

whether any of the short-deletion mutants in our collection is a selfer. If a short deletion, because it lacked one or two bases, affected the functioning of a gene by throwing off the triplet reading, then it is conceivable that the function could be restituted by the addition or subtraction of a base through selfing.⁸

Summary.—A “selfer” is a mutant that gives rise to wild-type recombinants in matings with itself. Evidence is presented that such mutants are found among auxotrophs of *Salmonella typhimurium*. It is proposed that unequal crossing-over, involving adjacent bases of the DNA of a gene, is responsible for this phenomenon.

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SELECTION FOR GEOTAXIS IN MONOMORPHIC AND POLYMORPHIC POPULATIONS OF *DROSOPHILA PSEUDOOSCURA*

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Carson^{1, 2} has been successful in obtaining by selection strains of *Drosophila robusta* which differed in their behavior. The behavioral character involved is a complex one, a phototactic response combined with a general vigor and an ability to respond quickly to outside interference. The selection was more effective in populations which were karyotypically monomorphic (i.e., structurally homozygous) than in polymorphic ones in which many individuals were inversion heterozygotes. Carson ascribes this to the blockage of gene recombination in inversion heterozygotes, and to relatively free recombination in the homozygotes. Hirsch and his students³⁻⁵ have devised an apparatus which permits selecting flies which are positively or negatively geotactic, the procedure being easy, accurate, and not time consuming. They have shown that populations of *Drosophila melanogaster* contain enough genetic variance to respond rapidly to the selection. The genetic basis of the geotactic response is complexly polygenic, and Erlenmeyer-Kimling and Hirsch⁵ found that at least three of the four pairs of the chromosomes are involved. We have used a similar apparatus, constructed under the supervision of Professor Hirsch, to study the response to selection for positive and for negative

geotaxis in chromosomally polymorphic and monomorphic populations of *Drosophila pseudoobscura*. The apparatus is, very briefly, a classification maze, in which the flies have to make their "choices" of going up or down; a fly which goes 15 times upward ends in the terminal tube No. 1; going always downwards leads to the terminal tube No. 16; going up and down with equal frequency leads, irrespective of the order, to tubes Nos. 8 or 9, etc. The selection is made simply by breeding the flies which are found in the uppermost, or in the lowermost tubes. After some generations of selection the flies become distinctly different in their preferences for upward or downward movements.

Material and Technique.—The experimental populations are derived from 12 strains homozygous for the CH gene arrangement, and 12 strains homozygous for the AR gene arrangement, in their third chromosomes. The wild ancestors of these strains were collected at Piñon Flats, Mount San Jacinto, California, some 15 years ago; the strains were kept in regular mass cultures in a constant temperature room at 16°C. The three experimental populations were monomorphic for AR, monomorphic for CH, and polymorphic for AR and CH respectively. The populations were made by intercrossing all the AR strains, or all the CH strains, or all the AR to all the CH strains, and using the hybrids so obtained. The "monomorphic" populations were, accordingly, structurally homozygous, but were presumably genically heterogeneous. The polymorphic one was both chromosomally and genically heterogeneous, the initial frequencies of the AR and CH chromosomes being 50 per cent.

In every generation approximately 250 virgin females and 250 males, aged separately 2–10 days on ordinary culture medium, were run through the maze. The maze stood in a constant temperature room at 20°C, the light being a fluorescent lamp, vertically placed near the terminal tubes of the maze (see Hirsch³). In general, the flies were introduced into the maze in the afternoon, and by next afternoon or morning, almost all of them sorted themselves out in the terminal tubes. The females and the males were run, of course, separately. For selection, 25 females and 25 males were taken from the uppermost, or from the lowermost tubes of the maze. At the beginning of the experiment, the uppermost (No. 1) and the lowermost (No. 16) tubes had too few flies, and then the flies from two, three or more upper or lower tubes were used. The females and the males of a given selection were placed together in a culture bottle, and transferred to fresh culture bottles daily for about a week, whereupon the parents were discarded. The oviposition and the development of the progeny took place at 25°C. When the adults of the next generation hatched, females and males were collected daily, separated, and aged at 16°C until enough flies accumulated to be placed in the maze.

