EFFECTS OF DISRUPTIVE SELECTION

I. GENETIC FLEXIBILITY

J. M. THODAY
Genetics Department, Sheffield University

Received 14.vi.58

THIS article, and those which will follow it, concern the results of experiments using artificial selection of the type that Mather (1953*a*) has called *disruptive* and Simpson (1944) has called *centrifugal*. Such selection may be said to occur when we maintain a single population by choosing more than one class of individuals to provide the parents of each generation. In its extreme form disruptive selection involves choosing both extreme classes and discarding intermediates.

The antithesis of disruptive selection is *stabilising selection* (Simpson's centripetal selection), which occurs when we choose, as parents of each generation, individuals at, or as close as possible to, the mean of the population from which they come.

Mather's third type of selection is the more usual *directional selection* whose effects have been widely studied.

Cyclic selection (Thoday, 1956) provides a fourth type which would occur if we were to reverse the direction of selection in different generations. It clearly has something in common with disruptive selection as Mather (1955*a*) has pointed out.

Waddington (1953, 1958) has classified selection according to the effects it may be expected to produce, rather than according to the measurable characters of the individuals selected. While of value for theoretical discussion, such a classification cannot be used in designing selection experiments and is not therefore used here.

Schmalhausen (1949), Mather (1953*a*, 1955*a*, *b*) and Waddington (1953, 1958) have discussed the consequences that might be expected to result from different types of selection. In principle we must expect effects of two kinds. Responses might occur as changes in the effective variety of genotypes, or as changes in the variability of development. The first would involve change in the amount of effective genetic variation in the population. The second would involve change in the responsiveness of the developmental system to the environmental variance to which the population is exposed, or changes in the amount or effectiveness of the accidental sources of developmental variance that Waddington, Graber and Woolf (1957) call developmental noise. We may therefore expect stabilising selection to reduce the genetic variation in a population (Waddington's normalising selection) or to increase the stability of the developmental processes mediated by the genotypes in the population (Waddington's stabilising or canalising selection), or to do both. Disruptive selection might be

expected to have the opposite effects, increasing genetic variation and/or increasing developmental flexibility by producing epigenetic systems with alternative pathways. It might also act to reduce developmental stability or the canalisation of existing pathways.

Mather (1955*a*) has further argued that disruptive selection should have more profound effects. Provided that the two or more types selected are necessary to one another, disruptive selection might be expected to give rise to a polymorphic situation based on alternative pathways of development. Development might be switched into one or other path by a genetic switch mechanism, or by an environmental switch which, if available, should be equally effective and might equally well be exploited. On the other hand, if the two or more types selected are not dependent on one another, then disruptive selection could put a premium on the development of an isolation barrier and lead to the separation of different populations with different characteristics.

Mather's predictions imply that disruptive selection may be of the greatest evolutionary significance. Yet few experiments have been carried out to determine how effective either disruptive selection or stabilising selection may be. Falconer and Robertson (1956) compared the effects of stabilising and disruptive selection for weight in mice and Falconer (1957) has studied the effect of stabilising selection on abdominal chaeta-number in *Drosophila*. Neither of these experiments gave marked results though there was some reduction in variance in the mouse stabilising line. The present paper describes the results of similar experiments using sternopleural chaeta-number in *Drosophila melanogaster*. A preliminary account has already been published (Thoday, 1958*a*).

1. MATERIAL AND CULTURE METHODS

All the experiments have been carried out in lines that originate from a single wild stock " Dronfield." This wild stock derived from a single fertilised female captured near Sheffield in May 1954, and has been maintained at 25° C. (approximately) ever since, usually by 4-pair transfers. It is the same stock as was used for the directional selection experiments described by Thoday (1958*b*).

