A TEST OF COINCIDENT RECOMBINATION IN CLOSELY LINKED GENES OF NEUROSPORA¹

DAVID R. STADLER AND AGNES M. TOWE

Department of Genetics, University of Washington, Seattle, Washington 98105

Received September 16, 1967

TETRAD analyses of intragenic recombination in *Ascobolus* (LISSOUBA *et al.* 1962; RIZET and ROSSIGNOL 1966; MOUSSEAU 1966) and in *Neurospora* (STADLER and TOWE 1963) have shown that mutant sites in one part of a functional gene may show markedly different frequencies of non-reciprocal segregation from those shown by sites in another part of the same gene. Selection of prototrophic recombinants in crosses between allelic mutants (MURRAY 1963, SIDDIQI and PUTRAMENT 1963; STADLER and TOWE 1963; PEES 1965) yields patterns of outside marker combinations which may result from the same kind of polarity. Such results are compatible with the "fixed pairing region" concept suggested by STAHL (1961) and by MURRAY (1961). Such a hypothesis follows:

1) A chromosome is made up of a series of fixed pairing regions (FPR), each region being the length of one or a few genes; the ends of FPR's may coincide with the ends of functional genes.

2) When homologous chromosomes synapse during the first meiotic prophase, only a small fraction of the FPRs (perhaps one per cent) are paired effectively for recombination.

3) Within such a paired FPR, the involved chromatids may show two or three or more exchanges, which are not required to be reciprocal with respect to the exact point of exchange or to the number of exchanges; it is required only that both have an odd number of exchanges or both have an even number, so that reciprocal (2:2) segregation will be insured at both ends of the FPR.

4) Sites near the ends of an FPR may be involved in recombination events with a different frequency than sites near the middle of the region.

5) Coincident exchanges in the same FPR produce negative interference and there is positive (chiasma) interference between separate FPRs.

Assuming that the hypothesis is correct, one can test whether two mutant sites lie in the same FPR by selecting recombinants between them in a cross segregating for linked markers on both sides (Figure 1). If both of the selected sites *m-1+* and *m-2+* are in the same FPR, the selected exchange between them may frequently be accompanied by exchanges to the left of *m-1* and to the right of *m-2*, and all four marker combinations may be found among the *m+* recombinants. If *m-1* and *m-2* are in separate FPRs, coincident exchanges to the left of *m-1* and to the right of *m-2* will not occur, and one of the non-parental marker

¹ This investigation was supported by a grant from the National Science Foundation.

FIGURE 1.—Production of m^+ recombinants with various marker combinations, according to the Fixed Pairing Region (FPR) model. It is assumed that exchange can take place in only one FPR in the marked region, but there is no limit to the number of exchanges in that region. The left-hand column represents the cross in which the selected sites $m-1^+$ and $m-2^+$ are located in the same FPR, while the right-hand column shows them in separate FPRs.

combinations ($A m^+ b$) will be absent. Tests of seven mutants in the *cys-2* locus of *Neurospora* (STADLER and TOWE 1963) indicated that all seven were in the same FPR. The present report deals with such an experiment involving one of these same seven mutants and a mutant in the nearby but separate functional gene *cys-1*. The results indicate that the *cys-1* mutant is not in the same FPR as the *cys-2* mutant site. A preliminary report of part of this work was made earlier (STADLER, TOWE and MURRAY 1965).

