THE GENETICS OF A SMALL CHROMOSOME REGION OF *DROSOPHILA MELANOGASTER* CONTAINING THE STRUCTURAL GENE FOR ALCOHOL DEHYDROGENASE. IV: SCUTOID, AN ANTIMORPHIC MUTATION

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ABSTRACT

Exchange mapping locates the dominant mutation Scutoid to the right of *Adh* on chromosome arm 2L of *D. melanogaster*. However, deletion mapping indicates that *Sco* is to the left of *Adh*. The phenotype of *Sco* is sensitive to mutation, or deletion, of *noc*$^+$ and of three genes, *el*, *l(2)br22*, and *l(2)br29* mapping immediately distal to *noc*. The four contiguous loci, *el*, *l(2)br22*, *l(2)br29* and *noc*, although separable by deletion end points, interact, because certain (or all) alleles of these four loci show partial failure of complementation, or even negative complementation. The simplest hypothesis is that *Sco* is a small reciprocal transposition, the genes *noc*, *osp*, and *Adh* exchanging places with three genes normally mapping proximal to them: *l(2)br34*, *l(2)br35* and *rd*. The *Sco* phenotype is thought to result from a position effect at the newly created *noc/l(2)br28* junction.

MAPPING close to the structural gene for alcohol dehydrogenase (*Adh*) on chromosome arm 2L of *Drosophila melanogaster* is the dominant mutation Scutoid (*Sco*). This mutation was induced with X rays by KRIVSHENKO (1959) and, when heterozygous, results in a specific pattern of loss of bristles from the head and thorax of the adult fly. The map location of *Sco* made it an obvious marker to use for the genetic analysis of *Adh* and for the analysis of the genetic structure of the environs of *Adh*. It soon became apparent, however, that *Sco* is a rather exceptional mutation. For example, the map position of *Sco* determined by recombination and that determined by deletion analysis are contradictory. Moreover, *Sco*, although normally a stable mutation, can be reverted by X rays at a high frequency. Analysis of the revertants of *Sco* revealed an unexpected genetic complexity in the structure of the *Sco* chromosome. This and a following paper (M. ASHBURNER *et al.*, unpublished results) are devoted to a genetic analysis of *Sco* and its revertants. It will probably help the reader if we begin by summarizing the structure of the *Sco* mutation that we consider the data warrant.

MODEL

In Figure 1 we show a genetic map of part of the "*Adh* region" of chromosome arm 2L, that is to say an approximately 40-polytene chromosome band region

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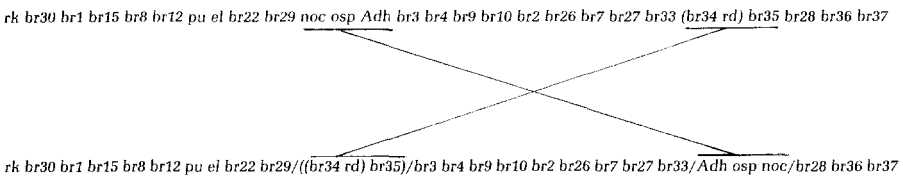

FIGURE 1.—Genetic map of region 35 in wild type (above) and *Sco* (below) chromosomes, showing the *Sco* transpositions. Data for the wild-type map is from O'DONNELL *et al.* (1977), WOODRUFF and ASHBURNER (1979a, 1979b) and from M. ASHBURNER and colleagues (unpublished).

between 34F1-2 and 35E1-2. This region, which is approximately 2.7 map units long, includes 29 identified "lethal" complementation groups and nine "visible" loci. These genes have been ordered by both recombination and deletion mapping (see O'DONNELL *et al.* 1977; WOODRUFF and ASHBURNER 1979a, 1979b; M. ASHBURNER *et al.*, unpublished results; and below).

Sco is a reciprocal transposition of two small segments within this chromosome region. As a result of a four-break event the three contiguous loci *noc*, *osp* and *Adh* have exchanged positions with at least three loci normally located more proximally, *i.e.*, *l(2)br34*, *rd* and *l(2)br35*. The new gene order of the *Sco* chromosome is shown in Figure 1. The order of the *noc*, *osp*, *Adh* region is as shown on this map, *i.e.*, inverted in its new position. The order of the *l(2)br34 rd l(2)br35* segment has not been determined. The Sco phenotype is a consequence of the juxtaposition of the normally separated loci noc^+ and $l(2)br28^+$.

MATERIALS AND METHODS

Stocks: The *Sco* chromosome presumably originates from KRIVSHENKO's original stock, as we know of no other occurrence of this mutation. Indeed all of our attempts to make new alleles of *Sco* have failed. We derived a *Sco*-carrying chromosome from the $Y^S X \cdot Y^L$,*In(1)EN,y*; *In(2L)Cy* + *In(2R)Cy,Cy* cn^2/*Sco* stock of Dr. D. LINDSLEY. Most of the data are from a stock carrying this chromosome balanced with *In(2L)Cy* + *In(2R)Cy,al*^{2} *Cy pr Bl* cn^2 *vg c* sp^2. Marked *Sco* chromosomes were made either by exchange with standard stocks or by mutation. Markers other than *Sco* will only be mentioned when relevant to the data. Other balancer chromosomes used were *In(2LR)O,Cy* dp^{hd} *pr* cn^2*(CyO)*, *In(2LR)Gla,Gla l(2)br16*^{SF16}*(Gla)* and *In(2L)Cy,Cy* dp^2 *b pr,(Cy dp b pr)*. Other stocks have either been described before (WOODRUFF and ASHBURNER 1979a, 1979b; O'DONNELL *et al.* 1977; M. ASHBURNER *et al.*, unpublished results) or will be described in the text (see Table 1).

Culture conditions: For routine purposes 4- x 1-inch vials or 200-ml bottles were used with Philipp-Harris Instant Drosophila medium. The culture temperature was 25°, and the crosses were scored until the 18th day after being set up. For cytology, larvae were grown on a yeast-glucose medium.

Scoring of Sco: Wild-type flies have seven pairs of dorsal head macrochaetae and 13 pairs of macrochaetae on their dorsal thorax (*i.e.*, 40 bristles/fly). The phenotype of *Sco* was scored by counting these bristles (AO, MO, PO = anterior, middle and posterior orbitals; PVt = postverticals; AV, PV = anterior and posterior verticals; O = ocellars; UH, LH = upper and lower humerals; PSt = presuturals; AN, PN = anterior and posterior notopleurals; AS, PS = anterior and posterior supraalars; AD, PD = anterior and posterior dorsocentrals; AP, PP = anterior and posterior postalars; ASc, PSc = anterior and posterior scutellars). Unless stated otherwise, bristle numbers are the means of ten males and ten females.

Nomenclature: By convention we use the "—" sign to denote the absence of a gene, resulting from deletion. Thus *el/el*$^-$ indicates a heterozygote between a mutant *el* allele and a deletion that includes (at least) the *el* locus. Viability data is normally from crosses between stocks carrying

TABLE 1

Description of deletions

Deletion	Cytology
Df(2L)fn1	*Df(2L)34F4-A1; 35D5-7*
Df(2L)fn2	*Df(2L)35A3; 35B2-4*
Df(2L)fn3	*Df(2L)35B1; 35B3-4*
Df(2L)fn27	*Df(2L)35B1; 35D1-2*
Df(2L)A48	*Df(2L)35B3; 35D5-7*
Df(2L)A63	[a]
Df(2L)A72	*Df(2L)35B2-3; 35B7*
Df(2L)A178	*Df(2L)35B2-3*
Df(2L)A263	*Df(2L)34E5-F1; 35C3-5*
Df(2L)A266	*Df(2L)35B2-3*
Df(2L)A267	*Df(2L)35B2; 35B10*
Df(2L)A379	[b]
Df(2L)A400	*Df(2L)35A1-4; 35B10*
Df(2L)A446	*Df(2L)35B1; 35E1-2*
Df(2L)AR-R1	*Df(2L)35A3-4; 35B10-C1*
$Df(2L)el^{4D}\ R15^{P}$	*Df(2L)35A2-4; 35B10-C1*
$Df(2L)el^{4D}\ A80^{P}$	*Df(2L)35A2-4; 35A3-4*
Df(2L)64j	*Df(2L)34D1-2; 35B8-9-C1*
Df(2L)75c	*Df(2L)35A1-2; 35D4-7*
Df(2L)do-1	*Df(2L)35B1; 35D2*
Df(2L)osp-18	*Df(2L)35B1-2; 35C4-5*
Df(2L)osp-29	*Df(2L)35B1-2; 35E6*[c]
Df(2L)osp-144	[a]
$Df(2L)Adh^{n78i3}$	*Df(2L)35B1; 35D5-7*
Df(2L)W	*Df(2L)35A2-3; 35B3-5*
$Df(2L)Sco^{R+4}$	*Df(2L)35B1-2; 35D5-7*
$Df(2L)C158.1^{L}\ Sco\ R + 11^{R}$	*Df(2L)35B3; 35C±*
Df(2L)b81a1	*Df(2L)34D3; 35B1*
Df(2L)b80e3	*Df(2L)34C3; 35A4*

[a] Not cytologically deficient.
[b] Associated with breakpoint of *In(2LR)A379* = *In(2L)35B3-5; 57A8-10* + *In(2)35B3-5; 40-41.*
[c] *osp29* is mutant, but not deleted, for osp.

chromosomes balanced over Cy and is expressed as the number of Cy^{+} progeny over the total number of progeny (or as a percentage).

