CHROMATID INTERFERENCE IN NEUROSPORA CRASSA

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THE study of chromatid interference is crucial for the understanding of the mechanisms underlying the distribution and the pattern of crossovers among the chromatids. It is of interest also to find out whether the double exchanges are distributed uniformly along the entire length of a pair of homologous chromosomes or whether exchanges are distributed differently in different regions of the chromosomes.

Many contradictory results concerning the occurrence of chromatid interference have been reported in the literature (see review by EMERSON 1963). Both in the cases cited by EMERSON, and in other reports on *Neurospora* (LINDEGREN and LINDEGREN 1942; WHITEHOUSE 1956, 1958; RIFAAT 1956; PERKINS 1956, 1962; BOLE-GOWDA, PERKINS and STRICKLAND 1962), on *Saccharomyces* (SHULT and LINDEGREN 1959), on *Chlamydomonas* (LEVINE and EBERSOLD 1959; EBERSOLD and LEVINE 1959), and on *Sphaerocarpus* (KNAPP 1960), the results are extremely heterogeneous both between experiments and between particular combinations of regions "within arms" and "across centromeres" of the linkage groups studied. Sometimes there is an excess of 2-strand doubles, sometimes a deficit of 3-strand doubles and sometimes even no chromatid interference.

In view of such a poor agreement between the values reported in different organisms, within the same very organism, or even for the same linkage group, no general conclusions can be drawn. Further study of the pattern of chromatid interference seems to be desirable under a known genetic and environmental control. An attempt is made here to report the extent to which the interference pattern is modifiable by treatment with the chelating agent, ethylenediamine tetra-acetic acid (EDTA). EDTA has been used because it is presumed that this agent facilitates crossing over by breaking the linear continuity of the chromatids incidental to crossing over, as it chelates metallic ions, especially calcium and magnesium which are essential to the maintenance and integrity of chromosomes (LEVINE 1955; STEFFENSEN, ANDERSON and KASE 1956; EVERSOLE and TATUM 1956; KAUFMANN, GAY and McELDERRY 1957). Modifying effects on the frequency of genetic exchanges mediated by EDTA have been recorded in *Drosophila* (LEVINE 1955; STEFFENSEN, ANDERSON and KASE 1956; RASMUSON 1961), in *Chlamydomonas* (EVERSOLE and TATUM 1956), and in *Neurospora* (PRAKASH 1963c). A high increase in the frequency of gene recombination in *Escherichia* and the frequency of transduction in *Salmonella* and of certain phage mutants have been recorded by EISENSTARK and KIRCHNER (1956). LEVINE and EBERSOLD (1958) obtained, however, negative results with EDTA in *Chlamydomonas*.

The full tetrad data are published in the present paper in Table 1. These data have been analyzed elsewhere with respect to crossover frequencies (PRAKASH 1963c), and with respect to position interference (PRAKASH 1964), which is sometimes called chiasma or chromosomal interference. Significant differences in the frequency of crossing over were found in almost all regions as a result of the treatment. Significant positive position interference was absent in the control, was present among certain pairs of regions when treated with $4 \times 10^{-5}M$ and $10 \times 10^{-5}M$ EDTA, but vanished on treatment with $20 \times 10^{-5}M$ EDTA. The localization and intensity of negative position interference were affected by the treatment, more in linkage group I than in linkage group VI. The present paper, in addition to presenting the data in full, analyses them with respect to chromatid interference.

MATERIALS AND METHODS

The markers employed in this study were: *A/a*, mating type; *ad-8* (74A-Y152-M7), adenine requiring; *arg-3* (30300), arginine requiring; *col-4* (70007), colonial; *cr* (original allele number unknown), crisp; *hist-2* (C94), histidine requiring; *me-6* (35809), methionine requiring; *pan-2* (74A-YU370-1A), pantothenic acid requiring; *rib-1* (51602), riboflavin requiring; *tryp-2* (75001), anthranilic acid requiring; *ylo* (Y30539y), yellow conidia. *A/a*, *arg-3*, *hist-2*, *cr* and *me-6* are in linkage group I; *col-4* is in linkage group IV; *ad-8*, *ylo*, *pan-2*, *rib-1* and *tryp-2* are in linkage group VI. To minimize extraneous genetic differences and to improve fertility, all the strains were backcrossed, before use, for at least six successive times to the standard LINDEGREN wild-type strain. The latter was used as a recurrent perithecial parent while the fertilising parent was always an isolate from the preceding generation. Only second-division segregants were selected in each backcross for subsequent backcrossing so as to ensure the inclusion of LINDEGREN wild-type centromeres (PRAKASH 1963b). The following "Multi-marker parental strains" were constructed after inbreeding: (1) *a arg-3 cr me-6; ylo rib-1 tryp-2*. (2) *A hist-2; col-4; ad-8 pan-2*. (3) *a hist-2 me-6; col-4; ylo rib-1*. (4) *A arg-3 cr; ad-8 pan-2 tryp-2*. The marker *col-4* was introduced to aid in detection of the occurrence or nonoccurrence of meiotic nuclear passing (because it is close to the centromere on linkage group IV), to facilitate recognition of spore pairs, and to study some interchromosomal relationships (this will be reported elsewhere). Tetrad analysis from the control crosses showed *hist-2* 0.9 map unit right of the centromere and 7.3 units from *arg-3*, which was 6.4 map units left of the centromere (all values uncorrected).

All stock cultures were maintained on malt-bacto peptone medium which was prepared by adding 0.2 percent bacto peptone (British Drug Houses), 1 percent liquid malt extract (British Pharmacopoeia), 1.5 percent glucose and 1.2 percent Difco agar to the standard salt solution containing trace elements and biotin as described by WESTERGAARD and MITCHELL (1947). The liquid crossing medium was bacto peptone-asparagine medium and was prepared by adding 0.25 percent bacto peptone; 0.25 percent sucrose; 2.0 percent glucose and 0.03 percent DL-Asparagine to the standard salt solution. Media were buffered at pH 6.8 with a phosphate buffer. Crosses were carried out at 25°C in 150 ml Erlenmeyer flasks on cottoned liquid crossing medium (PRAKASH 1963d) which was supplemented for biochemical requirements where necessary. Deionised distilled water was used for preparing all solutions. Reciprocal crosses were made by adding a conidial suspension of one parent (antheridial parent) 48 hours after inoculation of the other parent (protoperithecial parent). Six hours later, EDTA was added and solutions were adjusted to the specific molar concentrations. The following crosses were made: *a arg-3 cr me-6; ylo rib-1 tryp-2* $\times$ *A hist-2; col-4; ad-8 pan-2* (crosses 31 to 34). *a hist-2 me-6; col-4; ylo rib-1* $\times$ *A arg-3 cr; ad-8 pan-2 tryp-2* (Crosses 39 to 42). Crosses 31 and 39 served as controls. Uncorrected map lengths of the component intervals from control values are: *a-arg-3* (region I): 2.3; *arg-3-centromere* (II): 6.4; *centromere-hist-2* (III): 0.9; *hist-2-cr* (IV): 4.9; *cr-me-6* (V):

10.1; centromere-*col-4* (VI): 8.1; *ad-8-ylo* (VII): 7.1; *ylo*-centromere (VIII): 4.0; centromere-*pan-2* (IX): 1.7; *pan-2-rib-1* (X): 1.9; *rib-1-tryp-2* (XI): 10.2. The EDTA concentrations used were: $4 \times 10^{-5}M$ (crosses 32 and 40); $10 \times 10^{-5}M$ (crosses 33 and 41); $20 \times 10^{-5}M$ (crosses 34 and 42).

The method for tetrad dissection in order was essentially the same as previously described (PRAKASH 1963a). Each of the eight ascospores from an ascus was germinated separately in a $3 \times \frac{3}{8}$ inch test tube on an agar slant containing minimal medium (2.5 percent glucose; 1.2 percent Difco agar; standard salt solution) with biochemical supplements added (20 $\mu g/ml$ L-arginine monohydrochloride; 10 $\mu g/ml$ L-histidine monohydrochloride; 35 $\mu g/ml$ adenine; 10 $\mu g/ml$ riboflavin; 35 $\mu g/ml$ anthranilic acid; 20 $\mu g/ml$ D-pantothenic acid, calcium salt; 35 $\mu g/ml$ DL-methionine). Nutritional requirements for all germinated cultures were scored in plates of appropriately supplemented sorbose medium (0.4 percent sorbose which was recrystallised from CH_3OH , before use); 0.2 percent sucrose; 2 percent Difco agar; with standard salt solution). Scoring for mating-type was carried out in duplicate tubes using tester suspensions of both mating-types so as to ensure that false negatives were not obtained.

