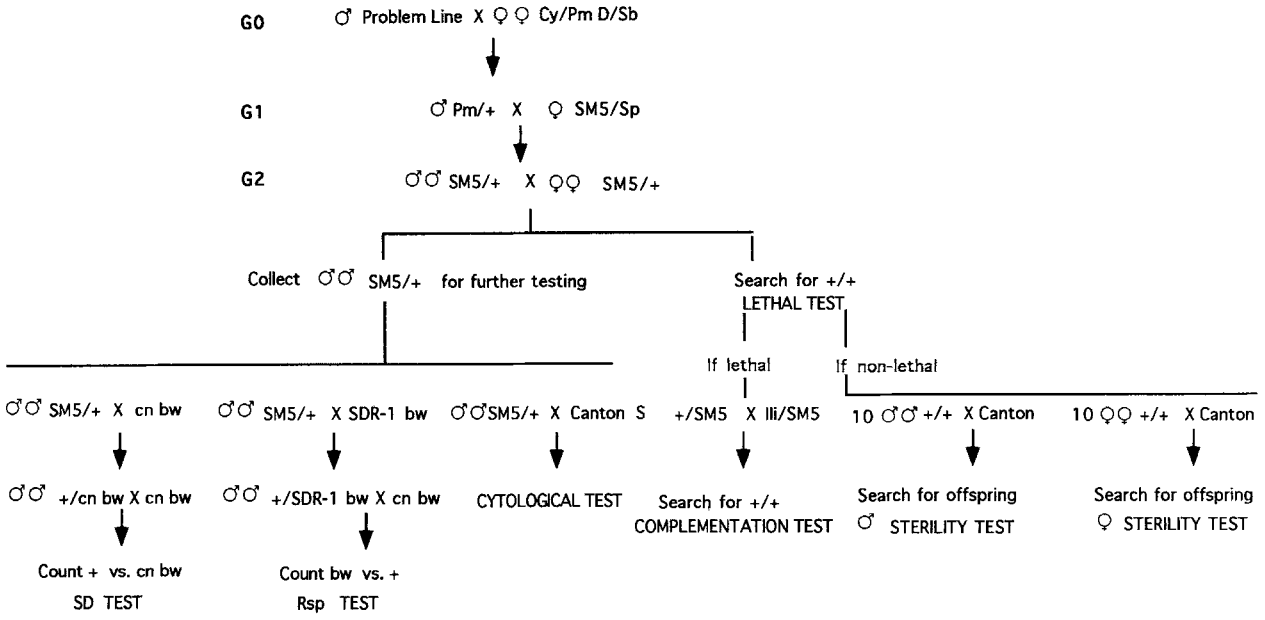

Fig. 1. Matings to test chromosome for *SD*, *Rsp*, lethality, sterility, and inversions. Each male from a sample of the problem line is mated in a separate vial to *Cy/Pm; D/Sb* females (in some instances the G0 cross was the reciprocal, see Materials and methods). One *Pm* male from each G1 is selected and crossed to *SM5/Sp* in order to obtain in G2 several identical copies of one chromosome per G0 individual. Matings between *SM5/+* males and females provide a test for lethality and at the same time allow us to keep the chromosomes balanced with *SM5* for further testing

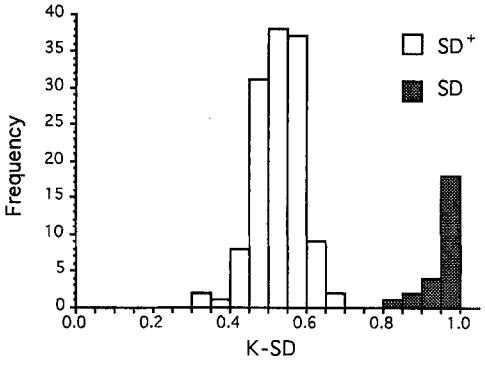

Fig. 2. Distribution of k values of the 1989 chromosome sample against the standard SD^+ chromosome *cn bw*

