COMPETITION BETWEEN MUTANTS IN EXPERIMENTAL POPULATIONS OF *DROSOPHILA MELANOGASTER*¹

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ONE of the truisms of modern biology is that organisms are adapted to their physical and biological environments. No evolutionary change is possible which does not at the same time leave the organism adapted to its environment. Although the forces of natural selection, mutation, migration and random genetic drift may interact to produce evolutionary changes, natural selection has, since the time of Darwin, assumed a dominant role because it is the mechanism of adaptation. Natural selection and hence adaptation hinge on differential reproduction, a greater proportion of the better adapted types surviving to reproduce. Despite the fundamental role played by adaptation in relation to a great variety of biological problems, and despite the widespread interest in adaptive phenomena, a feeling exists that much still remains to be learned about adaptation. One of the major changes in SIMPSON's "The Major Features of Evolution" (1953) as compared to his "Tempo and Mode in Evolution" (1944) was the inclusion of an extensive discussion of adaptation. And in his review of this latest book by SIMPSON, STEBBINS (1954) writes, in relation to the section on adaptation, "Perhaps the greatest gap in modern evolutionary knowledge is our paucity of precise information on just how and why certain characters are selected under a given set of environmental conditions." A similar opinion was expressed by WADDINGTON (1953) who further felt that although the mathematical theories of population genetics have had considerable impact on evolutionary thought, the validity and usefulness of some of the concepts have yet to be adequately demonstrated. The current discussion of the significance to evolution of random genetic drift is a case in point.

The experiments to be reported are attempts to explore some of the problems related to the adaptive value of particular genes. It has recently been suggested (DOBZHANSKY and WALLACE 1954) that the study of adaptive differences should involve polygenically controlled traits rather than single factor differences. Since it is impossible to set up separate classes of major and minor genes, and since so far as is known the same principles govern the behavior of genes of all kinds, an approach which involves genes causing major phenotypic and adaptive differences may help to extend the theories and point the way to the more complex studies involving polygenic traits. Our knowledge of the adaptive values of even the simply inherited, clear-cut traits is still rather sketchy. On the list of "frankly deleterious variants" cited by DOBZHANSKY and WALLACE were Huntington's chorea and sickle cell anemia. However, Huntington's chorea has been shown to raise the reproductive level of carriers above that of their normal sibs (REED and PALM 1951), and ALLISON

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(1954) has recently presented evidence showing that persons with sickle cell trait (the heterozygotes for the gene producing sickle cell anemia) are less susceptible to subtertian malaria. Hence, the evaluation of the adaptive value, even of a gene which seemingly must be deleterious, needs to rest on a careful appraisal of all of its effects in the population. At the present time, the most rapid progress toward an increased understanding of the concept of adaptive value seems possible from work with genes having well-defined effects and clear-cut inheritance.

METHODS

In order to determine the relative adaptive value of a pair of alleles, flies carrying these genes were placed in a "population bottles" devised by REED and REED (1948) and LUDWIN (1951). A population unit consists of two half-pint milk bottles joined together by a 3-inch section of automobile radiator hose. A $\frac{3}{4}$ -inch hole for ventilation is cut into the hose and plugged with cotton. The food is poured into bottles as they lie on their sides and hardens in a "slant". A fresh slant of food is used to replace each bottle alternately as its food is exhausted. In this way, a population can be maintained for an indefinite period of time with a minimum amount of handling or disturbance. A major advantage of the population bottles over population cages (e.g. WRIGHT and DOBZHANSKY 1946) is that the units are small and easily handled so that a number of replicas of each experiment can be run.

The food used was a standard corn meal, corn syrup, brewer's yeast, agar medium containing Moldex, to which were added a few drops of live yeast suspension. The populations were maintained in a constantly lighted room held at $21 \pm 1^\circ\text{C}$ and 50% relative humidity.

The populations were sampled by removing the cotton plug from the hose connection and placing a vial over the hole, with the vial held horizontally toward a fluorescent light. The samples were taken a few days after a new slant had been added so that the females had had an opportunity to lay their eggs on the fresh food. The flies usually walked slowly rather than flew into the vial so that position with relation to the opening rather than activity seemed to govern their movement into the vial.

