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Segregation of centric *Y*-autosome translocations in *Drosophila melanogaster*

II. Segregation determinants in females

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SUMMARY

This is a study of the chromosomal segregation patterns in females of 15 Experimental stocks of *Drosophila melanogaster*, each carrying one element of a T (Y; 2) with a centric break-point. In each Experimental stock the relative frequency of all eight possible meiotic configurations of four relevant chromosomal elements was followed: an attached-*X* chromosome, a multiply-inverted chromosome 2, a free arm of chromosome 2, and a half-translocation element. Although the 15 translocation elements were broken at different sites, there were no basic differences among the Experimental stocks in their segregation patterns. The three two-by-two configurations were the most common. Comparison of this pattern with that of the segregation pattern of stocks similar but for an inversion-free chromosome 2, showed that in the Experimental stocks exchange pairing did not play a significant role in the determination of the segregation pattern.

The results of these experiments, together with the analysis of results from other published studies provide evidence against the model that had been forwarded by Grell. According to this model, chromosomes that did not participate in exchange pairing undergo another pairing cycle, in which total chromosome length is a factor in the determination of segregation.

We support a modified version of Novitski's model of premetaphase chromocenter-like chromosome aggregation. Disjunction of non-exchange chromosomes is regulated by determinants located in the proximal heterochromatin of the sex chromosomes and the autosomes. However, the specificity, especially that of the autosomal determinants, is not high. Thus, if an autosome and a sex chromosome are available, their determinants may interact-to-disjoin by default. More frequently, the determinants of the left-arm autosomal element may interact-to-disjoin with those of the right-arm chromosomal element.

1. INTRODUCTION

Despite many efforts, it must be admitted that the factors that determine regular disjunction of homologuous chromosomes are still not well understood. In the present series of papers an attempt has been made to reexamine the role of

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chromosomal segments proximal to the centromere of an autosome (chromosome 2) and of the *Y* chromosome in determining chromosome disjunction in Drosophila. The experimental procedure for recovering T (Y; 2) with centric break-points and for constructing a series of Experimental stocks that varied, as far as possible, only in the particular half translocation carried has been described by Falk, Baker & Rahat (1984). In that paper the experimental procedure for estimating the relative frequencies of all eight possible meiotic configurations in such stocks was also described. The segregation pattern in males of experimental stocks with 15 different half translocations has also been described (Falk *et al.* 1984). Here we present the segregation pattern in females of the same series of Experimental stocks.

Ever since the classical experiments of Bridges & Anderson (1925), and later of Dobzhansky (1933, 1934), on crossing over and disjunction in Drosophila females, the role of exchange pairing in chromosome disjunction has been well established. However, it has always been recognized that although exchange between homologues is a sufficient condition for orderly chromosomal disjunction in females, it is not a necessary condition. Approximately 5% of the *X* chromosomes and practically 100% of the small fourth chromosomes disjoin regularly without ever exchanging. Even more significantly, although heterozygosity for multiple inversions disrupts the exchange pairing of homologues, it does not necessarily interfere with the disjunction of the chromosomes (at least as long as the pairing disturbances are limited to one pair of chromosomes: see Cooper, Zimmering & Krivshenko, 1955).

Intensive studies of segregation in the presence of various chromosomal aberrations in Drosophila oocytes were carried out by Grell (see Grell, 1976). These studies led Grell to conclude that segregation of non-exchange chromosomes was controlled by a pairing event that occurred after 'exchange pairing' took place. This second, 'distributive pairing', determined the segregation of all chromosomes that had not been determined before by 'exchange pairing'. Total chromosome length, rather than homology, was considered to be the significant determinant at 'distributive pairing'. This concept of a less efficient homologue-disjunction mechanism acting *after* the more efficient one did, has been questioned on theoretical grounds by Novitski (1964). Experiments by Novitski (1975, 1978) and others (e.g. Portin, 1975) have shown that chromosomes that participated in the presumed 'distributive pairing' were not necessarily the ones excluded from 'exchange pairing'. This refuted the claim for separate disjunction determination events for exchange and non-exchange chromosomes. The demonstration by Nokkala & Puro (1976) and by Dävring & Sunner (1977) that the chromosomes in the oocytes of Drosophila assembled in a chromocenter-like configuration during meiotic prophase, provided a material basis for Novitski's model of nonspecific association of *all* chromosomes at prophase. According to this model, all chromosomes were held together in one bundle, at their proximal heterochromatic segments. Some chromosomes disjoin as a consequence of the ensuing exchange pairing, the others that are left in the chromocentric-like aggregate, may find a partner by default, and segregate from it. Yet, there are indications for some genetic control of disjunction of the non-exchange chromosomes. For example,

