NEW EVIDENCE OF HETEROSIS IN NATURALLY OCCURRING INVERSION HETEROZYGOTES IN *DROSOPHILA PSEUDOOBSCURA*

HOWARD LEVENE * and THEODOSIUS DOBZHANSKY †
Departments of Mathematical Statistics and Zoology, Columbia University

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1. REVIEW OF THE PROBLEM

THE occurrence in natural populations of *Drosophila* of inversion heterozygotes has long been known. Positive evidence that this chromosomal polymorphism has an adaptive function came with the finding that the frequencies of certain gene arrangements in some populations of *Drosophila pseudoobscura* undergo cyclic changes which follow the annual succession of seasons (Dobzhansky, 1943). Wright and Dobzhansky (1946) then made experimental populations in which progenies of flies collected in nature were allowed to breed for a series of generations in population cages. The proportions of chromosomes with different gene arrangements were observed to change from generation to generation. In populations of uniform geographic origin (*i.e.* composed of progenies of flies collected in the same locality) the changes usually obeyed a simple rule. Apparently stable equilibria became established, at which the chromosomes with different gene arrangements continued to occur in the populations. This behaviour is consistent with the hypothesis that the chromosomal polymorphism is balanced ; the inversion heterozygotes are heterotic, and the corresponding homozygotes are adaptively inferior to the heterozygotes. Later it was found (Dobzhansky, 1950) that in geographically mixed populations (derived from flies collected in different localities) heterosis is no longer the rule ; the heterozygotes may be equal, superior, or inferior to the homozygotes.

The hypothesis of heterosis was verified both in experimental and in natural populations. Dobzhansky (1947) compared the frequencies of inversion homo- and heterozygotes among individuals grown under optimal conditions with those among flies which developed in severely crowded population cages. The frequencies obeyed the binomial square rule among the former, but among the latter there was an excess of heterozygotes and a deficiency of homozygotes. Dobzhansky and Levene (1948) then compared the frequencies of inversion homo- and heterozygotes among eggs deposited by wild-caught females of *Drosophila pseudoobscura*, and among adult males of the same species

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collected in their natural habitats. The binomial square rule was obeyed quite well in the egg samples. Among the wild-caught males, the deviations from the proportions demanded by the binomial square rule were not statistically significant in most samples. But the combined data, for males collected in 22 localities mostly in California, showed a quite significant excess of heterozygotes. This is as expected if the inversion heterozygotes are favoured by differential survival in most populations most of the time.

Da Cunha (1953) found some natural populations of *Drosophila willistoni* in which more than 50 per cent. of the females are heterozygous for certain inversions in the X-chromosomes. To be sure, frequencies of heterozygotes in excess of 50 per cent. may be observed without heterosis in populations which are in the throes of rapid genetic changes, and which therefore are not at equilibrium. This difficulty was removed when da Cunha (1956) found several inversions which maintained frequencies of heterozygotes in excess of 50 per cent. in experimental populations of *D. willistoni*, even after these populations reached stable genetic equilibria. Dobzhansky and Pavlovsky (1955) described a population of *D. tropicalis* from a locality in Central America in which about 70 per cent. of the individuals were heterozygous for a certain inversion. An experimental laboratory population derived from the flies from this locality contained 96 per cent. of heterozygotes for the same inversion. Pavan, Dobzhansky, and da Cunha (1957) observed in a locality in Peru a population of *D. paulistorum* with 79 per cent. of heterozygotes for a certain inversion. A somewhat lower frequency, about 60 per cent., of heterozygotes for another inversion was encountered in *D. willistoni* in north-eastern Brazil. The interest of this case is, however, heightened by the fact that the excess of heterozygotes was met with not in one but in several localities, the most remote ones separated by a distance of at least 200 kilometres, and in one of these localities the excess was ascertained at different seasons of the year.

