INTERCHROMOSOMAL EFFECTS ON CROSSING OVER IN DROSOPHILA MELANOGASTER. II. A REEXAMINATION OF X CHROMOSOME INVERSION EFFECTS[1]

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INTEREST in interchromosomal effects on crossing over in *Drosophila melanogaster* has been renewed recently (COOPER, ZIMMERING and KRIVSHENKO 1955; OKSALA 1958; HART and SANDLER 1961; RAMEL 1962; SUZUKI 1962a; ROBERTS 1962). As a result of the new approaches taken in these studies, two general types of mechanisms, one physiological in nature (STEINBERG and FRASER 1944; RAMEL 1962; ROBERTS 1962), the other mechanical (SCHULTZ and REDFIELD 1951; OKSALA 1958; SUZUKI 1962a, b) have been suggested to explain these effects. Although, as SCHULTZ and REDFIELD (1951) indicate, a clear-cut distinction between these hypotheses is difficult, for the present paper the physiological mechanism has been interpreted as an alteration of gene action (e.g., position-effect), and the mechanical effect as altered chromosome behavior (e.g., loop formation, asynapsis). While the mechanical hypotheses have been more readily tested, the number of conditions known to cause interchromosomal effects is extensive, and no mechanical hypothesis yet proposed adequately accounts for all of the observations. On the other hand, while physiological explanations are sufficiently general to encompass most known situations, no critical experiments have been carried out testing their validity.

By interpreting the interchromosomal effects on crossing over on a mechanical basis, it is possible to separate chromosomes having such effects into two groups: those that are postulated to synapse as loops or large rings (SUZUKI 1962a) and those postulated to have a definite frequency of asynapsis (SUZUKI 1962b). It is possible to minimize such influences of loop configurations and abnormal crossover values by testing autosomal exchange in X chromosome inversion homozygotes. Such tests might indicate whether the effects of inversion heterozygotes are due to loop formation, to heterozygosity *per se*, or to the intrinsic properties of the rearrangement. It was also hoped that inversion-homozygote tests would

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provide data on the contribution of specific chromosome regions to the interchromosomal effects.

METHODS AND MATERIALS

Crossing over in all experiments was measured in chromosome 3 using the following markers (followed by map distances as listed in BRIDGES and BREHME 1944): *ru* = roughoid 0.0, *h* = hairy 26.5, *st* = scarlet 44.0, p^p = pink-peach 48.0, *ss* = spineless 58.5, e^s = ebony-sooty 70.7. The region from *ru* to *h* is designated as 1, from *h* to *st* as 2, *st* to p^p as 3, p^p to *ss* as 4, and *ss* to e^s as 5. Note that Region 3 spans the centromere and that the distal half of 3R remains unmarked.

Eight different X-chromosome inversions were tested (see Figure 1 for the positions of the breakpoints). Three of the inversions, *In(1)*yellow^4 (y^4), *In(1)*scute^9 (sc^9), and *In(1)*delta-49 (*dl-49*), are completely euchromatic, whereas the rest have right breaks at different points in proximal heterochromatin. Two, *In(1)*roughest^3 (rst^3) and *In(1)*white-mottled^4 (w^{m4}), have left breaks in salivary region 3C and their right breaks between heterochromatic blocks hC and hD (COOPER 1959). The remaining three, *In(1)*scute^8 (sc^8), *In(1)*yellow^{3P} (y^{3P}), and *In(1)*scute^4 (sc^4) have left breaks in region 1A and right breaks either very close to the centromere (sc^8 and y^{3p}) or very close to euchromatin (sc^4). More detailed descriptions of the inversions can be found in BRIDGES and BREHME (1944).

All of the inversions were tested in the heterozygous and homozygous condition. In addition, crossing over was measured in sc^4/sc^8 females and in females heterozygous for the crossover products between sc^8 and sc^4 (sc^8 sc^4 and sc^4 sc^8). As controls, crossing over in chromosome 3 of females bearing normal X chromosomes was measured concurrently with each inversion experiment.

