REVERSAL OF POLARIZED RECOMBINATION OF ALLELES IN NEUROSPORA AS A FUNCTION OF THEIR POSITION[1]

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WHEN recombinant tetrads are selected from crosses between alleles affecting ascospore color in Ascobolus, a recombinant (wild-type) spore is usually shown to arise from a nonreciprocal event. Such a nonreciprocal event has been called conversion and one of the two alleles may be converted to wild type more frequently than the other. If on the basis of inequalities of conversion, a series of sites can be ranked in an unambiguous order, then recombination is polarized (LISSOUBA and RIZET 1960).

When allelic recombinants are selected from the random products of meiosis and classified with respect to markers flanking the selected gene, polarity of allelic recombination is suggested by an inequality of the classes that have parental combinations of flanking markers. If on the basis of such inequalities, a series of alleles can be ranked in an unambiguous order, then allelic recombination is shown to be polarized (MURRAY 1961). Alternatively, this phenomenon may be described in terms of an asymmetric distribution of apparent exchanges coincident with the selected one. Within a region of polarized recombination the asymmetry is always in the same direction (SIDDIQI 1961).

It seems likely that polarized recombination detected either from random spores or from tetrads is a manifestation of the same phenomenon. In a few cases, both random spores and tetrad data have been obtained using the same alleles (e.g. STADLER and TOWE 1963; FOGEL and HURST 1967) and the results indicate that the parental combination of flanking markers identifies the allele that has been converted.

Explanations of polarized allelic recombination have required either that recombinational events are discontinuously distributed (STAHL 1961; MURRAY 1961; HOLLIDAY 1964; HASTINGS and WHITEHOUSE 1964) or that a component of the recombination process is polarized either within small subunits (polarons) of the chromosomes (RIZET, LISSOUBA and MOUSSEAU 1960) or with respect to the gross organization of the chromosome (SIDDIQI 1961).

The early models demanding fixed regions of pairing (STAHL 1961; MURRAY 1961) and the hybrid DNA models invoking fixed points of primary nucleotide breakage (HOLLIDAY 1964; HASTINGS and WHITEHOUSE 1964) both predict a

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reversal of polarity depending on propinquity of sites to one or the other end of the paired region. The Fixed Pairing Region model predicts that among prototrophic recombinants selected as random spores, the more frequent class having flanking markers of parental combination represents conversion of the mutant site further from an end of the pairing region; the hybrid-DNA model, on the contrary, predicts that the more frequent class represents conversion of the site nearer an end of the pairing region. In tetrads, a similar relation is predicted for frequencies of conversion, which are expected to be highest in the middle of a Fixed Pairing Region model and vice versa for a hybrid-DNA model.

Early observations from both tetrads (e.g. gene 46 of Ascobolus—LISSOUBA and RIZET 1960) and random spores (e.g. the *me-2* gene of Neurospora—MURRAY 1963) indicated that polarity was uniformly in one direction. This could be interpreted on either the Fixed Pairing Region model or a hybrid-DNA model as indicating that all the sites were located towards one end of the recombination region, or alternatively, that polarity was dependent on some process with unidirectional polarity.

These implications prompted the screening of a further sample of *me-2* (linkage group IV) alleles in a search for sites located either proximally or distally to those mapped previously. The mapping of two proximal mutants has permitted the demonstration of a reversal of polarity in the proximal region of the *me-2* gene.

Inseparable from the determination of the direction of polarity with respect to the ends of the pairing region is the definition of the ends of such a region. If pairing regions were discrete, crosses between closely linked mutants in adjacent pairing regions should be characterized by the absence of recombinants having flanking markers of the minority *non*parental combination, as was found for crosses between the closely linked genes *cys-1* and *cys-2* in linkage group VI of Neurospora (MURRAY 1965; STADLER, TOWE and MURRAY 1965; STADLER and TOWE 1968). An additional test was made using a different pair of closely linked genes, *me-7* and *me-9* in linkage group VII. *me-7* has provided another example of strong polarity with some evidence of polarity reversal. It seemed particularly desirable to examine this system since the presence of markers in an adjacent gene offered the possibility of identifying the end of a pairing region.

