FURTHER NOTES ON THE NATURE OF NON-RANDOM DISJUNCTION IN DROSOPHILA MELANOGASTER[1]

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THE nature of meiosis in ordinary diploid organisms is such that homologous chromosomes are usually present in gametes with equal frequencies. One exception to this rule in *Drosophila melanogaster* has been termed non-random disjunction (NOVITSKI 1951). Here it has been found that homologs are recovered unequally frequently from females when they are heteromorphic, or of unequal size. When this is the case, the smaller of the two homologs is recovered about twice as frequently as the larger. The genetic analysis has suggested, as the basis for this phenomenon, the formation of an asymmetric dyad as a consequence of crossing over, followed by the preferential inclusion into the egg nucleus of the smaller of the two chromatids making up the dyad. It was suggested, at the time the phenomenon was first described, that one might imagine this result to be brought about by the dragging of the longer chromatid of the dyad at first anaphase, leading to an orientation of the centromere region at second metaphase of such a nature that the shorter chromatid would tend to become included in an egg nucleus. Such a sequence of events is purely hypothetical and was proposed primarily as an aid in understanding the genetic results.

The following two points will be considered below. 1. A hypothesis to explain non-random disjunction in mechanical terms is discussed and discarded. The experimental results, however, reveal a deficiency of newly generated single ring X chromosomes from females carrying tandem metacentric compound X chromosomes (for a description of the compound chromosomes, see NOVITSKI 1954) with no homolog. It is shown that this same phenomenon extends to the single rings generated by tandem compound ring X chromosomes, and also to the single rod chromosomes generated by tandem acrocentric compound X chromosomes. 2. Non-random disjunction in the tandem acrocentric compound X chromosome is now demonstrated to occur; its extent being considerably greater than in any previously analyzed case.

THE BEHAVIOR OF TANDEM METACENTRIC COMPOUND X CHROMOSOME WITHOUT AN HOMOLOGOUS CHROMOSOME

A hypothesis to explain, in mechanical terms, the phenomenon of non-random disjunction was tested during the course of the present work. Although the tests did not confirm the initial hypothesis, the results obtained proved to be of considerable interest in another connection and hence are reported here.

The hypothesis which was tested depended upon assuming that paired heterochromatic regions tend to separate later, or with more difficulty, than paired euchro-

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matic regions. If such were the case, and if two homologous chromosomes differed from one another in that one of them had a distally placed heterochromatic segment, then, following a single exchange, the dyads separating from one another are each composed of a longer and a shorter chromatid, the longer, in each case, possessing the heterochromatic distal region. If these heterochromatic regions remain paired for some time after the more proximal regions have separated, then both of the dyads should become so oriented that the shorter chromatid faces an outer, and hence a potentially functional, egg nucleus. This would result in an excess recovery of shorter chromatids, which is the observed result to which the name non-random disjunction has been given. In fact, the structural situation just described (actually sc^4 sc^8/sc^8) represents one of the major evidences for the phenomenon.

An experiment which would test such a hypothesis immediately suggests itself. Asymmetric dyads are produced not only from homologs which differ structurally from one another, but are also generated by some of the compound X chromosomes. One such compound is the tandem metacentric compound X chromosome (known, in older usage, as the tandem attached-X) which produces, following certain types of exchanges, dyads composed of a tandem metacentric compound X chromosome and a single ring X chromosome. These single rings have been shown to disjoin non-randomly from the compound chromosome (NOVITSKI 1951). The tandem metacentric compound used in those experiments was heterozygous for $In(1)sc^8$, and hence possessed a distal heterochromatic segment. The parental females carried, in addition to the compound, a heterochromatic homolog (the Y chromosome) which regularly separates from the compound at anaphase I. A delay in the separation of the Y chromosome from the distal heterochromatin of the compound chromosome would, according to the hypothesis, orient the dyad so as to give the observed excess of recovered single ring X chromosomes. A test of the hypothesis, consequently, is simply to remove the homolog, which should eliminate the orientation, and hence the excess of recovered single rings.

