THE MEIOTIC EFFECT OF A DEFICIENCY IN *DROSOPHILA MELANOGASTER* WITH A MODEL FOR THE EFFECTS OF ENZYME DEFICIENCY ON RECOMBINATION

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ABSTRACT

The meiotic effects of heterozygosity for a deficiency of the zeste-white region of the *X* chromosome include reduced recombination and increased nondisjunction of the entire chromosome complement. Reduced dosage of a gene or genes in the zeste-white interval, rather than structural heterozygosity, is responsible for the meiotic effect. A model for the recombination effects of reduced enzyme concentration has been developed, and its consequences are comparable with the results obtained for deficiency heterozygosity. Thus, all of the observations can be accounted for by imagining a dosage-sensitive locus in the zeste-white region that codes for an enzyme involved in the recombination process. The interaction of the interchromosomal effect of heterozygous inversions with the deficiency has been examined, and the possibility of using the model for the analysis of other meiotic phenomena is considered.

SINCE the initial systematic search for mutants of *Drosophila melanogaster* that affect meiotic chromosome behavior (SANDLER *et al.* 1968), numerous papers have appeared recounting the analysis of these mutants, the analysis of mutants discovered earlier, and the analysis of more recently isolated mutants (see BAKER *et al.* 1976b for review).

A broad spectrum of mutants has been found with remarkably high frequency both in natural populations and after mutagen treatment. For example, BAKER and CARPENTER (1972) tested 189 EMS-treated *X* chromosomes and found eleven *X*-linked mutants that cause from 7-fold to over 400-fold increased *X* chromosome nondisjunction in females. Whether or not the wild-type alleles of all or most of these genes are directly involved in the meiotic process remains, however, unproven.

Two explanations are possible for the evidently large number of genes that, when mutant, affect meiosis. The process may be controlled directly by a large number of genes, or the process may be intricate, delicate, and sensitive to a variety of physiologic alterations that are not unique to meiosis. That the latter may be true does not vitiate the use of meiotic mutants in analyzing the control flow of meiosis, but does require some care in the inferences one draws about the role of the wild-type gene as opposed to the effect of the mutant.

The strongest of the meiotic mutants have proven most tractable for the analysis of meiotic control, and some of these mutants are indeed in genes directly involved in DNA metabolism (BAKER *et al.* 1976a; BOYD, GOLINO and SETLOW 1976). The weaker mutants, however, are less easily used for the analysis of meiotic control and have received less scrutiny.

Without knowledge of the actual molecular basis of a meiotic effect, conclusions about the wild-type function are necessarily inferential. Though it is possible to devise some hypothesis about the meiotic function altered by a mutant, it is generally not possible to ask whether that effect is a direct one or is an indirect, pleiotropic one. The analysis of the meiotic effects of a deficiency adds one element to the base from which inferences may be drawn; the nature of the defective gene is known—it is absent. It is possible to determine whether a point mutant is a neomorph, an amorph, or a hypomorph (though that has not yet been accomplished for any of the meiotic mutants), but it is not possible by genetic analysis alone to determine the molecular basis of the defect. For example, alteration of substrate binding, catalytic activity, turnover rate, or enzyme production could all be effects of hypomorphic mutants at a single locus. For a deficiency, however, one can at least ask if the meiotic anomaly is consistent with a direct meiotic effect of reduction of the amount of a gene product.

It was fortuitously noticed in the course of a mutant screen that heterozygosity for *Df(1)w*^{rJ1}, a small *X*-chromosome deficiency, affects chromosome behavior. An examination of the nature and cause of these effects was undertaken to ask whether the effects of *Df(1)w*^{rJ1} heterozygosity could be ascribed to reduction in amount of a gene product required for normal meiosis. This paper presents: (1) evidence that heterozygosity for *Df(1)w*^{rJ1} causes abnormal behavior of both the *X* chromosomes and autosomes, (2) a demonstration that these effects result from the abnormal gene dosage of the deficiency heterozygote, (3) an examination of the nature of the defective recombination and disjunction processes of the deficiency heterozygote, and (4) a model for the recombination effects expected from reduction in the amount of a gene product.

CROSSES AND RESULTS

Except where noted, the chromosomes and markers used in these experiments are described in LINDSLEY and GRELL (1968).

The existence of a meiotic effect of Df(1)w^{rJ1} *heterozygosity*

To determine whether behavior of the entire complement is affected by heterozygosity for *Df(1)w*^{rJ1}, disjunction of the *X*, second and fourth chromosomes, and exchange in the *X* and second chromosomes were examined.

Recombination and disjunction of the *X* chromosomes was examined by crossing *Df(1)w*^{rJ1}, *y*^{2} *sn*^{3}/*Dp(1;1)sc*^{v1}, *y pn v·y*$^{+}$ and control, *y*/*Dp(1;1)sc*^{v1}, *y pn v·y*$^{+}$, females to *Y*^{S}*X·Y*^{L}, *In(1)EN*, *y B/O* males. The results are shown in Table 1. *Dp(1;1)sc*^{v1}, *y pn v·y*$^{+}$ allows recombination to be scored in two nearly equal segments covering almost the entire length of the *X* chromosome,

TABLE 1

X-chromosome recombination and disjunction in females heterozygous for a deficiency of the zeste-white region

Female tested	Regular females	Exceptional Males	Exceptional Females	Regular males: Non-crossover	Regular males: Single crossover *pn-v*	Regular males: Single crossover *v-y*+	Regular males: Double crossover
$\frac{y\ rst^2}{y\ pn\ v{\cdot}y+}$	5372	2	0	3869	1763	1851	363
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y+}$	5386	45	37	2417	726	745	14

Female tested	Map distance *pn-v*	Map distance *v-y*+	Coefficient of coincidence	Exchange rank E_0	Exchange rank E_1	Exchange rank E_2	Nondisjunction/10^3 gametes
$\frac{y\ rst^2}{y\ pn\ v{\cdot}y+}$	27.1	28.2	0.61	0.079	0.736	0.185	0.3
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y+}$	19.0	19.5	0.10	0.246	0.740	0.014	12.3
Effect	0.30	0.31	0.84	——	−0.01	0.92	——

The frequency of nondisjunction was calculated as described in the text, while the parameters of exchange were calculated from the frequencies of crossover and noncrossover regular males. The effect of deficiency heterozygosity on exchange parameters is calculated as the fractional reduction of that parameter in the deficiency heterozygote compared to the control $\left(= 1 - \frac{\text{parameter in deficiency heterozygote}}{\text{parameter in control}}\right)$. The effect is positive if the parameter is reduced by deficiency heterozygosity and negative if it is increased.

and *X*-chromosome nondisjunction is readily detected by the production of B^+ matroclinous females and *B* patroclinous males. Calculation of the frequency of nondisjunction would have to be handled differently for second division nondisjunction than for first division nondisjunction in deficiency heterozygous females, as deficiency homozygotes would be lethal. There is, however, no indication that any of the nondisjunction occurs at the second division, as none of the matroclinous offspring were homozygous for the $Dp(1;1)sc^{v1}$ markers. Thus, since half of the nondisjunctional gametes produced by both deficiency heterozygotes and by control females are recovered as surviving zygotes, the number of exceptional progeny is doubled in calculating the frequency of nondisjunction. In addition, since $Df(1)w^{rJ1}/O$ zygotes do not survive, the number of regular males is doubled in calculating the frequency of nondisjunction in the deficiency heterozygotes.

Nondisjunction is substantially more frequent in the deficiency heterozygotes and recombination is reduced in both halves of the *X* chromosome. The frequency of double exchanges is more severely affected by deficiency heterozygosity than is the frequency of single exchanges, and the coefficient of coincidence is reduced.

TABLE 2

Second chromosome recombination in females heterozygous for a deficiency of the zeste-white region

Female tested	Noncrossovers	Single crossovers				Double crossovers						Triple crossovers	
		1	2	3	4	1,2	1,3	1,4	2,3	2,4	3,4	1,2,3	1,2,4
$\frac{y\ rst^2}{+}\ \frac{b\ pr\ c\ px\ sp}{+}$	3401	248	1059	1266	394	115	101	29	97	38	6	5	2
$\frac{Df(1)w^{rJ1}}{+}\ \frac{b\ pr\ c\ px\ sp}{+}$	3039	94	436	721	222	20	35	2	17	9	2	0	0

	Map distances				Exchange rank			Coefficient of coincidence						
	1	2	3	4	E_0	E_1	E_2	Average	1,2	1,3	1,4	2,3	2,4	3,4
$\frac{y\ rst^2}{+}\ \frac{b\ pr\ c\ px\ sp}{+}$	7.3	19.4	21.8	6.9	0.12	0.65	0.23	0.54	1.2	0.94	0.85	0.34	0.42	0.06
$\frac{Df(1)w^{rJ1}}{+}\ \frac{b\ pr\ c\ px\ sp}{+}$	3.3	10.5	16.9	5.1	0.36	0.57	0.07	0.44	1.3	1.4	0.26	0.21	0.37	0.05
Effect	0.55	0.46	0.22	0.26	—	0.12	0.70	0.19	—0.1	—0.5	0.7	0.4	0.1	0.2

Recombination in the regions from *b* to *pr* (region 1), *pr* to *c* (region 2), *c* to *px* (region 3), and *px* to *sp* (region 4) was scored in females heterozygous for $Df(1)w^{rJ1}$ and in controls. The females indicated were crossed to $+ / Y$; *b pr c px sp / b pr c px sp* males. The effect of the deficiency on the various recombination parameters is calculated as indicated for Table 1. The average coefficient of coincidence is calculated as the sum of the observed double crossovers divided by the sum of those expected in each pair of marked regions if exchange were independent.

Recombination of the second chromosomes in deficiency heterozygotes and in controls was measured using the markers *b pr c px sp*, which mark a region of the second chromosome from near the base of the euchromatin in the left arm to near the tip of the right arm. The results of these crosses are shown in Table 2. As in the *X* chromosome, recombination in the second chromosome is reduced in all regions, and this reduction is accompanied by a similar shift of the rank distribution of exchange.