However, the reliability of this sampling method was tested because of the possibility that differences in activity or in response to light either between the sexes or between mutant types might result in biased samples. In order to make this test, eight populations of glass versus wild type were sampled in the usual manner and then the rest of the flies were removed from the bottles and also counted. The results in table 1 show that there was no significant difference between the sampled flies and the remaining flies with respect to either sex ratio or frequency of the mutant types. These results do not completely eliminate the possibility that bias existed when other alleles were involved. However, they do show that when a highly disadvantageous mutant (see below) affecting the eyes was sampled, the samples obtained were not grossly biased, either with respect to sex ratio or frequency of the mutant type.

One set of experiments involved a group of genes at or near the white locus on the X chromosome. The mutants used were white, apricot, coral, eosin, and satsuma.

TABLE 1

Comparison of samples with remaining adult populations in 8 populations of glass vs. wild type

Population	Sample			Remainder		
	Males	Females	gl/gl	Males	Females	gl/gl
1	18	23	0	63	67	3
2	38	24	0	85	87	0
3	11	11	1	23	17	0
4	25	37	0	99	94	0
5	55	58	0	96	115	0
7	57	72	0	62	49	2
9	35	40	0	77	80	0
10	12	24	0	33	65	1
Totals	251	289	1	538	574	6
	% males = 46.5% $P = .3$ % gl/gl = 0.19% $P = .16$			% males = 48.4% $P > .3$ % gl/gl = 0.54% $P > .3$		

LEWIS (1952) has shown white and apricot to be pseudoalleles, and MACKENDRICK and PONTECORVO (1952) have shown white and coral to be pseudoalleles, but did not find crossovers between white and satsuma, eosin and apricot, or eosin and satsuma. Both coral and apricot belong to the so-called "apricot" group in which the eye color is darker in the male than in the female and the Pale modifier darkens the eye color. (However, it should be noted that MULLER (1950) states that no certain difference in eye color can be distinguished between the apricot males and females.) White and eosin belong to the "eosin" group, which shows a lighter eye color in males than in females, and in which the Pale modifier lightens the eye color. Satsuma shows no sexual dimorphism and is not modified by Pale.

The white stock was made relatively isogenic by single pair, brother-sister matings for 12 generations. During this period of inbreeding, the other four mutant stocks were repeatedly backcrossed to white so that by the end of this time all five stocks should have been rather similar genetically except at the mutant locus and probably closely adjacent regions. The backcrossing was carried out by first single pair mating a male sib from the white line to an eosin female, for example, and then backcrossing a heterozygous w^e/w female to a white male sib from the next inbred generation of white.

After the inbreeding, 5 populations of each mutant in competition with white were started, with 10 mutant males, 10 white males, and 10 heterozygous females as the initial population, the genes thus being present with equal frequency at the outset. The populations were sampled at intervals roughly of 30 days. Since the heterozygous females can be distinguished from the homozygotes, except for heterozygous white-satsuma females, it was possible to determine the exact gene frequencies in the samples at all times.

Another set of experiments involved competition between sex-linked and autosomal recessive genes and their wild type alleles. The mutants used were the sex-linked

recessives, yellow (*y*) and raspberry (*ras*²), and the autosomal recessives, vestigial (*vg*) and glass (*gl*). Ten populations of each recessive mutant were started from laboratory stocks. After these populations were well established and were estimated to consist of over 200 adult flies, a single freshly emerged wild type (Lausanne Special) male was introduced into each population on the 20th day after the mutant population had been started. The male was placed in the slant of fresh food and allowed to recover completely from the ether before this bottle was connected to the other by means of the rubber hose. The initial frequency of the wild type allele at the time of introduction of the male was then, at a maximum, about 0.005, and was probably less in most cases.

A comparison was made of the viability of the mutant types and their heterozygous wild type sibs by counting the progeny from a backcross of heterozygous females to mutant males reared in half-pint culture bottles under the conditions given above. Mating tests of the "female choice" type (MERRELL 1949, 1950) were conducted by placing 10 females in a creamer with 10 mutant and 10 wild type males, all of these flies being the progeny of a backcross of heterozygous females to mutant males. After 2 days, each of the females was isolated in a creamer, and her progeny were examined to determine the genotype of the father.