In addition to the inversion tests reported by SUZUKI (1961b), sc^8 $sc^4/+$, sc^4 $sc^8/+$, sc^8/sc^4, $w^{m4}/+$, and w^{m4}/w^{m4} females were also tested at the University of Chicago. Eight to ten pairs of flies were mated per half-pint bottle; the parents were removed after five days of laying and offspring counted until the 19th day after introduction of the parents. Laboratory temperature was maintained at 25° ± 1.0°C but humidity was not controlled. This procedure was used for the crosses in Lines 1–12, Table 1. After a discussion with DR. JACK SCHULTZ, it was decided that the autosomes of the inversion-bearing females should be as coisogenic as possible with those of the controls to rule out autosomal inversions or genes which might be present in the inversion stocks and which might influence

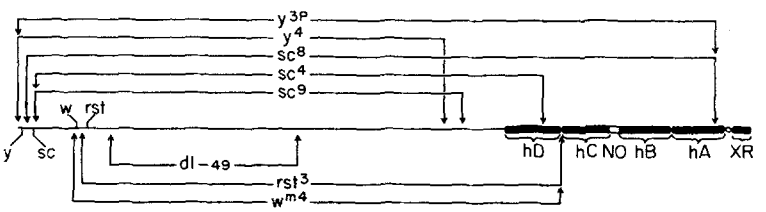


FIGURE 1.—Positions of the breakpoints and sizes of each X chromosome inversion.

TABLE 1

Crossover values in chromosome 3 with different X chromosome inversions

	X chromosome tested	Number counted	Crossover percentages, chromosome 3 region					Total map length	Strand ratio†
			1	2	3	4	5		
1.	$sc^4\ sc^8/+$	1,141	26.3	21.2	4.0	10.0	16.0	77.5	0.319
2.	$sc^8\ sc^4/+$	1,778	23.3	24.3	7.3	15.3	16.9	87.1	0.406
3.	sc^8/sc^4	1,611	24.5	23.3	5.6	15.3	15.9	84.6	0.371
4.	sc^8/sc^8	4,612	25.4	22.1	5.0	11.9	16.7	81.1	0.391
5.	$sc^8/+$	7,489	26.6	23.9	5.7	13.1	16.7	86.0	0.397
6.	sc^4/sc^4	2,348	24.2	21.3	6.7	10.6	16.1	78.6	0.314
7.	$sc^4/+$	2,428	23.5	22.0	5.3	13.3	15.7	79.8	0.309
8.*	rst^3/rst^3	1,298	23.0	22.5	4.7	10.9	14.6	75.7	0.304
9.*	$rst^3/+$	1,237	25.9	23.8	7.4	17.7	13.8	88.6	0.422
10.	w^{m4}/w^{m4}	1,972	21.0	23.1	5.8	12.8	14.2	76.9	0.337
11.	$w^{m4}/+$	1,408	24.3	24.9	5.7	14.1	14.6	83.6	0.404
12.	$+/+$	3,933	22.8	20.4	3.8	10.7	12.8	70.5	0.290
13.*	y^{3P}/y^{3P}	1,359	. . .	19.4	4.6	7.9	13.2	45.1	0.146
14.*	$y^{3P}/+$	1,299	27.8	19.5	4.6	9.5	11.1	72.5	0.273
15.	$+/+$	1,220	22.8	14.7	1.2	6.1	9.3	54.1	0.161
16.*	y^4/y^4	1,796	23.5	18.0	4.1	10.7	12.9	69.2	0.232
17.*	$y^4/+$	1,801	25.5	20.5	4.7	11.5	13.9	76.1	0.311
18.	$+/+$	1,114	24.4	14.6	2.4	6.0	12.8	60.2	0.193
19.*	*dl-49/dl-49*	1,995	23.8	16.9	2.9	7.2	10.9	61.7	0.199
20.*	*dl-49/+*	2,568	26.8	21.5	4.1	10.4	13.4	76.2	0.357
21.	$+/+$	1,547	24.8	17.9	2.5	8.0	12.2	65.4	0.249
22.*	sc^9/sc^9	697	23.7	17.4	2.2	9.2	11.9	64.4	0.201
23.*	$sc^9/+$	2,227	28.2	21.3	3.5	9.8	13.6	76.4	0.297
24.	$+/+$	1,896	24.5	16.7	1.9	7.8	10.4	61.3	0.197

* Indicates females coisogenic with their control females.
† Multiple crossovers:single crossovers.

