

HIGH MUTATION FREQUENCY INDUCED BY HYBRIDIZATION

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The increase in variability that is a familiar result of the rearing of second generations from crosses between different races is certainly due chiefly to segregation and recombination of genes in which the parental races differed. There is, however, a persistent feeling that perhaps interracial crossing also induces the production of new mutations. The first attempt to test this view experimentally with *Drosophila* led to negative results (Duncan 1915). Belgovsky (1937) reported an increased frequency of somatic mutations in the hybrids between *D. melanogaster* and *D. simulans*, in x-ray experiments. The differences reported were not very striking, and in any case have little bearing on questions concerning spontaneous frequencies.

Casual observations have led me to suspect an increased mutation frequency in the hybrids between the two semi-cross-sterile races (*A* and *B*) of *Drosophila pseudoobscura*. The present note describes experiments planned to measure the rate quantitatively in such hybrids.

Two different interracial crosses were carried out, using appropriate "marker" genes. Females of the scutellar scarlet (race *B*) stock were mated to males of the beaded (race *A*) stock. The F_1 females were mated to yellow compressed short (race *A*) males, and the daughters (first back-cross—1 *BC*) of this mating were tested individually by yellow compressed short males, to give the 2 *BC* generation. In the second experiment, yellow compressed short (*A*) females were mated to pointed (*B*) males, and the F_1 females were mated to scutellar scarlet (*B*) males to give the tested 1 *BC* females. In both cases females of the 2 *BC* generation were also tested for lethals, by mating to males of the strain to which their respective fathers belonged. The table shows the sex-linked lethals recovered (referred to the generation to which the first detected heterozygous female belonged), and the number of "visible" mutant types observed in the males (referred to the generation to which the males themselves belonged—in most cases presumably one generation later than that in which the actual mutation occurred).

The totals (denominators) shown in the table represent, for lethals, twice the number of tested females. This is because 12 of the 31 recovered lethals were in paternal *X*-chromosomes, which had evidently undergone mutation soon after fertilization had introduced them to the hybrid zygote. For the visibles the total given is that of the males counted in the generation concerned. Each separate mutation is counted once, though several of them

appeared in several offspring of single mothers. These relations show that few, if any, of the mutations occurred at meiosis. They are, therefore, scarcely to be referred to crossing-over or recombination.

The "visible" types recovered were mostly previously known types. Thus, forked (or singed—probably both are present, but the tests are not yet completed) was found five times, beaded three times, scutellar twice and dusky, bobbed, ascute, slender and short each appeared once. In the

TABLE 1
DETECTED MUTATIONS

GENERATION	BACKCROSSES TO RACE A		BACKCROSSES TO RACE B		TOTAL (PERCENTAGES)	
	LETHALS	VISIBLES	LETHALS	VISIBLES	LETHALS	VISIBLES
1 BC	0/38	1*/124	9/66	0/243	8.7	0
2 BC	6/106	0/911	16/152	10/1046	8.5	0.56
3 BC	...	5/2135	4/3796	...	0.15

* This was a somatic mutation—there was a large patch of forked (or singed) bristles on the thorax. The mutation is not included in the totals, since it is not comparable to the other "visibles," which presumably occurred in the mothers of the males recorded.

4 BC generation (not shown in the table because the pedigrees were varied in order to carry out tests of suspected mutant types) there were found white, bobbed, miniature and another forked (or singed).

The lethal frequencies given are to be taken as minimum values. As has been shown by Lancefield and others (see Sturtevant 1937a), the sex-ratio from *A-B* hybrids is variable. For this reason all sex-linked lethals were tested, and none were entered in the table unless they resulted not only in a 2:1 sex-ratio but also in typical lethal ratios for the sex-linked genes heterozygous in the culture. This requirement was met in at least two successive generations. From several probable lethals no satisfactory test was obtained in the following generation, and these have not been recorded, though the chromosomes concerned do appear in the totals. Incidentally, this test also showed that the loci of the lethals were scattered throughout the *X*-chromosome.

Owing to the complications just mentioned, and to the small number of cultures reared, it is not possible to judge whether there was an increased mutation frequency in the F_1 generation. The point is of theoretical interest, in connection with the hypothesis outlined below, but will have to be studied in experiments especially designed for the purpose.

In addition to the mutations shown in the table there were three dominants in the females of the 3 BC generation (Smoky, an extreme minute-bristle, and a sex-linked wing character). In the regular series no autosomal recessives could have been detected, but in testing one of the early sex-linked recessives, hybrids were mated together, and among their offspring was found the well-known second chromosome recessive, bithorax.

These experiments were carried out on a small scale, and no specific control is available. Nevertheless, the mutation frequencies—about 9 per cent of lethals and one-half of 1 per cent sex-linked visibles—are so much higher than any other recorded spontaneous rates that their significance cannot be doubted. It may be added that I have detected only one sex-linked lethal in *pseudoöbscura* in experiments not concerned with *A-B* hybrids.

The theoretical implications of the results just described may be deduced from the effects that natural selection should have on mutation rate. I have argued (Sturtevant 1937b) that natural selection must operate to keep the general mutation rate of a species at a minimum—a conclusion also reached by Shapiro (1938). I have suggested that different populations may achieve this result by different genetic means, and that crossing such different races should, through recombination, lead to an increase in mutation frequency. The results here recorded constitute a verification of this prediction. The increase here is unexpectedly great, but it may be pointed out that the cross made is about as extreme a one as it is possible to study in later generations.

These results indicate that a species may escape the impasse toward which the automatic decrease in mutation frequency is constantly pushing it, by the occasional interbreeding of semi-isolated populations within the species.

The general method of crossing may also be of use in the study of the nature of the mutation process, since there is no indication of an increase in major chromosome aberrations such as accompany x-ray treatment. Further study will be required to answer the question whether small rearrangements (deficiencies, small inversions) occur more frequently.

Summary.—The offspring of the backcrosses from hybrids between the two races (*A* and *B*) of *Drosophila pseudoöbscura* show a large increase in mutation frequency.

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