RESULTS

The white series

The changes in gene frequency in the populations can be followed in figures 1, 2, 3, and 4 (the complete data on which these figures and figures 5 through 8 are based are on file in the GENETICS editorial office). With the sex-linked genes only the changes in the males are shown because they adequately reflect what happened in the populations. Figures 1 through 4 show that rapid, consistent shifts in gene

FIGURE 1.—Competition between eosin and white.

frequency, attributable to strong selection pressure against one of the genes involved, do not occur. However, trends do appear in most cases, suggesting that the genes are not completely neutral in effect.

The frequency of the genes tends in most cases to differ between males and females (tables 2 and 3). Only in the satsuma group is there no evidence of differences. In the apricot group, when individual samples were compared, no significant difference emerged, but when the totals for each population were examined, the frequency of *w* was higher in the males than in the females in all five populations.

The expected numbers of heterozygous and homozygous females were calculated for each sample from the Hardy-Weinberg formula and from the observed gene fre-

FIGURE 2.—Competition between apricot and white.

FIGURE 3.—Competition between coral and white.

quencies in the females, and compared with the observed numbers. No comparison could be made involving satsuma because w^{sat}/w females were indistinguishable from w^{sat}/w^{sat} females. In the populations of eosin and white, the individual samples did not differ significantly from the expected numbers, but observed numbers were

FIGURE 4.—Competition between satsuma and white.

TABLE 2

Comparison of the frequency of w in males and females

Population	w^e-w %w		$apr-w$ %w		$w^{co}-w$ %w		$w^{sat}-w$ %w	
	Males	Females	Males	Females	Males	Females	Males	Females†
1	36.6	42.0	62.6	47.8	73.8*	65.6*	48.0	49.2
2	28.2	30.7	67.8	66.7	78.6	66.5	38.9	36.6
3	39.8	46.3	47.4	41.8	68.0	49.1	53.5	35.2
4	31.3	39.9	57.9	52.4	68.1	56.9	38.7	31.6
5	38.0	39.2	66.0	63.2	68.3	56.8	65.4	64.5
	34.8	39.7	58.7	52.6	71.9*	59.6*	47.1	42.3

* Omitting last two samples in population 1 when $w = 100.0\%$.

† Estimated from frequency of w/w females.

TABLE 3

Comparison of the frequency of w in males and females

Populations	Samples compared	$qf > qm$	$qf < qm$	χ^2
w^e-w	46	38	8	19.56†
$apr-w$	47	22	25	0.19
$w^{co}-w$	49	13	36	10.80†
$w^{sat}-w$	35	17	18	0.03

† Highly significant.

greater than expected somewhat more often than they were less (table 4). However, highly significant excesses of heterozygous females were observed in the apricot-white and coral-white populations.

The sex ratios deviated from equality in these populations (table 5). In all cases

TABLE 4
Comparison of observed and expected frequency of heterozygous females

Populations	Samples compared	$O > E$	$O = E$	$O < E$	χ^2
w^e-w	46	30	0	16	4.26*
$apr-w$	48	44	0	4	33.34†
$w^{co}-w$	48	33	3	12	9.80†

* Significant.

† Highly significant.

TABLE 5
Sex ratios in populations containing members of the white series

Population	w^e-w		$apr-w$		$w^{co}-w$		$w^{sal}-w$	
	Total of samples	% males	Total of samples	% males	Total of samples	% males	Total of samples	% males
1	1326	61.4	370	51.4	1127	51.4	752	66.0
2	811	61.3	653	55.6	861	60.8	684	67.2
3	670	61.8	1177	48.3	571	59.2	711	64.7
4	896	55.7	831	53.2	314	63.0	682	67.7
5	717	63.9	698	54.0	1176	56.4	342	68.4
	4420	60.7	3729	52.0	4049	56.8	3171	66.6

FIGURE 5.—Competition between vestigial and wild type.

FIGURE 6.—Competition between glass and wild type.

FIGURE 7.—Competition between yellow and wild type.

FIGURE 8.—Competition between raspberry and wild type.