MATERIALS AND METHODS

The mutant genes which were segregating in these crosses are in the left arm of linkage group VI in the following order: *lys-5* (lysine-requiring), *cys-2* (cysteine-requiring), *cys-1* (cysteine-requiring), *γlo* (yellow conidia), *ad-1* (adenine-requiring). The *cys-2* allele employed here is the one referred to as *cys*⁴ in the earlier recombination study (STADLER and TOWE 1963) and was obtained from UV-treated material. The *cys-1* mutant (isolation number 84605) is the

TABLE 1

Cysteine prototrophs from crosses between cys-1 and cys-2

Cross	Parents*	Percent germination	Total spores	Total <i>cys</i> ⁺	<i>cys</i> ⁺ per 10 ³ spores	Markers with <i>cys</i> ⁺			
						<i>lys</i> ⁺ <i>cys</i> ⁺ <i>γlo</i> ⁺	<i>lys</i> <i>cys</i> ⁺ <i>γlo</i>	<i>lys</i> ⁺ <i>cys</i> ⁺ <i>γlo</i>	<i>lys</i> <i>cys</i> ⁺ <i>γlo</i> ⁺
1	<i>cys-1 a</i> × <i>lys cys-2 γlo A</i>	60	29,200	76	2.6	16 (5.5)**	23 (7.9)	37 (12.7)	0
2	<i>cys-1 (G2) a</i> × <i>lys cys-2 γlo A</i>	85	22,400	100	4.5	20 (8.9)	15 (6.7)	65 (29.0)	0
3	<i>cys-1 (G3) a</i> × <i>lys cys-2 γlo A</i>	75	5,250	26	4.95	3 (5.7)	4 (7.6)	19 (36.2)	0
4	<i>cys-1 (G4) a</i> × <i>lys cys-2 γlo A</i>	80	4,700	51	10.9	4 (8.5)	6 (12.8)	41 (85.0)	0
5	<i>cys-1 (G2') a</i> × <i>lys cys-2 γlo A</i>	75	38,500	150	3.9	29 (7.5)	32 (8.3)	88 (22.8)	1
6	<i>cys-1 (NA) a</i> × <i>lys cys-2 γlo A</i>	60	31,100	124	4.0	14 (4.5)	30 (9.6)	79 (25.4)	1
7	<i>cys-1 (15) a</i> × <i>lys cys-2</i> <i>γlo ad A</i>	65	40,600	329	8.1	61 (15.0)	59 (14.5)	204 (50.3)	5
8	<i>cys-1 (27) a</i> × <i>lys cys-2</i> <i>γlo ad A</i>	55	26,900	333	12.4	73 (27.1)	46 (17.1)	211 (78.4)	3
9	<i>lys cys-1 A</i> × <i>cys-2 γlo a</i>	70	18,200	99	5.4	0	65 (35.7)	26 (14.3)	8 (4.4)

* All parents of all crosses were also *cot*.** Numbers in parentheses are frequencies per 10⁴ total spores.

only mutant allele known at this locus and was induced with X-rays. MURRAY (1965) has shown by complementation tests and nutritional studies that *cys-2* and *cys-1* probably represent separate functional genes.

All of the nine crosses reported here were of the form *cys-1* × *cys-2*, and they were heterozygous for the outside markers *lys* and *γlo*. A single stock of *lys cys-2 γlo A* was used as fertilizing parent in crosses 1–6 (Table 1). The first four represent an inbreeding series, i.e. after each successive cross was analyzed, a single *cys-1 a* ascospore culture from the progeny was crossed back to its *lys cys-2 γlo A* parent. Crosses 1 and 5 represent the start of a second inbreeding series which was carried no further. Number 6 is an attempt at outbreeding—here the *cys-1* parent was isolated from the progeny of a cross of the original *cys-1 a* stock to the wild-type strain known as North Africa I. Crosses 7 and 8 were segregating for *ad-1* as well as for all the loci involved in the other crosses; the *cys-1* parents in these two crosses were progeny of cross 4. The markers *lys* and *γlo* were coupled in the parentage of the first eight crosses, but in 9 they were in repulsion.

All strains used here carried the temperature-colonial mutant *cot*, so that the germinating ascospores, when incubated at 33°, produced compact colonies which could be isolated free of neighboring spores even on crowded plates.