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Carpenter (1973) isolated a mutation that affects specifically the disjunction of non-exchange chromosomes. Indeed, in recent years both Sandler & Szauter (1978) and Carpenter & Baker (1982) found evidence for the direct involvement of the proximal heterochromatic segments of the fourth and *X* chromosome, respectively, in determining chromosome segregation. Similarly, our previous experiments (Falk, 1983) led us to believe that there were factors in the proximal heterochromatin of the *X* chromosome that directed chromosome disjunction during meiosis in oocytes.

In the present study we concentrated on the disjunction of non-exchange chromosomes in oocytes. It will be shown that the four chromosomal elements of all Experimental stocks segregated according to a similar basic pattern, in which the three possible two-by-two configurations were the most prevalent ones, irrespective of their contents. This pattern is completely different from the segregation pattern of the same chromosomal elements in the meiosis of spermatocytes. A model will be presented according to which the disjunction determinants for the autosomes or the sex-chromosomes function neither very efficiently nor very specifically in determining non-exchange chromosome segregation in oocytes.

2 MATERIALS AND METHODS

Detailed descriptions of the recovery of the T (Y; 2)'s, the construction of the Experimental stocks, and the experimental procedures for determining their segregation patterns were given by Falk *et al.* (1984). Here only those details essential for the argument that follows will be summarized. For further details on markers and on the structure of chromosomes, see also Lindsley & Grell (1968).

The Experimental stocks. Fourteen half-translocations that were induced by Falk & Baker (1984) were recovered in Experimental stocks, the segregation pattern of which were studied. In each Experimental stock the segregation of four chromosomal elements was followed:

X – a compound reversed metacentric *X*-chromosome, C(1)RM, y^2 *su*(w^a) w^a.

A – a chromosome 2 with multiple inversions, In(2LR)CyO, *Cy* dp^{lvl} *pr* cn^2.

F – a chromosome 2 from which either the left arm or the right arm had been deleted: free right arm and free left arm chromosomes, respectively. The free left arm, F(2L), *dp*, was found to have a rather long right heterochromatic arm on cytological examination. The free right arm, F(2R), *bw*, was found to carry only a minute left arm on cytological examination.

T – one element of a T (Y; 2), with either the left arm of chromosome 2 (Experimental stocks 110, 112, 148, 170, 312, 442, 750, 890, and 980) or the right arm of chromosome 2 (Experimental stocks 101, 126, 311, 726, and 880), capped or captured by a *Y*-chromosome fragment. The *Y*-chromosome fragment was marked with either y^+ (marking the tip of the short arm of the original *Y*-chromosome) or by B^s (attached to the tip of the long arm of the original *Y* chromosome).

The Experimental stocks were designated XATF and XAFT, according to whether the half-translocation carried 2L or 2R, respectively. The structure of the Experimental stocks was confirmed by cytological examinations of mitoses of

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larval brain ganglion cells. In all stocks only few non-Cy flies were recovered. That is, flies homozygous for the T and F elements were inviable.

In three of the XAFT stocks (126, 311 and 726) a spontaneous process of transfer of the y^+ marker from the T element carrying 2R to the F element carrying 2L took place before the segregation pattern of the Experimental stocks was determined. This must have been a kind of exchange between the heterochromatic left arm of the T element and the heterochromatic arm right of the F element (see figure 7 and discussion in Falk *et al.* 1984). This meant that the T and F elements in these stocks changed roles: the stocks were tested as XATF rather than as the originally intended XAFT.

An additional Experimental stock, originally from the *Y*-autosome translocation collection of Lindsely *et al.* (1972), was obtained from the Umeå Drosophila Stock Centre. This stock, B190, is a T(Y; 2) broken in section 60 of the polytene chromosomes, which has lost its B^s marker. The y^+ marker was found to be located on the right half of the translocation. Because in this stock both half translocation elements were present (rather than one T element and one F element), it was designated XATT.

Segregation of the four chromosomal elements can occur in eight different configurations, giving 16 different types of gametes (see left columns of Table 1 of the present paper, and figure 2 of Falk *et al.* 1984). In order to measure the frequency of each gamete type the Experimental stocks were mated to five different Tester stocks as described by Falk *et al.* (1984).