TABLE 6
Comparison of viability of mutant and wild type sibs

Genotype	+/ <i>gl</i>	<i>gl</i> / <i>gl</i>	+/ <i>vg</i>	<i>vg</i> / <i>vg</i>
Males	795	723	863	802
Females	822	745	962	851
Total	1617 1.000	1468 .908	1825 1.000	1653 .906
Genotype	+ or +/ <i>ras</i>	<i>ras</i> or <i>ras</i> / <i>ras</i>	+ or +/ <i>y</i>	<i>y</i> or <i>y</i> / <i>y</i>
Males	1476	1420	444	477
Females	1399	1418	475	440
Total	2875 1.000	2838 .987	919 1.000	917 .998

TABLE 7
Female "choice" mating tests

Female Genotype	Total females	Successful males		Double matings
		Wild type	Mutant	
A. Equal numbers of mutant and wild type males				
+/ <i>y</i> *	73	62	3	1
<i>y</i> / <i>y</i> *	97	68	8	1
Total	170	130	11	2
+/ <i>ras</i> *	68	40	21	0
<i>ras</i> / <i>ras</i> *	76	39	18	1
Total	144	79	39	1
+/ <i>gl</i>	49	26	1	0
<i>gl</i> / <i>gl</i>	48	30	0	1
Total	97	56	1	1
+/ <i>vg</i>	48	42	4	1
<i>vg</i> / <i>vg</i>	48	41	4	0
Total	96	83	8	1
B. 18 mutant to 2 wild type males				
<i>gl</i> / <i>gl</i>	43	22	12	0
<i>vg</i> / <i>vg</i>	41	15	22	0

* MERRELL 1949.

TABLE 8
Sex ratios in populations with vg, gl, y or ras

Type of population	Total of samples	% males
A. Mutant and wild type		
<i>vg</i> —10 populations	7281	50.5
<i>gl</i> —9 populations	6537	45.9
<i>y</i> —3 populations	3381	46.3
<i>ras</i> —5 populations	7726	48.9
B. Mutant only		
<i>gl</i> —1 population	328	36.0†
<i>y</i> —6 populations	2533	41.8†
<i>ras</i> —5 populations	3125	47.4†

† Highly significant difference from sex ratio in comparable populations under A.

there was a significant excess of males, the satsuma-white populations showing the greatest deviation, 2 males to 1 female. Although there were fluctuations in the ratio from sample to sample, each group of populations appears to have a more or less characteristic sex ratio.

Wild type vs. mutants

The changes in frequency of the mutant types, *vg*, *gl*, *y*, and *ras*, in competition with the wild type are shown in figures 5, 6, 7, and 8. The changes in frequency were so uniform in the ten populations of *vg* and nine of *gl* in which the wild type became established that the data have been combined to give a single curve in each case. In each of these 19 populations the frequency of the mutant phenotype had dropped from more than 99% at the outset to less than 10% by the 55th day. The course of events in the populations with *y* and *ras* can be followed from the changes in gene frequency observed in the males. However, each population is shown separately because the course of events in each was unique. The wild type became established in all ten *vg* populations, and nine of ten *gl* populations, but only in three out of nine *y* populations, and five out of ten *ras* populations.

The outcome of the tests for viability and mating success is shown in tables 6 and 7. The mutants appear to have a more drastic effect on mating success than on viability under the conditions of the experiments.

The sex ratios in the various populations are shown in table 8. A comparison has been made between the sex ratios in the populations in which the wild type became established and those populations remaining homozygous for the mutant.

DISCUSSION

The w series

There was no great difference in selective value among the alleles and pseudoalleles of white. Rapid changes in frequency, usually observed in competitions between wild type and mutant alleles, did not occur. These *w* genes presumably have never been in competition before. Nevertheless, the indications are that they can not be considered to be altogether adaptively neutral. Trends were observed in three of the

four sets of experiments. Only w^{sat} and w appeared to be comparable to each other and under different conditions they might also show selective differences. It would be interesting to know whether, in a more heterozygous background, modifiers would accumulate due to selection which would cause one gene to become decidedly superior to the other.

However, although the genes did not change frequency rapidly, they apparently differed in their effects in the males and females. A sex ratio of 1:1 was approached most closely in the w vs. apr populations, apparently due to heterosis in the $apr +/+ w$ females. A general statement could be made that the females, with two doses of any of these genes, were less viable than the males, with only a single dose.