RESULTS

Each cross was made in duplicate (reciprocal crosses); the data from duplicates were homogeneous and were therefore pooled. The ordered tetrad data from the eight crosses thus studied are given in Table 1 for the five regions between *A/a* and *me-6* in linkage group I and for the five regions between *ad-8* and *tryp-2* in linkage group VI. This allows a study of the strand relationship between contiguous exchanges among 20 pairs of regions at a time, and critical evaluation of the double exchanges across the centromeres. The main body of the table includes completely analyzable regular tetrads, i.e. those with either three or four products represented. Unused tetrads in which two, one or zero genotypes were recovered, or which were the result of some irregularity, are enumerated at the end of the table. Completely analyzable regular tetrads, with germination of ascospores 89 percent, make up over 93 percent of the total tetrads dissected. All four products were recovered in 397 tetrads, which constituted 95 percent of the 417 completely analyzable tetrads giving information on chromatid interference for both the linkage groups I and VI (with germination of ascospores over 96 percent). No significant departures were apparent in an analysis where tetrads with three products were excluded. All completely analyzable tetrads including the ones with three products have, therefore, been utilized in the subsequent Tables 2 to 6 and for Figures 1 to 4. Segregating markers located near the centromeres of the three linkage groups I, IV and VI showed no coincident pattern of asymmetrical (alternating) second division segregation. This indicates that meiotic nuclear passing is either negligible or absent in the crosses studied.

Comparative frequencies of 2-strand, 3-strand and 4-strand pairs of contiguous exchanges are given in Tables 2 and 5 for linkage group I and in Tables 3 and 6 for linkage group VI. In linkage group I, regions I and V are designated as distal and regions II, III and IV proximal to the centromere. In linkage group VI, regions VII and XI are designated distal and regions VIII, IX and X proximal to the centromere. The two types among 3-strand doubles i.e. bc-ac or bd-ad; bc-ad or ac-ad pairs in the terminology of Table 1, show a 1:1 ratio to one another in the individual crosses as well as in the total data. Deficiency of 3-strand doubles

in both linkage groups I and VI, and in all crosses, is highly probable as shown in the raw as well as in the derived totals (Tables 4 to 6). There is a marked excess of 2-strand doubles, indicating the presence of negative interference, in

TABLE 1

Ordered tetrads from the eight crosses (four treatments). Genotypes for three linkage groups I, IV and VI are given to the left. Exchanges occurred in regions where letters are present to indicate the strand relationship. The strands involved in an exchange in the leftmost regions of linkage group I (from regions I to V), in linkage group IV (region VI) and in the leftmost regions of linkage group VI (from regions VII to XI) are arbitrarily designated bc. A dash indicates no exchange. The number of completely analysable tetrads for each cross is given to the right

Crosses: 31 to 34

	a	arg-3	C	+	or	me-6	C	+	+	rlo	C	+	rib-1	tryp-2
Strand a	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Strand b	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Strand c	A	+	C	hist-2	+	+	C	col-4	ad-8	+	C	pan-2	+	+
Strand d	A	+	C	hist-2	+	+	C	col-4	ad-8	+	C	pan-2	+	+
Regions:	I	II	III	IV	V	VI	VII	VIII	IX	X	XI			
Linkage group:	I					IV			VI					

Crosses: 39 to 42

	a	+	C	hist-2	+	me-6	C	col-4	+	rlo	C	+	rib-1	+
Strand a	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Strand b	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Strand c	A	arg-3	C	+	or	+	C	+	ad-8	+	C	pan-2	+	tryp-2
Strand d	A	arg-3	C	+	or	+	C	+	ad-8	+	C	pan-2	+	tryp-2
Regions:	I	II	III	IV	V	VI	VII	VIII	IX	X	XI			
Linkage group:	I					IV			VI					

Strands involved in exchanges in regions											Control		4x10 ⁻⁵ M EDTA		10x10 ⁻⁵ M EDTA		20x10 ⁻⁵ M EDTA		Total	
I	II	III	IV	V	VI	VII	VIII	IX	X	XI	31	39	32	40	33	41	34	42		
No exchanges:																				
-	-	-	-	-	-	-	-	-	-	-	159	93	87	68	94	68	78	71	718	
Single exchanges:																				
bc	-	-	-	-	-	-	-	-	-	-	0	2	0	5	2	1	1	0	11	
- bc	-	-	-	-	-	-	-	-	-	-	6	2	7	2	0	0	1	0	18	
- - bc	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	0	4	0	4	
- - - bc	-	-	-	-	-	-	-	-	-	-	6	0	6	2	2	0	5	0	21	

2

Strands involved in exchanges in regions																													
I	II	III	IV	V	VI	VII	VIII	IX	X	XI	Control			4x10 ⁻⁵ M EDTA			10x10 ⁻⁵ M EDTA			20x10 ⁻⁵ M EDTA			Total						
-	-	-	-	bc	-	-	-	-	-	-	21	7	11	13	1	0	13	8	74										
-	-	-	-	-	bc	-	-	-	-	-	10	4	1	0	2	1	6	3	27										
-	-	-	-	-	-	bc	-	-	-	-	4	5	12	4	8	6	11	0	50										
-	-	-	-	-	-	-	bc	-	-	-	1	3	0	0	0	7	2	0	13										
-	-	-	-	-	-	-	-	bc	-	-	0	2	0	0	0	3	3	0	8										
-	-	-	-	-	-	-	-	-	bc	-	0	3	0	0	0	1	0	0	4										
-	-	-	-	-	-	-	-	-	-	bc	25	11	19	14	4	0	2	2	77										
Total Singles:																	73	39	56	40	19	19	48	13	307				
Double exchanges:																													
i) Two in linkage group I; none in linkage group IV; none in linkage group VI:																													
bc	-	-	bc	-	-	-	-	-	-	-	1	1	1	0	0	0	0	0	0	3									
-	bc	-	bc	-	-	-	-	-	-	-	2	4	0	0	0	0	0	0	0	6									
-	bc	-	bc	-	-	-	-	-	-	-	2	1	0	0	0	1	0	0	0	4									
-	-	bc	bc	-	-	-	-	-	-	-	0	1	0	0	0	0	0	0	1	3									
-	-	-	bc	bc	-	-	-	-	-	-	2	0	0	0	0	0	0	0	0	1									
bc	-	-	-	ac	-	-	-	-	-	-	0	0	0	0	1	0	0	0	1	1									
bc	-	bd	-	-	-	-	-	-	-	-	0	0	0	0	0	0	0	1	1										
-	bc	-	bd	-	-	-	-	-	-	-	1	0	0	0	0	0	0	0	1	1									
bc	-	-	ad	-	-	-	-	-	-	-	0	0	0	0	0	0	0	1	1										
bc	-	-	-	ad	-	-	-	-	-	-	1	0	0	0	1	0	0	2	4										
-	bc	ad	-	-	-	-	-	-	-	-	0	0	0	0	0	0	0	1	1										
-	bc	-	ad	-	-	-	-	-	-	-	0	2	0	1	0	0	0	0	3										
-	bc	-	-	ad	-	-	-	-	-	-	1	0	0	0	0	0	0	1	2										
-	-	bc	-	ad	-	-	-	-	-	-	0	0	0	0	0	0	0	1	1										
-	-	-	bc	ad	-	-	-	-	-	-	0	0	1	0	0	0	0	0	1	1									
-	-	-	-	-	-	-	-	-	-	-	0	0	1	0	0	0	0	0	1	1									
bc, ad	-	-	-	-	-	-	-	-	-	-	1	1	0	0	0	0	0	0	2										
-	-	-	-	-	-	-	-	-	-	-	1	1	0	0	0	0	0	0	2										