It would certainly be wrong to conclude, as some authors did from the above data, that excesses of heterozygotes must be present at all times in all populations. The occurrence in some natural populations of rapid seasonal changes in the frequencies of chromosomes with different gene arrangements is in itself evidence that the relative fitness of at least some inversion homo- and heterozygotes varies in different environments. An extraordinary sensitivity to environmental changes was already found in *Drosophila pseudoobscura* by Wright and Dobzhansky (1946). At 25° C., the fitness of a certain inversion heterozygote was more than double that of a certain homozygote, while at 16° C. both were apparently alike in fitness. Conversely, certain karyotypes in *D. persimilis* were about equal in fitness at 25° but very different at 16°. In this connection, it is probably not accidental that *D. pseudoobscura* is more at home in warmer and *D. persimilis* in cooler habitats. Da Cunha (1951) and Dobzhansky and

Spassky (1954) induced changes in the relative adaptive values of heterozygotes and homozygotes for some inversions in *D. pseudoobscura* by feeding experimental populations on different species of yeasts. When fed on a nutrient medium with a certain species of yeast, a normally heterotic inversion heterozygote became adaptively inferior to one of the homozygotes at 21°, although not at 25° nor at 16°. As a consequence, stable genetic equilibria were established in some but not in other experimental populations. Yet, no differences in the behaviour of experimental populations of *D. willistoni* fed on different species of yeasts were detected by da Cunha (1956).

Perhaps the most striking demonstration of a delicate sensitivity of inversion homo- and heterozygotes in *Drosophila pseudoobscura* to the environment was adduced in experimental populations in which as many as six different karyotypes were simultaneously present (Levene, Pavlovsky, Dobzhansky, 1954). The adaptive value of a karyotype depends not only on such variables as temperature and food but also on what other karyotypes are living in the same medium. Thus, A may be superior to B in the absence of C, but it may become inferior to B when C is present. A different kind of sensitivity was discovered in *D. robusta* (Levitan, 1951, 1954, 1955). The gene arrangements in the two limbs of a metacentric chromosome show, in at least some populations of this species, a non-random association, which suggests that the chromosome acts as an organised unit rather than as a mechanical aggregate of genes. Moreover, this non-randomness is more pronounced in males than in females ; seasonal changes in the frequencies of the gene arrangements are also more evident in the male than in the female sex. It should also be noted that in *D. pseudoobscura* and in *D. persimilis* seasonal changes occur in populations of some geographic localities but not in others (Dobzhansky, 1956 and older work). It certainly does not follow that the carriers of the different karyotypes are differentiated in fitness in the former but not in the latter localities.

The purpose of the present article is to report some new, and quite uncomplicated, evidence that the heterozygotes for chromosomal inversions naturally occurring in *Drosophila pseudoobscura* and *Drosophila persimilis* are indeed superior in fitness to the corresponding homozygotes.

2. THE DATA

Strains of *Drosophila pseudoobscura* and *D. persimilis* have been maintained for a number of years in our laboratory. With rare exceptions, each strain is derived from a single fertilised female collected in the natural habitats of the respective species, mostly by one of the authors (Th. D.). The dates of collecting have been recorded. The chromosomal constitution which these strains possessed soon after their establishment in the laboratory is also recorded on the basis of the examination of the giant chromosomes in the larval salivary

glands. Some of the strains carried one or more kinds of heterozygotes for inversions in the third chromosomes ; this is, of course, as expected, since at the start each strain must have contained at least four third chromosomes, two derived from the original female, and two from the original male progenitor. The question, then, is this : Does the chromosomal polymorphism persist in the laboratory strains for as long or longer than it may be expected to persist owing to chance alone ?

Laboratory strains are maintained by periodic transfer of samples of flies from the old culture bottles to fresh cultures ; therefore, the unfixed genetic variants in each strain are exposed in every generation to the risk of not being included among the parents of the succeeding generation. If these variants are adaptively neutral, the risk is a function of the number of flies of the preceding generation which become the parents of the succeeding generation. This number can be only approximately estimated, because for maintenance of routine laboratory stocks the flies are transferred without being counted. Mr B. Spassky, who has maintained most of these stocks during most of the time which they have been kept in this laboratory, estimates that the average numbers of the flies transferred from culture to culture were close to twenty, and the maximum numbers close to forty, in each case about equally divided between females and males. For our present purposes an overestimate of this number is preferable to an underestimate ; we shall, therefore, use both the probable and the upper estimates in the calculations. The strains are normally kept in a constant temperature room at about 16° C., but most of them were kept for shorter or longer periods at room temperatures, especially during the early years. They are transferred to fresh cultures about once in six weeks. We shall use six weeks as the estimate of the length of a generation, although when the strains were kept at room temperatures they had to be transferred at shorter intervals.