Nondisjunction of the fourth chromosomes, and of the *X* chromosomes as well, was assayed by crossing $Df(1)w^{rJ1}$, y^2 sn^3/y; spa^{pol}/spa^{pol} females and control females to $Y^SX{\cdot}Y^L$, *In(1)EN*, *v f B*$\cdot y^+/O$; *C(4)RM*, *ci* ey^R/O males. As before, half of the zygotes resulting from nondisjunction of the *X* chromosomes are lethal aneuploids, and the number of *X*-chromosome nondisjunctional progeny is therefore doubled in calculating the frequency of *X*-chromosome nondisjunction. For the crosses of deficiency heterozygotes, one half of the *X/O* regular zygotes will not be recovered, and the number of males resulting from normal *X*-chromosome disjunction is therefore doubled. Half of the zygotes resulting from normal disjunction of the fourth chromosomes are *haplo-4 Minute*, and, although some survive, they are excluded from these data. One half the zygotes formed by fertilization of *diplo-4* nondisjunctional eggs will carry four fourth chromosomes, and though they may sometimes survive, they would be phenotypically indistinguishable from the products of normal fourth-chromosome disjunction. One half the zygotes formed by fertilization of *nullo-4* eggs will be lethal. Though scoring of surviving *tetra-4* exceptional progeny as normal disjunctional progeny will cause a slight underestimate of the frequency of fourth-chromosome nondisjunction, no attempt to correct for this has been made in the calculations.

The results of these crosses, and the calculated frequencies of *X*- and fourth-chromosome nondisjunction, are shown in Table 3. Fourth-chromosome nondis-

TABLE 3

X and fourth-chromosome disjunction in females heterozygous for a deficiency of the zeste-white region

Female tested	Regular females	Regular males	4^{th} chromosome exceptions		*X* chromosome exceptions		*X* and 4^{th} chromosome exceptions		Nondisjunction/ 10^3 gametes	
			Females	Males	Female	Males	Female	Males	*X*	4
$\frac{y\ spa^{pol}}{y\ spa^{pol}}$	1037	1132	0	0	0	0	0	0	0	0
$\frac{Df(1)w^{rJ1},\ y^2\ sn^3}{y}$ $\frac{spa^{pol}}{spa^{pol}}$	3247	2392	8	5	13	24	2	4	10.6	3.7

X and fourth-chromosome nondisjunction were scored for $Df(1)w^{rJ1}$ heterozygotes and controls crossed to $Y^SX{\cdot}Y^L$, *In(1)EN*, *v f B*$\cdot y^+/0$; *C(4)RM*, *ci* $ey^R/0$ males. To calculate the frequencies of nondisjunction, the numbers of *X* chromosome and *X* and 4^{th} chromosome exceptional progeny are doubled for both the control and the deficiency crosses, and the numbers of regular males and 4^{th} chromosome exceptional males are doubled for the deficiency cross to account for the relative recoveries of *X* exceptional progeny and the lethality of *deficiency/0* zygotes.

junction, as well as *X*-chromosome nondisjunction, is increased by heterozygosity for *Df(1)w^{rJ1}*.

This experiment indicated that *Df(1)w^{rJ1}* also produces a maternal effect on mitotic chromosome behavior in the progeny of deficiency heterozygous females. Forty-seven progeny (not included in Table 3) in which mitotic recombination or chromosome loss occurred were recovered from the cross of *Df(1)w^{rJ1}, y^2 sn^3/y; spa^{pol}/spa^{pol} females*. Of these forty-seven anomalous progeny, thirty-three involved loss of *X*-chromosome material from the paternally derived *Y^{S}X·Y^L, In(1)EN, v f B·y$^+$* chromosome to yield *y/y$^+$Y* or *y sn^3/y$^+$Y* males; four were mosaic for this event, one involving loss of material from the *Y^{S}X·Y^L, In(1)EN, v f B·y$^+$* chromosome to yield a *y/(yellow$^+$ deficient) v f B* female; four were mosaic for fourth chromosome markers; and seven were gynandromorphs. The presence of a normal *X* chromosome and of a complete *y$^+$Y* chromosome in the apparent detachments of the attached-*XY* chromosome were confirmed by progeny tests. No cases of mitotic recombination or chromosome loss were detected in the control cross, and there was no clustering of the mitotic events to indicate the presence of a detachment chromosome in the *Y^{S}X·Y^L* stock. (Mitotic events have also been routinely recovered from a variety of other crosses of *Df(1)w^{rJ1}* heterozygotes to *Y^{S}X·Y^L, In(1)EN, v f B·y$^+$/O* males. The crosses were done for other purposes and will be reported in a subsequent publication.)

Nondisjunction of the second chromosomes was examined in crosses of deficiency heterozygotes and control females to *C(2)EN, c px* males [*C(2)EN* = *2^{R}2^L·2^{L}2^R*, NOVITSKI 1976]. As only nondisjunctional gametes can be recovered in these crosses, an absolute frequency of nondisjunction cannot be determined. Relative frequencies were, however, determined by measuring the fecundity of these matings by egg counts of a sample of the matings. These results are shown in Table 4. The frequency of second chromosome nondisjunction is also increased by heterozygosity for *Df(1)w^{rJ1}*.

TABLE 4

Second chromosome nondisjunction in Df(1)w^{rJ1} *heterozygotes*

Female tested	Number mated	Progeny recovered: Normal *X* disjunction Males	Progeny recovered: Normal *X* disjunction Females	Progeny recovered: *X* chromosome nondisjunction	Eggs/ female/24 hrs	Exceptional offspring per Female	Exceptional offspring per Egg
$\frac{y\ rst^2}{y\ rst^2}$	1000	25	27	12	19.3	0.076	0.004
$\frac{Df(1)w^{rJ1}}{y\ rst^2}$	930	73	115	59	21.9	0.408	0.019

Females heterozygous for *Df(1)^{rJ1}, y^2 sn^3* and control females were crossed to *+/Y; C(2)EN, c px/0* males. Egg counts were obtained by placing ten pairs per bottle in fifteen bottles for each cross. Eggs laid in the first 24 hrs after mating were discarded, and eggs laid in the next 24 hrs were collected and counted. Progeny were scored from vial matings of five pairs per vial.

For the control matings the number of progeny simultaneously nondisjunctional for the *X* and second chromosomes was doubled in calculating the frequency of exceptions, while for matings of deficiency heterozygotes the number of male offspring resulting from normal disjunction of the *X* chromosomes and nondisjunction of the second chromosomes was also doubled to account for the inviability of *Df(1)w^{rJ1}/0* zygotes.

The cause of abnormal chromosome behavior in deficiency heterozygotes

Two alternative causes for the abnormal chromosome behavior observed in *Df(1)w^{rJ1}* heterozygotes may be suggested; hypoploidy for one or more genes in the deficient region, or mechanical distortion of chromosome pairing resulting from structural heterozygosity.

The observation that deficiency heterozygosity for the zeste-white region of the *X* chromosome affects disjunction of all the chromosomes, decreases recombination on at least the *X* and second chromosomes, and has a maternal effect on the mitotic chromosome behavior of offspring that have not themselves received the deficiency chromosome, suggests that it is unlikely that the effect of deficiency heterozygosity results from structural heterozygosity. An additional possibility, that a linked dominant or semi-dominant meiotic mutant is responsible for the meiotic effect, is not tenable since other, independently derived, deficiencies in this region also show the meiotic defect. A direct method is available, however, for examination of the relationship between the effect of this deficiency on chromosome behavior and the genetic material that is absent: examination of the effect of the deficiency in the presence of a duplication carrying the segment involved. In that circumstance the deficiency's physical presence remains intact, and effects that are a consequence of the structure of the deficiency would also remain. Genes contained within the deficient segment would, however, be present in normal dose, and effects that are a consequence of hypoploidy would be absent.

These experiments employed a duplication, supplied by B. JUDD, which was originally isolated by M. GREEN. The duplication, which has not been previously described, consists of a small part of the tip of the *X* chromosome from *2B7-C1* to *3C1–2* inserted at *102F* in the fourth chromosome. Genetically, it includes all of the loci deficient in *Df(1)w^{rJ1}* that are necessary for viability but is mutant or deficient for the *w* locus and extends distally through the *pn* locus. The duplication will be referred to in the remainder of this report as *Dp(1;4)mg*.

X-chromosome recombination and disjunction were examined in females of four different genotypes: (1) females having one dose of the zeste-white region (*Df(1)w^{rJ1}, y^2 sn^3/Dp(1;1)sc^{V1}, y pn v·y$^+$; spa^{pol}/spa^{pol}*), (2) females having two doses of the zeste-white region but structurally heterozygous for the deficiency (*Df(1)w^{rJ1}, y^2 sn^3/Dp(1;1)sc^{V1}, y pn v·y$^+$; Dp(1;4)mg/spa^{pol}*), (3) females having two doses of the zeste-white region and structurally normal (*y/Dp(1;1)sc^{V1}, y pn v·y$^+$; spa^{pol}/spa^{pol}*), and (4) females having three doses of the zeste-white region (*y/Dp(1;1)sc^{V1}, y pn v·y$^+$; Dp(1;4)mg/spa^{pol}*).

The mating scheme used to generate the four genotypes tested is shown in Figure 1. *spa^{pol}* was used to mark the normal fourth chromosomes in order to monitor the presence of the duplication in these matings, and it was also used in the test generation crosses to *FM7/Y; spa^{pol}/spa^{pol}* males to insure that duplication-bearing and nonduplication-bearing offspring could be distinguished.

Though *spa^{pol}* was a convenient marker for these purposes, *pn* could not be reliably distinguished from *pn$^+$* among *spa^{pol}* progeny. This was of no consequence in matings of *Df(1)w^{rJ1}, y^2 sn^3/Dp(1;1)sc^{V1}, y pn v·y$^+$* females since

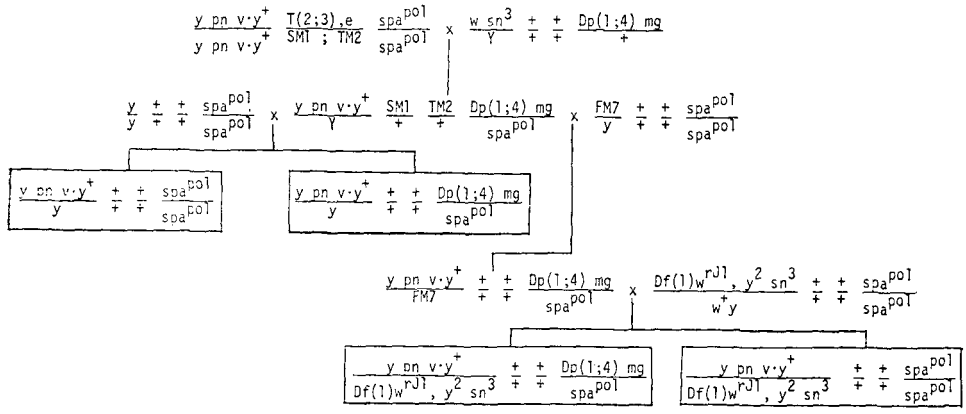

FIGURE 1.—Matings used to generate genotypes with various doses of the zeste-white region for analysis of recombination and disjunction. The matings diagrammed were used to generate the four classes of females shown in boxes. Individual females of these genotypes were mated to *FM7/Y*; spa^{pol}/spa^{pol} males.

the tight linkage of pn^+ and $Df(1)w^{rJ1}$ results in survival of only one of each reciprocal recombinant class. Unambiguous classification was obtained in crosses of $y/Dp(1;1)sc^{v1}$, *y pn v*·y^+; spa^{pol}/spa^{pol} females by progeny testing of female offspring and in crosses of $y/Dp(1;1)sc^{v1}$, *y pn v*·y^+; $Dp(1;4)mg/spa^{pol}$ females by progeny testing of nonduplication-bearing daughters.

