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Studies on Genetic Organization in Higher Organisms, II. Complementation and Fine Structure of the Maroon-like Locus of *Drosophila melanogaster**

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Abstract. Mutants of the maroon-like complex, representative of the five known complementation classes, were subjected to fine structure mapping experiments utilizing a nutritional selective procedure which permits the survival of rare *ma-l*$^+$ progeny from large-scale crosses. The analysis provides an internally consistent, unique map, colinear with the complementation map. Noncomplementers exhibit a polarized mapping distribution. In addition to *ma-l*$^+$ recombinants, the selective medium permitted the survival of *ma-l*$^+$ exceptionals not associated with recombination for adjacent markers. Analysis of the exceptionals favors their origin as convertants.

Current views concerning the nature of elementary genetic units in multicellular organisms focus upon notions of genetic organization which have emerged largely from investigations with microbial systems. The recombinational and functional features of a simple cistron in *Drosophila* are clearly identical to those of microbial systems.[1] One extensively studied, but poorly understood, class of genetic units in higher organisms is collectively referred to as "complex genes." Although these units probably do not represent a single class of genetic elements, they do exhibit features which distinguish them from simple cistrons, and which have led to interpretations involving operons,[2] allele complementation,[3] and gene duplication.[4]

The maroon-like mutants (*ma-l*: 1–64.8)[5] of *Drosophila melanogaster* were chosen as a model system for the investigation of a complex gene. In addition to a brownish eye color resulting from a reduction in red (drosopterin) pigments, *ma-l* mutants exhibit loss of activity of xanthine dehydrogenase, pyridoxal oxidase, and aldehyde oxidase, three enzyme activities which appear to be associated with distinct molecular species. Although several lines of evidence relate the eye color defect solely to xanthine dehydrogenase, the biochemistry underlying this pleiotropy remains obscure. Investigation of a large group of *ma-l* mutants, induced with various mutagens, led to their classification into two categories: (*1*) A group of lethal *ma-l* mutants were shown to be deficiencies which extended into the *ma-l* region and (*2*) a set of 19 fully viable *ma-l* mutations, which fall into five complementation groups with respect to eye color and xanthine dehydrogenase activity in mutant heterozygotes (Fig. 1).[6] Ignoring the lethal *ma-l* mutants, which behave as Group I noncomplementers,

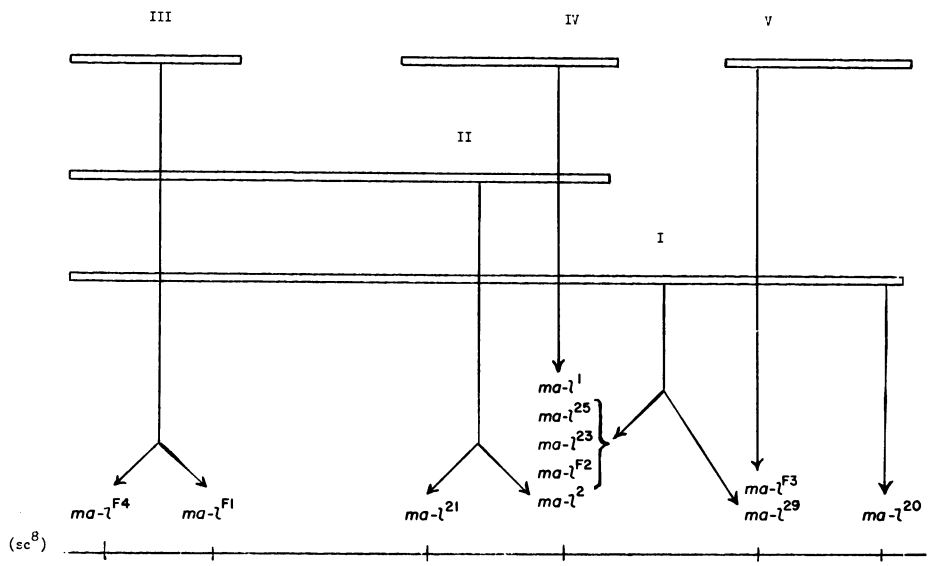

FIG. 1.—Colinearity of genetic and complementation maps.