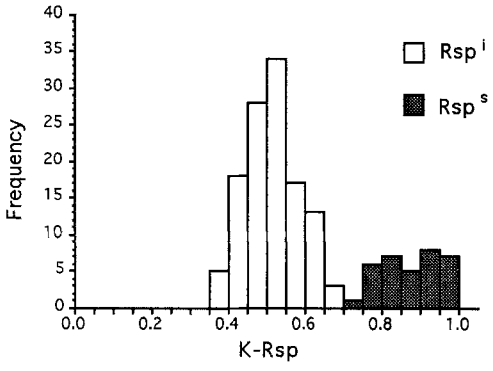

Fig. 3. Distribution of k values of the 1989 chromosome sample against the standard *SD* chromosome *SDR-1 bw*

Results

The frequencies of lethal-bearing chromosomes in screens carried out in the years 1987 and 1989, and those previously reported, are presented in Table 1. None of the lines S-27S, S-27P, Ac-27S or N-21 showed any chromosome II-lethal to be stably maintained over time.

However, line Ac-27P presented chromosomal lethals which were maintained over the period under study. Lethal frequencies in 1985 were estimated from male genotypic frequencies while those of 1987 and 1989 were from female gametic frequencies (females from Ac-27P were used in G0, see Fig. 1). Thus, frequencies of chromosomes other than II_3 in 1985 were underestimated since 48% of males transmited only the lethal II_3. Some lethals were found in a single copy for each chromosomal extraction and their pooled frequency is given in the table. None of the chromosomes sampled in 1987 carried more than one lethal and only two chromosomes from 1989 carried two lethals.

Preferential transmission of lethal II_3 has been shown previously within the Ac-27P line (Domínguez et al. 1987). In order to ascertain if it was due to *SD*,

Table 1. Frequencies of lethals and the frequency of SD within each lethal type. In parenthesis, number of chromosomes tested

Line	Lethal	1985[a]	1987		1989	
		Freq.	Freq.	Freq. *SD*	Freq.	Freq. *SD*
Ac-27P			(48)		(40)	
	II_3	0.36	0.26	1	0.37	0.93
	II_4	0.05	0.08	0	0	
	II_5	0.05	0.07	0.66	0	
	II_6	0.16	0.13	0.12	0.20	0.25
	Single-copy	0.08	0.05	0.25	0.07	0.33
	Lethal-free	0.06	0.41	0.45	0.40	0.06
	Not sampled	0.24				
Ac-27S			(28)		(24)	
	Lethal-free	1	1	–	1	0.33
S-27P			(30)		(30)	
	II_1	0.07	0		0	
	Lethal-free	0.93	1	–	1	0
S-27S			(28)		(30)	
	II_2	0.17	0.07	–	0	
	Lethal-free	0.83	0.93	–	1	0
N-21					(29)	
	II_7	0	–		0.10	0
	Lethal-free	1	–		0.90	0

– Not tested
[a] Data from Domínguez et al. (1987)

chromosomes extracted from that line in 1987 and 1989 were tested against the *SD*-sensitive strain *cn bw* and classified as *SD* or SD^+. The overall frequency of *SD* was 0.51 and 0.43 respectively with a mean k = 0.99 against *cn bw*. Disequilibrium between lethals and *SD* was large, *SD* is mainly associated with lethal II_3. Only one II_3 chromosome out of the 27 tested was SD^+. Thus, preferential transmission of lethal II_3 within the line is due to its association with *SD*. Distortion was not restricted to this lethal but was also found in chromosomes with other lethals (II_5, II_6 and single-copy lethals) and also in lethal-free chromsomes.

The 40 chromosomes extracted from Ac-27P in 1989 were also tested for *Rsp* as well as for inversions and, those that were homozygous-viable, for male and female sterility genes. The different classes of chromosomes according to all the tested characteristics and their frequencies are presented in Table 2. Besides lethals and *SD*, Ac-27P segregates for *Rsp*, the inversion In(2*L*)*t*, and female-sterile genes. There was disequilibrium between *Rsp*, the inversion In(2*L*)*t*, and *SD*. Twenty-two out of twenty-three SD^+ chromosomes were Rsp^s. The inversion In(2*L*)*t* was associated with lethal II_6 and SD^+. Two different recessive female-sterile genes were found in one single copy, one in an SD^+ chromosome and the other in the only *SD* chromosome free of lethals found in this sample. One of the