Recombination in $Df(1)w^{rJ1}$, y^2 $sn^3/Dp(1;1)sc^{v1}$, *y pn v*·y^+ females could be scored directly from the phenotypes of their sons, and could also be scored directly among female offspring since the *FM7* chromosome used (MERRIAM and DUFFY 1972) carries y^2, w^a, sn^{z2} and *v*. In addition, in matings of $Df(1)w^{rJ1}$, y^2 $sn^3/Dp(1;1)sc^{v1}$, *y pn v*·y^+; $Dp(1;4)mg/spa^{pol}$ females, duplication-bearing and nonduplication-bearing sons could be differentiated. In crosses of females heterozygous for $Df(1)w^{rJ1}$ all males were scored, and all the females from a subset of the matings were scored.

The results of the tests of the four genotypes are shown in Table 5. Within each of the genotypes tested, the various groups of offspring which yield information on recombination (duplication- and nonduplication-bearing males, females) are homogeneous, and the data were grouped for calculation. Table 6 presents the calculated values of the various exchange and disjunctional parameters.

These results indicate that the effect of $Df(1)w^{rJ1}$ on chromosome behavior is the result of abnormal gene dosage in the deficiency heterozygote. In the deficiency heterozygote the map length of the *X* chromosome is reduced and the pattern of exchange is altered (reduced coincidence, reduced frequency of double exchange tetrads) while the frequency of nondisjunction is increased. (The lower frequency of nondisjunction calculated here as compared to those of preceding tables is largely the result of the inviability of the *FM7/O* exceptional male class.) The combination of the deficiency and the duplication has a more nearly normal *X*-chromosome map length, a quite normal exchange distribution, and a normal frequency of nondisjunction.

TABLE 5

X-chromosome recombination and disjunction data for females having various doses of the zeste-white region

Genotype	Offspring scored	Non-crossovers	Single crossovers *pn-v*	Single crossovers *v-y+*	Double crossovers	Reciprocal products	Total regular Males	Total regular Females	Exceptional Males	Exceptional Females
Deficiency	males (from 127 matings)	3087	1580	1164	97	——	5928	9631	1	26
	females (from 57 matings)	1422	660	497	36	1875				
Deficiency and duplication	nonduplication males (from 135 matings)	1723	930	868	243	——	8163	13566	0	4
	duplication males (from 135 matings)	1116	534	576	145	2028				
	nonduplication females (from 35 matings)	444	230	191	43	844				
	duplication females (from 35 matings)	382	201	179	48	751				
Normal	females (progeny tests)	318	196	180	60	——	7191	7034	0	2
Duplication	females (progeny tests)	310	191	184	70	——	4921	5646	2	2

Females heterozygous for *Df(1)w^{rJ1}*, *Dp(1;4)mg*, both or neither were crossed to *FM7/Y*; *spa^{pol}/spa^{pol}* males. For the deficiency heterozygotes all regular male offspring and regular female offspring from a sample of matings were scored for crossovers. Where reciprocal classes are of indeterminate crossover type they are listed separately.

A sample of female offsping of those females having structurally normal *X* chromosomes were progeny tested to score crossovers.

The results for females having three doses of the zeste-white region suggest that an additional dose of the region increases recombination still further, but homogeneity tests do not reveal a significant difference between these data and those from females having two doses of the region. If there is any increase in recombination resulting from hyperploidy for the region, it is assuredly less than the decrease resulting from hypoploidy.

The pattern of recombination in Df(1)w^{rJ1} *heterozygotes*

In deficiency heterozygotes the frequency of double exchange tetrads is more severely reduced than is the frequency of single exchange tetrads for both the *X* and second chromosomes. Not only is the rank distribution of exchange altered

TABLE 6

Parameters of recombination and disjunction for females having various doses of the zeste-white region

Genotype		Deficiency	Deficiency and duplication	Normal	Duplication
Number of copies of zeste-white region		1	2	2	3
Map distances	*pn-v*	28	30	34	35
	v-y+	21	29	32	34
	Total	49	59	66	69
Coefficient of coincidence		0.26	0.70	0.74	0.80
Exchange rank	E_0	0.09	0.06	0	0.01
	E_1	0.85	0.70	0.68	0.62
	E_2	0.06	0.24	0.32	0.37
Nondisjunction/10^3 gametes		2.5	0.33	0.28	0.76

X-chromosome map distances, coefficient of coincidence, tetrad rank and the frequency of nondisjunction are calculated from the data in Table 5.

by heterozygosity for $Df(1)w^{rJ1}$, but the regional distribution of exchange is altered as well.

The data for second-chromosome recombination have already been presented in Table 2. Heterozygosity for $Df(1)w^{rJ1}$ reduces recombination by 55% in the *b–pr* region, by 46% in the *pr–c* region, by 22% in the *c–px* region and by 26% in the *px–sp* region. This result is different from that found for any of the previously reported meiotic mutants. Normally, recombination is relatively frequent for a given physical length in medial regions of a chromosome arm, is somewhat less frequent towards the tips, and is much less frequent near the centromere. Although a number of meiotic mutants have been found that diminish these regional differences, none have been reported that accentuate them as does heterozygosity for $Df(1)w^{rJ1}$.

Since single exchanges and double exchanges do not normally have the same regional distributions, at least part of this regional effect could result from the greater suppression of double exchanges than single exchanges. There could, however, also be differential sensitivity to the effect of $Df(1)w^{rJ1}$ heterozygosity in different regions. To explore the possibility of regional effects on exchange, maximum likelihood estimates of the frequencies of single exchange in each region, and of double exchange in each pair of regions, were obtained by numerical approximation.* Several conditions were examined: (1) single and double exchange frequencies uniformly and equally affected by $Df(1)w^{rJ1}$ heterozygosity, (2) single and double exchanges affected differently, but uniformly in all

* Maximum likelihood estimates were obtained with an interactive, time sharing, program for maximum likelihood and minimum chi-square estimation written by the author. Copies are available on request.

regions, (3) single exchange affected differently in each region but double exchanges reduced uniformly, and (4) double exchange affected differently in each pair of regions, but single exchanges uniformly affected. Expected numbers of noncrossovers, single crossovers and double crossovers based on these estimates were tested for goodness of fit by χ^2. The results are: (1) the frequencies of single and double exchanges are not equally and uniformly reduced ($\chi^2 = 79.4$, 9 df, $P << 0.001$), (2) a uniform reduction of the frequency of double exchange different from a uniform reduction of the frequency of single exchange is not sufficient to account for the regional differences ($\chi^2 = 31.1$, 8 df, $P < 0.001$), (3) a uniform reduction of the frequency of double exchanges accompanied by regionally different effects on the frequency of single exchange does account for the observed differences ($\chi^2 = 10.3$, 5 df, $0.05 < P < 0.1$), while (4) a uniform reduction of the frequency of single exchange accompanied by a non-uniform effect on the frequency of double exchange does not account for the observed differences ($\chi^2 = 14.9$, 3 df, $0.001 < P < 0.01$). Thus, not only are the frequencies of single and double exchanges altered differently by *Df(1)w*^{rJ1} heterozygosity, but different chromosomal regions are differently sensitive. Furthermore, these regional differences are more pronounced for single than for double exchanges.

Interference also appears to be affected differentially in different regions. Individual estimates of the coefficient of coincidence, however, include the combined errors of several small numbers. To provide a test for uniformity of effect on the coefficient of coincidence that uses all of the data, maximum likelihood estimates for the total frequencies of exchange in each region and for the coefficients of coincidence for each pair of regions were obtained. Expected numbers of non-, single and double crossovers based on these estimates were compared to the data. Two hypotheses were tested: (1) that the coefficient of coincidence is uniformly affected by *Df(1)w*^{rJ1} heterozygosity, and (2) that the coefficient of coincidence for pairs of regions on opposite sides of the centromere is affected differently than is the coefficient of coincidence for pairs of regions in the same arm. For both tests no restriction was placed on the effect of *Df(1)w*^{rJ1} on the frequencies of total exchange in each region. In the first test, the maximum likelihood estimate for a uniform effect on the coefficient of coincidence is 0.006, but does not account for the observed differences ($\chi^2 = 11.6$, 5 df, $P < 0.05$). Under the second hypothesis, the maximum likelihood estimate for the effect on the coefficient of coincidence for pairs of regions in opposite arms is 0, while the estimate for the effect within an arm is 0.29. This does adequately account for the observed differences ($\chi^2 = 8.6$, 4 df, $0.05 < P < 0.1$). Thus, although the effect of *Df(1)w*^{rJ1} heterozygosity on the coefficient of coincidence may differ for each pair of regions, the most that can be said from these data is that the coefficient of coincidence is not reduced by *Df(1)w*^{rJ1} heterozygosity in pairs of regions around the centromere that normally show no interference, but is decreased by *DF(1)w*^{rJ1} heterozygosity in pairs of regions in which interference occurs in the control.

To examine the details of the effects of *Df(1)w^{rJ1}* heterozygosity on *X*-chromosome exchange, *Df(1)w^{rJ1}, y^{2} sn^{s}/Dp(1;1)sc^{V1}, y pn cv m f·y^{+}; spa^{pol}/spa^{pol}* and control females were crossed to *Y^{s}X·Y^{L}, In(1)EN, v f B/0; C(4)RM, ci ey^{R}/0* males. The data from these crosses are given in Table 7. Though the *X* chromosome is well marked, the data present two problems that the second chromosome data do not. The first of these is the lethality of one of each reciprocal pair of products. For comparison of the control and deficiency crosses, the calculations in Table 7 are based on only those classes that survive in both crosses. Nevertheless, the estimated exchange parameters are influenced by additive marker viability effects that would not affect the calculations where both reciprocal products are recovered.

