THE RELATIONS OF INVERSIONS IN THE X CHROMOSOME OF DROSOPHILA MELANOGASTER TO CROSSING OVER AND DISJUNCTION*

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INTRODUCTION

STUDIES of chromosome aberrations such as polyploidy and translocations have contributed much to the understanding of the meiotic behavior of chromosomes. One of the commonest types of structural difference in chromosomes within a species is that in which a segment of a chromosome has been inverted. These cases have not contributed as much as might have been expected toward an understanding of chromosome mechanics. It has been apparent for some time that they needed systematic study, and that the series of X chromosome inversions accumulated in X-ray experiments furnished the necessary material. The present paper represents the results of a study made with these points in mind.

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Recent papers on inversions illustrate the difficulties encountered in such studies. GERSHENSON (1935) and STONE and THOMAS (1935) found that the chromatids resulting from single crossing over are not recovered, and by making egg counts showed that there is no detectable mortality that can be invoked to account for them. They concluded that single exchange is so rare as to be negligible. SIDOROV, SOKOLOV, and TROFIMOV (1935) showed by the use of attached-X females that single exchanges do occur with a high frequency; but they appear to have been unaware that egg counts fail to show any corresponding mortality. The dates show that at least the second and third papers mentioned and our own preliminary note (BEADLE and STURTEVANT, 1935) were all sent to press inde-

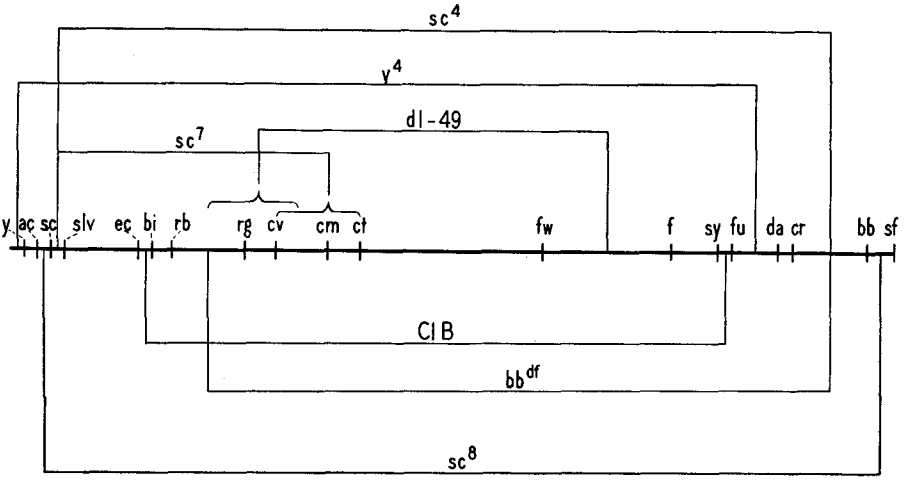

FIGURE 1.—Diagram showing the nature of the inversions used in the present study.

pendently. Our account, of which the present paper is the full presentation, included both the proof that single exchanges occur (using the same method as the Russian investigators), and the proof that there is no corresponding egg mortality. We were faced with a seeming paradox, the only escape from which was the assumption that the single crossover chromatids are produced but are not included in the egg nucleus. We developed a scheme that gives this result (pp. 591–596, and figs. 6 and 7), and that is in good quantitative agreement with the data in other respects.

INVERSIONS STUDIED

There follows a descriptive catalogue of the inversions we have studied. Figure 1 shows the lengths of these inversions. The data on the extent of each inversion are largely from the experiments with females heterozygous for two inversions, which are described below. The egg mortalities associated with the inversions are given in a later section.

Inversion scute-4

AGOL (1929) subjected yellow flies to X-rays, and obtained an extreme scute allelomorph, sc^4. This was found to be associated with a long inversion in the X chromosome, shown below to extend from a point between *sc* and *slv* to a point between *cr* and *bb*. Females heterozygous for this inversion give about 9 percent crossing over among their regular offspring, and also produce about 6 percent of patroclinous sons, as shown in table 1. All the recovered crossovers are doubles.

Our best experiments are those in which *y*, *cv*, *v*, and *f* are followed, since here it is probable that few or no undetected doubles occur. The table shows a few crossovers entered as singles; these are evidently all really doubles in which the second crossover has occurred in the unmarked region between *f* and the inversion point. In another experiment, in which *cr* and *bb* were present, but the rest of the chromosome was not so well controlled, two such apparent singles were tested and found in fact to represent *cr bb* crossovers as well.

Table 1 shows a total of 108 crossover males to 63 patroclinous from XX females; the ratio between these classes, 1.71:1, will be discussed below.

TABLE 1

Tests of females heterozygous for inversion sc-4. In this and following tables the crossover classes are labelled according to the standard sequence of loci, unless otherwise indicated. In cases where two contrary classes are entered under one heading, the right-hand or lower one of the two carries the mutant gene at the leftmost locus concerned.

MOTHERS	♀		REGULAR ♂♂															EXC. ♂♂
	REG.	EXC.	0		1		2		3		1,2		1,3		2,3		TOTAL	
sc^8 *cv v f*/*y* sc^4	344	0	115	150	1	2	2	1	1	0	1	0	3	5	4	6	291	18
y^2 *cv v f*/*y* sc^4	331	0	154	86	3	0	0	0	1	2	1	0	4	7	5	3	266	14
v/*y* sc^4 *cv f*	801	1	294	291	2	3	7	6	0	2	3	2	10	11	6	4	641	31
y^2 *cv v f*/*y* sc^4/Y	397	11	144	105	3	1	4	3	1	4	3	2	9	9	4	7	299	52

The total crossover percentage among regular sons is 9.3 from the XX females, 16.7 from the XXY females. The latter value needs correction, however. Half of the exceptional gametes die, so the totals should be taken as regulars plus twice the exceptional females; this gives 50:299+22, or 15.6 percent. It seems clear that the presence of a Y significantly increases the frequency of recovered double crossovers.

Crossing over in sc-4/sc-4 is approximately normal. Three experiments are recorded (table 2). The third experiment also gave a total of 14 reversions of Bar and 6 occurrences of double-bar (in 8,523 flies), all of them *f-fu* crossovers. In many of these cultures the *B* flies were not classified

for *f-fu*. This serves to confirm the report of MULLER and WEINSTEIN (1933), based on sc-8 experiments, that unequal crossing over occurs only between non-sister strands even when the *B* locus is far removed from the spindle attachment.

TABLE 2

Crossing over in homozygous inversion sc-4. Regular males only are recorded in the first experiment; in the second and third both males and females are included.

MOTHERS	0	1	2	3	1, 2	1, 3	2, 3	TOTAL
cv cr/w^{e}f	66 73	14 8	43 42	9 16	2 3	1 1	1 2	281
vf/cv	93 94	31 20	24 37		3 0			302
B/f B fu	2707	103						2810

Inversion scute-7

DUBININ (1930) has described scute-7. It was obtained by X-raying apricot (w^a) flies, and is a recessive scute allelomorph resembling but definitely different from scute-1.

Females heterozygous for scute-7 have shown no crossing over for any loci to the left of *ct*, and a reduction of crossing over for the interval from *ct* to *lz*. To the right of *lz* substantially normal values have been obtained (table 3). Tests of crossovers have shown that the decrease of crossing over is due to something lying to the left of *sn*, in the region most affected.

TABLE 3*

LOCI	sc-7/+		sc-7/sc-7	
	N	PERCENT	N	PERCENT
sc-w	6213	0	—	—
w-cv	3103	0	—	—
fa-sn	—	(0.4)	603	2.8
cv-ct	1030	0	—	—
cv-sn	1395	0.4	—	—
cv-v	938	7.5	—	—
sn-lz	1395	1.6	292	5.1
lz-v	—	(5.5)	292	3.4
v-f	678	24.9	350	22.6

* These values are all from XX females. Less extensive data are available for XXY females in the case of sc-7/+; they show no significant differences from the above values.

Owing to the complete absence of crossing over to the left of *ct* it was at first impossible to test this region in homozygous sc-7. However, in a sc-7 chromosome a mutation occurred to an allelomorph of facet, found in an X-ray experiment by Mrs. C. E. RUCH. The results obtained with this chromosome, tested against genes introduced by crossing over (table 3), show that the reduction of crossing over in heterozygous sc-7 is due to an inversion that includes *fa* but not *sn*.

The extent of this inversion has not been determined accurately by genetic methods, since it does not give viable crossovers with any other inversion we have used, unless special methods are used. Salivary gland chromosomes have, however, been seen to give typical heterozygous inversion figures that show the existence of a short terminal uninverted piece. Dr. J. SCHULTZ has studied such preparations more carefully, and we are indebted to him for the information that the left inversion point lies close to the right of scute, the right one not far from the locus of crossveinless.

Inversion scute-8

SIDOROV (1930) subjected apricot (w^a) flies to X-rays and obtained a bristle mutant described as a new scute allelomorph. The relations of this to the scute and achaete series are peculiar; but it is most convenient to retain the name scute-8 for it. There is an associated inversion which has been studied by several investigators (PATTERSON and STONE 1935; STONE and THOMAS 1935). These authors have described its properties; the data given here are in essential agreement with their account.

As will be shown below, the inversion extends from a point between *ac* and *sc* to a point to the right of *bb*. Its right end has been shown by GERSHENSON to be located in the inert region of the X.

The crossing over shown by sc-8/+ is illustrated in table 4. Our other experiments are less satisfactory in that fewer or less well-spaced loci are concerned, but they agree in indicating that these are about the usual values. As in other cases, the classes listed as single crossovers are obviously really doubles, with the second crossover between forked and the right inversion point.

No adequate data are available for crossing over in XXY sc-8/+ females.

Table 4 shows that crossing over is of about the normal frequency in sc-8/sc-8, though (as briefly stated by OFFERMAN and MULLER, 1932) there are local differences from the standard values. The w^a-*cv* interval gives 6.1 percent, as opposed to the usual value of about 12 percent, whereas *f-cr* gives 9.5 as opposed to about 6 percent. Thus in both cases the same section gives more crossing over when it lies far from the spindle attachment.

Inversion scute-8 deficiency

The scute-8 inversion reaches from a point between *ac* and *sc* to a point to the right of *bb*. We have found, as NOUJDIN (1935) has recently reported, that any series of sc-8, in which appropriate tests are made, produces occasional *y-ac* deficiencies, that is the left inversion point involves an unstable union of parts. The resulting chromosome is deficient for *y*, *ac*, and probably *Hw*, and for no other known loci. All the remaining known

loci are in reverse sequence. We have used this "Df sc-8" in some of our inversion experiments.

TABLE 4

Crossing over in inversion sc-8 females.

	In/+		In/In			
CLASSES	sc-8 w^a cv v f / y^2	ct / sc-8 w^a cr	w^a ct cr / cv f	+ / w^a cv v f	w^a cv / v f	w^a v / cv f
0	764 913	341 277	490 509	407 257	173 123	78 79
1	0 0	1 1	33 47	26 31	13 11	9 5
2	4 3	1 4	29 42	97 75	52 27	18 21
3	9 14		345 326	110 94	54 43	25 20
4	0 4		74 71			
1, 2	0 0	6 14	0 1	1 1	0 1	0 0
1, 3	0 0		13 13	3 5	4 2	4 4
1, 4	0 1		6 9			
2, 3	2 3		9 10	18 5	10 2	3 1
2, 4	8 12		6 2			
3, 4	20 13		12 15			
1, 3, 4	0 0		0 1			
2, 3, 4	0 0		0 1			
Exc. males	57	21				

As in the cases of sc-4/+ and sc-8/+, the apparent single crossovers are evidently all really doubles, in which the second crossover was to the right of *f*. The relative numbers of double crossover males (30) and patroclinous males (31) need correction for comparison with other series, since only half the crossovers survive while the other half carry the deficiency. As thus corrected the ratio becomes 60:31 = 1.9:1.

Tables 4 and 5 indicate that there are about twice as many crossovers recovered from Df (sc-8)/+ as from sc-8/+. Analysis of a few other crosses,

TABLE 5*

sc cv v f / Df (sc-8) w^a × y^2 *cv v f*

INTERVAL	MALES		FEMALES	
0	211		245	245
1	2		4	5
2	2			
3	7		16	9
4	1		1	6
1, 3	0		1	1
2, 3	0			
1, 4	1		2	5
2, 4	7			
3, 4	10		8	7
Total	241		555	
Ex.	31			

* Df sc-8 is lethal, so that each crossover class of males is represented only once. The females could not be classified for w^a, so intervals 1 and 2 were not separable in them. In the female row the not-yellow class is entered to the left in each case. Egg counts made by Miss M. Groscurth show that the males carrying Df sc-8 die in the egg stage.

not here reported in detail because they include fewer genes or for similar reasons, suggests that the difference, if present, may be less than indicated. More experiments are needed.

Females of the constitution Df (sc-8)/sc-8 have all their genes in the same sequence, but are heterozygous for a terminal *y-ac* deficiency. Table 6 gives the crossing over observed.

TABLE 6

Crossing over in sc^8B/Df (sc-8) *cv v f* ♀ ♀.*

0	1	2	3	4	1.2	1.3	2.3	TOTAL
89 62	26 16	8 6	2 5	0 0	29 2	25 27	7 9	332

* This table gives the results of a cross to *y cv v f*; it includes both sexes, and contrary classes are therefore not equivalent because of the lethal nature of the deficiency. In reality the sequence is Df *B f v cv*; the classes above, renumbered on this basis, become, in the order given: 0; 1; 1.4; 1.3; 1.2; 4; 3; 3.4).

From table 6 values for comparison with sc-8/sc-8, have been calculated:

	w^a-*cv*	*cv*-*ct*	*cv*-*v*	*v*-*f*	*f*-*B*	*f*-*cr*	*B*-Df
sc-8/sc-8	6.1	4.8	17.4	21.3	—	9.5	—
sc-8/Df (sc-8)	—	—	24.1	22.6	0	—	19.0

In the case of *cv v* the data suggest a difference; other experiments (involving fewer loci) with sc-8/Df (sc-8) give values of 18.7 (in 215 flies) and 16.6 (in 380 flies). Both series are therefore to be taken as giving not far from 18 percent.