Table 2. Chromosome classes in Ac-27P females

Chromosome class				No. of chromosomes
Lethal II_3	*SD*		Standard	13
Lethal II_6	SD^+	Rsp^s	In(2*L*)*t*	4
Lethal II_6	SD^+	Rsp^i	In(2*L*)*t*	1
Lethal II_6	*SD*		?	1
Lethal II_3 II_6	*SD*		Standard	1
Lethal II_3 II_6	SD^+	Rsp^s	In(2*L*)*t*	1
Lethal single copy	*SD*		Standard	1
Lethal single copy	SD^+	Rsp^s	Standard	1
Lethal single copy	SD^+	Rsp^s	Standard	1
Female-sterile single copy	*SD*		Standard	1
Female-sterile single copy	SD^+	Rsp^s	Standard	1
Lethal and sterile free	SD^+	Rsp^s	Standard	14

SD lethal-free chromosomes coming from the sample of 1987 that had been kept in stock was tested and shown to be also homozygous female-sterile. But those two chromosomes containing female-sterile genes complement each other as well as the six *SD* lethal chromosomes to which they were tested for female strility. Thus, the only two *SD* lethal-free chromosomes tested for sterility were found to be female-sterile. The other eight *SD* lethal-free chromosomes sampled at generation 135 were not maintained and could not be tested for sterility.

Lethals II_3, II_4, II_5 and II_6 were roughly mapped by recombination with the laboratory strain *all*. Lethal II_3 is located between the markers *b* (48.5) and *pr* (54.5), as is *Sd*; 2 out of 14 recombinants obtained between these markers recombined between II_3 and *pr*. Lethal II_4 is linked to the marker *pr*; it did not recombine with *pr* in the four recombinants studied between this marker and *b*, nor in 11 recombinants between *pr* and *c*. Lethal II_5 was located between *dp* (13.0) and *b*; 5 out of 12 recombinants in the region recombined between *dp* and II_5. Lethal II_6 is tightly linked to In(2*L*)*t*. No recombinants in the left arm were recovered from *all*/In(2*L*)*t* II_6 females and in none of the 12 recombinants between *pr* and *c* was there recombination between In(2*L*)*t* and II_6.

SD was also found in the Ac-27S line. Its gametic frequency in males was 0.33 (Table 1) with a mean k of 0.97 against *cn bw*. The strength of distortion in the line was calculated by extracting eight chromosomes per individual from a sample of 50 males and 50 females of Ac-27S (Fig. 4) and classifying them as *SD* or SD^+. The distribution of sampling frequencies of *SD* chromosomes in males and females is shown in Fig. 5. SD/SD^+ males ($k = 0.55 \pm 0.03$) did not differ significantly from females ($k = 0.48 \pm 0.03$) in their k value denoting that there is no noticeable distortion within the line. Genotypic and genic frequencies based on a progeny

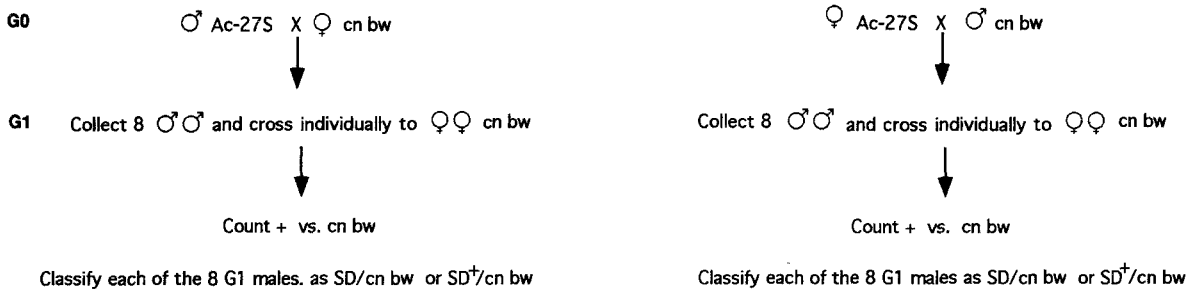

Fig. 4. Mating scheme to estimate SD/SD^+ distortion within the line Ac-27S. Fifty males and 50 females were crossed individually to *cn bw* mates. Eight male offspring of each G1 were individually tested for *SD* by crossing them to *cn bw* females and classified as *SD/cn bw* or $SD^+/cn\ bw$, hence the G0 individual genotype was found. The k value for each SD/SD^+ heterozygous G0 male was estimated by the proportion *SD/cn bw* males in G1. The mean k of SD/SD^+ males, compared to that of the females, provided a test of distortion within the line