the complementation pattern seen in heterozygotes may be interpreted on two general models of genetic organization. One model would consider maroon-like as a single cistron whose biologically active product is a dimer or higher multiple aggregate of a single polypeptide. Complementation between different mutants then reflects the production of hybrid aggregates which possess some biological activity. On the second model, Group III, IV, and V mutants (Fig. 1) represent mutations in each of three adjacent cistrons. The viable Group I and II mutants would include site mutants as well as deficiencies, the site mutants reflecting the direction of translation of a polycistronic message. Group II site mutants would be polar mutants in the second cistron, while the Group I site mutants might include lesions at sites concerned with regulation or initiation of transcription as well as polar translational mutants in the first cistron. Clearly, fine structure mapping of a representative sample of the various classes of *ma-l* mutants is essential to an understanding of the organization of this region.

Materials and Methods. A set of fully viable *ma-l* mutations induced with various mutagens on the X chromosome, or a Y-borne duplication of the *ma-l* region comprise the basic raw material of this study. These mutants, as well as *ma-l* deficiencies and other genetic markers in the *ma-l* region, used in this investigation, are described elsewhere.[6]

Selective system: Genetic fine structure analysis: Females heterozygous for a pair of *ma-l* mutants are mated to tester males and their progeny reared on a purine-enriched medium which permits survival only of rare *ma-l*$^+$ offspring.[7] Matings of 15 pairs of parents for each half-pint milk bottle are made on standard cornmeal-molasses medium maintained at 23–26°C, and the parents are transferred to fresh cultures at 2-day intervals to permit a total of 10 days of egg-laying. Immediately after transfer, 1 ml of 0.2% aqueous purine (Sigma Chemical Co.) is added to each developing culture which contains approximately 50 ml of standard medium. Preliminary trial experiments revealed that such purine supplementation effectively kills *ma-l* mutant zygotes while

more than 90% of *ma-l*$^+$ zygotes survive. Egg hatchability of both classes is normal on purine-enriched medium. Estimation of the total number of zygotes sampled in each cross is obtained by omitting purine from $^1/_{60}$ of the cultures in each experiment, and counting total progeny in those bottles. Map distances are estimated as 2 × the frequency of *ma-l*$^+$ recombinants × 100.

In order to increase recombination in the *ma-l* region, the entire study was made with *sc*^{8} and *sc*^{81L} *sc*^{8R} inversions which move *ma-l* from a position proximal to the centromere to the distal end of the X chromosome.[5] Consider a cross involving a pair of separable *ma-l* mutants, *ma-l*^{x} and *ma-l*^{y}. Heterozygous females of the genotype *y sc*^{S1} *ma-l*^{x} *l-t2-4a f sc*^{8}/*y*$^+$ *sc*^{8} *ma-l*^{y} *l-t2-4a*$^+$ *f*$^+$ *sc*^{8} are crossed to tester males of the genotype *In(1)dl-49,v,In(1)B*^{M1}*,Df(1)ma-l*^{6}/*y*$^+$*Yma-l*^{106}. On these chromosomes, yellow (*y:* 1–0.0)[5] and lethal-t2-4a (*l-t2-4a:* 1–64.3),[8] serve as nonselective outside markers 3.7 and 0.5 units from *ma-l*, respectively. The relative position of any given pair of *ma-l* mutants is obtained from the pattern of recombination of the outside markers associated with the *ma-l*$^+$ survivors. Thus, if *ma-l*^{x} is located to the left of *ma-l*^{y}, then the *ma-l*$^+$ recombinant chromosomes should be *y*$^+$ *ma-l l*$^+$*-t2-4a*. If *ma-l*^{y} were located to the left of *ma-l*^{x}, then the wild-type recombinants should be *y ma-l*$^+$ *l-t2-4a*$^+$. Surviving *ma-l*$^+$ daughters will carry the *In(1)dl-49,v,In(1)B*^{M1}*Df(1)ma-l*^{6} chromosome which is deficient for *ma-l*, yet covers *l-t2-4a*, and serves as a balancer for the scute inversion as well as the entire maroon-like region.[5, 6] The *ma-l*$^+$ sons will carry *y*$^+$*Yma-l*^{106}. This Y chromosome carries a duplication of the *ma-l* region which permits survival of the male parent carrying *Df(1)ma-l*^{6}. It covers *l-t2-4a* and has a noncomplementing *ma-l* mutation (*ma-l*^{106}).[6] Thus, all eggs carrying a *ma-l* mutant X chromosome will produce a mutant male or female zygote upon fertilization by gametes from the tester male. All such progeny will die on the purine-enriched selective medium. However, any egg bearing a *ma-l*$^+$ X chromosome, regardless of other markers present, will produce a phenotypically *ma-l*$^+$ zygote which survives on purine-enriched medium. Fine structure crosses involving females heterozygous for certain complementing *ma-l* mutants produce an additional class of progeny which survive as rare single females, which upon testing, were shown to be nondisjunctional progeny carrying the complementing *ma-l* mutant alleles on identifiable maternal chromosomes. These offspring survive, presumably due to the complementation levels of enzyme activity.[6] However, since they are rare and easily identified upon test, no effort was made to screen out this "experimental noise." They are not included in the analysis.