Experimental Data.—The results of the experiments are summarized in Tables 1 and 2 in Figures 1 and 2. It can be seen that the flies in the original populations were either neutral to gravity or only slightly positively geotactic. The mean values for the females were between 9 and 10, and for the males between 7.8 and 9.4. The point of neutrality being 8.5, this indicates either a weak positive geotaxis or simply that a fly is more likely to fall down than it is to crawl up in the maze. The negative selection (moving upward) may have been slightly more rapid in the early generations than the positive selection (moving toward gravity), but by the ninth generation the means of the positive lines were between 10.0 and 11.7, and of the negative lines between 4.7 and 6.4. Some further progress was accomplished in the next nine generations, and in the 18th generation the means of the positive lines were between 11.4 and 13.0, and of the negative lines between 3.4 and 5.2. The variation curves of the positive and negative selection lines continued to overlap, but they became, if considered jointly, very distinctly bimodal.

After eight generations of selection, the polymorphic populations were subjected to cytological analysis. Chromosomes in the salivary gland cell were examined in 150 larvae from the population selected for a positive and 150 from that selected

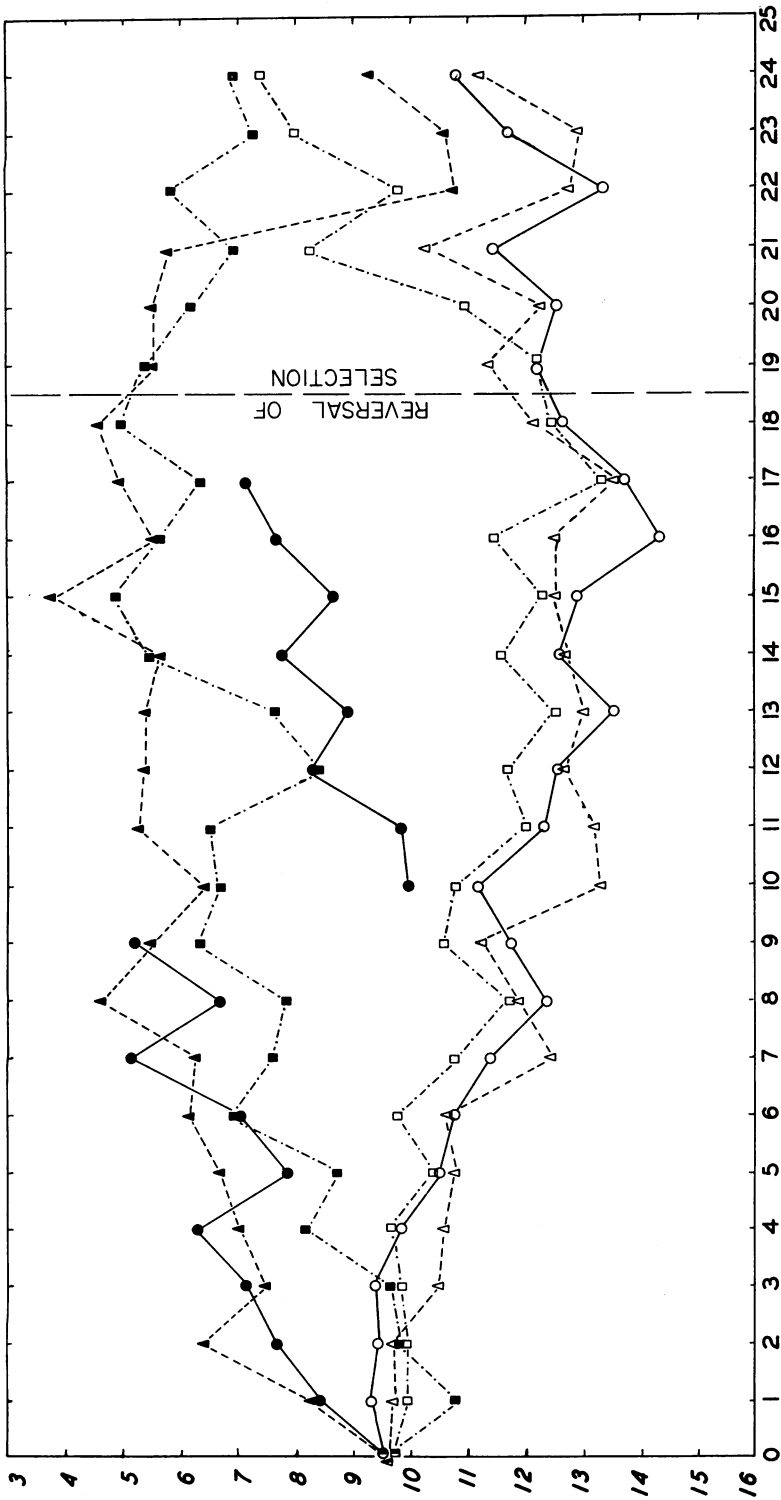


FIG. 1.—Selection for positive and negative geotaxis in *Drosophila pseudobscura* females. Ordinate, the geotactic score; abscissa, generations of selection. Solid lines and circles, polymorphic populations; dashed lines and squares, monomorphic AR; dot and dash and triangles, monomorphic CH. Black symbols, negative selection; white symbols, positive selection.