Two points must be mentioned at this juncture. First, an excess in the recovery of single rings is manifest in tandem metacentric data of STURTEVANT and BEADLE (1936). These workers used a tandem metacentric compound which did not possess a distal heterochromatic segment. (Their compound was an attached-X heterozygous for $In(1)y^4$, an inversion which has its distal break to the left of *y* and its proximal break just to the right of *fu*). Since the hypothesis which was tested requires the separation of basal heterochromatin, distally placed on the compound, from the Y chromosome (which was present in the experiments of STURTEVANT and BEADLE) non-random disjunction in this case represents critical negative evidence against the hypothesis. For this reason, a tandem metacentric compound similar to that of STURTEVANT and BEADLE has been constructed and tested. The results obtained are in full agreement with those of the earlier work (see below), and hence the hypothesis would, on this basis alone, have to be discarded. Secondly, it should be noted that after the experiments to be described were completed, further (and extremely convincing) evidence against the hypothesis was reported by WELTMAN (1954) who demonstrated non-random disjunction in an especially constructed attached-X chromosome, tested in females which did not carry a homolog for the attached-X.

In conclusion then, the data of STURTEVANT and BEADLE, the repetition of their results in the present work, and finally the data of WELTMAN are sufficient to eliminate the initial hypothesis. The experiments to be described below therefore, although originally done with this particular hypothesis in mind, are not considered from that point of view.

Experimental results

Two tandem metacentric compound X chromosomes have been used in the present study. The first of these is designated as the *Hw f* tandem metacentric; its origin has been described in detail previously (NOVITSKI and LINDSLEY 1950). The particular properties of this compound which are of interest here are: (1) the single ring X chromosomes produced by crossing over are viable in both males (XY or XO) and females; and (2) the distal portion of one arm of the compound, having been derived from $In(1)sc^8$, possesses a distal heterochromatic segment containing the *bb* locus and the nucleolus organizing region (*NO*).

The second tandem metacentric compound studied, designated here as the y^4 tandem metacentric, had been synthesized in a triploid female carrying an attached-X chromosome homozygous for *y v f*, and a rod X chromosome containing the y^4 inversion. An exchange, in such a female, between the attached-X chromosome and the inverted chromosome, taking place proximal to the y^4 inversion, produced the tandem metacentric compound. The properties of this compound which are of interest here are: (1) the single rings generated by crossing over are deficient for the tip of the X chromosome and duplicated for the proximal uninverted section of $In(1)y^4$, and hence are almost invariably male lethal although they are recoverable in heterozygous females; (2) the compound possesses no distally placed heterochromatin; and (3) the compounds are heterozygous for the markers *v* and *f*.

Data have been collected from three pairs of parallel crosses. First, females carrying the *Hw f* tandem metacentric compound both with and without a Y chromosome were crossed to Canton-S (wild type) males. The results from these matings are given in table 1. A similar pair of matings was made between females carrying the y^4 tandem metacentric compound, both with and without a Y chromosome, by Canton-S males. The results from this pair of crosses are given in table 2. The y^4 tandem metacentric was also tested in females which either carried no homolog for the compound, or which carried FR2 as a homolog. (FR2 is a heterochromatic chromosome fragment equiva-

TABLE 1

The results from crosses of females carrying the Hw f *tandem metacentric compound X chromosome, both with and without a Y chromosome, by Canton-S (wild type) males*

Type of progeny	Phenotype of progeny	Number of progeny from	
		♀♀ with a Y	♀♀ without a Y
Compound X ♀♀	Hw f ♀♀	285	369
Patroclinous ♂♂	+ ♂♂	2,121	2,061
Ring-bearing ♀♀	+ ♀♀	802	570
Ring-bearing ♂♂	f ♂♂	765	598

TABLE 2

The results from crosses of females carrying the y^4 *tandem metacentric compound X chromosome heterozygous for* v *and* f, *both with and without a Y chromosome, by Canton-S (wild type) males. Occasional crossovers which occurred outside of the* y^4 *inversion are included with the* y *female class. The numbers in parenthesis are the observed numbers corrected for viability according to the method shown in the text*

Type of progeny	Phenotype of progeny	Number of progeny from	
		♀♀ with a Y	♀♀ without a Y
Compound X ♀♀	y ♀♀	911	764
Patroclinous ♂♂	+ ♂♂	4,734	3,964
Ring-bearing ♀♀	+ ♀♀	1,191 (1,575)	740 (979)
Homozygous ♀♀	y v ♀♀	29	20
	y f ♀♀	0	2

