GENETICS OF NATURAL POPULATIONS. XXIII. BIOLOGICAL ROLE OF DELETERIOUS RECESSIVES IN POPULATIONS OF DROSOPHILA PSEUDOOBSCURA[1]

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GENES, or polygene complexes, which are deleterious in double dose occur in heterozygous condition in natural populations of every species of Drosophila so far studied in this respect. There is good reason to believe that harmful recessives are frequent in heterozygous condition in many, and possibly in all, Mendelian populations in which inbreeding is not too prevalent. The biological role played by the deleterious recessives concealed in natural populations is, however, not understood. DOBZHANSKY and WRIGHT (1941) and WRIGHT, DOBZHANSKY, and HOVANITZ (1942) inferred that at least some of the apparently recessive lethals in populations *of Drosophila pseudoobscura* are to some extent deleterious also in heterozygotes. Certain alternative interpretations, which would have made the assumption of an incomplete recessivity of the lethals unnecessary, were, however, not excluded. STERN *et al.* (1952) showed that most of the sex-linked lethals arising in laboratory cultures of *D. melanogaster* were incompletely recessive, and WALLACE and KING (1952) found a like situation with autosomal lethals. CORDEIRO (1952) and PROUT (1952) adduced similar evidence for naturally occurring autosomal lethals in *D. willistoni*. MULLER (1950) advanced theoretical arguments to show that recessive hereditary defects in man should produce mildly incapacitating effects in heterozygotes.

However, not all lethals affect adversely the fitness of heterozygotes. Heterotic lethals were found in *D. melanogaster* by MASING (1938), TEISSIER (1942), WALLACE and KING (1952), and STERN *et al.* (1952). CORDEIRO and DOBZHANSKY (1954) observed that at least 4 out of 52 second-chromosome lethals found in natural populations of *D. willistoni* were heterotic in combination with some other chromosomes from the same populations. GUSTAFSSON (1946) and GUSTAFSSON, NYBOM, and WETTSTEIN (1950) discovered mutants in barley which were poorly viable in homozygotes but advantageous in heterozygotes. For other examples, see LERNER (1954). More data on the effects in heterozygous condition of various classes of genetic variants which occur in natural populations are obviously needed.

The most important gap in present knowledge is the complete dearth of information on the fitness of heterozygotes for genes and gene combinations which are not lethal but only mildly deleterious when homozygous. It is now becoming customary to distinguish complete lethals (genotypes which make the viability of their carriers equal to zero in a certain environment), semilethals (viability above zero but less than 0.5 of the average for a given population), subvitals (viability above 0.5 but sig-

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nificantly less than 1.0), normals (viability within two standard errors from 1.0), and supervitals (viability significantly above 1.0). For more precise definitions of subvitality and supervitality, and for a description of methods used to estimate the frequencies of subvital and supervital chromosomes, see WALLACE and MADDEN (1953) and DOBZHANSKY and SPASSKY (1953). The present article reports the results of experiments comparing the behavior of subvital and supervital chromosomes found in a natural population of *D. pseudoobscura*. We hope to show that there is no correlation between the viabilities of homozygotes and heterozygotes for such chromosomes, and that combining different chromosomes from the same population results in a great variety of reaction norms the adaptedness of which varies in different environments.

VIABILITY OF HOMOZYGOTES IN A TEXAS POPULATION

Samples of the population of *D. pseudoobscura* were collected in the neighborhood of Austin, Texas, in March–May of 1953 by one of the authors (TH.D.) in cooperation with DRS. M. J. D. WHITE, M. R. WHEELER, MESSRS. W. HEED, L. METTLER, and other colleagues. The wild males, or single sons of wild females, were crossed (in the laboratory in New York) to laboratory strains with suitable mutant markers used to analyze the viability of the homo- and heterozygotes for second chromosomes in *D. pseudoobscura*. This experimental procedure has been described by DOBZHANSKY and SPASSKY (1953) and in earlier papers, and need not be re-described here in detail. Its essence is that individuals homozygous for a given wild chromosome are obtained in cultures which produce also flies heterozygous for the same chromosome and for another chromosome carrying a dominant mutant gene marker (Bare = short bristles). This is done by intercrossing females and males heterozygous for a certain wild chromosome and a chromosome with Bare and a crossover suppressor. Provided that the homozygotes and the Bare heterozygotes are equally viable, the offspring of the intercross should consist of 33.3% non-Bare flies (homozygotes) and 66.7% Bare heterozygotes. In reality, the proportion of non-Bare flies varies in different cultures from 0 (if a wild chromosome is lethal to homozygotes) to 33.3% and above. The data actually obtained in the experiments with the chromosomes from Texas are summarized in table 2. These data were obtained in cultures raised in incubators at 25°C, and on culture medium inoculated with Fleischmann's yeast.