The *cys-1* parent of each cross was inoculated onto slants of crossing medium supplemented

with 500 mg/liter L-methionine (which gave higher fertility in these crosses than did cysteine-supplemented medium) five days before being fertilized with conidia of the *cys-2* parent. The crosses were allowed to mature at least three weeks at 25° before being analyzed for *cys*⁺ recombinants. The perithecia were then teased apart in sterile water to release the ascospores. This mixture was shaken vigorously and filtered through surgical gauze to remove clumps and pieces of perithecial wall. The resulting ascospore suspension was added to 1% agar at 60° and incubated 25 minutes to activate the ascospores. Aliquots were pipetted onto plates of minimal medium plus 50 mg/liter L-lysine. (The plating medium for crosses 7 and 8 was supplemented with adenine also.) These plates were incubated at 33° for three days, at which time the *cys*⁺ colonies were clearly visible on the selective medium. They were isolated and grown on slants of complete medium, scored for color, and conidial suspensions were made to determine nutritional requirements by drop tests on sorbose plates.

Some of the cysteine-independent colonies on these plates were pseudowild types (PWT's; MITCHELL, PITTINGER and MITCHELL 1952), and it was necessary to exclude these before tabulating the results. In the first two crosses all the *cys*⁺ progeny were screened for PWT's in two ways:

- 1) Vegetative test: duplicate inocula of a conidial suspension were plated on minimal medium supplemented with lysine and on minimal with both lysine and cysteine—PWT's gave a much larger number of macroscopic colonies on the latter medium than the former, while true *cys*⁺ recombinants gave equal numbers on both plates.

- 2) Cross test: the putative *cys*⁺ recombinant was crossed to one of the *cys* mutant parents—if it was a PWT, nearly all the progeny of this cross were cysteine mutants, but if the parent was a true *cys*⁺ recombinant, half the progeny were *cys*⁺.

The two tests gave corresponding results in all cases, so the simpler and quicker vegetative test was used for subsequent analyses. It was found that all the PWT's came from colonies that were noticeably smaller than most of the true *cys*⁺ recombinants at the time of isolation from the germination plates. All the PWT's were not only cysteine-independent, but were also lysine-independent and most, but not all, of them were orange (*γlo*⁺). In the subsequent experiments (crosses 3–9), PWT tests were performed on all the small-colony isolates and all other isolates which were *lys*⁺ *cys*⁺ *γlo*⁺. Isolates of the "critical class" (*lys cys*⁺ *γlo*⁺) were also tested.

To determine map distances between the marked loci, germinated ascospores from each cross were picked up and scored for segregating markers. (It was possible to distinguish *cys-1* from *cys-2* by growth tests on minimal sorbose plates supplemented with thiosulfate.) Many of the *cys-1* progeny conidiated poorly, making the classification of *γlo* uncertain. As a result, the linkage maps were derived from the *cys-2* progeny exclusively. This was facilitated by the observation that *cys-2* ascospores show a distinct difference in germination from *cys-1* on deficient medium (minimal plus lysine). Approximately 250 *cys-2* ascospores from each cross were scored for recombination.

RESULTS

Asci from crosses 1, 2 and 5 (*cot cys-1 a* × *cot lys cys-2 γlo A*) were dissected on 4% agar blocks of minimal medium supplemented with lysine. They were heat-shocked (60° for 30 min.) and incubated 24 hours at 33° before microscopic examination. At this time the *cys*⁺ recombinants were clearly distinguishable on the selective medium. Among approximately 1500 asci in which at least three spore pairs germinated there were fifteen which each contained a *cys*⁺ spore pair and one which contained a single *cys*⁺ spore. The spores of the sixteen asci were isolated in separate slants of complete medium, allowed to grow, and then were classified. The results are shown in Table 2.