The second problem is that the *Dp(1;1)sc^{V1}* chromosome carried *f* while the *Df(1)w^{rJ1}* chromosome bore the marker *sn^{s}*. While there is no difficulty discriminating *sn^{s}* from *f*, the difference between *sn^{s}* and *sn^{s} f* is elusive. Therefore, all of the single crossover products are distinguishable, but several double crossover types are not. This introduces uncertainty in the estimates of the map length of the *m* to *f* and *f* to centromere regions of the deficiency heterozygote, as indicated in the table. This limits the information that can be obtained about the regional distribution of exchange and about regional differences in the coefficient of coincidence.

Recombination along the *X* chromosome, like recombination along the second chromosome, is not uniformly reduced by heterozygosity for *Df(1)w^{rJ1}*; the centromere region is most affected and the interstitial regions least. If there is any local effect of the structural heterozygosity, it must be very slight. Since several of the double crossover classes are indistinguishable, the analysis of regional variation in the *X* chromosome data must be less complete than that of the second chromosome data. Maximum likelihood estimates of the frequencies of single and double exchange were obtained for two hypotheses: (1) that the frequencies of single and double exchange are uniformly and equally affected by *Df(1)w^{rJ1}* heterozygosity, and (2) that the frequencies of single and double exchange are uniformly but differently affected by *Df(1)w^{rJ1}* heterozygosity. Expected numbers of non-, single, and double crossovers based on these estimates were then compared to the observations. Since there were very few double crossovers recovered in the *m–f* and *f*-centromere pair of regions, the double crossover classes were combined as: (1) *pn–cv, cv–m*, (2) *pn–cv, m–f* combined with *pn–cv, f*–centromere, and (3) *cv–m, m–f* and *cv–m, f*–centromere combined with *m–f, f*–centromere. The observations cannot be accounted for by a uniform and equal effect on the frequencies of single and double exchange ($\chi^2 = 72.2$, 3 df, $P << 0.001$) nor by regionally uniform but different effects on the frequencies of single and double exchange ($\chi^2 = 9.9$, 2 df, $0.001 < P < 0.01$). Thus, for the *X* chromosome, as for the second chromosome, the regional differences in the effect of *Df(1)w^{rJ1}* do not result solely from the change in the ratio of single to double exchanges, but reflect regional differences in sensitivity to the effect of the deficiency. A contingency test of the double crossover classes alone does not

TABLE 7

Recombination along the X *chromosome and disjunction of the* X *and* 4th *chromosomes in* Df(1)w^{rJ1} *heterozygotes*

RECOMBINATION

Female tested	Non-crossovers	Single crossovers: 1	2	3	4	Double crossovers: 1,2	1,3	1,4	1,3 or 1,4	2,3	2,4	2,3 or 2,4	3,4	Triple crossovers
Deficiency	1632 ——	204 ——	491 ——	202 ——	41 ——	3 —	— —	— —	11 —	3 —	10 —	10 —	5 —	0 —
Control	783 1810	358 190	739 716	239 368	132 178	23 34	46 26	26 29	——	52 52	46 73	——	2 3	4* 2†

DISJUNCTION

Female tested	Regular males	Regular females	4th chromosome exceptions: Females	Males	X chromosome exceptions: Females	Males	X and 4th chromosome exceptions: Females	Males
Deficiency	2612	2404	38	4	70	79	13	22
Control	5931	5796	3	4	1	0	0	0

PARAMETERS OF RECOMBINATION AND DISJUNCTION

Female tested	Map lengths: 1	2	3	4	Exchange rank: E_0	E_1	E_2	Coincidence: 1,2	1,3 & 1,4	2,3 & 2,4	Nondisjunction/10^3 gametes: X	4
Deficiency	8.3	19.8	8.0–8.8	2.1–1.9	0.25	0.69	0.06	0.07	0.46	0.40	45	14
Control	18.6	35.1	14.0	8.6	—0.19	0.88	0.32	0.14	0.70	0.50	0.1	0.6
Effect	0.55	0.44	0.37–0.43	0.66–0.76	—	0.22	0.81	0.5	0.3	0.2		

Df(1)w^{rJ1}, y^2 sn^3/Dp(1;1)sc^{V1}, y pn cv m f·y+; spa^{pol}/spa^{pol} and *y/Dp(1;1)sc^{V1}, y pn cv m f·y+; spa^{pol}/spa^{pol}* control females were crossed to *Y^{S}X·Y^L, In(1)EN, v f B/0; C(4)RM, ci ey^R/0* males. Crossovers in regions 1 (*pn-cv*), 2 (*cv-m*), 3 (*m-f*), and 4 (*f-y+*) are indicated. Only one of each reciprocal pair is recovered from the deficiency heterozygotes because of the lethality of *deficiency/0* zygotes. The reciprocal products are listed separately for the control cross, and the exchange parameters were calculated from only those classes recovered in both crosses. Because of the presence of *sn^3* on the deficiency chromosome, some double crossover classes are indistinguishable from each other. Map distances for regions 3 and 4 are calculated with all the confused individuals in either one or the other region to indicate the uncertainty in the estimates. Regions three and four are considered a single region for calculating the coefficient of coincidence. The effect of deficiency heterozygosity is calculated as in previous tables.

* One each in *1,2,3, 1,2,4, 2,3,4* and *1,3,4.*

† One in *1,2,4* and one in *1,3,4.*

indicate significant regional variation in the effect on the frequency of double exchange ($x^2 = 3.3$, 2 df, $0.1 < P < 0.2$) and, as for the second chromosome, much of the variation reflects differences in sensitivity of the frequency of single exchange from region to region.

The measured effect of deficiency heterozygosity on the coefficient of coincidence is slightly greater in the *pn–cv* and *cv–m* pair of regions than in the other sets of regions. Unlike the second chromosome results, however, these results for a set of regions within a single chromosome arm are compatible with a uniform effect on coincidence. A maximum likelihood estimated uniform reduction of the coefficient of coincidence of 0.17, with the total frequency of exchange affected differently in each region, yields $x^2 = 2.5$ with 2 degrees of freedom ($0.2 < P < 0.3$).

The second chromosome recombination data also provide a test, though a weak one, of the independence of recombination in the *X* and second chromosomes. The *Df(1)w*^{rJ1} chromosome, in addition to being deficient for the zeste-white interval, also carries the mutants *y*^{2} and *sn*^{3}. In the cross of *Df(1)w*^{rJ1}, *y*^{2} *sn*^{3}/+; *b pr c px sp*/+ females, the sons were scored for recombination between *y*^{2} and *sn*^{3}, as well as for recombination of the second chromosomes; the data are given in Table 8. The frequencies and distribution of crossovers on the second chromosome are the same in progeny where the *X* chromosome had a crossover between *y*^{2} and *sn*^{3} and in those progeny where the *X* chromosome was noncrossover in that region. Thus, recombination in the *X* and second chromosomes appears to be independent. This is, however, a weak test not only because the number of *y*^{2} *sn*^{3} crossover progeny is small, but because a majority of the chromosomes that are noncrossover between *y*^{2} and *sn*^{3} have nevertheless been derived from exchange tetrads. This test then assures only that no gross coincidence or interference of exchange in the two nonhomologs occurs.

The possibility of interaction between the meiotic effect of hypoploidy for the zeste-white region and the interchromosomal effect of heterozygous inversions was also examined. Females heterozygous for *Df(1)w*^{rJ1} and *Dp(1;1)sc*^{V1}, *y pn v y*$^+$ that were, in addition, heterozygous for a multiply inverted second chromosome (*SM1*), a multiply inverted third chromosome (*TM2*), both, or neither, were tested. The fourth chromosomes were also marked by *spa*^{pol}, and

TABLE 8

The independence of recombination of the X *and* 2nd *chromosomes in* Df(1)w^{rJ1} *heterozygotes*

X chromosome	Non-crossover	Single crossovers				Doublecrossovers						Map length
		b-pr	*pr-c*	*c-px*	*px-sp*	*b-pr pr-c*	*b-pr c-px*	*b-pr px-sp*	*pr-c c-px*	*pr-c px-sp*	*c-px px-sp*	*b-sp*
Noncrossover	885	25	134	194	70	6	6	0	7	2	0	33
Crossover between *y*^{2} and *sn*^{3}	172	3	22	46	23	0	1	0	0	1	0	37

The male progeny included in Table 2 are separated here into *y*^{2}-*sn*^{3} *X* chromosome crossover progeny and those that were noncrossover in that region.

the females were crossed to $Y^{S}X{\cdot}Y^{L}$, *In(1)EN, v f B/0*; *C(4)RM, ci ey^{R}/0* males so that disjunction of the *X* and fourth chromosomes, as well as *X*-chromosome recombination, could be monitored. The results of these crosses with respect to recombination are presented in Table 9. In controls and in deficiency heterozygotes, heterozygosity for heterologous inversions increases the frequency of *X*-chromosome recombination and shifts the tetrad distribution toward an increased frequency of double-exchange tetrads. Hypoploidy for the zeste-white region, in the presence or absence of the inversions, reduces the frequency of recombination, and reduces the relative frequency of double exchange tetrads.