This finding raises certain questions about the theory of dosage compensation advanced by MULLER (1932, 1950). Since males and females usually show rather similar phenotypes for traits controlled by sex-linked genes despite two doses of these genes in females and only one in males, MULLER has suggested that the differences in gene dosage have in some way been compensated. This dosage compensation is presumed to be due to the action of modifiers in the X chromosome, an intrachromosomal balance being achieved between the mutant and the modifiers. He further suggests that the dosage compensation system functions primarily to make the effects of the wild type genes the same in both sexes. The system of modifiers is thought to have evolved in relation to the wild type, but shows up best in the presence of hypomorphic mutants.

Since the expression of the eye mutants in these populations showed no apparent differences from the usual descriptions (BRIDGES and BREHME 1944), with slight differences or none between hemizygous males and homozygous females, presumably a normal system for dosage compensation was present. However, if such modifiers adjust a trait like eye color to more or less comparable values in males and females, then they would also be expected to adjust the viability of the males and females to comparable levels (see discussion below on the sex ratio). Furthermore, these modifiers might be expected to produce comparable viabilities as well as eye colors even if the differences in viability were due to sex-linked genes other than the w series itself. However, the most extreme sex ratio, 2 males:1 female, occurred in the satsuma-white populations where there was no sexual dimorphism for either satsuma or white. Hence, it seems clear that the expression of each trait, eye color and viability, was independent of the other, whether due to pleiotropic effects of the w genes or to the separate action of the w series on eye color and of other sex-linked genes on viability. In either case, if dosage modifiers were present, they would be expected to have modified both eye color and viability under MULLER's hypothesis. Hence, the suggestion (GOLDSCHMIDT 1938, 1954) that similarities in eye color are due to a threshold effect during development may be more useful in this instance since under this hypothesis, it is possible for eye colors to be similar but viabilities different when there are differences in gene dosage.

It might be expected that the most pigmented eye would be the best adapted, but this is not so. The sequence of genes from best adapted to least adapted is not the same as the sequence from most pigmented to least pigmented. The adaptive relations are roughly as follows: $w^e > w \cong w^{sat} > apr > w^{co}$, while the sequence

with regard to amount of pigment is $w^{sat} > w^{co} > w^e > apr > w$. Similar results have been reported by TIMOFÉEFF-RESSOVSKY (1933). These differences may be due to other viability genes closely linked to the w locus, but they may also be due to the effects of the mutants themselves. If so, the mutants' effects on eye color are only one aspect of their overall selective value.

The frequency of the less favored allele was generally lower in the males than in the females. Thus in w^e vs. w populations, the less favored w was less frequent in males than in females, whereas in w^{co} vs. w populations, the less favored w^{co} was less frequent in males than females. No difference was found in the w^{sat} vs. w or the apr vs. w populations between frequencies in males and females; in w^{sat} vs. w apparently because of the equivalence in adaptive value, in apr vs. w probably because of the heterosis involved in the females. This result is in accord with expectation since there are only two types of males, but three types of females. Selection can thus be expected to be more effective in the males because they do not carry the less favored gene in the heterozygous condition.

This result presents an apparent paradox since selection seems to be more effective in the males, but the total numbers of males exceed the totals for the females. Actually selection can be thought of as being more discriminating in the males than in the females, gametic selection being more effective than zygotic (which is essentially the difference here). This effect, then, is in addition to the effects of dosage discussed above.

The heterosis observed in females heterozygous for white and either of its pseudoalleles, apricot or coral, and possibly for white and eosin, requires comment. Heterosis has also been reported for the pseudoalleles in the lozenge region in *Drosophila melanogaster* by OLIVER and GREEN (1944). These authors ascribed the heterosis to interaction between the lozenge genes. Another possibility is that the heterosis is due to the presence of a wild type allele at each locus. Still another explanation may be that the heterosis is due to residual differences at loci closely linked to the mutants which did not become uniform during the backcrossing to white. If the latter is the case, it is a rather interesting coincidence that the known pseudoalleles should produce the maximum heterosis while eosin showed little. If the heterosis is due to the genes within the white region, then the second explanation, that heterosis is due to the presence of a wild type allele at each locus, seems more probable than the first. If heterosis is, indeed, characteristic of pseudoalleles, and if pseudoallelism is as common as recent studies (in *Drosophila*, LEWIS 1952; GREEN and GREEN 1949; IVES AND NOYES 1951; MACKENDRICK and PONTECORVO 1952; in mice, DUNN and CASPARI 1943; in *Neurospora*, GILES 1951; BONNER 1951; and in *Aspergillus*, PONTECORVO 1953) seem to indicate, this relationship may have considerable importance. It lies in the fact that new phenotypes may be exposed to selection without being completely divorced from the adaptive value of the wild type.