Reciprocal recombination between the *cys* mutants has occurred in three of the asci (#2, 6, 13). These asci establish the order of the loci as *lys*—*cys-2*—

TABLE 2

Analysis of Tetrads Containing cys⁺ Recombinants

<i>reciprocal recombination between the cys loci:</i>											
+	cys-1	+	lys	cys-1,2	+						
+	+	ylo	lys	cys-2	ylo						
3 asci (#2, 6, 13)											
<i>non-reciprocal events at cys-2:</i>											
+	cys-1	+	lys	cys-1	+	+	+	ylo			
+	cys-1	+	+	cys-1	+	+	cys-1	+			
lys	+	ylo	lys	cys-2	ylo	lys	cys-2	ylo			
lys	cys-2	ylo	+	+	ylo	lys	cys-1	+			
7 asci (#3, 4, 5, 8, 11, 14, 15)			1 ascus (#12)			1 ascus (#7)					
<i>non-reciprocal events at cys-1:</i>											
+	+	+	+	cys-1	+	lys	cys-2	+	+	cys-1	+
+	cys-1	+	lys	cys-2	ylo	+	cys-1	+	+	cys-1/+	+
lys	cys-2	ylo	lys	cys-2	ylo	lys	cys-2	ylo	lys	cys-2	ylo
lys	cys-2	ylo	+	+	+	+	+	ylo	lys	cys-2	ylo
1 ascus (#10)			1 ascus (#16)			1 ascus (#1)			1 ascus (#9)		

The asci with the same recombination events in the marked region have been grouped, even though the order of the two spore pairs in the same half of the ascus was reversed in some cases.

There were eight cases in which a single member of a spore pair failed to germinate and was assumed to have the same genotype as its sister spore. In two asci (#3, 9) both members of the last spore pair were ungerminated, and the genotype has been inferred by comparison to other tetrads.

These asci were also classified for mating type, which confirmed the pairings based on the other segregating traits.

* One member of this spore pair was *cys-1*, the other was *cys+*.

cys-1—*ylo*, and all three can be accounted for by single crossovers on that basis. The remaining thirteen asci are the result of non-reciprocal events: nine show 6:2 segregation at the *cys-2* site, three show 6:2 segregation at *cys-1*, and one (#9) segregated 5:3 at *cys-1*. Three of the asci (#1, 7, 12) with non-reciprocal events involving *cys* had reciprocal recombination between *lys* and *ylo*, and in each case the *cys*⁺ “convertant” was one of the two crossover spore pairs.

Random spores from the nine crosses were plated on minimal medium containing lysine to select *cys*⁺ recombinants. These were then classified for the unselected flanking markers (*lys* and *ylo*) and tested to exclude the pseudowild types. The results are shown in Table 1. The “critical class” which should not occur if the mutant sites of *cys-1* and *cys-2* are in separate pairing regions is *lys cys*⁺ *ylo*⁺ for the first eight crosses and *lys*⁺ *cys*⁺ *ylo*⁺ for cross 9. Less than one per cent (ten out of 1288) of the *cys*⁺ recombinants are in the critical class.

The interpretation of these results would be simplified if the Fixed Pairing

Region hypothesis predicted the *complete absence* of the critical class among recombinants between sites in separate FPRs. However, the prediction is not absolute. The critical class can result only from coincident events in two FPRs. The hypothesis states that there is positive interference between separate FPRs, but an earlier observation (STADLER 1959a) revealed that this interference is not complete. It was shown that interallelic recombination at the *cys-2* locus differs from intergenic recombination in its interference properties. Progeny with non-parental combinations of *lys* and *ylo* did show interference, i.e. they had a much lower frequency of recombination in the adjacent *ylo-ad* region than did the general population. However, recombination between the two *cys-2* alleles did not by itself cause interference; the *cys*⁺ recombinants with parental combinations of the surrounding markers (*lys* and *ylo*) showed the normal frequency of recombination in the *ylo-ad* region. A similar relationship between interallelic recombination and interference has recently been demonstrated for another genetic region in *Neurospora* by N. E. MURRAY and D. D. PERKINS (unpublished) and for the *hi-1* locus in yeast by FOGEL and HURST (1967).