RESULTS

The Sco *phenotype:* When heterozygous with a wild-type second chromosome, *Sco* results in the loss of between 11 and 15 bristles per fly. The pattern of loss is quite specific, for example, the ASc, PSc, AN, PN, UH and AP sites are those most strongly affected (M. ASHBURNER *et al.*, unpublished results) and, unlike some mutations with superficially similar phenotypes (e.g., Hairless), *Sco* does not affect cell hairs and removes from bristle sites both tormogen and trichogen cell derivatives. *Sco* is normally regarded as a recessive lethal, although when care is taken to remove extraneous lethals from the *Sco* chromosome by recombination a few *Sco* homozygotes survive to adulthood. In one such experiment, 12 homozygotes among 7700 progeny were found. These flies

had a very extreme *Sco* phenotype, with only eight or so bristles/fly, and with the loss of other macrochaetae such as the sternopleurals and (in males) the sex combs. These *Sco* homozygotes also had small, very rough, eyes, resembling those of *ast* in shape but with the central facets forming a prominent, irregular excrescence. The ocelli of the homozygotes were normal. *Sco* homozygotes are sterile and short lived.

Mapping of Sco: O'DONNELL *et al.* (1977) mapped *Sco* 0.02% to the right of *Adh*, on the basis of two *Adh-Sco* recombinants in 9281 flies. We have done similar experiments, for example, in 10,846 progeny of *b Sco pr/b* Adh^{n2} *l(2) br4*^{AR6} *pr* females we recovered a single *Adh-Sco* recombinant whose phenotype was consistent with *Sco* being located to the right of *Adh* (see Figure 1). However, it was clear that the *Sco* chromosome very strongly reduced exchange in the immediate vicinity of *Adh*. In another experiment no *Adh-rd*^{s} recombinants were found in 15,946 progeny of *b Sco pr/*Adh^{nC1} *rd*^{s} *pr cn* females when, in control crosses, the *Adh* to *rd*^{s} distance was of the order of 0.4%.

A summary of some of the effects of *Sco* on exchange is shown in Figure 2. The notable feature of the data is that the effects of *Sco* on exchange are very local, limited to the *el* to *rd* interval. The genetic distance between *b* and *pr* is not reduced, indeed it may even be increased, in *Sco*/+ heterozygotes.

In independent experiments MARONI (1980) recovered, in the presence of a compound X-chromosome, a recombinant between *el* and *Sco* that is consistent with *Sco* mapping to the right of elbow. However, MARONI correctly concluded that the structure of the *el-Sco* crossover chromosome was not consistent with the hypothesis that *Sco* is a simple mutation mapping proximal to *Adh*. We will return to the nature of MARONI's recombinant chromosome below. We now conclude that (1) *Sco* is a strong, but local, suppressor of exchange in the *Adh* region, and that (2) the limited recombination data suggest that *Sco* maps to the right of *Adh*.

The cytology of Sco: These exchange data clearly call for a cytological study of the *Sco* chromosome. On cursory examination the polytene chromosomes of

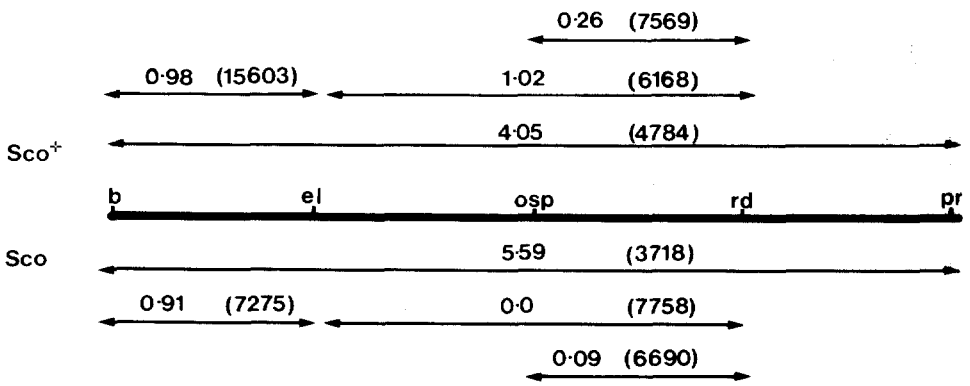

FIGURE 2.—The effects of *Sco* on exchange in the black (*b*) to purple (*pr*) interval. Map distances (in % exchange) in marker/+ and marker/*Sco* females (with progeny numbers) are shown. The *osp-rd* distance in the *osp rd*/+ experiment is probably rather low, because the mean of seven independent determinations of the *Adh-rd* distance is 0.43% (n = 120163).

Sco/+ appear to be normal and it is only on close inspection that something appears to be wrong in region 35 of chromosome arm 2*L*. It is impossible to say, from the cytological picture alone, just what is wrong; all that is seen is a disturbance of synapsis in region 35 and the absence of a puff normally active in 35B2-5. The polytene chromosomes of *Sco*/+, both synapsed and asynapsed, are shown in Figure 3. A more detailed consideration of the cytology of *Sco* is made by M. ASHBURNER (unpublished) who concluded that the cytological and genetic interpretations of *Sco* are quite compatible.

Deletion mapping of Sco: *Sco* has been crossed to most of the 70 or so deletions that include all or part of the 34D to 35E region in the hope that the data would unambiguously locate *Sco*. Representative data are shown in Figure 4. A long deletion, such as *Df(2L)fn1*, clearly "includes" *Sco* because *Sco*/*Df(2L)fn1* heterozygotes are semilethal, and those flies that do eclose are phenotypically similar to *Sco* homozygotes with respect to both their bristle and eye phenotypes. Two deletions, *Df(2L)W* and *Df(2L)osp29*, conveniently divide the *Df(2L)fn1* region into distal and proximal parts, respectively. The phenotype of *Sco*/*Df(2L)W* is similar to that of *Sco*/*Df(2L)fn1*; on the other hand, *Sco*/*Df(2L)osp29* heterozygotes are viable and do not have an enhanced Scutoid phenotype. This leads to the conclusion that *Sco* is located within the region common to *Df(2L)fn1* and *Df(L)W*, that is to say, to the region between *l(2)br1* and *Adh*. Two deficiencies, *Df(2L)A400* and *Df(2L)el*^{4D}*R15*^{P}, that include only the *pu-Adh* region in common with *Df(2L)W*, both give a "homozygous" Scutoid phenotype with *Sco* suggesting that, in fact, *Sco* is

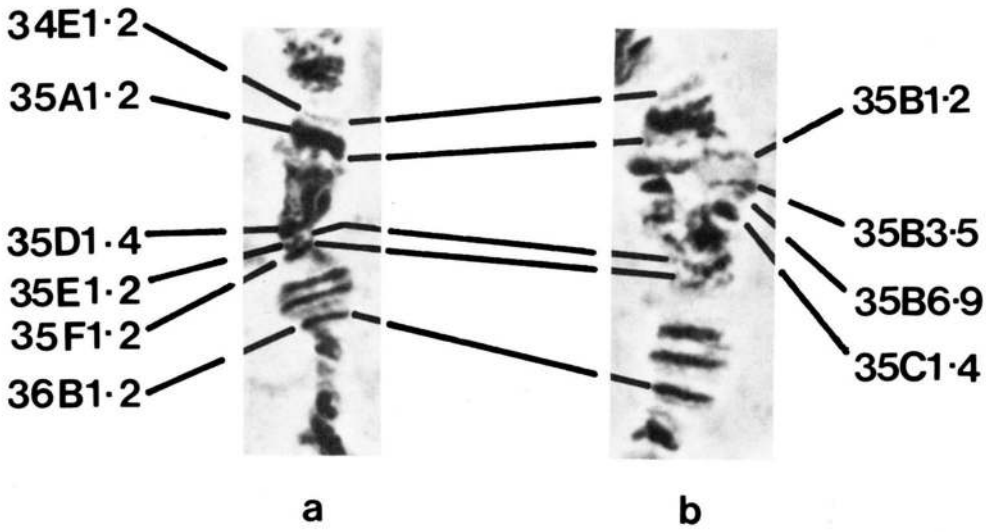

FIGURE 3.—The polytene chromosomes of *Sco*/+. (a) Synapsed and (b) asynapsed. When synapsed, the confused banding pattern between 35B1 and 35D1 is obvious. When asynapsed the 35B1-3 puff is clearly absent from the *Sco* homologue (left) and the banding of this homologue differs from that of the wild (right). It looks as if the *Sco* homologue is inverted for 35B3 to 35C4. However, a reciprocal transposition of 35B3-5 and 35C1-4 would have a similar form since the bands between these (*i.e.*, 35B6 to 35B10) are rather symmetrical.