3. RESULTS

The number of progeny corresponding to the different types of maternal gametes obtained by mating the Experimental stocks to the five Tester stocks are given in Table 1. The number of culture bottles for each of the matings with the different Tester stocks, is given at the bottom of each column.

The frequencies of the different meiotic configurations, relative to that of configuration I, for all 15 Experimental stocks are given in Table 2. Included are also the results from a control stock with two free *X* chromosomes (no attached-*X*) and both left and right F elements (no T element). This control stock is designated X/X; A/F/F. The translocation arm of each stock, as well as the *Y*-chromosome marker attached to its T element, are indicated below the Experimental stocks' serial numbers.

The data are based on the pooled calibrated results of all repeats, according to the procedure described by Falk, *et al.* (1984). Where viability differences between complementary genotypes exceeded 50% of the more viable one, the data were corrected by ignoring the less viable genotype and doubling instead the number of flies of the more viable genotype. In each case the corrected values are given in parentheses. This correction was not done where the number of progeny of the more frequent type did not exceed a dozen flies. No such corrections were attempted with progeny of matings to Tester sock D_1, because in this Tester stock inequality between complementary genotypes is the rule (see e.g. Falk, 1983). Whenever non-disjunction in the Tester stocks was observed, and the progeny

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Table 1. *Total numbers of progeny obtained by mating females of the Experimental stocks to males of five Tester stocks, according to types of maternal gametes*

(For configurations VII and VIII: results of mating to D_1 to the left and to D_2 to the right. In the few cases where it was not possible to identify a genotype, the number was set equal to the complementary genotype and put in parentheses.)

Configurations		Experimental stocks															
		126	311	442	726	880	750	312	110	890	170	112	101	980	148	B190
I	X A	168	154	365	120	176	139	121	226	130	181	108	204	175	108	484
	T F	205	155	384	120	187	147	105	153	145	216	147	209	141	132	495
II	X T F	29	10	30	21	16	9	9	24	16	5	6	17	20	16	40
	A	32	17	40	20	20	7	20	15	17	11	3	27	17	13	11
III	X F	71	99	193	129	190	152	92	181	283	227	188	52	228	403	172
	A T	82	307	194	324	373	153	89	252	394	307	281	143	433	523	130
IV	X A T	1	2	1	23	9	3	0	2	5	5	5	2	3	4	0
	F	4	3	3	1	5	2	10	2	(5)	5	0	11	1	12	27
V	X T	37	246	289	123	382	68	62	106	114	187	28	55	130	82	125
	A F	48	309	468	305	509	199	195	307	314	346	123	85	267	217	355
VI	X A F	4	27	23	20	50	23	16	53	30	20	17	13	43	44	54
	T	8	11	28	16	35	9	37	21	21	16	9	4	15	18	33
VII	X	2 10	(13)	22 26	2 0	2 16	8 21	4 2	6 25	4 22	16 47	6 7	48 34	9 28	6 14	1
	A T F	41 16	13	101 25	11 0	61 22	67 21	36 8	50 31	32 49	72 75	50 16	31 69	77 42	53 12	5
VIII	X A T F	0 2	2	0 1	0 0	0 1	0 0	1 0	0 0	0 0	0 3	0 4	0 8	0 1	0 3	0 3
	0	2 16	(2)	2 (1)	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 8	0 0	0 0	0 0
		Number of culture bottles														
	A	4	3	7	3	3	2	3	2	2	2	2	4	2	3	4
	B	1	3	5	5	5	6	3	5	5	5	5	5	5	10	4
	C	1	4	4	7	5	5	4	5	5	5	5	3	5	5	5
	D_1	5	3	3	4	5	5	2	5	2	5	5	6	5	5	5
	D_2	2	–	4	2	5	5	2	5	2	10	5	7	5	5	–

Table 2. *Corrected and calibrated relative frequencies of gametes from different meiotic configurations (I to VIII)*
(Numbers in parentheses: corrected for viability differences.)