In November 1956 samples of eggs deposited by the flies from the different strains were taken, and placed in culture bottles in a way to avoid overpopulation and crowding of the larvæ. Salivary glands from about ten larvæ from each strain, one gland per larva, were stained in acetic orcein. The preparations were made by Mrs N. Spassky ; the gene arrangements in the third chromosomes were examined and recorded by one of us (Th. D.). The results are summarised in table 1.

Table 1 lists 28 strains of *Drosophila pseudoobscura* and 11 strains of *D. persimilis*. For each strain are given the name of the locality in which the wild progenitor was collected, the date of collecting, an estimate of the number of generations during which the strain was kept in the laboratory, and the gene arrangements in the third chromosomes which were found in November of 1956. For descriptions of these gene arrangements, and for drawings of the chromosome configurations in some of the inversion heterozygotes, see Dobzhansky

(1944). In only three strains, marked in table 1 by asterisks, have the results of the examination in 1956 deviated from those of the

TABLE 1

The gene arrangements in the third chromosomes in laboratory strains of Drosophila pseudoobscura *and* Drosophila persimilis

Geographic origin	Collected	Generations	Chromosomes
D. pseudoobscura			
Alturas, Calif.	June 1940	143	AR
Amecameca, Mexico	March 1938	166	TL*
Atitlan, Guatemala	Feb. 1928	167	TL
Black Mesa, Ariz.	June 1940	143	AR
Chichicastenango, Guat.	Feb. 1938	167	TL, SC
Coffee Creek, Calif.	July 1940	142	ST, AR
Cuernavaca, Mex.	March 1928	166	CU, TL
Estes Park, Colo.	Aug. 1941	132	EP, TL, PP
Flagstaff, Ariz.	June 1940	143	AR
Huehuetenango, Guat.	Feb. 1938	167	TL*
La Grande, Wash.	Aug. 1932	211	AR, ST
Mara Lake, B. Col.	Aug. 1934	193	AR, ST
Mariposa, Cal.	July 1940	142	AR
Methow, Wash.	June 1940	143	AR, ST
Morelia, Mex.	March 1938	166	SC, TL
Oaxaca, Mex.	Sept. 1935	184	CU, OX
Orizaba, Mex.	March 1938	166	CU, TL
Pachuca, Mex.	March 1928	166	TL
Patzcuaro, Mex.	March 1938	166	SC, TL
Perpetua, Ore.	June 1940	143	AR, ST
Pikes Peak, Colo.	Aug. 1941	132	AR, PP
St Helena, Calif.	July 1940	142	AR, ST
Seattle, Wash.	Aug. 1932	211	ST
Tehuacan, Mex.	March 1938	166	EP, TL
Totonicapan, Guat.	Feb. 1938	167	CU, SC
Whitman N. F., Ore.	June 1940	143	AR, ST
Yollo Bolly, Calif.	July 1940	142	AR, ST
Yuma, Ariz.	Apr. 1941	130	AR, ST
D. persimilis			
Coffee Creek, Calif.	July 1940	142	KL, MD
Deer Creek, Calif.	July 1940	142	KL, WT
Hope, B. Col.	Aug. 1934	193	KL
Nojogui, Calif.	? 1934	192 (?)	WT
Orick, Calif.	July 1940	142	KL, MD
Quesnel, B. Col.	Aug. 1934	193	KL
St Helena, Calif.	July 1940	142	KL, MD
Sequoia N. P., Calif.	Aug. 1940	141	ST
Stony Creek, Calif.	July 1940	142	ST, KL
Weott, Calif.	July 1940	142	KL*
Yollo Bolly, Calif.	July 1940	142	MD