Inversion ClB

The "ClB" chromosome was first briefly described by MULLER (1928), and has been very extensively used since in special experiments. The most detailed account of its properties is that given by GERSHENSON (1935). PAINTER (1934) has figured the inversion that is visible in the salivary-gland cells of ClB heterozygotes. As described by MULLER, this chromosome has an inversion (shown below to extend from a point between *ec* and *bi* to a point between *sy* and *fu*), and carries a lethal and the mutant genes *sc*, *t*, *v*, *se*, and *B*. The leftmost of these, *sc*, lies outside the inversion and separates from it by crossing over occasionally. The other mutant genes lying in the inversion are also occasionally lost by double crossing over. We should interpret the "reinverted" ClB chromosome described by GERSHENSON (1930) as having arisen from a triple crossover—a double within the inversion and a simultaneous single to the left of it. GERSHENSON (1935) records a total of 1 percent crossing over for the whole chromosome (*sc* to *cr*), a value that is, if anything, slightly higher than general experience would lead one to expect. About three-fourths of this crossing over is made up of singles to the left of the inversion. Our own data are less extensive than GERSHENSON'S, and need not be presented since they add nothing of importance.

GERSHENSON has also studied crossing over in XXY females heterozygous for ClB. He found, as have we, that the exceptional females produced are practically always non-crossovers. After correcting his observed crossover values by adding the non-disjunctional eggs to the observed non-crossover regulars, he arrived at the conclusion that approximately the same amount of crossing over occurs as in XX females. His values are 1.29 percent for crossing over to the left of the inversion, .07 percent for doubles within the inversion, the differences from the XX values being opposite in sign and insignificant in amount; the percentages are, however, too small to be useful for such comparisons.

GERSHENSON has added one other essential bit of evidence, concerning a relation we have not studied. He determined (the method used is not stated) the frequency of XX and XXY females among the regular daugh-

ters of XXY ClB females. His table IV shows that among the regulars carrying the ClB chromosome there were 47 XXY:49 XX; among those carrying the non-inverted chromosome there were 68 XXY:63 XX. Evidently, in the regular eggs the Y is distributed at random.

A similar relation was recorded by BRIDGES (1916) for XXY females carrying no inversion, half the regular daughters being shown to be XXY, the other half XX. KIKKAWA (1932) reports that in *D. virilis*, significantly less than half are XXY. This result is based on cytological observations and seems to us to be doubtful. The Y of *virilis* is not visibly different from the X's or from eight of the autosomes; under these circumstances wholesale counts made on the minute oögonial chromosomes seem questionable.

TABLE 7*

$$\text{♀}\ \frac{\text{dl-49}\ cm^2 \quad bb}{v\ cr} \times \text{♂}\ v\ B\ bb$$

	XX ♀♀		XXY ♀♀	
Regular (*B*) ♀				
0	220	201	134	255
1	30	40	152	57
Exc. (+) ♀	0		578	
Reg. (not-*B*) ♂				
cm or *cr* (*v* or not-*v*)	419		567	
v	19		40	
Exc. (*v B*) ♂	1		480	

* In the male classes *bb* cannot be identified, and *cm* and *cr* are not separable. The *v-cr* crossing over can only be determined by doubling the *v* class of males, the contrary crossover, *cm cr*, not being identifiable. In the female classes the crossing over detected is that between *v* and *bb*; in the case of the XXY females *bb* is suppressed by the Y present in some of the regular daughters so the observed classes are misleading. Using *bb* classes only the numbers are: non-crossovers 134, crossovers 57.

Inversion delta-49

Inversion dl-49 was first described in an abstract by MULLER and STONE (1931). The left break was shown to lie between *rb* and *cm*, the right between *fw* and *f*. According to PAINTER (1934) unpublished data of these workers show that the right break lies between *fw* and *g*. PAINTER (1934) showed from a study of salivary chromosomes of females heterozygous for inversion dl-49 that the left break occurred between *rb* and *cv*. Since the method that we have used for determining the ends of inversions could not (with the material at our disposal) be used with dl-49, we can add no further information.

Females heterozygous for Inversion dl-49 give few or no crossovers within the inversion among their offspring. We have not collected any ex-

tensive series of data showing this to be true since it seemed quite unnecessary. Inversion dl-49 is extensively used in "balanced" stocks and, so far as we know, no case of double crossing over within the inverted segment has occurred in heterozygous females; the opportunities for detecting such, had they occurred, have been abundant.

Females homozygous for inversion dl-49 show approximately normal crossing over both within the inversion and outside it, according to STONE and THOMAS (1935).

Females heterozygous for inversion dl-49 do give recoverable crossovers outside the limits of the inversion, those to the left occurring with considerably lower frequency than those to the right. Among 533 progeny of the cross inversion dl-49 *cm*^{2} *f*/*y ec cv ct*^{6} *v g*^{2} *f* × *y ec cv ct*^{6} *v g*^{2} *f*, 3 or 0.56 percent were crossovers between *y* and *ec*.

The data of table 7 show, from XX females, *v-cr* = 8.7 percent, *v-bb* = 14.3 percent. The latter value may be taken as giving the amount of crossing over between the inversion and the spindle attachment; it is in reasonable agreement with the value of 13.4 obtained by SCHULTZ (quoted by L. V. MORGAN 1933).

Table 7 also shows the crossing over from XXY females heterozygous for inversion dl-49. After correcting for the inviable non-disjunctional gametes the values are *v cr* = 4.5, *v bb* = 10.1. Another series of XXY females, of the constitution dl-49 *cm*^{2} *bb*/*y*^{2}, gave (corrected) *y*^{2}*cm*^{2} = 0.5, *y*^{2}*bb* = 13.4, based on 275 regular males and 70 *bb* regular females, respectively. The conclusion seems warranted that the Y somewhat decreases crossing over between the spindle attachment and the inversion.

Inversion yellow-4

According to DUBININ and FRIESEN (1932), the y-4 inversion was found by SEREBROVSKY. It presumably arose as the result of X-ray treatment and is inseparably associated with a mutation of the yellow gene to an allelomorph very closely resembling the original *y*^{1}. As shown below, the leftmost inversion break is located very near to or at the yellow locus (to the left of it according to MULLER and PROKOFJEVA 1935); the rightmost break is located between the genes *fu* and *da*.

Females heterozygous for inversion y-4 give, among their regular offspring, about 2.7 percent of double crossovers within the inversion; about 2.4 percent of the sons of such females are patroclinous. The data from which these percentages are obtained are presented in table 8. Certain of the crossovers appear as singles within the inversion; they are presumably doubles with the second crossover in the short uncontrolled region between *f* and the end of the inversion. The ratio of recovered double crossovers among male offspring of XX mothers (57) to patroclinous males (51) is 1.12:1.

The data from XXY females (table 8) can be compared with those from XX females, since the XXY mothers were sisters of approximately half of the XX mothers and since the two lots of XX data gave similar results (2.8 and 2.3 percent of males patroclinous, 2.7 and 2.0 percent of regular males crossovers). The percentage of crossovers among regular sons of XXY mothers is 6.1, or 5.8 when corrected for exceptional offspring. As in the case of inversion sc-4, the frequency of recovered double crossovers is increased by the presence of a Y chromosome.

TABLE 8

Crossing over in In y-4/sc cv v f and in sister In y-4/sc cv v f/Y females by B or sc B males.

	XX FEMALES		XXY FEMALES	
B ♀♀	2106		548	
+ ♀♀	1		39	
B ♂♂	51		56	
Regular males				
0	1019	1044	287	250
1–2	2	3	3	3
1–3	16	11	9	9
1-(4)	0	1	1	0
2-3	11	8	7	6
2-(4)	3	1	0	0
3-(4)	0	1	0	0
Total regular males		2120		575

Inversion bobbed deficiency

From X-ray treated males SIVERTZEV-DOBZHANSKY and DOBZHANSKY (1933) got an X chromosome carrying a deficiency for the proximal third of the somatic metaphase X chromosome, and a small-wing (*sl*) allelomorph. Females heterozygous for this and a normal X chromosome gave very low crossover values, a result ascribed by the above workers to the presence of the deficiency in heterozygous condition. We have obtained clear evidence that the bobbed deficiency chromosome carries an inverted segment extending from between *rb* and *rg* to between *cr* and the spindle attachment.

SIVERTZEV-DOBZHANSKY and DOBZHANSKY published data on crossing over in females heterozygous for Df (bb). Our data are substantially the same (table 9). The *y-ec* interval lies outside the inversion and shows (in XX females), 0.8 percent of recovered single crossovers. This is a marked reduction as compared with the standard crossover value for this interval. The region from *ec* to *ct* is partly outside and partly within the inversion. To get the frequency of recovered double crossovers within the inversion, apparent singles in this region (four in number) are assumed to be actually

doubles since the greater part of the region must lie inside the inversion. Recovered doubles within the inversion, assuming apparent singles to be doubles with the second single in the unmarked *f*-spindle attachment region, constitute 3.9 percent of the regular males. The relation between double crossovers and patroclinous males will be considered in connection with the mechanism of disjunction in inversions.

TABLE 9

Data from the cross sc sl² Df(bb)/ec ct⁶ g² f×w B. The XX and XXY females were sisters.

	XX FEMALES		XXY FEMALES	
B ♀ ♀	1244		1622	
+ ♀ ♀	0		255	
w B ♂ ♂	21		292	
Regular males				
0	443	601	695	774
1	5	4	4	10
2–(6)	1	3	5	2
3–(6)	12	10	13	17
4–(6)	1	2	4	1
5–(6)	1	0	2	0
2–3	0	0	1	0
2–4	0	0	0	1
2–5	0	1	2	1
3–4	1	6	3	0
3–5	3	1	5	3
4–5	1	0	0	0
1–3–(6)	0	0	0	1
Total regular males		1096		1544

Females heterozygous for Df (bb) and carrying a Y chromosome gave about the same frequency of double crossovers within the inversion as did their XX sisters, 3.7 (corrected for non-disjunction) as compared with 3.9 percent. There is no indication here of an increase in crossing over in the presence of a Y chromosome such as that shown by the sc-4 and y-4 inversions.

Crossover data from XXY females homozygous for Df (bb) are given in table 10. (XX homozygotes do not survive, as shown by SIVERTZEV-DOBZHANSKY and DOBZHANSKY.) The *y-f* interval gives a crossover value of 37.1 percent which is higher than is given by this segment in its normal position in the chromosome (8 plus 10 units). The remaining intervals show less than normal crossing over with the decrease becoming more marked toward the spindle attachment. Presumably we are here dealing with the so-called spindle attachment effect, that is, segments moved away from the spindle attachment show increased crossing over; distal

segments moved near the spindle fiber show a decrease in crossing over (OFFERMAN and MULLER 1932; BEADLE 1932).

TABLE 10

Data from the cross y^2 f v Df(bb)/sc g^2 ct^6 Df(bb)/Y×w B.

		B ♀♀	2269		
		+ ♀♀	69		
		w B ♂♂	84		
Regular males					
0	478	434	1–4	15	17
1	304	312	2–3	0	2
2	72	107	2–4	3	5
3	46	52	3–4	1	1
4	33	37	1–2–4	1	1
1–2	23	19	1–2–3	1	0
1–3	25	27			
			Total regular males		2016

Region	Percentage of crossovers
1	37.1
2	11.6
3	7.7
4	5.7

COMBINATIONS OF DIFFERENT INVERSIONS

In females carrying overlapping inversions, single crossovers within the region common to the two inverted segments should give chromatids with single spindle attachments, in contrast to the chromatids with two or with no spindle attachments resulting from single crossing over within the inverted segment in a female heterozygous for a single inversion. If two overlapping inversions are not too different in length such single crossovers should be viable in the heterozygote. Actually we know this to be the case in several combinations of X chromosome inversions. GERSHENSON (1932) has reported a bobbed deficiency chromosome resulting from single crossing over between In sc-4 and In sc-8.

Crossovers between different inversions will of course give different results depending on the relative positions of the inversion points. Thus, representing the normal sequence of segments of a chromosome such as *A B C D E F*, inversions differing only at one end, $\frac{A\ B\ D\ C\ E\ F}{A\ B\ E\ D\ C\ F}$, will give crossovers *A B D C F*, a single deficiency and *A B E D C E F*, a single net duplication (fig. 2). If both ends differ in position, there are two more possibilities. Thus $\frac{A\ B\ D\ C\ E\ F}{A\ E\ D\ C\ B\ F}$ gives *A B D C B F*, a duplication

for *B* and a deficiency for *E*, and the complementary duplication-deficiency *A E D E F* (fig. 3). The third possibility $\frac{A\ B\ E\ D\ C\ F}{A\ D\ C\ B\ E\ F}$ gives the double duplication *A B B D C B E F* and the double deficiency *A D C F* (fig. 4). We shall consider examples of all of these possibilities.

TABLE 11

Chromosomes resulting from single crossing over within common inverted regions.

