GENETICS OF NATURAL POPULATIONS. XIII. RECOMBINATION AND VARIABILITY IN POPULATIONS OF DROSOPHILA PSEUDOOBSCURA

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INTRODUCTION

SPECIES of Drosophila show little variability as insect species go. Apart from a size variation which is mostly environmental, individuals that compose natural populations are as a rule uniform in appearance. Notwithstanding this external uniformity, natural populations of Drosophila contain a great store of genetic variants. The principal components of this store are recessive autosomal genes which, when homozygous, modify the viability, development rate, fertility, and other properties of their carriers. These genes are present in the populations mostly concealed in heterozygous condition (for further reference see DOBZHANSKY 1941; DOBZHANSKY and SPASSKY 1944; DUBININ 1946; IVES 1945; SPENCER 1944).

The concealed recessive variants are detected with the aid of experimental procedures, the essential part of which is obtaining individuals homozygous for chromosomes or chromosome sections which were carried in wild individuals in heterozygous state. Homozygotes display in their phenotype the effects of the recessives that were hidden in heterozygotes. The most frequently used version of this technique consists in crossing wild flies to laboratory strains which have some chromosomes marked by appropriate mutant genes and inverted sections. Flies are eventually obtained which carry a certain wild chromosome in duplicate, while the sibs of these flies carry the same chromosome only once. Comparison of the homozygotes and heterozygotes for the chromosome permits the detection of any recessive factors which this chromosome may carry.

It is evident that the above technique reveals only the net effects of homozygosis for whole chromosomes. How many genes may be involved in the production of these effects is not immediately apparent. Suppose, for example, that the homozygotes for a certain wild chromosome have a lower viability, a slower development rate, and some visible morphological peculiarity not present in their heterozygous sibs (such diversified effects of homozygosis for wild chromosomes are frequently met with in the actual experiments). What is the genetic basis of these changes? It is possible that the chromosome in question contains a gene for the low viability, another gene for the slow development, and still another for the morphological change. It is likewise possible that this chromosome carries a single gene with manifold effects responsible for the whole complex of characters. Finally, several or many genes may be involved in the production of each character, some of these genes having manifold effects and others apparently restricted fields of action. Experiments described in the present article have been devised to discriminate

between these possibilities. The importance of this problem from the standpoint of population genetics is considerable. The amount of potential variability stored in natural populations will be much greater if the properties of wild chromosomes are determined by multiple genes than if they depend upon single genes or very few genes. The amount of variability potentially available to the species determines its evolutionary plasticity. In the present experiments, the gene contents of three wild second chromosomes of *Drosophila pseudoobscura* from Mount San Jacinto, California, have been analyzed. It can be shown that these chromosomes carry complexes of genes which are capable of giving rise to a large amount of variability by recombination.

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THE BACKGROUND OF THE PRESENT INVESTIGATION

DOBZHANSKY, HOLZ, and SPASSKY (1942) have analyzed 302 wild second chromosomes of *Drosophila pseudoobscura* from three localities (Andreas Canyon, Piñon Flats, Keen Camp) on Mount San Jacinto, California. A very considerable amount of concealed variability was revealed by this analysis. The experimental methods, described and illustrated in the paper just referred to, are essentially as follows.

A wild male is crossed to females homozygous for the second chromosome recessive gene glass (*gl*). A single male from the offspring is outcrossed to females which carry in one of their second chromosomes the recessive *gl*, the dominant mutant gene Bare (*Ba*), and an inversion which causes a strong reduction of crossing over in the second chromosomes. This male must of necessity have one wild second chromosome and one second chromosome with the gene *gl*. In the progeny of the outcross, *Ba* females and males are selected and intercrossed. These *Ba* flies have a wild second, and a *Ba gl* inversion second chromosomes. In the offspring of the *Ba* flies, three classes of zygotes are formed: (1) wild type (non-Bare), homozygous for the wild second chromosome being tested; (2) Bare, heterozygous for the wild second and the *Ba gl* inversion second chromosomes; and (3) Bare glass, homozygous for the *Ba gl* inversion chromosome. The *Ba gl* homozygotes seldom survive as adults and are ignored in the counts. The theoretically expected ratio of the wild type to Bare flies is, therefore, 1:2, or 33.3 percent wild type to 66.7 percent Bare. This theoretical ratio, however, is realized only if the viability of individuals homozygous for the wild second chromosome and that of individuals heterozygous for the wild and for the *Ba gl* inversion second chromosomes are alike. In practice, this is far from always the case. The deviations from the expected ratios 33.3 percent wild to 66.7 percent Bare furnish a measure of the influence of homozygosis for the wild second chromosomes on the viability of the flies.

About 10 percent of the 302 wild second chromosomes tested contained

recessive lethal genes; the lethals are detected because in the crosses involving them the wild type class fails to appear, and the offspring of the *Ba gl* inversion females and males are Bar flies only. About 11 percent of the wild second chromosomes contain semilethals. A recessive semilethal is defined as a gene which destroys more than half of the homozygotes. The cultures involving semilethals consequently produce more than 0 but less than 16.7 percent of wild type individuals (the remainder, of course, being Bare). About 21 percent of the wild second chromosomes contain recessive genes which reduce the viability of the homozygotes to an extent not great enough to be classed as semilethals. The cultures with such "minus modifiers of the viability" produce more than 16.7, but significantly less than 33.3 percent, of wild-type individuals. Finally, a few of the chromosomes contain "plus modifiers of the viability" and give cultures which contain significantly more than 33.3 percent wild type.

The effects of homozygosis for wild second chromosomes on the duration of the development (development rate) of the flies are detected in a way similar in principle to the detection of the viability effects of the same chromosomes. The flies emerging from the pupae are classified and counted at frequent intervals (usually on alternate days) in the cultures in which the progenies of the wild/*Ba gl* inversion ♀ × wild/*Ba gl* inversion ♂ crosses are developing. Now, if the development rates of the wild type homozygotes and of the wild/*Ba gl* inversion heterozygotes are alike, then the ratios of wild:Bare flies in the successive counts will also be alike, within the limits of experimental errors. If, however, the wild chromosome carries a recessive gene, or genes, which slow down the development of homozygotes, then the proportions of wild type flies hatching in the cultures will be low in the first counts and will be relatively high in the later counts. This will, of course, be true regardless of the proportion of wild type individuals in the total count of the flies emerging in a given culture—in other words, regardless of the effects which a given second chromosome may have on the viability of the homozygotes. About 50 percent of the wild second chromosomes analyzed proved to contain recessive genes which, when homozygous, prolong the development of the flies; these genes are referred to as "minus modifiers of the development rate." A few chromosomes contain recessive "plus modifiers of the development rate": the homozygotes for these chromosomes hatch from the pupae significantly earlier than the Bare heterozygotes.

The detection of the recessive factors that produce externally visible morphological changes in the homozygotes requires no extended explanation. If the wild second chromosomes carry such factors, the non-Bare flies deviate from the wild type condition in their morphology.