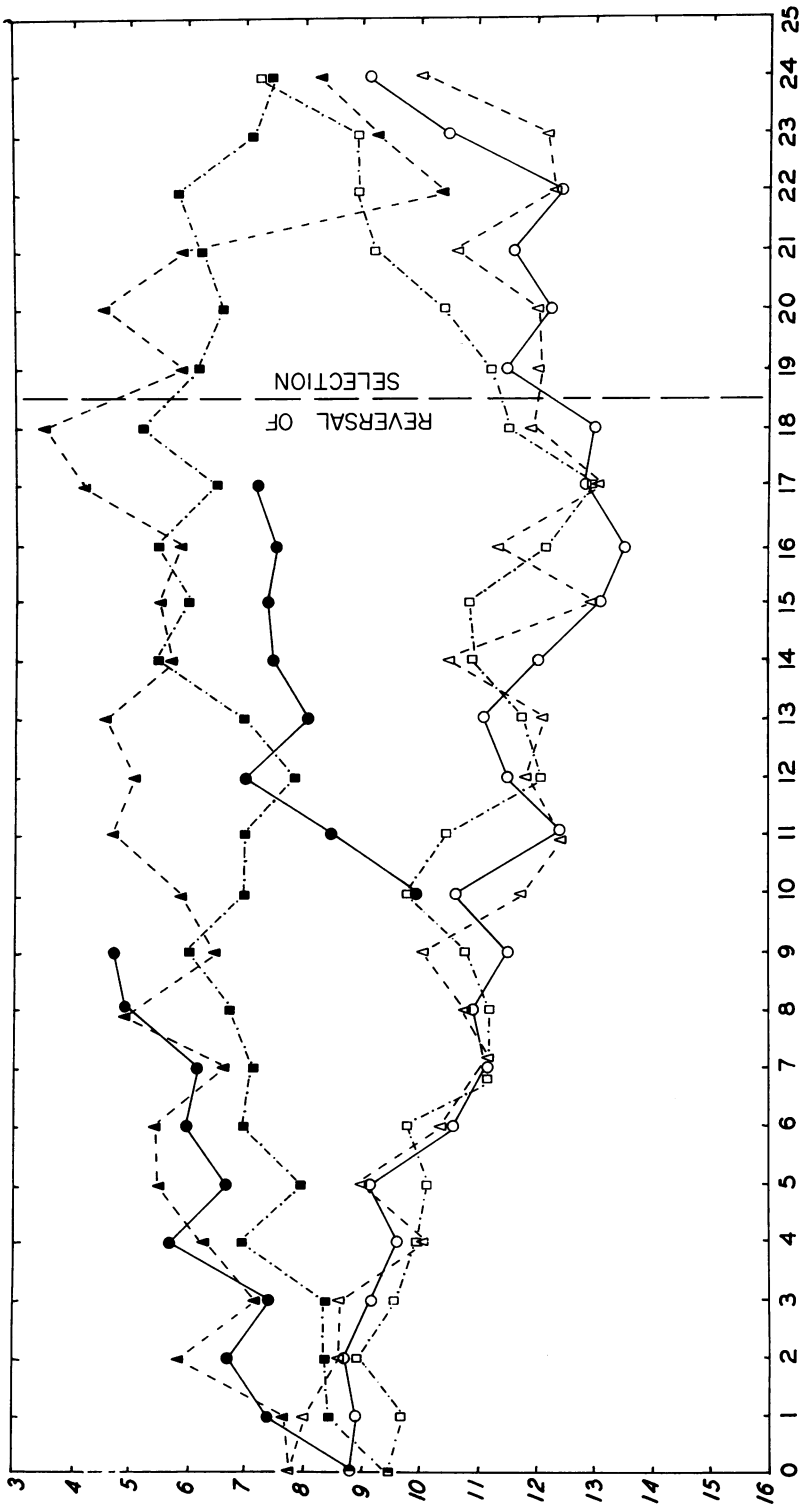


FIG. 2.—Selection for positive and negative geotaxis in *Drosophila pseudoobscura* males. The meaning of the symbols is given in the caption for Figure 1.

TABLE 1
SELECTION FOR POSITIVE GEOTAXIS IN MONOMORPHIC AND POLYMORPHIC POPULATIONS OF
Drosophila pseudoobscura

(The highest possible score is 16, the lowest 1. In Tables 1 and 2, the scores of the females are placed on the left and of the males on the right. Further explanation in text.)

Genera- tion	Monomorphic AR		Monomorphic CH		Polymorphic	
P	9.67 ± 0.21	7.77 ± 0.26	9.72 ± 0.22	9.45 ± 0.20	9.51 ± 0.24	8.80 ± 0.25
1	9.63 ± 0.25	7.97 ± 0.24	9.89 ± 0.24	9.62 ± 0.23	9.25 ± 0.22	8.92 ± 0.22
2	9.63 ± 0.27	8.54 ± 0.24	9.85 ± 0.25	8.90 ± 0.22	9.41 ± 0.26	8.67 ± 0.27
3	10.35 ± 0.25	8.57 ± 0.26	9.72 ± 0.22	9.45 ± 0.20	9.29 ± 0.24	9.10 ± 0.24
4	10.43 ± 0.25	10.03 ± 0.26	9.66 ± 0.23	10.00 ± 0.25	9.85 ± 0.31	9.26 ± 0.21
5	10.69 ± 0.23	8.99 ± 0.26	10.24 ± 0.25	10.16 ± 0.24	10.46 ± 0.20	9.11 ± 0.26
6	10.65 ± 0.25	10.38 ± 0.26	9.62 ± 0.25	9.76 ± 0.22	10.70 ± 0.28	10.53 ± 0.25
7	12.23 ± 0.24	11.18 ± 0.26	10.68 ± 0.26	11.11 ± 0.23	11.29 ± 0.27	11.59 ± 0.24
8	11.85 ± 0.29	10.81 ± 0.27	11.67 ± 0.24	11.14 ± 0.23	12.23 ± 0.22	10.91 ± 0.26
9	11.16 ± 0.26	10.00 ± 0.28	10.44 ± 0.27	10.74 ± 0.24	11.68 ± 0.24	11.43 ± 0.24