crossing over. A small number of the appropriate crosses for each inversion were carried out at Oak Ridge so that heterozygous and homozygous females were sisters as well as coisogenic with their controls. The mating procedure followed to derive the proper females is shown in Figure 2. The following stocks are symbolized in Figure 2: (1) a stock containing multiple inversions in each of the major chromosomes (*FM6; SM1; Ubx*), (2) eight X-chromosome inversion stocks (Inv), (3) Oregon-R_{369}, a wild-type stock maintained by brother-sister pair matings for 369 generations, and (4) a stock bearing the third chromosome markers (3-ple) which had been rendered isogenic previously by the use of balancers. Where differences from the original observations (SUZUKI 1961a) were noted, more matings were set up, and these data are reported here. In the work reported here, when the autosomes of three inversion stocks (rst^3, y^{3P}, and sc^9), which had apparent decreases in crossing over were replaced, crossover values were found to increase. In one stock, (rst^3), cytological inspection of salivary chromosomes revealed a small inversion close to the centromere in 3R. It is probable that the initial observations reflected the presence of some re-

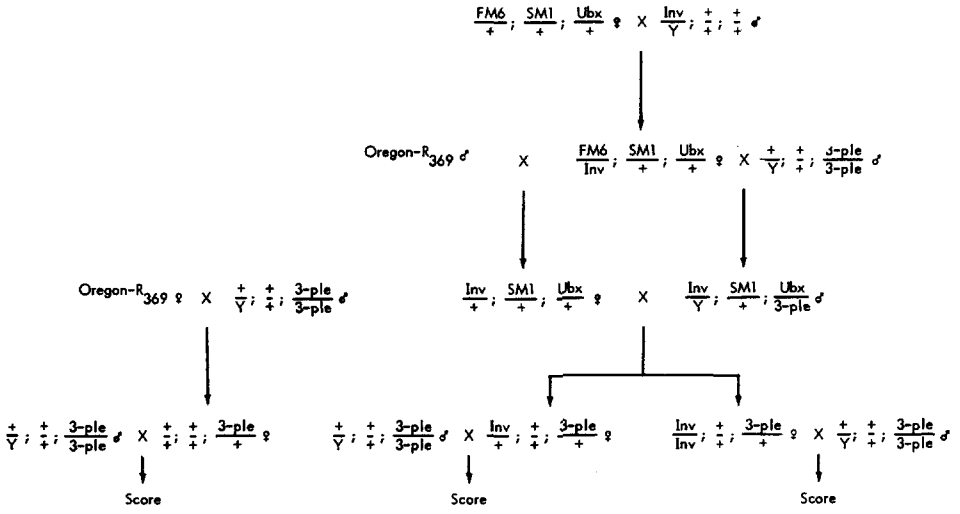


FIGURE 2.—The mating procedure followed to obtain females with a similar genetic background. See text for explanation of the symbols.

arrangement that suppressed crossing over in these stocks. The latter group of experiments was carried out by pair matings in quarter-pint bottles at 25° ± 0.5°C and a relative humidity over 70 percent. The medium used at each institution was also different, (BAKER's medium at Chicago, Cal Tech's at Oak Ridge).

To test for the effect of heterochromatin located distally on the X chromosome, the Fragment-1 chromosome (FR-1) obtained by NOVITSKI (1952) was used. FR-1 is a normal X chromosome with the short arm of the Y attached to the tip (symbolized as $Y^{S}X\cdot$). Two Y arm attachments to the centromeres of normal X's ($X\cdot Y^{L}$ and $X\cdot Y^{S}$) were tested to determine whether X–Y arm attachment or presence of a Y arm *per se* influences autosomal exchange.

Owing to the presence of markers on the X chromosome of some of the inversions and on the X–Y arm attachments which interfered with the autosomal eye markers, only the female offspring of heterozygous and homozygous rst^{3}, w^{m4}, y^{3P}, sc^{9}, $X\cdot Y^{L}$, $X\cdot Y^{S}$, and $Y^{S}X\cdot$ females were scored. Crossing over was not scored in region 1 of Y^{3P}/y^{3P} females owing to the presence of a marker which interfered with *ru*.

RESULTS

Table 1 lists the crossover percentages for each region of chromosome 3 and total progeny counted in each cross. A chi-square test for homogeneity of control data for the tests carried out in Chicago (lines 1–12, Table 1) indicated that they were homogeneous; the four separate controls were then combined (line 12, Table 1). The control data of separate tests collected at Oak Ridge were significantly different from each other and from the Chicago controls. Therefore each set of experiments must be compared with its respective control. The dividing spaces in all of the tables indicate the limits within which valid com-

parisons may be made. The radical difference between control crossover values obtained in Chicago (line 12, Table 1) and in Oak Ridge (lines 15, 18, 21, and 24, Table 1) indicates the influence of environment on crossover values since the flies used at both laboratories were derived from the same stocks. The major differences between the experiments conducted in the two laboratories were in food, humidity, number of parents per bottle, and bottle size.