SOURCE OF		♀			♂
LEFT END	RIGHT END	DUPLICATION FOR	DEFICIENCY FOR	HETEROZYGOUS FOR NORMAL CHROMOSOME	
sc-4	sc-7	*ct-cr*	none	Inviable	Inviable
sc-4	sc-8	*sc*	*bb*	Normal; fertile	Normal; fertile; inviable without Y
sc-4	Clb	*fu-cr*	*slv-ec*	Inviable	Inviable
sc-4	dl-49	*g-cr*	*slv-rb*	Inviable	Inviable
sc-4	y-4	*y-sc, cr*	none	Normal	Normal
sc-7	sc-4	none	*ct-cr*	Inviable	Inviable
sc-7	sc-8	*sc*	*ct-bb*	Inviable	Inviable
sc-8	sc-4	*bb*	*sc*	Fertile; legs often abnormal	Nearly completely lethal; sterile; extreme sc
sc-8	sc-7	*ct-bb*	*sc*	Inviable	Inviable
sc-8	Clb	*fu-bb*	*sc-ec*	Inviable	Inviable
sc-8	dl-49	*g-bb*	*sc-rb*	Inviable	Inviable
sc-8	y-4	*y-ac, cr-bb*	none	*Hw* effect of sc-8; fertile	*Hw* effect of sc-8
Clb	sc-4	*slv-ec*	*fu-cr*	Inviable	Inviable
Clb	sc-8	*sc-ec*	*fu-bb*	Inviable	Inviable
Clb	dl-49	*g-sy*	*bi-rb*	Inviable	Inviable
Clb	y-4	*y-ec*	*fu*	Fertile; abnormal eyes, wings, hairs	Inviable
Clb	Df(bb)	none	*bi-rb, fu-bb*	Poorly viable; sterile; minute bristles	Inviable
dl-49	sc-4	*slv-rb*	*g-cr*	Inviable	Inviable
dl-49	sc-8	*sc-rb*	*g-bb*	Inviable	Inviable
dl-49	Clb	*bi-rb*	*g-sy*	Inviable	Inviable
dl-49	y-4	*y-rb*	*g-fu*	Inviable	Inviable
y-4	sc-4	none	*y-sc, cr*	Poorly viable; fertile; minute bristles	Inviable
y-4	sc-8	none	*y-ac cr-bb*	Poorly viable; fertile; minute bristles	Inviable
y-4	Clb	*fu*	*y-ec*	Inviable	Inviable
y-4	dl-49	*g-fu*	*y-rb*	Inviable	Inviable
y-4	Df(bb)	none	*y-rb cr*	Inviable	Inviable
Df(bb)	Clb	*bi-rb, fu-cr*	none	Fertile; wings slightly narrowed	Sterile; wings notched at tip
Df(bb)	y-4	*y-rb, cr*	none	Fertile; wings narrow, bristles abnormal	Inviable

The recoverable single crossovers with either one or two deficient segments are useful in determining genetically the position of the inversion points. Thus if such a crossover shows a deficiency for gene B but not for genes *A* and *C*, we can say that one inversion end is located between genes *A* and *B*, the other between *B* and *C*. The precision of this method is limited only by the extent and accuracy of the genetic map and by the fact that only recessive mutant effects are available for deficiency tests.

From many combinations of two inversions we have collected data on non-disjunction (table 14) which are discussed below.

Table 11 gives a summary of the available information concerning the properties of the chromosomes derived from single crossing over in the region common to two inversions. Where we have recorded a given crossover chromosome as being inviable, this is to be understood as meaning "under ordinary conditions." It is quite likely that some of the types in question could be brought to maturity by special culture techniques, which we have not used in any case.

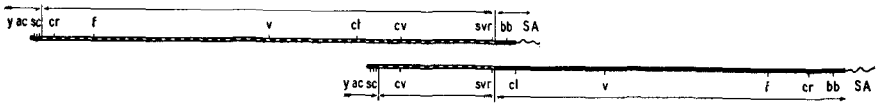

FIGURE 2.—Inv sc-4 (above)/Inv sc-7 (below). Diagram showing conjugation of the common inverted regions. The arrows point in the direction in which the loci are arranged in "normal" chromosomes, reading from the distal end to the spindle attachment.

Inversion sc-4/Inversion sc-7

In this case both left inversion points lie very close to *sc*, and to the right of it; they must be nearly or exactly at the same level. The right point is much further from this level in sc 4. Singles within the common inverted region would be either duplications or deficiencies for the long section from near *cv* to *cr* (fig. 2), and it is accordingly in agreement with expectation that they were not recovered in crosses to normal males. The only other type of crossover that might be expected to appear is the double within this *cv-cr* section, and a few of these were obtained.

From *y sc*^{4} *cv f*/*sc*^{7} *w*^{a} ♀ (×various ♂♂) were obtained 459 regular ♀♀ (no crossovers were observed in those 2 of the 4 cultures where they could have been identified, but detailed counts were not recorded), 228 *sc w*^{a}♂♂, 176 *y sc cv f*♂♂, 8 *sc w*^{a} *f*♂♂, 3 *y sc cv*♂♂,

By mating sc-4/sc-7 heterozygotes to translocation 1,2-7 (break between *rb* and *cv* in X and attached to the right of *sp* in II) or translocation 1, 3–3 (break between *rb* and *cv* in X, attached to the right of *ca* in III) we were able to save the crossovers in the common inverted segment which are deficient for the long segment from the right end of the sc-7 inversion

(near *cv*) to the spindle attachment (fig. 2). From the cross *y sc*^{4} *v f cr*/ *sc*^{7} *w*^{a} *fa*^{2} *sn v* by T 1, 2–7, 455 normal ♀ ♀, 2 + ♂ ♂, 181 *y sc*^{4} *v f cr* ♂ ♂, 184 *sc w*^{a} *fa sn v* ♂ ♂ were obtained. In addition there were 16 males carrying the deficiency crossover plus the proximal X segment from the translocation. Of these 13 were *sc*, 1 was *sc w*^{a} *fa* and 2 were *sc fa*. All were strong scutes, otherwise normal. Of these 11 were tested; none was fertile (they are of course expected to be XO). The 16 males constitute 4.05 percent of the regular males, which would indicate, since the contrary class is lost, a frequency of 8.1 percent crossing over in the common inverted segment. It is assumed that the translocation males produce four types of gametes in equal numbers.

Females of the same constitution as above mated to T 1, 3–3 males gave essentially similar results. There were 407 regular non-crossover males and 6 crossovers of the type considered above. Here the frequency of single crossovers, corrected for the class not recovered, is 2.9 percent. Three of these males were tested and, as expected, were sterile.

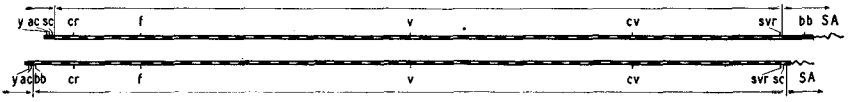

FIGURE 3.—Inv sc-4 (above)/Inv sc-8 (below). Conjugation of the common inverted regions.

In both of the above cases the percentages of recovered crossovers indicate minimum values of crossing over in the common inverted segment. Since the recovered crossover individuals carry a net duplication (difference between sc-7 right break and translocation break) they are probably lower in viability than non-crossover males. Likewise if the translocations give more regular than non-disjunctional gametes the observed frequency of crossing over will be lower than the real value.

Inversion sc-4/Inversion sc-8

The sc-8 inversion is slightly longer than the sc-4 one at both ends, the resulting single crossovers carrying either a deficiency for *sc* and a duplication for *bb* or a duplication for *sc* and a deficiency for *bb*. The conclusions as to their limits depend in part on the results obtained from the heterozygote here under discussion, so the argument may now be presented.

GERSHENSON (1932) has already described the crossover that receives the left end of sc-4 and the right end of sc-8 (fig. 3), showing that it acts as though it carried a lethal allelomorph of *bb*, both the lethal and the bobbed effects being suppressed by a Y. This shows that the *bb* locus is absent, that is, that it is present in the inverted portion of sc-8 and in the uninverted portion of sc-4, both of which are absent in this crossover.

GERSHENSON has also studied the deficient chromosome cytologically in the oögonia of heterozygous females; he finds it to be reduced in length by about one quarter. This can only mean that a large section (not far from half) of the inert region is included in In sc-8 and not in In sc-4. The latter presumably includes little or no inert region. Finally, GERSHENSON showed that this chromosome did not carry a deficiency for *cr*. It follows that In sc-4 has its right break between *cr* and *bb*, while In sc-8 has it to the right of *bb*, conclusions which our own data confirm.

The other crossover, that must carry two *bb* loci, is usually lethal in the male. We have found that it does not carry a deficiency for *ac*, *slv*, or *br*. These three loci must thence be alike in the two inversions, that is, either in both or outside of both, since the crossover studied by GERSHENSON also carries no deficiency for them. When tested against scute allelomorphs this chromosome behaves as an extreme scute, but so does sc-4 itself, so this is not a critical result. However, we have been able to obtain a few males carrying this chromosome. Occasionally they emerge but only live a few hours. Examination of their bristles shows that they have many fewer than sc-4 males; the only named ones observed were the inner verticals, posterior supra-alars, and the dorsocentrals, that is, the "achaete" as opposed to the "scute" bristles, and even these were frequently absent. Dr. J. SCHULTZ informs us that a study of the salivary gland chromosomes also indicates that the sc-8 break is to the left of the *sc* band, the sc-4 one to the right of it. It must be concluded that these males represent the occasional survival of specimens in which the scute locus is wholly absent.

Females heterozygous for this chromosome often have some of their legs abnormal. The abnormality, which is most frequent in the posterior pair, may consist in bifurcation, shortening and twisting, or basal fusion of the two members of one pair.

The above results show that In sc-4 runs from a point between *sc* and *slv* to a point between *cr* and *bb*; In sc-8 from a point between *ac* and *sc* to a point between *bb* and the spindle attachment.

TABLE 12

	f v cv w^a (sc-8) × various ♂♂			
♀	*y sc*^{4}			
Except. ♂♂	456		1, 2	1 3
Regular ♂♂	0		1, 3	7 3
0	52	76	1, 4	1 1
1	0	28	2, 4	2 3
2	1	37	3, 4	3 1
3	0	30	1, 2, 4	0 1
4	0	10	Total ♂♂	269

Table 12 shows the crossing over from sc-4/sc-8. Since one type of single crossover is practically lethal, the simplest way of calculating crossing over seems to be to use in each case only the larger of the two contrary classes. If this is done the values become: total 201; *y-f*, 19.9; *f-v*, 17.9; *v-cv*, 21.4; *cv-w*^{a}, 9.0. These values are, as expected, not different from those for sc-8/sc-8 or sc-8/Df sc-8. Classification for *sc*^{8} was not attempted. The *y* males were typical *sc*^{4}; the *y w*^{a} were nearly wild-type for bristles, carrying both *sc*^{4} and *sc*^{8}.

Both of the crossovers recovered from sc-4/sc-8 have been tested for crossing over and disjunction, and have given the expected results. The one with the left end of In sc-8 (the sc deficiency) when tested against a normal chromosome gave the following results: Df (sc) *f*/*y w*^{a} ♀ × various males: 453 regular ♀ ♀, no exceptions; 337 *y w*^{a} ♂ ♂, 7 *sc* (extreme) *f* ♂ ♂, 17 *y w*^{a} *f* ♂ ♂, 1 extreme *sc* ♂, 1 *y* ♂, 47 exceptional ♂ ♂. (In some cases *sc*^{1}, *sc*^{10}, or *slv* were used instead of *y*.) Calculating the frequency of exceptional males by doubling the *y* class (since the deficiency is nearly lethal), there were 47/767 or 6.1 percent exceptions. In other words this chromosome gives results both as to crossing over and as to disjunction comparable to those shown by the inversions from which it was derived. This result is confirmed by a small series in which the crossover was tested against In sc-8. Here there was about 32 percent crossing over between *sc* and *f*, and only 0.7 percent exceptional males were produced.

The other crossover (*sc* duplication, *bb* deficiency) behaves similarly. Females of the constitution *y w*^{a} *cv* Df(bb)/*f* gave 347 regular sons (of which 10 were crossovers, 3 clearly doubles and the others presumably so) and 11 exceptional sons. The totals for all experiments of this type show 12/391 = 3.1 percent exceptions. This same chromosome was also tested against In sc-4. There resulted 826 regular ♀ ♀, no exceptional ♀, 657 regular ♂ ♂, 4 exceptional ♂ ♂. Among the regular males crossing over could be checked, and the following values were obtained: *sc-w*^{a}, 0.5; *w*^{a}*-cv*, 7.0; *cv-v*, 18.3; *v-f*, 21.3. Here again the crossover, as expected, behaves much like the inversions from which it was derived.

Inversion sc-4/Inversion ClB

The ClB inversion lies wholly within that of sc-4. ClB/+ gives very few crossovers, so that doubles would be expected to be rare here, and none was found. Of the singles within the common inverted region, one type should be a deficiency for *slv-ec* and a duplication for *fu;* the other should be a duplication for *slv-ec*, and a deficiency for *fu*. Neither was obtained; evidently both are inviable in males and also in heterozygous females.

From ClB (*sc v B*)/*y sc*^{4} *cv f* ♀ × *y*^{2} *cv v f* ♂ were obtained 254 *v B* ♀ ♀, 238 *y cv f* ♀ ♀, 2 *sc B* (exceptional) ♀ ♀, 182 *y sc cv f* ♂ ♂, 1 *y*^{2} *cv v*

f (exceptional) ♂. An XXY ♀ of the same constitution gave 27 *v B* ♀ ♀, 33 *y cv f* ♀ ♀, 61 *sc B* ♀ ♀, 24 *y sc cv f* ♂ ♂ and 52 y^2 *cv v f* ♂ ♂.

Inversion sc-4/Inversion dl-49

Scute-4 inversion includes the segment from just to the right of *sc* to between *cr* and *bb*, the greater portion of the chromosome (fig. 1). Delta-49 extends from between *rb* and *cv* to between *fw* and *f* and is consequently entirely included within the sc-4 inversion. From the cross *y* sc-4/dl-49 *y-Hw* cm^2 m^2 g^3 × *t v m* g^2, 1,752 males were recorded, all non-crossovers. This result might have been expected from our knowledge of the behavior of females heterozygous for each of these inversions separately. Doubles within the sc-4 inversion and outside In dl-49 either do not occur or are very rare. Since heterozygous dl-49 gives single crossovers within the inversion (p. 587), it is probable that in the sc-4—dl-49 combination some singles occur in the inverted segment common to the two inversions. Such crossovers result in either a *slv-rb* duplication and *f-cr* deficiency or the complementary deficiency-duplication. Both of these products would be expected to be inviable.

XX females heterozygous for In sc-4 and In dl-49 give few or no exceptional daughters and a frequency of exceptional sons not significantly higher than normal.