The manifestation of recessive genes borne in the wild second chromosomes is frequently different in different environments. As shown by DOBZHANSKY and SPASSKY (1944), this environmental sensitivity is sometimes very high. Individuals homozygous for a certain wild chromosome, for example, may survive fairly well at some temperatures and may be little viable, or even com-

pletely lethal, at other temperatures. Apart from temperature, the manifestation of many genetic variants depends upon other culture conditions. Thus, the viability of homozygotes for some wild chromosomes may be relatively higher in cultures with low population densities than in more crowded cultures. Some homozygotes do, and others do not, respond to changes in the quality of the food on which the larvae develop. Chromosomes which in a certain environment produce similar effects may behave very differently in other environments.

The more the effects produced by homozygosis for wild chromosomes are investigated, the clearer it becomes that natural populations of *Drosophila pseudoobscura* contain a great variety of chromosomes with different gene contents. What is called the "normal" or "wild type" phenotype of the species is the average condition found in heterozygotes for *different* second, third, and fourth chromosomes. The number of these chromosomes with different gene contents present in natural populations is apparently high enough so that homozygotes for any one chromosome are in a minority. Furthermore, only few of the chromosomes may be called "normal," in the sense that individuals homozygous for them are indistinguishable from the average phenotype of the heterozygotes.

MATERIAL AND METHOD

Some 20 of the wild second chromosomes studied by DOBZHANSKY, HOLZ, and SPASSKY (1942) and by DOBZHANSKY and SPASSKY (1944) have been preserved in the laboratory in the form of balanced strains. In these strains, females and males carrying a given wild second chromosome and a *Ba gl* inversion second chromosome are selected and intercrossed in each generation. Since the inversion suppresses most of the crossing over, the wild chromosome is transmitted from generation to generation without change, except for the possible occurrence of mutations. Three wild second chromosomes have been picked for the present investigation. These are: chromosome No. 1015 from Andreas Canyon (to be referred to as "chromosome A"), No. 863 from Piñon Flats (chromosome B), and No. 975 from Andreas Canyon (chromosome C). A cytological examination in salivary gland cells showed all three chromosomes to have the normal gene arrangement. The other properties of these chromosomes are as follows (based on the data of DOBZHANSKY and SPASSKY 1944).

Chromosome A

Viability of homozygotes nearly normal at the temperature of 16½°C, semilethal at 21°, and completely lethal at 25½°. At temperatures at which some of the homozygotes survive, the development rate of the latter is considerably slower than that of the heterozygotes; the flies emerging from the pupae during two or more beginning days of hatching in a given culture are all Bare, wild type flies appearing only in later counts. Relatively more homozygotes survive in crowded than in underpopulated cultures.

Chromosome B

Viability of homozygotes normal or above normal at 16½° and 21°, normal

or slightly below normal at 25½°C. The results obtained in different cultures are uniform, regardless of the population density. Development rate is normal at all the temperatures tried.

Chromosome C

Viability of homozygotes normal or slightly above normal at 16½° and 21°, normal at 25½°. The results obtained in different cultures are uniform, regardless of the population density. Development rate is slightly slower in homo-

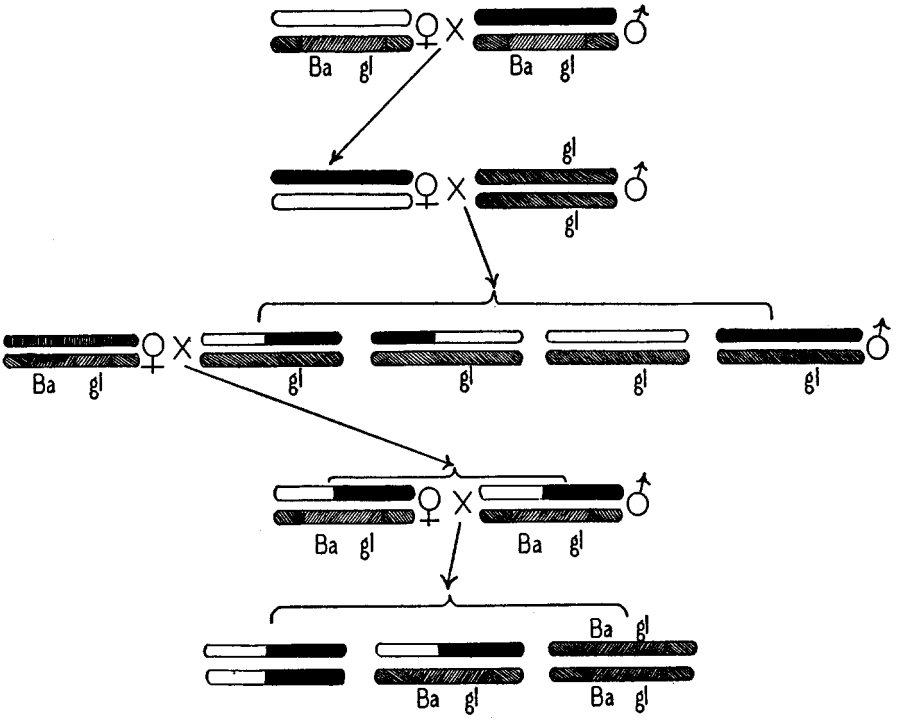

FIGURE 1.—The experimental procedure used to analyze the effects of recombination of genes in two wild second chromosomes (shown in white and black respectively). The laboratory chromosomes containing various marking genes or inverted sections are shown with the diagonal lines. *Ba*—the dominant Bare; *gl*—the recessive glass.

zygotes than in heterozygotes, but the difference is much less striking than in chromosome A.

To obtain crossing over between chromosomes A, B, and C, the experiments were arranged as shown in figure 1. Females carrying one of these chromosomes, say chromosome A (shown in figure 1 in white), and the balancing *Ba gl* inversion chromosome (diagonal lines), were crossed to males with chromosome B (black) and the same balancing chromosome. The wild type individuals obtained in the progeny all carry one chromosome A and one chromosome B. Such wild type females were crossed to males homozygous for

the recessive glass (*gl*). In the offspring of this cross, all flies carry a paternal chromosome with *gl* and a maternal wild chromosome. The maternal chromosome, however, may be an intact chromosome A, or an intact chromosome B, or it may be a chromosome compounded of sections of A and B by crossing over. It is, of course, impossible to tell by inspection of the phenotype of the fly which kind of a chromosome it carries; an examination of the properties of the chromosomes, however, is possible if flies homozygous for them are obtained.

A total of 100 wild/glass males (the third line in fig. 1) were selected and crossed individually to females having the *Ba gl* inversion chromosome. In the offspring, females and males showing the character Bare, but not showing glass, were selected and inbred. The composition of these flies is evidently wild/*Ba gl* inversion (fig. 1). From each culture, 12 females and an equal or greater number of males were taken, aged together for four days in a vial with food, and then transferred five times to fresh culture bottles at one day intervals. The five cultures containing the offspring of the same group of parents were placed in an incubator at 25½°C to develop. When the progeny in these cultures started to hatch, counts were made on alternate days. Just as in the above discussed experiments of DOBZHANSKY, HOLZ, and SPASSKY, the ratios of wild type to Bare flies obtained in the cultures can be used to measure the relative viabilities of homozygotes and heterozygotes for chromosomes A, B, and their crossover derivatives. The ratios obtained in the successive counts in the same cultures furnish a yardstick for measuring the relative development rates of the homo- and heterozygotes.