The ratios of crossover values obtained by dividing experimental (p_1) by control (p_0) values for each region of chromosome 3, are plotted together with their 95 percent confidence limits in Figures 3 to 9. A ratio of 1 indicates that the crossover values compared are not different. The method used in calculating confidence limits was suggested by Dr. Paul Meier and has been outlined previously (Suzuki 1962a).

Figures 3–5 indicate that, with the exception of *sc*^{4} *sc*^{8}/+, all of the other inversion heterozygotes increased crossing over in chromosome 3 in the typical manner, the increase being greatest in the centromere region (Steinberg and Fraser 1944; Schultz and Redfield 1951). The data for *sc*^{4}, *sc*^{8}, *y*^{4}, and *dl-49* heterozygotes are qualitatively similar to those of Steinberg and Fraser (1944).

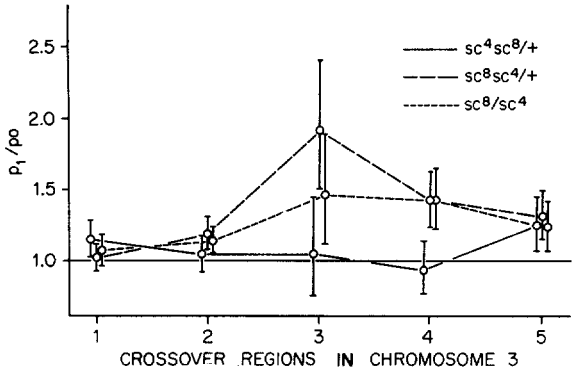


Figure 3.—Ratio of crossover values in each region of chromosome 3 of *sc*^{4} *sc*^{8}/+, *sc*^{8} *sc*^{4}/+, and *sc*^{8}/*sc*^{4} females to the control values.

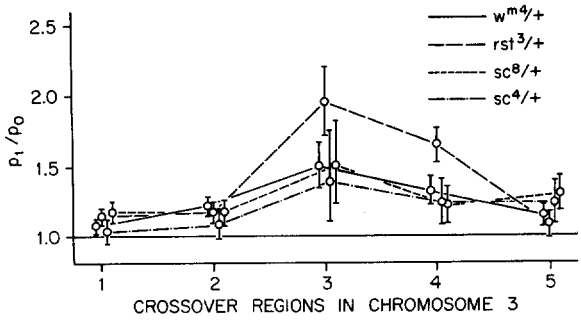


Figure 4.—Ratio of crossover values in each region of chromosome 3 of *w*^{m4}, *rst*^{3}, *sc*^{4}, and *sc*^{8} heterozygotes to the control values.

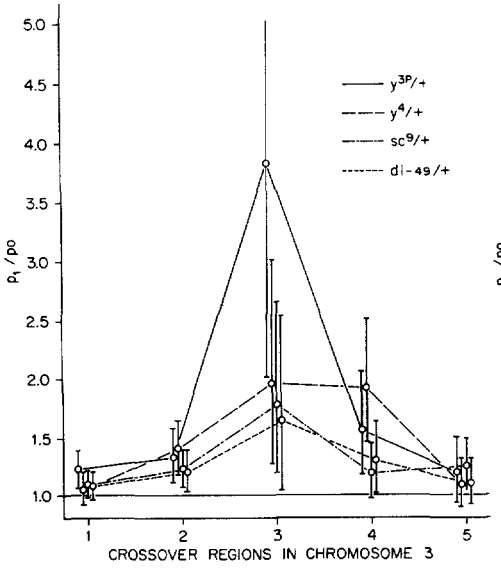


FIGURE 5.—Ratio of crossover values in each region of chromosome 3 of y^{3P}, y^4, sc^9, and *dl-49* heterozygotes to their respective control values.