Test crosses of *ma-l*$^+$ progeny: The X chromosomes from surviving *ma-l*$^+$ progeny are established in balanced stocks, and tested to assay the other genetic markers in the experiment as follows: (1) If the *ma-l*$^+$ individual is a forked (*f*) male, it is crossed by *y sc*^{S1} *ma-l*^{F3} *l-t2-4a f sc*^{8}/*yIn(1)49, sn*^{x2} *In(1)B*^{M1}, *Df(1)ma-l*^{6} females. The absence of forked females identifies *l-t2-4a*, while the *y* marker is determined from the surviving progeny. (2) If the *ma-l*$^+$ individual is a *f*$^+$ male, it is crossed to two kinds of females, (*a*) *y v f ma-l* attached-X females with a standard Y chromosome produce no male progeny if *l-t2-4a* is present, and (*b*) *y sc*^{S1} *ma-l*^{F3} *sc*^{8}/*y sc*^{S1} *ma-l*^{F3} *sc*^{8} females serve as a test cross for the presence of the *y* marker. (3) If the *ma-l*$^+$ individual is a female, it is crossed by *y sc*^{S1} *ma-l*^{F3} *sc*^{8} males with a standard Y chromosome. The absence of male progeny identifies *l-t2-4a* while the *y* marker may be diagnosed from the female progeny.

Enzyme preparation and assays: These are described elsewhere.[6]

Results. Fine structure crosses on purine medium: The results of 21 fine structure crosses assaying approximately 6 × 10^7 zygotes are summarized in Table 1. Of 63 *ma-l*$^+$ progeny recovered from these crosses, a total of 61 reproduced to permit their classification into two categories: (1) Those associated with recombination for the adjacent markers *y* and *l-t2-4a* (R^1 and R^2), and (2) *ma-l*$^+$ exceptionals not associated with marker recombination (P^1 and P^2). Since the recombination distance between *y* and *l-t2-4a* in the scute-8 inversion