We can restate the relationship of the FPR model to positive interference by saying that those events which result in an odd number of exchanges per strand in one FPR do interfere with recombination in neighboring regions, while even-number events do not. This means that some *cys*⁺ recombinants should occur in the critical class even if the fixed pairing region model is correct and if the two *cys* mutants are in separate pairing regions. [The segregating site at *ad-1* was added to the parentage of crosses 7 and 8 to permit a test of the effect of recombination between the two *cys* loci on the frequency of crossing over in the neighboring *ylo-ad* region. However, the test could not be performed. It would have required a marked demonstration of interference in the control progeny (those without recombination between the *cys* mutants), and this was not observed. The frequency of recombination between *ylo* and *ad* in these crosses was about eight per cent, and it was nearly this frequent (six per cent) among the progeny with recombination between *lys* and *ylo*.]

If we assume that no interference results from the even-number recombination events involving the *cys* mutants in the present study, we can calculate the expected coincidence of a *cys*⁺ event giving a parental marker combination with intergenic recombination in the region required to yield the markers of the critical class. These calculations are shown in Table 3, and the number of critical class recombinants expected to result from these double events are compared with the observed numbers. The observed numbers are somewhat *lower* than the expected. This may mean that even-number recombination in the *cys* region does cause some interference for the genetic region very near it, even though it does not extend as far as the *ylo-ad* region. Or it could mean that the interference properties of recombination between the two *cys* genes are somewhat different from those of recombination within *cys-2*. In any case, the observed recombinants in the critical class are fully accounted for on this basis, and the results are in full agreement with the predictions for *cys* mutants in two separate fixed pairing regions.

TABLE 3

Frequencies of the critical class of cys+ recombinants expected to result from coincident crossing over within the marked region

Cross	Recombination frequencies		cys+ recombinants with parental marker combinations		Critical class (<i>lys cys+ γlo+</i>)	
	<i>lys-cys</i>	<i>cys-γlo</i>	+ + +	<i>lys + γlo</i>	Expected	Observed
1	0.015	0.025	16	23	0.81**	0
2	0.04	0.04	20	15	1.4	0
3	0.069	0.017	3	4	0.27	0
4	0.077	0.072	4	6	0.74	0
5	0.032	0.04	29	32	2.2	1
6	0.127	0.036	14	30	1.9	1
7	0.098	0.084	61	59	10.9	5
8	0.082	0.084	73	46	9.8	3
9*	0.061	0.015	8	26	0.88	0

* For this cross the parental marker classes were *lys cys+ γlo+* and *lys+ cys+ γlo*, and the critical class was *lys+ cys+ γlo+*.

** Method of calculation: expected critical class = $16(0.015) + 23(0.025) = 0.81$

DISCUSSION

The FPR hypothesis was originally designed to account for the distribution of outside marker combinations among selected recombinants between allelic mutants. It was observed that the two parental marker combinations might occur with significantly different frequencies. There is evidence from tetrads (STADLER and TOWE 1963; FOGEL and HURST 1967) that such a recombinant with a parental marker combination usually represents a non-reciprocal (3:1) segregation (which we shall call NR) at the site of the mutant which came into the cross with that marker combination. Thus a cross between a high-NR and a low-NR mutant gave unequal frequencies of the two parental marker combinations among the selected recombinants. Analyses of these marker combinations from pairwise crosses of numerous alleles at the same locus showed a clustering of alleles with similar NR frequency in *Neurospora* (MURRAY 1963; STADLER and TOWE 1963) and in *Aspergillus* (SIDDIQI and PUTRAMENT 1963). This indicated that the position of a mutant site within the gene determined its frequency of NR, and this could be explained if the probability of these recombination events were different for a site near the end of a fixed pairing region from that for a site near the middle of the region. More direct evidence of the relation of NR frequency to the position of a mutant site in the gene came from tetrad analyses of crosses involving ascospore color mutants in *Ascobolus* (LISSOUBA *et al.* 1962; RIZET and ROSSIGNOL 1966). However, a detailed analysis of tetrads from crosses involving seven allelic color mutants in *Ascobolus* was reported by KRUSZEWSKA and GAJEWSKI (1967), and their results conflict with the conclusion from earlier studies that frequency of NR depends on position in the locus. These authors found that one very high-NR mutant and a very low-NR mutant mapped at the