TABLE 3

The results from crosses of females carrying the y^4 *tandem metacentric compound X chromosome heterozygous for* v *and* f, *both with and without FR2 (a heterochromatic chromosome fragment equivalent to YL and carrying* y^+), *by* y B *males carrying the YSX·YL chromosome plus a normal Y chromosome. Occasional crossovers which occurred outside of the* y^4 *inversion are included with the* y *female class. The "patroclinous males" are* y^+ *when they receive FR2 from the parental females. The numbers in parenthesis are the observed numbers corrected for viability according to the method shown in text*

Type of progeny	Phenotype of progeny	Number of progeny from	
		♀♀ with FR2	♀♀ without FR2
Compound X ♀♀	y ♀♀	923	1,134
Patroclinous ♂♂	(y or y^+) B ♂♂	4,241	5,585
Ring-bearing ♀♀	y B ♀♀	1,249 (1,652)	1,076 (1,423)
Homozygous ♀♀	y v ♀♀	43	45
	y f ♀♀	1	1
Exceptional ♀♀	+ or B ♀♀	10	—
Exceptional ♂♂	y B ♂♂	100	—

lent to the long arm of the Y chromosome and carrying the normal allele of *y* from the distal uninverted section of *In(1)sc*^{8}. These females were crossed to *y B* males carrying a YSX.YL chromosome plus a normal Y chromosome. The results from this pair of experiments are given in table 3.

Although the single rings generated by the y^4 inversion are recoverable in the heterozygous condition as females in spite of the fact that the rings carry a rather sizable duplication, it might be suspected that there would be an adverse effect on the viability of such ring-bearing females. To test for such a possibility (both in the case of the rings from the y^4 tandem metacentric as well as for the case of the *Hw f* tandem metacentric), rings from each type of tandem metacentric were tested in the following way: ring/y^2w^a *B*, M-5 females were crossed to Canton-S (wild type) males. The results from these crosses are given in table 4. The two types of female progeny from this cross (i.e. those which get the M-5 chromosome from the parental female

TABLE 4

Tests for the viability of single ring X chromosomes generated by the Hw f *and the* y^4 *tandem metacentric compound X chromosomes. The cross in both cases was as follows: ring/*y^2 w^a *B, M-5* ♀♀ × *Canton-S (wild type)* ♂♂

Type of progeny	Phenotype of progeny	Ring from *Hw f* tandem metacentric	Ring from y^4 tandem metacentric
Ring-rod ♀♀	+ ♀♀	196	570
Rod-rod ♀♀	B/+ ♀♀	223	754
Ring-bearing ♂♂	f ♂♂	208	0
Rod-bearing ♂♂	y^2 w^a B♂♂	146	522
Exceptional ♂♂	+ ♂♂	0	21

and hence are *B*, versus those which get the ring and are therefore wild type) give a measure of the viability of the ring in each case. In the case of the ring from the *Hw f* tandem metacentric, it can be seen that 196 rings are recovered to 223 rods. Thus the viability of ring-bearing females carrying the ring from the *Hw f* tandem metacentric is not greatly depressed. The ring from the y^4 tandem metacentric, on the other hand, does show a depression. As can be seen from table 4, there were 754 rods recovered as compared with only 570 rings. As a consequence, in analyzing each test involving the y^4 tandem metacentric, the ring-bearing female class must be increased to account for this viability depression. Such a viability correction may be calculated simply according to the relationship: 570:754 = observed number of rings: corrected number of rings. The corrected numbers for the ring classes are given in parenthesis next to the observed figures in tables 2 and 3. It is the corrected figures which will be used in all of the calculations to follow; it should be noted, however, that the conclusions to be drawn from these experiments do not depend upon these corrections.

Analysis of the data

An examination of the data given in tables 1, 2, and 3 reveals a consistent difference between the experiments in which the parental females carried a homolog for the tandem metacentric compound as compared with those in which they did not. Thus for each set of experiments there are proportionately fewer rings produced by females which carried no homolog for the compound than from females which did carry such a homolog.