Details of culture are similar to those previously described (Thoday, 1958*b*). Each line is maintained by 4 cultures in each generation (three weeks per generation), each culture having a single pair of parents. The 4 cultures are labelled according to the origin of their mothers and represent 4 separate female sub-lines. A culture is assayed by counting chaeta-numbers on both sides of 20 flies of each sex, and the best 8 of each sex are selected. Of any such 8 the best is intended to continue the line, but the second, third and fourth are set up as insurance cultures in case the first fails. (When the best successful culture seemed likely to produce very few flies, virgins were sometimes collected from a second culture and used to provide extra flies to complete the assay.) The remaining 4 are set up together in a fifth (" mass ") culture to ensure absolutely against the loss of a female line. (It has only been necessary to use 8 of these in the experiments described here.) Thus each line is

set up as 16 single-pair cultures and 4 four-pair cultures, though the aim is only to use 4 single-pair cultures, one from each female line. This procedure is designed to ensure against loss of female lines, and is necessitated by the insistence on single-pair cultures.

If, in selection, choice had to be made between two flies of equal chaeta-number, the more bilaterally symmetrical was chosen.

2. MATING AND SELECTION SYSTEMS

(i) Disruptive selection with negative assortative mating: the D⁻ line

The first disruptive selection line to be established was primarily intended to assess the possibility that selection might be able to bring

TABLE 1

The mating and selection systems

	Parents of Generation	Culture (*i.e.* female sub-line)							
		A		B		C		D	
		♀	♂	♀	♂	♀	♂	♀	♂
(*a*)	D⁻								
	n	HA × LC		HB × LD		LC × HA		LD × HB	
	n+1	HA × LD		HB × LC		LC × HB		LD × HA	
	n+2	HA × LC		HB × LD		LC × HA		LD × HB	
	n+3	HA × LD		HB × LC		LC × HB		LD × HA	
	etc.								
(*b*)	D⁺								
	n	HA × HC		HB × HD		LC × LA		LD × LB	
	n+1	LA × LD		LB × LC		HC × HB		HD × HA	
	n+2	HA × HC		HB × HD		LC × LA		LD × LB	
	n+3	LA × LD		LB × LC		HC × HB		HD × HA	
	etc.								

The entries designate the parents used to produce the culture in the generation shown in the first column. H indicates the highest, and L the lowest chaeta-number fly found in the appropriate culture. A, B, C and D indicate the culture from which the fly was selected.

about responses in the cytoplasm, and a preliminary report has been given (Thoday, 1958*c*) of the results from this point of view. The mating and selection system is given in table 1*a*.

(ii) Disruptive selection with positive assortative mating: the D⁺ line

This line was set up specifically to test the effects of disruptive selection, and was designed to ensure that cytoplasmic variables, if any, would not be subjected to consistent selection. The mating and selection system used is given in table 1*b*. This system ensures that there is selection for high and for low chaeta-number flies in each generation, but that high and high will be mated together, and low and low will be mated together in separate cultures.

At generation 21 of this line an unfortunate error was made in selection. *For this one generation the whole line was selected for low chaeta-number.* This must be borne in mind when the results are considered.

(iii) Stabilising selection: the S line

This line is maintained by exactly the same mating system as shown in table 1*b*, and originated from the generation 1 cultures of the D^+ line. It was intended to provide a comparative line. The flies selected in each generation are those with chaeta-numbers nearest to the mean of the wild stock from which the lines originated. This mean has varied from 17 to 18 chaetæ, and, as males usually have rather fewer chaetæ than females, the aim is always to select females with 9 chaetæ on each side, and males with 9 on one side and 8 on the other. This aim has usually but, of course, not always been achieved. This mean of 17·5 proved a little low, so that there has been slight directional selection as well as stabilising selection.

(iv) Divergent-directional selection

Certain divergent-directional selection experiments have been carried out on the lines to test their responsiveness to directional selection. Each of these involved taking coincidentally a high selection line and a low selection line and observing their divergence over three generations. Each of these lines was maintained with 4 single-pair cultures per generation, a rotational mating system being used exactly as described in Thoday (1958*b*). The four initial cultures always included all four female sub-lines of the line under test. These test lines were run at a generation every two weeks (not three weeks as for the main lines) for three generations.