TABLE 9

The interaction of interchromosomal effect and deficiency heterozygosity

Females tested	Non-crossover	Single crossover *pn-v*	Single crossover *v-y^{+}*	Double crossover	Map length *pn-v*	Map length *v-y^{+}*	Exchange rank E_0	Exchange rank E_1	Exchange rank E_2	Coefficient of coincidence
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{+}{+}$ $\frac{+}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	1474	349	322	19	16.9	15.8	0.37	0.59	0.04	0.33
$\frac{y}{y\ pn\ v{\cdot}y^{+}}$ $\frac{+}{+}$ $\frac{+}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	977	480	463	134	29.9	29.1	0.08	0.66	0.26	0.75
Deficiency effect					0.43	0.46		0.11	0.85	0.56
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{SM1}{+}$ $\frac{+}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	1352	570	396	88	27.4	20.2	0.20	0.65	0.15	0.69
$\frac{y}{y\ pn\ v{\cdot}y^{+}}$ $\frac{SM1}{+}$ $\frac{+}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	906	685	568	344	41.1	36.4	0	0.45	0.55	0.92
Deficiency effect					0.33	0.45		−0.44	0.73	0.25
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{+}{+}$ $\frac{TM2}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	1171	438	413	56	23.8	22.5	0.18	0.71	0.11	0.50
$\frac{y}{y\ pn\ v{\cdot}y^{+}}$ $\frac{+}{+}$ $\frac{TM2}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	1214	767	761	436	37.9	37.7	0.04	0.41	0.55	0.96
Deficiency effect					0.37	0.40		−0.73	0.80	0.48
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{SM1}{+}$ $\frac{TM2}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	787	419	360	192	34.8	31.4	0.11	0.45	0.44	1.0
$\frac{y}{y\ pn\ v{\cdot}y^{+}}$ $\frac{SM1}{+}$ $\frac{TM2}{+}$ $\frac{spa^{pol}}{spa^{pol}}$	741	605	606	464	44.2	44.3	0	0.23	0.77	0.98
Deficiency effect					0.21	0.29		−0.96	0.43	−0.02

Females of the indicated genotypes were crossed to $Y^{S}X{\cdot}Y^{L}$, *In(1)EN, v f B/0*; *C(4)RM, ci ey^{R}/0* males.

The qualitative effects of interchromosomal effect then appear to be the converse of those of zeste-white hypoploidy. Though not demonstrable from these data, interchromosomal effects are the converse of the effect of *Df(1)w^{rJ1}* heterozygosity in yet another respect; the effect of heterologous inversions, like that of the deficiency, is most pronounced in those regions in which exchange is least frequent normally (SCHULTZ and REDFIELD 1951).

Though the qualitative effects of interchromosomal effect are the reverse of those of heterozygosity for *Df(1)w^{rJ1}*, the two effects are not independent. As the frequency of recombination and the relative frequency of double exchange tetrads are increased by interchromosomal effect, the effectiveness of deficiency heterozygosity in reducing both of these parameters declines. Thus, deficiency heterozygosity causes a reduction of *X*-chromosome map length of 45 percent in flies having normal autosomes, 39 percent in *SM1* heterozygotes, 39 percent in *TM2* heterozygotes and 25 percent in *SM1*; *TM2* heterozygotes. The frequency of double exchange tetrads is reduced 85 percent in flies having normal autosomes, 73 percent in *SM1* heterozygotes, 80 percent in *TM2* heterozygotes, and 43 percent in *SM1*; *TM2* heterozygotes.

The pattern of disjunction in Df(1)w^{rJ1} *heterozygotes*

Most of the characteristics of the disjunctional anomaly of *Df(1)w^{rJ1}* heterozygotes are analogous to those of the majority of recombination defective meiotic mutants (BAKER *et al.* 1976b). The data, described below, indicate that: (1) nondisjunction of the *X* and fourth chromosomes are correlated but they do not disjoin from each other, (2) the *X* and second chromosomes tend to disjoin from one another, and (3) nondisjunctional chromosomes are generally nonexchange chromosomes.

Disjunction of the *X* and fourth chromosomes was followed in several experiments. The data from all of these experiments have been collected in Table 10 where the nondisjunctional progeny are listed according to the chromosome constitution of the eggs that produced them.

Were disjunction of the *X* and fourth chromosomes independent, the frequency of *X*-chromosome nondisjunction among fourth chromosome exceptions would be the same as the frequency among all gametes, with the reciprocal statement true for fourth-chromosome nondisjunction among *X* exceptional gametes. For the first of these comparisons, the numbers of progeny exceptional for the *X* chromosome and of regular *X* male progeny exceptional for the fourth chromosome must be doubled to account for the relative recovery of the *X* exceptions and the lethality of deficiency hemizygous zygotes. Doing so, one finds that 44 percent of fourth chromosome exceptional gametes are also exceptional for the *X* chromosome, and 17 percent of *X* chromosome exceptional gametes are also exceptional for the fourth chromosome. The *X* and fourth chromosomes are not behaving independently. Nevertheless, there is no evidence of disjunction of the *X* and fourth chromosomes from each other, since no excess of the gamete types expected from nonhomologous disjunction (*XX* ; *OO* and *OO* ; *44*) is

TABLE 10

The pattern of X *and* 4th *chromosome nondisjunction in* Df(1)w^{rJ1} *heterozygotes*

Female tested	Genotype of egg											
			X;44		*X;0*						*X;4*	
	XX;4	*0;4*	Males	Females	Males	Females	*XX;44*	*0;0*	*XX;0*	*0;44*	Males	Females
$\frac{Df(1)w^{rJ1}}{y}$ $\frac{+\ +\ spa^{pol}}{+\ +\ spa^{pol}}$	13	24	2	3	3	5	1	0	1	4	2392	3247
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{+\ +\ spa^{pol}}{+\ +\ spa^{pol}}$	28	40	7	10	3	7	3	4	3	9	2164	4241
$\frac{Df(1)w^{rJ1}}{y\ pn\ cv\ m\ f{\cdot}y^{+}}$ $\frac{+\ +\ spa^{pol}}{+\ +\ spa^{pol}}$	70	79	2	15	2	23	6	10	7	10	2612	2404
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{SM1\ +\ spa^{pol}}{+\ +\ spa^{pol}}$	11	10	3	7	3	6	1	1	0	0	2401	2413
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{+\ TM2\ spa^{pol}}{+\ +\ spa^{pol}}$	36	41	4	10	2	6	1	1	1	3	2082	3978
$\frac{Df(1)w^{rJ1}}{y\ pn\ v{\cdot}y^{+}}$ $\frac{SM1\ TM2\ spa^{pol}}{+\ +\ spa^{pol}}$	10	17	8	12	1	11	10	2	0	1	1757	2432
Sum	168	211	26	57	14	58	22	20	12	27	13408	18715

X- and fourth-chromosome nondisjunctional progeny from several crosses of deficiency heterozygotes are listed according to the genotypes of the eggs from which they were derived.

observed in either the individual experiments, where the numbers are small, or in the aggregate data.

The pattern of chromosome distribution among second chromosome exceptional progeny may also be examined. The data from crosses to *C(2)EN* shown in Table 4 are classified in Table 11 according to the chromosome constitutions of the eggs that were recovered. These results also provide an interesting observation about the behavior of the compound second chromosome, *C(2)EN*, that is worth noting, though it is of no particular import for the present study. This compound chromosome was constructed recently by NOVITSKI and was chosen for these crosses in preference to isochromosome compound second chromosomes (*i.e.*, *C(2L)RM*; *C(2R)RM*) because *C(2)EN* males would not produce *diplo-2*^{L}; *nullo-2*^{R} and *nullo-2*^{L}; *diplo-2*^{R} sperm. Surprisingly, however, no progeny derived from fertilization by *C(2)EN*-bearing sperm were recovered in either control or deficiency heterozygote crosses. Recent results (unpublished data and I. DUNCAN, personal communication) suggest that this chromosome causes a suicidal version of meiotic drive. For present purposes, the only consequence of this is that, of the four possible products simultaneously nondisjunctional for the *X* and second chromosomes, only two can be recovered (*XX* ; *22* and *OO* ; *22*).

Nondisjunction of the *X* and second chromosomes in deficiency heterozygotes is clearly not independent. Among gametes exceptional for the second chromosome, eighteen percent are also exceptional for the *X* chromosome. (Note that in making this calculation, as in calculating the frequency of nondisjunction per egg, the number of recovered regular *X*-chromosome male progeny must be doubled to account for the inviability of *deficiency/O* zygotes.) Not only are *X* chromosome and second chromosome nondisjunction correlated, but it is apparent that the *X* and second chromosomes preferentially disjoin from one another. Of the two classes of diplo-second gametes recovered, the one expected from nonhomologous disjunction (*OO* ; *22*) is recovered far more frequently than is the other.

Nondisjunction in *Df(1)w*^{rJ1} heterozygotes generally involves nonexchange chromosomes. In *Df(1)w*^{rJ1}, *y*^{2} *sn*^{3}/*Dp(1;1)sc*^{V1}, *y pn v y*$^{+}$ females, for example, single exchange followed by nondisjunction at first meiotic anaphase would

TABLE 11

The pattern of X *and second chromosome nondisjunction in deficiency heterozygotes*

Female tested	Genotype of egg: *X;22* Males	*X;22* Females	*X;0* Males	*X;0* Females	*0;22*	*XX;0*	*XX;22*	*0;0*
$\frac{Df(1)w^{rJ1}}{y\ rst^{2}}$	73	115	0	0	57	0	2	0
$\frac{y\ rst^{2}}{y\ rst^{2}}$	25	27	0	0	12	0	0	0

The nondisjunctional progeny from the crosses enumerated in Table 4 are listed according to the *X* and second chromosome egg genotypes.

result in the homozygosis of markers distal to the exchange in one-quarter of the gametes, and one-third of the matroclinous females recovered from such eggs would be mutant for the distal markers, since deficiency homozygous progeny would die. Similarly, nondisjunction of double-exchange tetrads would result in the recovery of mutant homozygous matroclinous progeny one-quarter of the time (from two- and four-strand double exchanges with exchanges in the *deficiency–sn* and *pn–v* regions or *sn–v* and *v*–centromere regions), one-third of the time (from three-strand double exchanges) or one-half the time (from two- and four-stranded doubles with exchanges in the *deficiency–sn* and *v*–centromere regions). Of the thirty-four matroclinous females recovered from the cross of $Df(1)w^{rJ1}$, $y^2\ sn^3/Dp(1;1)sc^{v1}$, $y\ pn\ v{\cdot}y^+$ females having normal autosomes, none was homozygous for any of the recessive markers.

$Df(1)w^{rJ1}$, $y^2\ sn^3/Dp(1;1)sc^{v1}$, $y\ pn\ cv\ m\ f{\cdot}y^+$ females yielded eighty-three matroclinous offspring. Only one was homozygous for a marker. Seventy of the matroclinous females were also progeny tested to detect homozygosis of wild-type alleles or changes in coupling of markers. Sixty-five matings were fertile and only one crossover (a single crossover between *m* and *f*) was found. Finally, all of the matroclinous females were heterozygous for the y^+ centromere marker, confirming the first meiotic division origin of the nondisjunction.