10	13.22 ± 0.21	11.73 ± 0.29	10.66 ± 0.24	9.76 ± 0.23	11.09 ± 0.24	10.55 ± 0.27
11	13.15 ± 0.21	12.39 ± 0.23	11.98 ± 0.23	10.42 ± 0.24	12.23 ± 0.22	12.36 ± 0.24
12	11.67 ± 0.23	11.79 ± 0.25	11.62 ± 0.24	12.05 ± 0.21	12.52 ± 0.22	11.41 ± 0.25
13	12.90 ± 0.22	12.08 ± 0.27	12.42 ± 0.21	11.72 ± 0.20	13.45 ± 0.20	11.06 ± 0.26
14	12.57 ± 0.22	10.41 ± 0.29	11.52 ± 0.22	10.84 ± 0.23	12.51 ± 0.22	11.98 ± 0.23
15	12.42 ± 0.24	12.96 ± 0.23	12.18 ± 0.19	10.87 ± 0.22	12.90 ± 0.21	13.07 ± 0.21
16	12.44 ± 0.24	11.26 ± 0.24	11.39 ± 0.20	12.12 ± 0.23	14.21 ± 0.16	13.50 ± 0.21
17	13.55 ± 0.18	13.08 ± 0.21	13.27 ± 0.20	12.85 ± 0.18	13.78 ± 0.19	12.73 ± 0.22
18	12.02 ± 0.24	11.79 ± 0.31	12.37 ± 0.21	11.45 ± 0.23	12.52 ± 0.21	13.00 ± 0.18
Selection Reversed						
19	9.31 ± 0.19	11.95 ± 0.24	12.15 ± 0.22	11.15 ± 0.22	12.14 ± 0.23	11.45 ± 0.21
20	12.25 ± 0.23	11.98 ± 0.23	10.87 ± 0.24	10.28 ± 0.24	12.53 ± 0.21	12.13 ± 0.24
21	10.13 ± 0.17	10.56 ± 0.17	8.23 ± 0.27	9.06 ± 0.28	11.34 ± 0.29	11.60 ± 0.27
22	12.85 ± 0.19	12.35 ± 0.22	9.77 ± 0.23	8.87 ± 0.23	13.30 ± 0.19	12.39 ± 0.28
23	12.94 ± 0.20	12.11 ± 0.24	7.91 ± 0.24	8.84 ± 0.25	11.66 ± 0.24	10.46 ± 0.26
24	11.18 ± 0.25	9.97 ± 0.29	7.21 ± 0.20	7.16 ± 0.20	10.72 ± 0.23	9.03 ± 0.24
25	10.24 ± 0.26	10.51 ± 0.26	7.59 ± 0.21	6.72 ± 0.21	9.96 ± 0.21	8.63 ± 0.23