Strands involved in exchanges in regions							Control	4x10 ⁻⁵ M EDTA			10x10 ⁻⁵ M EDTA			20x10 ⁻⁵ M EDTA			Total
I	II	III	IV	V	VI	VII VIII IX X XI		31	39	32	40	33	41	34	42		
ii) None in linkage group I; none in linkage group IV; two in linkage group VI:																	
-	-	-	-	-	-	bc	bc	-	-	2	0	0	0	1	0	0	3
-	-	-	-	-	-	bc	ad	-	-	0	0	0	0	1	0	0	1
-	-	-	-	-	-	bc	-	bc	-	0	0	0	0	1	0	0	1
-	-	-	-	-	-	bc	-	bc	-	0	0	0	0	0	0	1	0
-	-	-	-	-	-	bc	-	bc	-	1	1	0	0	0	1	0	3
-	-	-	-	-	-	-	bc	-	bc	0	0	0	0	1	0	0	1
-	-	-	-	-	-	-	-	bc	bc	1	0	0	0	0	0	0	1
-	-	-	-	-	-	bc	bd	-	-	1	0	0	0	0	0	0	1
-	-	-	-	-	-	bc	-	bd	-	0	0	0	0	1	0	0	1
-	-	-	-	-	-	-	bc	bd	-	1	0	0	0	0	0	0	1
-	-	-	-	-	-	bc	-	ad	-	0	0	0	0	2	0	0	2
-	-	-	-	-	-	bc	-	ad	-	0	0	1	1	2	1	1	6
-	-	-	-	-	-	-	bc	ad	-	0	0	0	0	2	0	0	2
-	-	-	-	-	-	-	bc	-	ad	0	0	0	0	1	0	0	1
-	-	-	-	-	-	-	-	bc	bc	0	0	0	0	0	1	0	1
-	-	-	-	-	-	-	-	bc	ad	0	0	0	0	1	0	0	1
-	-	-	-	-	-	-	-	bc	ad	0	0	0	0	1	0	0	2
-	-	-	-	-	-	bc, ad	-	-	-	1	0	0	1	0	2	0	4
-	-	-	-	-	-	-	bc, ad	-	-	0	0	0	0	1	0	0	1
-	-	-	-	-	-	-	-	bc, ad	-	1	0	0	1	0	0	0	2
iii) One in linkage group I; none in linkage group IV; one in linkage group VI:																	
bc	-	-	-	-	-	bc	-	-	-	1	0	2	1	0	0	1	5
bc	-	-	-	-	-	-	-	-	bc	0	0	2	2	3	0	1	8
-	bc	-	-	-	-	bc	-	-	-	3	0	0	1	0	0	0	4
-	bc	-	-	-	-	-	bc	-	-	3	0	0	0	0	0	0	3

3	Strands involved in exchanges in regions						Control	$4 \times 10^{-5} M$ EDTA	$10 \times 10^{-5} M$ EDTA	$20 \times 10^{-5} M$	Total				
	I	II	III	IV	V	VI VII VIII IX X XI									
-	bc	-	-	-	-	bc	0 0	2 3	0 0	0 0	5				
-	bc	-	-	-	-	bc	0 0	0 4	0 0	0 0	4				
-	-	bc	-	-	-	bc	0 1	0 0	0 0	0 0	1				
-	-	bc	-	-	-	bc	0 0	0 0	0 1	0 0	1				
-	-	bc	-	-	-	bc	0 0	0 0	0 3	0 0	3				
-	-	bc	-	-	-	bc	0 0	0 0	2 0	2 0	4				
-	-	bc	-	-	-	bc	2 1	0 0	1 0	0 0	4				
-	-	bc	-	-	-	bc	0 0	0 0	0 0	1 0	1				
-	-	bc	-	-	-	bc	0 1	2 5	0 1	0 0	9				
-	-	bc	-	-	-	bc	4 0	0 0	2 3	0 2	11				
-	-	bc	-	-	-	bc	8 2	9 3	11 8	7 7	55				
-	-	bc	-	-	-	bc	2 0	0 0	0 0	0 1	3				
-	-	bc	-	-	-	bc	0 0	0 0	0 0	1 3	4				
-	-	bc	-	-	-	bc	0 0	2 0	7 2	0 1	12				
-	-	bc	-	-	-	bc	12 2	13 11	9 10	5 3	65				
(iv) One in linkage group I; one in linkage group IV; none in linkage group VI:															
bc	-	-	-	-	-	bc	0 0	0 0	3 1	0 0	4				
-	bc	-	-	-	-	bc	2 2	3 4	0 0	0 0	11				
-	-	bc	-	-	-	bc	0 2	5 5	0 0	1 0	13				
-	-	bc	-	-	-	bc	3 0	2 0	4 5	6 1	21				
(v) None in linkage group I; one in linkage group IV; one in linkage group VI:															
-	-	-	-	-	-	bc	5 0	2 0	2 0	3 0	12				
-	-	-	-	-	-	bc	0 2	0 1	2 0	0 0	5				
-	-	-	-	-	-	bc	0 1	0 3	2 0	0 0	6				
-	-	-	-	-	-	bc	0 0	1 0	2 0	1 0	4				
-	-	-	-	-	-	bc	4 0	3 0	1 1	0 3	12				
Total Doubles:							69	26	51	47	67	41	33	29	363

Strands involved in exchanges in regions											Control	4x10 ⁻⁵ M EUTA	10x10 ⁻⁵ M EUTA	20x10 ⁻⁵ M EUTA	Total	
I	II	III	IV	V	VI	VII	VIII	IX	X	XI						
Triple exchanges:																
i) Three in linkage group I; none in linkage group IV; none in linkage group VI:																
-	-	-	bc	-	-	-	-	-	-	-	1	0	0	0	0	1
-	-	bc	ad	-	-	-	-	-	-	-	1	0	0	0	0	0
ii) Two in linkage group I; one in linkage group IV; none in linkage group VI:																
bc	-	bc	-	bc	-	-	-	-	-	-	0	0	0	0	0	1
bc	-	bc	-	bc	-	-	-	-	-	-	1	0	0	0	0	2
bc	ad	-	bc	-	-	-	-	-	-	-	0	0	0	0	1	0
bc	-	ad	bc	-	-	-	-	-	-	-	0	0	0	0	1	2
-	bc	-	bc	-	-	-	-	-	-	-	1	0	0	0	0	1
-	bc	-	bc	-	-	-	-	-	-	-	0	2	0	0	0	2
-	bc	bd	bc	-	-	-	-	-	-	-	1	1	0	0	0	2
-	bc	ad	bc	-	-	-	-	-	-	-	1	0	0	0	0	2
-	bc	bc	bc	-	-	-	-	-	-	-	1	0	0	0	1	0
-	bc	ad	bc	-	-	-	-	-	-	-	0	0	0	0	1	0
-	bc	-	bc	bc	-	-	-	-	-	-	0	0	0	0	0	1
-	bc	-	bd	bc	-	-	-	-	-	-	0	0	0	0	1	0
-	-	bc	bc	bc	-	-	-	-	-	-	1	1	0	0	1	3
iii) Two in linkage group I; none in linkage group IV; one in linkage group VI:																
bc	-	bc	-	-	-	-	-	bc	-	-	0	0	0	0	1	0
bc	-	bc	-	-	-	-	-	bc	0	0	0	0	0	0	0	2
bc	-	bc	-	-	bc	-	-	-	0	0	0	0	0	1	0	0
bc	-	bc	-	bc	-	-	-	bc	1	0	0	0	0	0	0	2
bc	-	bc	-	bc	-	-	-	bc	0	0	0	0	0	1	0	0
bc	-	ac	-	-	-	-	-	bc	1	0	0	0	0	0	0	1
bc	-	-	bd	-	-	-	-	bc	-	-	1	0	0	0	0	1
bc	-	-	ac	-	-	-	bc	-	-	-	0	0	0	0	1	0

5	Strands involved in exchanges in regions										Control	4x10 ⁻⁵ M EDTA				10x10 ⁻⁵ M EDTA				20x10 ⁻⁵ M EDTA				Total
	I	II	III	IV	V	VI	VII	VIII	IX	X		XI	31	39	32	40	33	41	34	42				
-	-	-	bc	-	-	-	bc	-	-	ad	0	0	1	0	0	0	0	0	0	1				
-	-	bc	-	-	-	-	-	bc	-	ad	0	0	1	0	0	0	0	0	0	1				
-	-	bc	-	-	-	-	bc, ad	-	-	-	0	0	0	0	1	0	0	0	0	1				
-	-	bc	-	-	-	-	-	-	-	bc, ad	0	0	1	1	0	0	0	0	0	2				
-	-	-	bc	-	-	-	bc	-	-	-	1	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	ad	-	-	0	0	0	0	0	0	0	1	0	1				
-	-	-	bc	-	-	-	bc	-	-	bc	1	1	0	1	0	0	1	0	1	4				
-	-	-	bc	-	-	-	bc	-	-	bd	0	1	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	-	-	ac	0	0	0	1	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	-	-	ad	1	0	0	0	1	1	0	1	0	4				
-	-	-	bc	-	-	-	bc	ad	-	-	0	0	0	0	0	1	0	0	0	1				
-	-	-	bc	-	-	-	bc	-	-	bc	0	1	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	-	-	bc	0	0	1	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	ad	-	-	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	-	-	bc	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc	-	-	bc	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	bc, ad	-	-	-	0	0	0	0	0	0	0	1	2	3				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	1	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	1	2				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0	0	0	0	0	0	1				
-	-	-	bc	-	-	-	-	-	-	bc, ad	0	0	0	0										