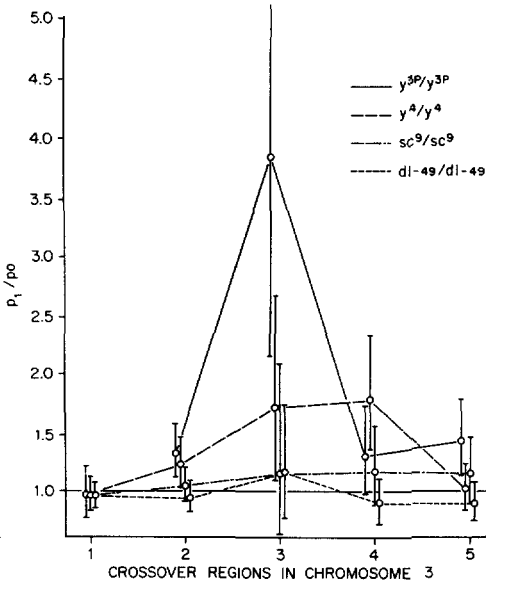


FIGURE 6.—Ratio of crossover values in each region of chromosome 3 of y^{3P}, y^4, sc^9, and *dl-49* homozygotes to their respective control values.

The extreme increase (three- to fourfold) in crossing over recorded for region 3 of $y^{3P}/+$ and y^{3P}/y^{3P} females (Figures 5 and 6) is in large part due to the fact that the control values for this region were exceptionally low (line 15, Table 1). While an increase in crossing over is definitely indicated, the amount of increase due to y^{3P} is probably 2 to 2½-fold only.

In contrast with the results of SCHULTZ and REDFIELD (1951) and RAMEL (1962), who demonstrated decreases in autosomal crossing over in different X-inversion tests, no combination of inversions in these experiments was found to depress crossing over significantly below the control levels in the centromere region. REDFIELD (personal communication) has obtained increases in crossing over in the centromere region of chromosome 3 in recent preliminary tests of sc^8 homozygotes, a combination previously reported to decrease crossing over by 50 percent.

Although both sc^9 and *dl-49* heterozygotes significantly increase crossing over in chromosome 3 (Figure 5), the homozygotes have no effect (Figure 6). This is evidence against interpreting interchromosomal effects as resulting from the intrinsic properties of the rearrangement *per se*, unless it is maintained that one class contains rearrangements interacting in such a way that their individual effects are nullified, whereas other inversions have effects in both homozygotes and heterozygotes. The increase in exchange in y^4 homozygotes (Figure 6) shows that the absence of effect in sc^9 and *dl-49* homozygotes is not a property peculiar to completely euchromatic inversions. Since one difference between y^4 and sc^9 is

in the position of their left breakpoints (Figure 1), the position of the region which lies between these two breakpoints (from yellow to scute) with respect to proximal heterochromatin may be important. I have tested (unpublished data) the effects on crossing over in chromosome 3 of duplications of the X-tip region which are inserted into proximal heterochromatin of the X (from *Tp(1)sc*^{2}) or which are attached to the centromere of a normal X chromosome as a second arm (from *Inp(1)sc*^{V1}). Significant increases were detected with both aberrations, but since no attempts were made to standardize autosomes, the results can only be taken as possible evidence for a specific role of the X tip in interchromosomal effects. However, SCHULTZ and REDFIELD (1951) reported effects of a distal duplication (w^{m}) and SUZUKI (1962a) noted effects of a proximal duplication (B^{S}), and it is possible that duplications in general evoke interchromosomal effects.

The last column of Table 1 is the ratio of multiple crossovers to single crossovers for each experiment; an increase in this ratio over the control ratio is interpreted as a decrease in interference. However, as RAMEL (1962) has pointed out, an increase in crossing over without a change in the amount of interference per unit length of chromosome will nevertheless appear as an increase in the frequency of multiple exchanges. Therefore, although it can be seen that the frequency of multiple crossovers is considerably increased in the presence of all conditions in which crossing over is increased, a change in interference may not necessarily be indicated.

All of the inversions involving breaks in the proximal heterochromatin (and therefore having varying amounts of distally located heterochromatin) increase crossing over in chromosome 3 when homozygous (Figures 6 and 7). SCHULTZ (personal communication) has suggested that these distally located blocks of heterochromatin may pair nonspecifically with proximal heterochromatin in a chromocenter-like region, thus giving a loop configuration whose consequent effects would be similar to those of inversion heterozygotes. To test the possibility that distally located heterochromatin *per se* may have an effect on crossing over, FR-1 was tested in the heterozygous and homozygous condition (Table 2, Figures 8 and 9). It can be seen that attachment of Y^{S} to the tip of a normal X induces a response much greater than that of any of the inversions tested. The

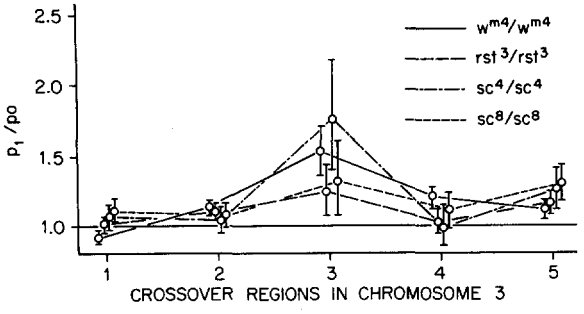


FIGURE 7.—Ratio of crossover values in each region of chromosome 3 of w^{m4}, rst^{3}, sc^{4}, and sc^{8} homozygotes to their control values.