		X/X; A/F	126 XATF y^+	311 XATF y^+	442 XATF y^+	726 XATF y^+	880 XAFT B^s	750 XATF B^s	312 XATF B^s	110 XATF B^s	890 XATF y^+	170 XATF y^+	112 XATF y^+	101 XAFT y^+	980 XATF B^s	148 XATF y^+	B190 XATT (B^s) y^+
I	X A / T F	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
II	X T F / A	1	0·16	0·09	0·10	0·17	0·10	0·06	0·13	0·10	0·12	0·04	0·04	0·11	0·12	0·12	(0·08) 0·05
III	X T F / A T	1·52	3·28	(3·97) 2·63	1·19	(3·24) 2·27	1·86	0·71	1·60	0·92	1·97	1·08	1·47	(1·11) 0·76	1·67	2·32	0·60
IV	X A T / F	1·52	0·11	0·03	0·02	(0·23) 0·12	0·46	0·01	0·09	0·01	0·03	0·02	0·02	(0·09) 0·05	0·01	0·04	(0·11) 0·06
V	X T / A F	1·50	1·82	2·69	2·83	(2·18) 1·53	2·95	(1·11) 0·75	(2·59) 1·71	(1·30) 0·87	(1·83) 1·25	1·07	(0·77) 0·47	0·90	(1·35) 1·01	(2·17) 1·49	(1·16) 0·78
VI	X A F / T	1·50	0·26	(0·26) 0·18	0·19	0·13	0·28	(0·13) 0·09	(0·49) 0·35	(0·22) 0·16	0·15	0·07	0·08	(0·17) 0·11	(0·22) 0·15	(0·44) 0·31	0·14
VII	X / A T F		0·37	0·17	0·62	0·22	0·23	0·22	0·40	0·18	0·26	0·21	0·16	0·41	0·29	0·28	0·01
VIII	X A T F / 0		0·05	0·03	0·01	0·04	0·003	0	0·003	0	0	0·003	0·01	0·03	0	0·008	0·05

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could be classified according to their maternal meiotic configuration, the figures were added to the appropriate classes.

The Experimental stocks are presented in the same order as in tables 4 and 5 of Falk *et al.* (1984), in order to facilitate comparisons.

The most conspicuous aspect seen in Table 2 is that all 15 Experimental stocks have a quite similar segregation pattern. The frequencies of configurations I, III and V are common, all other configurations are rarer, although configuration VII, and in some cases also configuration VI, are not very rare in relation to configuration I. This pattern is very different from that obtained for the segregation of males of the same Experimental stocks, where stocks were divided into two groups by their segregation pattern, and in one group the stocks were further differentiated by the degree of expression of the specific segregation pattern (Falk *et al.* 1984).

The three most common configurations are the three possible combinations in which the four chromosomal elements segregate two-by-two. Actually, these three configurations are not equally frequent, and in most Experimental stocks, configurations III and V are more frequent than configuration I: the mean relative (corrected) frequency of configuration III is 1·88 and that of configuration V, 1·92 (the XATT Experimental stock B190 was not considered here). On closer inspection it can be seen that mating Experimental stock females to Tester stock B males did not allow us to discriminate progeny of configuration III from those of configuration VII. Thus, it would seem that the frequency of configuration III could be inflated. This, however, is not the case because it has been shown that Tester stock B males produce hardly any gametes that complement those of configuration VII (Falk *et al.* 1984).

There is no direct indication why the relative frequencies of configurations III and V are lower in some Experimental stocks (750, 110, 112, 101 and B190) than in others. If one accepts the classification of the Experimental stocks according to their relative breakpoint, as given in figure 8 of Falk *et al.* (1984), one may compare the relative frequencies of configurations III and V to configuration I in the five Experimental stocks with the longest T elements (126, 311, 442, 726, and 880) and the five with the shortest T-elements (101, 112, 148, 170, and 980). It appears that the ratio for the stocks with the shorter T elements is lower (mean value: 1·39) than that for the stocks with the longer ones (mean value: 2·60). This means that, if anything, the more different in length the T and F elements were, the more frequently they segregated from each other (or, put otherwise, the more similar the length of the T element to that of the X or A element, the less often it segregated from them).

In these experiments we intended to study the segregation of the chromosomal elements as far as possible in the absence of recombination. The CyO balancer is a pericentric inversion superimposed upon a chromosome 2 carrying a paracentric inversion in each arm. Although these inversions would interfere with homologue pairing and exchange, the possibility must be considered that some pairing and exchange did occur between the A element and the T and F elements. Most of such exchange products would either not be included in the oocyte nucleus, or cause zygote lethality when included in the nucleus. Thus there is no direct way to

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recognize the extent of exchange events during meiotic prophase. In the presence of exchange, the disjunction of the A element from both the T element and the F element (configuration I) should prevail, relative to the non-disjunction of the T element (configuration III) or the F element (configuration V) from the A element. The segregation pattern of four of the Experimental stocks in which the multiply-inverted A element was replaced by a non-inverted, normal chromosome 2 is presented in Table 3. In such females, obviously the A element could recombine freely with both the T and F elements. As can be seen in the table, the disjunction of the T and F elements from the multiply-inverted A element is dramatically different from that found when exchange between these elements could occur freely. 'Exchange pairing' was not a significant factor in determining the segregation pattern of our Experimental stocks.