Experiments on recombination of genes in chromosomes A and C, and in B and C, were arranged as described above for the A–B combination, except that fewer chromosomes were tested in each case.

RECOMBINATION OF GENES IN THE CHROMOSOMES A AND B

A total of 97 chromosomes obtained in the offspring of females heterozygous for A and B chromosomes were successfully tested for their effects on the viability of homozygotes. The results obtained in the cultures raised at 25½°C are summarized in table 1, which shows the total numbers of the flies examined in the test generation (the last generation shown in fig. 1) as well as the percentages of wild type individuals among these flies. As indicated above, five cultures were raised for each chromosome (only three cultures, however, were fully counted for most of the lethal chromosomes). Although table 1 shows only the total counts in all the cultures involving each chromosome, the last column, marked "χ^2," gives the chi-squares that measure the degree of heterogeneity observed among the five cultures of each series. Each chi-square has four degrees of freedom. No chi-squares can be calculated for the lethals and extreme semilethals.

Inspection of table 1 shows that 37 out of the 97 chromosomes tested proved to be lethal when homozygous, as demonstrated by the failure of wild type individuals to appear in the cultures. Since one of the parental chromosomes (chromosome A) is also lethal to homozygotes at 25½°C (see above), these 37

chromosomes may be supposed to represent non-crossover A chromosomes; it will be shown below that some of them nevertheless are crossovers. Only four chromosomes (Nos. 3, 26, 73, and 91) produce normally viable homozygotes, as attested by the appearance of more than 30 percent of wild type individuals in the cultures. Homozygotes for four other chromosomes (Nos. 33, 44, 45, and 77) have viabilities only slightly below normal—they give between 25 and 30 percent of wild type flies in the cultures. Since the viability of homozygotes for the parental chromosome B is normal or subnormal (30.6 percent wild type among 1549 flies, see DOBZHANSKY and SPASSKY 1944, page 275), these eight chromosomes may be supposed to represent non-crossover chromosomes B. However, it is possible to show that at least two out of the eight possess properties which the original chromosome B did not possess. Namely, the homozygotes for chromosome No. 26 show a recessive visible effect, rather short and thin bristles. Homozygotes for chromosome No. 44 develop very slowly; only Bare flies emerge in the cultures during the first two to four days after the beginning of the hatching, while the late hatches consist of only or mostly wild type individuals. The homozygotes for chromosome B have normal bristles and develop at the same rate as heterozygotes. Barring mutation, the only way in which chromosomes Nos. 26 and 44 could have acquired new properties not present in chromosome B is by crossing over between chromosomes A and B. Therefore, only six out of 97 chromosomes tested may be said to be indistinguishable from the ancestral chromosome B.

Nine chromosomes (Nos. 13, 16, 20, 57, 59, 60, 67, 71, and 98, table 1) gave more than 16.7 percent but less than 25 percent of wild type flies in the cultures. In other words, the viability of homozygotes for these chromosomes is definitely below normal, but not low enough to be included in the class of semilethals. These chromosomes are obviously identical with neither the ancestral chromosome A nor B, and are derived from the latter by crossing over. Furthermore, these nine chromosomes are not alike among themselves. Homozygotes for chromosome No. 60 seem to develop faster than the heterozygotes ($\chi^2 = 5.03$, probability with two degrees of freedom about 0.08). Homozygotes and heterozygotes for chromosome No. 59 have the same development rates. The remaining seven chromosomes slow down the development of homozygotes very significantly. Chromosomes Nos. 13 and 71 give significantly different percentages of wild type individuals in different cultures of the same series, which indicates that the viability of homozygotes for these chromosomes is modified by some environmental agent that varies from culture to culture. In the case of chromosome No. 71, this agent is almost certainly the population density, since cultures which produced fewer flies gave higher proportions of wild type individuals than cultures with many flies, as follows:

Flies per culture	78	128	166	204	205
Percentage wild type	37.2	33.6	25.9	15.7	15.6

No such correlation with the population density is noticeable in the case of chromosome No. 13, although cultures with different numbers of flies have been obtained.

TABLE 1

Viability of homozygotes for each of the 97 second chromosomes obtained in the offspring of females carrying chromosomes A and B. Experiments at 25½°C.

CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2	CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2
1	641	2.5	—	48	1070	5.4	7.47
2	770	0.0	—	49	902	16.3	43.12
3	708	35.6	2.81	50	365	1.4	—
4	729	0.0	—	51	352	0.0	—
5	688	0.1	—	52	974	6.0	4.30
6	348	0.0	—	53	548	0.0	—
7	474	0.0	—	54	1006	3.0	44.85
8	547	0.0	—	55	366	0.0	—
9	711	4.4	26.49	56	1110	14.4	5.62
10	1079	7.2	13.96	57	1578	20.91	4.28
11	524	0.4	—	58	486	0.0	—
12	631	0.0	—	59	1049	21.0	0.23
13	1378	22.1	32.47	60	828	17.3	9.78
14	844	0.0	—	61	757	0.0	—
15	1113	6.8	13.82	62	592	5.1	—
16	1171	24.8	6.08	63	440	0.0	—
17	851	13.3	37.86	64	924	11.2	44.30
18	1385	0.0	—	65	860	13.0	24.44
19	729	0.0	—	66	838	0.7	—
20	709	22.8	5.25	67	622	19.8	5.10
21	347	1.4	—	68	811	5.5	13.62
22	861	13.2	5.90	69	442	5.4	—
23	699	10.7	8.84	70	695	4.6	—
24	1207	4.3	—	71	781	22.9	19.06
25	833	0.0	—	73	1163	36.3	3.09
26	1626	33.8	1.62	74	501	0.0	—
27	995	9.8	4.70	75	861	0.0	—
28	615	0.0	—	76	982	0.0	—
29	990	0.0	—	77	1007	28.3	10.82
30	519	0.0	—	78	1145	0.0	—
31	1533	0.0	—	79	636	16.0	11.83
32	1359	11.8	13.06	80	345	2.3	—
33	625	26.1	6.31	81	805	0.0	—
34	384	0.0	—	82	471	0.0	—
35	1312	5.6	23.46	83	659	0.0	—
36	463	0.0	—	84	536	2.4	—
37	1000	11.0	16.51	85	479	1.0	—
38	443	0.0	—	86	614	0.0	—
39	449	0.0	—	87	634	13.1	42.73
40	500	0.0	—	88	953	8.5	30.15
41	611	0.9	—	89	920	4.6	6.71
42	554	0.0	—	91	938	34.3	3.19
43	427	1.2	—	93	998	3.5	—
44	1015	27.8	2.92	94	1039	16.3	23.20
45	1087	29.2	3.16	95	811	3.9	—
46	643	0.0	—	96	787	13.8	86.69
47	643	0.0	—	97	829	4.6	13.12
				98	461	19.3	4.78
				99	462	0.0	—
				100	324	1.5	—

As many as 13 chromosomes gave percentages of wild type individuals ranging from ten to 16.7 percent, and ten chromosomes gave percentages below ten but above five per cent. Moderate recessive semilethals are evidently present in these 23 chromosomes. We may designate as extreme semilethals the 20 further chromosomes that gave less than five but more than zero percent wild type (table 1). Since neither chromosomes A nor B is semilethal at 25½°C (see above), these 43 chromosomes are crossovers between A and B. There is also no doubt that the semilethals do not represent a uniform group; rather, a collection of chromosomes with different properties is included in the semilethal class. This is confirmed by consideration of properties of these chromosomes other than their effects on the viability of the homozygotes.