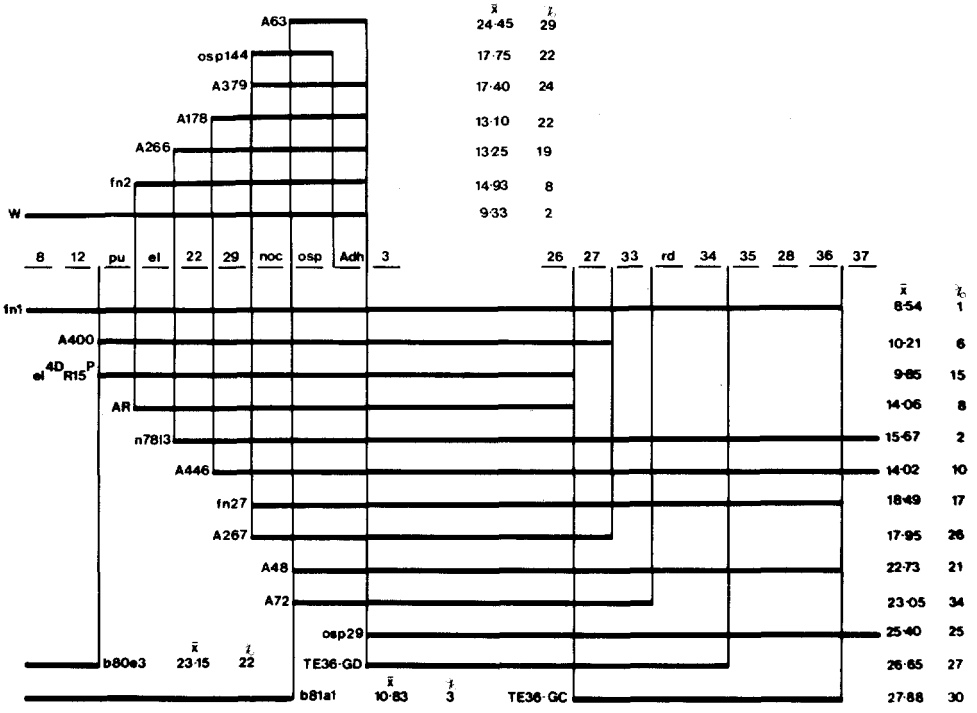

FIGURE 4.—The interaction between deletions of region 34-35 and *Sco* with respect to viability and bristle phenotype. % is the relative viability of the *Sco*/Df progeny from Df/Cy × *Sco*/Cy *Bl* crosses; $\bar{x}$ is the mean bristle number of the Df/*Sco* flies. *Sco*/Cy have mean bristle numbers in the range of 25 to 28 bristles/fly. The genetic limits of the deletions on a wild-type genetic map, which is interrupted between *l(2)br3* and *l(2)br7*, are shown (data as for Figure 1).

between *l(2)br12* and *Adh*. All of 22 other deficiencies that include the entire *pu* to *Adh* interval have similar phenotypes when heterozygous with *Sco*, enhancing the *Sco* phenotype to some 10 to 12 bristles/fly.

These data are unexceptional, except they indicate that *Sco* maps to the left, rather than to the right, of *Adh*. Matters become rather more complicated, however, when an attempt is made to map *Sco* more precisely within the region between *l(2)br12* and *Adh*, by using deletions that end between these loci.

Two deletions have their distal limits between *pu* and *el*: *Df(2L)fn2* and *Df(2L)AR-R1*. When heterozygous with these deletions *Sco* has a bristle phenotype of about 14 bristles/fly, considerably less enhanced than, for example, *Soc/Df(2L)W* or *Sco/Df(2L)el^{4D}R15^{P}* (both about nine bristles/fly). These differences cannot be caused by factors to the right of the *l(2)br12-Adh* region because *Df(2L)fn2* and *Df(2L)W* have the same proximal limit (between *Adh* and *l(2)br3*), and *Df(2L)AR-R1* and *Df(2L)el^{4D}R15^{P}* actually share their proximal breakpoint, *i.e.*, that of *T(Y;2)R 15*. The next series of deletions to be considered is that broken between *el* and *l(2)br22*. Data for two of these, *Df(2L)A266* and *Df(2L)Adh^{n7813}* are shown in Figure 4. When heterozygous with these deletions, *Sco* flies have between 13 and 16 bristles/fly, similar to, for example, *Sco/Df(2L)fn2* heterozygotes. When heterozygous with deficiencies broken

between *l(2)br22* and *l(2)br29* (e.g., *Df(2L)A446, Df(2L)A178*), the phenotype of *Sco* is similar, 13–14 bristles/fly. However, deletions that are broken more proximal, i.e., between *l(2)br29* and *noc*, for example, *Df(2L)osp144, Df(2L)A267, Df(2L)A379* and *Df(2L)fn27*, have a weaker effect on *Sco*: they enhance, but only by 10 or so bristles, to 17–18 bristles/fly.

Finally, deletions broken to the right of *noc*, either between *noc* and *osp* or between *Adh* and *l(2)br3* (see Figure 4), have little, if any, effect on *Sco*'s expression. Only two deletions are available that have their proximal, rather than distal, limits between *l(2)br12* and *osp: Df(2L)b80e3* broken between *l(2)br12* and *pu* and *Df(2L)b81a1* broken between *noc* and *osp*. *Df(2L)b80e3* has no effect on the expression of *Sco* whereas *Df(2L)b81a1* acts like all other deletions of the entire *pu-noc* interval, enhancing the expressivity of *Sco* to about 10 bristles/fly.

These data point inexorably to the conclusion that *Sco* cannot be simply located to any discrete genetic interval defined by deletion endpoints. The interaction of deletions of all, or part, of the *l(2)br12* to *Adh* interval with *Sco* depends upon just how much of this region the deletion removes: if the entire interval is absent (e.g., *Df(2L)W*) then *Sco*/Df flies are poorly viable (typically less than 5% survive) and they have an extreme phenotype, only 8–10 bristles/fly. If, however, only the *el-Adh, br22-Adh* or *br29-Adh* regions are missing from the deletion, then the viability of *Sco* heterozygotes increases, (although not very consistently) and their phenotype is less extreme, 13–15 bristles/fly. If the deletion removes even less of the *l(2)br12-Adh* region, *i.e.*, the *noc-Adh* or *noc-osp* intervals, then there is only relatively minor (if any) lowering of the *Soc/Df* viability and a lesser enhancement, to 17–18 bristles/fly, of their phenotype. Finally deletions that leave the entire *pu-noc* region intact, but remove *osp* and *Adh*, are viable with *Sco* and have little effect on its phenotype.

These data emphasize (1) that deletions cannot be used to map *Sco* to a single simple genetic region and (2) that both the semilethality and bristle phenotypes of *Sco* map to a region to the left of *Adh*, in fact, to the left of *osp*, and not to the right as the recombination data, albeit limited, suggested.

The interaction of Sco *with other mutations in the* Adh *region:* We have crossed *Sco* to representative alleles of all the lethal and visible complementation groups identified in the 34D–35E interval, analyzing the progeny with respect to both their relative viability and the phenotypes of the *Sco* heterozygotes. The majority of loci, and the majority of chromosome aberrations, mapped to this small chromosome region, have no effect on the expressivity of *Sco* (data not shown). The only mutations that do interact with *Sco* map to the four contiguous loci, elbow, *l(2)br22, l(2)br29* and no-ocelli—that is to say mutations that map to the region which, when deleted, enhances *Sco*'s expression.

elbow: Mutant alleles of elbow are recessive and, when homozygous or hemizygous, result in a characteristic "bent" wing phenotype and reduced halteres. Weak *el* alleles are most readily scored by the small size and low bristle number of their alulae. el^1 is clearly a hypomorphic mutation; the wings of el^1 homozygotes are much larger than those of el^1/el^- deficiency heterozygotes. The deletion mapping of *el* is unambiguous, it maps between *pu* and *l(2)*

br22, that is to say between the distal limits of, for example, *Df(2L)fn2* and *Df(2L)A266*.