TABLE 2

Crossover values in chromosome 3 with different X–Y arm attachments

	X chromosome tested	Number counted	Crossover percentages, chromosome 3 region					Total map length
			1	2	3	4	5	
1.*	$Y^SX\cdot/Y^SX\cdot$	1,549	19.9	23.9	10.4	12.1	15.4	81.7
2.*	$Y^SX\cdot/+$	1,174	22.3	26.5	11.1	14.9	16.9	91.7
3.	+/+	1,766	24.4	21.6	2.9	9.6	13.0	71.5
4.	$X\cdot Y^S/X\cdot Y^S$	722	19.8	19.5	4.6	9.1	11.4	64.4
5.	$X\cdot Y^L/X\cdot Y^L$	523	19.9	17.4	4.4	6.3	12.8	60.8
6.	+/+	1,121	21.4	17.6	4.1	10.2	12.5	65.8
7.	$X\cdot Y^S/+$	2,222	27.9	15.3	2.3	6.6	12.2	64.3
8.	$X\cdot Y^L/+$	1,953	23.9	15.1	1.6	5.9	12.5	59.0
9.	+/+	1,492	25.3	16.5	2.1	8.4	11.9	64.2

* Coisogenic with their control females.

lack of effect of the Y^S and Y^L attachments to an X centromere (Table 4, Figures 7 and 8) indicates that the presence of a Y arm or its attachment to the X as such is not the condition responsible for the effect of FR-1.

A tetrad analysis of each X-Y arm experiment using the method of WEINSTEIN (cited by SUZUKI 1962a) indicated that the introduction of FR-1 increases the frequency of multiple-exchange tetrads whereas the frequencies of no-exchange

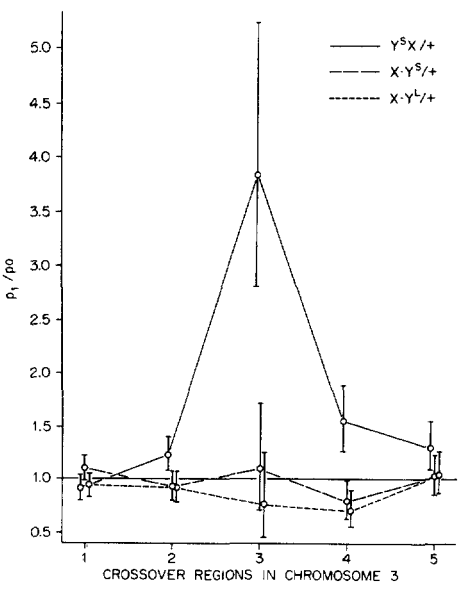


FIGURE 8.—Ratio of crossover values in each region of chromosome 3 of $Y^SX\cdot$, $X\cdot Y^S$, and $X\cdot Y^L$ heterozygotes to their respective control values.

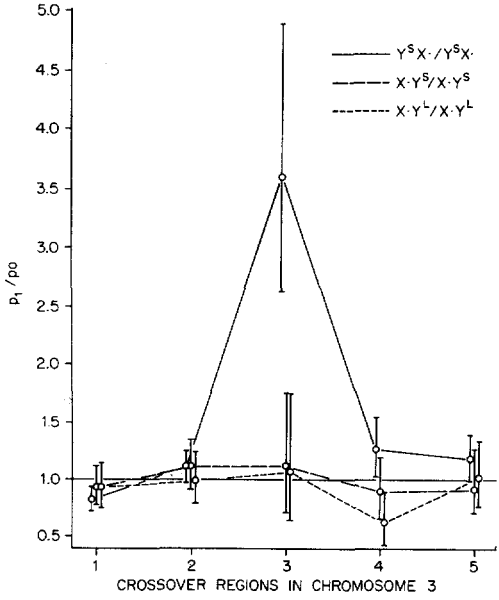


FIGURE 9.—Ratio of crossover values in each region of chromosome 3 of $Y^SX\cdot$, $X\cdot Y^S$, and $X\cdot Y^L$ homozygotes to their respective control values.

and single-exchange tetrads are decreased. The data of X·Y^{S} and X·Y^{L} tests, while not conclusive, indicate a slightly decreased frequency of multiple-exchange tetrads.