As a first approach, it might be imagined that this reduction in the recovery of single rings is a reflection of a change in the amount of non-random disjunction; specifically, a reduction or an elimination of such non-randomness (since when non-randomness operates it causes an excess in the recovery of single rings). That this is, in fact, not the case may be shown in two ways, the second of which is of particular interest. First, an examination of the raw data in tables 1, 2, and 3 shows that in every case (of specific interest at present, of course, are those cases in which the parental females carried no homolog for the compound) the number of rings recovered in either sex exceeds the number of compound-X females recovered. This, barring a gross viability depression of the compound-X female class, is equivalent to a direct observation of non-randomness. This follows from a simple consideration of the expecta-

TABLE 5

The ratio of single ring X chromosomes recovered as females to recovered patroclinous males, and the ratio of recovered tandem metacentric compound X chromosomes to recovered patroclinous males for all of the tandem metacentric tests reported. The figure used for the rings generated by the y^4 *tandem metacentric has been corrected for viability by the method shown in text. The column headed "Table" gives the source of the data from which the ratios have been obtained*

Cross	Table	Ring ♀♀ /Pat. ♂♂	Tandem metacentric ♀♀ /Pat. ♂♂
Hw f/Y × Canton-S	1	0.38	0.13
Hw f/0 × Canton-S	1	0.28	0.18
y^4/Y × Canton-S	2	0.33	0.20
y^4/0 × Canton-S	2	0.25	0.20
y^4/FR2 × YSX·YL	3	0.38	0.22
y^4/0 × YSX·YL	3	0.25	0.21

tions from the various types of exchanges (for diagrams, see NOVITSKI 1951): in the absence of non-randomness, from no-exchange tetrads there are produced only compound X's, whereas from the single and double-exchange tetrads there is produced a compound X for each single ring, and, consequently, if there were no non-randomness, there should be at least as many compounds recovered as rings (in either sex). Since an excess of rings is apparent in the data, it may be concluded that non-randomness is operative in tandem metacentric compounds even in the absence of a homolog.

Another way of considering the depression of rings in cases in which the compound-bearing females carried no homolog is as follows. If the depression of rings were a consequence of a shift (of any sort) in the relative recovery of rings and compounds, then, if the relative proportion of rings is reduced, the proportion of compound-X's would go up. In table 5, the ratio of rings to patroclinous males and the ratio of compound X's to patroclinous males is given for all of the cases reported. From this table it can be seen that, in general, the relative proportion of recovered compounds remains constant (considering pairs of parallel runs with and without a homolog), but in every case the proportion of rings is sharply reduced when the homolog is absent. From the data it appears, then, that there is a reduction in the number of rings produced by females carrying a tandem metacentric compound with no homolog, without, however, a concomitant increase in any of the other classes. Since there are more rings than compound-X's observed, and since none of the classes is increased to account for the depression in rings, it would appear most reasonable to attribute this depression to a lethality of some percentage of the rings newly generated by the compound chromosome.

In this connection there is an observation of considerable interest. Crosses have been made of females carrying tandem compound ring X chromosomes both with and without FR2 (NOVITSKI 1954) to identical males. In the case in which the females carried FR2, the ratio of ring males to patroclinous males was 0.33, while the ratio of compound-bearing females to patroclinous males was 0.09. In a parallel run in which the females carried no homolog, the ratios were 0.25 and 0.09, respectively. Hence it appears that in the tandem ring, as well as in the tandem metacentric, there is a depression of recovered single rings when the parental females lack a homolog for the

compound. This observation renders it all the more likely that this depression of rings is a lethality, since the expectations from the various types of exchanges are rather different for the two compounds.

Measurements of the degree of non-randomness

The extent of non-random disjunction is given by the numerical value of the coefficient c, where a value of 0.5 represents random disjunction (no non-randomness) and one of 1.0 represents 100 percent recovery of one of the two chromatids of the asymmetric dyad. In estimating c values in experiments with compounds, it is convenient to derive special equations in order to circumvent difficulties that arise because of the complexity of the genetic set-up. The equation for c for the case of the tandem metacentric had been given earlier (NOVITSKI 1951) as

$$c = \frac{X^c}{2 \text{ Pat } ♂♂ - XX - X^c} - \frac{E_2(1 - c)}{4E_1 + 3E_2}.$$

The last term in the expression is ordinarily disregarded in calculating, being a correction factor of small magnitude.