Table 3. *Relative frequencies of configurations I–VI in females of four Experimental stocks: The A element carries multiple inversions (Cy) or is free of inversions (no-Cy)*

(In parentheses: total number of progeny from gametes of each configuration in matings with no-Cy flies (In two cases culture bottles were transferred only once, and thus were counted only 2/3).)

		4 4 2 XATF y^+		8 8 0 XAFT B^s		7 5 0 XATF B^s		1 0 1 XAFT y^+	
		Cy	no-Cy	Cy	no-Cy	Cy	no-Cy	Cy	no-Cy
I	X A / T F	1	1 (1142)	1	1 (1551)	1	1 (1340)	1	1 (930)
II	X T F / A	0·10	0·25 (283)	0·10	0·30 (464)	0·06	0·19 (259)	0·11	0·29 (266)
III	X F / A T	1·19	0·66 (375)	1·86	0·32 (74)	0·71	0·16 (117)	1·11	0·45 (113)
IV	X A T / F	0·02	0·08 (47)	0·28	0·02 (8)	0·01	0·03 (112)	0·09	0·03 (28)
V	X T / A F	2·83	0·23 (163)	2·94	0·19 (168)	1·11	0·25 (143)	0·90	0·19 (158)
VI	X A F / T	0·19	0·02 (16)	0·28	0·02 (11)	0·13	0·07 (39)	0·17	0·05 (11)
		Number of culture bottles							
	A	4		4		$4\frac{2}{3}$		4	
	B	4		2		3		5	
	C	5		$2\frac{2}{3}$		4		3	

In five Experimental stocks a free *Y* chromosome was added to the XATF genome of the females. Females of these stocks were mated to males of Tester stock A only (Table 4). In configuration I the X element segregates from the T element (and F element), while in configuration II it segregates with the T element (and F element). In only one of the five matings did the relative frequency of configuration II to configuration I significantly increase when a free *Y* chromosome was added. It seems that of the five Experimental stocks, only in one (442) was

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there a significant preferential disjunction of the X and T elements that could be challenged by the competing free *Y* chromosome. In the other four stocks the presence of the *Y* chromosome did not affect the segregational relations between the chromosomal elements. The preferred X–T disjunction in Experimental stock 442, as compared to its relative absence in Experimental stock 750, can also be seen in the segregation pattern of non-Cy females of these two stocks (Table 3).

Table 4. *Ratio of configuration II* ($XTF \leftrightarrow A$) *to configuration I* ($XA \leftrightarrow TF$) *in females of Experimental stocks with no free* Y *and with a free* Y *chromosome*

	442 XATF y^+	750 XATF B^s	890 XATF y^+	170 XATF y^+	112 XATF y^+
No free *Y*	0·10	0·06	0·12	0·04	0·04
Free *Y*	1·15	0·08	0·10	0·11	0·11

4. DISCUSSION

The evidence presented allowed us to be quite confident that the segregation of the experimental chromosome-elements in this study took place essentially in the absence of exchange pairing. This would mean that chromosomes either did not pair at all, or, if they did, pairing was limited to only a few points along the homologous arms or, alternatively, to a time when exchange did not occur. Yet, the non-random recovery of gametes from the eight (a priori equally possible) meiotic configurations indicates that there was some conjunction (at least in the narrow sense of 'interaction') between the chromosome elements. The segregation pattern in the females is, however, so different from that in males, that we can abandon any speculation on a possible common denominator for the factors involved in non-exchange segregation in females and in males. This is in agreement with Grell (1976) and others (e.g. Carpenter, 1973).

Had we obtained a segregation pattern in which the three two-by-two configurations, I, III and V, were equally frequent, we would have had to conclude that although the non-exchange chromosomes tended to conjoin in pairs, there was no specificity in the choice of the partners they interacted with. As it happened, however, configurations III and V were usually more frequent than configuration I, and configurations VI and VII were not too rare either.