DISCUSSION

The reports of RAMEL (1962) and SUZUKI (1962a) indicate that none of the existing mechanical or physiological hypotheses for interchromosomal effects on crossing over is compatible with all of the data. It is necessary, therefore, to try to determine whether a distinction can be made between possible mechanical or physiological effects of rearrangements based on the general features of each model.

If the interchromosomal effects of inversions are due to the intrinsic properties of the rearrangements, it might be expected that females bearing two homologous, rearranged chromosomes would have more heterologous crossing over than females bearing only one inversion chromosome. None of the X-inversions tested has a greater effect in the homozygous condition than in the heterozygous, and some homozygotes show a smaller effect (*sc^{4}*, *rst^{3}*, *y^{4}*), or none at all (*sc^{9}*, *dl-49*). These observations cannot be easily reconciled with physiological hypotheses that attribute the effects of rearrangements directly to the rearrangement itself, for this would not lead to the expectation that the presence of two inversions would be suppressive.

The different pattern of effect of *sc^{4} sc^{8}* would appear anomalous since all other inversion heterozygotes have typical interchromosomal effects. It is possible that the deletion of most of the proximal heterochromatin in the *sc^{4} sc^{8}* chromosome prevents it from completing a loop with its normal homolog during synapsis. One obvious feature common to inversion heterozygotes is that their synaptic configurations have been altered. However, the increase in crossing over in inversion homozygotes such as *y^{4}/y^{4}*, which are not expected to synapse as loops, shows that the loop configuration, as such, of inversion heterozygotes may not necessarily be the condition responsible for the interchromosomal effects of these rearrangements.

If, as SCHULTZ and REDFIELD (1951) and OKSALA (1958) postulate, a pattern of polarized meiotic chromosomes exists at the time of crossing over, homozygosity for certain inversions may lead to disturbances in the polarity of paired chromosomes; for example, either distally located heterochromatin may lead to loop formation or a region responsible for the initiation of polarization may be affected. The former possibility is excluded by the effects noted in *y^{4}/y^{4}* females (Figure 6), where the inverted segment is completely euchromatic. The apparent importance of the integrity of the tip region (compare effects of homozygous *y^{4}* with *sc^{9}*, Figure 5) for normal autosomal exchange suggests a possible role of the tip in a polarization process. Displacement of the tip region (as in *y^{4}*) or the apposition of heterochromatin to the tip (as in FR-1 and the inversions with heterochromatic breaks) may interfere with the activity of the tip. BRAVER (1961) has shown that crossing over in the distal region of the X of FR-1 homozygotes is suppressed. This indicates that distally located heterochromatin

can have disruptive effects within the X, and it can be seen (Figures 8 and 9) that FR-1 has a strong effect on chromosome 3. One scheme that is roughly consistent with the suggested importance of the relative positions of the tip and heterochromatin is shown in Figure 10. Here the tip region is exaggerated to demonstrate that the chromosomes having interchromosomal effects have the tip near heterochromatin. These considerations do not exclude the possibility that changes in chromosome polarization may result in a physiological change in the nucleus which is responsible for changed crossover values.

The intrabrachial effects on crossing over in X chromosomes heterozygous for inversions appear to be physiological effects of the inversions (GRELL 1962; ROBERTS 1962) or of distal heterochromatin (BRAVER 1961). GRELL (1962) studied the effects of X chromosome inversions of different sizes and in different parts of the X on crossing over within the X in the presence and absence of a Y chromosome. It is instructive to note that she finds several factors involved in the crossover frequencies. She finds that whereas crossing over is suppressed near the breakpoints of the inversions, presumably owing to mechanical interference with pairing, it is enhanced in the region most distant from the breakpoints. Thus, the distal X inversions, *sc*^{7} and *65*, show a significant increase in crossing over proximally in the X, whereas the proximal inversion, B^{M1}, shows a possibly significant distal increase. Furthermore, the Y (in XXY females) eliminates the intrabrachial increase observed proximally with *sc*^{7} and *65*, but increases crossing over distally in the normal X and heterozygous *In(1)AB*. At the