TABLE 1. *Surviving progeny in fine structure crosses.*

Series	Experimental cross	*ma-l*⁺ Chromosomes R¹	R²	P¹	P²	Total progeny × 10^{-3}	Map distance × 10^{4}
	$ma\text{-}l^{F3}/ma\text{-}l^{2}$	0	5	1	1	1848	5.4
	$ma\text{-}l^{F3}/ma\text{-}l^{21}$	0	3	0	1	765	7.8
	$ma\text{-}l^{2}/ma\text{-}l^{21}$	0	1	0	1	4760	0.4
A	$ma\text{-}l^{F4}/ma\text{-}l^{2}$	2	0	0	0	511	7.8
	$ma\text{-}l^{F4}/ma\text{-}l^{21}$	1	0	0	0	767	2.6
	$ma\text{-}l^{F1}/ma\text{-}l^{21}$	3	0	3	2	8590	0.7
	$ma\text{-}l^{F1}/ma\text{-}l^{2}$	0	0	1	0	1500	—
	$ma\text{-}l^{F4}/ma\text{-}l^{F1}$	2	0	0	1	3000	1.3
	$ma\text{-}l^{1}/ma\text{-}l^{F3}$	2	0	1	5	2500	1.6
B	$ma\text{-}l^{1}/ma\text{-}l^{2}$	0	0	0	1	3389	—
	$ma\text{-}l^{F4}/ma\text{-}l^{1}$	2	0	4	1	1922	2.1
	$ma\text{-}l^{F1}/ma\text{-}l^{1}$	1	0	0	0	2071	1.0
	$ma\text{-}l^{2}/ma\text{-}l^{20}$	1	0	0	0	507	3.9
	$ma\text{-}l^{2}/ma\text{-}l^{29}$	1	0	0	2	3078	0.7
C	$ma\text{-}l^{2}/ma\text{-}l^{25}$	0	0	0	0	1675	—
	$ma\text{-}l^{2}/ma\text{-}l^{23}$	0	0	1	3	1701	—
	$ma\text{-}l^{2}/ma\text{-}l^{F2}$	0	0	0	0	7970	—
	$ma\text{-}l^{1}/ma\text{-}l^{F2}$	0	0	0	0	4460	—
	$ma\text{-}l^{F3}/ma\text{-}l^{20}$	1	0	3	3	4025	0.5
D	$ma\text{-}l^{F3}/ma\text{-}l^{29}$	0	0	0	0	4068	—
	$ma\text{-}l^{F3}/ma\text{-}l^{23}$	0	0	1	0	500	—

R^1, y^+ *ma-l*⁺ *l-t2-4a* recombinant; R^2, *y ma-l*⁺ *l-t2-4a*⁺ recombinant.
P^1, *y ma-l*⁺ *l-t2-4a* parental; P^2, y^+ *ma-l*⁺ *l-t2-4a*⁺ parental.

is 4.2 units, the fact that 25/61 (41%) of the *ma-l*⁺ chromosomes exhibited such marker exchange points to a recombinational interpretation of their origin.

Fine structure mapping with the *ma-l*⁺ recombinants: For each heterozygote, $ma\text{-}l^{x}/ma\text{-}l^{y}$, the left allele, $ma\text{-}l^{x}$ was present on a chromosome carrying both recessive markers, *y* and *l-t2-4a*. The right allele, $ma\text{-}l^{y}$ was present on a chromosome carrying the wild-type alleles of these outside markers. As indicated, only one class of *ma-l*⁺ recombinant chromosomes was recovered from any cross (R^1 or R^2), and the relative position of the *ma-l* mutants is inferred from the pattern of marker recombination. Thus, in the first cross, $y\ ma\text{-}l^{F3}l\text{-}t2\text{-}4a/y^{+}ma\text{-}l^{2}l\text{-}t2\text{-}4a^{+}$ females yielded 5 *ma-l*⁺ recombinant chromosomes, all confirmed upon subsequent test as *y ma-l*⁺ *l-t2-4a*⁺. On the basis of this observation, $ma\text{-}l^{2}$ is placed to the left of $ma\text{-}l^{F3}$ in the scute-8 inverted chromosome, with a map distance estimate of 5.4×10^{-4} units. Analysis of the remaining data of Table 1 follows this logic. The first three crosses of Series A establish the order, $ma\text{-}l^{21} - ma\text{-}l^{2} - ma\text{-}l^{F3}$. The remaining crosses of Series A place $ma\text{-}l^{F4}$ and $ma\text{-}l^{F1}$ to the left of both $ma\text{-}l^{2}$ and $ma\text{-}l^{21}$, with $ma\text{-}l^{F4}$ located to the left of $ma\text{-}l^{F1}$. The Series B crosses position $ma\text{-}l^{1}$ to the left of $ma\text{-}l^{F3}$ and to the right of both $ma\text{-}l^{F4}$ and $ma\text{-}l^{F1}$, inseparable from $ma\text{-}l^{2}$ in the indicated sample size. The series C crosses test a sample of five of the viable Group I noncomplementers against either $ma\text{-}l^{2}$ or $ma\text{-}l^{1}$. Only two crosses yielded recombinants. In both cases, the recombinants place the mutants to the right of $ma\text{-}l^{2}$. Subsequent tests of these mutants against the rightmost mutant, $ma\text{-}l^{F3}$, place one of the Group I noncomplementers, $ma\text{-}l^{20}$, to the right of $ma\text{-}l^{F3}$ (Series D). The recombination data of Table 1 is summarized in the genetic map illustrated in Figure 1. Major features of the map are: (1) Mutants of complementation