The group of 13 moderate semilethals which gave between ten and 16.7 percent of wild type in the cultures may be considered first. Among them, three chromosomes (Nos. 17, 23, and 32) have development rates which do not differ perceptibly in homo- and heterozygotes. Nos. 37, 64, and 94 make homozygotes develop slightly but significantly slower than the corresponding heterozygotes. The other seven chromosomes produce more or less striking delays in the development of homozygotes. If we take chi-squares greater than 9.49 (which, with four degrees of freedom corresponds to a probability of about 0.05) to indicate significant heterogeneities among cultures of the same series, it follows that the viability of homozygotes for chromosomes Nos. 17, 32, 37, 49, 64, 65, 79, 87, 94, and 96 is sensitive to culture conditions, while that of the homozygotes for Nos. 22, 23, and 56 displays no such sensitivity (table 1). Examination of the data, however, discloses no significant correlations between the percentages of wild type individuals and the population densities in the cultures.

The ten semilethals that gave between five and ten percent of wild type individuals are an equally diversified group. Homozygotes for chromosomes Nos. 15, 27, and 69 have small wings that are usually bent arc-like over the back of the fly; the character is frequently asymmetrical, and some flies appear normal. Homozygotes and heterozygotes for chromosome No. 52 develop equally fast; Nos. 10, 68, and 88 slow down the development of homozygotes to a slight extent. Other chromosomes produce more or less striking delays in the development of the homozygotes. The percentages of wild type in different cultures testing the same chromosome are particularly variable for chromosomes Nos. 35, 52, 69, and 88. In no case, however, is there a suggestion of a correlation between this variability and the population density in the cultures. The 20 extreme semilethals are probably not a uniform group either, but very little can be said about them because only few flies homozygous for any given chromosome have been encountered.

It is obvious, therefore, that a considerable variety of chromosomes with different properties are produced as a result of crossing over between chromosomes A and B.

INFLUENCE OF LOW TEMPERATURE ON THE BEHAVIOR OF SOME LETHALS

The experiments described above have been carried at the temperature of

25½°C. In these experiments, 37 chromosomes completely lethal to homozygotes and 20 chromosomes that behaved as extreme semilethals were found in the progeny of females heterozygous for chromosomes A and B. Now, the ancestral chromosome A is known from the experiments of DOBZHANSKY and SPASSKY (1944) to behave very differently at different temperatures: it is lethal to homozygotes raised at 25½°, semilethal at 21°, while at 16½° these homozygotes survive nearly as well as do the heterozygotes. It was therefore

TABLE 2

Viability at 16½°C of homozygotes for second chromosomes obtained in the offspring of females carrying chromosomes A and B. These chromosomes were lethal or semilethal at 25½°C (cf. table 1).

CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2	CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2
1	834	34.9	2.03	46	751	32.8	4.78
2	911	30.2	24.33	47	888	34.4	6.47
4	1061	25.6	8.01	50	392	27.3	3.65
5	1457	33.3	2.15	51	1286	34.5	7.65
6	1295	30.5	8.56	53	709	33.9	0.89
7	780	26.0	7.90	55	595	22.2	2.73
8	1349	35.0	0.90	58	957	30.5	2.84
11	1378	23.7	5.30	61	1097	36.3	3.81
12	1088	30.9	5.77	62	277	34.7	2.25
14	1149	28.9	5.76	63	792	0.0	—
18	877	0.0	—	66	979	29.8	4.99
19	363	30.3	4.63	69	539	34.7	4.43
21	180	32.8	3.17	74	1006	35.9	8.89
25	1554	31.8	11.72	75	458	32.8	5.44
28	798	24.7	10.65	76	1488	25.2	50.51
29	1077	31.0	13.69	78	672	34.4	4.27
30	264	24.6	4.14	80	402	30.0	6.44
31	1202	21.7	19.19	81	1258	26.6	22.35
34	942	33.5	24.85	82	753	31.1	1.72
36	856	19.2	12.64	83	754	26.1	14.68
38	706	32.7	1.70	84	955	29.6	7.85
39	127	29.1	3.99	85	550	31.3	4.11
40	1321	31.4	4.36	86	1767	34.4	2.66
41	358	0.0	—	93	532	30.1	4.52
42	1070	29.2	11.59	95	514	34.1	5.76
43	730	29.5	1.42	99	483	33.9	9.51
				100	486	30.7	9.54

decided to test the behavior of the 37 lethal and 20 semilethal chromosomes at the low temperature, 16½°. The experimental technique remained the same as used for the experiments at the high temperature; the wild/*Ba gl* inversion flies were allowed to oviposit for about 24 hours at room temperature, five cultures being raised for each chromosome. The cultures then developed in a cold room at 16½°. The results are summarized in table 2, which is constructed like the previously discussed table 1.

Examination of table 2 shows that only three out of the 53 chromosomes tested (Nos. 18, 41, and 63) are completely lethal to homozygotes at $16\frac{1}{2}°$ as well as at $25\frac{1}{2}°$. The appearance of these chromosomes is very interesting, since neither the ancestral chromosome A nor B are lethal or even semilethal at $16\frac{1}{2}°$. The origin of the three lethal chromosomes must be due, disregarding mutation, to crossing over between chromosomes A and B. Chromosomes A and B evidently contain genes, or groups of genes, which taken separately are not lethal to homozygotes raised at $16\frac{1}{2}°$ but which become lethal when combined by crossing over. In view of their known origin by crossing over, chromosomes Nos. 18, 41, and 63 may be said to carry "synthetic lethals." No synthetic semilethals have appeared; the lowest proportion of wild type individuals given by any of the non-lethal chromosomes listed in table 2 is 19.2 per cent for chromosome No. 36, which is outside the semilethal range.