Inversion sc-4/Inversion y-4

Inversion sc-4 runs from a point between *sc* and *slv* to a point between *cr* and *bb;* In y-4 from a point near *y* (to the left of *ac*) to a point between *fu* and *cr*. One of the single crossovers is deficient for *y* (?) *ac-sc* and *cr;* the other is a duplication for both these sections. The former is lethal in males but survives occasionally in heterozygous females as a minute-bristled type. The latter (duplication) crossover is viable in offspring of both sexes.

Owing to the presence of *y* in both inverted chromosomes and of an extreme *sc* allelomorph in sc-4, the tests for deficiencies for these two loci are inconclusive. Fully satisfactory tests have shown, however, that the minute crossover is deficient for the loci *ac* and *cr*, not for *rst*, *pn*, *sy*, nor for *od*. The other (duplication) crossover showed no deficiency effects for any of these loci. That is, the inversions differ with respect to *ac* and *cr;* In sc-4 was shown above to include *cr* but not *ac*. Hence y-4 includes *ac* but not *cr*. Both include *rst* and *pn*, as follows from this analysis and from the direct test. In sc-4 includes *sy* and *od;* therefore In y-4 has its right break between these two and *cr;* other data show that it is also to the right of *fu* which is 0.3 units to the right of *od* and *sy*.

The crossing over in In sc-4/In y-4 is similar to that in In sc-4/In sc-8. Here again one single crossover class of males dies, and the data have been treated by using the larger member of each pair of contrary classes. The results are then: total 433; *sc-f*, 20.3; *f-v*, 7.9; *v-cv*, 11.3; *cv-w*^{a}, 10.2; *w*^{a}*-sc*, 1.2.

The *w*^{a} *sc* value appears here and not in the corresponding series for In sc-4/In sc-8 because In y-4 carries a *sc* gene that is clearly dominant to *sc*^{4}, whereas the allelomorph present in In sc-8 gives with *sc*^{4} a variable type not always clearly separable from *sc*^{4}.

Data from XXY In sc-4/In y-4 show the same type of crossing over and roughly the same amount; the experiments however include too few flies to be valuable for detailed comparisons.

Inversion sc-7/Inversion sc-8

This combination of inversions is essentially the same as sc-4/sc-7 already discussed. Females heterozygous for the two inversions give progeny carrying chromosomes derived by crossing over within the common inverted segment. As in the case of the sc-4/sc-7 both of these crossovers are inviable. Doubles within the sc-8 inversion but outside the short sc-7 inversion are recovered.

From the cross sc-8 *w*^{a}/sc-8 *v*/Y by various males the following offspring were recovered:

Regular	♀ ♀	589	
Exceptional	♀ ♀	70	
Exceptional	♂ ♂	103	
Regular	♂ ♂		
0		247	246
2-(3)		11	10

In addition there was one exceptional male expected to be *y*^{2} *cv v B* which did not show *y* but which did show a hairy wing effect. This male was sterile. Evidently he carried a duplication for *y*.

From crosses of sc-7/sc-8 to T 1, 2–7 or T 1, 3–3 males (as in the case of sc-4/sc-7) males were recovered which carried the crossover deficient for the long segment from the right break in sc-7 to *bb*. These were enabled to survive by the proximal X segment from the translocation males. Such males differ from those obtained from sc-4/sc-7 (fig. 2) in not carrying a *bb* duplication and in carrying a duplication for the *sc* locus. From the cross sc-8 *w*^{a} *cv v f*/sc-7 *w*^{a} *fa*^{2} *sn v* by translocation males the following flies were recorded:

		♂♂ T 1,2–7	♂♂ T 1,3–3
Regular females		844	867
matroclinous	♀♀	1	0
v minute	♀♀	0	1
Patroclinous	♂♂	4	5
Regular	♂♂	796	728
sc w^a	♂♂	17	19
sc w^a *fa*	♂♂	0	1

The *v* minute female recorded above carried the long crossover chromosome, tandem attached-X chromosomes deficient for the common inverted segment of the parent inversions. This deficiency was partly covered by the distal X segment from the translocation.

The *sc* w^a and *sc* w^a *fa* males carry the short crossover chromosome. The actual frequency was 2.1 and 2.7 percent of regular males. These males carry both the sc^7 and sc^8 genes and were intermediate between sc^7 and sc^8 males for the scute character. Their wings were spread. All of them that were tested (seven) were sterile as expected and were presumably XO.

Assuming that the translocation males produce four types of gametes in equal numbers, and that the above mentioned males have normal viability the true percentages of crossovers in the common inverted segment would be obtained by doubling the crossover male classes (the contrary crossover is not recovered) which would give values of 4.1 and 5.2 percent. Since these males are almost certainly of lower viability than the regular males, these percentages represent minimum values. The real value is probably considerably higher.

Inversion sc-7/Inversion ClB

These two inversions overlap in the rather short region from *bi* to near *cv*. Singles would be expected to be rare within this region and would be inviable. None was recovered. From the behavior of each when heterozygous for a normal chromosome it is inferred that few crossovers of any kind would be recovered. In fact, sc-7 w^a/ClB *sc v B* females gave 327 regular sons with one crossover which was sc^7 w^a *v* that is, a double within that part of In ClB not common to In sc-7. Similar XXY females gave 270 regular males with no crossovers.

Inversion sc-7/Inversion dl-49

The right break in In sc-7 is near *cv*, the left break in dl-49 between *rb* and *cv*. In the absence of more accurate information we cannot say definitely whether or not these two inversions overlap although it seems more probable that there is a short overlapping segment. The data from

sc-7 w^a/dl-49 cm^2 XX females by *w B* males are limited; 157 males show no crossovers but the region to the right of the dl-49 inversion where one might expect a low frequency of crossovers is not under control. From XXY mothers, similarly marked, 206 non-crossover males were recorded.

Inversion sc-7/Inversion Df(bb)

In the combination of In sc-7 and In Df(bb) there is probably a short overlapping segment between *rb* and *cv*. From the cross sc-7 $w^a/y\ sl^2$ Df (bb)- × *sc ec ct t* g^2 *sl*, 1651 regular males were recorded of which 19 or 1.15 percent were apparent single crossovers between w^a and *sl*. Presumably all of these were actually doubles with the second crossover in the uncontrolled region between *sl* and *bb*. Several sc-7 $w^a\ sl^2$ males and *sc sl* females were tested and found not to carry Df (bb) showing that they were double crossovers. Presumably an appreciable number of undetected double crossovers occurred in the rather long unmarked region between the right end of In sc-7 and the locus of *sl*.

In the above cross 22 patroclinous males were recorded. Exceptional females could not be distinguished from one crossover class but since there were only 18 females in this class and 12 in the contrary crossover class, the number of exceptional females could not have been large.

Inversion sc-8/Inversion ClB

Inversion ClB is wholly within the limits of In sc-8, and few or no recovered crossovers of any kind are to be expected—the case being very similar to that of In sc-4/In ClB. In fact none was obtained among 21 regular sons of XX females or 160 sons from XXY females.

Inversion sc-8/Inversion dl-49

This combination is essentially similar to the combination of In sc-4 and In dl-49 already considered; the discussion given there applies in the present combination. From the cross sc-8 w^a/dl-49 cm^2 by *w B*, 1742 non-crossover regular males were recorded and 6 patroclinous males. From 5 additional cultures not recorded in detail, 2 apparent w^a *cm* males were obtained. These proved, on testing, to be the result of mutation of an eye color gene in the dl-49 chromosome rather than of crossing over. The locus of the mutation was not determined. From XXY females of the above constitution mated to *w B* males 576 non-crossover regular males and 444 patroclinous males were recorded.

STONE AND THOMAS (1935) also studied this combination. They obtained one double crossover (outside of the dl-49 inversion, inside of the sc-8 one) in experiments carried out at 30°C.

Inversion sc-8/Inversion y-4

Inversion y-4 extends to the left further than In sc-8 by the locus of *ac* (and *y*?); In sc-8 extends further to the right by the *cr- bb* section. No crossovers are to be expected outside the inversions; of the singles within the common inverted region, one is a duplication for *ac* (and *y*?) and for *cr-bb;* the other is a deficiency for both these sections. The latter is lethal in males, the former survives; in heterozygous females the former (duplication) is fully viable, the latter gives a minute-bristled individual that has reduced viability.

Tests against recessives show that the "minute" crossover is deficient for *ac* and *cr*, not for *slv;* the other one (duplication) is deficient for none of these loci. Therefore the inversions differ in that one includes *cr*, the other does not; likewise they differ for *ac;* both or neither include *slv*. These results are in agreement with the conclusions from sc-4/sc-8 and sc-4/y-4, which show that *slv* is included in both, *cr* in sc-8 but not in y-4, *ac* in y-4 but not in sc-8.

The crossing over tests for this combination show results similar to those from sc-4/y-4 but they are too scanty to permit detailed comparisons.

The duplication crossover, tested against a normal chromosome gave no exceptions among 314 daughters, 18 among 332 sons (5.4 percent). These values, as expected, are comparable to those from the In sc-4—In sc-8 crossovers.

Inversion ClB/Inversion dl-49

The delta-49 inversion is entirely included within the ClB inversion. From the cross ClB *sc v sl B*/dl-49 cm^2 $bb^x \times$ *sc cv v f cr*, 629 regular non-crossover males (cm^2) and 2 patroclinous males were obtained. Among 1266 females, 3 (0.24 per cent) were crossovers between *sc* and the left break of ClB; one was of the constitution *sc B* presumably a primary exception equational for the scute gene. XXY females of this combination were not studied.

Single crossovers in the inverted segment common to ClB and dl-49 presumably occur but are evidently inviable.

Inversion ClB/Inversion y-4

The right inversion points here are very similar, differing only in that In y-4 includes *fu*, In ClB does not. At the left In y-4 is considerably longer. Crossing over might occur between the inversions and the spindle attachment, but tests have not been made. Of the singles within the common inverted region, one gives a long deficiency for (*y*?) *ac* to *ec*, and a short duplication for *fu*, the other has the corresponding duplication and

deficiency. Both crossovers are lethal in males. The one with the long (*ac-ec*) deficiency is also lethal in heterozygous females; the other is viable. This latter crossover usually carries the *B* gene of ClB, and in that case the resulting *B*/+ females have very narrow bar eyes similar to those of *B*/*B*. They also have irregularly arranged acrostical hairs, and their wings are slightly reduced in size and are less convex than is normal on the posterior margin. Tests of this crossover chromosome show that it carries a deficiency for *fu*, not for *y*, *ac*, *br*, *w*, *ec*, *f*, *vb*, *sy*, *od*, *cr*. The negative results could all have been predicted from conclusions already established in this paper; the positive case constitutes our proof that *fu* is in the inverted section of y-4, not in that of ClB.

From y-4 w^a/ClB *sc v B* only one of the 280 regular sons was a crossover. This one, y^4 w^a *v*, was a double within the common inverted region. The females from these same mothers (excluding the mating to *fu* ♂ because of the low viability of *fu*/Df) gave 218 broad bar non-crossover ♀ ♀, 237

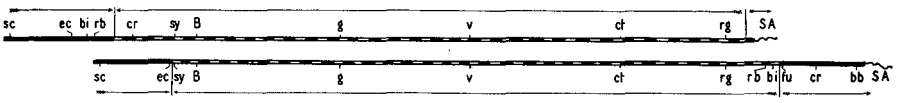

FIGURE 4.—In Df (bb) (above)/In ClB (below). Conjugation of the common inverted regions.

not-bar non-crossover ♀ ♀ and 72 narrow bar crossover ♀ ♀. From the mating to *fu* ♂ one of the 6 *fu*/Df daughters was not-bar, and must have resulted from crossing over between *B* and the inversion point of ClB, a distance of less than two units on the standard map.

Inversion ClB/Inversion Df (bb)

The left break of ClB is between *bi* and *ec*, the right between *sy* and *fu*. The left break of Df (bb) is between *rb* and *rg*, the right between *cr* and *bb*. That these statements are correct will be shown below from studies of single crossovers between ClB and Df (bb). Both breaks of Df (bb) are to the right of those of ClB. Consequently one single crossover should give duplications for the *bi-rb* and *fu-cr* segments (fig. 4). The contrary crossover should give a deficiency for these two segments plus the deficiency for bobbed from the Df (bb) chromosome (fig. 4). Both of these crossovers are viable and can be recovered in heterozygous females. The duplication chromosome is viable in the male. Such males are small with wings having a less convex outer margin than normal and usually with one or more notches at the tips; they are sterile. Dissections by Professor DOBZHANSKY show that the testes are collapsed like those of very old males. Females heterozygous for the double deficiency survive as extreme minutes with wings of a characteristic shape. They have normal ovaries as shown by

dissections made by Professor DOBZHANSKY but according to many tests are sterile. Males carrying this deficiency chromosome are inviable.

Tests of the deficiency-carrying crossover which gets the right end from Df (bb) and the left end from ClB give positive evidence that the *rb* and *cr* loci are absent. From crosses of ClB/Df (bb) to *bi* and *fu* males no deficiency heterozygotes were obtained. We conclude that both of these loci are included in the deficiency crossover. The results from ClB/y-4 establish this for *fu*. The number of flies examined was in each case adequate to have given many deficiency crossover females were they not inviable. Similar tests have shown that the *ec*, *rg*, *f*, *bb*, and *sy* loci are not included in these deficiencies. These results confirm the conclusion already drawn that the right break of ClB is between *sy* and *fu*. The left break must lie between *ec* and *bi*. These conclusions confirm and extend those of PAINTER (1934) derived from studies of salivary chromosomes. In a similar way it is clear that the left break of Df (bb) lies between *rb* and *rg* and that the right one lies to the right of carnation.

Frequency and distribution of single crossovers

Among 2010 regular females from ClB/Df (bb) mothers, 48 or 2.4 per cent carried the deficiency crossover. The contrary crossover could not be classified accurately in the females; if they were of equal frequency, the recovered single crossovers would be 4.8 percent of the total. Among 749 regular males, 26 or 3.5 percent carried the double duplication crossover. The contrary class dies but half the non crossovers likewise die because of the ClB lethal so that this value represents a direct measure of the frequency of singles. It is quite certain that both of the above values are much too low; the crossover-carrying individuals in both cases are of very poor viability and no precautions were taken to prevent overcrowding in the cultures.