An analysis of recombination in the *me-6* region of linkage group I, initiated because the orientation of this region may be inverted by means of a chromosome rearrangement (MURRAY 1968), has subsequently provided a third example of polarity reversal dependent on the positions of sites within a gene. The three examples of polarity reversal, *me-2*, *me-7* and *me-6*, representing regions of otherwise different recombination characteristics, are presented and discussed in this paper.

MATERIALS AND METHODS

Media, methods of crossing, ascospore isolation and scoring were as described by PERKINS (1959); ascospores were plated according to the procedure outlined by MURRAY (1963). When large numbers of ascospores were required, the interallelic crosses were made in Erlenmeyer flasks of liquid medium containing pleated filter papers.

methionine-2: The *me-2* strains and the flanking markers, *tryp-4* (Y2198) and *pan-1* (5531), have been described previously (MURRAY 1960; 1963). The density of plating was increased to between 10,000 and 40,000 viable spores per plate to compensate for the low recombination frequencies.

methionine-7: The *me-7* strains were isolated following ultraviolet irradiation of the wild-type strain Emerson *a* (alleles with the prefix NM were isolated by the author, that with the prefix Hy by JULIAN HARTLEY). *me-7* is located close to the centromere of linkage group VII approximately 2 to 3 units right of *thi-3* (thiamine-3) and 1 to 2 units left of *wc* (white collar) (PERKINS, GLASSEY and BLOOM 1962; MURRAY unpublished). *thi-3* (18558) and *wc* (P829) were used as flanking markers. The selective media were supplemented with thiamine (10 μg/ml) and the ascospores were plated at a density of 10,000 to 40,000 viable spores per plate.

methionine-6: Three strains were used. *me-6* (35809) and *mac* (65108) have been used previously (see MURRAY 1968). *me* (S2706) was selected from among a series of methionine mutants kindly provided by E. L. TATUM. The available evidence, presented here for the first time, suggests that *me-6* (35809), *mac* (65108) and *me* (S2706) are probably allelic.

Analyses were performed as described by MURRAY (1968) using *thi-1* (56501) and *ad-9* (Y154M37) as flanking markers and with the albino markers *al-2* (albino-2, 15300) and *aur* (aurescent, 34508) entering in repulsion; true wild types are expected to be albino in phenotype whereas pseudo-wild types are orange. All isolates of orange (wild-type) color were backcrossed to test whether they were true or pseudo-wild types.

RESULTS

me-2: The doubly marked *me-2* strains—*tryp-4* (Y2198) *me-2* (K44) *pan-1* (5531) and *tryp-4 me-2* (H98) *pan-1*—were constructed and ten unmarked *me-2* strains that had not been used in previous analyses were crossed to these tester strains. K44 was the extreme proximal marker and H98 was close to the distal end of the *me-2* gene. Of the ten strains, one (K18) was shown to map proximally to K44 and a second (P152) distally not only to H98 but to all the mutants mapped previously.

In all the crosses reported by MURRAY (1963) inequalities between prototrophs with the parental combinations of flanking markers indicated that the more distal allele (i.e., the one closer to *pan-1*) was more frequently converted to wild type. The data in Table 1 show that K18 and K43 provide exceptions to this rule. A reversal in the direction of polarity is found when K18 is crossed to either K44 or P140, or when K43 is crossed to K44. The order of these mutants is shown at the head of Table 1; K18 is placed proximal to K43 on the basis of the higher prototroph frequencies in crosses to either K44 or P140. K43 was known to be located in the proximal region of *me-2* (MURRAY 1963), but only a few ascospores were analysed previously.