A control experiment consists in intercrossing Bare females and Bare males heterozygous for second chromosomes derived from *different* wild flies. The non-Bare flies obtained in the offspring are heterozygotes which carry two second chromosomes of different derivation. The viability of such flies is normal by definition (see DOBZHANSKY and SPASSKY 1953). The control data are reported in table 1. It can be seen that the mean frequency of non-Bare flies in control progenies is $34.20 \pm 0.26\%$. This is slightly but significantly higher than the ideal 33.33%. It follows that the Bare chromosome depresses slightly the viability of its carriers.

The data in table 2 may now be considered. The 27 wild second chromosomes which have produced test cultures with no non-Bare flies are evidently lethal when homozygous. Test cultures with more than 0 but less than 17.1% of non-Bare flies (half of the control value, 34.2%) contain semilethal second chromosomes; such chromosomes numbered 29. The lethal and semilethal chromosomes together were

TABLE 1

Percentages of non-Bare flies in 110 intercrosses which produce heterozygous flies

Percent non-Bare	Intercrosses	Percent non-Bare	Intercrosses
29	5	37	16
31	15	39	4
33	37	41	2
35	29	43	2

Mean percentage 34.20 ± 0.26%.

TABLE 2

Viability of homozygotes for 178 second chromosomes derived from the Texas population. The figures show the numbers of chromosomes that produce cultures with different percentages of non-Bare flies

Percent non-Bare	Chromosomes	Percent non-Bare	Chromosomes
0	27	19	2
1	7	21	2
3	2	23	3
5	1	25	7
7	6	27	10
9	6	29	21
11	0	31	31
13	2	33	26
15	2	35	12
17	3	37	7
		39	1
Total lethals & semilethals	56	Total quasi-normals	122

56, or 31.5 ± 3.5% of the total. The remaining 122 chromosomes gave test cultures with from 19% to 39% non-Bare flies; these chromosomes are designated "quasi-normals." Among the quasi-normals, there are included subvitals, normals, and supervitals.

THE SUBVITAL AND SUPERVITAL CHROMOSOMES

Among the 178 chromosomes the performance of which in the homozygosity tests is reported in table 2, we have chosen, for the experiments to be described below, 10 chromosomes which gave cultures with between 18.5% and 25% of non-Bare flies, and 10 chromosomes which gave cultures with more than 35% of non-Bare flies. The former are presumably subvital and some of the latter supervital and others normally viable when homozygous. The percentages are based on counts of several hundred flies, and thus have a standard error of about 2%. To reduce this error further, we re-tested these chromosomes by raising more cultures, all of them at 25° and on Fleischmann's yeast. One of the subvitals proved to contain a peculiar condition expressed in production of varying proportions of dwarf flies. This condition was caused possibly by transmission of an infecting agent. This chromosome was eventually lost. The summary records of the other chromosomes are shown in table 3.

TABLE 3

Viability records of the subvital and supervital chromosomes used in the experiments

Supervitals			Subvitals		
No. of the chromosome	Flies counted	Percent non-Bare	No. of the chromosome	Flies counted	Percent non-Bare
10	2743	36.1	81	1264	28.6
158	4843	34.9	14	1438	28.4
62	3495	34.8	120	1502	27.6
202	3123	34.1	121	1400	27.6
150	5024	33.8	39	2037	27.1
57	1914	33.6	53	1530	25.8
1	3519	33.4	43	1948	23.7
106	1688	32.8	31	1878	22.4
16	1971	32.2	140	1471	16.2
50	2026	31.5			

The homozygotes for the chromosomes Nos. 10, 158, 62, and 202 may be classed as normal or supervital under the conditions of the experiment, and Nos. 150, 57, 1, 106, 16, and 50 as normally or very slightly subnormally viable. These ten supervital and normal chromosomes produce, then, homozygotes of high viability, and will be symbolized below by an H. Chromosomes Nos. 81, 14, 120, 121, 39, and 53 are mildly subvital, Nos. 43 and 31 strongly subvital, and No. 140 falls just within the conventional range of semilethality. These nine chromosomes will be referred to as "low" and symbolized by an L.

The 19 chromosomes listed in table 3 are perpetuated in the laboratory as balanced strains; the balancing chromosome has the dominant marker Bare, the recessive glass, and an inversion which suppresses most of the crossing over (see DOBZHANSKY and SPASSKY 1953).