It is of interest to determine how the single crossovers in the common inverted segment are distributed. In all experiments *v* was carried by the ClB chromosome. We can then separate crossovers in males into those which occurred between *rg* and *v* and those which occurred between *v* and *sy*. When this is done, the following results are obtained:

Crossover interval	Standard map lengths	Number of crossovers
rg to *v*	22+	111
v to *sy*	27.2	141

The ratios of standard map lengths of these intervals is 1:1.24−; that of singles within these regions 1:1.26. We can conclude that the distribution of single crossovers within the common inverted segment is approximately normal.

Crossing over in heterozygotes for the duplication crossover

Crossing over in females heterozygous for the Df (bb)-ClB crossover has been studied in two experiments. Only one of these is reported here. The other, although involving larger numbers of individuals, is not as well controlled for crossing over in different regions. The data from females carrying the duplication chromosome and a bobbed deficiency chromosome are given in table 13.

TABLE 13

Data from the cross y^2 *f v* dup/*sc* g^2 ct^6 *Df (bb)* ♀ ♀ by *w B* ♂♂. *The females of this experiment were sisters of those used in the experiment summarized in Table 10, homozygous Df (bb) of the same constitution.*

		B ♀♀	1471		
		+ ♀♀	0		
		w B ♂♂	5		
*Regular ♂♂					
0	91	411	1–5	0	6
1	99	14	2–3	0	2
2	60	14	2–4	0	3
3	55	7	3–4	0	1
4	31	6	3–5	0	1
5	7	0	1–3–4	1	0
1–2	0	8	1–2–4	1	0
1–3	3	14			
1–4	0	8	Total		844

* In each case the smaller of the two contrary classes represents the males carrying the duplication.

In comparison with the Df (bb) chromosome, the double duplication crossover chromosome carries one net duplication, namely a segment including *rb-bi-f-cr* from the ClB chromosome. This segment together with the bb segment is simply added to the Df (bb) chromosome which of course carries the *bi-rb-cv-f* segment (no difference in arrangement) at the left end. The data of table 13 show the following crossover values as measured in the classes not carrying the duplication:

y-f	19.4
f-g	10.6
g-v	10.5
v-ct	6.4
ct-dup	2.1

For these same regions in homozygous Df (bb) sister females with a Y chromosome the values for the first four regions above (Table 13) are 37.1, 11.6, 7.7, 5.7 respectively. The fifth region cannot be measured in Df (bb) /Df (bb); its standard map length is 10 units.

It is clear from the above that the duplication crossover chromosome crosses over freely with Df(bb), one of the inversions from which it was derived. As compared with Df(bb)/Df(bb)/Y, crossing over is reduced in the *y-f* interval but is the same in the other intervals which can be compared. The reduction in the *y-f* interval is presumably the result of the duplication which is of course homologous with a segment included in the *y-f* interval.

Inversion dl-49/Inversion y-4

From the cross y-4 w^a/dl-49 *y Hw* m^2 g^3 ♀ ♀ by *t v m g* ♂ ♂, 1506 regular sons showed no crossovers. There were two patroclinous males. There were 1,651 regular females, all non-crossovers, and five exceptional females, four from 1 of the nine cultures.

From a cross of XXY females of the above constitution with *w* or *w B* males, 428 regular non-crossover, 487 patroclinous males, 446 regular females and 506 exceptional females were recorded.

It is clear that recoverable crossovers are practically absent in females of this combination, unless they occur between the right break of y-4 inversion and the spindle attachment. Data from attached-X females heterozygous for y-4 (p. 564) indicate that singles in this interval are very rare.

Single crossovers in the segment common to the two inversions, presumably occur and are lethal both in heterozygous females and in males.

Inversion y-4/Inversion Df (bb)

The location of the breaks in both y-4 and Df(bb) have already been discussed; both breaks in Df (bb) are to the right of those of y-4. Consequently single crossovers in the common inverted segment of these two inversions will give either a double duplication or a double deficiency. The latter is inviable both in males and in heterozygous females; the former is viable in females heterozygous for a normal chromosome. Such a female usually has stubby outer verticals, disarranged scutellars, and outer wing margins less convex than normal. If such a duplication female is heterozygous for *B*, the eyes are usually as narrow as those of a female homozygous for *B*. These crossover females are fertile but produce very few offspring. Their viability is good considering the number of loci carried in the two duplications.

From the cross y-4 w^a *cv v* s^2/*sc* sl^2 Df(bb) by *sc B* males there were recorded one exceptional female (+), 330 regular ♀ ♀ (*B* and *sc B*), 4 *sc B* ♂ ♂, 123 *sc sl* ♂ ♂, 85 *y* w^a *cv v s* ♂ ♂ and 38 duplication ♀ ♀. The frequency of crossover females in percent of regular females is 10.7. From sister females of those used in the cross above, but XXY in constitution, mated to *sc B* males, the following offspring were obtained: 264 + ♀ ♀, 390 *B* ♀ ♀, 236 *sc B* ♀ ♀, 272 *sc B* ♂ ♂, 159 *sc sl* ♂ ♂, 198 *y* w^a *sv v s* ♂ ♂,

and 144 duplication ♂♂. Here duplication females constitute 18.7 percent of the regular females. Since only one crossover is recovered here the true percentage of singles from these data will be 18.7 for XX and 19.8 (corrected) for XXY. The frequencies are not significantly different.

Since females heterozygous for the duplication crossover produce very few offspring, few studies of them were made. It is known that crossing over between the duplication chromosome and a normal chromosome is very low and that a few patroclinous males are produced. These results are expected since the crossover chromosome is in effect an inversion plus an intercalated duplication.

NON-DISJUNCTION

Table 14 is a summary of the available data on the production of matroclinous females and patroclinous males.

In many of these experiments the exceptional females could not be distinguished and only the males are recorded, in others the male exceptions were known to have very low viability and only the females are recorded. It follows that the numbers of individuals in the two sexes from a given combination are often not comparable. ClB and Df(sc-8) are lethal in the males; accordingly in all series involving these the observed number of regular males has been doubled in calculating the recorded total, a point to be remembered in judging the significance of the values given. In many of the combinations of two inversions, single crossovers between the two inversions occur; some of these are lethal and others have reduced viability. No corrections have been made for this; therefore in several of these cases if is certain that the totals are too low and the percentages of exceptions too high.

In the case of ClB/+ we have added our own data to those recorded by GERSHENSON (1935) though in the XXY experiments we obtained somewhat higher values than he records. We have excluded the males from his XX experiment in which the father was bb^1, since the exceptions (having no Y) would be inviable. We have also excluded one unexplained XX culture of our own that gave 9 exceptional females to 223 regulars and 11 exceptional males to 133 regulars. We have observed in some other combinations a suspiciously high frequency of cultures that gave more than one exception when others of the same constitution gave none. In no case were the resulting frequencies high enough to be interpreted as due to the presence of an unsuspected Y. The frequencies are about those that result from the presence of a short duplication carrying the X spindle attachment, but we have not studied the descendants of such females with this possibility in mind.

The results of STONE and THOMAS (1935) for sc-8/+ and dl-49/+ have not been included in the table.

TABLE 14

Summary of non-disjunction data.

	XX MOTHERS						XXY MOTHERS					
	FEMALES			MALES			FEMALES			MALES		
	TOTAL	EXC.	% EXC.	TOTAL	EXC.	% EXC.	TOTAL	EXC.	% EXC	TOTAL	EXC.	% EXC.
sc-4/+	6287	1	0.02	5861	337	5.75	933	40	4.3	817	109	13.4
sc-4/sc-4	953	0	0.00	600	0	0.00						
sc-7/+	5386	5	0.09	4919	14	0.28	1518	195	12.9	1697	256	15.1
sc-7/sc-7	1610	0	0.00	1370	1	0.07						
sc-8/+	4703	1	0.02	5138	164	3.20	1310	130	9.9	1847	255	13.8
sc-8/sc-8	574	0	0.00	481	0	0.00	310	4	1.3	252	5	2.0
Df (sc^8)/+	641	2	0.31	1053	47	4.46	85	9	10.6	80	12	15.0
sc-8/Df (sc^8)	631	0	0.00	504	9	0.00						
ClB/+	5693	14	0.25	3438	16	0.47	7478	2729	36.6	7172	2712	37.8
dl-49/+	3238	0	0.00	3168	6	0.19	4355	1985	45.6	4145	1747	42.2
dl-49/dl-49							126	5	4.0	99	12	2.0
y-4/+	2007	1	0.05	2171	51	2.34	587	39	6.8	631	56	8.9
y-4/y-4	206	1	0.49	169	0	0.00						
Df (bb)/+	1244	0	0.00	3437	67	1.95	1877	255	13.6	1836	292	15.9
Df (bb)/Df (bb)							2338	69	2.9	2100	84	4.0
sc-4/sc-7	459	0	0.00	422	7	1.66	341	34	10.0	280	43	15.3
sc-4/sc-8	456	0	0.00	264	0	0.00						
sc-4/dl-49	2084	0	0.00	1755	3	0.17						
sc-4/y-4	1187	3	0.26	954	0	0.00	413	33	8.0	224	30	13.4
sc-7/sc-7	439	0	0.00	350	12	3.43	659	70	10.6	617	103	16.7
sc-7/Df (sc^8)	523	0	0.00	531	7	1.32						
sc-7/ClB	754	0	0.00	658	4	0.61	894	322	35.8	824	284	34.5
sc-7/dl-49	169	2	1.18	157	0	0.00	355	138	38.8	346	140	40.5
sc-7/y-4	479	0	0.00	297	1	0.34						
sc-7/Df (bb)				1673	22	1.31						
sc-8/dl-49	1959	5	0.26	1748	6	0.34	1146	541	47.3	1020	444	43.5
sc-8/y-4	316	0	0.00	240	1	0.42	906	70	7.7	968	134	13.8
ClB/dl-49	1270	4	0.32	1260	2	0.16						
ClB/y-4				561	1	0.18	101	4	4.0	57	5	8.8
ClB/Df (bb)	1557	2	0.13	1200	6	0.50	1622	520	32.0	1351	561	41.5
dl-49/y-4	1656	5	0.32	1508	2	0.13	952	506	53.2	915	487	53.2
y-4/Df (bb)	370	1	0.27	194	4	2.06	1034	264	25.5	629	272	43.2

PRESENCE OF SINGLE CROSSOVERS

Representing a normal X chromosome schematically as *B C D E* a and an homologous chromosome with the *CD* segment inverted as *B D C E* a (a in both cases representing the spindle attachment), then single crossovers in the *CD* segment will give the products (1) *B C D B* (duplication for *B*, deficiency for *E*, and having no spindle attachment) and (2) a *E C D E* a (deficiency for *B*, duplication for *E*, and having two spindle attach-

ments). Product (1) would be expected to be lost because of its lack of a spindle attachment. Product (2), because of its two spindle attachments, should form a tie between the two poles of the first meiotic division. It is known from the cytological studies of McCLINTOCK (1931, 1933) on Zea, MATHER (1934) on Vicia, STONE (1933) on Tulipa, and SMITH (1935) on Trillium that, for these plants, single crossovers do occur between segments relatively inverted and that the results are as described above. In order to understand the mechanism of disjunction in inversion heterozygotes in Drosophila it is essential to know whether such crossovers occur in this organism and, if so, with what frequency. The most direct method of answering these questions, namely, cytological examination as used in the cases cited above, is very difficult in the case of oögenesis in *Drosophila melanogaster*. We have resorted to less direct genetic methods.

From the data already presented on single crossing over in combinations of two overlapping inversions it seems highly probable that single crossovers occur within the inverted segment in females heterozygous for a single inversion. Inversion scute-8 represents an inversion of the entire X chromosome with the exception of the *y* and *ac* loci and the spindle attachment. It can be considered as representing essentially a transfer of the spindle attachment from the right to the left end of the chromosome.

As regards crossing over it should behave essentially like a normal chromosome. In the heterozygote of sc-8 and sc-4 crossing over is practically normal as has already been shown. We can therefore argue that in the heterozygote sc-4/+, single crossovers should be of approximately normal frequency. Similarly in the combination sc-7/sc-8 we have shown that single crossing over occurs in the common inverted segment. From this we can conclude that single crossing over occurs in the inverted segment of sc-7/+. Here the data from the combination sc-7/sc-8 and also from sc-4/sc-7 suggest that the frequency is reduced below that for the sc-7 inverted segment normally arranged. The same general kind of an argument can be made for several of the other combinations considered in the previous section.

In a female heterozygous for a single X chromosome inversion, crossing over can be more or less directly measured by using attached-X females, (see also SIDOROFF, SOKOLOV, and TROFIMOV 1935). By selecting the appropriate crossover from a triploid of the constitution y-4/$\widehat{XX}$ we obtained an attached-X female heterozygous for the y-4 inversion. In such a female, exchange in the inverted segment will give either (1) a closed chromosome carrying a duplication for *cr-bb* and a deficiency for the small segment to the left of *y*, or (2) a chromatid with two spindle attachments plus a chromatid with none (fig. 5). The Y chromosome that is usually

present disjoins from the attached-X chromosomes at the first division. The results described above and shown in figure 5 take place during the second division. The types and relative frequencies of gametes expected

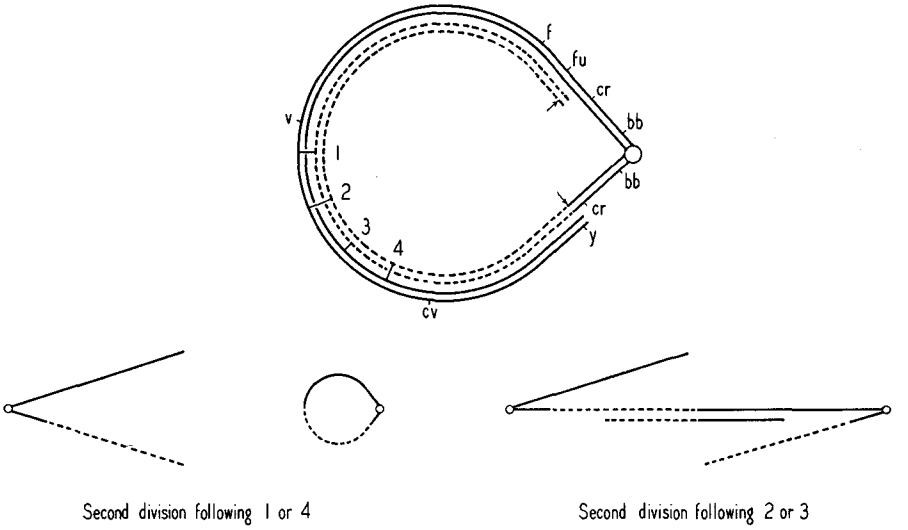

FIGURE 5.—Attached-X, heterozygous for In y-4. Above, conjugation of inverted section. Below, chromatids resulting from the indicated single exchanges. Chromatid with no spindle attachment omitted in lower left.

following single and double exchange are summarized in table 15. Data from the cross y^4cr/y^2v for attached-X females mated to *t v f* males are given in table 16.