AR—Arrowhead, CU—Cuernavaca, EP—Estes Park, KL—Klamath, MD—Mendocino, OX—Oaxaca, PP—Pikes Peak, SC—Santa Cruz, ST—Standard, TL—Tree Line, WT—Whiteney.

original examination. In all three cases, two different arrangements were originally found but only one was still extant in 1956. More precisely, the Amecameca, Mexico, strain contained in 1938 CU as well as TL chromosomes, but only TL has been preserved. In the Huehuetenango, Guatemala, strain TL and SC chromosomes were present in 1938, but SC was lost. In the Weott, California, strain

of *Drosophila persimilis* KL and MD chromosomes were found in 1940, and only KL in 1956. In 12 strains, only a single third chromosome gene arrangement was found at the original examination, and the same chromosome structure was seen again in 1956. In 23 strains, two different third chromosomes were originally found, and the same two found again in 1956; and in 1 strain three different third chromosomes were found and recovered again. Most of the strains have, evidently, maintained their chromosomal composition during more than 100 generations which they spent in the laboratory cultures.

3. MATHEMATICAL ANALYSIS

Sewall Wright (1931) investigated inbreeding in a random mating population. If the population consists of N_m males and N_f females the effective population size, N, is defined by $1/N = 1/(4N_m)+1/(4N_f)$. If $N_m = N_f$, $N = N_m+N_f$. In the present material, each culture was started with N′ flies chosen at random from the previous culture. Thus N_m fluctuated at random about a mean value of $N'/2$, and because the sexes were not precisely equally frequent, the effective population size over a period of time is close to $N'-1$. Since N′ is only known very roughly, we can take $N = N'$ with no serious error.

Wright (1931) gave a recurrence relation for the coefficient of inbreeding F, and for the panmictic index $P = 1-F$. The relation for P is

$$P_t = \left(1-\frac{1}{N}\right) P_{t-1}+\frac{1}{2N} P_{t-2}, \qquad . \qquad . \qquad . \qquad (1)$$

where the subscript refers to the time in generations since the establishment of the population. The explicit solution of (1) in terms of N and t is easily obtained, and was first given, to the best of our knowledge, by Malécot (1946). The exact formula is

$$P_t = \left(\frac{1-\frac{1}{N}-\sqrt{1-\frac{1}{N^2}}}{2\sqrt{1-\frac{1}{N^2}}}\right)\left(\frac{1-\frac{1}{N}+\sqrt{1-\frac{1}{N^2}}}{2}\right)^t - \left(\frac{1-\frac{1}{N}+3\sqrt{1-\frac{1}{N^2}}}{2\sqrt{1-\frac{1}{N^2}}}\right)\left(\frac{1-\frac{1}{N}-\sqrt{1-\frac{1}{N^2}}}{2}\right)^t \qquad (2)$$

The exact value of P_0 and P_1 is 1. For t greater than 1, the simplified approximate formula

$$P_t = \left(1+\frac{1}{2N}\right)\left(1-\frac{1}{2N}\right)^t \qquad . \qquad . \qquad . \qquad (3)$$

differs from the exact value by a quantity of the order of $t/(16\ N^4)$,

which can almost always be neglected. (*E.g.* for N as small as 20 and t as large as 200, the error is of the order $1/12{,}800 \simeq \cdot 0001$). The even simpler form

$$P_t = e^{-\frac{t}{2N}} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

has an absolute error of at most $1/2N$ and a relative error of approximately $(1/2N)-(t+1)/8N^2$. Table 2 gives the estimated values of t, the number of elapsed generations, the number of cultures with each such value, and the value of P_t calculated from (3) for the most probable N, 20, and for the upper bound of 40.