Heterozygotes between el^1 and *Sco* are indistinguishable from *Sco*/+ flies (Table 2). However, three new *el* alleles all enhance the expression of *Sco*. The first of these to be studied was the EMS-induced temperature-sensitive allele, el^3 (WOODRUFF and ASHBURNER 1979b). el^3 is a weak *el* allele (by comparison with el^1), and is, therefore, not a deletion. The heterozygotes, el^3/Sco, are viable, but the flies have some seven bristles less than *Sco*/+. The second elbow allele found to enhance *Sco* was also EMS induced, but is a translocation to the Y chromosome. This translocation ($T(Y;2)el^4$) is broken in chromosome 2L between *l(2)br12* and *pu* because a synthetic deletion made using the 2 distal-Y proximal element of $T(Y;2)el^4$ and the Y distal-2 proximal element of the LINDSLEY-SANDLER translocation *T(Y;2)R15* (i.e., $Df(2L)el^{4D}R15^P$) is deleted for *pu* to *l(2)br26*. $T(Y;2)el^4$ is, phenotypically, very similar to el^1, that is to say, el^4/el^1 flies resemble el^1 homozygotes and el^4/el^- heterozygotes resemble el^1/el^- heterozygotes. It is, therefore, unlikely that el^4 is a deletion for *el*. Yet el^4/Sco heterozygotes, although viable, have a considerably enhanced Scutoid phenotype (Table 2). The enhancement of *Sco* by $T(Y;2)el^4$ can be shown to be caused by the proximal element of the translocation, because this effect can be covered by the distal element of *T(Y;2)A80*.

$Df(2L)el^{4D}A80^P$ (which is, genetically, $l(2)br12^+pu^-el^+$) has little effect on the expression of *Sco*. The relationship between the translocation of $T(Y;2)el^4$ and the el^4 mutation is not clear in the light of genetic evidence that the translocation is broken distal to pupal. The breakpoint and the elbow mutation could be independent events or the elbow phenotype of the translocation could result from a position effect. The absence of any position effect on pupal may be a result of nonautonomy.

The third *el* allele studied was el^{GM2}, EMS induced by G. MARONI (unpublished). Like el^3 this is a very weak elbow allele, but it is not temperature sensitive. It enhances *Sco* to an even greater degree than either el^3 or el^4;el^{GM2}/Sco flies have some 11 bristles less than their *Sco*/+ sibs. el^{GM2} differs from el^3 in another respect: it shows reduced viability when heterozyous with *l(2)br22* and *l(2)br29* alleles (Table 3). Despite this, el^{GM2} can neither be deleted for *el*, nor can it be deleted for *l(2)br22* or *l(2)br29* because, if it were, it would give an extreme elbow phenotype with el^1 and would be lethal, and not semilethal, with mutant alleles of *l(2)br22* and *l(2)br29*.

l(2)br22: Four EMS-induced mutations define *l(2)br22*. These are all lethal *inter se* and their lethality maps between *el* and *l(2)br29*. However, there are strong grounds for considering that *l(2)br22* is in some way related to the three other loci of the *el-noc* interval because (1) three of the *l(2)br22* alleles are also weak *el* alleles, (2) all *l(2)br22* alleles are semilethal with $l(2)br29^{ScoR+1}$ and (3) three are weak *noc* alleles. However, they define a locus distinct from *l(2)br29* because *Df(2L)A446* is completely lethal with $l(2)br29^{ScoR+1}$ but is viable with all *l(2)br22* alleles (Table 4). Of the four alleles of *l(2)br22*, one, $l(2)br22^{AR10}$, is a leaky lethal; hemizygotes do survive and if the deletion includes either (or both) *el* and *noc* then the escapers show a weak phenotype characteristic of either (or both) of these loci.

TABLE 2

Interaction of Sco *with* el *and* br22 *alleles*[a]

	Mutant/*Sco*			Control/*Sco*			Deviation in bristle no.
	N	%	$\bar{x}$	N	%	$\bar{x}$	
el^1	561/1152	48.7	28.85 ± 0.28	478/978	48.9	27.00 ± 0.58	+1.85
el^3	300/1305	23.0	20.80 ± 0.42	111/367	30.2	27.30 ± 0.32	−6.50
el^4	357/1350	26.4	20.00 ± 0.49	157/521	30.1	27.25 ± 0.38	−7.25
el^{GM2}	262/1134	23.1	14.90 ± 0.32	57/195	29.2	28.30 ± 0.82	−13.40
$br22^{AR10}$	173/1780	9.7	11.60 ± 0.41	132/400	33.0	24.60 ± 0.55	−13.00
$br22^{FT1}$	190/1195	15.9	13.35 ± 0.41				−11.25
$br22^{HG33}$	268/1182	22.7	15.20 ± 0.55	216/434	49.8	25.40 ± 0.47	−10.20
$br22^{HG46}$	104/564	18.4	16.40 ± 0.37	36/119	30.3	27.75 ± 0.68	−11.35

Genotypes (and control chromosomes in brackets): *b* el^1 rd^s *pr cn* (Canton-S); $el^3 Adh^{uf3}$ *cn/CyO* ($l(2)br1^{SF11}$ Adh^{uf3} *cn/CyO*); *b* $T(Y;2)el^4$ Adh^{nc2} *pr cn bw/CyO* (*b* $l(2)br15^{HG6}$ Adh^{nc2} *pr cn bw/CyO*); *b* el^{GM2} Adh^F/Cy *Roi* (*b* $l(2)br1^{GM2}$ Adh^F/*CyRoi*); $l(2)br22^{AR10}$ Adh^{n11} *cn vg/Gla*, $l(2)br22^{FT1}$ Adh^{n11} *cn vg/CyO* (Adh^{n11} $l(2)br26^{HG21}$ *cn vg/CyO*); $l(2)br22^{HG33}$ Adh^{n7} *cn vg/CyO* (Adh^{n7} *cn vg*); *b* $l(2)br22^{HG46}$ *pr/CyO* (*b pr* $l(2)HG44$/CyO).

[a] For each *el* and *l*(2)br22 allele the viability and bristle number of *mutant/Sco* heterozygotes is compared with that of an appropriate control chromosome. The difference in bristle number of *mutant/Sco* and *control/Sco* is shown on the right. *N* shows the number of *mutant/Sco* progeny (or *control/Sco*) over total progeny number in crosses to *Sco/CyBl*.

TABLE 3

Relative viabilities of el *and* noc *alleles with* $l(2)br22^{FT1}$ *and* $l(2)br29^{ScoR+1}$ [a]

	FT1	%	Sco^{R+1}	%
el^1	275/525	52.3	234/444	52.7
el^3	173/531	32.6	275/1444	19.0
el^4	268/920	29.1	338/1186	28.5
el^{GM2}	202/1288	15.7	157/1091	14.4
noc^2	235/740	31.8	225/1073	21.0
noc^3	205/632	32.4	192/640	30.0
noc^4	217/972	22.3	21/611	3.4
noc^{18}	123/371	35.8	158/764	20.7
noc^{19}	94/337	27.9	98/987	9.9
noc^{TE146}	265/1098	24.2	13/9063	0.1

[a] Number of *noc/l* or *el/l* flies over total progeny from crosses of *noc/Cy* × *l/Cy* or *el/Cy* × *l/Cy* except for el^1, which was homozygous.