for a negative geotaxis. The gene arrangements were thus determined in 300 third chromosomes from each population. The negative population proved to have only AR chromosomes, while in the positive one the frequencies were 66.0 per cent AR and 34.0 per cent CH chromosomes. The negative "polymorphic" population has, thus, become a monomorphic AR. It was discarded, and a new population was started, in order to test whether the elimination of CH in the negatively selected polymorphic population might have been accidental.

The initial material for this new polymorphic population was obtained by crossing AR flies from the positively selected monomorphic AR, with CH flies from the negatively selected monomorphic CH population. The F₁ flies were run through the maze, and gave a mean score of 9.97 in both sexes. They were, thus, weakly positively geotactic. Since the parents had scores of between 10 and 11 (the AR population), and 6 (the CH population), the performance of the hybrids is intermediate, perhaps with a tendency toward dominance of the positive geotaxis. The new population was subjected to a negative selection, responded quickly (Figures 1 and 2), and after seven generations of selection (corresponding to the 17th generation in the other populations) achieved a record of about 7. A cytological examination showed that it had lost its CH chromosomes, and became monomorphic AR.

At the same time (the 17th generation) the positively selected polymorphic population had 53.0 per cent AR and 47.0 per cent CH. It has increased the fre-

TABLE 2

SELECTION FOR NEGATIVE GEOTAXIS IN MONOMORPHIC AND POLYMORPHIC POPULATIONS OF *Drosophila pseudoobscura*