Furthermore, those cases of heterosis which have been reported as involving alleles at a single locus may be indicative of pseudoallelism. For instance, the marked heterosis noted by KERR and WRIGHT (1954) in heterozygotes of spine-

less (*ss*) and aristapedia (*ss^a*) compared to both homozygotes may indicate that they are pseudoalleles, a possibility made even more likely by the rather different nature of their morphological effects. Also, when interallelic interaction has been reported as supporting evidence for the overdominance theory of heterosis (SINGLETON 1943; GUSTAFSSON 1952; and others), the heterosis may actually have been due to pseudoallelic interaction interpretable in terms of the dominance hypothesis.

Wild type versus mutants

In contrast to the results with the *w* series, the wild type genes showed a decided superiority over their mutant alleles. The changes in frequency of the *vg* vs. + and *gl* vs. + populations were characterized by an initial precipitous drop in the frequency of the mutant type followed by a more gradual decline. Although a similar leveling off has been interpreted to indicate that an equilibrium has been attained when the mutant reached a low frequency (L'HERITIER and TEISSIER 1937), the rate of elimination is so slow at low frequencies that the decision as to whether or not equilibrium has been reached is very difficult unless the experiment is continued for a long period. Although the viability of the mutants is fairly high, about 90% that of the wild type under favorable conditions, the clue to their low adaptive value apparently lies primarily in their effect on mating behavior. It should be noted that the mode of decline in frequency of the mutants in these populations fits the type of change theoretically expected when there is complete selection against an autosomal recessive gene.

In those *y* vs. + and *ras* vs. + populations in which the wild type gene became established, the decline in frequency of the mutant type was more gradual than in the populations carrying the autosomal recessives. The most rapid shifts in frequency of the mutant type came at intermediate frequencies, with the changes being more gradual at both high and low frequencies of the mutant type. This finding is in accord with the predictions of population genetics, which have indicated that selection is most effective at intermediate gene frequencies. Again the mating behavior seems very closely tied to the results in the populations. When tested, neither *y* nor *ras* showed significant differences from the wild type as measured by the number of adults produced, but both reduced the mating efficiency of the males, *y* considerably more than *ras*. The more rapid decline of *y* in the populations in which the wild type became established as compared to *ras* indicates agreement between the mating tests and the changes in the populations.

On the basis of the tests made of viability and mating success, the mutants compared to each other could be rated as follows: all + alleles > *ras* > *y* > *vg* $\cong$ *gl*. These ratings are borne out by the relative success of the mutants in the populations, for the rate of change in frequency in the populations is much slower for *ras* than it is for *vg* or *gl*, where the selection coefficient is so much greater. A further prediction of population genetics especially emphasized by WRIGHT is that when selection is weaker, chance events play a greater role in the course of events in the populations. This prediction is borne out in a crude way by the fact that in the *y* vs. + and *ras* vs. + populations, the wild type became established in only 8 of 19

populations while it became established in 19 of 20 *vg* vs. + and *gl* vs. + populations. Hence, where the selective advantage of the wild type gene was less, it had a lower probability of becoming established in the population.

Sex ratios

The sex ratios involved in the wild type-mutant competitions showed an excess of females over males or else a 1:1 sex ratio in contrast to the results with the *w* series where males outnumbered females. Since all of the populations were sampled in the same fashion, it becomes unlikely in view of these results that sex was responsible for sampling bias. Other authors have reported that in *Drosophila melanogaster* populations they have usually obtained an excess of females over males (MOENKHAUS 1911; REED and REED 1950; LUDWIN 1951). A further observation from the above data is that the sex ratio in populations containing both the wild type and the mutant type is generally closer to 1:1 than is the ratio in homozygous mutant populations (table 8). These results can be interpreted to indicate that the various mutant genes were more deleterious in one sex than the other. The wild type genes, on the other hand, came closer to producing equal viability in both sexes. If such is generally the case, then presumably the secondary sex ratio has been adjusted by natural selection toward unity in the adults. FISHER (1930a) and SHAW and MOHLER (1953) have reasoned that natural selection should always act toward producing equality of the sexes at maturity. These results would appear to bear out their conclusion. However, no answer can be suggested as to whether the equality produced is due to the selection of modifying factors or to the selection of those among the wild type isoalleles which have equivalent effects in males and females.