Although these characteristics of nondisjunction in $Df(1)w^{rJ1}$ heterozygotes are analogous to those of recombination-defective meiotic mutants, exchange in the deficiency heterozygotes is, in one circumstance at least, not sufficient to ensure normal disjunction. In deficiency heterozygotes that are heterozygous for *SM1* and *TM2* as well, the matroclinous female progeny frequently arise from *X*-chromosome exchange tetrads. Of the twenty matroclinous females recovered, six (including one also exceptional for the fourth chromosomes) were homozygous for *pn* and *v*, one was homozygous for *sn* and one was homozygous for *pn* and *sn*. One out of the twelve matroclinous females recovered from $Df(1)w^{rJ1}$; *SM1* heterozygotes was also homozygous for a marker (*pn*), though none of the thirty-eight matroclinous females from $Df(1)w^{rJ1}$; *TM2* heterozygotes was homozygous for a marker. *SM1* and *TM2* exert a potent interchromosomal effect on recombination even in the presence of $Df(1)w^{rJ1}$ heterozygosity, and the frequency of *X*-chromosome no-exchange tetrads is low. Of all of the meiotic mutants, only one, *abo*, exists where heterozygous inversions continue to exert an interchromosomal effect, and where the mutant is mild enough that the frequency of no-exchange tetrads is low (CARPENTER and SANDLER 1974). Since *abo* is itself a second chromosome recessive mutant, the effect of interchromosomal effect of only *TM2* was examined. Unfortunately, CARPENTER and SANDLER recovered only five matroclinous females, none of which were homozygous for any *X*-chromosome markers. Thus, it cannot be determined whether the recovery of crossover exceptional chromosomes in $Df(1)w^{rJ1}$; *SM1*; *TM2* heterozygotes is a general property of nondisjunction when the availability of non-exchange tetrads is near zero, or is a property specifically of the meiotic effect of $Df(1)w^{rJ1}$.

DISCUSSION

Heterozygosity for $Df(1)w^{rJ1}$ causes both increased nondisjunction and reduced exchange. The disjunctional effect is quite similar to that produced by recombination-defective meiotic mutants, with the exception of the recovery of crossover exceptional chromatids in *SM1*; *TM2* heterozygotes. As no parallel observations exist for the meiotic mutants, the disjunctional effect will be assumed to be a consequence of the effect on the recombination process, and the discussion will focus on the aberrant pattern of recombination in the deficiency heterozygote. This assumption may not be correct; but in the absence of further data, it is the simplest available.

A model of the meiotic effect of a deficiency

Recent evidence, both direct and indirect, indicates that altered gene dosage in higher organisms leads to a proportionate change in the amount of gene product (for examples in Drosophila see review of MACINTYRE and O'BRIEN 1976; see CARLSON 1972 and FARBER 1973 for examples in Datura and in human cells, respectively). It is, therefore, of interest to inquire whether the effects of $Df(1)w^{rJ1}$ on recombination would be those expected to be produced by halving the level of an enzyme involved in exchange. Exchange itself must, however, involve many processes that affect whole regions of chromosomes, whole chromosomes, or the whole nucleus. In developing this model, the quantity of an enzyme rather than its mode of action is of interest. One might be tempted to pursue this by developing a set of differential equations analogous to the classical description of reaction kinetics. In this case, however, that would require modeling a nonequilibrium, time and diffusion-limited reaction of an enzyme of unknown function. Faced with this unencouraging prospect, a simpler stochastic approach has been attempted.

Approximations of the frequencies of total exchange in a region, double exchange, single exchange, and the coefficient of coincidence will first be derived for this model. Subsequently, the effects of enzyme deficiency on each of these parameters will be examined.

Consider an enzyme that mediates one step in the exchange process. Assume that, prior to exchange, L enzyme molecules are synthesized and that these contact the chromosomes at random. Then in a given region that occupies fraction s_x of the genome, the probability of M enzyme contacts is:

$$\binom{L}{M} s_x^M (1 - s_x)^{L-M}$$

More than one event must occur at that site for an exchange to take place: local synapsis, nicking, unwinding, hybrid formation, ligation, etc. The enzyme of interest mediates but one of these processes and the probability of completion of the other events need not be uniform for all chromosome regions. Let the probability that the other local events occur, whether before or after the action

of the enzyme, be γ. Then the probability that M enzyme contacts results in one or more exchange in the region is:

$$1 - (1 - \gamma)^M$$

Not only is a sequence of events at the site of enzyme action required, but processes at other locations may be required for completion of exchange as well. Some of these might be processes affecting whole regions of chromosome (completion of premeiotic S or establishment of synapsis in the region, for example). Others might be local events that occur at sites different from the site of action of the enzyme. For example, nicking and unwinding may proceed from a point, but affect a substantial region. Let P be the probability that these regional processes are completed, whether they precede or follow the time at which action of the particular enzyme is required.

Then the probability of one or more exchanges in the region given the presence of L enzyme molecules in the cell is:

$$\begin{aligned} & P\left[\Sigma \binom{L}{M} s_x^M (1 - s_x)^{L-M} (1 - (1-\gamma)^M)\right] \\ & \quad = P\left[\Sigma \binom{L}{M} s_x^M (1 - s_x)^{L-M} - \Sigma \binom{L}{M} s_x^M (1 - s_x)^{L-M} (1-\gamma)^M\right] \\ & \quad = P\left[1 - (s_x - s_x\gamma + 1 - s_x)^L\right] \\ & \quad = P\left[1 - (1 - s_x\gamma)^L\right] \end{aligned}$$

If the number of enzyme molecules in the cell is large enough that the distribution of enzyme contacts may be approximated by a Poisson distribution, then the probability of one or more exchanges in a region is:

$$P\,(1 - e^{-\lambda\gamma})$$

where λ is the average number of enzyme contacts in the region. The remainder of the derivations will continue to employ the binomial distribution of enzyme contacts so that the possible case of an enzyme produced in very small numbers may be considered. Except for low L, or λ, the curves will coincide unless $s_x\gamma$ is near unity. It may also be noted that L need not be strictly the number of enzyme molecules. It could as well represent the total number of contacts of enzyme molecules with the genome for an enzyme that does not bind exactly once each meiosis.

To examine exchange rank, divide the region of length s_x in two parts. Let the fraction of the region in one part be s_1 and the fraction of the length in the second part be $(1 - s_1) = s_2$. To determine the frequency of simultaneous exchange in both subregions, it will be necessary to include interference between events in the two regions. Though SANDLER *et al.* (1968) and CARPENTER and SANDLER (1974) have in different ways distinguished between "precondition" or "nodal" events that affect interference and "exchange" events that do not, those processes that cause interference could be either local or regional in nature. Therefore, let γ_1 and γ_2 be the probabilities of local processes being completed in each region, and let $C_L\gamma_1$ and $C_L\gamma_2$ be the probabilities of local processes being completed, such that exchange occurs in both regions. Similarly, let P_1 and P_2 be the probabilities

of completion of regional processes in the two regions, and let $C_R P_1 P_2$ be the probability of completion of regional processes in both regions simultaneously.

Of M enzyme contacts in the entire region, any number, k, from 0 to M, may occur in one region with probability:

$$\binom{M}{k} s_1^k s_2^{M-k}$$

and the probability of one or more exchanges in the first region, given M enzyme contacts in the entire region, is:

$$P_1 \Sigma \binom{M}{k} s_1^k s_2^{M-k} (1 - (1-\gamma_1)^k) = 1 - (1-s_1\gamma_1)^M$$

This expression must be summed for all possible numbers of enzyme contacts, M, from 0 to L which may occur in the combined regions. The probability of one or more exchanges in one region given the presence of L enzyme molecules in the cell is then:

$$P_1[\Sigma \binom{L}{M} s_x^M (1-s_x)^{L-M} (1 - (1-s_1\gamma_1)^M)] = P_1 [1 - (1-s_x s_1\gamma_1)^L]$$

Although this is a measure of the frequency of one or more exchanges in one region, where that region is small it approximates the frequency of single exchanges in that region (whether accompanied by exchanges in the second region or not) and will be denoted as:

$$E_{\text{region 1}} = P_1 [1 - (1-s_x s_1\gamma_1)^L]$$

For exchange to occur in both regions, regional and local events must be completed in both regions. Thus, the probability of one or more exchanges in each of the two regions given M enzyme contacts is:

$$\begin{aligned} &C_R P_1 P_2 [\Sigma \binom{M}{k} s_1^k s_2^{M-k} (1 - (1-C_L\gamma_1)^k) (1 - (1-C_L\gamma_2)^{M-k})] \\ &= C_R P_1 P_2 [\Sigma \binom{M}{k} s_1^k s_2^{M-k} - \Sigma \binom{M}{k} s_1^k s_2^{M-k} (1-C_L\gamma_1)^k \\ &\quad - \Sigma \binom{M}{k} s_1^k s_2^{M-k} (1-C_L\gamma_2)^{M-k} + \Sigma \binom{M}{k} s_1^k s_2^{M-k} (1-C_L\gamma_1)^k (1-C_L\gamma_2)^{M-k}] \\ &= C_R P_1 P_2 [1 - (1-C_L s_1\gamma_1)^M - (1 - C_L s_2\gamma_2)^M + (1 - C_L s_1\gamma_1 - C_L s_2\gamma_2)^M] \end{aligned}$$

When summed for all possible values of M from 0 to L this is the probability of one or more exchanges in both regions. Where the regions are small this will approximate the frequency of one exchange in each region and is:

$$E_2 = C_R P_1 P_2 [1 - (1-s_x C_L s_1\gamma_1)^L - (1 - s_x C_L s_2\gamma_2)^L + (1 - s_x C_L s_1\gamma_1 - s_x C_L s_2\gamma_2)^L]$$

The frequence of exchange in only the first region is the total frequency of exchange in that region less the frequency of simultaneous exchanges in the two regions and is:

$$\begin{aligned} E_{\text{1-region 1}} = P_1 [1 - (1-s_x s_1\gamma_1)^L] - C_R P_1 P_2 [1 - (1-s_x C_L s_1\gamma_1)^L \\ - (1-s_x C_L s_2\gamma_2)^L + (1 - s_x C_L s_1\gamma_1 - s_x C_L s_2\gamma_2)^L] \ . \end{aligned}$$