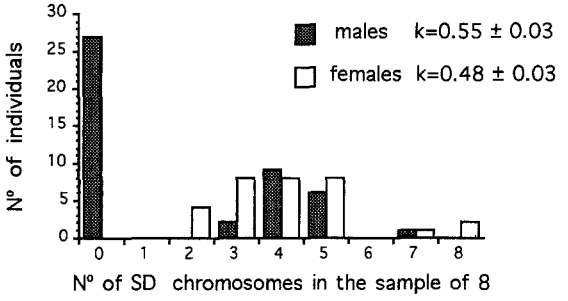

Fig. 5. Distribution of sampling frequencies of *SD* chromosomes in Ac-27S males and females. Eight chromosomes were extracted from each individual and classified as *SD* or SD^+ as outlined in Fig. 4

Table 3. *SD* genotypic frequencies in Ac-27S

Sex	No. of indiv.	Genotypes			Freq. of *SD*
		SD^+/SD^+	SD^+/SD	SD/SD	
Males	45	0.60	0.40	0	0.20
Females	31	0	0.94	0.06	0.53

test differed between the sexes (Table 3). Almost all females leaving offspring were SD/SD^+ heterozygotes. This could be related to the fact that 19 out of 50 females from Ac-27S crossed to *SM5/Sp* males did not leave descendants suggesting that some genotypes were female-sterile. A survey among the females in the line showed a 30% (74/243) sterility.

A new sample of chromosomes was extracted, one from each of 30 Ac-27S females and tested for lethals, *SD*, *Rsp*, inversions, and sterilty (Table 4). Line Ac-27S segregates for *SD*, In(2*L*)*t*, and a female-sterile gene. There are two main types of chromosomes in the line: *SD* chromosomes with the standard arrangement (60%) and SD^+ chromosomes carrying In(2*L*)*t* and a female-sterile gene (30%). Insensitivity of SD^+ chromosomes agreed with the lack of distortion in SD/SD^+ males within the Ac-27S line. Although no complete male sterility was observed, *SD* homozygous males left reduced offspring. The female-sterile gene in line Ac-27S is tightly linked to In(2*L*)*t*. None of the 18 recombinants between *pr* and *c* showed recombination between the female-sterile locus and In(2*L*)*t*. Several complementation tests were carried out to study the relationships between the sterility genes in Ac-27P and Ac-27S. The sterile gene from Ac-27S is different from those sampled from Ac-27P. It was also shown that the inverted lethal chromosomes from Ac-27P lack the sterile gene from Ac-27S.

Table 4. Chromosome classes in Ac-27S females

Chromosome class			Frequency
Sterile-free	SD^+	Standard	0.03
Female sterile	SD^+	In(2*L*)*t*	0.30
Sterile-free	*SD*	Standard	0.60
Sterile-free	*SD*	In(2*L*)*t*	0.07

No *SD* chromosomes were found in any of the other three lines, S-27P, S-27S and N-21 (Table 1). Chromosomes extracted from these lines in 1989 were also tested for *Rsp*, inversions, and sterility genes. Lines S-27P and S-27S lack inversions and all the sampled chromosomes were insensitive to distortion. Inversion In(2*L*)*t* was found in N-21 at a frequency of 0.41 and all the inverted chromosomes were sensitive to *SD* while all the standard chromosomes were not. No sterility genes were sampled from any of these three lines.

Discussion

The equilibrium frequency of *SD* in nature seems to be lower than 5%. This equilibrium is achieved with both sensitive and insensitive responders segregating in the

population (Temin and Marthas 1984) and can be accounted for by the theoretical model of Charlesworth and Hartl (1978), given some limitations in the fitnesses of genotypes. When a laboratory strain is established, SD^+ chromosomes would tend to be fixed since balancing selection is ineffective as a factor retarding fixation in small populations when the equilibrium gene frequency lies near to 1 or 0 (Robertson 1962). The frequency of *SD* in the Ac lines is around 30–50% and it has been maintained in these lines since they were established 14 years ago. This leads to the notion that *SD* has increased in frequency well above 5% by stochastic events. Presumably Rsp^s became fixed in SD^+ chromosomes in the first generations and then caused a rapid increase in *SD* frequency.