The four *l*(2)br22 alleles are, therefore, somewhat enigmatic. Although their lethal phenotype maps unambiguously to a discrete genetic interval, they interact with mutant alleles of three adjoining loci. They are assuredly not deletions for the *el-noc* interval. If they were, $l(2)br22/el^-$ would have a strong, and not a weak, elbow phenotype; $l(2)br22/l(2)br29^{ScoR+1}$ would be lethal and not semilethal; and $l(2)br22/noc^{TE146}$ would have a strong, and not a rather weak, *noc* phenotype. Moreover, $l(2)br22^{AR10}$ would not be a leaky lethal. Yet all *l*(2)br22 alleles strongly enhance *Sco* and three of them, at least (*AR10*, *FT1*,

TABLE 4

Deletion mapping of mutations in the pu *to* noc *interval showing that the* el, l(2)br22 (FT1, AR10, HG33), l(2)br29 (Sco^{R+1}) *and* noc *phenotypes can be clearly separated by deletion end points*[a]

	Df(2L)A400	*Df(2L)fn2*	*Df(2L)fn3*	*Df(2L)A446*	*Df(2L)A267*	*Df(2L)A72*
pu	*pu*	+	+	+	+	+
el	*el*	*el*	+	+	+	+
FT1	0/108	0/214	0/348	101/400	210/659	$155/451^{+}$
AR10	1/396(el)	31/1506(el)	$65/1053(el^{+})$	$122/430(el^{+})$	$223/855(el^{+})$	$61/372(el^{+})$
HG33	0/202	0/174	0/277	112/337	282/877	115/365
Sco^{R+1}	0/198	0/528	0/1008	9/1863	159/784	355/1152
noc	*noc*	*noc*	*noc*	*noc*	*noc*	+

[a] The vertical line indicates the extent of each deletion in this region.

and *HG46*), have a considerably reduced viability with *Sco* (Table 2). The polytene chromosomes of all *l(2)br22* alleles appear to be normal in structure.

l(2)br29: This lethal is defined by a single mutant chromosome, the X-ray-induced revertant of *Soc*, Soc^{R+1} (M. ASHBURNER *et al.*, unpublished results). This revertant is recessive lethal and this phenotype maps between *l(2)br22* and *noc* (Table 4). Soc^{R+1} is completely lethal with *Sco*. It is very unlikely that Sco^{R+1} is a deletion. On the one hand no deletion is absolutely lethal with *Sco*. More compelling is the fact that Soc^{R+1} is a synthetic lethal with some alleles of *noc* which, themselves, are fully viable as homozygotes or when heterozygous with *l(2)br29*$^{-}$ deletions (see Tables 3 and 4). Thus, the Sco^{R+1} chromosome must "do something" and cannot merely be an absence of "*br29*" function (see below and M. ASHBURNER *et al.*, unpublished). Indeed there is other evidence (M. ASHBURNER *et al.*, unpublished and M. ASHBURNER, unpublished) that loss of "*br29*" function is not lethal.

noc: The no-ocelli (*noc*) locus maps immediately distal to *osp* and several EMS and gamma-ray induced *noc* alleles have been isolated (M. ASHBURNER, S. TSUBOTA and N. SPOEREL, unpublished). In addition, one allele is known as a consequence of the insertion into *noc* of a $w^{+}rst^{+}$ Transposing Element (see ISING and RAMEL 1976). Some e.g., noc^{2}, noc^{4}, noc^{TE146}, noc^{19}, but not all, e.g., noc^{3}, noc^{18}, alleles of *noc* enhance the expression of *Sco* and some show a reduced viability when heterozygous with *Sco* (Table 5). Although some *noc* alleles are chromosome aberrations (e.g., *In(2L)noc*^{2}, *In(2L)noc*^{4}), there is no correlation between their effects on *Sco* and their chromosomal nature; for example, both noc^{18} and noc^{19} are cytologically normal; they were induced by EMS in the same screen: the former allele does not affect *Sco*, the latter enhances it. *noc* is not a vital locus, not only are flies that are homozygously deleted for *noc* viable (e.g., *Df(2L)A178/Df(2L)A267*) but all *noc* alleles are either homozygous viable or viable with a *noc*$^{-}$ deletion. Some *noc* alleles that enhance *Sco* are either lethal or semilethal with Sco^{R+1} (Table 3), an example of negative complementation. In fact, all alleles of *noc* that are lethal (or semilethal) with Sco^{R+1} also enhance *Sco*, but not *vice versa* (e.g., noc^{2}, Table 3).

TABLE 5

Interaction of Sco *with* noc *alleles*[a]

	noc/Sco			Control/*Sco*			Deviation in bristle no.
	N	%	$\bar{x}$	N	%	$\bar{x}$	
noc^{2}	138/475	29.1	17.60 ± 0.47	71/207	34.3	28.20 ± 0.72	−10.60
noc^{3}	168/561	29.9	26.00 ± 0.63	69/176	39.2	27.05 ± 0.47	−1.05
noc^{4}	141/858	16.4	14.10 ± 0.49	233/446	52.2	24.95 ± 0.36	−10.85
noc^{18}	141/390	36.2	27.00 ± 0.44	165/530	31.1	23.35 ± 0.55	+3.65
noc^{19}	59/251	23.5	16.95 ± 0.72				−6.40
noc^{TE146}	233/1060	22.0	16.30 ± 0.59	478/978	48.9	27.00 ± 0.58	−10.70

Genotypes (control chromosomes in brackets): b $l(2)br1^{HG10}$ noc^{2} Adh^{nC1} pr cn bw/CyO (b $l(2)br1^{HG10}$ Adh^{nC1} pr cn bw/CyO); noc^{3} Adh^{n5} pr/CyO (Adh^{n5} pr); b noc^{4} Adh^{F} cn bw/CyO (b Adh^{F} cn bw); b noc^{18} Adh^{F} $l(2)br4^{AR1}$ pr/CyO, b noc^{19} Adh^{F} $l(2)br4^{AR1}$ pr/CyO (b Adh^{F} $l(2)br4^{AR1}$ pr/CyO); w; al dp b noc^{TE146}/CyO (Canton-S).

[a] The difference in bristle number between *noc/Sco* and noc^{+}/*Sco* is shown where, except for noc^{TE146}, the noc^{+} chromosome was the base chromosome on which the *noc* allele was induced. For noc^{TE146} the deviation is shown from *Sco*/+ where "+" is a Canton-S *2nd* chromosome. *N* shows the number of *noc/Sco* progeny (or noc^{+}/*Sco*) over total progeny in crosses to *Sco/CyBl*.

In summary, four complementation groups have been mapped between *pu* and *Adh*; two are recessive lethal, *l(2)br22* and *l(2)br29*, and two are recessive visible, *el* and *noc*. The mapping of these groups with deletions is quite clear; all are separated by several different deletion end points (see Table 4). Yet some, or all, known alleles of each interact with *Sco*, either to enhance the mutation's visible phenotype or to reduce its viability, or both. None of these mutations show any of the characteristics of deletions, a point we emphasize. The evidence for this statement, although indirect, is compelling.

Duplications and Sco: The conclusion that *Sco* maps to the left of *Adh* is supported by the interaction between *Sco* and three duplications for parts of region 34–35 (Table 6). Two of these duplications partially suppress *Sco*: they are *Dp(2;2)Adh3* and *Dp(2;2)GY*. The former duplication extends from 34B1-2 to approximately 35B3; it covers *Adh* but not *l(2)br7* (ASHBURNER 1982). Its proximal limit has not been determined genetically, but, to judge from its cytology, is near the *l(2)br3*. The second duplication is from 33B1-2 to 35C1-2 and, genetically extends to *l(2)br33*.

The third duplication used, $Dp(2;2)C143.41^{L}C158.1^{R}$, does not affect the expression of *Sco*. The cytological limits of this duplication are 35B3 and 35E1-2. Genetically the duplication covers *l(2)br3*, but not *Adh*, *osp*, or *noc*. This is known because the *In(2L)C158.1* has been used, with other inversions broken near to 35B3, to construct deletions (e.g., *Df(2L)C75RL* and $Df(2L)C158.1^{L}Sco^{R+11R}$) one of whose end points lie between *Adh* and *l(2)br3*.