The main experiment

Crosses were arranged to produce homozygotes for high (ten crosses), homozygotes for low (nine crosses), and heterozygotes for the following 27 combinations of H and L chromosomes:

H × *H*	*H* × *L*	*L* × *L*
1 × 10	1 × 14	14 × 31
10 × 16	10 × 31	31 × 39
16 × 50	16 × 39	39 × 43
50 × 57	50 × 43	43 × 53
57 × 62	57 × 53	81 × 120
62 × 106	106 × 81	120 × 121
106 × 150	150 × 120	121 × 140
150 × 158	158 × 121	140 × 14
158 × 202	202 × 140	
202 × 1		

All these 46 crosses were arranged in a similar way. Namely, groups of 12 females and 12 males carrying the Bare-glass-Inversion chromosome and the desired wild

second chromosomes were placed together in bottles with the standard cream of wheat-molasses medium used in the laboratory. The parents were transferred every day to fresh culture bottles, so that the oviposition period in each culture was limited to about 24 hours. Thus many bottles with eggs representing the progenies of the same group of parents were obtained. Each bottle was then subjected to one of the following four conditions: (a) incubator at 25°C; (b) constant temperature room at 16°; (c) 3 days at 16°, followed by 4 days at 4°, by 1 day at 25°, by 3 days at 16°, by 4 days at 4°, etc., until all the flies emerged; this variable temperature series is recorded in the tables below as "4°"; (d) incubator at 27° until the adults began to emerge, then at 25°. Equal numbers of cultures were placed in each of these four environments and the bottles obtained on successive days were always placed in different environments.

The first series of experiments under these four conditions was made with non-autoclaved food inoculated with Fleischmann's yeast (F). The second series used the yeast *Kloeckeraspora apiculata* (K), and the third series the yeast *Zygosaccharomyces dobzhanskii* (Z). These yeasts were supplied by PROFS. H. PHAFF and A. B. DA CUNHA, and were used in some previous work (e. g., DOBZHANSKY and SPASSKY 1954). For the experiments with these yeasts, the bottles with the Drosophila culture medium were autoclaved, on cooling inoculated with a suspension of the proper yeast, and left stoppered for 3 days to let the yeast grow before the flies were introduced.

In all series of experiments, 6 replicate bottles were used for each temperature-yeast combination. When the flies began to emerge, counts were made at 3-day intervals until the eclosion was complete or until there was a possibility that the next generation was appearing. All cultures were made moderately overpopulated; the mean number of hatching adults counted per culture (for 2214 cultures) was 135.5, the numbers being in general highest at 16° and lowest at 27°. The total number of flies counted in this main experiment was 299,508. The results are summarized in table 4.

In table 4 are given the numbers of flies counted and percentages of the non-Bare class in the totals for each series of experiments. Now, as indicated, above, we have studied the homozygotes for 10 different supervital (H) and 9 different subvital (L) chromosomes, and also the heterozygotes for, respectively, 10, 9, and 8 combinations of H × H, H × L, and L × L chromosomes. Since the different chromosomes and chromosome combinations yield different viabilities, table 4 shows also the chi-squares, degrees of freedom (df) and probabilities (P) of obtaining heterogeneities as large as those observed from sampling errors.

Influence of temperature on homozygotes

As stated above, the ten "high" and nine "low" chromosomes were selected because they produced, in cultures fed on Fleischmann's yeast and at 25°C (F 25° in table 4 and in figures 1 and 2), highly viable and subvital homozygotes respectively. The viability of the homozygotes for each of these chromosomes under these conditions is shown in figures 1 and 2 by black squares (cf. also table 3). It is obviously desirable to know how viable are these homozygotes under environmental conditions other than those in which they were selected. Table 4 and figures 1 and 2 supply the answer.

TABLE 4

Numbers of the flies counted and percentages of non-Bare flies among them. Experiments at different temperatures, and with food inoculated with Fleischmann's yeast (F), with Kloeckeraspora (K), or with Zygosaccharomyces (Z) yeasts. In the H and L series the non-Bare flies were homozygous for chromosomes giving respectively high or low viability in double dose; in the H × H, H × L, and L × L series the non-Bare flies were heterozygous for different combinations of "high" and "low" chromosomes. Further explanation in text