Most SD^+ chromosomes in line Ac-27P were sensitive to distortion. This observation agrees with the distortion previously found for lethal II_3, the most common *SD* chromosome (Domínguez et al. 1987), and explains the high frequency of *SD* in that line. However, no distortion was observed in Ac-27S and correspondly SD^+ chromosomes were insensitive. It seems likely that responders in Ac-27S were at first sensitive to allow the increase in *SD* frequency. Insensitive responders would then have replaced the sensitive ones later in the history of the line. This suggestion is supported by the observation that SD^+ in Ac-27S is associated with In(2*L*)*t*. The inversion was also found in lines Ac-27P and N-21 but there the In(2*L*)*t* chromosomes were sensitive. Inverted insensitive chromosomes in Ac-27S may have arisen by recombination, even though its frequency is reduced by In(2*L*)*t*. Another possibility is that some In(2*L*)*t* Rsp^s chromosomes had changed to Rsp^i in line Ac-27S since it has been suggested that *Rsp* may be unstable in some conditions (Wu et al. 1988). Chromosomes In(2*L*)*t* $SD^+ Rsp^i$ must have replaced the sensitive ones due to the high frequency of *SD* which gives them a strong relative advantage. It is interesting to note that the generation and rapid increase in frequency of $Sd^+ Rsp^i$ chromosome has been shown in population cages initiated with 50% $SdRsp^i$ and 50% $Sd^+ Rsp^s$ chromosomes (Hiraizumi et al. 1960; Hartl 1977).

Most *SD* chromosomes carry the cosmopolitan inversion In(2*R*)*NS* and may also carry one or more unique inversions around the centromere or in the right arm. These play a role in the perpetuation of the *SD* system by preventing recombination between the distorter and its target locus (Charlesworth and Hartl 1978) or between the distorter and enhancers linked in coupling to it (Thompson and Feldman 1974). The only *SD* chromosomes without rearrangements come from the Mediterranean area. Our results provide more examples of Mediterranean inversion-free *SD* chromosomes. It was interpreted that inversion-free chromosomes represent ancestral forms of *SD* that subsequently evolved by trapping inversions that restrict recombination among the elements of the complex and then spread world-wide (Lyttle 1991; Temin et al. 1991). The Ac lines had accumulated deleterious genes in both *SD* and SD^+ chromosomes. The different content of detrimentals in the two Ac lines suggests that they were accumulated after the subdivision of the initial line at generation 16. Though it would be impossible to reconstruct the processes that led to the precise situation we now observe, there can be no doubt that the balancing effect of distortion and chance events due to small population size is responsible for the accumulation of detrimentals. *SD* chromosomes are usually associated with recessive deleterious genes (Hartl and Hiraizumi 1976). This has been attributed to the chance fixation of lethal mutations in haplotypes largely closed to recombination and subject to strong genetic drive (Lyttle 1991). In fact, lethals linked to *SD* in nature must behave like neutral genes in a population restricted to *SD* chromosomes, due to its low equilibrium frequency. In our laboratory strains, lethal or detrimental genes linked in coupling to *SD* would have been accumulated by the balancing effect of distortion. Following Crow (1991), in a population containing only *SD* and SD^+-sensitive chromosomes, a lethal *SD* chromosome can accumulate until it reaches an equilibrium frequency which depends on the fitness of the three possible genotypes and the strength of distortion (e.g., the equilibrium frequency for $k = 0.8$ and selection acting solely against the lethal is 0.3). A detrimental non-lethal *SD* chromosome can quickly increase its frequency and even be fixed in the population provided that insensitive responders or modifier genes reducing distortion do not accumulate. Presumably, line Ac-27P is near the equilibrium: *SD* causes distortion in the line but carries linked lethal or female-sterile genes which are not easily removed by recombination. *SD* chromosomes from Ac-27S are lethal and sterile-free but that line has accumulated SD^+-insensitive chromosomes opposing the action of *SD*.