same site, and some of the other mutants failed to suggest any simple relationship between map position and NR frequency.

The present study concerns a somewhat different feature of the FPR model, and its interpretation does not depend directly on the relationship between position in the pairing region and frequency of non-reciprocal segregation. We are dealing here with the frequencies of the various outside marker combinations accompanying recombination between two linked mutants ($m-1$ and $m-2$ in Figure 1). When $m-1$ and $m-2$ represent linked genes several map units apart, the $m+$ recombinants are nearly all $a m+ B$. When $m-1$ and $m-2$ are hetero-alleles, the recombinants include high frequencies of all four possible marker combinations. In this study $m-1$ and $m-2$ represent separate but closely-linked cistrons, and the selected recombinants include high frequencies of three marker combinations, while the remaining (non-parental) combination drops to a negligible frequency. One explanation for such results would be a series of physically discrete regions (like FPR) involved in recombination, with a junction between two such regions occurring between *cys-1* and *cys-2*.

The observation that the *cys-1* and *cys-2* mutant sites are in separate pairing regions is compatible with the proposition that each cistron is a pairing region. However, a recent observation of N. E. MURRAY (unpublished) does not fit this interpretation. She has selected recombinants between two methionine mutants in *Neurospora* which are very closely linked but appear to represent separate cistrons. In this case the frequency of the outside marker combination of the critical class is too high for mutants in separate FPRs. This result seems to rule out an exact correspondence between cistrons and fixed pairing regions.

The FPR hypothesis is designed to account for both reciprocal and non-reciprocal recombination by a single mechanism. However, several studies have suggested that these two kinds of recombination result from different events (MITCHELL 1957; ROMAN and JACOB 1958; STADLER 1959a,b). One such observation (STADLER 1959b) involved the effect of the genetic background on the frequencies of the two kinds of recombination. Comparison of five different crosses with the same segregating markers revealed that the frequency of recombination between the outside markers could fluctuate over a three-fold range while the frequency of recombination between the two *cys-2* alleles remained constant. The present data may be examined in the same way. Inbreeding has been shown to cause increasing intergenic recombination in *Neurospora* (STADLER and TOWE 1962), so it is interesting to compare the frequencies for the series represented by crosses 1, 2, 3, 4 and by crosses 1, 5. Inbreeding results in a rising rate both for *cys+* recombinants (Table 1) and for recombination between *lys* and *ylo* (Table 3). However, the breakdown of the *cys+* frequencies into the different marker combinations (see figures in parenthesis in Table 1) reveals a particularly interesting point. The frequencies of *cys+* recombinants with parental marker combinations remain relatively constant while the majority non-parental class rises several fold. It is notable that the classes of unchanging frequency are those which have been attributed to non-reciprocal recombination, while the expanding class is the *cys+* type found in the three reciprocal recom-

ination asci of Table 2. This suggests that reciprocal recombination increases with inbreeding while NR does not. This is consistent with the observation on *cys*⁺ recombination in crosses between allelic mutants at the *cys*-2 locus: the frequency does not increase with inbreeding, and tetrad analysis shows that the recombinants result exclusively (or nearly so) from NR events (STADLER and TOWE 1963). We should point out, however, that even the putative NR classes fluctuate in crosses 7, 8 and 9.