It may be worth while to make a few remarks here about the nature of this " inbreeding " in random mating finite populations, since many non-mathematical geneticists find it a confusing subject. Let us suppose a population segregating for a pair of alleles or karyotypes A and A', and suppose that in the founding population (generation O) A has the frequency q_0 in both males and females. Then in the next generation ($t = 1$), the probability that an individual chosen at random is heterozygous is $2q_0(1-q_0)$. The probability that an individual chosen at random from the t-th generation will be a heterozygote will be $P_t \cdot 2q_0(1-q_0)$, and in this sense P_t measures the loss of heterozygosis due to inbreeding. However, in fact, the loss of heterozygosis is entirely due to genetic drift from random sampling errors, and if q_t is the actual frequency of A in the t-th generation, then the probability that an individual chosen at random in the t-th generation will be a heterozygote is $2q_{t-1}(1-q_{t-1})$. In other words the Hardy-Weinberg equilibrium will be maintained in the population, so long as it is calculated from *current* gene frequencies, and any " inbreeding " is only relative to a particular reference point in the past. This is quite different from the real departure from the Hardy-Weinberg equilibrium in a population where close relatives mate more frequently than would be expected by chance.

Thus the probability that a random individual will be homozygous is $1-2P_tq_0(1-q_0)$. But what is the probability that a second individual chosen at random will be, say, A A, given that the first one was A A ; what is the probability that two individuals chosen at random will be homozygotes of the same kind ? The answer to these questions is not obvious. It is even less obvious what the probability is that all the individuals in the t-th generation are homozygotes of the same kind ; that is that $q_t = 0$ or 1, although this probability must be large if P_t is close to zero. This probability can be obtained by the methods of Markoff chains, although the labour increases with N, or for large N by consideration of a diffusion process. Kimura (1954) has given the solution for large N in the form

$$H_t = 6q_0(1-q_0)e^{-t/2N} + 14q_0(1-q_0)[1-5q_0(1-q_0)]e^{-6t/2N} + R, \quad (5)$$

where H_t is the probability that both alleles are still present and R is of the order of magnitude of $e^{-15t/2N}$. For $6t/2N$ greater than 7

or t greater than $2 \cdot 4N$, even the third term is less than 0·001, and we have

$$H_t = 6q_0(1-q_0)e^{-t/2N} \quad . \quad . \quad . \quad . \quad (6)$$

This probability of no fixation is largest if $q_0 = 1/2$, as would be expected on intuitive grounds, so that even in this least favourable case for fixation, the probability that fixation has not occurred is only

$$H_t = \frac{3}{2} e^{-t/2N}, \quad . \quad . \quad . \quad . \quad (7)$$

or approximately $1 \cdot 5\ P_t$.

TABLE 2

Estimated number of generations, t, *number of originally heterozygous cultures for each* t, *number of cultures no longer heterozygous, and values of the panmictic index* $P_t = 1 - F_t$ *and of the maximum probability of remaining heterozygous for the most probable population size,* $N = 20$, *and the upper limit of population size,* $N = 40$

t	No. of cultures	No. not heterozygous	N = 20		N = 40	
			P_t	Prob. het.	P_t	Prob. het.
130	1	0	0·041	0·059	0·202	0·296
132	2	0	0·040	0·056	0·197	0·288
142	9	1	0·031	0·044	0·174	0·255
143	3	0	0·030	0·042	0·172	0·250
166	6	1	0·017	0·024	0·129	0·189
167	3	1	0·017	0·022	0·127	0 186
184	1	0	0·011	0·015	0·103	0·150
193	1	0	0·009	0·012	0·092	0·134
211	1	0	0·006	0·007	0·074	0·106
Total	27	3				

Table 2 gives the value of H_t, calculated from (7), for all cultures for $N = 20$ and $N = 40$. In table 2 the largest probability that both alleles are still present is for $N = 40$, $t = 130$ and is approximately 0·3. Even if we took this largest value as the actual probability for all the cultures, the probability that 24 out of the original 27 cultures with more than one chromosome present would not lose any chromosome is less than 10^{-7}. If we take account of the actual time values, and the fact that in one case all of *three* original chromosomes were preserved, this probability would become negligible. Evidently then, some agency was acting to maintain heterozygosis, and the most likely candidate is selection in favour of heterozygotes.