3. CHAETA-NUMBER, ASYMMETRY AND VARIANCE IN THE LINES

Fig. 1 shows the mean chaeta-numbers, arithmetic asymmetries and within-culture-and-sex mean squares for the three lines. The asymmetry values are means of the differences between the sides of the flies, sign ignored. No correction for relation between asymmetry and mean (Thoday, 1955, 1958*b*) has been made. Neither are the variances corrected for any comparable relation to mean.

The generation numbers in the figure are those applicable to the D^- line. Coincident generations for the three lines as plotted were cultured coincidentally.

(i) The D⁻ line

The selection practised on the D^- line clearly had negligible effect on mean chaeta-number in the first 10 generations. Neither variance nor asymmetry show evidence of a trend during this period.

From generation 10 to generation 17, the mean rose slowly but

steadily and this was accompanied by wide fluctuations of variance which, however, was higher after this period. At the same time asymmetry rose sharply to a new level, a rise that coincided with and appears to have been confined to the period of most rapid response

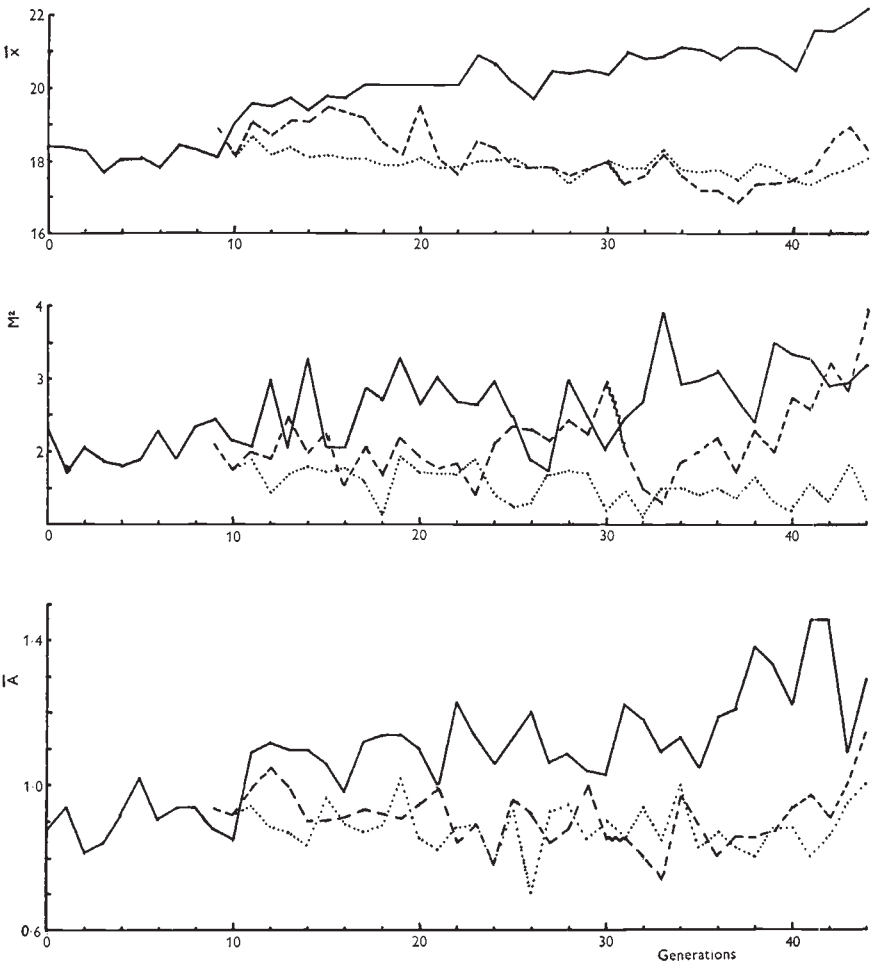

FIG. 1.—Mean chaeta-numbers ($\bar{x}$), within-sex-and-culture mean squares (M^2) and asymmetries ($\bar{A}$) in the three lines. Solid line D^-: broken line D^+: dotted S. The generations are those applicable to D^-: points plotted together represent data obtained from coincidentally raised cultures. The generation at which the selection error was made in D^+ is marked by a wavy line.

in mean. It is clear that events during this period were complex. Variance and asymmetry can both be correlated with mean and part of their rise is likely to be due to this correlation. But the fluctuations of variance, and the suddenness of the rise in asymmetry suggest that other factors are involved.