Generation	Monomorphic AR		Monomorphic CH		Polymorphic	
P	9.67 ± 0.21	7.77 ± 0.26	9.72 ± 0.22	9.45 ± 0.20	9.51 ± 0.24	8.80 ± 0.25
1	8.18 ± 0.25	7.52 ± 0.26	10.87 ± 0.26	8.34 ± 0.25	8.73 ± 0.25	7.35 ± 0.23
2	6.24 ± 0.24	5.83 ± 0.21	9.67 ± 0.27	8.38 ± 0.27	7.57 ± 0.26	6.63 ± 0.23
3	7.37 ± 0.26	7.19 ± 0.23	9.54 ± 0.24	8.39 ± 0.25	7.07 ± 0.24	7.34 ± 0.25
4	6.98 ± 0.23	6.26 ± 0.25	8.04 ± 0.25	6.97 ± 0.21	6.25 ± 0.23	5.66 ± 0.21
5	6.64 ± 0.26	5.42 ± 0.23	8.72 ± 0.27	7.92 ± 0.20	7.80 ± 0.22	6.26 ± 0.26
6	6.06 ± 0.25	5.33 ± 0.22	6.91 ± 0.25	6.94 ± 0.31	6.93 ± 0.25	5.93 ± 0.26
7	6.11 ± 0.24	6.52 ± 0.25	7.52 ± 0.25	7.12 ± 0.23	5.08 ± 0.23	6.10 ± 0.22
8	4.60 ± 0.19	4.81 ± 0.21	7.88 ± 0.26	6.64 ± 0.23	6.61 ± 0.28	4.87 ± 0.26
9	5.45 ± 0.24	6.39 ± 0.25	6.17 ± 0.22	5.96 ± 0.25	5.10 ± 0.28	4.66 ± 0.25
10	6.35 ± 0.31	5.84 ± 0.25	6.48 ± 0.23	6.59 ± 0.24	Re-Started	
11	5.18 ± 0.24	5.70 ± 0.23	6.42 ± 0.23	6.39 ± 0.22	9.97 ± 0.27	9.97 ± 0.31
12	5.22 ± 0.27	5.08 ± 0.34	8.25 ± 0.25	7.74 ± 0.30	9.89 ± 0.28	8.45 ± 0.31
13	5.31 ± 0.22	4.57 ± 0.20	7.54 ± 0.25	6.97 ± 0.27	8.15 ± 0.27	6.96 ± 0.21
14	5.62 ± 0.21	5.65 ± 0.18	5.48 ± 0.22	5.48 ± 0.23	8.91 ± 0.28	8.01 ± 0.27
15	3.80 ± 0.19	5.42 ± 0.24	4.70 ± 0.23	5.98 ± 0.25	7.76 ± 0.29	7.47 ± 0.29
16	5.45 ± 0.24	5.83 ± 0.25	5.48 ± 0.23	5.33 ± 0.23	8.61 ± 0.28	7.33 ± 0.27
17	4.92 ± 0.25	4.13 ± 0.23	6.21 ± 0.24	6.44 ± 0.25	7.61 ± 0.30	7.60 ± 0.27
18	4.40 ± 0.18	3.41 ± 0.19	4.81 ± 0.20	5.22 ± 0.21	7.06 ± 0.29	7.19 ± 0.29
	Selection Reversed					
19	5.43 ± 0.23	5.85 ± 0.28	5.23 ± 0.24	6.17 ± 0.22
20	5.42 ± 0.24	4.51 ± 0.23	6.14 ± 0.24	6.55 ± 0.29
21	5.78 ± 0.23	5.88 ± 0.26	6.88 ± 0.27	6.18 ± 0.22
22	10.83 ± 0.27	10.30 ± 0.26	5.78 ± 0.25	5.72 ± 0.22
23	10.50 ± 0.23	9.26 ± 0.21	7.12 ± 0.29	7.01 ± 0.28
24	9.14 ± 0.25	8.28 ± 0.25	6.91 ± 0.25	7.28 ± 0.22
25	9.00 ± 0.20	7.61 ± 0.21	6.82 ± 0.22	7.25 ± 0.22

quency of CH, while the negatively selected population lost its CH chromosomes. Polymorphic AR and CH populations kept in population cages at 25°C, but not selected for geotaxis, reach equilibria at about 70 per cent AR and 30 per cent CH. The conclusion is inescapable that selection for negative geotaxis favors the carriers of AR chromosomes, while that for positive geotaxis gives an advantage to the AR/CH heterokaryotype. The evidence that it is the heterokaryotype, and not simply the carriers of CH chromosomes that is favored, is twofold. In the first place, the AR chromosomes are not lost in the positively selected polymorphic population. Secondly, this population shows a disturbance of the Hardy-Weinberg equilibrium in favor of the heterokaryotype. In the 17th generation of selection, 64 per cent of the larvae examined from this population belonged to the AR/CH heterokaryotype. In this population, the selection has evidently favored a gene pool, which made the AR/CH and CH/CH homokaryotypes semilethal, and thus achieved a population in which almost two thirds of the individuals were the heterokaryotypes AR/CH. Populations of this sort are known in some species of *Drosophila* also in nature.^{6, 7}

Since by the 17th generation the selection gains were becoming small, the experiment was redirected as follows. The negatively selected polymorphic population which lost its CH chromosomes was discarded. The remaining five populations were each subdivided in two; in one division the selection was relaxed, the flies being transferred to fresh cultures, generation after generation, without being run through the maze; in the other division the selection was reversed, the old positive populations being now selected for negative geotaxis, and vice versa.