SD^+ chromosomes from Ac lines also harbor detrimental genes. They would have accumulated by a mechanism similar to Muller's ratchet (Felsenstein 1974) which predicts that deleterious mutants would accumulate in chromosome regions with restricted recombination in finite populations. In a population where *SD* frequency becomes high, most individuals would be heterozygotes since: (1) distortion itself leads to an excess of heterozygotes due to different gametic frequencies between the sexes (Hedrick 1988) and (2) *SD* homozygotes are lethal or detrimental. In such a situation, recessive detrimental genes linked in repulsion to *SD* can become fixed in SD^+ chromosomes by drift in a generation and can not then be subsequently eliminated due to linkage that prevents the production of detrimental-free chromosomes. This process is also

related to that proposed by Madalena and Robertson (1975) to explain the accumulation of lethals, without effect over the selected trait, linked either in coupling or in repulsion to an artificially selected lethal. This process would eventually lead to a balanced system where all individuals are lethal heterozygotes and then further linked recessive-deleterious mutants would be driven only by chance events. After reaching this state, *SD* chromosomes are trapped and would remain segregating independently of their distorting ability.

The previous discussion explains the accumulation of detrimentals linked in cis or in trans to *SD* in Ac lines. In fact, all the main unfavorable genes mapped in the left arm at the region limited by the left break-point of In(2*L*)*t* and the centromere. In(2*L*)*t* (22D3-E1; 34A8-9) is linked to *SD*: the *Adh* locus, close to the right break point of the inversion is 3.9 map units from the *Sd* locus and the effective recombination in inversion heterozygotes would probably be lower since the action of inversions as cross-over suppresors usually spreads outside the inversions themselves (Roberts 1976). The two Ac lines went to a essentially balanced system. In line Ac-27P, *SD* mantains its distorting ability and most individuals are *SD*-lethal II_3 heterozygotes. Different SD^+-lethal chromosomes at fluctuating frequencies were sampled from that line, the evolution of these chromosomes being ruled by drift. Ac-27S has evolved to a different balance, SD^+ has fixed a linked female-sterile that make difficult eliminate *SD* despite the accumulation of insensitive responders. Presumably SD^+ female sterility is balanced by the reduced fertility of *SD* homozygous males. It is interesting that Lyttle (personal communication) has found similar results in his studies, where isofemale lines established from wild samples of *D. melanogaster*, identified in the first generation as segregating for *SD* and In(2*L*)*t* among others, quickly evolved to self-balanced *SD*/In(2*L*)*t* lines.

Event though the high frequency of deleterious genes can be explained, the number of different lethal and sterile genes that were sampled from line Ac-27P seems striking. Besides the four main lethals (II_3, II_4, II_5 and II_6) we have found 16 single-copy lethals and three female- sterile genes. The line also segregates for the mutant *black*. Some unusual phenomena, such as the possible induction of mutations (Hartl and Hiraizumi 1976) or the genetic instability of the elements of the complex (Golic 1990), have been sometimes reported in relation to *SD*. Consideration of such events has lead to the notion that transposable elements could be involved in the *SD* system (Sandler and Golic 1985; Golic 1990) though there is no direct evidence for this possibility. Our observation of so many different mutants in the Ac-27P line is likely to involve the mobilization of transposable elements but could not be related to *SD* since the sister line Ac-27S, also harboring *SD*, did not exhibit such an amount of variability.

Our results raise the possibility that some other cases of persisting lethals in laboratory strains may have been associated with *SD*. This may explain the findings of Skibinski (1986) and could apply to other studies since meiotic drive would not ordinarily be detected and is not usually looked for. *SD* can be found in almost all natural populations, usually associated with inversions and detrimental genes, at low equilibrium frequencies. Whenever the equilibrium conditions are broken down in small populations (e.g., by artificial selection, genetic drift, or environmental changes which alter the relative fitnesses of the components of the system), leading to an increase in *SD* frequency, deleterious genes linked in disequilibrium with the complex can be fixed in SD^+ chromosomes by chance and can not then be eliminated. This process would eventually lead to a balanced population where all chromosomes were lethal carriers.

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