Among the 50 non-lethal chromosomes in table 2, six chromosomes gave between 19.2 and 25 percent of wild type individuals in the cultures, 12 chromosomes between 25 and 30 percent, 30 chromosomes between 30 and 35 percent, and two chromosomes (Nos. 61 and 74) 36.3 ± 1.4 percent and 35.9 ± 1.5 percent wild type respectively. Since all these chromosomes behaved as lethals or extreme semilethals at $25\frac{1}{2}°$, their performance at $16\frac{1}{2}°$ is truly remarkable: a change of only 9°C causes a shift all the way from lethality to normal survival (fig. 2). This is, of course, what the ancestral chromosome A does as well; in the experiments of DOBZHANSKY and SPASSKY (1944) chromosome A homozygotes were lethal at $25\frac{1}{2}°$, while at $16\frac{1}{2}°$ as many as 29.7 ± 1.4 percent wild type appeared in the cultures. What is important for us here is that the 50 chromosomes are not an uniform lot. Some of them make the homozygotes survive more and other less frequently than the ancestral chromosome A. They have evidently acquired new properties through crossing over between chromosomes A and B.

Individuals homozygous for chromosome A develop, at $16\frac{1}{2}°$, appreciably more slowly than do the heterozygotes. It is, therefore, not unexpected that every one of the chromosomes listed in table 2 also slow down the development of homozygotes (the lethals must, of course, be disregarded since nothing can be told about the development rate of lethal homozygotes). The degree of the prolongation of the development is, however, not alike in all cases. Thus, the homozygotes for chromosomes Nos. 5, 14, and 55 seem to have their development slowed down more than in the homozygotes for other chromosomes.

The case of chromosome No. 76 is particularly interesting since in this case the decrease of the development rate is partly dominant. The hatching of the adult flies in the cultures involving this chromosome started about five days later than in other cultures made on the same date. The hatching continued in some of the cultures for as long as three weeks. The adult flies are small, paler than normal in coloration, and have relatively large and heavy bristles. At $25\frac{1}{2}°$ this chromosome is lethal to homozygotes, but the heterozygotes show only a slight delay in their development.

The last column in table 2 gives chi-squares that measure the heterogeneities among the five cultures raised to study each chromosome. Each of these chi-

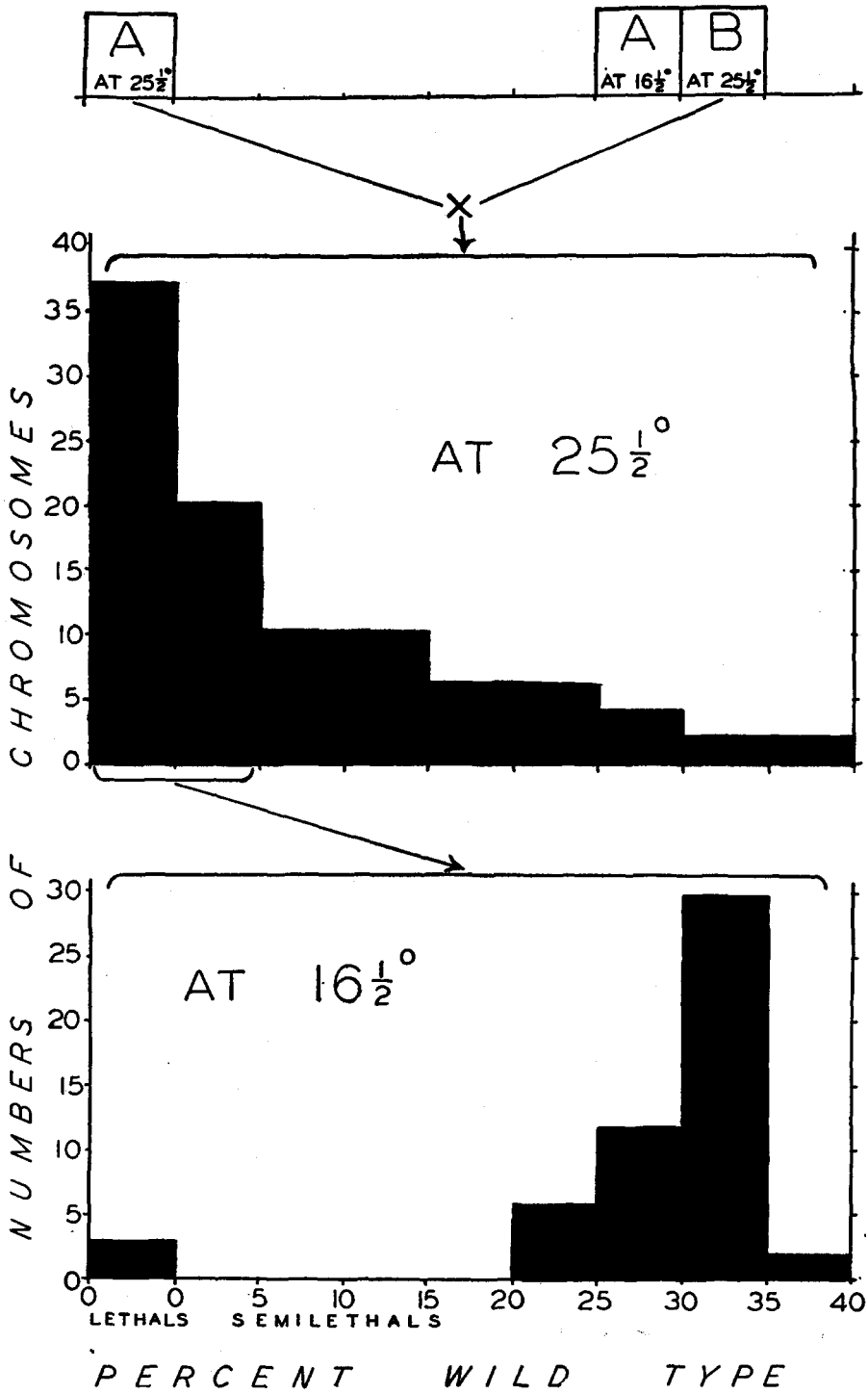

FIGURE 2.—Results of recombination of the viability genes carried in chromosomes A and B. The viability is measured through observing the proportions of wild type individuals in the cultures. Cultures containing between 30 and 35 percent wild type arise when the viability of homozygotes for a given chromosome is about equal to that of the heterozygotes. Failure of wild type individuals to appear in the cultures indicates that the chromosome involved is lethal to homozygotes.

squares has four degrees of freedom. Here as before, significant chi-squares indicate that the relative viability of homozygotes for a given chromosome is sensitive to differences in culture conditions that may occur among cultures made on successive days. Inspection of table 2 shows that most of the chi-squares are small. However, chromosomes Nos. 2, 31, 34, 76, 81, and 83 show very significant heterogeneities. The origin of these heterogeneities is obscure; the most obvious factor that could produce such differences among cultures, namely differences in population densities (different numbers of flies developing in different culture bottles), does not seem to be involved here.

TABLE 3

Viability at 25½°C of homozygotes for second chromosomes obtained in the offspring of females carrying chromosomes A and C.

CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2	CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2
1	801	0.0	—	16	1028	29.6	5.87
2	996	11.3	32.00	17	883	31.8	5.43
3	905	32.9	4.36	18	1055	0.0	—
4	1496	36.4	9.36	19	438	0.0	—
5	1069	17.1	2.69	20	1181	32.5	8.10
6	824	31.2	0.47	21	809	0.0	—
7	738	18.8	21.14	22	695	25.0	34.04
8	871	39.4	0.50	23	813	16.1	11.19
9	1148	7.5	5.45	24	996	31.4	9.50
10	1281	30.6	2.17	25	1021	32.8	5.81
11	1202	32.0	3.75	26	1095	34.1	2.31
12	837	4.3	—	27	1023	35.4	5.39
13	642	0.0	—	28	1148	33.9	1.52
14	1195	32.7	0.99	29	1104	30.3	0.97
15	783	0.0	—				

RECOMBINATION OF GENES IN CHROMOSOMES A AND C

The experiments on chromosomes A and C were arranged like those with the A-B combination, except that only 29 chromosomes obtained in the offspring of females heterozygous for A and C were tested. The data for the tests carried at 25½°C are summarized in table 3. It should be kept in mind in interpreting these data that chromosome A is lethal to homozygotes at 25½°, while homozygotes for chromosome C are normal in viability and have a development rate slightly but significantly slower than do the heterozygotes.

Only six of the chromosomes shown in table 3 are lethal when homozygous; these six chromosomes may represent the non-crossover chromosomes A. As many as 16 chromosomes gave percentages of wild type ranging from 29.6 per cent to 39.4 per cent; individuals homozygous for these chromosomes have, then viabilities approaching those of the heterozygotes. Some, but not all, of these 16 chromosomes may be non-crossover chromosomes C. That some of

them are in fact crossovers, is shown by heterogeneities too great to be explained by chance alone. Thus, as many as 39.4 ± 1.6 percent wild type appeared in the cultures involving chromosome No. 8, which indicates that homozygotes for this chromosome have viabilities greater than the heterozygotes. Furthermore, individuals homozygous for chromosomes Nos. 4, 10, 11, 14, 27, and 29 develop more slowly than do heterozygotes, while the remaining 10 chromosomes produce little or no prolongation of the development.

Chromosomes Nos. 9 and 12 are strong semilethals, while No. 2 is a moderate semilethal. Nos. 5, 7, and 23 are near the upper boundary of the semilethal range, while No. 22 decreases the viability of homozygotes to an extent far less than semilethal. All these chromosomes carry recombinations of genes contained in chromosomes A and C. Their effects on the development rate are heterogeneous. The development rates of the homo- and heterozygotes for chromosomes Nos. 2, 9, 12, 22, and 23 are alike or nearly so. A slight but significant delay occurs in homozygotes for No. 5, while the development of homozygotes for No. 7 is very strikingly slower than that of heterozygotes—the hatching of wild type individuals begins several days after Bare individuals have started to emerge from the pupae. Chromosomes Nos. 2, 7, 22, and 23 give heterogeneous results in different cultures (see the chi-squares in table 3). In Nos. 2 and 7 the heterogeneities seem to be uncorrelated with population densities in the cultures. There is an indication that low population densities are favorable for the survival of homozygotes for chromosome No. 23, as shown by the following figures:

Flies per culture	68	101	108	245	291
Percentage wild type	29.4	18.8	13.9	11.8	16.5

Conversely, homozygotes for chromosome No. 22 survive relatively better than do the heterozygotes in cultures with medium population densities. The data are as follows:

Flies per culture	40	74	178	191	212
Percentage wild type	0.0	4.1	28.1	36.7	24.1

Despite their lethality at $25\frac{1}{2}$°C, individuals homozygous for chromosome A survive nearly normally at $16\frac{1}{2}$° (see above). It may, then, be inferred that the lethal chromosomes shown in table 3 are non-crossover chromosomes A. The six lethals (Nos. 1, 13, 15, 18, 19, and 21) and the two semilethals (Nos. 9 and 12) shown in table 3 were, therefore, re-tested at $16\frac{1}{2}$°. A summary of the results appears in table 4.

As expected, all these chromosomes proved not to be lethal to homozygotes at $16\frac{1}{2}$°. Furthermore, every one of these chromosomes causes more or less striking delays in the development of the homozygotes as compared with heterozygotes. This is also a property of the ancestral chromosome A at $16\frac{1}{2}$°. And yet, it can be shown that some of the eight chromosomes listed in table 4 have properties which chromosome A did not possess. The viability of homozy-

gotes for chromosome No. 9 is lower than that of the other homozygotes, although a reference to table 3 will show that at 25½°C this chromosome behaved as a semilethal while other chromosomes (except No. 12) behaved as complete lethals. The homozygotes for No. 12 develop only slightly less rapidly than the corresponding heterozygotes, while the other homozygotes show more or less striking delays in their development.

RECOMBINATION OF GENES IN CHROMOSOMES B AND C

A great variety of chromosomes differing in viability, development rate, and other characters have been obtained by recombination of genes borne in

TABLE 4

Viability at 16½°C of homozygotes for second chromosomes obtained in the offspring of females carrying chromosomes A and C. These chromosomes were lethal or semilethal at 25½°C (cf. table 3).

CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2	CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2
1	1610	30.7	4.90	15	1068	33.3	6.31
9	783	18.9	10.86	18	988	32.2	3.99
12	1140	28.4	1.30	19	776	28.4	6.50
13	1468	29.6	2.84	21	952	26.5	15.31

chromosomes A and B or in A and C. The problem arises whether such results can be regarded typical for gene recombination in wild chromosomes in general. The ancestral chromosome A is, to be sure, exceptional in the wide range of behaviors which individuals homozygous for it display in different environments: they are nearly normally viable at 16½°, semilethal at 21°, and lethal at 25½°. Experiments on recombination of genes in chromosomes B and C should help to elucidate this problem; homozygotes for either of these chromosomes show normal or slightly below normal viabilities at 25½°, normal or slightly above normal at 16½°. Homo- and heterozygotes for chromosome B are alike in development rate; homozygotes for C develop slightly slower than the heterozygotes (cf. p. 273).

The experimental techniques used were the same as employed for the A-B and A-C combinations. The data for the tests carried at 25½° are summarized in table 5. Only 19 among the 33 chromosomes studied produced 30 or more percent of wild type flies in the cultures. Two other chromosomes (Nos. 2 and 23) produced 28.7 and 28.2 percent wild type respectively. The homozygotes for these 21 chromosomes may, then, be said to be about equal in viability to the corresponding heterozygotes, and to the homozygotes for the ancestral chromosomes B and C. The remaining 12 chromosomes are clearly different from both B and C. Among them, nine chromosomes gave between 21 and 27 percent wild type. These nine chromosomes produce slight but perceptible deleterious effects on the viability of homozygotes. Most remarkable are chro-

mosomes Nos. 1, 19, and 31, which produced 5.7 percent, 6.4 percent, and 10.3 percent wild type individuals respectively. These chromosomes fall, consequently, well within the semilethal range. Since neither chromosomes B nor C are semilethal to homozygotes, the three semilethal chromosomes may well be called "synthetic semilethals," analogous in their mode of origin to the synthetic lethals mentioned on p. 279. Recombination of genes in two wild chromosomes each of which makes the homozygotes normally viable may, then, give rise to chromosomes that act as semilethals.