TABLE 15

EXCHANGE	$\widehat{XX}$ GAMETES				X^c GAMETES	SECOND DIVISIONS WITH CHROMATID TIE	Y GAMETES
	NON-CROSSOVER	RECIP-ROCAL	EQUA-TIONAL-a	EQUA-TIONAL-b			
None	1						1
Single	1				1	2	4
Double* 2-s	1	1	1	1			4
3-s a					2	2	4
3-s b			1	1	2		4
4-s						4	4
Total Doubles	1	1	2	2	4	6	16

* Double exchanges are designated by the number of strands that undergo crossing over. Thus, in a 2-strand (2-s) double exchange, the same two strands cross over at the two levels.

The daughters showing *y* and *cr* carry attached-X chromosomes. Those which show neither *y* nor *cr* carry the closed chromosome derived by single crossing over in the inversion. From the fact that the sex ratio approaches 2 males to 1 female we infer that those cases in which a double spindle attachment arises by crossing over within the inversion result in lethal eggs.

TABLE 16

Progeny of the cross y^4cr/y^2v f cr attached-X females by t v f males. Four egg-laying periods; 3, 2, 2 and 3 days.

$\widehat{XX}$ FEMALES		+/X^c FEMALES		MALES	
y^2cr	304	*f*	137	*t v f*	1098
y^2v *cr*	11	*v f*	197	*y cr*	1
y^2v *f cr*	1	*v*	3		
Total	316		337		

In such cases the X chromosomes are not simply eliminated for we should then expect a ratio of 2+ males to 1 female. Males carrying the closed chromosome are almost completely inviable. The *y cr* male recorded in table 16 apparently carried such a chromosome. This male had narrow wings, other characteristics of duplication-carrying males, was *y* (not y^2) and was sterile. We have not made a cytological study of this closed-X; this has been done by SIDOROV, SOKOLOV, and TROFIMOV (1935) for the closed-X they obtained in the same way (using an unspecified inversion). They have published a drawing of one metaphase plate showing the closed-X.

From the data given in table 16 and the information summarized in table 15, we can make an approximate calculation of the frequencies of single and double exchanges within the inverted segment. Doubles are measured by equationals for genes within the inverted segment (*v* and *f*). Since equationals for one chromosome only are detected, there is one chance in eight of detecting a crossover from a double exchange tetrad. Thus the twelve equationals indicate that there were actually 96 double exchange tetrads. Since a part of the females are eliminated, a corrected total must be used and the most direct way of getting this is to double the number of males. This gives 2196 as a corrected total. The frequency of double exchanges is then 4.4 percent. Using the information in table 15 we can subtract from the observed numbers of individuals those which carry products of double exchange. The remainder should give a measure of single exchanges. Single crossovers are directly recovered as closed chromosomes. The frequency of single exchanges is also measured by the deficiency of females as compared with males. The average of these two

measures of single exchange is 90.8 percent (assuming 50 percent as the value given by recovered closed chromosomes). The summary of the above operations is as follows:

	$\widehat{XX}$ females	X/X^c females	males	Excess of males over females
Observed	316	337	1098	445
Double exchange (4.4%)	36	24		36
Remainder	280	313		409
Single exchange (90.8%)	298.7	248.4		454.9

The two measures of single exchange agree with one another only approximately. However it is quite clear that the frequency of single exchange is high and approaches the frequency characteristic of the segment normally arranged. The distribution of the single crossovers in the inversion heterozygote is indicated by the data, and for the regions *y-v* and *v-f*, is approximately the same as that for normal chromosomes.

Crossing over in the segment between the right break of the inversion and the spindle attachment is very low as indicated by the low frequency of forked equationals. The one y^2 *v f c r* female recorded in table 16 is assumed to have resulted from double exchange within the inverted segment rather than from single exchange to the right of it.

In the case of $\widehat{XX}$ females heterozygous for short inversions, the closed chromosomes resulting from crossing over within the inverted segment are inviable in heterozygous condition and so cannot be recovered unless the duplications and deficiencies are compensated for in some way. However it is clear from the above discussion of attached-X In y-4 heterozygotes that the distortion of the sex ratio in itself can be used as a measure of crossing over.

Early experiments with $\widehat{XX}$ females heterozygous for In sc-7 consistently gave an excess of males over females. The results of three such experiments are summarized in table 17. These experiments indicated relatively high frequencies of exchange in the inverted segment and approximately normal crossing over between the inversion and the spindle-attachment, the latter result being in substantial agreement with those from free-X In sc-7 heterozygotes (p. 557). Since no particular precautions were taken to insure that male and female offspring were of comparable viability in these experiments, stocks more satisfactory with respect to the mutant genes used were made up and the experiments repeated. To decrease viability differences, relatively short egg-laying periods were used.

The results are summarized in tables 18 and 19. These data are in agreement with those from the first experiments in showing that crossing over to the right of the inversion is about normal (the sc-7 chromosome of the females whose progeny are summarized in table 19 apparently carried a semi-lethal mutant of unknown origin and the raw data must be corrected accordingly). However these experiments indicate a lower exchange frequency within the inverted segment than did the earlier ones. The inversion involves a segment 13 to 20 map units long. The data of tables 18 and 19 give crossover values of 9 and 10 percent (one half exchange frequencies).

TABLE 17

Progeny of $\widehat{XX}$ females heterozygous for inversion sc-7 mated to various males.

CONSTITUTION OF DAUGHTERS*	CONSTITUTION OF MOTHERS		
	sc-7 w^a v f	sc-7 w^a f	sc-7 w^a v B
	y^2 w^a ec f	y^2 w^a ec f	y^2 w^a ec f
+	267	206	155 (B/+)
sc-7	6	45	10 (B/+)
y^2 ec	53	24	18 (B/+)
sc-7 v	53		14 (B/+)
y^2 ec f			4
sc-7 v, B/B			5
B/B			2
f			1
y^2 ec, B/B			1
Total females	379	275	210
Corrected total females†	385	296	216
Total males	493	483	309
Exchange (%)	29.2	51.6	40.1

* Constitutions are given only with respect to genes heterozygous in the mother.

† Corrected total females obtained by adding to non-crossover phenotype, twice the number of equationals for the sc-7. The correction is for the indicated lower viability of equationals for y^2.

Experiments were made with In dl-49 using the same technique as for the later experiments with In sc-7. The results of two experiments with controls are summarized in table 20. The extent of the distortion of the sex ratio in the two series is not the same. The control experiments indicate that the difference is due to the difference in relative vaibility of the two kinds of males used. Making appropriate corrections of the number of males, the two series indicate exchange values for the inverted segment of 11.5 and 12.5 percent. Exchange in the segment between the right inversion break and the spindle attachment is measured by equationals for

genes within the inversion limits. The values indicated are 3.8 and 10.4 percent for the two series. The cause of the rather large difference is not known. Exchange in the segment to the left of the inversion is measured by equationals for *y* and by equationals for the genes *v* which are not equational for *y*. About all that can be said about the exchange frequency for this terminal segment is that it is low (less than 2 percent).

TABLE 18

Progeny of the cross sc-7 w^acr/y^2ct v f cr attached-X females by wild type males. Egg-laying periods; 3, 2 and 2 days.

FEMALES								TOTAL*	MALES	PERCENT EXCHANGE
cr	sc-7 w^acr	*y ct cr*	*y ct v cr*	*y ct v f cr*	*f cr*	*v f cr*	*v cr*			
629	124	27	79	45	2	3	1	937	1088	18.5

* Total corrected for indicated lower viability of sc-7 w^a

TABLE 19

Progeny of the cross sc-7w^a/y^2v f cr attached-X females by wild type males. Egg-laying periods 3, 2 and 2 days.

FEMALES										TOTAL*	MALES	PERCENT EXCHANGE
+	sc-7w^a	*y*	*y v*	*y v f*	*y v f cr*	*v f*	*f cr*	*f*	*v*			
393	2	14	66	8	1	1	1	1	1	575	679	20.4

* Total corrected as in table 18.

From the evidence considered above it is clear that single crossovers do occur between segments of chromosomes inverted relative to one another. The frequency of such crossovers evidently depends on the length of the

TABLE 20

Progeny of the cross dl-49 cm^2/y^2 v f cr attached-X females×Bar and + males and from control crosses of y^2 v f cr/y^2 v f cr attached-X females by Bar and + males. In each case, three egg-laying periods; 3, 2 and 2 days.

PROGENY	INVERSION		CONTROL	
	×B	×+	×B	×+
+ ♀♀	984	1672		
cm ♀♀	11	46		
y ♀♀	0	1		
y v ♀♀	2	10		
y v f ♀♀	4	28		
y v f cr ♀♀	5	18		
v f cr ♀♀	0	1		
Total ♀♀	1006	1776	590	841
♂♂	1004 (1101)*	2076 (1960)*	538	891

* Numbers in parentheses are corrected totals obtained by multiplying the observed numbers of males by the ratio of females to males in the appropriate control.

inverted segment and its position in the chromosome. These relations will be discussed in more detail in another connection (page 596). In any case we can say that long inversions such as In sc-8, In sc-4, and In y-4 show, with a normal chromosome, a high frequency of single crossing over between the inversion segments. These frequencies are of the same order of magnitude as those characteristic of these same segments arranged in the normal way.

EGG AND LARVAL-PUPAL MORTALITY

We have shown in the preceding section that single crossovers occur with a relatively high frequency in inversion heterozygotes. The question that we shall consider now is whether or not such crossovers result in inviable zygotes. This question can of course be directly answered by determining the amount of mortality in the progeny of heterozygotes for inversions known to give a high frequency of single crossing over within the inverted segment.

Technique

The method that we have used in determining the amount of mortality is essentially the same as that commonly used by other workers (e.g., L. V. MORGAN 1933). Certain modifications were found useful. Paper spoons have usually been used as containers for the medium on which the eggs are collected. They have two disadvantages: (1) the surface of the medium is usually not flat and (2) the depth of the medium varies which often results in drying out around the edges. To overcome these disadvantages small metal (nickel has been found satisfactory) containers about 38 mm long, 17 mm wide and 3 mm deep were made. A handle of the same material about 10 mm wide was soldered to the bottom so that it projected about 3 cm.

The standard cornmeal-molasses-agar medium with the addition of animal charcoal (to increase the contrast between eggs and medium) was liquified, pipetted into the containers and allowed to cool. The flat surface was then painted with a rather heavy yeast suspension. The addition of fermented banana, alcohol or wine was found to be of no advantage. A single female was allowed to deposit eggs on the medium for a period of 24 hours. The container was then removed from the vial and replaced with one containing fresh medium. After removing the container the food was removed from it with a strip of cardboard of appropriate size. The eggs, including those already hatched, were then counted and recorded. The food was placed in a vial at 25°C in a moist incubator for 28 hours after which time the unhatched eggs were counted. The food block was then placed in a standard half pint culture bottle and the flies allowed to develop to maturity. Unless care is taken to have the outside of the food con-

tainer dry there is danger in error from eggs deposited on the sides of the container. The larvae from these eggs may hatch and crawl onto the food block. There is also some error in losing or killing a few larvae in handling the food blocks. The magnitude of these errors can be kept reasonably low with careful manipulation.

Our experience indicates that the percentage of egg mortality is dependent upon the genetic constitution of the mother as well as upon the genetic constitution of the eggs themselves. Thus females from inbred stocks or females homozygous for several recessive genes generally give relatively high mortality regardless of the type of males to which they are mated. Because of this fact, strictly comparable controls cannot be had. To minimize this "residual" egg mortality, crosses between more or less unrelated stocks were made wherever possible and the F_1 females from not overcrowded cultures were used in the egg-laying experiments. Normal controls more or less comparable in genetic constitution were run simultaneously with the experiments on inversion heterozygotes.

Results

The results of our experiments on In sc-4, In sc-8, In y-4, and In dl-49 heterozygotes are summarized in table 21. The answer to the question that we set out to study is quite clear: single crossovers do not give rise to inviable zygotes. In the cases of In sc-4, In sc-8 and In y-4 exchange is approximately normal in frequency. If the distribution of the four strands of a tetrad were random at meiosis, we should expect about half the products to be single crossovers or their equivalent. Since such crossovers are not recovered in the viable zygotes they would have to be eliminated as inviable zygotes. However, it is evident that inviable zygotes do not approach 50 per cent in frequency. Since these inversion heterozygotes produce an appreciable number of patroclinous males (about 3 to 5 percent of the viable zygotes) we know that there should be a corresponding frequency of inviable zygotes (no-X eggs fertilized by Y-carrying sperms). In these cases crossing over could be followed sufficiently well to know that the inversion heterozygotes were giving the usual results. In addition the frequency of patroclinous males was determined and found to be approximately "normal" for the inversion heterozygotes under consideration. When the data are considered in connection with the frequencies of patroclinous males produced (page 595) and with the controls, and when allowance is made for the difference in genetic constitution between inversion heterozygotes and controls, we can conclude that the only zygotes whose death is the direct result of the presence of the inversion in the parent females are those corresponding to patroclinous males and differentiated from them by the sperm.