However, since the equation was first derived, evidence has been presented indicating that one of the two classes of four strand doubles from the tandem metacentric gives rise to a double second anaphase bridge which, unlike the lethal single second anaphase bridges, yields a nullo-X egg (NOVITSKI 1955). In the absence of a special genetic situation which will distinguish between the patroclinous males that arise regularly in crosses involving females carrying compound X chromosomes, and those from four strand doubles, the observed patroclinous male class will include both types. It is of some importance, therefore, to correct the formulae presented earlier for the tandem metacentric, taking into account the additional contribution to the patroclinous male class from four strand doubles. The equation given previously as

$$\text{Pat. } ♂♂ = \tfrac{1}{2}(E_0 + E_1 + E_2)$$

should be modified to

$$\text{Pat. } ♂♂ = \tfrac{1}{2}(E_0 + E_1 + E_2 + \tfrac{1}{8} E_2).$$

When the final formula for c for the tandem metacentric is modified to take into account this change, it becomes

$$c = \frac{X^c}{2 \text{ Pat. } ♂♂ - XX - X^c} - \frac{E_2(2 - 3c)}{8E_1 + 7E_2}$$

The only difference between this equation and that presented above is in the last term of the expression, the correction factor. Since the absolute magnitude of the revised term must be less than that of the original one, and since this term represents a correction factor of small magnitude indicating an overestimate in the calculated c values, it follows that the equation used earlier to obtain c values for the tandem metacentric is probably more accurate than was thought at the time. Consequently, in the calculations of c values given in table 6, the correction factor has been ignored.

The values for the tests in which the parental females carry no homolog are not

TABLE 6

The c *values for all of the tandem metacentric tests made. The column headed "Table" refers to the table from which the data for the calculations were taken. The formula for* c *is given in text. Rings = 2(ring-bearing ♀ ♀). X-Y = YSX·YL,* y B

Cross	Table	2(Pat. ♂♂)	2 (compound ♀♀)	Rings	c
Hw f/Y × Canton-S	1	4,242	570	1,604	0.78
y^4/Y × Canton-S	2	9,468	1,880	3,150	0.71
y^4/FR2 × X-Y/Y	3	8,682	1,936	3,322	0.97

given since the reduction of the single ring classes would render the determination of *c* spurious.

One of the *c* values given (that of the y^4 tandem metacentric/FR2 × YSX·YL/Y; table 3) is obviously too high and requires some comment. The patroclinous males from that cross carried the YSX·YL chromosome plus FR2, and might possibly suffer from a viability depression since they would carry a duplication for the *y* region (and possibly a triplication, since the YSX·YL chromosome may itself carry a duplication for the *y* region). If this class were depressed, then the *c* value would indeed be inordinately high. That this is, in fact, very possibly the case is shown by the following argument. If it is assumed that the *c* value for the y^4 tandem metacentric is the same for the case with FR2 (table 3) as it is for the case with a normal Y (table 2) and is equal to 0.71, then it is possible, using the formula for *c*, to get an estimate of the number of patroclinous males that should have been observed in the case with FR2. The observed number of patroclinous males was 4,241, whereas the figure obtained in the manner just outlined is 4,869. The validity of this number can be checked by comparing the ring to patroclinous male and compound-X to patroclinous male ratios. They become 0.33 and 0.19 respectively, agreeing very closely with the other tests recorded. It can be seen that the other *c* values obtained agree very well with previously published values (NOVITSKI 1951).

NON-RANDOMNESS IN THE TANDEM ACROCENTRIC COMPOUND X CHROMOSOME

The tandem acrocentric compound X chromosome regularly generates single X chromatids by crossing over within itself. Asymmetric dyads are thus produced, and it would be expected that the short single X chromatids would be recovered preferentially. However, the earliest results (NOVITSKI 1954) from this compound were interpreted as indicating no non-randomness. It was postulated at that time that the presence of the long arm of the Y chromosome, which was appended as a second arm of the compound, might have been responsible for diminishing the amount of non-randomness, possibly by some effect such as increasing the mass of the dyad and therefore decreasing, percentage-wise, the difference between the two chromatids.