SUMMARY

Recombinants have been selected in crosses between two cysteine-requiring mutants which are in separate but closely-linked genes, and they have been classified for the unselected flanking markers. Three of the marker combinations occurred with high frequency, but one (non-parental) combination was essentially absent. This result is consistent with the hypothesis that recombination events are restricted to a single Fixed Pairing Region in the marked segment and that the two cysteine mutants are located in separate pairing regions. The analysis of a series of backcrosses indicates that the cysteine-independent recombinants arise by two distinct processes: reciprocal recombination which increases with inbreeding, and nonreciprocal recombination which remains at a constant frequency through the inbreeding series.

LITERATURE CITED

- FOGEL, S., and D. D. HURST, 1967 Meiotic gene conversion in yeast tetrads and the theory of recombination. *Genetics* **57**: 455-481.
- KRUSZEWSKA, A., and W. GAJEWSKI, 1967 Recombination within the Y locus in *Ascobolus immersus*. *Genet. Res.* **9**: 159-177.
- LISSOUBA, P., J. MOUSSEAU, G. RIZET, and J. L. ROSSIGNOL, 1962 Fine structure of genes in the Ascomycete *Ascobolus immersus*. *Advan. Genet.* **11**: 343-380.
- MITCHELL, H. K., 1957 Crossing over and gene conversion in *Neurospora*, pp. 94-113. *The Chemical Basis of Heredity*. Edited by W. D. McELROY and B. GLASS. The Johns Hopkins Press, Baltimore, Maryland.
- MITCHELL, MARY B., T. H. PITTENGER, and H. K. MITCHELL, 1952 Pseudo-wild types in *Neurospora crassa*. *Proc. Natl. Acad. Sci. U.S.* **38**: 569-580.
- MURRAY, NOREEN E., 1961 Polarized recombination with the *me*-2 gene of *Neurospora*. (Abstr.) *Genetics* **46**: 886. — 1963 Polarized recombination and fine structure within the *me*-2 gene of *Neurospora crassa*. *Genetics* **48**: 1163-1184. — 1965 Cysteine mutant strains of *Neurospora*. *Genetics* **52**: 801-808.
- MOUSSEAU, J., 1966 Sur les variations de fréquence de conversion au niveau de divers sites d'un même locus. *C. R. Acad. Sc. Paris* **262**: 1254-1257.
- PEES, E., 1965 Polarized negative interference in the *lys*-51 region of *Aspergillus nidulans*. *Experientia* **21**: 514-516.
- RIZET, G., and J. L. ROSSIGNOL, 1966 Sur la dimension probable des échanges reciproques au sein d'un locus complexe d'*Ascobolus immersus*. *C. R. Acad. Sci. Paris* **262**: 1250-1253.
- ROMAN, H. L., and F. JACOB, 1958 A comparison of spontaneous and ultraviolet-induced allelic recombination with reference to the recombination of outside markers. *Cold Spring Harbor Symp. Quant. Biol.* **23**: 155-160.

- SIDDIQI, O. H., and A. PUTRAMENT, 1963 Polarized negative interference in the *paba-1* region of *Aspergillus nidulans*. Genet. Res. **4**: 12-20.
- STAHL, F., 1961 A chain model for chromosomes. J. Chim. Phys. **58**: 1072-1077.
- STADLER, D. R., 1959a The relationship of gene conversion to crossing over in *Neurospora*. Proc. Natl. Acad. Sci. U.S. **45**: 1625-1629. — 1959b Gene conversion of cysteine mutants in *Neurospora*. Genetics **44**: 647-655.
- STADLER, D. R., and A. M. TOWE, 1962 Genetic factors influencing crossing-over frequency in *Neurospora*. Genetics **47**: 839-846. — 1963 Recombination of allelic cysteine mutants in *Neurospora*. Genetics **48**: 1323-1344.
- STADLER, D. R., A. M. TOWE, and N. E. MURRAY, 1965 Intragenic and intergenic recombination in *Neurospora*. (Abstr.) Genetics **52**: 477.