The results presented here can be best understood on the basis of a modification of Novitski's (1964) model (see Introduction), assuming the existence of determinants that direct the disjunction of the non-exchange chromosomes from the chromocentere-like aggregate. Two kinds of determinants suggest themselves: (*a*) sex-chromosome determinants that direct the disjunction of the X and T elements, with good specificity, (*b*) autosomal disjunction determinants, with poor specificity. More specifically, there appears to be no difference between the determinants of the left arm and those of the right arm.

In Table 5 are listed the results expected on the assumption that determinants lead to the disjunction of one of the possible pairs, while the other two elements either interact-to-disjoin by default, or segregate at random. If only sex chromosome

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determinants were involved (line *a*), equal frequencies of configurations I, III, VI and VII would be expected. Although all four configurations were quite frequent (Table 2), the frequency of the first two was considerably higher than the last two. Furthermore, on this assumption no explanation for the prevalence of configuration V is offered. The excess of configurations I and III over configurations VI and VII indicates that the A and F elements did not segregate at random either; rather, there was also some interaction between the autosomal elements.

Table 5. *Configurations expected when one pair of chromosomal elements is determined to disjoin and the other elements disjoin or segregate by default or do not segregate*

Elements determined to disjoin	Remaining elements	Disjoin/ segregate by default	Do not segregate (non-disjunction)
(*a*) X T	A F	I III	VI VII
(*b*) A F	X T	I III	II IV
(*c*) A T	X F	I V	II VI
(*d*) T F	X A	III V	IV VI
(*e*) X A	T F	III V	II VII
(*f*) X F	A T	I V	IV VII

If we assume that only autosomal determinants were involved, i.e. that the A element could interact with either the F element (line *b*), or the T element (line *c*), the high frequency of configurations I, III and V could be explained. Note, however, that on an assumption that only autosomal disjunction determinants were involved (only lines *b* and *c*), configurations I and II, III and IV, and V and VI should have been equally frequent, which is not the case. The possibility that both the T and F elements disjoined from the A element could also be excluded, because this would have led to the prevalence of configuration I, and, in the absence of sex-chromosome determinants, also the prevalence of configuration II.

Assuming that the X element is determined to disjoin from the T element (line *a*), or the A element from the F element (line *b*), or the A element from the T element (line *c*) in a given oocyte, the overall excess of configurations III and V over configuration I would still remain unexplained. Obviously we must also accept segregation of the left autosomal arm from the right arm (T–F segregation). The low specificity of autosomal disjunction determinants that is predicted here is compatible with the absence of much variation between Experimental stocks in their segregation patterns.

But, before these conjectures are carried further, we must examine how far our results contribute to the refutation of previous models, notably that of Grell.

Grell's claim that the non-exchange chromosome pool must be *assembled* after exchange pairing takes place, was based mainly on the well known observation that no reduction was observed in exchange frequencies between the disjoining X chromosomes in XXY females, as compared to that in XX females (Grell, 1962). Falk (1983) has shown that this claim was probably due to an artifact of pooling the recombination frequencies of all intervals along the X chromosome. Reanalysing Grell's own data revealed that there *was* a reduction in recombination frequencies in the proximal segments of the X chromosomes of XXY females as compared to

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those of XX females. This reduction was, however, compensated by increased recombination frequencies in the distal segments: the 'intra-chromosomal' effect described by Grell in the same study. The recent findings of Lüning (1982*b*) that exchange in the distal-most intervals of the non-disjunctional X chromosomes of XXY females was much higher than suspected earlier, further refute the claim that non-disjoining chromosomes are necessarily non-exchange chromosomes, and thus, strongly supports Falk's (1983) interpretation. Furthermore, a careful analysis of Lüning's phenotypic deviants, presumed to have a more complex origin than single crossing-over (see table 10 of Lüning, 1982*a*), reveals that most could be due to exchange events between two or all three elements of X–X–Y trivalents (i.e. one X conjoining with both the Y and the other X, and hence disjoining to give X and XY gametes), as suggested by Falk (1983).