8 Strands involved in exchanges in regions							Control	4x10 ⁻⁵ M EDTA	10x10 ⁻⁵ M EDTA	20x10 ⁻⁵ M EDTA	Total
I	II	III	IV	V	VI	VII VIII IX X XI					
vii) One in linkage group I; none in linkage group IV; three in linkage group VI:											
-	-	-	-	bc	-	bc, - ad	0 0	0 0	0 0	0 1	1
-	-	-	-	bc	-	bc, - ad	0 0	0 0	0 0	0 1	1
Total quadruples:							10 10	13 11	12 16	14 16	102
Quintuple exchanges:											
i) Two in linkage group I; one in linkage group IV; two in linkage group VI:											
bc	bc	-	-	bc	-	- - bc ac	1 0	0 0	0 0	0 0	1
bc	ac	-	-	bd	bc	- - bc -	0 0	0 0	0 0	0 1	1
bc	-	ad	-	bc	bc	- - ad -	0 0	0 0	0 0	0 1	1
bc	-	ad	-	bc	-	bc - ad	0 0	0 1	0 0	0 0	1
bc	-	-	bc	bc	bc	- - ad -	0 0	0 0	0 0	1 0	1
bc	-	bc	-	bc	-	bc - bc	0 1	0 0	0 0	0 0	1
bc	-	ad	-	bc	-	bc, - ad	0 0	0 0	0 1	0 0	1
bc	-	-	ad	bc	bc	- - ad	0 0	0 0	0 0	1 0	1
bc	-	-	ad	bc	bc	- - ad -	0 0	1 0	0 0	0 0	1
bc	-	-	ad	bc	bc	- - bc -	0 0	0 0	1 0	0 0	1
bc	-	-	ad	bc	bc	- - bc bc	0 0	1 0	0 0	0 0	1
bc	-	-	ad	bc	bc	- - bc -	0 0	0 0	0 0	1 0	1
bc	-	-	ad	bc	bc	- - bc bc	0 0	0 0	0 0	1 0	1

Strands involved in exchanges in regions						Control 31 39	4x10 ⁻⁵ M EDTA	10x10 ⁻⁵ M EDTA	20x10 ⁻⁵ M EDTA	Total
I II III IV V VI VII VIII IX X XI XII										
- bc - - bc	bc	- bc - ad -	0 0	0 0	0 1	0 0	1			
- bc - - bc	bc	- bc - - ac	1 0	0 0	0 0	0 0	1			
- bc - - bd	bc	ad - -	0 0	0 0	1 0	0 0	1			
- bc - - ac	bc	bc - - ad	0 1	0 0	0 0	0 0	1			
- bc - - ad	bc	bc - -	0 1	0 0	0 0	0 0	1			
- bc - - ad	bc	bc - - ad -	0 0	0 0	0 0	1 0	1			
- bc - - ad	bc	bc - - bc	0 0	0 0	0 0	0 1	1			
- bc - - ad	bc	bc - - bd	0 0	0 0	1 0	0 0	1			
- - bc bc - bc	bc	ac - -	0 0	0 0	1 0	0 0	1			
- - bc ad - bc	bc	bc - ad -	0 0	0 0	0 0	0 1	1			
- - bc - bc	bc	bc - - bc	1 0	0 0	0 0	0 0	1			
- - bc - ad	bc	- bc bc -	0 0	0 0	0 0	1 0	1			
- - bc bc	bc	bc - - ad	0 0	1 0	0 0	0 0	1			
- - bc bc	bc	- - bc ad	0 0	0 0	0 0	1 0	1			
- - bc bd	bc	bc - - ad -	0 0	0 0	0 1	0 0	1			
- - bc ad	bc	bc - - bc -	0 0	0 1	0 0	0 0	1			
- - bc ad	bc	- - bc, - ad	0 0	0 0	0 1	0 0	1			
- - bc ad	bc	- - - bc, ad	0 0	0 0	0 0	1 0	1			
- - bc, - ad	bc	- bc - - ad	0 0	0 0	1 0	0 0	1			
- - - bc, bc ad	bc	bc - - ad	0 0	0 0	0 0	1 0	1			
- - - bc, bc ad	bc	bc, bc ad	0 0	0 0	1 0	0 0	1			
- - - bc	bc	bc - - bc, bc ad	0 0	0 0	0 0	0 0	1			
bc - - ad bc -	bc	bc - - bc -	0 0	0 0	1 0	0 0	1			
- - bc bc, - ad	bc	bc ad - - -	0 0	1 0	0 0	0 0	1			

9	Strands involved in exchanges in regions											Control		4x10 ⁻⁵ M EDTA	10x10 ⁻⁵ M EDTA	20x10 ⁻⁵ M EDTA	Total			
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	31	39	32	40	33	41	34	41	Total
iii) Two in linkage group I; none in linkage group IV; three in linkage group VI:																				
		bc	-	bc	-	-	-	-	bc, in-ad	ad	1	0	0	0	0	0	0	0	0	1
		-	bc	-	bc	-	-	bc	ad	bd	-	0	0	1	0	0	0	0	0	1
		-	bc	-	ac	-	-	-	bc	bc	bc	1	0	0	0	0	0	0	0	1
iv) Three in linkage group I; one in linkage group IV; one in linkage group VI:																				
		-	bc	-	bd, ac	-	bc	-	-	bc	-	0	0	0	1	0	0	0	0	1
		-	bc	-	-	bd, ac	bc	-	-	-	-	0	0	0	0	0	0	0	1	1
		-	-	bc	bc, ad	bc	-	bc	-	-	-	0	0	0	0	1	0	0	0	1
v) One in linkage group I; one in linkage group IV; three in linkage group VI:																				
		-	bc	-	-	bc	-	-	-	bc	bc, ad	0	0	1	0	0	0	0	0	1
		-	-	bc	-	bc	-	bc	-	bc	-	0	1	0	0	0	0	0	0	1
vi) Four in linkage group I; none in linkage group IV; one in linkage group VI:																				
		bc	-	ac, bd	-	-	-	-	-	bc	-	0	0	0	0	0	0	1	0	1
Total quintuples:												5	4	7	5	9	4	10	6	50
Sextuple exchanges:																				
i) Three in linkage group I; none in linkage group IV; three in linkage group VI:																				
		bc	bc	-	-	bd	-	bc	ac	bd	-	-	1	0	0	0	0	0	0	1
		-	bc	ad	bc	-	-	-	bc	ad	bc	-	0	0	0	1	0	0	0	1
		-	bc	-	bc	ad	-	bc	-	ac	-	bd	0	0	1	0	0	0	0	1

Strands involved in exchanges in regions						Control		4x10 ⁻⁵ M EDTA		10x10 ⁻⁵ M EDTA		20x10 ⁻⁵ M EDTA		Total					
I	II	III	IV	V	VI	VII	VIII	IX	X	XI	31	39	32	40	33	41	34	42	Total
ii) Three in linkage group I; one in linkage group IV; two in linkage group VI:																			
bc	ad	bd	-	-	bc	bc	-	ad	-	-	0	0	0	0	0	0	0	1	1
bc	bc	-	-	bc	bc	bc	-	-	ac	-	0	1	0	0	0	0	0	0	1
bc	-	bc	ad	-	bc	-	bc	-	ac	-	0	0	0	0	1	0	0	0	1
bc	-	-	ad	ad	bc	bc	ad	-	-	-	0	0	0	0	0	1	0	0	1
-	bc	ac	bd	-	bc	-	-	bc	ad	-	0	0	0	1	0	0	0	0	1
-	bc	ad	bd	-	bc	-	-	bc	-	bc	0	0	1	0	0	0	0	0	1
-	bc	ad	ad	-	bc	bc	ad	-	-	-	0	0	1	0	0	0	0	0	1
-	bc	-	bd	bd	bc	-	-	bc	bc	-	0	0	0	0	0	1	0	0	1
-	bc	-	ad	bc	bc	bc	-	ad	-	-	0	0	0	0	0	0	1	0	1
-	-	bc	ac, bd	-	bc	bc	-	-	ad	-	0	0	0	0	0	0	0	1	1
-	-	-	bc, in-ad	bd	bc	-	-	-	bc	ad	0	0	0	0	0	0	1	0	1
iii) Two in linkage group I; one in linkage group IV; three in linkage group VI:																			
bc	bc	-	-	-	bc	-	bc	ad	-	bc	0	0	1	0	0	0	0	0	1
bc	-	-	bd	-	bc	bc	bc	-	bc	-	0	0	0	0	0	1	0	0	1
-	bc	ad	-	-	bc	bc, ad	-	-	ac	-	0	0	0	0	0	0	1	0	1
-	bc	-	-	bc	bc	bc, ad	-	bd	-	-	0	0	0	0	0	0	0	1	1
-	-	bc	-	ad	bc	-	-	bc	ad	ac	0	0	0	0	0	0	0	1	1
-	-	-	bc	bc	bc	bc	bd	-	ac	-	0	1	0	0	0	0	0	0	1
-	-	-	bc	ad	bc	-	bc	ad	bc	-	0	0	0	0	0	1	0	0	1
iv) Four in linkage group I; one in linkage group IV; one in linkage group VI:																			
bc	-	bc	ac	bd	bc	bc	-	-	-	-	1	0	0	0	0	0	0	0	1