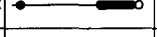
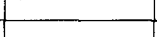
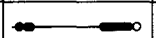
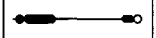
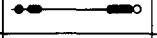
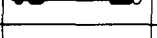
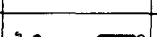
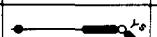
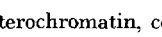
CHROMOSOME TYPE	CONFIGURATION	EFFECT OF HOMOZYGOTE ON CROSSING-OVER
NORMAL ROD-X		0
DELTA-49		0
SCUTE^{9}		0
YELLOW^{4}		+
SCUTE^{4}		+
SCUTE^{8}		+ +
ROUGHEST^{3}		+
WHITE-MOTTLED^{4}		+
YELLOW^{3P}		+ +
FRAGMENT-1		+ + +
X·Y^{S}		0

FIGURE 10.—Relative positions of heterochromatin, centromere, and X tip of X chromosome rearrangements. Thin line, euchromatin; heavy line, heterochromatin; •, X chromosome tip; +, significant increase in crossing over.

intrachromosomal level then, both mechanical and physiological factors can affect exchange frequencies although it cannot be determined whether they are interdependent or independent.

Addition of a Y chromosome to females bearing different compound-X chromosomes results in an increase in crossing over in chromosome 3 when the X is a reversed metacentric, a decrease when it is either a reversed acrocentric or a tandem metacentric, and in no effect when the X is a reversed compound ring (SUZUKI 1962a). These results were taken to indicate that the Y chromosome affects pairing and, therefore, exchange within the X. This, in turn, presumably influences autosomal crossover frequencies. The correlation between pairing properties in one chromosome pair and crossover frequencies in another pair (SUZUKI 1961a, b) and between the pattern of disjunction of the X's and crossing over in the autosomes (see SCHULTZ in MORGAN, BRIDGES and SCHULTZ 1935; ZIMMERING 1958) indicates a mechanical basis for interchromosomal effects. However, it must be stressed that chromosome conditions which evoke interchromosomal effects may be expressed through physiological means. It can only be suggested that the conditions of loop configuration, asynapsis, and displacement of the tip of the X chromosome may all result in a disruption of chromosome orientation with a consequent interchromosomal effect on crossing over in an unspecified way.

The qualitatively similar effects on crossing over in centromeric regions by different intrinsic changes as well as extrinsic factors, such as temperature (PLOUGH 1917) and radiation (MULLER 1925), indicate that the meiotic nucleus is very sensitive to change and that it responds similarly to a variety of unrelated agents. It is of primary interest to determine whether this sensitivity is primarily physiological, or whether it is to a greater or a lesser extent dependent on the mechanical orientation of the chromosomes at the time of crossing over. While further genetic analyses of chromosome aberrations (e.g., effect of translocations) are warranted, it is possible that no clear-cut differentiation between mechanical and physiological bases will result.

SUMMARY

To distinguish between a mechanical and a physiological basis for interchromosomal effects on crossing over in *Drosophila melanogaster*, tests of the effects of X chromosome inversions on chromosome 3 were carried out. The inversions tested were sc^4, sc^8, sc^9, w^{m4}, rst^3, y^4, y^{3P}, and *dl-49*. In addition, crossing over was measured in females carrying FR-1 ($Y^sX\cdot$), $X\cdot Y^L$, and $X\cdot Y^s$ and in sc^4/sc^8, $sc^4\ sc^8/+$ and $sc^8\ sc^4/+$ females.

The following results were obtained: (1) Crossing over in all inversion heterozygotes except $sc^4\ sc^8/+$ was increased in the typical manner, the increase being greatest near the centromere, the least, distally. (2) Crossing over was increased in females homozygous for sc^4, sc^8, w^{m4}, rst^3, y^4, and y^{3P}, but was not affected in sc^9 or *dl-49* homozygotes. (3) Crossing over was greatly increased in FR-1-bearing females, but was not affected in $X\cdot Y^L$ or $X\cdot Y^s$ homozygotes and heterozygotes. (4) It is suggested that a disruption in chromosome orientation

initiates the interchromosomal effects although the increase in crossing over may be mediated through a physiological mechanism.

The results suggest that the relative position of the tip of the X chromosome with respect to the centromere and to heterochromatin may influence autosomal exchange. It is suggested that the tip of the X may play a role in the orientation of chromosomes and that the apposition of heterochromatin to the tip or its change in position disrupts this role.

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