When P152, placed at the distal end of the locus is used in crosses, there is no change in the direction of polarity, but in marked contrast to crosses between markers at the proximal end of the gene, ordering of mutants is difficult, since there is very little inequality between the two classes of prototrophs that have nonparental combinations of flanking markers.

Ascospores from crosses which were homozygous with respect to the *me-2* alleles were screened for reversion to methionine prototrophy. Data have been published (MURRAY 1963) for all the *me-2* alleles used except K18 and P152. K18 gave no prototrophs among 2.7×10^6 viable ascospores and P152 none in 3.5×10^6

TABLE 1

Analysis of methionine prototrophs from interallelic crosses involving the most proximal and distal me-2 *alleles*

Map order of mutants used: tryp-4 K18 K43 K44 P140 H98 P24 P152 pan-1

Genotypes of parents							Methionine prototrophs		Classification of methionine prototrophs			
tryp	me^P	*pan*	×	*tryp*	me^D	*pan*	Number	Frequency per 10^8	P^P	P^D	R^1	R^2
+	K18	+	×	—	K44	—	96	2.9	25(26%)	19(20%)	46(48%)	6(6%)
—	K18	+	×	+	K44	—	114	4.2	34(30%)	16(14%)	55(48%)	9(8%)
+	K18	—	×	—	K44	+	105	8.4	24(23%)	8(8%)	54(51%)	19(18%)
—	K18	+	×	+	P140	—	111	9.5	29(26%)	23(21%)	45(41%)	14(13%)
+	K18	—	×	—	P140	+	123	6.4	30(24%)	18(15%)	56(46%)	19(15%)
+	K18	+	×	—	H98	—	229	38.9	46(20%)	91(40%)	74(32%)	18(8%)
+	K43	+	×	—	K44	—	68	1.7	15(22%)	11(16%)	39(57%)	3(4%)
—	K43	+	×	+	K44	—	68	2.1	21(31%)	10(15%)	36(44%)	7(10%)
+	K43	—	×	—	K44	+	50	1.5	18(36%)	7(14%)	19(38%)	6(12%)
—	K43	+	×	+	P140	—	81	3.1	13(16%)	20(25%)	40(49%)	8(10%)
+	K43	—	×	—	P140	+	110	2.3	29(26%)	29(26%)	42(38%)	10(9%)
—	K44	+	×	+	P140	—	34	1.1	4(12%)	14(41%)	11(32%)	5(15%)
+	K44	—	×	—	P140	+	84*	1.4	8(10%)	36(43%)	27(32%)	13(16%)
—	K44	—	×	+	P152	+	148	43.7	16(11%)	83(56%)	32(22%)	17(12%)
—	H98	—	×	+	P152	+	156	26.3	19(12%)	75(48%)	35(22%)	27(17%)
—	P24	+	×	+	P152	—	171	2.9	30(18%)	73(43%)	40(23%)	28(16%)
+	P24	—	×	—	P152	+	87	2.7	14(16%)	44(51%)	18(21%)	11(13%)

* Data published in MURRAY (1963).

P^P, parental combination of flanking markers entering with proximal (left-hand) *me-2* allele.

P^D, parental combination of flanking markers entering with distal (right-hand) *me-2* allele.

R^1, majority nonparental combination of flanking markers indicating order shown at head of table.

R^2, minority nonparental combination of flanking markers.

viable ascospores. The absence of prototrophs indicated that prototroph formation in crosses between alleles was not usually the result of reversion.

me-7: The data from crosses between *me-7* alleles are presented in Table 2. Many crosses between *me-7* alleles show pronounced asymmetries between the two classes of methionine prototrophs with parental combinations of flanking markers. In general, the asymmetries are such as to identify the right-hand *me-7* site (the one closer to *wc*) as the one more frequently converted to prototrophy. However, the map can be divided into two regions around the point represented by the alleles NM21t and NM254. Crosses within the right-hand region, and most particularly, crosses of either NM21t or NM254 with alleles to their right, show strong polarity with the right-hand allele being preferentially converted. Crosses of either NM21t or NM254 with alleles to their left suggest either a weak polarity in the reverse direction or an equality of conversion. The reversal is more readily appreciated by comparison of crosses between a right-hand allele (NM73) and a left-hand allele (e.g. NM250 or NM251) with those of the same right-hand allele (NM73) and the more centrally located alleles NM21t and NM254. The asymmetries are more extreme in the latter case, i.e., conversion of a left-hand