10	Strands involved in exchanges in regions										Total								
	I	II	III	IV	V	VI	VII	VIII	IX	X		XI							
v)	One in linkage group I; one in linkage group IV; four in linkage group VI:																		
	-	-	-	bc	bc	-	ac	bd	ad	0	0	0	0	1	0	0	1		
	-	-	-	bc	bc	-	bc	ac, in- bd det.		0	0	0	0	1	0	0	1		
vi)	Two in linkage group I; none in linkage group IV; four in linkage group VI:																		
	bc	bc	-	-	-	bc	ad	ac	bd	-	0	0	0	0	0	1	0	1	
	bc	-	-	ac	-	bc	ac	-	bd	ac	0	0	0	0	1	0	0	1	
	bc	-	-	ad	-	-	bc	-	ac, in- bd det.		0	0	0	0	0	1	0	1	
	-	-	-	bc	ac	-	bc	-	ad	bc	ac	0	0	0	0	1	0	0	1
vii)	Four in linkage group I; none in linkage group IV; two in linkage group VI:																		
	-	bc	ad	bd	ac	-	-	bc	-	-	ad	0	0	0	0	1	0	0	1
Total sextuples:																			
2 2 4 2 3 7 5 4 29																			
Septuple exchanges:																			
i)	Three in linkage group I; one in linkage group IV; three in linkage group VI:																		
	bc	bc	-	ad	-	bc	-	bc	ad	-	ac	0	0	0	0	0	1	0	1
	bc	-	-	bc	ad	bc	-	bc	-	bc	ad	0	0	0	0	1	0	0	1
	bc	-	-	ad	bc	bc	-	bc	-	ad	bc	0	0	0	0	1	0	0	1
	bc	-	-	ad	ad	bc	-	-	bc	ad	ac	0	0	0	0	1	0	0	1
	-	bc	ad	-	bc	bc	bc	ad	-	bc	-	0	0	0	0	0	0	1	1
	-	-	bc	ad	bc	bc	-	-	-	bc	bc, ad	0	0	0	0	1	0	0	1
iii)	Three in linkage group I; none in linkage group IV; four in linkage group VI:																		
	bc	bc	ad	-	-	-	bc	bc	ad	-	bd	0	0	0	0	0	1	0	1
	bc	ad	-	bd	-	-	bc	bc	bd	ad	-	0	0	0	0	1	0	0	1
	-	bc	ad	ad	-	-	bc	bc	ac	bd	-	0	0	0	1	0	0	0	1
	-	-	bc	ac	bd	-	bc	-	bd	bd	ad	0	0	0	0	1	0	0	1

Strands involved in exchanges in regions											Control	4x10 ⁻⁵ M EDTA	10x10 ⁻⁵ M EDTA	20x10 ⁻⁵ M EDTA	Total				
I	II	III	IV	V	VI	VII	VIII	IX	X	XI									
iiii) Four in linkage group I; none in linkage group IV; three in linkage group VI:																			
bc	ad	-	ad	bc	-	bc	ad	bc	-	-	0	0	0	0	1				
-	bc	bd	bd	ac	-	-	bc	-	ad	bd	0	0	1	0	0				
iv) Two in linkage group I; one in linkage group IV; four in linkage group VI:																			
bc	ad	-	-	bc	bc	-	ad	bd	bd	0	0	0	0	0	1				
bc	-	ad	-	bc	-	-	bc	ac	in- bd det.	0	0	0	0	0	1				
-	bc	-	-	bc	bc	ac	bc	ac	in- bd det.	1	0	0	0	0	0				
-	bc	-	-	ad	bc	bc	bc	ac	bd	-	0	0	0	0	1				
-	-	-	bc	ac	bc	bc	ac	bd	ad	-	0	0	0	1	0				
v) Four in linkage group I; one in linkage group IV; two in linkage group VI:																			
bc	ad	bd	-	ac	bc	bc	-	-	bc	-	0	0	0	0	1				
vi) Five in linkage group I; none in linkage group IV; two in linkage group VI:																			
bc	ac	-	ac	in- bd det.	-	-	bc	-	ad	-	0	0	0	0	1				
Total septuples:											1	0	2	1	7	3	3	2	19
Octuple exchanges:																			
i) Four in linkage group I; one in linkage group IV; three in linkage group VI:																			
bc	bc	ad	bd	-	bc	-	bc	ad	bd	-	0	0	0	1	0	0	0	1	
bc	ac	bd	-	ac	bc	bc	-	ad	-	bc	0	0	0	0	1	0	0	1	
bc	ad	-	bd	ac	bc	bc	-	-	bd	ac	0	0	0	0	0	1	0	1	
-	bc	-	ac	ac	bc	-	bc	ac	bd	-	0	0	1	0	0	0	0	1	
-	bc	bd	ac	-	bc	-	bc	-	ad	bd	0	0	0	0	1	0	1	0	

	Control	$4 \times 10^{-5} M$ EDTA	$10 \times 10^{-5} M$ EDTA	$20 \times 10^{-5} M$ EDTA	Total
A. Tetrads with 4 products: 8 ascospores analyzed	184 114	147 111	119 120	101 108	1004
7 " "	99 34	47 25	38 31	33 28	335
6 " "	12 7	8 11	10 4	15 6	73
5 " "	5 2	2 3	6 1	4 4	27
4 " "	1 1	0 0	3 0	2 0	7
B. Tetrads with 3 products: 6 ascospores analyzed	43 24	10 19	26 15	18 13	168
5 " "	15 5	14 19	27 9	24 11	124
4 " "	2 4	13 10	8 7	22 4	70
3 " "	0 1	0 1	1 0	2 0	5
C. Tetrads with 2 products: 3 ascospores analyzed	6 2	5 8	3 2	6 10	42
D. Tetrads with 1 product: 3 ascospores analyzed	7 3	2 7	5 7	7 8	46
E. Tetrads with 0 products: 3 ascospores analyzed	3 2	0 4	1 2	2 3	17
F. Technical error or abnormal asci:	3 1	2 2	3 2	4 5	22
Total ordered tetrads dissected	380 580	250 470	250 450	240 440	1940

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Strands involved in exchanges in regions											Control	$4 \times 10^{-5} M$ EDTA	$10 \times 10^{-5} M$ EDTA	$20 \times 10^{-5} M$ EDTA	Total				
I	II	III	IV	V	VI	VII	VIII	IX	X	XI									
ii) Three in linkage group I; one in linkage group IV; four in linkage group VI:																			
bc	ad	-	-	ac	bc	bc	ad	-	bc	bc	0	0	0	0	0	1			
bc	-	ad	-	bc	bc	bc	-	bc	bc	ac	0	0	0	0	1	0			
bc	-	-	ad	ac	bc	bc	ad	bd	-	ac	0	0	0	0	0	1			
-	bc	-	bc	ad	bc	bc	ac	bd	bd	-	0	0	0	0	0	1			
-	bc	-	ad	bc	bc	bc	bd	ac	-	ad	0	0	0	0	1	0			
iii) Four in linkage group I; none in linkage group IV; four in linkage group VI:																			
-	-	bc	bd	ac	-	-	bc	ad	bd	bd	0	0	0	0	0	1			
iv) Three in linkage group I; none in linkage group IV; five in linkage group VI:																			
bc	-	ad	-	bd	-	bc	bc	bd	ad	ad	0	0	0	0	0	1			
bc	ad	bd	-	ad	-	bc	bd	ac	-	bd	0	0	0	0	1	0			
v) Two in linkage group I; one in linkage group IV; five in linkage group VI:																			
-	-	-	bc	ad	bc	bc	ac	ac	in- bd	ad	0	0	0	0	1	0			
Total octuples:																			
											0	0	1	1	2	3	3	4	14
Novuple exchanges:																			
i) Four in linkage group I; one in linkage group IV; four in linkage group VI:																			
bc	bc	-	bd	ac	bc	bc	ad	-	bd	ac	0	0	0	0	1	0	0	1	
bc	ad	ac	bd	-	bc	bc	bd	-	ad	bc	0	0	0	0	0	1	0	0	
bc	-	-	ac	ac	bc	bc	bd	ac	-	bd	0	0	0	0	1	0	0	0	
ii) Five in linkage group I; one in linkage group IV; three in linkage group VI:																			
bc	-	bd	ac	ad	bc	bc	-	-	ac	bd	0	0	0	0	1	0	0	1	
Total novuples:																			
											0	0	0	0	3	1	0	0	4
Total completely analyzable tetrads:																			
											361	192	241	199	238	187	221	174	1813
Total for the treatment:																			
											553	440	425	395	1813				