Cross	t°C	Yeast	Flies counted	Percent non-Bare	χ^2	df	*P*
H	25	F	11,203	32.89	20.90	9	0.01
L	25	F	9,084	27.93	92.57	8	<0.001
H × H	25	F	12,662	33.60	14.87	9	0.09
H × L	25	F	12,413	33.67	4.04	8	0.85
L × L	25	F	10,762	33.60	9.53	7	0.22
H	16	F	16,805	33.28	11.50	9	0.25
L	16	F	13,319	33.13	13.96	8	0.08
H × H	16	F	18,151	33.70	21.43	9	0.01
H × L	16	F	16,009	33.54	10.45	8	0.22
L × L	16	F	13,450	33.69	3.44	7	0.85
H	27	F	5,712	25.44	46.60	9	<0.001
L	27	F	5,052	19.70	222.03	8	<0.001
H × H	27	F	6,144	32.68	15.31	9	0.08
H × L	27	F	5,053	32.83	6.72	8	0.56
L × L	27	F	6,174	31.32	5.95	7	0.52
H	4	F	10,185	33.24	14.86	9	0.09
L	4	F	9,111	31.92	13.88	8	0.08
H × H	4	F	10,389	38.10	13.25	9	0.15
H × L	4	F	9,402	36.94	21.55	8	0.006
L × L	4	F	7,977	37.07	7.02	7	0.42
H	25	K	15,874	31.87	39.51	9	<0.001
L	25	K	15,293	29.94	36.94	8	<0.001
H × H	25	K	16,380	34.49	33.70	9	<0.001
H × L	25	K	13,567	34.45	28.54	8	<0.001
L × L	25	K	12,824	33.92	11.57	7	0.12
H	16	K	19,408	32.41	17.88	9	0.04
L	16	K	17,515	32.71	31.18	8	<0.001
H × H	16	K	19,857	32.66	18.61	9	0.03
H × L	16	K	17,323	33.52	12.29	8	0.14
L × L	16	K	15,944	34.01	44.39	7	<0.001
H	27	K	4,558	29.22	45.90	9	<0.001
L	27	K	3,893	28.41	16.63	8	0.04
H × H	27	K	5,598	34.30	18.08	9	0.03
H × L	27	K	5,823	34.79	5.11	8	0.75
L × L	27	K	6,196	32.44	15.36	7	0.03
H	25	Z	12,593	31.33	15.06	9	0.09
L	25	Z	10,322	26.43	165.78	8	<0.001
H × H	25	Z	11,313	33.58	11.99	9	0.20
H × L	25	Z	10,281	33.42	9.51	8	0.30
L × L	25	Z	11,568	32.57	14.89	7	0.04
H	27	Z	5,978	29.49	16.64	9	0.06
L	27	Z	5,480	25.20	244.48	8	<0.001
H × H	27	Z	7,922	36.23	32.46	9	<0.001
H × L	27	Z	6,987	35.69	18.78	8	0.02
L × L	27	Z	9,339	34.87	15.65	7	0.03

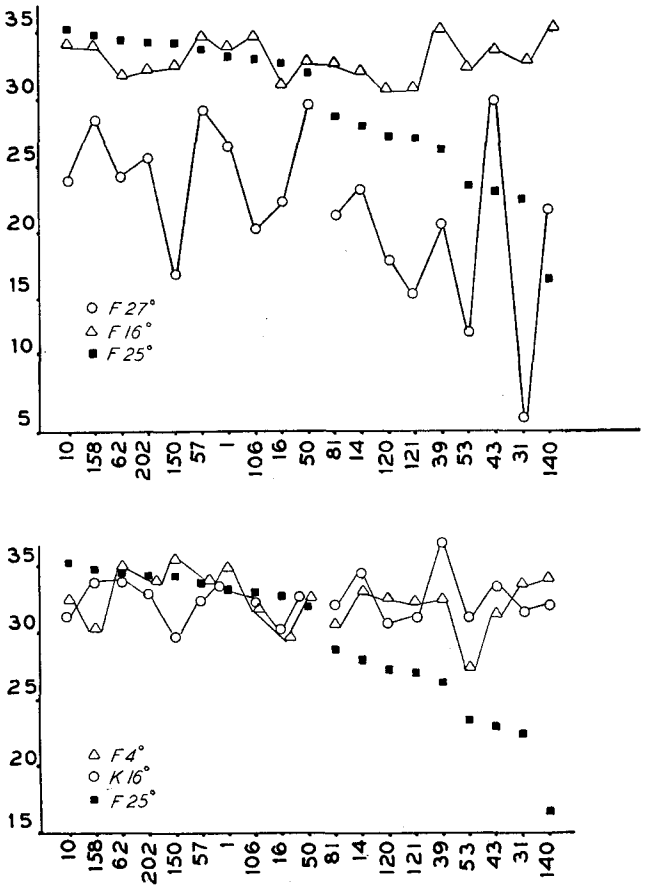

FIGURE 1.—Percentage of non-Bare flies emerging in various environments for homozygotes indicated by numbers (see text). Black squares indicate "standard" environment where homozygotes 10–50 are "high" and 18–140 are "low".