The results of the reversed selection are shown in Tables 1 and 2 and in Figures

TABLE 3
THE GEOTAXIS SCORES BEFORE AND AFTER THE RELAXATION OF SELECTION

	Monomorphic AR		Monomorphic CH		Polymorphic	
	♀	♂	♀	♂	♀	♂
Positive Selection						
Before relaxation	12.07	11.79	12.37	11.44	12.52	13.00
After relaxation	10.09	9.76	12.28	10.85	11.94	11.18
Negative selection						
Before relaxation	4.40	3.41	4.81	5.22
After relaxation	4.71	3.59	6.19	5.68
Difference						
Before relaxation	7.67	8.38	7.56	6.22
After relaxation	5.38	6.17	6.09	5.17

1 and 2. The populations responded rapidly; in fact, the back-selection acted even more quickly than the forward selection did in the original populations. After six generations of back-selection (the 24th generation in the Tables and Figures) the differences between the lines which were originally so striking almost disappeared. The relaxation of the selection resulted also in some losses of the differences previously achieved, as can be seen in Table 3. However, the relaxation of the selection gave, unsurprisingly, a smaller degree of convergence than the back-selection.

A cytological examination of the populations in which the selection was relaxed or reversed gave most interesting results. The polymorphic population selected for 18 generations for positive geotaxis, and then having passed 11 generations without selection, contained 50 per cent of AR and of CH chromosomes. Among the 150 larvae examined, 78 were AR/CH heterozygotes, a good fit to the Hardy-Weinberg expectation of 75. The population back-selected for 7 generations in the negative direction after the 18 generations of the positive selection had, in a sample of 200 larvae, 99 AR/CH heterokaryotypes and 101 CH/CH homokaryotypes, and not a single AR/AR. Here the AR chromosomes have evidently become lethal in double dose. This is the more unexpected, since the negative selection in the original polymorphic population resulted in the diminution of CH and in fixation of AR.

The selection has not been equally efficient in the different populations. In Figures 1 and 2 it can be seen at a glance that, while the polymorphic and the monomorphic AR populations were for the most part close at all stages of selection, the monomorphic CH lagged behind. Table 4 makes this fact even more evident.

TABLE 4
DIFFERENCES BETWEEN THE GEOTAXIS SCORES IN POLYMORPHIC AND MONOMORPHIC POPULATIONS
SELECTED FOR POSITIVE AND NEGATIVE RESPONSES

Generation	Mono AR	Mono CH	Polymorphic	Generation	Mono AR	Mono CH
1	0.95	0.15	1.22	14	6.85	5.70
2	3.05	0.35	1.95	15	8.08	6.18
3	2.18	0.62	1.99	16	6.21	6.35
4	3.60	2.32	3.60	17	8.79	6.74
5	3.81	1.87	2.58	18	8.02	6.92
6	4.82	2.76	4.19	Selection Reversed		
7	5.34	3.53	5.14	19	5.00	5.95
8	6.62	4.15	5.83	20	7.15	4.23
9	7.59	4.53	6.69	21	4.52	2.12
10	6.38	3.68	...	22	2.04	3.57
11	7.83	4.78	...	23	2.65	1.30
12	6.53	3.84	...	24	1.86	0.09
13	7.55	4.81	...			

This table shows the divergence achieved after various generations of selection between the scores of the populations selected in the opposite directions (females and males combined). The divergence is consistently greater in the monomorphic AR than in the monomorphic CH populations. The selection in the polymorphic population is about as effective as it is in the monomorphic AR, and more so than in the monomorphic CH.