TABLE 2

Strand relationships of double exchanges (contiguous) in linkage group I

Regions	Control				4×10 ⁻⁵ M EDTA				10×10 ⁻⁵ M EDTA				20×10 ⁻⁵ M EDTA				Total
	Double exchanges				Double exchanges				Double exchanges				Double exchanges				Double exchanges
	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	2-st 3-st 4-st (P*, d.f.=2)
A. Within arms																	
a. Left arm																	
I and II	31	2:0:1*	(1)		32	1:0:1			33	1:1:3			34	1:0:3			
	39	1:0:0			40	1:0:0			41	0:1:3			42	1:1:3			
Pooled		3:0:1				2:0:1				1:2:6				2:1:6			8:3:14 (<0.001)
b. Right arm																	
(i) Adjacent regions																	
III and IV	31	1:1:0			32	2:1:2			33	1:1:2			34	1:1:1*	(1)		
	39	0:0:0			40	1:1:2			41	1:1:1			42	1:1:3			
Pooled		1:1:0				3:2:4				2:2:3				2:2:4			8:7:11 (0.05 to 0.02)
IV and V	31	3:0:1*	(1)		32	1:1:3*	(2)		33	2:3:7*	(3)		34	3:0:3*	(3)		
	39	3:1:0			40	1:0:1			41	2:3:6			42	1:1:3			
Pooled		6:1:1				2:1:4				4:6:13				4:1:6			16:9:24 (<0.001)
(ii) Nonadjacent regions																	
III and V	31	2:1:0			32	0:0:0			33	0:1:0*	(1)		34	0:1:5			
	39	1:0:0			40	0:1:1			41	0:1:2			42	1:0:3			
Pooled		3:1:0				0:1:1				0:2:2				1:1:8			4:5:11 (0.02 to 0.01)
Total (right arm)		10:3:1				5:4:9				6:10:18				7:4:18			28:21:46
(P)		(0.02 to 0.01)				(0.3 to 0.2)				(0.05 to 0.02)				(<0.001)			(<0.001)
		d.f. = 6				d.f. = 6				d.f. = 6				d.f. = 6			d.f. = 6
Total (within arms)		13:3:2				7:4:10				7:12:24				9:5:24			36:24:60
(P)		(0.02 to 0.01)				(0.2 to 0.1)				(<0.01)				(<0.001)			(<0.001)
		d.f. = 8				d.f. = 8				d.f. = 8				d.f. = 8			d.f. = 8
B. Between arms																	
(i) Proximal regions																	
II and III	31	0:0:0			32	0:2:2			33	0:2:0			34	0:2:2			
	39	0:0:0			40	0:1:3			41	0:1:2			42	0:1:2			
Pooled		0:0:0				0:3:5				0:3:2				0:3:4			0:9:11 (0.01 to 0.001)
II and IV	31	5:2:2			32	2:1:4			33	0:1:5*	(1)		34	1:0:1			
	39	4:2:2			40	1:2:4			41	0:2:1			42	1:1:1			
Pooled		9:4:4				3:3:8				0:3:6				2:1:2			14:11:20 (<0.001)
(ii) Distal regions																	
I and V	31	2:1:1			32	1:0:1			33	0:2:4			34	3:1:6			
	39	1:0:0			40	1:1:0			41	1:1:3			42	3:3:7			
Pooled		3:1:1				2:1:1				1:3:7				6:4:13			12:9:22 (<0.001)

TABLE 2—Continued

Regions	Control				4 × 10 ⁻⁵ M EDTA				10 × 10 ⁻⁵ M EDTA				20 × 10 ⁻⁵ M EDTA				Total
	Double exchanges				Double exchanges				Double exchanges				Double exchanges				Double exchanges
	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	2-st 3-st 4-st (P*, d.f. = 2)
(iii) Proximal/ distal																	
I and III	31	2	0	0	32	2	0	1	33	1	1	0	34	1	0	2	
	39	0	0	0	40	1	0	1	41	0	0	1	42	2	1	2	
Pooled		2	0	0		3	0	2		1	1	1		3	1	4	9:2:7 (<0.001)
I and IV	31	2	2	0	32	1	1	0	33	1	1	3	34	1	1	0	
	39	2	0	0	40	0	0	1	41	1	3	4	42	0	0	2	
Pooled		4	2	0		1	1	1		2	4	7		1	1	2	8:8:10 (0.2 to 0.1)
II and V	31	5	3	1	32	1	0	1	33	1	2	1	34	2	1	2	
	39	6	3	1	40	1	0	0	41	1	0	1	42	2	1	2	
Pooled		11	6	2		2	0	1		2	2	2		4	2	4	19:10:9 (<0.001)
Total (between arms)		29	13	7		11	8	18		6	16	25		16	12	29	62:49:79
(P)		(<0.001)				(0.3 to 0.2)				(0.1 to 0.05)				(0.02 to 0.01)			(<0.001)
		d.f. = 12				d.f. = 12				d.f. = 12				d.f. = 12			d.f. = 12

* Plus the indicated number of pairs (indeterminate type), owing to a 4-strand double exchange within one of the regions.

P-values are from chi-square, testing agreement with $\frac{1}{4}:\frac{1}{2}:\frac{1}{4}$ for 2-strand:3-strand:4-strand double exchanges.

TABLE 3

Strand relationships of double exchanges (contiguous) in linkage group VI

Regions	Control				4 × 10 ⁻⁵ M EDTA				10 × 10 ⁻⁵ M EDTA				20 × 10 ⁻⁵ M EDTA				Total
	Double exchanges				Double exchanges				Double exchanges				Double exchanges				Double exchanges
	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	2-st 3-st 4-st (P*, d.f. = 2)
A. Within arms																	
a. Left arm																	
VII and VIII	31	5	2	2* ⁽¹⁾	32	2	0	3	33	2	2	6	34	2	0	3	
	39	3	1	1	40	1	0	2	41	2	4	6	42	0	1	3	
Pooled		8	3	3		3	0	5		4	6	12		2	1	6	17:10:26 (<0.001)
b. Right arm																	
(i) Adjacent regions																	
IX and X	31	2	0	1	32	1	1	2	33	2	1	3* ⁽³⁾	34	3	2	3	
	39	0	0	0	40	2	0	2	41	1	2	2	42	2	1	4	
Pooled		2	0	1		3	1	4		3	3	5		5	3	7	13:7:17 (<0.001)
X and XI	31	2	1	0	32	1	1	1	33	0	0	1	34	0	1	1	
	39	1	0	0	40	1	1	1	41	0	1	1	42	1	1	2	
Pooled		3	1	0		2	2	2		0	1	2		1	2	3	6:6:7 (0.3 to 0.2)

TABLE 3—Continued

Regions	Control				4×10 ⁻⁵ M EDTA				10×10 ⁻⁵ M EDTA				20×10 ⁻⁵ M EDTA				Total
	Double exchanges				Double exchanges				Double exchanges				Double exchanges				Double exchanges
	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	Cross No.	2-st	3-st	4-st	2-st 3-st 4-st (P*, d.f. = 2)
(ii) Nonadjacent regions																	
IX and XI	31	2:0:0*	(¹)	32	2:0:3*	(¹)	33	1:3:5*	(⁴)	34	2:0:4*	(¹)					
	39	2:0:0		40	0:1:2		41	2:2:5		42	1:1:2						
Pooled		4:0:0			2:1:5			3:5:10			3:1:6						12:7:21 (<0.001)
Total (right arm)		9:1:1			7:4:11			6:9:17			9:6:16						31:20:45
(P)		(<0.01)			(0.1 to 0.05)			(0.05 to 0.02)			(0.05 to 0.02)						(<0.001)
		d.f. = 6			d.f. = 6			d.f. = 6			d.f. = 6						d.f. = 6
Total (within arms)		17:4:4			10:4:16			10:15:29			11:7:22						48:30:71
(P)		(<0.01)			(0.02 to 0.01)			(0.05 to 0.02)			(<0.01)						(<0.001)
		d.f. = 8			d.f. = 8			d.f. = 8			d.f. = 8						d.f. = 8
B. Between arms																	
(i) Proximal regions																	
VIII and IX	31	0:2:1		32	0:2:2		33	0:2:2		34	0:2:3						
	39	0:1:0		40	0:1:2		41	0:1:3		42	0:1:2						
Pooled		0:3:1			0:3:4			0:3:5			0:3:5						0:12:15 (<0.01)
VIII and X	31	1:0:1*	(¹)	32	2:0:1		33	1:1:5		34	0:0:0*	(¹)					
	39	0:0:1		40	0:0:0		41	2:2:3		42	0:0:2						
Pooled		1:0:2			2:0:1			3:3:8			0:0:2						6:3:13 (<0.001)
(ii) Distal regions																	
VII and XI	31	4:2:1		32	1:1:3		33	1:1:3		34	2:1:4						
	39	6:3:2		40	2:1:3		41	1:2:3		42	2:1:2						
Pooled		10:5:3			3:2:6			2:3:6			4:2:6						19:12:21 (<0.001)
(iii) Proximal/distal																	
VII and IX	31	2:1:1		32	1:1:1		33	1:1:2		34	2:1:6						
	39	1:0:0		40	1:1:2		41	1:1:1		42	3:2:5						
Pooled		3:1:1			2:2:3			2:2:3			5:3:11						12:8:18 (<0.001)
VII and X	31	3:0:0		32	1:0:1		33	2:2:3		34	3:0:2						
	39	1:1:0		40	1:0:0		41	0:1:2		42	3:2:4						
Pooled		4:1:0			2:0:1			2:3:5			6:2:6						14:6:12 (<0.01)
VIII and XI	31	3:1:0		32	1:0:2		33	1:3:2		34	0:0:0						
	39	3:0:1		40	1:1:2		41	0:0:2		42	0:0:0						
Pooled		6:1:1			2:1:4			1:3:4			0:0:0						9:5:9 (0.05 to 0.02)
Total (between arms)		24:11:8			11:8:19			10:17:31			15:10:30						60:46:88
(P)		(0.05 to 0.02)			(0.2 to 0.1)			(<0.001)			(<0.001)						(<0.001)
		d.f. = 12			d.f. = 12			d.f. = 12			d.f. = 12						d.f. = 12