In cultures fed on Fleischmann's yeast but kept at 16° or at the variable low temperature (F 16° and F 4° in fig. 1 and table 4) the performance of the chromosomes is radically altered. In the first place, the homozygotes for H chromosomes are now, on the average, almost equal in viability to the homozygotes for L chromosomes (33.28% and 33.13% respectively at 16°, and 33.24% and 31.92% respectively at 4°, table 4). In other words, the average differences between the homozygotes which were supervital and subvital at 25° have largely disappeared at the lower temperatures. In fact, some of the highest proportions of non-Bare flies have been observed in cultures involving L chromosomes (chromosomes Nos. 39 and 140 at 16° and No. 140 at 4°, see fig. 1). It is interesting to note that the homozygotes for the chromosome No. 140 had the lowest viability at 25° (table 3 and fig. 1). Furthermore, at 16° the average viability of the homozygotes is only slightly lower (33.28% and 33.13%) than that of the heterozygotes (33.54% to 33.70%, table 4). At the variable low temperature

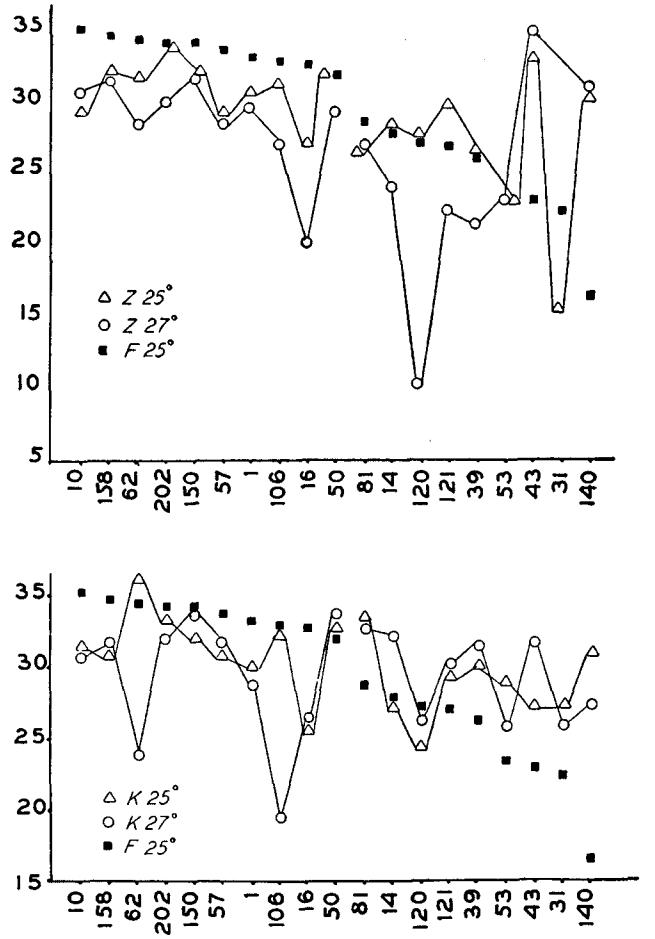

FIGURE 2.—Percentage of non-Bare flies emerging in various environments for homozygotes indicated by numbers (see text). Black squares indicate "standard" environment where homozygotes 10–50 are "high" and 18–140 are "low".

(4°, table 4) this is, however, not the case (31.92% and 33.24% for the homozygotes, 36.94% to 38.10% for the heterozygotes). It will be shown below that the homozygotes tend to be less fit than the heterozygotes in variable environments.

At high temperature and on Fleischmann's yeast (F 27° in fig. 1 and table 4) the situation changes again. The chromosomes which had similar records at 25° may behave quite differently at 27°, and vice versa. Thus, chromosome No. 43 produced semilethal homozygotes at 25°, but at 27° these homozygotes are as viable as any in either the "low" or the "high" groups. Conversely, the homozygotes for chromosome No. 31 are about as viable as No. 43 at 25°, but almost completely lethal at 27°. Chromosome No. 150 produced normally viable homozygotes at 25° but it is semilethal at 27°. The viability records of the different chromosomes at 27° are highly heterogeneous, as shown by the large chi-squares in the H 27 F and L 27 F lines in

table 4. The only respect in which the viability records at 25° and 27° are still consistent is that the mean viability of the homozygotes for H chromosomes is higher than that for L chromosomes (25.44% and 19.70%, table 4).

Influence of nutrition on homozygotes

Changing the nutritional variable without changing the temperature also causes alterations in the viability of the homozygotes. At 25° in cultures fed on Kloeckeraspora (K 25° in fig. 2 and table 4) some chromosomes improve their viability records (Nos. 62, 81, 121, 39, 53, 43, 31 and 140), while others change for the worse (Nos. 10, 158, 150, 57, 1, 16, 120). In general, the H chromosomes are more often the losers and L the gainers; in other words, the homozygotes which are supervital on Fleischmann's yeast are mostly subvital on Kloeckeraspora, while those subvital on Fleischmann's may gain on Kloeckeraspora, although not to the extent of becoming supervitals. The mean for H chromosomes (31.87%) is nevertheless higher than that for L chromosomes (29.94%, table 4). Comparison of the cultures fed on Fleischmann's with those fed on Zygosaccharomyces at 25° (Z 25°, fig. 2 and table 4) reveals a story similar to that in Kloeckeraspora cultures. The homozygote for chromosome No. 43 shows a spectacular improvement and is normal or even supervital on Zygosaccharomyces. A great improvement is also observed with No. 30, which is semilethal on Fleischmann's but normally viable on Zygosaccharomyces.