Groups III, IV, and V map as site mutants in an order consistent with the complementation map. (2) The tested Group II mutants, *ma-l*^{21} and *ma-l*^{2}, map as site mutants in a position consistent with the polar nature of their complementation. (3) The mapping data involving the Group I noncomplementers also are consistent with their interpretation as polar mutants. (4) Failure of separation in recombination tests is believed merely to reflect proximity rather than identity of mutational sites. This point is amplified by the fact that mutant members of two or more complementation groups have been localized to the same region, and have failed to be separated in recombination tests. Thus, *ma-l*^{F3} (Group V) and *ma-l*^{29} (Group I) have not been separated from each other nor have *ma-l*^{1} (Group IV), *ma-l*^{2} (Group II) and *ma-l*^{25}, *ma-l*^{23}, *ma-l*^{F2} (Group I) been separated (Figure 1).

Analysis of the *ma-l*$^{+}$ exceptionals: Turning next to those *ma-l*$^{+}$ exceptionals which arose without marker exchange (P^{1} and P^{2}, Table 1), several observations are pertinent to an understanding of their mode of origin. Crosses to preserve all *ma-l*$^{+}$ chromosomes as well as subsequent crosses to tester stocks, designed primarily to confirm and/or identify the markers in the maroon-like region, also preclude the possibility that dominant or recessive autosomal or recessive sex-linked suppressors are involved in the origin of any of the *ma-l*$^{+}$ chromosomes of Table 1. Second site mutations within *ma-l*, or closely linked dominant suppressor(s) were not eliminated by these tests. However, one would expect that dominant suppressors and second-site mutant reversions would not lead to uniform restoration of wild-type levels of xanthine dehydrogenase activity. A study of the enzyme activity of a random sample of eight different *ma-l*$^{+}$ recombinants and 11 exceptionals reveals that all exhibit at least wild-type levels of enzyme. Table 2 summarizes the results of one series of two experiments which demonstrates this point. In addition to wild-type and null activity controls, another control genotype was *lxd/lxd* which has been reported to substantially reduce activity.[9] This test (Tube 1, Table 2) lends confidence that the system is capable of recording significantly reduced activity in a genotype

TABLE 2. *Xanthine dehydrogenase activities of the indicated genotypes.*

Tube no.	Experiment 1		Experiment 2	
	Activity	Source	Activity	Source
1	0.6	*lxd*	3.0	E
2	3.0	X	3.6	E
3	3.5	X	3.0	E
4	3.0	X	3.6	E
5	3.7	X	0	*ma-l*^{F3}
6	3.0	X	3.1	*ma-l*$^{+}$
7	4.0	X	2.7	E
8	2.8	X	2.9	E
9	0	*ma-l*^{F3}	4.4	E
10	4.0	E	4.7	E
11	2.9	X	3.3	E
12	2.9	*ma-l*$^{+}$	3.1	E