* Plus the indicated number of pairs (indeterminate type), owing to a 4-strand double exchange within one of the regions.

P-values are from chi-square, testing agreement with $\frac{1}{4}:\frac{1}{2}:\frac{1}{4}$ for 2-strand:3-strand:4-strand double exchanges.

TABLE 4

Strand relationship in pairs of contiguous exchanges (regions pooled) according to EDTA treatments in linkage groups I and VI

Treatment	2-st	3-st	4-st	2-st	A†	B‡
				2-st + 4-st		
Control:						
Linkage group I	42	16	9(2)*	0.82	≪0.001	≪0.001
Linkage group VI	41	15	12(3)	0.77	≪0.001	≪0.001
Pooled	83	31	21(5)	0.80	≪0.001	≪0.001
4 × 10 ⁻⁵ M EDTA:						
Linkage group I	18	12	28(2)	0.39	0.2 to 0.1	≪0.001
Linkage group VI	21	12	35(1)	0.37	0.1 to 0.05	≪0.001
Pooled	39	24	63(3)	0.38	0.2 to 0.01	≪0.001
10 × 10 ⁻⁵ M EDTA:						
Linkage group I	13	28	49(5)	0.21	≪0.001	≪0.001
Linkage group VI	20	32	60(7)	0.25	≪0.001	≪0.001
Pooled	33	60	109(12)	0.23	≪0.001	≪0.001
20 × 10 ⁻⁵ M EDTA:						
Linkage group I	25	17	53(4)	0.32	<0.001	≪0.001
Linkage group VI	26	17	52(2)	0.34	<0.01	≪0.001
Pooled	51	34	105(6)	0.33	≪0.001	≪0.001
Total	206	149	298(26)	0.41	≪0.001	≪0.001

* Number of tetrads showing pairs of indeterminate type, owing to a 4-strand double within one of the intervals, is italicized in parentheses.

† A shows P-values testing the deviation from 1:1 for 2-strand doubles : 4-strand doubles.

‡ B shows P-values testing the deviation from 1:1 for (2-strand + 4-strand) doubles : 3-strand doubles.

the control crosses, and an excess of 4-strand doubles, indicating the existence of positive interference, in the crosses treated with 10 × 10⁻⁵M EDTA and 20 × 10⁻⁵M EDTA. No significant departure from a 1:1 ratio exists between 2-strand and 4-strand doubles in crosses treated with 4 × 10⁻⁵M EDTA. In Tables 5 and 6, totals were derived (derived totals) by (i) excluding data from adjoining regions to avoid errors due to misscoring, conversions, or mutations; (ii) excluding data from regions II and III in linkage group I and from regions VIII and IX in linkage group VI because of the indeterminate pairs of 2-strand doubles. (This error would result in a spuriously high ratio of 4-strand or even 3-strand to 2-strand types); (iii) adding data from regions located within left and right arms to avoid the intervening effects of the centromere; and (iv) adding data from regions 'across centromere' to compare with the data from 'within arms'. In linkage group I, all the derived totals except those from regions across centromere show a significant excess of 4-strand doubles over 2-strand doubles. In linkage group VI, all the derived totals except where adjoining regions are excluded show an excess of 4-strand doubles over 2-strand doubles, but only at about the 5 percent level of significance. It is obvious that the results in the last three columns in Tables 5 and 6 are obtained by pooling the data from differently treated crosses which are heterogeneous. On an examination of Tables 2 and 3, it becomes clear, however, that there is a significant excess of 2-strand doubles

TABLE 5

Strand relationship in pairs of contiguous exchanges according to the number of regions intervening and totals derived for various segments of the data in linkage group I (crosses within a treatment pooled)

Number of regions intervening	Control			4×10 ⁻⁵ M EDTA			10×10 ⁻⁵ M EDTA			20×10 ⁻⁵ M EDTA			2-st	A [†]	B [‡]
	2-st	3-st	4-st	2-st	3-st	4-st	2-st	3-st	4-st	2-st	3-st	4-st	2-st + 4-st		
0	10	2	2	7	6	14	7	13	24	8	7	20	0.35	<0.01	≤0.001
		*§					***			**					
1	14	5	4	6	4	11	1	6	9	6	3	14	0.42	0.2 to 0.1	≤0.001
		*§					**§								
2	15	8	2	3	1	2	4	6	9	5	3	6	0.59	0.3 to 0.2	≤0.001
		***§													
3	3	1	1	2	1	1	1	3	7	6	4	13	0.35	0.1 to 0.05	≤0.001
Total	42	16	9	18	12	28	13	28	49	25	17	53	0.41	<0.01	≤0.001
Derived totals:															
(a) Excluding adjoining regions	32	14	7	11	6	14	6	15	25	17	10	33	0.46	<0.01	≤0.001
	****						****			***					
(b) Within arms	13	3	2	7	4	10	7	12	24	9	5	24	0.37	0.02 to 0.01	≤0.001
	***§						***			***					
(c) Across centromere	29	13	7	11	8	18	6	16	25	16	12	29	0.44	0.2 to 0.1	≤0.001
	****			**			****			*					
(d) Excluding regions II and III	42	16	9	18	9	23	13	25	47	25	14	49	0.43	0.05 to 0.02	≤0.001
	****						****			***					

Deviation from 1 2-strand : 1 4-strand doubles for the individual entries is shown by: * denoting significance at the 5 percent level; ** 2 percent level; *** 1 percent level; **** 0.1 percent level.

[†] A shows P-values testing the deviation from 1:1 for 2-strand doubles : 4-strand doubles for the pooled data.

[‡] B shows P-values testing the deviation from 1:1 for (2-strand + 4-strand) doubles : 3-strand doubles for the pooled data.

§ After Yates' correction.

in the control crosses, and of 4-strand doubles in the crosses treated with 20 × 10⁻⁵M EDTA, (though in the latter, P-values across centromere over the totals in linkage group I are not significant) within arms and across centromeres in both linkage groups I and VI. In contrast to the three sets of crosses mentioned above, the crosses treated with 4 × 10⁻⁵M EDTA showed no deviation (except within arms in linkage group VI where P = 0.02 to 0.01) from the expected ratio of 1:2:1 of 2-strand : 3-strand : 4-strand doubles, totaled over the crosses. Variation in the occurrence of different strand relationships between pairs of regions can be seen in Figures 1 to 4. No doubt, the pairs of regions given in these figures can be arranged arbitrarily in many different orders, but joining the points here does not give spurious curves, because once a particular order for the pairs of regions is fixed on the graph, relative shapes between the curves, between the control and the different EDTA treatments, can be readily compared. The data concerning alteration in the type of double exchanges, with respect to the pairs

TABLE 6

Strand relationship in pairs of contiguous exchanges according to the number of regions intervening and totals derived for various segments of the data in linkage group VI (crosses within a treatment pooled)