At 27°C and with Zygosaccharomyces food (Z 27° in fig. 2 and table 4) the viability of all homozygotes for H chromosomes is reduced; most of the L chromosomes also lose, but Nos. 43 and 140 gain very strikingly. The mean for H chromosomes is higher (29.49%) than for L (25.20%). The Kloeckeraspora-fed cultures at 27° (K 27° in fig. 1 and table 4) behave somewhat differently. Compared to the Fleischmann's fed cultures, the homozygotes for H chromosomes become more or less strongly reduced in viability (except Nos. 150 and 50), but the L chromosomes are mostly improved (except No. 81). The result is that the average for H chromosomes (29.22%) is not significantly higher than for L chromosomes (28.41%).

At 16° and with Klockeraspora-fed cultures (K 16° in fig. 1 and table 4) the viabilities of the homozygotes for H and L chromosomes become alike on the average (32.41% and 32.71% respectively). This does not mean, however, that the viabilities of all homozygotes have become uniform; indeed, the chi-square shows that a very significant heterogeneity continues to exist, at least among H chromosomes.

Comparing homozygotes with heterozygotes

At 25° and in cultures fed on Fleischmann's yeast, the homozygotes for H chromosomes are, on the average, about as viable as the heterozygotes, while the L homozygotes are less viable (table 4). This means, of course, only that the chromosomes were selected to produce just these effects, and that they continue to produce them on re-testing.

A much more significant result is that, in F 27°, F 4°, K 25°, K 27°, Z 25°, and Z 27° cultures, the mean viability of the H homozygotes is significantly lower than that of the heterozygotes in the same environment. This is less strikingly apparent

TABLE 5

Chi-squares for heterogeneity, comparing the viabilities of the heterozygotes carrying two subvital (L × L), one subvital and one supervital (L × H), and two supervital (H × H) chromosomes. All chi-squares have two degrees of freedom

Environment	Chi-square	Probability
F 25°C	0.03	0.98
F 4°C	3.00	0.22
F 16°C	1.32	0.50
F 27°C	3.77	0.15
K 25°C	1.20	0.50
K 16°C	7.53	0.02
K 27°C	8.29	0.015
Z 25°C	2.99	0.22
Z 27°C	3.88	0.15

in F 16° and K 16° cultures, but in these cultures the viabilities of all classes have become relatively uniform. The conclusion which follows is this: When a homozygote possesses a normal or a superior-to-normal viability, it does so only in a narrow range of environments.

Recessivity of subvital effects

The problem which interests us most is whether chromosomes which produce subvital homozygotes produce, on the average, less fit heterozygotes than do chromosomes which give normally viable or supervital heterozygotes. Table 4 contains data bearing on this problem. In every environment tried, we tested ten H × H heterozygotes, nine H × L heterozygotes, and eight L × L heterozygotes. Table 5 reports the chi-squares for heterogeneity for each of the nine environments. Each chi-square has two degrees of freedom. Only two of the nine chi-squares are significant between 1% and 2% levels. These are for cultures kept at 16° and 27° and fed on Kloeckeraspora. Now, referring back to table 4, one can see that in the K 27° series the highest viability average is for the H × L cultures, followed by H × H, and the lowest for L × L. This might suggest that chromosomes which are subvital in homozygous condition are subvital also when heterozygous. This is, however, invalidated by the K 16° series, in which the L × L average is the highest, followed by H × L and finally by H × H. This is the reverse of what would be expected if the subvitals were incompletely recessive.

The conclusion that the effects of the chromosomes when homozygous and when heterozygous are not correlated, can be tested further. Indeed, we have seen in figures 1 and 2 that the effects of a chromosome when homozygous are strongly modifiable by environmental changes. The average differences between chromosomes selected in one environment for supervital and subvital effects, tend to be more or less strongly reduced when the homozygotes are tested in other environments. For this reason, we have, in accordance with the suggestion of our colleague, PROFESSOR HOWARD LEVENE, computed rank order correlations for the effects of L chromosomes when homozygous and when heterozygous in a given environment. The results are shown in table 6.