4. INBREEDING WHEN HETEROZYGOTES ARE FAVOURED

It is clear that when heterozygotes are favoured by selection, progress toward homozygosis under inbreeding will be greatly slowed. This process has been studied by the methods of Markoff chains by

Hayman (1953), Hayman and Mather (1953 and 1956), Reeve (1955), and Haldane (1956). Most of these authors considered regular systems of inbreeding, and the only connection with the present problem is that sib mating is equivalent to $N_m = N_f = 1$. Kimura (1955) has considered random mating in a finite population with genic selection, but not selection in favour of heterozygotes. The Markoff chain methods become excessively laborious for N as large as 20, involving 40×40 matrices, while Kimura's methods assume large N and might not be valid for N = 20, even if the formidable analytic difficulties were overcome. Accordingly recourse was had to Monte Carlo methods or in less elegant terms " bean bag genetics ", that is, to a sampling experiment. The model chosen gives the karyotypes A A, A A′, A′ A′, in the ratio $(1-s) : 1 : (1-s')$. Then if the gene frequency in the t-th generation is q_t, the expected gene frequency in the $(t+1)-th$ generation is

$$\tilde{q}_{t+1} = \frac{q_t - sq_t^2}{1 - sq^2 - s'(1-q)^2} \quad . \quad . \quad . \quad . \quad (8)$$

For a given value of s, the probability of fixation in a large number of generations is least for $s' = s$, since in this case equilibrium is at $q = 1/2$ and large or small values of q, with danger of fixation, are least likely. Accordingly s' was chosen to equal s, and (8) became

$$\tilde{q}_{t+1} = \frac{q_t - sq_t^2}{1 - s[q^2 + (1-q)^2]} \quad . \quad . \quad . \quad (9)$$

To minimise the chance of fixation, $\tilde{q}_0$ was then chosen to be $1/2$, and a sample of 2N was chosen from a binomial population with probability $1/2$. The resulting frequency of A was q_1. Then $\tilde{q}_2$ was calculated from (9) and a sample of 2N was chosen from a binomial population with the proportion $\tilde{q}_2$ of A's. The result of this sampling was the observed value of q_2, from which $\tilde{q}_3$ was calculated, and so on. The process was stopped after 170 generations (as representative of the actual cultures) unless fixation was reached before that time.

For N = 40, and $s = s' = 0{\cdot}1$, five trial populations reached fixation in 22, 29, 37, 45 and 55 " generations ". This result is significantly different from the observed 3 out of 27 using Fisher's exact test ($P = 0{\cdot}0002$). Evidently an advantage of 10 per cent. for the heterozygote is not enough to prevent fixation, even with the upper limit of 40 for the population size and with $q_0 = 1/2$, the value least favourable to fixation. Next the more probable population size of 20 was chosen, and $s = s'$ increased to $1/2$. Now two trials went 170 generations without reaching fixation. Finally two trials with N = 20 and $s = s' = 1/4$ gave no fixation in 170 generations, although a third reached fixation in only 14 generations. In general if q became small at some time t, but did not reach fixation, selection soon returned q to near $1/2$, so that the four artificial populations

that did not reach equilibrium in 170 generations ended with the rarer allele having a q of 0·35, 0·40, 0·42, and 0·45. Further trials with $s = 1/2$ and $s = 1/4$ were not made because of the labour and the fact that very many more trials would have had to be made before a significant difference from the observed proportion of 3 fixed out of 27 could be found. Thus it was not practicable to distinguish between $s = 1/2$ and $s = 1/4$ as the proper value, although $s = 0{\cdot}1$ was definitely too small. All that can safely be said is that for most of the chromosome pairs studied s and s' must have been greater than 0·1 and probably greater than 0·2. The three cultures that reached fixation may have been " unlucky " or may have had smaller values of s and s', or s and s' of opposite sign.