The coefficient of coincidence is:

$$C = \frac{E_2}{(E_{\text{region 1}})\ (E_{\text{region 2}})}$$

$$= \frac{C_R P_1 P_2 \left[1 - (1-s_x C_L s_1 \gamma_1)^L - (1-s_x C_L s_2 \gamma_2)^L + (1 - s_x C_L s_1 \gamma_1 - s_x C_L s_2 \gamma_2)^L\right]}{P_1 \left[1 - (1-s_x s_1 \gamma_1)^L\right] P_2 \left[1 - (1-s_x s_2 \gamma_2)^L\right]}$$

$$= \frac{C_R \left[1 - (1-s_x C_L s_1 \gamma_1)^L - (1 - s_x C_L s_2 \gamma_2)^L + (1 - s_x C_L s_1 \gamma_1 - s_x C_L s_2 \gamma_2)^L\right]}{\left[1 - (1-s_x s_1 \gamma_1)^L\right] \left[1 - (1-s_x s_2 \gamma_2)^L\right]} .$$

The effect of reducing the number of enzyme molecules

The effect of enzyme reduction may be measured for this model, as was done for the data, by the reduction of each exchange parameter in the deficiency compared to the control. As the overall length of the two regions, the relative lengths of the regions, and the probabilities of completion of local events in the regions are confounded, the parameters $z_1 = s_x s_1 \gamma_1$ and $z_2 = s_x s_2 \gamma_2$ will be substituted to simplify the expressions. Thus, the effect on total exchange in one region of reducing the number of enzyme molecules from L to $L/2$ is:

$$1 - \frac{P_1 \left[1 - (1-z_1)^{L/2}\right]}{P_1 \left[1 - (1-z_1)^L\right]}$$

$$= 1 - \frac{1 - (1-z_1)^{L/2}}{1 - (1-z_1)^L} \tag{1}$$

The effect on the frequency of exchange in just that region is:

$$1 - \frac{1-(1-z_1)^{L/2} - C_R P_2 \left[1-(1-C_L z_1)^{L/2} - (1-C_L z_2)^{L/2} + (1-C_L z_1 - C_L z_2)^{L/2}\right]}{1-(1-z_1)^L - C_R P_2 \left[1-(1-C_L z_1)^L - (1-C_L z_2)^L + (1-C_L z_1 - C_L z_2)^L\right]} \tag{2}$$

The effect on the frequency of double exchanges is:

$$1 - \frac{1 - (1-C_L z_1)^{L/2} - (1-C_L z_2)^{L/2} + (1-C_L z_1 - C_L z_2)^{L/2}}{1 - (1-C_L z_1)^L - (1-C_L z_2)^L + (1-C_L z_1 - C_L z_2)^L} \tag{3}$$

and the effect on the coefficient of coincidence is:

$$1 - \frac{\left[1-(1-C_L z_1)^{L/2} - (1-C_L z_2)^{L/2} + (1-C_L z_1 - C_L z_2)^{L/2}\right]\left[1-(1-z_1)^L\right]\left[1-(1-z_2)^L\right]}{\left[1-(1-C_L z_1)^L - (1-C_L z_2)^L + (1-C_L z_1 - C_L z_2)^L\right]\left[1-(1-z_1)^{L/2}\right]\left[1-(1-z_2)^{L/2}\right]} \tag{4}$$

These effects of reducing the level of an enzyme on the various parameters of exchange are not entirely obvious from inspection of the equations and have instead been evaluated numerically over a wide range of initial enzyme levels. Different chromosome regions may differ in length and in each of the probabilities and coincidences for regional and local events. The effects of enzyme reduction will first be considered for various pairs of regions of equal size with equal probabilities of completion of local events (*i.e.*, for $s_x s_1 \gamma_1 = s_x s_2 \gamma_2 = z$), under the condition that the two regions are always in an appropriate state for exchange

($P_1 = P_2 = 1$) and in the absence of either regional or local interference ($C_R = C_L = 1$). Variation of each of these will then be considered.

The effect of halving the level of an enzyme on the total frequency of exchange in one region is shown in Figure 2a, the effects on the frequencies of single and double exchanges are shown in Figures 2b and 2c, and the effect on the coefficient of coincidence is shown in Figure 2d. As one-half of all exchanges are detected as crossovers, the effect on the total frequency of exchange is equivalent to the effect of enzyme deficiency on map length. The maximum effect of reducing enzyme concentration is a fifty percent reduction of map length, and the effect decays to zero as the system becomes enzyme saturated.

In all circumstances, the frequency of double exchange tetrads is reduced more than is the frequency of single exchange tetrads. The maximum effect on single exchanges is a fifty percent reduction, while the maximum effect on double exchanges is complete elimination. That the maximum effect on the frequency

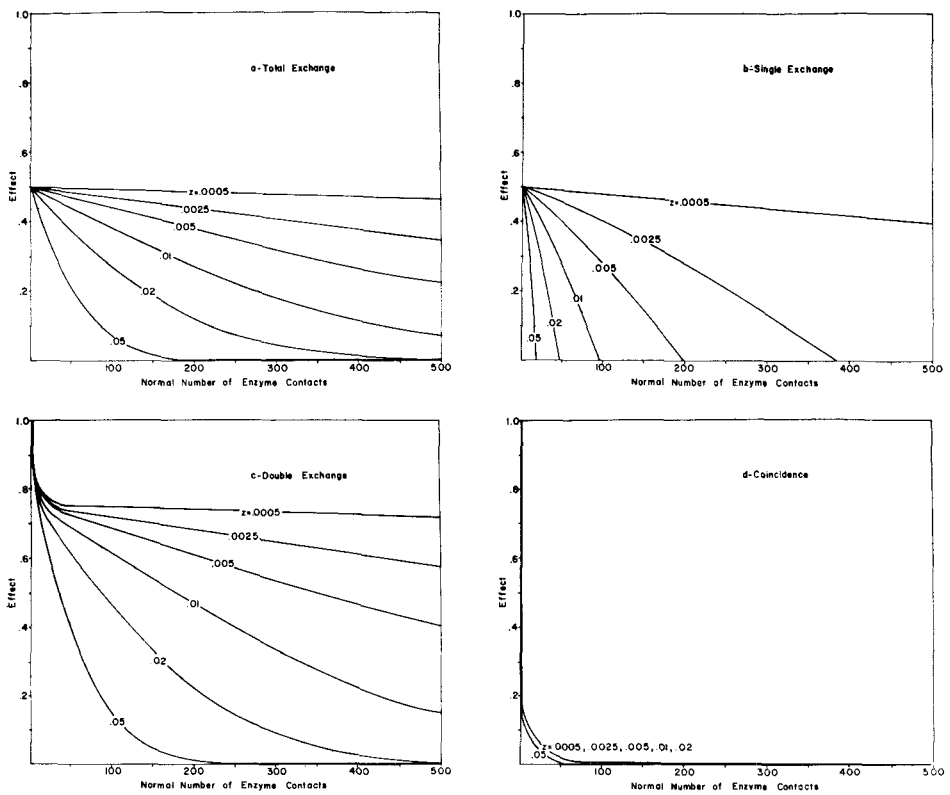

FIGURE 2.—The effect of enzyme reduction on the parameters of exchange. The simulated effect of halving the level of an enzyme is calculated as $1 - \frac{\text{Parameter (reduced)}}{\text{Parameter (normal)}}$ as described in the text. Each parameter as indicated in the graphs is calculated for one of a pair of equivalent regions ($s_x s_1 \gamma_1 = s_x s_2 \gamma_2 = z$) and the results are plotted against the normal number of enzyme contacts for different values of z.

of double-exchange tetrads would be complete elimination may be seen directly. When the number of enzyme molecules is reduced to one, no double exchanges can take place, though single exchanges could still occur. The limiting effect on single exchanges must be fifty percent, since halving the number of enzyme contacts can never reduce that number to zero. As the total frequency of exchange increases, reducing the enzyme level can result in an increase in the frequency of single exchanges, since what would have been double-exchange tetrads in the normal situation become single-exchange tetrads in the deficiency (*i.e.*, the effect on single exchange as measured here is negative).

A negative effect on double exchanges as triples are converted to doubles is also possible, but is eliminated here by the fact that the model is truncated at two regions. The concavity thus introduced into the effect on double exchange is not a serious matter for comparison with actual experiments since triples are, in any case, rare.

Since double exchanges cannot occur if only one enzyme contact occurs, the maximum effect on the coefficient of coincidene of reducing the number of enzyme molecules would be total elimination of coincidence. That effect, in the absence of any other contributions to interference, quickly decays to zero as the number of enzyme molecules increases. Note that normal levels of interference cannot result from enzyme limitation alone, as that would produce interference around centromeres, as well as in other pairs of small regions, no matter how far separated.

Regional differences in the effects of enzyme deficiency

The frequency and rank distribution of exchange is sensitive, under this model, to a variety of regional and local events. The effect of enzyme deficiency, however, on each of these parameters of exchange is not identically sensitive to these events. The effect of enzyme reduction on the total frequency of exchange in a region is sensitive only to the probabilities associated with events at the site of enzyme action (equation 1). The effect of enzyme reduction on the frequency of single exchanges is sensitive to the probability of regional events in regions other than the one being scored (and in identical fashion to interference between regional events), to the probabilities associated with events at the site of enzyme action, and to interference between those events (equation 2). The effects of enzyme reduction on double exchange and on interference are sensitive to only the probabilities of events at the site of enzyme action and to interference between those events (equations 3 and 4).