TABLE 6

Rank order correlations between the effects of subvital chromosomes in homozygous and in heterozygous condition

Environment	Low × high	Low × low
F 25°C	+0.03	+0.24
F 4°C	−0.53	−0.52
F 16°C	+0.08	−0.43
F 27°C	−0.53	−0.83
K 25°C	+0.52	−0.21
K 16°C	+0.67	+0.24
K 27°C	+0.12	−0.40
Z 25°C	+0.43	−0.12
Z 27°C	−0.10	+0.55

Of the 18 rank order correlation coefficients in table 6, exactly one half (9) are positive and the other half are negative. Now, a significant positive correlation would indicate that, for each environment, a chromosome which is favorable in homozygotes is favorable also in heterozygotes, and vice versa. A significant negative correlation would indicate an opposite conclusion. In reality, only one of the positive correlations (+0.67, for K 16°) is significant at about the 5% level, and the same is true for one negative correlation (−0.83, for F 27°). The algebraic sum of all the correlations in table 6 is -0.79 ± 1.55, which is clearly not significant. We may conclude that no correlation between the effects of a chromosome when homozygous and when heterozygous is apparent in our data.

Heterogeneity of heterozygotes

From the absence of a correlation between the viability effects of chromosomes in homozygotes and heterozygotes, it does not follow that the heterozygotes are simply "normal" flies which are all more or less alike. They are not. Table 4 supplies the evidence that of the 27 classes of heterozygotes (3 groups, each tested in 9 different environments), only 13 do not show evidence of heterogeneity (probabilities 0.1 or higher). Among the remainder, 2 correspond to probabilities between 0.05 and 0.10, 6 between 0.01 and 0.05, and 6 to probabilities below 0.01. The conclusion may also be re-stated as follows: The viability of a heterozygote in a given environment depends on the nature of the chromosomes (viz., gene complexes) which it carries, but not on the effects which these chromosomes would have in double dose.

A word of caution must be added at this point. Examination of table 4 shows that the percentages of non-Bare flies, in cultures producing heterozygotes, were lower in some environments (F 27°) than in other environments (F 4°, Z 27°). This does not necessarily mean that all the chromosome combinations studied do better or worse respectively in these environments. Indeed, all the cultures produced wild type (= non-Bare) flies and flies which carried a chromosome containing a dominant mutant gene Bare, which does have some effects on the viability of its carriers (table 1). These effects are, naturally, subject to modification by the environments used in our experiments.

DISCUSSION

Except for dominant lethals, a certain time interval, which may embrace several or many generations, elapses between the origin of a deleterious mutant and its elimination from a Mendelian population. This interval is especially long for recessive mutants whose deleterious effects are sheltered from natural selection by being concealed in heterozygotes. The existence in Mendelian populations of a concealed store of deleterious variants is, then, simply a consequence of the less than perfect efficiency of natural selection. This is, however, only a part of the story, and, possibly, biologically the least meaningful part. Since the genotypes which are adaptively negative in some environments may prove positive in other environments, the concealed genetic variability may be regarded as a store of genetic raw materials (cf. DOBZHANSKY 1937; MATHER 1943; and other work). Owing to sexual reproduction, recombination of the genetic components of this store yields a large variety of genotypes, some of which fit the changing demands of the environment. This point of view remains valid, but it now appears that it is also an oversimplification.

Investigation of the inversions found in many species of Drosophila has revealed that the adaptedness of some natural populations rests to a considerable extent on a high incidence in these populations of heterotic inversion heterozygotes (cf., DOBZHANSKY 1951 for a review; also WALLACE 1954). It is formally correct, but certainly not very enlightening, to say that the low fitness of the inversion homozygotes is due to "deleterious recessives." Anyway, natural selection acts to perpetuate these recessives in the population rather than to eliminate them. One may also argue about whether a population consisting only of homozygotes would necessarily be ill-adapted (CAIN and SHEPPARD 1954), but it is a fact that natural selection establishes equilibrium frequencies of the inversions at which the mean adaptive value of the population as a whole is maximized. Now, the inversions proved to be only one of the mechanisms for maintaining balanced heterozygosis in populations. Recent work has shown that a considerable majority of the chromosomes in Drosophila populations are deleterious in homozygotes (WALLACE and MADDEN 1953; DOBZHANSKY and SPASSKY 1953, 1954). The fate of a chromosome under selection depends chiefly on the fitness of the gene complex it contains when it is in heterozygous combinations with other gene complexes which occur in the same Mendelian population; the fitness of the homozygotes is in general less important because of their rarity (WALLACE and KING 1952; WALLACE 1955; CORDEIRO and DOBZHANSKY 1954; and especially LERNER 1954). Some "deleterious recessives" are, thus, not fleeting but relatively permanent components of the gene pool of Mendelian populations. The data reported in the present article bear directly on this point: The heterozygotes which contain chromosomes which are subvital when homozygous have the same fitness as do heterozygotes for chromosomes which are normally viable or even supervital when homozygous.