TABLE 2

Analysis of methionine prototrophs from me-7 *interallelic crosses*

Map order of mutants used: thi (251 56 250)‡ 254 21t 331 308 73 271 *wc*

Genotypes of parents						Methionine prototrophs		Classification of methionine prototrophs			
thi	me^L	*wc* ×	*thi*	me^R	*wc*	Number	Frequency per 10^5	P^L	P^R	R^1	R^2
—	251	+ ×	+	73	—	162	5.5	37(23%)	91(56%)	26(16%)	8(5%)
+	251	+ ×	—	73	—	98	11.8	25(26%)	49(50%)	18(18%)	6(6%)
—	250	+ ×	+	73	—	163	5.2	40(25%)	74(45%)	43(26%)	6(9%)
+	250	— ×	—	73	+	363	5.6	75(21%)	208(57%)	46(13%)	34(9%)
—	56	+ ×	+	73	—	104	12.0	18(17%)	58(56%)	20(19%)	8(8%)
+	56	— ×	—	73	+	113	4.0	34(30%)	63(56%)	13(12%)	3(3%)
—	21t	+ ×	+	73	—	106	1.9	8(8%)	63(59%)	28(26%)	7(7%)
+	21t	— ×	—	73	+	102	2.3	10(10%)	61(60%)	23(23%)	8(8%)
+	254	— ×	—	73	+	161	2.7	14(12%)	123(76%)	12(8%)	7(4%)
—	21t	— ×	+	308*	+	90	1.9	4(4%)	58(64%)	24(27%)	5(6%)
+	254	— ×	—	21t	+	0 in 3.2×10^6					
+	308*	— ×	—	73	+	0 in 2.4×10^6					
+	331	— ×	—	73	+†	76	1.0	13(17%)	48(63%)	11(15%)	4(5%)
—	331	+ ×	+	73	—†	80	1.6	11(14%)	57(71%)	11(14%)	1(1%)
—	73	+ ×	+	271	—	149	6.1	30(20%)	61(41%)	46(31%)	12(8%)
—	21t	— ×	+	271	+	53	. .	6(11%)	32(61%)	12(23%)	3(6%)
—	21t	+ ×	+	271	—	66	3.9	6(9%)	51(77%)	8(12%)	1(2%)
—	250	+ ×	+	21t	—	47	1.2	25(53%)	15(32%)	6(13%)	1(2%)
+	250	— ×	—	21t	+	56	0.5	29(52%)	18(32%)	7(13%)	2(4%)
—	56	+ ×	+	21t	—	97	0.5	43(44%)	39(40%)	10(10%)	5(5%)
+	251	— ×	—	21t	+	47	0.5	21(45%)	18(38%)	5(10%)	3(6%)
—	250	+ ×	+	254	—	244	1.4	109(45%)	101(41%)	25(10%)	9(4%)
—	251	+ ×	+	254	—	103	1.1	41(40%)	41(40%)	14(14%)	7(7%)

* Isolation number with prefix Hy; all other isolation numbers should be prefixed NM.

† Crosses heterozygous for temperature-sensitive *me-9* allele, but plated under permissive conditions.

me^L: Left-hand *me-7* allele.

me^R: Right-hand *me-7* allele.

P^L: Parental combination of flanking markers entering with left-hand *me-7* allele.

P^R: Parental combination of flanking markers entering with right-hand *me-7* allele.

R^1: Majority nonparental combination of flanking markers consistent with order at head of table.

R^2: Minority nonparental combination of flanking markers.