Enzyme activities associated with *ma-l*$^{+}$ recombinants (X) and exceptionals (E) measured as change in fluorescence units/min over a 15-min incubation period at 30 °C in extracts of ten adult males less than 24 hr from eclosion. Each measure is based upon straight line plots of six measurements at 3-min intervals. The X chromosome of each tested class was either a *ma-l*$^{+}$ recombinant (X) or *ma-l*$^{+}$ exceptional (E). The *ma-l*$^{+}$ control carried *In(1)sc*^{8}; the null activity control was *In(1)sc*^{S1L} *ma-l*^{F3}*sc*^{8}. All classes, including controls carried *y*$^{+}$*Yma-l*^{106}.

which has wild-type eye color and would survive the purine-selective system. While these observations do not absolutely preclude the possibility that one or more of the *ma-l*$^+$ exceptionals arose by means of a second-site mutation or a closely linked dominant suppressor, certainly only a minor fraction of the exceptionals can be attributed to this mode of origin.

A second possibility for the origin of the *ma-l*$^+$ exceptionals would argue that the *ma-l*$^+$ recombinants reflect separability between site mutants, and that the *ma-l*$^+$ exceptionals are the result of conventional two-strand double exchanges, one between the site mutants, and the second between *ma-l* and one or the other outside marker. Such an interpretation would require a tremendous negative interference since there are more exceptionals than *ma-l*$^+$ recombinants (Table 1). A further point about the exceptionals is revealed by an examination of their distribution with respect to the flanking markers, *y* and *l-t2-4a* (P^1 and P^2, Table 1). One may consider such exceptionals as derivatives of chromosomes which originally carried one or another *ma-l* mutant. Thus, the first row of Table 1 describes a cross in which *ma-l*^{F3} yielded *ma-l*$^+$ recombinants in test against *ma-l*^{2}, and the recombination data identifies *ma-l*^{F3} as the "proximal" allele (with respect to the centromere on the *sc*^{8} chromosome). This cross yielded 2 *ma-l*$^+$ exceptionals. One exceptional carried the flanking markers originally associated with the proximal allele, *ma-l*^{F3}, while the other carried the markers associated with the distal allele, *ma-l*^{2}. Inspection of Table 1 reveals that 15 proximally and 15 distally derived *ma-l*$^+$ exceptionals were recovered. Moreover, both classes may be recovered from a single cross. There are several crosses for which the exceptionals are not included since the relative position of the *ma-l* mutants is unknown. If the origin of the *ma-l*$^+$ exceptionals were via classical double exchanges, one of the two crossovers must occur between the *ma-l* mutants. If the second exchange occurred anywhere between the distal *ma-l* mutants and the distal outside marker, then a *ma-l*$^+$ would appear associated with the chromosome that originally bore that distal *ma-l* mutant. If the second exchange occurred between the proximal *ma-l* and the proximal outside marker, then a *ma-l*$^+$ would be recovered associated with the chromosome that originally bore the proximal *ma-l* mutant. Since the distal outside marker, *y*, is almost eight times further from *ma-l* than is the proximal outside marker, *l-t2-4a*, one would expect that the distally derived *ma-l*$^+$ exceptional would arise much more frequently than the proximally derived *ma-l*$^+$ exceptional. However, as noted above, both classes of exceptionals appear with equal frequency (Table 1). In light of these observations, we feel that it is unlikely that classical double exchanges play a significant role in the origin of the *ma-l*$^+$ exceptionals.

Finally, we may consider the likelihood that spontaneous reverse mutation is a significant factor in the origin of the *ma-l*$^+$ exceptionals. Traditionally, fine-structure recombination experiments include homozygous mutant controls to permit identification of background levels of reverse mutation. Despite the use of selective procedures which reduce the labor of scoring progeny, the enormous scale of rearing required for these experiments precluded the possibility of performing such controls without seriously limiting the investigation. Nevertheless, several pertinent points emerge from the study.