The interaction of changes in the probability associated with local events (z) with the effects of enzyme reduction is illustrated in Figure 3a. The interaction of differentially varying the probability of local events in the two regions ($z_1/(z_1 + z_2)$) with the effects of enzyme reduction is illustrated in Figure 3b. The interaction of the probability of completion of regional events (P_2) with the effects of enzyme reduction (which is identical to the interaction of interference between regional events (C_R) and the effects of enzyme reduction) is illustrated in Figure 3c. The interaction of interference between local events

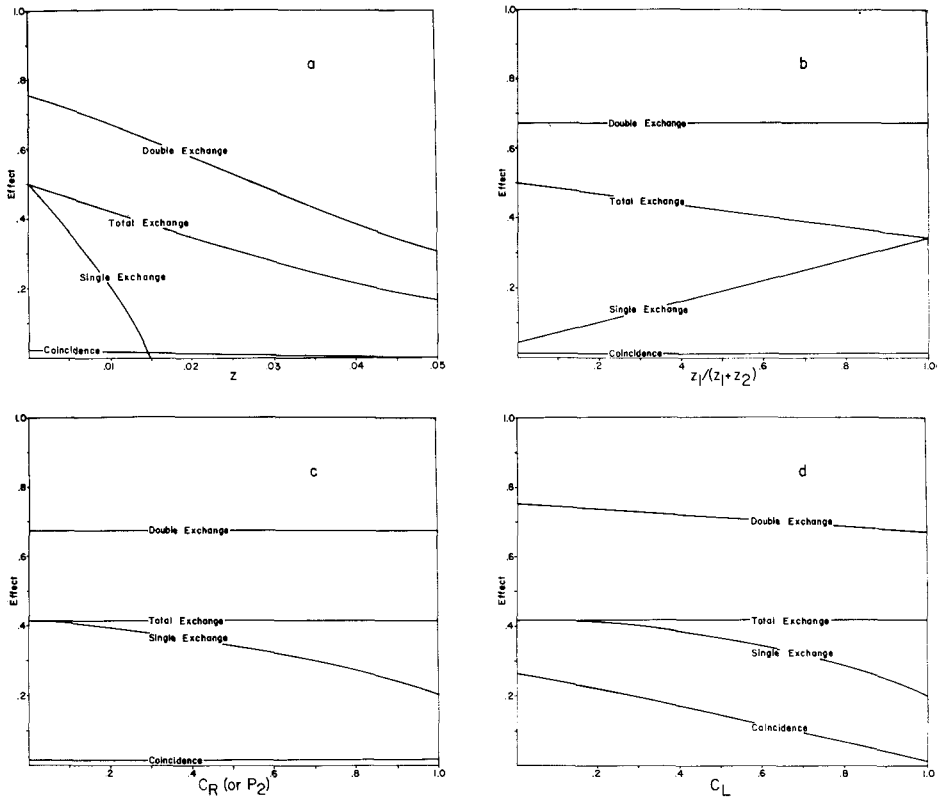

FIGURE 3.—The interaction of regional differences with the effects of enzyme reduction. The effects of enzyme reduction on the parameters of exchange are plotted against the variables of the model. Except for the variable indicated in each graph, the variables are fixed at: $L = 64$, $z = s_x s_1 \gamma_1 = s_x s_2 \gamma_2 = 0.01$, $C_L = C_R = P_2 = 1$. For the curves of effect versus $z_1/(z_1 + z_2)$, $z_1 + z_2$ is fixed at 0.02.

(C_L) with the effects of enzyme reduction is illustrated in Figure 3d. In each figure the curves are drawn with other variables fixed as indicated previously, but these curves are representative of the family of curves that is obtained for other values of the variables. In addition to the insensitivity of the effect of enzyme reduction on some exchange parameters to certain variables described above, the following may be noted from these curves: (1) in each case, differences that alter the effect of enzyme reduction on single exchange result in a smaller change, or no change at all, in the effect on double exchange. Thus, whatever differences exist along a chromosome that result in the normal nonuniform distribution of exchange, those regional differences will more strongly influence the effect of enzyme reduction on single exchange than the effect on double exchange. (2) The effect of enzyme reduction on the coefficient of coincidence is sensitive to interference between events at the site of enzyme action. Thus, in regions devoid of interference, one may expect no effect of enzyme reduction on coincidence, but in other regions there can be an effect of enzyme

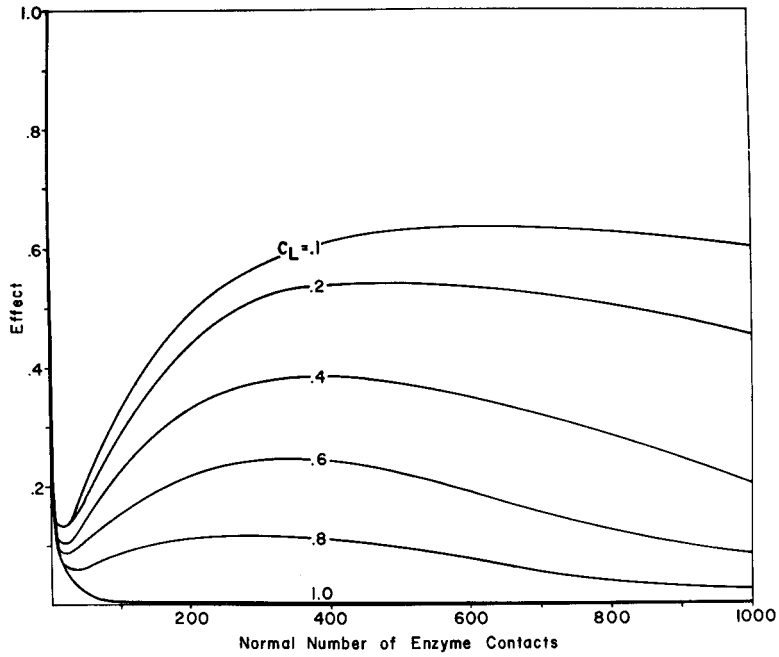

FIGURE 4.—The interaction of local interference with the effect of enzyme reduction on the coefficient of coincidence. The effect of enzyme reduction on the coefficient of coincidence is plotted against the normal number of enzyme contacts for various values of local coincidence (C_R). The other variables of the model are fixed at $z = s_x s_1 \gamma_1 = s_x s_2 \gamma_2 = 0.01$ and $C_R = P_2 = 1$.

reduction on the coefficient of coincidence even if the number of enzyme molecules is large. This interaction is illustrated explicitly in Figure 4. Although at sufficient enzyme concentration a reduction in enzyme level will have no effect on the coefficient of coincidence in any region, over a broad range of enzyme levels increased interference between events at the site of enzyme action results in increased depression of coincidence by enzyme deficiency.

Comparison of the model and the experimental results

This model, like any model, is an oversimplified representation of a more complex reality. Nevertheless, in all characteristics the effects of enzyme reduction on exchange predicted by this model are analogous to those observed for *Df(1)w*^{rJ1} heterozygotes:

(1) Map length is reduced, with a maximum reduction for a single region of about fifty percent.

(2) The frequency of double exchanges is reduced more severely than the frequency of single exchanges.

(3) Reduced exchange is accompanied by increased interference. This is not a simple consequence of the preceding, since, for example, a reduction of single exchange of 50% accompanied by a 75% reduction of double exchanges would not be detected as increased interference.

(4) Regions in which exchange is normally infrequent per unit physical length are more severely affected than regions in which exchange is normally more frequent per unit physical length.

(5) Regional differences in the effect of enzyme reduction are more pronounced for single exchanges than for double exchanges, even though the effect on double exchanges is more severe than that on single exchanges in a given region.

(6) Reduced enzyme level has less effect on the coefficient of coincidence in regions around a centromere than in other regions.

(7) Any increase in recombination in flies having three doses of the region should be less than the decrease produced in the deficiency heterozygotes. Though the curves of Figure 2 are drawn for changes from L to $L/2$, curves for changes from $1\frac{1}{2}$ L to L would be similar. As that change is itself smaller and as $1\frac{1}{2}$ L represents a greater strating number of enzyme contacts, the effect would be less.

At least one other deficiency, *Df(3R)sbd*^{105}, affects meiotic chromosome behavior, and the approach taken here might provide a partial description of its effects as well. *Df(3R)sbd*^{105} heterozygosity causes a decrease in X-chromosome map length of about thirty percent. That effect is at least superficially similar to that of *Df(1)w*^{rJ1} heterozygosity; the frequency of double exchanges is reduced more than is the frequency of single exchanges (HINTON 1966, with additional data in LINDSLEY *et al.* 1968). The numbers recorded are small, however, and no difference can be discerned in the regional distribution of exchange in *Df(3R)sbd*^{105} heterozygotes compared to controls. *Df(3R)sbd*^{105} is deficient for the locus of a strong, nearly recombinationless, meiotic mutant, *c(3)G* (GOWEN and GOWEN 1922), a mutator gene (GREEN 1970) and possibly other genes with meiotic effects. *c(3)G* itself has a dominant effect, but that effect is the reverse of its recessive effect and of the effect of *Df(3R)sbd*^{105}; recombination is enhanced by heterozygosity for *c(3)G* (GOWEN and GOWEN 1922; HALL 1972). Whether *c(3)G* is itself not an amorph, or whether the effect of *Df(3R)sbd*^{105} is a compound of the effects of hemizygosity for *c(3)G* and other loci, remains unresolved.

HINTON (1967) has also tested seventeen other small deficiencies for dominant effects on recombination. Eleven of them had detectable, though slight, effects in at least one nonhomologous region.

The model presented here was devised to ask whether the meiotic effect of one deficiency is comparable with the effects that might be expected to result from halving the level of an enzyme. It may also be a useful formalism for the analysis of other meiotic anomalies. A suggestion of this may be seen from consideration of the interaction of the interchromosomal effect of heterozygous inversions with heterozygosity for *Df(1)w*^{rJ1}.

One plausible hypothesis about the nature of the interchromosomal effect is that the time during which recombination can occur is lengthened because of delayed synapsis of the heteromorphic pair. (For a review of the phenomenology and hypotheses relating to interchromosomal effect and the presentation of

this particular hypothesis, see LUCCHESI and SUZUKI 1968). In terms of the model developed here, increasing the time span during which recombination could take place would increase the number of enzyme contacts if the number of contacts of each molecule were time dependent, and would increase the probabilities of completion of local and/or regional events. If only regional properties were altered by interchromosomal effect, only the effect of $Df(1)w^{rJ1}$ heterozygosity on single exchange would be altered by the presence of heterologous inversions. The effects of $Df(1)w^{rJ1}$ on all of the parameters of exchange, however, are reduced by interchromosomal effect. The model then suggests that, however interchromosomal effect works, it does not affect only regional processes.

The formal approach taken here is not universal; the same approach cannot be directly applied to all point mutant amorphs or hypomorphs. Both classes of phenotypic expression could arise as the result of a number of alterations in a gene product. For example, an enzyme that binds to the chromosomes, but that fails to react properly, might preclude the action of another enzyme at that site or might otherwise alter the state of the chromosome. That enzyme defect need not have the same effect on recombination as a defective enzyme that sometimes fails to bind at all. Either enzyme, however, could be the product of a hypomorphic mutant. Though it may be possible to extend the present model to a variety of different mutant types, that extension might require specification of the enzymatic reaction involved. Nevertheless, one might attempt the converse argument if a point mutant were found that altered exchange in the manner predicted by this model; it should be possible to delimit, to some degree at least, why the gene product fails to work.

A note on the zeste-white region

It has not escaped the author's notice that the region deficient in $Df(1)w^{rJ1}$ has been the subject of intensive cytogenetic investigation. A subsequent paper will recount attempts at the localization of the meiotic locus (or loci) within the zeste-white region.

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