An experiment was therefore set up to determine whether the degree of non-randomness might be affected by the presence of the long arm of the Y chromosome (=YL) carried basally on chromosomes which ordinarily (i.e. when the Y chromosome arm is not involved) show non-randomness. The two X chromosomes chosen differed in that one of them carried FR1 distally. The so-called FR1 chromosome

has been shown to be an X chromosome in normal sequence with the short arm of the Y chromosome at the free end (BRAVER 1955). Females carrying this chromosome, along with the normal one, produce eggs about two thirds of which carry the normal tip and one third, the FR1 tip. The long arm of the Y chromosome was attached to the base of the chromosome carrying FR1 by crossing over, and females carrying this chromosome, and a normal one, were tested. This, then, provides an ideal genetic set-up for determining whether dyads with the long arm of the Y attached basally behave in the same way as those with the normal subterminal X centromere, since both types of dyads are to be found in meioses of a given female. This is the equivalent of both an experimental and control situation in a single individual. The exact genetic constitution of the mating along with the results is given in table 7.

The data have been analyzed in the following way. Equations representing the expected frequencies of noncrossovers, singles, and doubles, under conditions of non-randomness, have been presented earlier (NOVITSKI 1951). These equations have been modified by assuming that there is not just one coefficient of non-randomness, but two; one when the dyad has the normal X centromere, and a second when the dyad carries YL at the base. These two coefficients of non-randomness are labelled c and c', respectively. The unknowns in the equations are c, c', and the frequencies of tetrads with no, one, and two exchanges. The numbers used in the analysis are those given under the male columns, corresponding to the recovered noncrossovers, singles, and

TABLE 7

Progeny of females of the constitution FR1 y cv v f·*YL*/car *mated to* y v car *males. Crossover regions are: 1′*, y-cv; *1″*, cv-v; *1*, y-v; *2′*, v-f; *2″*, f-car; *2*, v-car. *A dash indicates an unidentifiable class, and a vertical arrow through classes points to the more general class for which identification is unambiguous*

Crossover region	FR1 ♂♂	Non-y ♂♂	FR1 ♀♀	Non-y ♀♀
0	859	1,622	959	1,887
1′	201	308	↓	↓
1″	350	478	↓	↓
1	551	786	605	853
2′	328	531	↓	↓
2″	97	120	↓	↓
2	425	651	433	735
1′, 1″	7	11	—	—
1′, 2′	35	69	↓	↓
1′, 2″	22	27	↓	↓
1″, 2′	46	78	↓	↓
1″, 2″	21	35	↓	↓
1, 2	122	209	158	264
2′, 2″	2	8	—	—
Total in ♂♂				
non co	859	1,622		
singles	976	1,437		
doubles	124	217		

doubles, at the bottom of table 7. The maximum likelihood solution of these equations gives the following values: $c=0.652$, $c'=0.650$, $E_0=334$, $E_1=3{,}540$, and $E_2=1{,}350$. The exchange frequencies arrived at in this way represent percentages 6.4, 67.8, and 25.8, respectively. For a somewhat similar crossover experiment performed earlier (NOVITSKI 1951) in which the calculations of exchange frequencies were made by direct algebraic solution (which was not possible in this case) the values were 4.4, 68.4, and 27.1, respectively. This agreement serves to validate the method used. Of greatest interest, of course, is the astonishingly close agreement in the values of non-randomness for the dyads with and without YL. There seems to be no question but that the addition of YL to one of the chromosomes has not changed non-randomness appreciably.

These results indicate that the failure to find evidence for non-randomness in the tandem acrocentric compound (NOVITSKI 1954) was not due to the presence of YL, which was appended as a second arm to the centromere of the compound. This necessitates a re-evaluation of the tandem acrocentric data. The analysis referred to above was based upon an experiment in which approximately 80 percent of the progeny came from compound-bearing females which did not carry a free Y chromosome. As was shown above for the tandem metacentric and the tandem ring, the presence or absence of a Y chromosome in a compound-bearing female may affect the number of single chromosomes produced by crossing over which are recovered. It consequently becomes of some interest to consider results from tandem acrocentric females with and without a Y chromosome. Therefore, a number of tests of tandem acrocentric females, with and without a free Y chromosome, have been made. The results from these tests are given in tables 8 and 9. In table 10 are recorded the c values for these tests. The formula for c for the case of the tandem acrocentric has been given by NOVITSKI (1954). It should be noted, however, that the equation was given incorrectly in that work (although the c values recorded were calculated from the correct formula), and should be

$$c = \text{single chromosomes}/(4 \times \text{Pat. } ♂♂ - 4 \times \text{Tandem acrocentrics} - \text{single chromosomes}) + \text{C.F.}$$