One other duplication has been studied, $Dp(2;1)Soc^{R+23}$ (ASHBURNER *et al.*, unpublished results). This is derived by segregation from the insertional translocation $T(2;1)Sco^{R+23}$, an X-ray-induced revertant of *Sco*. This translocation involves three breaks on the *Sco* chromosome, one between *rk* and *l(2)br30*, one between *noc* and *l(2)br28* and one between *l(2)br36* and *l(2)br37*. The *l(2)* $br30^{+}$ to *noc* region translocated to the proximal heterochromatin of the X

TABLE 6

Effects of duplications for 34-35 on Sco *and* b el Sco *phenotypes*[a]

	Dp/Sco	*Dp/b el Sco*
Dp(2;2)Adh^{3}	+4.25	+2.45
Dp(2;2)GY	+4.62	+3.18
Dp(2;2)C163.41^{L}*C158.1*^{R}	+0.53	−0.53
Dp(2;1)Sco^{R+23}	+0.48	+0.61

[a] Shown is the difference in bristle number between *Dp/Sco* (and *Dp/b el Sco*) flies and their *Cy/Sco* and (*Cy/b el Sco*) sibs, except in the case of *Dp(2;1) Sco*$^{R+23}$, which is the difference between *Dp(2;1)Sco*$^{R+23}$/+; *b el*^{1}*rd*^{s} *pr cn/Sco* (or *b el Sco*) and *Basc/+*; *b el*^{1}*rd*^{s} *pr cn/Sco* (or *b el Sco*) females. Mean deviation of at least three independent crosses.

chromosome and the *l(2)br28*$^{+}$ to *l(2)br36*$^{+}$ region was lost, leaving the duplication shorter, by these two genes, than the deletion. *Df(2L)Sco*$^{R+23}$*/Sco* are semilethal (7/827) and have only 9.67 ± 0.30 bristles/fly; this deletion acts like any other long deletion in this respect. However, paradoxically, *Dp(2;1)Sco*$^{R+23}$ has no effect on *Sco* in either *Dp(2;1)Sco*$^{R+23}$*/+;Sco/+* or *Dp(2;1)Sco*$^{R+23}$*/+;Df(2L)Sco*$^{R+23}$*/Sco* genotypes. The former are just like *Sco/+* (with a mean bristle number of 28.50 + 0.31/fly), and the latter like *Df(2L)Sco*$^{R+23}$*/Sco* (with a mean of 10.65 + 0.27 bristles/fly). The explanation of this paradox is that the duplication is mutant for *noc* (M. ASHBURNER *et al.*, unpublished results) and only duplications carrying *noc*$^{+}$ suppress *Sco* (see DISCUSSION).

The b el Sco *crossover:* The recovery of a recombinant chromosome between *el* and *Sco*, by MARONI (1980), has already been mentioned. MARONI made the important observation that this chromosome is duplicated for *Adh*. The crossover was derived from *b el Adh*^{n1}*/Sco Adh*^{F} females; the *Adh*^{n1} mutation is of an *Adh*^{S} allele, and *Adh*^{n1}*/Adh*^{F} heterozygotes show an active ADH^{n1}ADH^{F} heterodimer on electrophoresis. MARONI found that *b el Sco/Adh*$^{-}$ also showed this heterodimer, indicating that this chromosome carries both *Adh*^{n1} and *Adh*^{F} alleles. This result led MARONI to suggest that the *Adh*^{F} gene of the *Sco* chromosome had been transposed to the right of its normal location.

In fact, the structure of the *b el Sco* crossover is even more interesting. Phenotypically *b el Sco/+* heterozygotes are Scutoid, but significantly less extreme than *Sco/+* (Table 7). *b el Sco/Sco* flies are semilethal (21/1064) and have a moderately enhanced Scutoid phenotype (with a mean of 19.00 ± 0.55 bristles/fly; $n = 19$). When heterozygous with deletions of the *Adh* region, *b el Sco* shows a similar pattern of interaction as *Sco*, although its phenotype is *never* enhanced below that characteristic of *Sco/+* (*i.e.*, 25–27 bristles/fly). The phenotype of *b el Sco* is enhanced by mutant alleles of *el*, *l(2)br22* and *noc* in a manner similar to that seen for *Sco* itself. Heterozygotes between *b el Sco* and *l(2)br29*$^{ScoR+1}$ are semilethal (188/2225) and have a phenotype similar to that of *Sco/+* (Table 7).

The *b el Sco* chromosome shows a very different pattern of lethality with deletions of the *Adh* region from that of *Sco* (Tables 7 and 8). The *Sco* chromosome is only semilethal with deletions that include the *pu-noc* interval. The *b el Sco* chromosome, on the other hand, is completely lethal with those

TABLE 7

Data showing the interaction of b el Sco *with region 35 deletions and mutations of* el, noc, br29 *and* br22[a]

Chromosome	Viability N	Viability %	Mean bristle no.	Deviation in bristle no. from control
Canton-S(+)	354/722	49.0	32.20 ± 0.30	—
Df(2L)W	8/564	1.4[b]	24.88 ± 1.22	−7.12
Df(2L)fn2	50/1027	4.9[b]	28.44 ± 0.41	−4.96
Df(2L)A266	216/637	33.9	27.25 ± 0.46	−5.45
Df(2L)A178	320/1125	28.4	26.90 ± 0.33	−5.60
Df(2L)A379	251/744	33.7	30.25 ± 0.40	−3.65
Df(2L)A63	159/508	31.3	31.00 ± 0.31	−0.80
el^{1}	211/723	29.2	32.00 ± 0.72	−0.20
el^{3}	104/412	25.2	29.55 ± 0.35	−2.25
el^{4}	168/523	32.1	29.70 ± 0.27	−2.40
el^{GM2}	76/238	31.9	27.05 ± 0.42	−3.30
$br22^{AR10}$	143/591	24.2	26.75 ± 0.38	−4.80
$br22^{FT1}$	219/804	27.2	26.95 ± 0.26	−4.60
$br22^{HG33}$	182/636	28.6	27.90 ± 0.36	−4.50
$br22^{HG46}$	105/348	30.2	27.20 ± 0.28	−5.30
$br29^{ScoR+1}$	188/2125	8.8	24.85 ± 0.36	−7.15
noc^{2}	195/593	32.9	29.90 ± 0.38	−2.65
noc^{3}	70/289	24.2	30.70 ± 0.37	−2.10
noc^{4}	111/495	22.4	27.90 ± 0.19	−3.65
noc^{18}	56/229	24.5	32.25 ± 0.29	−0.10
noc^{19}	186/576	32.3	28.76 ± 0.46	−3.59
noc^{TE146}	126/390	32.3	27.75 ± 0.34	−4.45

[a] For the deletions and *br29* control bristle counts were made of *Cy/b el Sco* sibs. For other mutations the deviation in bristle number is from that of *b el Sco* heterozygous with an isogenic chromosome (see footnotes to Tables 2 and 5).

[b] These genotypes are phenotypically extreme elbow, hence their relative inviability.

deletions that include a region far to the right of *noc*, i.e., deletions that include the locus of *reduced*. Moreover, *b el Sco/rd*^{s} heterozygotes show a strong reduced phenotype (*Sco* is *rd*$^{+}$). Because no lethal (but five viable) alleles of *rd* have been found (LINDSLEY and GRELL 1968; M. ASHBURNER and colleagues, unpublished), and because *rd/rd*$^{-}$ are viable, we suspected that the *b el Sco* chromosome may be a deletion including *rd* and one or more adjacent lethals.

Using EMS as a mutagen, we isolated a small number of recessive lethals mapping to the region of *rd* by selecting for lethals using either *Df(2L)fn1* or *Df(2L)A48*. Deletion mapping these lethals, and *inter se* crosses between the lethal-carrying chromosomes, identified five lethal complementation groups in the region of *rd*. All of these loci, and *rd* are separated by at least one deletion end point, with the exception of *rd* and *l(2)br34* (Table 8). In addition to these EMS-induced lethals, we have identified a new complementation group, mutation of which is associated with the X-ray-induced *T(2;3)H16*, *dpp*^{ho2} (=*T(2;3)*

TABLE 8

Lethality of the b el Sco *chromosome with deletions that include the 35C-35D*[a]

Deletion	*br26*	*br7*	*br27*[b]	*br33*	(br34	rd)	*br35*	*br28*	br36	*br37*[c]	b el Sco	*Sco*
AR-R1	0/515	0/2587	+	+	+	+	+	+	+	+	56/437	178/2189
$el^{4D}R15^{P}$	0/1332	0/501	+	+	+	+	+	+	+	+	112/518	131/881
64j	0/115	0/3139	27/487	+	+	+	+	+	+	+	166/1050	17/582
A267	0/393	0/217	0/391	+	+	+	+	+	+	+	242/858	153/600
Sco^{R+4}	0/676	0/1507	0/711	52/941[d]	+	+	+	+	+	+	65/484	86/897
A72	0/367	0/506	68/1706	0/217	+	+	+	+	+	+	148/532	250/723
A263	0/360	0/299	0/367	0/732	0/305	*rd*	+	+	+	+	0/269	80/1153
osp^{18}	0/108	0/262	0/114	0/336	0/194	*rd*	+	+	+	+	0/209	66/416
$C158.1^{L}ScoR+11^{R}$	0/336	0/625	0/348	0/325	0/317	*rd*	0/169	+	+	+	0/337	14/624
do-1	0/250	0/236	15/272	0/374	0/306	*rd*	0/224	0/356	+	+	0/270	17/425
A48	0/164	0/233	14/870	0/726	0/220	*rd*	0/111	0/386	0/222	+	0/227	207/986
75c	0/635	0/2883	10/788	0/633	0/155	rd	0/365	0/475	0/425	+	0/214	29/692
A446	0/194	0/189	0/558	0/210	0/216	*rd*	0/255	0/777	0/174	0/138	0/358	138/1445
osp^{29}	0/146	0/183	0/160	0/276	0/238	*rd*	0/243	0/405	0/196	0/377	0/181	68/272
b el *Sco*	129/418	107/359	526/1508	319/1176	0/731	*rd*	0/450	91/336	132/453	59/212	—	21/1064
Sco	356/1067	248/855	157/604	164/583	207/905	+	126/416	217/707	155/491	100/291	–	–

[a] The order of *l(2)br34* and *rd* is arbitrary.
[b] *l(2)br27* alleles are often leaky; the escapers have a "stubbly chaetae" phenotype. This locus may be *ck* of BRIDGES.
[c] *l(2)br37* is associated with the breakpoint of *T(2;3)H16*, at all other loci EMS-induced lethal alleles were used.
[d] No other deletion is semilethal with the $l(2)br33^{HG38}$ allele.