STONE and THOMAS (1935) have also published egg counts for In sc-8/+ and In dl-49/+. The mortality indicated is higher than in our data, as it is also for their controls. They have also not distinguished between egg mortality and larval-pupal mortality. It seems clear that the lowest adequately established mortality is the one that gives the best picture of the case; and it is to be noted also that STONE and THOMAS conclude, as do we, that single crossovers are not responsible for any detectable portion of the observed mortality.

TABLE 21

Egg and larval-pupal mortality data for inversion heterozygotes.

MATING	TOTAL EGGS	INVIABLE	PERCENT INVIABLE	HATCHED EGGS	ADULT FLIES	PERCENT EMERGENCE OF HATCHED EGGS
y sc-4 *v f cr*/+×*B*	2839	214	7.5	2625	2187	83.4
sc-8 w^a *cv v f*/y^2–×*B*	4190	284	6.8	3906	3745	96.0
y^{2S}/*B* (control for above)×*B*	3947	52	1.3	3895	3741	96.2
sc-8 *B*/w^a *v*/*Y*×y^{2S}	1313	184	14.0	1129	990	87.6
+/w^a *v* (control)×y^{2S}	1018	26	2.5	992	991	99.9
dl-49/+×*B*	1645	51	3.1	1594	1525	95.7
y-4/*v* g^3×*w*	884	68	7.7	816	753	92.4
y-4/y-4×*w*	570	113	19.8	457	375	82.2

Data from XXY In sc-8 heterozygotes are included in table 21. Here both egg and larval-pupal mortality is relatively high. This is of course expected from the fact that here secondary non-disjunction occurs with an appreciable frequency (page 582). The frequency of inviable eggs is of the same order of magnitude as that of exceptional males (YY or YX zygotes, depending upon the sperm) and larval-pupal mortality is of the same order of magnitude as exceptional females (XXX or XXY zygotes, depending upon the sperm).

In connection with studies of sister-strand crossing over, SCHWEITZER and KALISS (1935) have made extensive determinations of egg mortality in inversion heterozygotes. Their results are in agreement with the conclusion we have drawn that single exchanges between inverted segments do not result in inviable zygotes.

THE MECHANISM OF DISJUNCTION IN INVERSION HETEROZYGOTES

It has been shown in preceding sections that single exchanges occur within the inverted segment of inversion heterozygotes, and further, that the crossover products of single exchange are not recovered and do not result in inviable zygotes. It is evident that we must assume that such single crossover chromatids are selectively eliminated during the meiotic process.

It has also been shown that X chromosome inversion heterozygotes give rise to patroclinous males among their progeny. We have implied that the frequency of such exceptional males is a function of double exchange.

The problem that we shall consider is how these two results, (1) elimination of single crossover chromatids and (2) the production of no-X eggs, are brought about. We know from cytological studies on plants (Zea, McCLINTOCK 1933; Tulipa, STONE 1933; Vicia, MATHER 1934; Trillium, SMITH 1935) that double spindle attachment chromatids resulting from crossing over between segments inverted with respect to one another produce chromatin ties between the two poles of the first meiotic division (or under certain conditions to be considered below, between poles of second meiotic spindles). Knowing that the four nuclei resulting from meiosis in

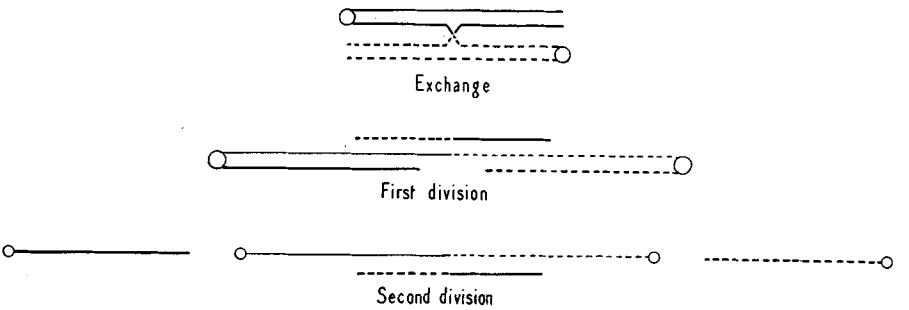

FIGURE 6.—Single exchange within a heterozygous inversion. The upper figure represents the two X's of a female in which one chromosome is practically wholly inverted. At the first meiotic division there results a chromatid tie; this leads to an orientation of the second division such that the two terminal nuclei receive only non-crossover chromatids; one of these is the egg nucleus. The result is the total loss of all single crossover chromatids to the polar body nuclei.

the Drosophila egg lie approximately on a single straight line (HUETTNER 1924), we are prompted to propose the following scheme for the X chromosome of Drosophila.

1. A single chromatid tie at the first meiotic division results in orientation of the spindle attachments in such a manner that only chromatids with a single spindle attachment get into the terminal nuclei, one of which will become the egg nucleus (HUETTNER 1924).

2. A double chromatid tie results in the formation of end nuclei with no X chromosome, and a no-X egg will result.

The behavior of various types of crossover tetrads expected according to this scheme is shown diagrammatically in figures 6 and 7.

As to the precise nature of the orientation of single exchange tetrads or their equivalent we have insufficient information; we know only the end result. It seems reasonable to suppose that the orienting influence of a double attachment chromatid is mechanical. However, we do not know

whether or not such chromatids in Drosophila break during the division as they are known to do in the plants mentioned above. If they break, the orientation probably results from the retardation prior to breakage. Single crossover chromatids without spindle attachments are probably not included in either daughter nucleus but lost in the cytoplasm during division as is known to be the case in plants (McCLINTOCK 1933).

From the diagrammatic representation of the suggested scheme (figs. 6 and 7), it is evident that certain quantitative relations should hold. These

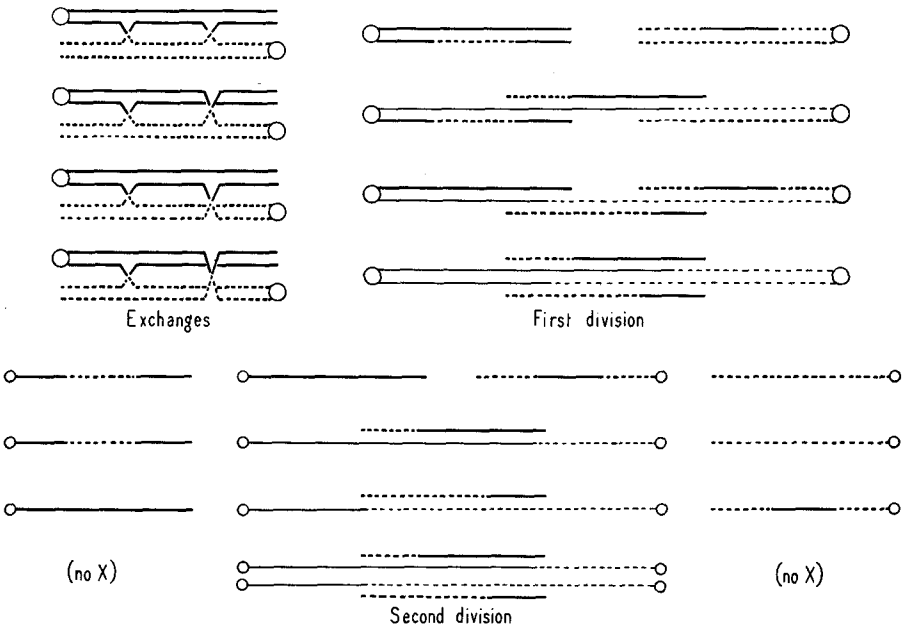

FIGURE 7.—The four possible types of double exchange within a heterozygous inversion. The two-strand exchange (upper row) leads to equal numbers of non-crossover and double crossover chromatids in the terminal nuclei, each of which will be the egg nucleus in half the cases. Three-strand doubles (second and third rows) result in chromatid ties at the first division, and also lead to equal numbers of non-crossover and double crossover chromatids in the egg nuclei. Four-strand double exchange (fourth row) leads to a double tie at the first division, and to no-X egg nuclei.

should serve as tests of the assumptions we have made. The types and frequencies of gametes expected to result from non-, single, double, and triple exchange tetrads are summarized in table 22. It is seen that from double exchange tetrads, double crossover and no-X gametes are expected to occur in the ratio of 3:2. This 3:2 ratio was also found experimentally by STONE and THOMAS (1935) for In sc-8 and for another long inversion that we have not studied. For the longer inversions some triple exchanges presumably occur and these give double crossover and no-X gametes in the ratio of 21:4. Since we have no way of measuring the relative frequencies

of double and triple exchanges in inversion heterozygotes (because triple crossover chromatids must be eliminated) we cannot predict precisely what the ratio of double crossover to no-X eggs should be. However, if we make the assumption that the frequency of triple relative to double exchanges in inversion heterozygotes does not exceed that of normal X chromosomes (about 1:10), then the ratio of double crossover to no-X gametes should lie between 3:2 and 3.4:2.

The numerical data showing the relation of double crossovers to patroclinous males are given in table 23. Half the no-X eggs are lost (fertilization with Y sperm) and in the cases recorded in the table, half the double crossovers were not detected since only male offspring were used to measure crossing over. Hence the zygotic ratios expected are the same as the gametic ratios mentioned above and given in table 22. The observed relative frequencies approach rather closely the ratio 3:2. In no case is the deviation from 3:2 statistically significant. The totals approach very closely a

TABLE 22

Relative frequencies of types of gametes produced following single, double, and triple exchange within the inverted segment of an X chromosome tetrad.

EXCHANGE	DESIGNATION*	NON-CROSSOVER	DOUBLE CROSSOVER	NO-X EGG
None		1	0	0
Single		1	0	0
Double	2 (1)	1	1	
	3 (2)	2	2	
	4 (1)			2
	Total	3	3	2
Triple	2, 3, 3 (4)	4	4	
	2, 4, 4 (2)		4	
	2, 2, 2 (1)	2		
	3, 4, 3 (2)			4
	3, 2, 3 (2)	1	3	
	3, 3, 4 (4)		8	
	4, 2, 4 (1)		2	
	Total	7	21	4

* Doubles are designated by the number of strands involved in the two exchanges; triples in the same way by considering them as three doubles, taking successive exchanges a, b and c in combinations of two in the order a-b, a-c, and b-c, and in this case, disregarding the direction (a-b-c is equivalent to c-b-a). Relative frequencies of different types among doubles or among triples are indicated by numbers in parentheses.

The frequencies of gametes (totals of last three columns) must in each case be proportional to the frequencies of occurrence of the types of exchange (numbers in parentheses). This is true even in the case of two-strand doubles, where the potentially good chromatids are twice as numerous as in the case of three-strand doubles, since each tetrad gives rise only to a single gamete. The same principle applies also to triples.

ratio of 3:2; the actual observed small deviation is in the direction expected to result from triple exchanges. The inversion heterozygotes known to give approximately normal crossing over (sc-4, sc-8 and (Df sc^8) actually are the ones that give the higher ratios. The results expected on the pro posed scheme of disjunction in inversion heterozygotes are thus in quantitative agreement with the experimental data.

TABLE 23

Relative frequencies with which double crossovers and patroclinous males are recovered from inversion heterozygotes. In all cases double crossovers as recovered in males only are recorded.

CONSTITUTION	DOUBLE CROSSOVER MALES	PATROCLINOUS MALES	CALCULATED (3:2)		ACTUAL RATIO
sc-4/+	108	63	102.6	68.4	3.4:2
sc-8/+	93	57	90.0	60.0	3.3:2
Df (sc-8)*/+	60	31	54.6	36.4	3.9:2
y-4/+	57	51	64.8	43.2	2.2:2
Df (bb)/+	93	66	95.4	63.6	2.8:2
sc-4/sc-7	11	7	10.8	7.2	3.1:2
	422	275	418.2	278.8	3.1:2

* Number of double crossovers corrected, owing to lethal nature of Df (sc-8).

The scheme proposed should enable one to predict quantitatively the results from closed-X heterozygotes. These have been studied by L. V. MORGAN (1933). Her results differ from those expected according to the scheme formulated from our knowledge of inversion heterozygotes in two important respects:

1. Among the progeny of X/X^c, X is recovered more frequently than X^c.

2. Egg mortality is too high relative to the frequency of recovered double crossovers.

The inequality of X and X^c among the progeny was ascribed by L. V. MORGAN to differential viability. The egg mortality data led her to conclude that single exchanges result in inviable zygotes. Fortunately a second closed-X chromosome was found by Mr. R. D. BOCHE of this laboratory. This closed-X has an advantage over the original X^c used in the experiments of L. V. MORGAN in that it has less effect on viability. We have made several experiments with X^{c-2} heterozygotes set up especially to test the scheme proposed in this paper. The results of these experiments are to be presented in another paper but we can say here that both discrepancies mentioned above appear now to be viability effects. The results obtained from X/X^{c-2} and X^{c-2}/X^{c-2} females are in as good agreement with those predicted from the assumptions we have made in this paper as could reasonably be expected.

We have pointed out that single exchange between two segments inverted relative to one another does not result in inviable zygotes. In the case of attached-X inversion heterozygotes we have pointed out that following certain types of single exchange a chromatid tie is formed during the second meiotic division. From the numerical data we concluded that the condition in which the X chromosome spindle attachment is tied to a spindle attachment in the nucleus lying next in line does result in an inviable egg. There is another case in which single exchange within the inverted segment should result in a chromatid tie at the second division. This is where a single exchange within the inversion is accompanied by a second exchange outside the inversion of such a nature that the two exchanges make a three-strand double exchange. SMITH (1935) has observed this result cytologically in Trillium. In the inversions dealt with in our experiments, lethal eggs from this source would be very infrequent except for the case of In sc-7. This inversion is the only one that we have used in which exchange in the heterozygote is frequent both inside and outside the inverted segment. Here, however, the mortality has not been studied.