It is this equation (ignoring, as above, the correction factor) which is used for determining the c values given in table 10.

TABLE 8

The results from a mating of females which carry a tandem acrocentric compound X chromosome homozygous for the mutant allele of y, *both with (A) and without (B) a Y chromosome—by* y B *males which carry the YSX·YL chromosome and no homolog*

Type of progeny	Phentotype of progeny	Number of progeny from	
		(A) ♀♀ with a Y	(B) ♀♀ without a Y
Compound X ♀♀	y ♀♀	272	208
Patroclinous ♂♂	y B ♂♂	907	687
Rod-bearing ♀♀	y B ♀♀	614	395
Rod-bearing ♂♂	y ♂♂	600	457

TABLE 9

The results from a mating of females which carry a tandem acrocentric compound X chromosome homozygous for the mutant allele of y *with no homolog, by males carrying the YSX·YL,* y B *chromosome both with (C) and without (D) FR2 (for description see text)*

Type of progeny	Phenotype of progeny	Number of progeny from	
		(C) ♂♂ with FR2	(D) ♂♂ without FR2
Compound X ♀♀	y or + ♀♀	580	561
Patroclinous ♂♂	y B ♂♂	2,113	1,956
Rod-bearing ♀♀	y B ♀♀	902	843
Rod-bearing ♂♂	y or + ♂♂	853	871
Exceptional ♂♂	y ♂♂	3	—
	B ♂♂	2	—

TABLE 10

The c *values for all of the tandem acrocentric tests made. The formula for* c *is given in text. The letters in parenthesis indicate the source of the data. T.A. = tandem acrocentric,*

X-Y = YSX·YL, y B

Cross	4(Pat. ♂♂)	4(T. A.)	Single chromosomes	*c*
T.A./Y × X-Y/0 (A)	3,628	1,088	1,214	0.92
T.A./0 × X-Y/0 (B)	2,748	832	852	0.80
T.A./0 × X-Y/FR2 (C)	8,452	2,320	1,755	0.40
T.A./0 × X-Y/0 (D)	7,824	2,244	1,714	0.44

Before analyzing the data, it is necessary to consider one point. It can be seen from the data given in tables 8 and 9 that sets B and D, which are given as genetically identical (although, indeed, sets A and B were done considerably earlier than sets C and D), do not, in fact, agree at all. Moreover, set B is itself suspect because there were many fewer rod-bearing females recovered than rod-bearing males, whereas in the other three sets there is the expected equality. Consequently, the results from set B will not be considered in the following discussion.

If set A (in which the compound-bearing females carried a Y chromosome) is compared with sets C and D (in which the parental females carried no homolog), it is

TABLE 11

The ratio of single rod X chromosomes recovered as females to patroclinous males, the ratio of rod X chromosomes recovered as males to patroclinous males, and the ratio of tandem acrocentric com pounds to patroclinous males, for all of the tandem acrocentric tests recorded. T.A. = tandem acrocentric; X-Y = YSX·YL, y B. *The letters in parenthesis refer to the source of the data*

Cross	Rod ♀♀/Pat.♂♂	Rod ♂♂/Pat. ♂♂	T.A. ♀♀ /Pat. ♂♂
T.A./Y × X-Y/0 (A)	0.68	0.66	0.30
T.A./0 × X-Y/0 (B)	0.57	0.67	0.30
T.A./0 × X-Y/FR2 (C)	0.43	0.40	0.27
T.A./0 × X-Y/0 (D)	0.43	0.45	0.29

evident that there is a reduction in the recovery of single rod-bearing progeny. This reduction can be seen more clearly by reference to table 11 in which the ratios of compound females to patroclinous males, rod-bearing females to patroclinous males, and rod-bearing males to patroclinous males are given. This reduction in the recovery of newly generated single chromosomes by the tandem acrocentric in the absence of a homolog parallels the reduction, noted in the last section, of recovered single rings from tandem metacentric and tandem ring compound X chromosomes without a homolog.