Grell (1964) observed that similarity in chromosome length specified the segregation of non-exchange elements. Moore & Grell (1972) claimed further that it was similarity in total chromosome length, rather than arm length, that served as the recognition cue for non-exchange chromosome segregation. The evidence for this last claim depended on two matings in which a compound metacentric chromosome 4 segregated from a duplication of X-chromosome origin. In one (Dp 1144), the duplication was as long as one arm of the compound chromosome 4, in the other (Dp 1346), the duplication was twice as long as the arm of the compound chromosome 4, i.e. as long as the total length of the compound. The frequencies of compound chromosome 4 and duplication non-disjunction and their standard errors were $0{\cdot}24 \pm 0{\cdot}06\,\%$ and $0{\cdot}16 \pm 0{\cdot}03\,\%$, respectively*. This difference is not significant. It is true that the difference was more significant when a third competing element was added, but as the authors showed, this reflects another process, and even there the difference disappeared when the data were broken down into the three possible pairwise non-disjunctions.

Both the results of our previous study on the segregation of a very long compound entire chromosome 2 from the X chromosomes (Falk, 1983), and the results of the present study do not support the hypothesis that total chromosome length determines the segregation pattern of non-exchange chromosomes. This still does not refute the claim that chromosome arm length is significant for the determination of the segregation of non-exchange chromosomes. But such an effect could actually be expected when chromosomes are aggregated into a chromocentere-like configuration before meiotic metaphase. Taken together with the reservations from Grell's model quoted in the Introduction, we may consider the hypothesis of a second 'distributive pairing' that determines the segregation of chromosomes which did not participate in 'exchange pairing', on the basis of similarity in length, rather than on the basis of segregation determinants, as refuted. We believe that our modification of the model suggested by Novitski is consistent both with the theoretical considerations, and with the experimental results.

The interpretation of the results offered here is also in agreement with the

* There are minor computation errors in table 4 of Moore & Grell (1972): The S.E. of $0{\cdot}16\,\%$ for a total of 13337 is $0{\cdot}03\,\%$ and not $0{\cdot}01\,\%$ as given for the Dp 1346 chromosome. Similarly the S.E. for chromosomes Dp 856, Dp 1173 and y^{+}Y are: 0·07, 0·06 and $0{\cdot}16\,\%$ rather than 0·06, 0·01 and $0{\cdot}17\,\%$ respectively.

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findings of Gershenson (1940) and of Lindsley & Sandler (1958), according to which female-specific disjunction determinants are present in the proximal heterochromatin of the sex chromosomes of Drosophila. The difference in the segregation pattern that we observed in the presence of a free *Y* chromosome, between Experimental stock 442, and the four other stocks, also indicates that there are specific sites for disjunction determination on the *Y* chromosome, that may be translocated or not, according to the location of the breakpoint in this chromosome. These claims were also upheld in our previous study (Falk *et al.* 1984). The results presented in this series further agree with Gershenson's observation that disjunction determinants active in females are at least partly different from those active in males.

That the function of determinants in females is less specific than that in males could have been expected also on theoretical grounds: while in females the main role of securing regular disjunction of homologues is played by exchange, in males these determinants are the only device available for securing proper disjunction of homologues.

In conclusion, we believe that we have shown in this series of studies that disjunction determinants are located in the proximal segments of the sex chromosomes as well as of chromosome 2. The disjunction determinants operating in females are different from those operating in males: while those in females are not very efficient and not highly specific, those in males are specific, and when a complete set is present, they are also very efficient in securing homologue disjunction at meiosis.

This paper was written while the senior author was a fellow at the Institute for Advanced Study in Berlin.

REFERENCES

BRIDGES, C. B. & ANDERSON, E. G. (1925). Crossing over in the *X*-chromosome of triploid females of *Drosophila melanogaster*. *Genetics* **10**, 418–441.

CARPENTER, A. T. C. (1973). A meiotic mutant defective in distributive disjunction in *Drosophila melanogaster*. *Genetics* **73**, 393–428.

CARPENTER, A. T. C. & BAKER, B. S. (1982). On the control of the distribution of meiotic exchange in *Drosophila melanogaster*. *Genetics* **101**, 81–89.

COOPER, K. W., ZIMMERING, S. & KRIVSHENKO, J. (1955). Interchromosomal effect and segregation. *Proceedings of the National Academy of Science U.S.A.* **41**, 911–914.

DÄVRING, L. & SUNNER, M. (1977). Late prophase and first metaphase in female meiosis of *Drosophila melanogaster*. *Hereditas* **85**, 25–32.

DOBZHANSKY, Th. (1933). Studies on chromosome conjugation II. The relation between crossing over and disjunction of chromosomes. *Zeitschrift für induktive Abstammungs- und Vererbungslehre* **64**, 269–309.