5. DISCUSSION

In *Drosophila pseudoobscura* and in *D. persimilis*, heterozygotes which carry two chromosomes of a pair with different gene arrangements but derived from the same geographic population are usually heterotic. However, Epling, Mitchell and Mattoni (1953, 1957) put forward what they believe to be an alternative hypothesis. It is well known that reduction of crossing over in a certain chromosome by a heterozygous inversion may be accompanied by increased recombination in some portions of the chromosomes in which crossing over is normally rare. Epling, Mitchell and Mattoni then postulate that under changing environmental conditions, the increased recombination in the residual genome of structural heterozygotes may aid in adapting to the changing conditions and consequently the offspring of structural heterozygotes will be favoured. It seems doubtful whether a second order effect such as this could actually give the heterozygotes as much advantage as they have in natural populations. As an explanation of the retention of the inversion heterozygotes under the fairly constant conditions of the laboratory cultures, the hypothesis of Epling *et al.* may safely be dismissed.

Nevertheless, heterosis is not an intrinsic property of inversion heterozygotes. Some inversions failed to display heterosis in experimental populations of *Drosophila pseudoobscura* kept at 16° C., or fed on nutrient media with certain yeasts (Dobzhansky and Spassky, 1954 and other work, see above). Yet it is exactly at that temperature that our laboratory strains have been kept and showed a persistence of the inversion polymorphism. This is not necessarily a contradiction ; relatively weak heterosis is hard to detect in experimental populations, and different geographic strains may have different temperature sensitivity ranges, just as the related species, *D. pseudoobscura* and *D. persimilis*, are known to have. It is even less necessary to suppose, as some writers have done, that the heterosis will lead to differential mortality of the inversion homozygotes and consequent disturbances of the ratios demanded by the binomial square rule. Such disturbances

have indeed been found in certain populations, both natural and experimental ones, but they are neither expected nor observed to be universal. In fact, an advantage of the heterozygote with respect to such factors as fertility and fecundity would not cause such disturbances.

Only a few studies have separated the individual components of adaptive value. Spiess, Ketchel and Kinne (1952) found the WT/KL inversion heterozygotes in *Drosophila persimilis* appreciably superior to the WT/WT and KL/KL homozygotes in fecundity. Spiess and Schuellein (1956) showed further that the WT/KL heterozygotes exceed the homozygotes in speed of development from egg to adult and in survival rates during the development. Finally, the heterozygotes possessed superior homeostatic buffering, expressed in lower environmental components of the variance estimates for the traits studied. Such superior homeostasis has also been found by Rosenbaum-Moos (1955) in *D. pseudoobscura* inversion heterozygotes. In this species, the over-all fitness of the ST/CH heterozygotes was found to be no higher than that of the ST/ST homozygotes, but much higher than that of the CH/CH homozygotes. However, the different components of fitness of these karyotypes are known to vary in their relative values quite appreciably in different environments (Heuts, 1947, 1948 ; Birch, 1955).

Inversion polymorphism is clearly a part of the adaptive machinery in natural populations of Drosophila. But no organic system is adaptive as such ; adaptedness is harmony between a living system and the conditions of its existence. The relative adaptive values of the heterozygous and homozygous karyotypes in Drosophila populations are exquisitely sensitive to variations in the environment ; and yet the populations are homeostatically buffered against environmental disturbances because they are composed of numerous genetic types with diverse environmental optima.

6. SUMMARY

Strains of *Drosophila pseudoobscura* and *Drosophila persimilis*, each descended from a single inseminated female collected in nature, have been kept in laboratory cultures for an estimated 130 to 211 generations (see table 1 for particulars). The strains were examined for inverted sections in their third chromosomes within a few generations after their capture. At that time, 26 strains contained two gene arrangements each, 12 strains one gene arrangement each, and 1 strain three gene arrangements. Re-examination of the same strains showed that only 3 of the 27 strains which were structurally polymorphic became uniform in the course of time.

Groups of flies estimated to consist of between 20 and 40 individuals were transferred to new food in each generation to maintain the strains. It can be calculated that, with this breeding system, the strains should have become homozygous with respect to most of the unfixed genes

and chromosomal structures which they contained originally. The failure of the 24 out of the 27 strains to become homozygous for the gene arrangements in third chromosomes shows that the inversion heterozygotes are superior in fitness to the inversion homozygotes.

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