DISCUSSION

It has been shown above that females carrying tandem compound X chromosomes without a homolog (a Y chromosome) produce proportionately fewer offspring carrying newly generated single chromosomes than do such females with a Y chromosome. The three compounds which have been considered, the tandem metacentric, the tandem acrocentric, and the tandem ring represent all of the compound X chromosomes which regularly generate single chromosomes by crossing over.

In order to make the results from the experiments differing by the presence or absence of the Y chromosome agree with each other, it is necessary to assume that approximately 25 percent of all new single rings from the tandem metacentric are not recovered when there is no Y chromosome present in the parental female, and that about 40 to 50 percent of single rods generated by the tandem acrocentric in the absence of a homolog are not recovered.

Determining the exact cause of a discrepancy of this sort is more difficult in the case of the compound chromosomes than free X chromosomes because of the complexity of the genetic situation. One might imagine, for instance, that this discrepancy could arise as a consequence of a shift in exchange frequencies depending upon whether or not a homolog was present. This, as well as a change in the degree of non-randomness, has been considered in the text and has been found not to be compatible with the data. Without going into detail here, it may be said that other deviations from normal meiosis have likewise been examined and found wanting. These deviations include the possibility of chromatid interference, an equational rather than reductional first division (in any proportion), a difference in the behavior of anaphase II bridges, misdivision of the centromeres and strand preference. The simplest interpretation of the genetic results appears to be that some fraction of the single chromosomes newly generated in the absence of a homolog are not recovered in the progeny. At the present time it is not at all clear why a considerable proportion of single chromosomes newly generated by compounds should be lost; it is conceivable, for instance, that chromosome reduplication and exchange in these compounds proceeds abnormally when there is no homolog present, but thoughts along this line are speculative.

In the light of this observation, it is clear why certain tandem acrocentric tests (NOVITSKI 1954; sets C and D, table 10) give no evidence for non-randomness. In fact, it was not realized that the parental females used in the initial test (NOVITSKI 1954) did not carry a Y chromosome in some 80 percent of all cases until this effect of the Y chromosome on the recovery of the single chromosomes became apparent and the pedigree for those crosses was rechecked. When the tandem acrocentric carries

a homolog, however, the c value is extremely high (0.92). This is not an entirely unexpected result. Single exchanges in the tandem acrocentric compound are of two distinct types which presumably occur equally frequently. The first of these types produces an asymmetric dyad composed of a single rod and a tandem acrocentric compound. The other type produces a dyad composed of a single rod and a compound composed of three X chromosomes. The equation given above for c assumes that there is the same amount of non-randomness in both types of dyad. It may very well be, however, that there is in fact a much greater degree of non-randomness in those dyads in which a single chromosome separates from a triple (perhaps even approaching 100 percent) than in the case in which the single chromosome separates from the double.

SUMMARY

Tests of females carrying tandem metacentric or tandem acrocentric compound X chromosomes, with and without a homolog (the Y chromosome) have been made. It has been found that in the absence of a homolog, there is a deficiency of recovered single chromosomes newly generated by crossing over within the compounds. This same effect is manifest in previously published data on the tandem compound ring X chromosome. This deficiency of single chromosomes is greater for the case of the tandem acrocentric than for the case of the tandem metacentric. (It is not, as yet, possible to measure it in the tandem ring.) Various possible reasons for this reduced recovery of single chromosomes are considered. The simplest interpretation of the data seems to be that some fraction of the newly generated chromosomes are lethal when the compound bearing female does not carry a homolog; it is not yet possible, however, to explain why such chromosomes should be lethal.

These results explain why certain tandem acrocentric tests do not give evidence for non-random disjunction. The non-random effect (which is a recovery of single chromosomes over expectation) is masked by the reduced recovery of single rods in the absence of a Y chromosome. When a Y chromosome is present in the parental female, the tandem acrocentric compound shows a high degree of non-randomness ($c=0.92$).

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