‡ The order of these three alleles with respect to each other is unknown.

allele makes more of a contribution than does the conversion of a centrally located allele. The alleles NM21t and NM254 give similar recombination patterns although these alleles are not identical, only the former being temperature-sensitive.

Characteristic of *me-7* interallelic crosses is the unusually high contribution of prototrophs having parental combinations of flanking markers. In any cross, 70 to 80% of the methionine prototrophs isolated are parental with regard to flanking markers.

Ascospores from crosses homozygous with respect to the *me-7* allele were screened for reversion to methionine prototrophy. The absence of revertants (see

TABLE 3

Control crosses with me-7 *alleles homozygous*

Isolation numbers of *me-7* alleles	Number of viable spores plated × 10^{-5}	Number of methionine prototrophs
NM21t	69	0
NM56	11	0
NM73	46	0
NM250	62	0
NM251	70	0
NM254	22	0
NM271	7	0
NM331	87	0

Table 3) indicates that prototroph formation in crosses between alleles was not usually the result of reversion.

me-6 region: Three methionine mutants are known to map in the *me-6* region. The data (Table 4) clearly place the mutants in the order *thi–mac–me–me-6–ad*, where *thi* is the proximal flanking marker. The absence of complementation indicates allelism of *mac* and *me*, but both of these mutants complement *me-6*. *mac*, but not *me-6*, was shown to grow better when adenine was added to the methionine (DUBES 1953). The following information (GILLIAN ROBERTS, personal communication) indicates that physiologically *me* resembles *me-6* rather than

TABLE 4

Analysis of methionine prototrophs from crosses between mutants of the me-6 *region*

Genotypes of parents						Methionine prototrophs						
thi	me^P	*ad*	×	*thi*	me^D	*ad*	Number	Frequency per 10^5	Classification of methionine prototrophs P^P	P^D	R^1	R^2
—	*mac*	—	×	+	*me-6*	+*	147	34.3	33	15	96	3
+	*mac*	+	×	—	*me-6*	—*	282	41.2	78	30	173	1
—	*mac*	+	×	+	*me-6*	—*	220	54.0	81	13	125	1
+	*mac*	—	×	—	*me-6*	+*	81	42.9	21	3	57	1
						Total	730	...	213(29%)	60(8%)	451(62%)	6(1%)
—	*mac*	—	×	+	*me*	+	144	16.2	43	18	82	1
—	*mac*	+	×	+	*me*	—	129	53.9	43	4	80	2
						Total	273	...	86(32%)	22(8%)	163(59%)	3(1%)
+	*me*	+	×	—	*me-6*	—	97	17.3	15	45	33	4
+	*me*	+	×	—	*me-6*	—	58	20.9	8	20	26	4
+	*me*	+	×	—	*me-6*	—	143	11.2	27	50	63	3
+	*me*	—	×	—	*me-6*	+	110	19.0	25	44	32	9
						Total	408	...	75(18%)	159(39%)	154(38%)	20(5%)

* Data published in MURRAY (1968).

P^P: Parental combination of flanking markers entering with proximal methionine mutant.

P^D: Parental combination of flanking markers entering with distal methionine mutant.

R^1: Majority nonparental combination of flanking markers indicating the order *thi mac me me-6 ad*.

R^2: Minority nonparental combination of flanking markers.

mac: neither *me-6* nor *me* is stimulated by the addition of adenine under normal conditions. However, in a CO_2-enriched atmosphere (air 70% v/v + CO_2 30% v/v) *me-6* fails to grow on methionine, *me* grows poorly, but *mac* is unaffected. Under these conditions *me-6* grows on methionine plus adenine and the growth of *me* on methionine was enhanced by adenine. *me* appears to differ from *me-6* only in that it is a more leaky mutant.

Analyses of methionine prototrophs from crosses between pairs of these methionine mutants (Table 4) indicate a high frequency of apparent coincident exchanges. This is particularly true for the cross of the complementing mutants *me-6* and *me*, where the presence of the minority recombinant class indicates that these sites fall within the same recombination region.