EFFECTS OF INVERSIONS ON FREQUENCY OF CROSSING OVER

a. Homozygous inversions. The data are in agreement with earlier conclusions (STURTEVANT 1931) that homozygous inversions show about the same total amount of crossing over as do homozygous normals. They are also in agreement with the conclusions of BEADLE (1932) and of OFFERMAN and MULLER (1932) that the distribution of this crossing over is altered by relation to the spindle attachment, a given section giving less crossing over if it is near the attachment, more if it is near the free end of the chromosome.

b. Heterozygous inversions. The effects on crossing over are, as might be expected, different for sections within the inversion and those outside it, and are also dependent on the length and position of the inversion concerned.

Crossing over within the inversion is evidently decreased in heterozygotes for In sc-7 and In dl-49 (pp. 586–588), and is probably decreased in In ClB since so few doubles are recovered. The other inversions studied here, all of them longer than these, seem to have much less effect on crossing over within the inversion, though the data are scarcely adequate to permit the conclusion that there is no effect.

Crossing over in sections outside the inversion is regularly reduced. In sc-4 and In sc-8 do not leave any sections uninverted in which crossing over occurs in normal flies and can be measured in inversion heterozygotes. The same is true for the sections to the left of In sc-7 and In y-4 and for that to the right of In Df (bb). The remaining seven uninverted

sections all show a reduction in crossing over, localized close to the inversion itself to the right of In sc-7, relatively slight to the right of In dl-49, and very marked in the other cases, namely, on both sides of In ClB, to the left of In dl-49 and of In Df (bb), and to the right of In y-4.

These data are in approximate agreement with expectations from the competitive pairing hypothesis of DOBZHANSKY (1931). A short inversion may be supposed to have its pairing more interfered with by the uninverted sections than does a long inversion which has shorter uninverted sections. Conversely, a long inversion may be supposed to interfere more seriously than a short one with the pairing of the uninverted sections.

One other relation is suggested here, as it is by the data on autosomal inversions (STURTEVANT 1931); namely that an inversion is more effective in suppressing crossing over in segments distal to itself than in proximal segments. This relation is difficult to analyze, and of the present series of inversions dl-49 seems to be the only one favorable for its study. What is needed is a comparative study of a larger series of more diverse types of inversions than we have used. This need is supplied in part by STONE and THOMAS (1935), who reach conclusions similar to the one just suggested.

THE EFFECTS OF THE Y CHROMOSOME ON CROSSING OVER

The most extensive series of data on the effects of a Y chromosome on crossing over is that of BRIDGES and OLBRYCHT (1926). DR. BRIDGES informs us that the XXY females there recorded gave, in addition to the published results, 246 exceptional offspring (2.5 per cent). Correcting the data (by adding twice the number of exceptions to the non-crossover class in the case of XXY females) gives the following comparisons:

	sc	*ec*	*cv*	*ct*	*v*	*g*	*f*	total	N
XX	6.7	8.8	8.2	14.4	11.3	12.3		54.5	11325
XXY	6.5	9.1	8.3	14.2	10.1	9.7		50.8	9461
XX/XXY	1.03	.97	.99	1.01	1.12	1.27		1.07	

Evidently the Y has no effect on crossing over in the region from *sc* to *v*, reduces *v-g*, and reduces *g-f* still more. This is in agreement with the results on duplications described by DOBZHANSKY (1934), since the Y is homologous only with the right end of the X, and reduces crossing over only in the portions of the X near this homologous section.

The results recorded in this paper for comparable XX and XXY females can also be interpreted in terms of the hypothesis of "competitive pairing" (DOBZHANSKY 1931). In Df(bb)/+ gives no effect of the Y, as might be expected, since Df(bb) presumably carries little or no material homologous to the Y. In the cases of sc-4/+ and y-4/+ there is an increase of double

crossing over within the inversion, which may be looked upon as due to interference of the Y with pairing of the attachment ends of the X's, this in turn leading to less interference of these attachment ends with full pairing of the inverted segment. In the case of dl-49/+ the crossing over studied is that between the inversion and the spindle attachment; the data are in agreement with the analysis just given in that they indicate a decrease in crossing over due to the Y. The one remaining case in which we have comparable data is that of y-4/Df(bb), where the frequency of singles within the common inverted region seems to be unaffected by the presence of a Y, as would have been expected.

SECONDARY NON-DISJUNCTION

XXY females of all kinds give segregation of two chromosomes to one pole, one to the other (X-XY or XX-Y). The inversions affect the relative frequencies of these two types, and therefore a fuller understanding of the meiotic behavior of inversions should throw light on the mechanism of secondary non-disjunction.

If p be taken as the frequency of XX-Y segregation, then assuming random fertilization by X sperm and Y sperm and death of the XXX and YY classes, the frequency of recovered exceptions, q, will be $\frac{p}{2-p}$.

The earlier analyses of secondary non-disjunction (BRIDGES 1916, ANDERSON 1929, GERSHENSON 1935) have been based on the assumption that the maximum frequency of XX-Y segregation occurred when one X separated from Y and the other X went to either pole at random. This gives $p=.5$, $q=.333\%$. GERSHENSON himself obtained, from In ClB/+, $q=.353\pm .0040$ in the female classes, a deviation about five times the probable error. Adding our data the value becomes $.366\pm.0038$, a deviation of .033 or nearly 9 times the probable error. In the case of In dl-49/+ the female data of table 14 give $q=.456\pm.0051$, a deviation of .123, 24 times the probable error.

There can be no doubt, then, that XX-Y segregation can occur with a frequency greater than 0.5. As a matter of fact the dl-49/+ value for q (.456) gives $p=.626$.

It becomes necessary, therefore, to search for a new interpretation of secondary exceptions. As pointed out by Bridges (1916), nearly all the exceptional females from +/+/Y mothers are non-crossovers, carrying the same two X's as their respective mothers. The same relation holds for In/+/Y exceptions, as shown by GERSHENSON (1935) and by our own data. In both types of experiments occasional exceptions are found with crossover chromosomes; but these are little, if any, more frequent than are

such crossover exceptions from XX mothers; they may safely be disregarded in analyzing the effect of the Y on non-disjunction. Secondary exceptions, then, carry two unlike non-crossover chromatids. The failure of separation must take place at the first meiotic division, rather than the second, since the latter would give two *like* chromosomes. This is true provided Drosophila agrees with plants in having the first division reductional for spindle attachments. Indirect evidence as well as direct cytological evidence (KAUFMANN, 1935) indicates that this assumption is correct. It may be concluded also that secondary exceptions result from X-*tetrads* in which no crossing over occurred, for otherwise one would have to assume that the orientation of sister chromatids on the second meiotic spindle was not random. This is contrary to what is known in other cases; and even this assumption would not suffice to account for 3-strand or 4-strand doubles.

If secondary exceptions arise from non-crossover X tetrads, the next step is to determine the frequency of such tetrads in various kinds of females and to compare this with the frequency of non-disjunction in such females. This can be done best in the case of In dl-49. As shown above, XXY dl-49/+ females gave about 1 percent exchange to the left of the inversion, 12 percent in the inversion, and 20 percent to the right of the inversion. There are probably not over 3 percent multiple crossovers here, so 30 percent is not far from the true value for the crossover X-tetrads. (Three-strand multiples where one crossover is in the inversion and one is outside it should give rise to inviable eggs; the data presented above show that these are negligible in frequency.) Therefore, among the 70 percent non-crossover X tetrads, 62.6 or 90 percent give rise to non-disjunctional gametes. If we use the frequency of exceptional females actually observed in the same experiment in which crossing over was studied, we find that 66/79 or 83 percent of the non-crossover X tetrads gave XX-Y segregation. This does not take into account exchanges within the inversion. There can be little doubt that 90 percent is too low rather than too high a value. If one assumes that this same proportion holds in all cases the resulting deduced frequencies of complete non-crossover X tetrads (for example 9 percent for +/+/Y) seem not unreasonable. In any case, the proportion .667 suggested by BEADLE and STURTEVANT (1935) by analogy with the fourth chromosome is clearly incorrect for dl-49/+.

Table 14 shows that the frequency of secondary exceptions rises as the total frequency of crossing over decreases in the various inversion combinations. Changes in the reverse direction have not been recorded in *D. melanogaster*, but other species give more crossing over; that is, they have longer crossing over maps and presumably fewer non-crossover tetrads. The available data are shown in table 24. The map lengths given are

probably too short, especially in *willistoni* and *pseudoobscura*, owing to fewness of available loci for study. Other species have been omitted because this element of uncertainty is even greater. It is clear that the table is in agreement with expectation.

TABLE 24

Comparison of species.

SPECIES	SECONDARY EXCEPTIONS		TOTAL MAP LENGTH OF X	
	%	AUTHORITY	UNITS	AUTHORITY
melanogaster	4.3	Bridges 1916	66	Bridges, unpubl.
simulans	2.9	Sturtevant 1929	70	Sturtevant 1929
willistoni	1.7	Lancefield and Metz 1921	84	Lancefield and Metz 1922
virilis	0.5	Kikkawa 1932	182	Kikkawa 1932
pseudoobscura	0	Schultz and Redfield, unpubl.	170	Lancefield 1922

The frequency of secondary exceptions thus shows strong negative correlation with the frequency of tetrad crossing over. Since the latter value is not greatly affected by the presence of a Y, whereas the former is, it may be concluded that the frequency of secondaries is dependent on the occurrence of non-crossover tetrads, rather than the reverse.

NORMAL DISJUNCTION OF X'S

In the case of dl-49/+ the data show about 14 percent crossing over (28 percent exchange) between the spindle attachment and the inversion. The attached-X data show about 12 percent exchange within the inversion. These results are from XXY females; in the cases of other inversions the presence of a Y has been shown to give a slight increase in crossing over within the inversion. There is a small percentage (about 1 percent) of exchange between the inversion and the free end. The indicated total frequency of exchange is thus 41 percent. There is a fairly large probable error attached to this value; but, since there are probably some double exchanges involved, it seems safe to conclude that at least half the tetrads undergo no exchange.

The data of table 14 show, from this combination, no matroclinous females in a total of 3238 daughters. It follows that exchange is not necessary for normal disjunction. This conclusion can be avoided only by supposing that undetectable exchanges occur between the known genes and the attachment end of the chromosome. This supposition has no evidence in its support and is made unlikely by the absence of matroclinous females from In Df(bb)/+ and their presence only in numbers similar to those given by +/+ in the cases of In sc-8/+ and In Df(sc-8)/+. These three cases

all involve inversions that upset the homology well within the inert region, and might well be expected to interfere with crossing over in the region concerned.

The results here reported may, then, be taken as supporting the conclusion, which is probable on other grounds, that crossing over is not a necessary requirement for regular disjunction of the X chromosomes of *Drosophila melanogaster*.

POPULATION MECHANICS OF INVERSIONS

The scheme for inversion crossovers here developed should apply in all cases of inversions that do not include spindle attachments, since singles within such inversions should always give ties between first meiotic nuclei. The resulting selective eliminations of crossover chromatids may be expected in any case where three of the four products of meiosis are eliminated, the effective one being terminal (in terms of the orientation of the second division spindles). These conditions hold in the oögenesis of most animals and in the megasporogenesis of most seed-plants. In such forms as the Ascomycete Neurospora, where all the products of meiosis are potentially functional but are still arranged in a line, inversions of the type under discussion should lead to non-functioning of "inner" nuclei in much higher proportions than terminal ones. In plants the result will be the production of numerous inviable pollen grains, but no increase in egg inviability. There will therefore be no decrease in fertility, a circumstance that must prevent the rapid elimination of inversions through a reduced rate of reproduction. In animals the aberrant sperm will presumably be viable and functional, but will lead to the production of inviable zygotes and therefore to reduced fertility. In Drosophila this result is not brought about because of the absence of crossing over in the male.

A mechanism that increases the number of gametes carrying a single complete haploid set of chromosomes exists also in the case of heterozygotes for reciprocal translocations, where there is a higher frequency of "regular" than of "irregular" gametes in most cases. Here, however, there is no marked sexual difference, and the frequency of irregulars is high enough to produce an appreciable decrease in fertility in most (probably in all) cases. These relations are probably responsible for the observation that, within a given species of Drosophila, wild populations carry inversions far more frequently than translocations.

Inversions that include the spindle attachment cannot produce a chromatid tie, and will therefore decrease fertility if single exchanges occur within them. This is probably the explanation of the fact that no such inversions have been found in wild populations of Drosophila, though they do occur as a result of X-ray treatment.

SUMMARY

1. Seven inversions are discussed. Their nature is illustrated in figure 1.

2. The results obtained from females heterozygous for two inversions are described. The properties of the chromosomes produced by single crossing over within the common inverted sections are summarized in table 11.

3. The frequencies of matroclinous females and patroclinous males from the combinations studied are shown in table 14.

4. Females carrying attached X's, in one of which there is an inversion, give rise to closed X's by single crossing over within the inversion.

5. Egg counts show that the mortality from inversion heterozygotes can all be accounted for as due to the fertilization of no-X eggs by Y sperm. This is very much less than the indicated frequency of single crossover chromatids.

6. Since single crossovers are produced but are not recovered, they must be eliminated from the egg at meiosis, leaving a non-crossover chromatid in the reduced egg.

7. A scheme for such oriented divisions is shown in figures 6 and 7. This is based on cytological observations on plants and on the observed geometrical relations of the meiotic divisions in the Drosophila egg.

8. According to this scheme, crossover chromatids with two spindle attachments form ties between two nuclei at the first meiotic division, resulting in the tied chromatid failing to pass to either terminal pole; or at the second division, resulting in death of the egg when the egg nucleus is concerned.

9. This scheme results in several numerical predictions, which are borne out by the data:

(a) matroclinous females from XX mothers are not increased in frequency by inversions.

(b) patroclinous males are to recovered double crossover males as 2:3.

(c) egg mortality is practically equal to the frequency of patroclinous males.

10. Inversions, and also the presence of a Y chromosome, decrease crossing over in accordance with the hypothesis of competitive pairing.

11. Females (XX) heterozygous for inversions may give many no-exchange tetrads; these segregate normally, with the production of no significant number of XX gametes.

12. In XXY females that are dl-49/+, 90 percent or more of the eggs in which no exchange occurs give XX-Y segregation. Similar frequencies are probable in all cases studied.

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