The fine structure experiments (Table 1) may be divided into two classes: (1) those yielding *ma-l*$^+$ recombinants and (2) those which failed to yield *ma-l*$^+$ recombinants. The frequency of *ma-l*$^+$ exceptionals in the first class is 29/34, 344,000, while that for the second class is 7/25,263,000. These frequencies are indeed significantly different ($P<0.01$).[10]

A second point of interest emerges from the following consideration: Assuming that the *ma-l*$^+$ exceptionals are the result of spontaneous reverse mutation, then the markers present on each of the *ma-l*$^+$ exceptional chromosomes identify the mutant allele which reverted in each case. Thus, of the 11 mutant alleles involved in the 21 fine-structure crosses, 9 have given rise to "revertants" (Table 1). We might now consider the "reversion frequency" on an allele basis, comparing the observed frequency of reversion of each *ma-l* mutant in crosses which produced *ma-l*$^+$ recombinants, to the reversion frequency seen for that allele in crosses not yielding *ma-l*$^+$ recombinants. If spontaneous reverse mutation were, in fact, the mode of origin of the *ma-l*$^+$ exceptionals, these frequencies should be the same for a given *ma-l* allele. Unfortunately, the 36 exceptionals are distributed among the nine alleles such that there are too few per allele to make a meaningful test for all but *ma-l*^{F3} which has yielded ten *ma-l*$^+$ exceptionals in six fine structure crosses involving that allele. Assuming that the *ma-l*$^+$ exceptionals are the result of spontaneous reverse mutations, then nine revertants of *ma-l*^{F3} were recovered from four crosses which yielded *ma-l*$^+$ recombinants, while only one revertant of *ma-l*^{F3} was recovered from the two crosses which failed to yield *ma-l*$^+$ recombinants. Assuming further than $^1/_2$ of the zygotes sampled in each cross reflect the total number of *ma-l*^{F3} gametes sampled, the frequency of spontaneous reverse mutation of *ma-l*^{F3} in crosses yielding *ma-l*$^+$ recombinants was 9/4,569,000, while that frequency in crosses failing to yield *ma-l*$^+$ recombinants was 1/2,284,000. The significance of the difference between these frequencies ($P < 0.01$) does not support the spontaneous mutation hypothesis.[10]

A final argument against the likelihood that spontaneous mutations of any sort (reversions of the *ma-l* mutants, second-site mutants or closely-linked dominant suppressors) may have played a significant role in the origin of the *ma-l*$^+$ exceptionals emerges from the following considerations: (1) Flies exhibiting reduced levels of xanthine dehydrogenase activity (i.e., complementing heterozygotes) escape death in the purine-selection system. (2) The *ma-l* mutants are nonautonomous.[9] (3) An extensive study of spontaneous visible mutation for a series of 13 sex-linked loci revealed that for every newly-arisen germinal mutant, there were three to four times that many somatic mutations.[11] In view of these facts, one can envisage the purine-selective scheme as an amplication system for the recovery and study of spontaneous somatic mutations as well as germinal mutations. Moreover, if spontaneous mutation played a significant role in the origin of the *ma-l*$^+$ appearing progeny, somatic mutants would be expected with a higher frequency than germinal mutants. These would be identifiable as *ma-l*$^+$ germinal mosaics or *ma-l*$^+$ phenotypes that did not transmit. However, there were only two *ma-l*$^+$ appearing progeny recovered in the entire study which did not transmit, and one of these was sterile. There were no germinal mosaics.

Observations of high negative interference, recovery of wild-type exceptionals, and nonreciprocal recombination products have been reported in prior studies of intragenic recombination in *Drosophila*.[12] In view of the present analysis of the *ma-l*$^+$ exceptionals, we propose that all of these observations may well be conversions. It should be noted that the present limited observations, while indicative of conversion, are inadequate to question whether the conversion events show frequency inequalities which reflect map position of the mutant alleles.[13]

Conclusion. The fine structure map of the various classes of *ma-l* mutants does not, by itself, permit a clear distinction between the single cistron-allele complementation model of genetic organization, and an operonlike model.‡ Nor do these results conflict with the observations reported elsewhere[6] which provide a compelling argument in favor of the allele complementation model.

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‡ **Note added in proof:** However, an independent confirmation of the allele complementation model comes from the analysis of certain double mutant chromosomes (Finnerty, V., and A. Chovnick, *Genet. Res.*, **15,** in press.)

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