35D5-7;85F6-8) recovered by W. M. GELBART (unpublished). Table 8 also shows the results of crossing these lethals to the *b el Sco* stock. Not only does this chromosome uncover reduced but also it is lethal with two nonallelic lethals very close to reduced, i.e., $l(2)br34^{HG39}$ and $l(2)br35^{HG35}$. The results from crossing *b el Sco* to deletions are fully consistent: *b el Sco* is only lethal with those deletions that uncover one or both of these two lethal loci. *Sco* is viable with lethal alleles of all loci in the neighborhood of reduced (Table 8).

These data clearly show that the *b el Sco* chromosome is, in addition to being duplicated for *Adh*, deficient for *rd* and two adjacent lethal complementation groups. From the analysis of the *Sco* revertants (M. ASHBURNER *et al.*, unpublished results) we have strong reasons to believe that the duplication on *b el Sco* includes not only *Adh* but also its adjacent loci, *noc* and *osp*. Since *b el Sco* originated as a recombinant between *Sco* and Sco^+ chromosomes its structure can best be understood if the original *Sco* chromosome included a reciprocal transposition of *noc*, *osp*, *Adh*, and *l(2)br34,rd* and *l(2)br35* (Figure 5).

DISCUSSION

The detailed genetic analysis of *Sco* shows it to be a rather unusual mutation; although limited, the recombination data suggest that *Sco* maps to the right of *Adh*, yet the viability and phenotype of *Sco* are unaffected by deletions that include only genes to the right of *Adh*, but are strongly affected by deletion of genes to the left of *Adh*. Moreover, the deletion mapping of *Sco* fails to define any single genetic region for which *Sco* is dosage sensitive, rather this mutation's expressivity is sensitive to the loss of chromosomal material stretching over a region that includes at least five well defined loci. The degree to which deletions enhance the Scutoid phenotype depends upon just how much of this region is deleted. There would appear to be three "incremental" points: one between *osp* and *noc* which, when crossed by a deletion, enhances the phenotype of *Sco*/Df genotypes by about ten bristles/fly, another between *noc* and *l(2)br29* (which when crossed results in three to four *extra* bristles/fly being lost) and the third between *el* and *pu* that causes a *further* loss of five or so bristles/fly. The effects of the deletions on the viability of *Sco*/Df genotypes increases in parallel with their effects on the phenotype, although this is rather more subject to variation.

The importance of the *pu-osp* interval on *Sco* expression is also shown by the fact that duplications for this region partially suppress the *Sco* phenotype (if they include noc^+) and, more surprisingly, by the interaction of *Sco* with mutations of genes in this region. Neither *pu* nor *osp* themselves appear to be involved. Heterozygotes between *Sco* and any of five independent *pu* "point" mutations are indistinguishable from *Sco*/+ in phenotype. The same is true for heterozygotes between *Sco* and any of 27 different "point" *osp* alleles. Similarly no nondeleted *Adh* mutations affect *Sco* expression. On the other hand 3 of 4 *el* alleles, all 4 known *l(2)br22* alleles and 7 of 11 "point" *noc* alleles (above and M. ASHBURNER and colleagues, unpublished) enhance the Scutoid phenotype, when heterozygous with this mutation. Although we view these as mutations in different genes, the fact that mutant alleles of these three loci, and of *l(2)*

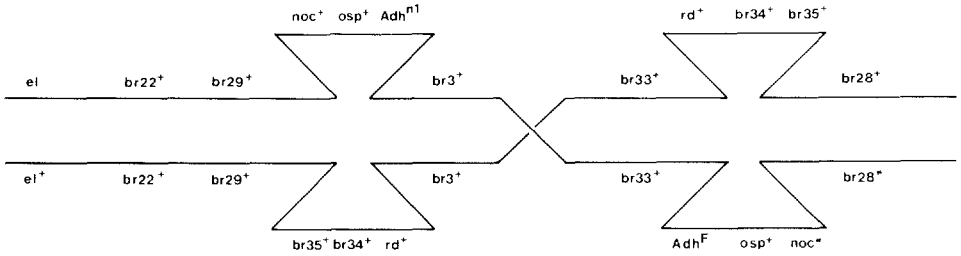

FIGURE 5.—The proposed origin of the *b el Sco* (i.e., *Dp(2;2), el* (*noc*$^+$ *osp*$^+$ *Adh*^{n1})(*Adh*^{F} *osp*$^+$ *noc**), *Df(2L)l(2)br34*$^-$ *rd*$^-$ *l(2)br35*$^-$, *Sco*) crossover chromosome of MARONI (1980). Exchange between *Sco* and the wild-type sequence *b el Adh*^{n1} chromosome occurred in the interval between *l(2)br3* and *l(2)br33*. The complementary crossover has not been recovered.

br29, may interact is obviously important for the interpretation of the role of this genetic region in the control of the *Sco* phenotype. We do not, as yet, have sufficient data at hand to understand the basis of the interaction between mutant alleles of *el*, *l(2)br22*, *l(2)br29* and *noc*. We can only presume that it reflects that these genes are under some sort of common control or that their gene products participate in a common process. Be that as it may, the important fact, from the point of view of the present discussion, is that the four *l(2)br22* alleles, the single *l(2)br29* allele and those three *el* alleles that enhance *Sco* (but not *el*^{1} that does not) all show a partial failure to complement *noc* alleles. It will simplify the present discussion if we view their effects on the expression of *Sco* as being a consequence of this fact.

The structure of the Sco *chromosome: Sco* is clearly a chromosome aberration. This is shown by the cytology of the *Sco*/+ polytene chromosomes and by the effects of *Sco* on exchange. *Sco* acts as a very local suppressor of recombination in the interval between *el* and *rd*. The model of the *Sco* chromosome that was proposed above was that *Sco* is a small reciprocal transposition: two small regions, *noc osp Adh* and *l(2)br34 rd l(2)br35*, having exchanged their chromosomal locations. The most critical evidence for this model comes from the study of MARONI's crossover between *Sco* and a wild-type sequence homologue and from a study of the nature of the induced revertants of *Sco* (M. ASHBURNER *et al.*, unpublished results).

The *b el Sco* chromosome, derived by exchange between *Sco* and a wild type sequence homologue (MARONI 1980), is deleted for at least three genes, *rd* and two adjacent lethals (we cannot rule out unidentified loci in this region). Moreover, it is duplicated for *Adh* and we shall argue below that there are good reasons for supposing that it is also duplicated for *noc*. The easiest way that a chromosome of this structure could originate by exchange between *Sco* and + is if the *noc osp Adh* and *l(2)br34 rd l(2)br35* regions had been transposed in *Sco* (Figure 5).

The nature of the induced revertants of *Sco*, which we shall discuss in detail in a subsequent paper (M. ASHBURNER *et al.*, unpublished results), is entirely consistent with this model; of the 23 revertants we have analyzed, 10 are deleted for both *noc* and *l(2)br28* (3 are also deleted for *l(2)br36* and 4 also for *osp*, *Adh* and *l(2)br36*). If these revertants had been induced on a chromosome of

standard sequence, they would represent noncontiguous deletions, an extraordinary occurrence. However, if they were induced on a chromosome whose gene order is as we propose for *Sco*, then they are all contiguous deletions and, therefore, not too remarkable.

The *b el Soc* chromosome is phenotypically Scutoid, albeit a rather weaker Scutoid than its parental chromosome (*b el Sco*/+ have 31 bristles/fly *vs.* 27 bristles/fly for *Sco*/+). This suggests that the Scutoid phenotype results from a mutational event mapping to the right hand transposition, and that the insertion of *l*(2)*br34*$^+$, *rd*$^+$, and *l*(2)*br35*$^+$ between *l*(2)*br29* and *l*(2)*br3* is irrelevant to the Scutoid bristle phenotype. This, of course, explains why, in conventional recombination experiments, *Sco* appears to map to the right of *Adh*.