The parental flanking-marker patterns (Table 4) indicate that in crosses of *mac* to either *me-6* or *me* the proximal site (*mac*) is converted more frequently. In contrast, a cross of *me* to *me-6* shows a marked reversal with the distal site (*me-6*) converted more frequently.

Since crosses homozygous for *me-6* or *mac* were not fertile, conidia were screened to obtain estimates of the reversion rates (MURRAY 1968). These rates were sufficiently low to suggest that the prototrophs isolated from heterozygous crosses resulted from recombination rather than reversion.

DISCUSSION

The finding that the direction of the polarity of allelic recombination changes as a function of the position of the sites within a locus, together with the demonstration that the direction of polarity is independent of orientation with respect to centromere (MURRAY 1968), supports the concept that polarity results from a discontinuous distribution of recombination regions.

The three systems described in this paper resemble the *lys-51* gene of Aspergillus (PEES 1965; 1967), the hi_1 gene of yeast (FOGEL and HURST 1967) and locus 19 of Ascobolus (MOUSSEAU 1966) in that the sites located close to the *ends* of the regions (or genes) are converted preferentially. These findings are difficult to accommodate on the early Fixed Pairing Region models but support a hybrid-DNA model in which the Fixed Pairing Region is envisaged as the restriction of the primary nucleotide breakage to fixed points at the ends of genes. From the premise that the proximity of a site to the point of primary nucleotide breakage enhances the chance of its inclusion in hybrid DNA, it follows that conversion will be more frequent towards the end of a pairing region (or towards both ends if hybrid DNA formation is initiated from both ends).

In contrast, for locus 75 of Ascobolus, RIZET and ROSSIGNOL (1966) reported a reversal of polarity with preferential conversion of the centrally located sites. This apparent contradiction was resolved by ROSSIGNOL (1967) when he subdivided the alleles into classes according to their conversion patterns in one-point tetrad analyses. For one class of alleles nonreciprocal segregations were equally frequent in either direction, i.e., conversion of mutant to wild type or of wild type to mutant. In contrast the alleles within a second class were characterized by

tetrads showing preferential conversion from wild type to mutant. Allelic crosses restricted to members of the same class showed a constant direction of polarity of conversion.

It is appropriate to emphasize that analyses of conversion by selective procedures produce a biased and incomplete picture. The conversion frequencies will be biased if conversion is not equally frequent in each direction (a good example of this is discussed in the previous paragraph). Recent data from yeast, where the mutations used were single base substitutions, showed conversion to be equally frequent in either direction (S. FOGEL, personal communication). However, selective analyses using transition mutations may give an incomplete picture for the following reason. Conversion results when the genetic information carried by a *segment* of DNA replaces the information carried by the corresponding segment in the homologous non-sister chromatid. When two sites are so closely linked that they fall within this *segment* of DNA, selective analyses will frequently fail to detect conversion to wild type because of the concomitant conversion of wild type to mutant. This concept is supported by data from unselected tetrads (e.g. CASE and GILES 1964) and recently has been elegantly demonstrated in yeast (FOGEL and MORTIMER 1968).