DOBZHANSKY, Th. (1934). Studies on chromosome conjugation III. Behavior of duplicating fragments. *Zeitschrift für induktive Abstammungs- und Vererbungslehre* **68**, 134–162.

FALK, R. (1983). The effect of an unusual chromosome architecture on disjunction and non-disjunction in Drosophila. *Genetical Research* **41**, 17–28.

FALK, R. & BAKER, S. (1984). Production of centric-autosomal-Y translocations. *Drosophila Information Service* **60**, 104–105.

FALK, R., BAKER, S. & RAHAT, A. (1985). Segregation of centric *Y*-autosome translocations in *Drosophila melanogaster*. I. Segregation determinants in males. *Genetical Research* **45**, 51–79.

GERSHENSON, S. M. (1940). The nature of so-called genetically inert parts of chromosomes. *Videnskap. Akad. Nauk. URSS* Kiev (in Ukrainian), pp. 3–116.

https://doi.org/10.1017/S0016672300021960 Published online by Cambridge University Press

GRELL, R. F. (1962). A new model for secondary non-disjunction. The role of distributive pairing. *Genetics* **47**, 1737–1754.

GRELL, R. F. (1964). Chromosome size at distributive pairing in *Drosophila melanogaster* females. *Genetics* **50**, 151–166.

GRELL, R. F. (1976). Distributive pairing. In *The Genetics and Biology of Drosophila*, vol. 1 a (ed. M. Ashburner and E. Novitski), pp. 435–486. Academic Press.

LINDSLEY, D. L. & GRELL, E. H. (1968). *Genetic Variations of Drosophila melanogaster*. Carnegie Institute of Washington, Publication, no. 627.

LINDSLEY, D. L. & SANDLER, L. (1958). The meiotic behavior of grossly deleted *X* chromosomes of *Drosophila melanogaster*. *Genetics* **43**, 547–563.

LINDSLEY, D. L., SANDLER, L., BAKER, B. S., CARPENTER, A. T. C., DENELL, R. F., HALL, J. C., JACOBS, P. A., MIKLOS, G. L. G., DAVIS, B. K., GETHMANN, R. C., HARDY, R. W., HESSLER, A., MILLER, S. M., NOZAWA, H., PARRY, D. M. & GOULD-SOMERO, M. (1972). Segmental aneuploidy and the genetic gross structure of the Drosophila genome. *Genetics* **71**, 157–184.

LÜNING, K. G. (1982*a*). Genetics of inbred *Drosophila melanogaster*. VI. Crossing-over in secondary non-disjunction exceptionals. *Hereditas* **96**, 161–174.

LÜNING, K. G. (1982*b*). Genetics of inbred *Drosophila melanogaster*. VII. Evidence of normal chromosome pairing in the distal ends of *X*-chromosomes in secondary non-disjunction. *Hereditas* **96**, 287–290.

MOORE, C. M. & GRELL, R. F. (1972). Factors affecting recognition and disjunction of chromosomes at distributive pairing in female *Drosophila melanogaster*. I. Total length *vs.* arm length. *Genetics* **70**, 567–581.

NOKKALA, S. & PURO, J. (1976). Cytological evidence for a chromocenter in *Drosophila melanogaster* oocytes. *Hereditas* **83**, 265–268.

NOVITSKI, E. (1964). An alternative to the distributive pairing hypothesis in Drosophila. *Genetics* **50**, 1449–1451.

NOVITSKI, E. (1975). Evidence for a single phase pairing theory of meiosis. *Genetics* **79**, 63–71.

NOVITSKI, E. (1978). The relation of exchange to nondisjunction in heterologous chromosome pairing in the Drosophila female. *Genetics* **88**, 499–503.

PORTIN, P. (1975). Non-homologous chromosome pairing in female Drosophila. Before or after exchange? *Hereditas* **80**, 59–68.

SANDLER, L. & SZAUTER, P. (1978). The effect of recombination-defective meiotic mutants on fourth-chromosome crossing over in *Drosophila melanogaster*. *Genetics* **90**, 699–712.

Note added in proof. Females of an XAFF control stock, i.e. flies with two free autosomal arms and no translocation element, gave nearly equal numbers of flies from configuration I and II gametes, and hardly any from the other configurations. This shows that in the absence of sex-chromosome determinants, the two single armed autosomal elements disjoin regularly from the (inverted) double armed autosome, as expected when autosomal disjunction determinants interact.

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