Number of regions intervening	Control			4 × 10 ⁻⁵ M EDTA			10 × 10 ⁻⁵ M EDTA			20 × 10 ⁻⁵ M EDTA			2-st	A ₁ ⁺	B ₁ ⁺
	2-st	3-st	4-st	2-st	3-st	4-st	2-st	3-st	4-st	2-st	3-st	4-st	2-st + 4-st		
0	14	6	5	8	5	18	10	17	32	10	8	24	0.35	<0.001	<0.001
		*			*			****			**				
1	7	2	3	6	4	6	5	6	13	6	5	16	0.39	0.1 to 0.05	<0.001
											*				
2	10	2	1	4	1	5	3	6	9	6	2	6	0.52	0.9 to 0.8	<0.001
		***	§												
3	10	5	3	3	2	6	2	3	6	4	2	6	0.48	0.9 to 0.8	<0.001
Total	41	15	12	21	12	35	20	32	60	26	17	52	0.40	<0.01	<0.001
Derived totals:															
(a) Excluding adjoining regions	27	9	7	13	7	17	10	15	28	16	9	28	0.45	0.3 to 0.2	<0.001
		****						***							
(b) Within arms	17	4	4	10	4	16	10	15	29	11	7	22	0.40	0.05 to 0.02	<0.001
		****	§					*							
(c) Across centromere	24	11	8	11	8	19	10	17	31	15	10	30	0.41	0.05 to 0.02	<0.001
		***						***			*				
(d) Excluding regions VIII and IX	41	12	11	21	9	31	20	29	55	26	14	47	0.43	0.05 to 0.02	<0.001
		****						***			**				

See Table 5 for footnotes.

of regions from crosses with the identical treatments, are homogeneous and are therefore pooled. Only contiguous exchanges were used for the figures.

DISCUSSION

If every exchange within a pair of intervals under study is detectable, the information is more reliable than when such detection is impossible. Since it is impossible to detect all multiple crossovers, an allowance may be made for undetected double exchanges by the use of WHITEHOUSE's (1956) correction. This correction is based on the occurrence of 4-strand double exchanges within intervals because 2-strand and 3-strand double exchanges within an interval remain unrecognized. In the data analyzed above, 4-strand double exchanges occurred within intervals in only 26 cases, which is less than 4 percent of the total number of contiguous double exchanges giving information on chromatid interference. WHITEHOUSE's correction was not applied both because 4-strand doubles were rare within intervals, and because the correction would serve only to provide a more precise estimate of the magnitude of chromatid interference if

FIGURES 1 and 3.—The variation in occurrence of 4-strand doubles in relation to 2-strand doubles with respect to the ten pairs of regions in *linkage group I*. (Figure 1, top left) and *linkage group VI* (Figure 3, top right). Deficiency of 4-strand doubles is indicated by a value falling below the null line and no chromatid interference is indicated by zero value (null line) based on the hypothesis of random strand exchanges.

FIGURES 2 and 4.—The variation in occurrence of 3-strand doubles in relation to 2-strand plus 4-strand doubles with respect to the ten pairs of regions in *linkage group I*. (Figure 2, bottom left) and *linkage group VI* (Figure 4, bottom right). A deficiency of 3-strand doubles is indicated by a value below the null line and an excess of 3-strand doubles by a value above the zero value (null line) based on the hypothesis of random strand exchanges. The letters a, b and c indicate respectively proximal/proximal, distal/distal and proximal/distal location of the pairs of regions across centromere.

it occurred, but would not provide evidence of the occurrence or nonoccurrence of chromatid interference.

Considering LINDEGREN and LINDEGREN's data, PERKINS (1955) shows that evidence for chromatid interference is greatly reduced if retabulation is made on the assumption that all the 2-strand double crossovers in a ratio of 20:3:1 of 2-, 3-, and 4-strand double exchanges in regions II and III (about 1 percent of asci) resulted from misassortment of centromeres. Whereas, accordingly, only their 15:7:6 double crossover ratio for regions I and IV shows evidence of negative chromatid interference not attributable to misassortment. Contrary to PERKINS' assumption that misassortment of centromere occurs more frequently in 2-strand double exchanges than in others, LINDEGREN and SHULT (1957) assert that misassortment, if it occurs at all, is independent of crossing over and observe that PERKINS' 1 percent frequency of misassortment is in conflict with the available data on *Neurospora* in the literature. An earlier reanalysis of part of their data by WHITEHOUSE (1942) had indicated the presence of chromatid interference not attributable to misassortment of centromeres. It is, however, clear that LINDEGREN and LINDEGREN's 1942 data enable assessments to be made of the occurrence of chromatid interference, and is the first record of such an occurrence.

The findings of WHITEHOUSE (1958) and of RIFAAT (1956), and the data reported here in the control crosses, as to the occurrence of negative chromatid interference across the centromere in linkage group I, are quite in conformity with those of LINDEGREN and LINDEGREN (1942). In the present investigation, an excess of 2-strand double exchanges obtained within arms of linkage group I is, however, in disagreement with these workers. HOWE (1956) and STADLER (1956) report that crossing-over events in one arm of a chromosome are independent of those in the other arm and that there exists no chromatid interference. HOWE obtained a 5:10:3 ratio for 2-strand, 3-strand and 4-strand doubles, across the centromere. STADLER (1956) feels that because of the low number of double crossovers, the result is compatible with quite a wide range of ratios of the 2-, 3-, and 4-strand types. STADLER's own ratio of 43:54:53 for 2-strand, detectable 3-strand, and 4-strand double crossovers is in good agreement with 1:1:1 ratio expected with no chromatid interference. It is most likely that the two types of 3-strand exchanges occur with equal frequency; STADLER's data are therefore good evidence for no chromatid interference in his strains. STADLER made use of markers on linkage group VI. The present results show, on the other hand, that there is consistently an excess of 2-strand doubles and a deficiency of 3-strand doubles within and between arms of linkage group VI in the control crosses. The departures in results arrived at by different workers may be a reflection of differences in the size of regions, the linkage groups, the genetic background of the markers used, and possibly in the techniques employed in collecting data.

It is striking in the present case that 4-strand double exchanges are in excess in the crosses treated with 10×10^{-5} M EDTA, compared with the control crosses, where 2-strand doubles are in excess. This suggests that negative chromatid interference can be changed to positive by EDTA.

In contrast to this effect with EDTA, MALING (1959) observed a deficiency of 3-strand double exchanges in a *Neurospora* cross treated with 5-bromouracil. EVERSOLE and TATUM (1956) observed an excess of the nonparental ditype class in crosses of *arg-1* $\times$ *arg-2* with EDTA treatment in *Chlamydomonas*. An excess of nonparental ditype over the expected number would mean either that the chromatid interference results in an excess of 4-strand double exchanges or that crossing over occasionally occurs at the 2-strand stage. It is important to note that a single crossover, if it occurs at the 2-strand stage, will give rise to an apparent 4-strand double exchange. Since the results obtained in the present investigation agree with those of EVERSOLE and TATUM (1956) in showing an excess of 4-strand double crossovers, it may be that EDTA is effective at the 2-strand stage.

With the use of tritiated thymidine, TAYLOR (1957, 1958, 1959, 1960) put forward convincing evidence for the existence of sister-strand exchanges, which lends support to the sister-strand exchange model discussed by SCHWARTZ (1953, 1954, 1955). At the 4-strand stage, if crossing over between homologous chromosomes is a result of an exchange between the newly formed chromatids, it is understandable that only 2-strand doubles would occur among multiple crossovers, and 3-strand or 4-strand doubles would require sister-strand exchanges in conjunction with the 2-strand doubles. It may be that EDTA treatment brings about alterations in the frequency of sister-strand exchanges in such a way that it favours a shift from 2-strand to 4-strand exchanges. There is thus a possibility that sister-strand exchanges are induced *simultaneously* with a higher frequency of odd than even numbers in each of the homologues, because of the occurrence of a uniform deficit in the 3-strand doubles and an overall excess of 4-strand doubles on treatment. The possibility of variation in the frequency of sister-strand exchanges has also been suggested by STRICKLAND (1961).

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SUMMARY

1813 completely analyzable ordered tetrads have been scored for 11 markers distributed on linkage groups I (five markers), IV (one marker), and VI (five markers). In all crosses, there is a statistically significant deficiency of 3-strand double exchanges. Chromatid interference is negative in the control crosses, with a marked excess of 2-strand doubles within arms and across centromeres of linkage groups I and VI. Chromatid interference is absent in crosses treated with $4 \times 10^{-5}\text{M}$ EDTA. A significant excess of 4-strand double exchanges is found in the crosses treated with $10 \times 10^{-5}\text{M}$ EDTA and $20 \times 10^{-5}\text{M}$ EDTA. This genetic analysis suggests that a negative chromatid interference is modifiable to positive chromatid interference when crosses are treated with an appropriate concentration of EDTA.

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