TABLE 5

Viability at 25½°C of homozygotes for second chromosomes obtained in the offspring of females carrying chromosomes B and C.

CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2	CHROMOSOME NO.	FLIES EXAMINED	PERCENTAGE WILD TYPE	χ^2
1	681	5.7	2.24	17	993	32.1	6.21
2	1177	28.7	3.99	18	1092	22.9	0.58
3	125	38.4	7.86	19	597	6.4	2.66
4	1037	26.3	6.33	20	878	34.2	4.71
5	759	31.6	4.27	21	1253	31.0	2.23
6	582	34.0	5.88	22	702	33.3	5.47
7	846	31.8	1.80	23	865	28.2	9.55
8	441	22.5	6.28	24	695	21.2	3.48
9	1372	32.7	3.35	25	903	33.2	4.54
10	620	25.2	2.04	26	957	31.5	1.32
11	928	30.8	2.56	27	1334	26.1	4.76
12	1295	30.3	3.94	28	907	32.7	7.86
13	830	34.0	5.92	29	933	32.5	2.88
14	1016	26.2	8.29	30	1392	26.7	16.44
15	972	26.3	1.98	31	672	10.3	0.71
16	800	32.1	2.48	32	835	34.6	5.58
				33	351	33.9	8.27

Analysis of the data for the development rates shows only a moderate variability. Namely, nine chromosomes (Nos. 4, 5, 10, 11, 12, 14, 24, 26, and 28) produce statistically significant delays in the emergence of homozygotes. Homo- and heterozygotes for the other 24 chromosomes develop at equal rates. Among the nine chromosomes which do slow down the development rates of the homozygotes, all but No. 14 produce only slight delays, more or less comparable with that produced by the ancestral chromosome C. A greater, but still not striking, prolongation of the development is characteristic of chromosome No. 14.

Inspection of the chi-squares in table 5 shows that the results obtained in different cultures of the same series are mostly quite uniform. The only sizeable chi-square (16.44) is found in the data for chromosome No. 30. The probability that such or greater chi-square may occur by chance is about 0.003,

but since it occurred in only one out of 33 chromosomes it is probably not significant.

The viability of homozygotes for chromosomes that behaved at 25½°C as "synthetic semilethals" (Nos. 1, 19, and 31) was re-tested at 16½°C. The proportion of wild type flies observed in the cultures proved to be 6.4 percent, 31.8 percent, and 32.8 percent among 408, 1480, and 919 flies respectively. Chromosome No. 1 is, consequently, semilethal at both temperatures, while Nos. 19 and 31 are normally viable at 16½°C.

DISCUSSION

It has been shown that recombination of genes carried in only three second chromosomes derived from natural populations of Mount San Jacinto gives rise to a remarkable variety of chromosomes with different properties. These chromosomes range all the way from complete lethality in homozygotes, through various grades of semilethals, relatively mild deleterious modifications, and to chromosomes which make homozygotes equal or even slightly superior to the respective heterozygotes in viability. Individuals homozygous for some chromosomes survive relatively better than the heterozygotes in cultures with low population densities, others in more crowded cultures, while still others are not affected by population density variations. The influence on the development rate ranges from cases when homo- and heterozygotes develop equally fast, through more or less noticeable delays, and to striking retardations of the homozygotes. One chromosome causes a semi-dominant, instead of a recessive, modification of the development rate. Some chromosomes produce slight modifications of the morphology of the flies, although the chromosomes from which they were derived did not have such effects.

Although the three initial chromosomes used in our experiments can hardly be considered a fair sample of second chromosomes in natural populations of *Drosophila pseudoobscura*, it is clear from the data that a tremendous amount of variability is released by recombination of genes in wild chromosomes. If a population of a locality were to start with only few chromosomes, it would contain an imposing variety of chromosomes in the following generations. This may seem inconsistent with the relative uniformity of at least the external appearance of the flies which prevails in natural populations of most species of Drosophila, including *D. pseudoobscura*. The solution of the paradox is that the variability here involved is mostly concealed or potential rather than actually manifest in the phenotype. The variability is concealed because most of the mutant genes are recessive and present in populations in low concentrations, and also because wild chromosomes differ not in single genes but in gene complexes.[1] Concealed variability is released, as we have seen, through recom-

[1] MATHER (see MATHER 1943 and 1944 for further references) has introduced the convenient expression "polygenic character" (a polygenic character is defined by MATHER as one "whose inheritance is controlled by many genes each having an effect which is small compared with non-heritable variation") to describe the long known phenomenon variously called inheritance through multiple genes or multiple factors, modifiers, duplicate genes, blending inheritance, etc. MATHER also uses the noun "polygenes" to mean "linked combinations of the genes determining

bination of the gene complexes carried in the chromosomes of a population by crossing over, and through manifestation of recessive genes and gene complexes in homozygotes.

The existence of a store of potential variability underlying the much more limited variation actually observed in sexually reproducing and cross-fertilizing populations has been realized for a long time, although the tremendous magnitude of this store is only now becoming apparent. The idea of accumulation in populations of concealed recessive variants is clearly implicit in the now classic SHULL-JONES theory of causation of heterosis through covering-up of deleterious recessives by their dominant "normal" alleles (see JONES 1917, 1925, EAST and JONES 1919, SINGLETON 1941, and others). Following a clear statement of the problem of concealed variability by CHETVERIKOV (1926), many investigators in various countries, among whom DUBININ and his school must be prominently mentioned, have found that populations of species of Drosophila indeed carry a profusion of autosomal recessive mutants concealed by heterozygosis (reviews in DOBZHANSKY 1939, 1941).

DOBZHANSKY, HOLZ, and SPASSKY (1942) have pointed out that the magnitude of the store of concealed variability and of heterosis are functions of the genetic population structure. In species which reproduce by self-fertilization or close inbreeding, deleterious recessive mutants and deleterious recombination products of the gene complexes are eliminated by natural selection almost as rapidly as deleterious dominants. Little heterosis is observed in such species. The more prevalent is outbreeding in a species, the less frequently will any individual chromosome or gene complex become homozygous. Deleterious recessives will be eliminated much less rapidly than deleterious dominants, and heterosis will be more or less strongly pronounced. Extreme outbreeding will cause chromosomes and gene complexes to become homozygous so rarely that the welfare of the species will depend upon the effects of these gene complexes in heterozygotes with other gene complexes present in the same population, rather than upon their effects in homozygotes. Natural selection will, accordingly, favor those gene complexes which produce optimal adaptations