Discussion.—The geotactic response of *Drosophila pseudoobscura* is evidently under a genetic control. Although the three initial populations in our experiments were originally approximately neutral to gravity, they responded to both positive and to negative selections, and gave rise to populations the members of which tended to move downward or upward respectively. The nature of the genetic variance which underlies these selection responses constitutes an interesting problem. By the 17th and 18th generations of the selection the increments gained per generation became small, indicating that a plateau was being approached. This did not, however, mean an exhaustion of the genetic variance; on the contrary, the reversal of the selection gave a rapid response, if anything more rapid than that to the original selection, and by the 24th generation the populations were almost back to their preselectional states as far as their geotactic scores were concerned. Some loss of the selectional gains has also occurred in the lines in which the selection was relaxed for 11 generations. This suggests, though does not completely prove, that the genetic variance was in part not simply additive. The modal geotactic reaction of the original populations, which happened to be close to the neutrality point, was a result of a gene pool held in a balanced state. The balance was displaced by the artificial selection, and upon relaxation of this selection, was partly restored by natural selection, perhaps owing to the adaptive advantage of the heterozygous state. This is an example of what Lerner⁸ has termed "genetic homeostasis." The remarkably rapid response to the back selection was due to the artificial and the natural selections reinforcing each other.

The selection, both in the plus and in the minus directions, was effective in populations monomorphic as well as polymorphic for the third chromosome gene arrangements, AR and CH. The observed variance was about equally large in all the populations, and it did not undergo any substantial change during the selection. The relatively less rapid selectional gains in the monomorphic CH populations may perhaps be related to the fact that CH chromosomes are not as frequent in nature as AR chromosomes in the geographic region from which the source material was derived.

The behavior of the polymorphic populations under selection is remarkable. The selection for a negative geotactic response favored AR chromosomes, while the heterokaryotype AR/CH induced a positive geotaxis on its carriers. This is the first recorded instance of chromosomal polymorphism derived from natural populations conditioning a behavior difference unconnected with sex; Spiess⁹ has, however, discovered differences in mating propensity among karyotypes of *Drosophila persimilis*. It must, however, be made clear that the behavior is not influenced directly by the gene arrangement as such, but rather by the gene contents of the chromosomes having certain gene orders. This is demonstrated by the chromosomal changes observed in the polymorphic populations selected first for a positive geotaxis and then back-selected in the negative direction. The original selection fa-

vored the AR/CH heterokaryotype, and made the homokaryotypes subvital; the back-selection favored an AR chromosome which happened to be lethal in double dose, and resulted in a population which consisted of CH/CH homokaryotypes and AR/CH heterokaryotypes, but lacked AR/AR entirely.

Summary.—Using a classification maze constructed by Professor Jerry Hirsch, we have selected populations of *Drosophila pseudoobscura*, for a positive and for a negative geotactic behavior. The three initial populations were respectively monomorphic for AR, monomorphic for CH, and polymorphic for AR and CH gene arrangements in their third chromosomes. All the initial populations were about neutral to gravity, yet all responded both to plus and to minus selection. The plus selection favored AR chromosomes, while the negative selection favored the AR/CH heterokaryotype. Relaxation of the selection resulted in a partial relapse towards the original state. Reversal of the selection gave an almost complete return to the original state. In the polymorphic AR/CH population the back-selection favored an AR chromosome which was lethal in double dose.

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MATERNAL EFFECT OF MA-1+ ON XANTHINE DEHYDROGENASE OF DROSOPHILA MELANOGASTER, II. XANTHINE DEHYDROGENASE ACTIVITY DURING DEVELOPMENT*

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At least two loci are now known which control xanthine dehydrogenase in *Drosophila melanogaster*.¹ One of these, maroon-like eye-color (*ma-l*), is located on the X-chromosomes; the other, rosy eye-color (*ry*), is on the 3rd chromosome.² The mutants show many similarities. Both have a reddish-brown eye color due to a partial deficiency of the red eye pigment, and both lack detectable amounts of the enzyme, xanthine dehydrogenase.¹ As a result of this deficiency, *ma-l* and *ry* mutants accumulate the enzyme substrates (hypoxanthine and 2-amino-4-hydroxypteridine) and show no trace of the products (uric acid and isoxanthopterin) formed from these compounds.³ Xanthine dehydrogenase was partially purified from wild-type flies, and no activity could be detected in extracts of the mutants.⁴