If this interpretation is correct, then the *Sco* phenotype results from a mutational lesion at either the *l*(2)*br33*/*Adh* breakpoint or at the *noc*/*l*(2)*br28* breakpoint. The fact that the expression of *Sco* is insensitive to mutation of either *Adh* or *l*(2)*br33*, but is very sensitive to mutation (or loss) of *noc* strongly suggests that the latter is the case.

The nature of the Sco *mutation*: It is a remarkable fact that of 23 induced revertants of *Sco* 19 are mutant for *noc* and that 12 have either deleted the *noc*/*l*(2)*br28* junction or are broken between these loci (M. ASHBURNER *et al.*, unpublished results). Moreover, most *noc* alleles, or mutations of other loci that show a partial failure of complementation with *noc* (*e.g.*, *el*, *l*(2)*br22*) and all *noc*$^-$ deletions, enhance the phenotype of *Sco*. Finally, we note that the bristle phenotype of *b el Sco*, which, *ex hypothesi* carries as a duplication an unaltered, wild-type allele of *noc*, is less extreme than that of *Sco* that carries only a transposed *noc*$^{"+"}$ allele.

These data suggest that, despite the fact that *Sco* is apparently *noc*$^+$, its *noc* allele is not wild type but is, in some way, mutant. For convenience we shall call the transposed *noc* allele of the *Sco* chromosome *noc**. One obvious, although not necessarily correct, way in which *noc** may differ from *noc*$^+$ is that it has fused with *l*(2)*br28*$^+$ as a result of the transposition and that now, instead of these two genes coding for quite separate gene products, they code for a single, novel, product (NOC*), perhaps as a result of transcriptional read through.

Since *Sco* is not mutant for *l*(2)*br28*, nor for *noc*, this novel gene product must, at least in part, be able to serve the functions of both the wild-type *noc* and *l*(2)*br28* gene products. (Note that this model would be unaffected, except in its precise detail, by the future discovery of a lethal gene mapping between *l*(2)*br35* and *l*(2)*br28*.)

The simplest model is that NOC* competes with NOC$^+$ and that the Scutoid phenotype is a consequence of this competition. If this were so, then it would follow that (1) duplication for *noc*$^+$ would suppress the Scutoid phenotype and (2) that mutation of *noc** or of *l*(2)*br28** (on *Sco*) would relieve the competition and lead to a reversion of the Scutoid phenotype. We have already indicated (and will document in M. ASHBURNER *et al.*, unpublished results) that the latter is true. That duplications for *noc*$^+$ partially suppress *Sco* is most clearly seen from the fact that *b el Sco*/+ have some four bristles/fly more than *Sco*/+. Two other duplications for *noc*$^+$ suppress *Sco*, but two duplications which

either do not include *noc* (*i.e.*, $Dp(2;2)C163.41^{L}C158.1^{R}$) or are mutant for *noc* (*i.e.*, $Dp(2;1)Sco^{R+23}$), do not.

Table 9 summarizes the various *Sco* and *b el Sco* genotypes we have studied with respect to both their phenotypes and the number of their noc^{+} and noc^{*} alleles. It is clear that as the ratio between the number of noc^{+} and noc^{*} alleles increases so the mutant phenotype of *Sco* decreases. This relationship is remarkably regular: Figure 6 is a graph of bristle number against the $\log_{10}$ of the noc^{+}:noc^{*} ratio. When we consider the "black box" that lies between these genes and the final bristle phenotype, the fit of the points to the line suggests that our hypothesis cannot be *too* far from the mark.

Sco is, therefore, an antimorphic mutation in the literal sense of MULLER (1932): "I would term such antagonistic mutant genes, having an effect actually contrary to that of the gene from which they were derived by mutation, as antimorphic".

The model that we have suggested for *Sco* does not, at least to our satisfaction, adequately explain why the phenotype of *Sco* should increase incrementally as deletions remove more and more of the region between *osp* and *pu*. We have alluded to the fact that the mutations of the four genes between these loci interact with each other, both with respect to viability and with respect to phenotype, yet they can all be demarcated quite unambiguously by deletion mapping. One possibility is that all four genes originated by duplication of, for example, *noc* and that, although they have subsequently diverged in function, all have retained a residual NOC^{+} activity. We only wish to point out here that there is evidence for another antimorphic mutation in this region: Sco^{R+1}. The lethality of this X-ray-induced revertant of *Sco* defines *l(2)br29*. Sco/Soc^{R+1} are lethal (0/1930) yet *Sco* is only semilethal with *l(2)br29*$^{-}$ deletions (*e.g.*, *Sco/Df(2L)fn2*: 166/2,297) whereas Sco^{R+1} is completely lethal with *l(2)br29*$^{-}$ deletions (0/16,475). Furthermore, Sco^{R+1} is a dominant lethal when heterozygous with some *noc* alleles (*e.g.*, noc^{TE146}) that are otherwise homozygous viable. We can only presume that Sco^{R+1} is not an amorph, and that its lethality results from the novel expression of a gene product.

The Sco *phenotype:* We have suggested that the *Sco* phenotype results from competition between NOC^{*} and NOC^{+} gene products. If this were true in the literal sense, we might expect *noc* alleles to have a recessive Scutoid phenotype. In fact, they do: *noc* homozygotes and *noc/noc*$^{-}$ heterozygotes very frequently lack their anterior notopleural and anterior postalar bristles. These two bristle sites are those most sensitive to loss in *Sco* and *Sco* revertant genotypes (M. ASHBURNER *et al.*, unpublished results).

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TABLE 9

The correlation between mean bristle number and the ratio of the number of noc$^+$ *and* noc* *alleles*[a]

Genotype[b]	No. of *noc*$^+$ alleles (a)	No. of *noc** alleles (b)	Ratio (a)/(b)	Approximate bristle phenotype
Sco/—	0	1	0	8
Sco/Sco	0	2	0	9-10
Sco/noc	<1	1	<1	14-27[c]
Sco/b el Sco	1	2	0.5	18-20
Sco/+	1	1	1	25-28
b el Sco/—	1	1	1	25-28
b el Sco/noc	>1	1	>1	27-32[c]
Sco/Dp noc$^+$	2	1	2	32-33
b el Sco/+	2	1	2	30-32
b el Sco/Dp noc$^+$	3	1	3	34-35

[a] See text.
[b] A "—" means a long region 34-35 deletion that includes the entire pu-osp interval (at least).
[c] Depending upon allele, see Tables 4 and 6.

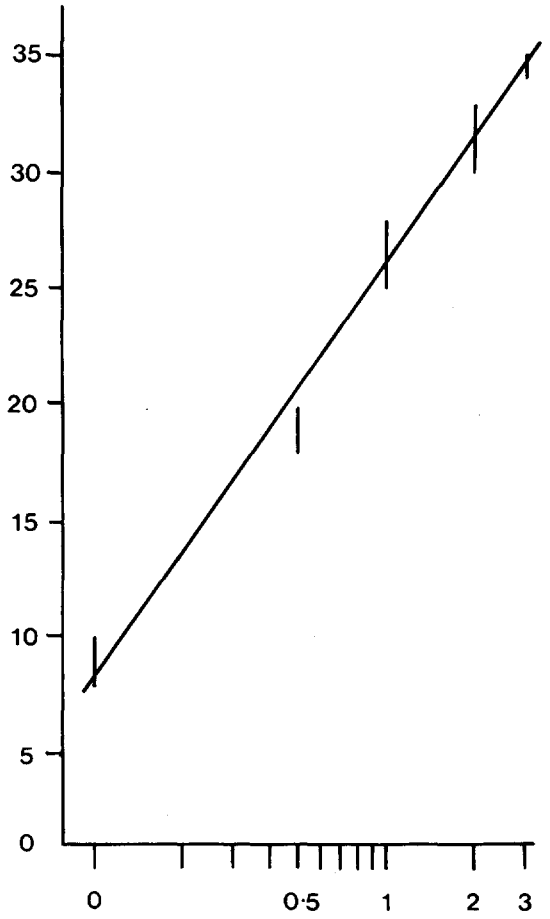

FIGURE 6.—A graph of the bristle numbers of flies heterozygous for *Sco* and chromosomes with various numbers of *noc*$^+$ alleles *vs.* the $\log_{10}$ of the ratio between the number of *noc*$^+$ and *noc** alleles (see Table 9 and text).

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