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quantitative variation". The gene complexes described in the present articles fit this definition of "polygenes." Since, however, a "polygenic character" is any character which is determined by many genes, regardless of whether these genes lie in the same or in different chromosomes, the noun "polygene" can only mean the sum total of the genes controlling a character which is "polygenic." To refer to individual genes entering in the determination of a polygenic character as "polygenes" would also be an etymological inconsistency. Furthermore, it must be emphasized that genes determining polygenic characters are not a separate category of genes, and that all transitions occur between polygenic characters and characters determined by single genes or few genes with large effects (MATHER'S "oligogenes"). In one of his papers, MATHER (1944) conjectures that genes which determine polygenic characters may be concentrated in heterochromatic chromosome sections, but MATHER'S evidence shows at most that some genes located in heterochromatin influence polygenic characters. Now, the history of genetics attests the futility of attempts to draw sharp distinction between the mechanisms of inheritance of qualitative and quantitative characters, even though the techniques of studying the extreme examples of these two classes are of necessity different.

in heterozygotes, largely regardless of their effects in homozygotes. The limiting case will be a species in which every chromosome is lethal when homozygous, and the degree of heterosis is, thus, at a maximum. Such a species is not known to exist, but, curiously enough, this limiting case is, as shown by MULLER as early as 1918, approached most closely by certain Oenotheras, but in them a singular chromosomal mechanism makes maintenance of heterosis compatible with self-pollination. MATHER (1941, 1943) refers to the effects of a chromosome (or of the genes it carries) in homozygotes as due to its "internal balance," while its effects in heterozygotes depend upon its "relational balance." MATHER's conception of heterosis (1943), p. 52 is however quite different from ours.

The ability of the gene complexes carried in second chromosomes of wild *Drosophila pseudoobscura* to produce, through recombination, a great variety of new gene complexes disrupts the notions of "normal" or "wild type" chromosome, genotype, or phenotype. In general, these notions exist because of the reluctance of human mind to abandon the idea of a finite number of static prototypes underlying the unmanageable, and yet fascinating, multiformity of the living nature. In Drosophila and in other forms in which the naturally occurring individuals of a species tend to be uniform in appearance, it is, nevertheless, convenient for descriptive purposes to contrast mutant or aberrant individuals or strains with normal or wild type ones. In polymorphic species, such as man and maize, geneticists distinguish normal and mutant alleles only for loci in which one of the alleles occurs much more frequently than all others. In *D. pseudoobscura* and *D. persimilis*, the idea of "normal" gene arrangement in the third chromosome had to be abandoned because so many gene arrangements occur in natural populations that designation of one of them as "Standard" has been arbitrary. Now, the polygenic nature of the variation found in the second chromosome leaves little doubt in that no single gene complex is likely to be prevalent enough in the populations to justify its being called the "normal" condition.

The objection may be raised that the observed variety of gene complexes concerns their manifestation only in homozygotes, while they are mutually so adjusted as to produce a "normal" phenotype in naturally occurring heterozygotes. To a great extent this is undoubtedly true; the potential variability far exceeds the effective one. The genetic population size in *Drosophila pseudoobscura* (DOBZHANSKY and WRIGHT 1943) is however sufficiently small to make it probable that gene complexes sometimes do become homozygous in nature. More important is that natural populations of this species, although they do seem uniform in morphology, show important variation in physiological properties. DOBZHANSKY (1943) and WRIGHT and DOBZHANSKY (1946) have shown that, at least in some localities, third chromosomes with the "Standard" gene arrangement are favored during summer, while chromosomes with the "Chiricahua" arrangement are favored during spring season. The adaptive values of individuals with these gene arrangements are very different in some environments. It seems probable that the different gene arrangements acquire

different adaptive properties through association with different genes, rather than through position effects. The polygenic nature of the variation shows how such associations become established. A gene complex which produces a phenotype well adapted to some environments in which the species occurs in nature is, of course, favored by natural selection. However, crossing over tends to break up gene complexes regardless of their usefulness. Inversions that prevent break-ups of superior gene complexes acquire, consequently, positive selective values and increase in frequencies. Since heterozygotes are better adapted than homozygotes, several gene arrangements exist in a population in a moving equilibrium.

The theory of genic balance, according to which plus and minus modifiers for various characters occur intermingled in chromosomes, was developed by BRIDGES (1922, 1939). The bearing of this distribution on the effectiveness of natural selection was pointed out by GOODALE (1937), and more recently discussed in detail by MATHER (1941, 1942, 1943), MATHER and WIGAN (1942), and WIGAN and MATHER (1942). Numerous genes lying in the same chromosomes (gene complexes) provide superior storage facilities for the genetic raw materials of evolution than would be possible with a few major genes, and recombination of genes in such gene complexes makes possible great advances in rebuilding the organism in directions favored by artificial or natural selection. This, with or without the concomitant occurrence of mutations, accounts for the rather spectacular results of systematic selection obtained in *Drosophila melanogaster* by PAYNE (1918, 1921), ZELENY (1922), and MATHER and WIGAN (*loc. cit.*). The data reported in the present article have a bearing on the problem of selection, even though they involve no selection experiments in the usual sense of the term. Some of the chromosomes obtained through crossing over between the three ancestral wild chromosomes have properties very different from the latter. It is, therefore, possible to "select" products of recombination of the gene complexes that deviate greatly from the ancestral types, being completely outside the limits of variability of these ancestors. The "synthetic" lethals and semilethals, obtained by crossing over between chromosomes that are normally viable in homozygotes, provide the most striking illustration of the above statement.

SUMMARY

Three wild second chromosomes, derived from the population of *Drosophila pseudoobscura* of Mount San Jacinto, California, were chosen as material for experiments. One of these chromosomes is remarkable because individuals homozygous for it are highly sensitive to environmental influences: they survive nearly normally at $16\frac{1}{2}^{\circ}$, are semilethal at 21°, and completely lethal at $25\frac{1}{2}^{\circ}$C. Homozygotes for the other two chromosomes have viabilities about equal to those of the respective heterozygotes.

By means of appropriate crosses, females were produced that were heterozygous for any two of the above three chromosomes. The eggs of these females contained chromosomes some of which were identical with the ancestral ones

(non-crossovers) and some were new (crossovers). A sample of these chromosomes was analyzed for their effects in homozygous condition. A great variety of chromosomes with different properties were thus obtained. The viability of the homozygotes for some of the chromosomes is equal to or even slightly superior to that of the respective heterozygotes; other chromosomes act as recessive deleterious modifiers, still others as semilethals, and finally some act as complete lethals. Homozygotes for some chromosomes are relatively more viable than heterozygotes in crowded cultures, others are favored in cultures with low population densities, and still others are not sensitive to population density variations. Many of the chromosomes produce varying degrees of retardation of the development of the homo- as compared to the heterozygotes.

Particularly interesting is the appearance of "synthetic" lethal and semilethal chromosomes, which arise through crossing over between chromosomes lacking these properties. One chromosome has a dominant effect on the development rate of its carriers; no such effects were present in the ancestral chromosomes. At least two chromosomes have "synthetic" effects on the visible morphology of the flies.

It is concluded that chromosomes in natural populations of *Drosophila pseudoobscura* differ in complexes of linked genes most of which have small individual effects. These gene complexes afford a great store of potential genetic variability which may be released by crossing over and recombination, and then utilized for evolutionary changes. Genes with large individual effects also occur in wild chromosomes.

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