CORDEIRO and DOBZHANSKY (1954) showed that different heterogeneous combinations, which carry pairs of chromosomes taken at random from the same population, vary in fitness in the same environment. The experiments described above confirm and extend this observation. "Normal" or "wild type" flies are an assem-

blage of many different genotypes, with different reaction norms and presumably also different ecological optima. In a way, this proves for Drosophila only what is so obvious in human populations, in which no two individuals are alike and often show their unlikeness by different reactions to the environment. But it is not obvious, and would be hard to foresee on theoretical grounds that the great variety of the reaction norms is an outcome of different combining ability of gene complexes which are mostly deleterious when homozygous. The load of mutations which a population carries is a dead weight only insofar as these mutations are deleterious both in homozygous and heterozygous condition, and in combination with most other genetic variants in the gene pool of the population. There is at least presumptive evidence that this is the case for many, though not for all, major mutations. We do not yet know how often the minor mutational changes are thus unconditionally harmful. But it is now apparent that the adaptive "norm" of a species established by natural selection is not genetically monolithic; it encompasses a large diversity of genetic elements, many of which show unexpected and unwelcome properties when homozygous.

SUMMARY

The effects in homozygous condition of 178 wild second chromosomes from a Texas population were studied at 25°C and in cultures fed on Fleischmann's yeast (*Saccharomyces cerevisiae*). From this sample, 10 chromosomes were selected which produced normally viable or supervital homozygotes (these chromosomes are denoted H), and 9 chromosomes which produced subvital homozygotes (these chromosomes are denoted L). The effects of these chromosomes when homozygous, and also when heterozygous in H × H, H × L, and L × L combinations, were studied at 4 different temperatures and in cultures fed on 3 different yeasts. The viability of the homozygotes proved to be highly sensitive to environmental modification (see figs. 1 and 2, and table 4). The viability of the heterozygotes is relatively more uniform and stable; nevertheless, the different heterozygotes are not all alike. It may be inferred that each heterozygous combination of chromosomes has a reaction norm somewhat different from other combinations. The important point is, however, that the heterozygotes which carry chromosomes which are subvital when homozygous, are not systematically inferior in fitness to those carrying chromosomes which are normally viable or supervital when homozygous. In this sense, the subvitality of most chromosomes found in natural populations, may be said to be completely recessive. However, since the heterozygous combinations are diversified, the chromosomes, or more precisely the gene complexes which they contain, do vary in their effects in heterozygotes. The subvitality in homozygous condition of most chromosomes found in a Mendelian population is a consequence of the gene pool being organized by natural selection to function as a coadapted system of numerous genetic variants.

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APPENDIX

Genetic variability of marginal populations

An hypothesis has been put forward that the amount of adaptive polymorphism present in a Mendelian population is positively correlated with the diversity of ecological niches which this population has mastered (DA CUNHA, BURLA, and DOBZHANSKY 1950). One of the tests of the validity of this hypothesis has been made by TOWNSEND (1952). He found that populations of *D. willistoni* which inhabit the margins of the distribution area of the species (Florida, Cuba) contain fewer chromosomal inversions than do populations of the central portion of the distribution area (central Brazil). The incidence of chromosomes which were lethal when homozygous was, however, only slightly lower in Florida than in central Brazil. Low frequencies of lethal chromosomes have, however, been recorded by CORDEIRO (unpublished) in certain populations from southern Brazil, near the southern margin of the distribution of *D. willistoni*. The population of *D. pseudoobscura* which has yielded the chromosomes used in the investigation described in the present article is a marginal one, since this species is rare or absent to the east of Austin, Texas (PROF. J. T. PATTERSON personal communication). The data in tables 1 and 2 permit the making of certain comparisons with other populations of the same species.

The frequency of lethal and semilethal second chromosomes in the Texas population is 31.5 ± 3.5% of the total (see above). This agrees very well with the figure for the populations of the Yosemite region of California, which is 33.0 ± 4.5%, but is higher than that for San Jacinto population, which is 21.3 ± 1.8% (see table 6, DOBZHANSKY and SPASSKY 1954). The California populations are not marginal. There is no evidence in our data that the marginal population in Texas has fewer lethals than do at least some non-marginal populations.

Another comparison is more instructive. Consider the 122 quasi-normal chromosomes listed in table 2. The mean frequency of non-Bare flies produced in cultures involving these chromosomes turns out to be 30.66 ± 0.38%. This can be compared with the mean frequency of 34.20 ± 0.26% in control cultures (table 1). Dividing the two figures we conclude that the mean viability of homozygotes for quasi-normal chromosomes from the Texas populations is 89.65 ± 1.11% of normal viability. The corresponding figure for Yosemite populations is 75.00 ± 1.22% (table 7 in DOBZHANSKY and SPASSKY 1954). The difference is clearly significant.

The data on the San Jacinto populations are, unfortunately, not quite comparable. The problem of genetic variability in marginal populations of a species is wide open. It seems possible that different classes of genetic variants do not behave in the same way. A marginal population may contain a more limited diversity of variants which serve as materials for construction of balanced polymorphic systems than a central population. Lethals and other drastic genetic changes may obey different rules.

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