Since these genes do affect the sex ratio so markedly, their adaptive values must be different in males and females. This conclusion indicates the possibility, as FISHER (1930b, 1932) has suggested, that balanced polymorphism could arise because a mutant which is advantageous in one sex may be disadvantageous in the other. This suggestion has been more or less neglected in the more recent discussions of the mechanism of balanced polymorphism (DOBZHANSKY 1951; FORD 1953), which have emphasized the superiority of the heterozygote over both homozygotes, fluctuating selection pressures, or ecological differences as instrumental in producing balanced polymorphism. The above data do not demonstrate this type of balanced polymorphism, but they do demonstrate the validity of the basic assumption, that the same gene may have different adaptive values in males and females. LEVITAN (1951) has presented evidence which indicates that there are differences in the adaptive value of different gene arrangements in the males and females of *Drosophila robusta*. Therefore, the polymorphism in gene arrangements, common to many species of *Drosophila*, could also be due to this cause as well as to adaptively superior heterozygotes.

SUMMARY AND CONCLUSIONS

1. Competition between alternative genes was followed in experimental populations of *Drosophila melanogaster*. In one set of experiments, white was placed in

competition with coral, eosin, satsuma, or apricot. Another set involved the sex-linked recessives yellow (*y*) and raspberry (*ras*), and the autosomal recessives vestigial (*vg*) and glass (*gl*), each in competition with its respective wild type allele.

2. In the experiments with white, the genes used came closer to being adaptively neutral than any tested thus far, but even so, trends were noted in favor of one or the other gene in all of the competitions except white vs. satsuma. Hence, the concept of the completely neutral gene pair is not generally supported by these results.

3. In the white vs. apricot and white vs. coral experiments there was a decided excess of heterozygous over homozygous females. In the white vs. eosin experiments there was possibly a slight excess of heterozygous females, but not to the degree seen with apricot and coral. Since apricot and coral have been shown to be pseudo-alleles of white, this heterosis may be due to the respective wild type alleles of these genes. These results further suggest the possibility that instances of heterosis reported as due to the interaction of alleles to produce overdominance may be of this kind.

4. The overall sex ratio in the white populations showed an excess of males over females, the highest being 2 males: 1 female in white-satsuma. This result is interpreted as being due to two doses of these deleterious genes in the females as compared to only one in the males. Since the effect of these genes on viability appears to be unrelated to their effect on eye color, the theory of dosage compensation for sex-linked genes does not seem to apply in this case.

5. The decline in frequency of the autosomal recessives, *vg* and *gl*, approximates the theoretical curve expected for complete selection against an autosomal recessive. The primary selection pressure was apparently not due to loss of viability, which was approximately 90% of the wild type on test in both cases, but rather to the reduction of mating success by the mutant males.

6. The decline in frequency of the sex-linked recessives, *y* and *ras*, was more gradual. The prediction from theory that the most rapid decrease in frequency of the less favored allele should occur at intermediate gene frequencies, with the decline more gradual at both high and low frequencies of the mutant, was borne out experimentally. Again the selection pressure was apparently due to reduced mating success rather than loss of viability.

7. The overall sex ratio in populations in which the wild type became established came closer to equality than the ratio in those populations which remained homozygous for the mutants. This result supports the theoretical conclusion that natural selection always tends to shift the secondary sex ratio in the direction of equal numbers of both sexes.

8. The variety of sex ratios observed indicates that genes may have different selective values in males and females. This observation suggests a further mechanism for balanced polymorphism.

9. The relationship between strength of selection pressure and chance events was demonstrated by the fact that when selection against the mutants was strong, as in *vg* and *gl*, the favored wild type became established in 19 of 20 populations. On the other hand when the selective advantage of the wild type was not so great, it was lost from 11 out of 19 *y* and *ras* populations.

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