The polaron model of WHITEHOUSE and HASTINGS (1965) equated the recombination region with the gene. Primary nucleotide breakage was restricted to the ends of genes and reversal in the direction of polarity resulted because hybrid-DNA formation could proceed from either end of the gene. On this model the gene was a discrete recombination region and crosses between closely linked non-allelic genes would be characterized by the absence of the minority class with nonparental flanking markers. Some support for this notion came from crosses between the closely linked *cys-1* and *cys-2* genes of Neurospora (STADLER, TOWE and MURRAY 1965; STADLER and TOWE 1968; MURRAY 1965) where crosses of *cys-1* by *cys-2* differed dramatically from all *cys-2* by *cys-2* crosses only in the absence of one of the classes having marker genes recombined, both parentally marked classes of cysteine prototrophs being present and numerous. In contrast, crosses of *me-7* by *me-9* (MURRAY, in preparation) gave an appreciable frequency (5%) of prototrophs in that minority class having marker genes recombined. It was concluded that the complex recombinational event can include sites within more than one gene. Similar conclusions were derived by PUTRAMENT (personal communication) and by MURRAY (unpublished data) when selection was made for recombination in one gene while, in addition to flanking markers, a nonselective marker is present in the neighboring gene. These findings were subsequently accommodated by the suggestion (WHITEHOUSE 1966) that, although initiation of hybrid DNA is restricted to a point at one end of a gene, the length of hybrid DNA may *exceed* that of the gene. On this model, the absence of polarity at one end of a gene, e.g. *cys-2* of Neurospora (STADLER and TOWE 1963) or *paba-1* of Aspergillus (SIDDIQI and PUTRAMENT 1963) or the reversal of polarity at the end of the gene opposite to the point of hybrid DNA initiation, is due to hybrid DNA initiated from the neighboring gene. These theoretical implications lend added

interest to the analysis of recombination between sites located close to the ends of genes.

The above model (WHITEHOUSE 1966) postulates that allelic recombinants having parental arrangements of flanking markers result from a double crossover. The first crossover requires hybrid-DNA formation to one side of the point of initial DNA breakage and the second (the "reverse crossover") requires hybrid-DNA formation to the opposite side of the initial breakage point. Polarity reversal at the proximal end of *me-2* would be the result of "reverse crossovers" initiated at the distal end of the proximally adjacent gene. Polarity reversal is therefore predicted to be associated with an excess of parental combinations of flanking markers. However, the present data for *me-2* are not in agreement with this prediction.

Early Fixed Pairing Region models (STAHL 1961; MURRAY 1961) and the hybrid-DNA model of HOLLIDAY (1964) predict an equality of parental and nonparental arrangements of flanking markers. The data for *me-2* (MURRAY 1963 and this paper) are at variance with this prediction, as has been discussed by CATCHESIDE (1966). More difficult to explain are the *me-7* data (Table 2) which show that prototrophs with parental arrangements of flanking markers comprise the majority (at least 70%) of the total recombinants for any cross analysed.

In the *me-6* region, crosses involving *mac* may yield up to 70% of the prototrophs with flanking markers recombined. One possibility, supported by the low frequency (1%) of the minority nonparental arrangement, is that there is a discontinuity located between the allelic markers *mac* and *me*. HOLLIDAY (1967) has pointed out that there are some precedents for discontinuities falling within a gene, e.g., in gene 46 of Ascobolus (ROSSIGNOL 1964). Results of the type observed for crosses of *mac* by *me* or *mac* by *me-6* would be unremarkable for interallelic crosses in Aspergillus.

In conclusion, the present examples of reversal in the direction of polarity of allelic recombination support the concept of discontinuous distribution of recombination regions, in particular according to a hybrid-DNA model. The marked excess of parental arrangements of flanking markers (e.g. for *me-7*) is not readily explained on any model. The finding that the direction of polarity changes within a given region and that parental arrangements of flanking markers may be in great excess, emphasizes the importance, when constructing intragenic maps, of using the asymmetries between those two classes with flanking markers recombined.

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SUMMARY

Data for the genes *me-2*, *me-7* and *me-6* demonstrate that the direction of the polarity of allelic recombination changes as a function of the position of sites

within a gene. For each of these regions the polarity is such that the sites of preferential conversion are located towards the end of the gene. Both recombinant combinations of the flanking markers are characteristically found among methionine prototrophs from allelic crosses of *me-2* and *me-7*, but not among those from some *me-6* crosses. This supports the concept that the *me-2* (or *me-7*) alleles comprise one pairing region but allows that *me-6* alleles may be located in separate pairing regions.

LITERATURE CITED

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