From generation 17 to generation 22 the mean was very steady

indeed and the variance, though fluctuating, showed no overall change. Thereafter the mean fluctuated a little but rose slowly, variance fluctuated widely but showed a further overall rise, and asymmetry behaved similarly though its rise seems more striking in recent generations.

Apart from the rise of mean chaeta-number there is little clear evidence of any change in this line that could be attributed to disruptive selection, and the results are essentially the same as those of the corresponding mouse line of Falconer and Robertson (1956). The overall rises in variance and in asymmetry may be attributable to correlations of these measures with mean. However, inspection of the curves does suggest that changes are occurring. The relative steadiness of variance at the beginning of the experiment suggests that the fluctuations that occurred later have some real meaning, and the correlation of asymmetry with mean seems far from complete. There is also a suggestion of a cyclic behaviour of asymmetry which is subject to rises and falls, as if selection were occasionally picking out developmentally unstable genotypes, but that these were then being eliminated by natural selection. It seems that both variance and asymmetry are subject to complex causes of changes. Some of these causes may counteract one another, and some will be independent of the artificial selection. The comparatively negative results for variance cannot therefore be critical evidence that variance is little affected by the artificial selection.

(ii) The D+ line

The mean chaeta-number of this line rose during the first 9 generations and then fell until it coincided with that of the S line. Variance behaved likewise at first. There were two fluctuations of mean, the more notable being that at generation 11 (Generation D^- 20 in fig. 1). Since this coincides with a period of very stable mean in D^-, and is not reflected in S, it seems at first rather unlikely that some environmental fluctuation can have been responsible. However, the single generation rise in mean occurred in all four cultures of the line and an environmental factor to which only the D^+ line was responsive seems to be the most probable cause.

After these fluctuations the D^+ mean remained virtually identical with that of S until, at generation 21 (D^- 30), the error of selection was made and it fell 0·5 chaetæ. It then remained below that of S until the most recent generations. During the period of stable mean, variance rose until at generation 21 (D^- 30) it had reached the level characteristic of line D^-. Over this period the variance of D^+ was clearly greater than that of S, though their means were the same. There is no suggestion that their asymmetries were different, and it therefore seems very likely that disruptive selection during this period caused an increase in the effective genetic variation in the D^+ line, though of course asymmetry can only be a very partial measure

of non-genetic variance. The error in selection made in generation 21 (D^+ 30) resulted in the loss of this increased within-sex-and-culture variance. It has, however, been regained since. Variance has now risen above that of D^- and is still rising.

TABLE 2

Coefficients of within-sex-and-culture variation (per cent.) and coefficients of asymmetry ($A/T \times 1000$)

D^- Generations		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
D^-	CV	8·4	7·1	8·4	7·7	7·4	7·6	8·4	7·5	8·4	8·7	7·7	7·5	8·9	7·2	9·4
	A/T	48	51	45	47	51	56	50	51	51	49	45	55	58	55	57
D^+	CV										7·5	7·3	7·5	7·3	8·2	7·2
	A/T										49	51	52	56	53	48
S	CV											7·3	7·5	6·5	7·1	7·5
	A/T											51	51	49	48	47

D^- Generations		15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
D^-	CV	7·1	7·3	8·4	8·2	9·0	7·3	8·9	8·3	7·8	8·2	7·9	6·9	6·4	8·5	7·7
	A/T	53	50	55	57	57	55	50	62	55	51	56	61	52	53	51
D^+	CV	7·6	6·3	7·6	6·8	8·2	7·0	7·3	7·8	6·3	7·9	8·6	8·6	8·1	8·9	8·4
	A/T	45	48	48	50	50	49	55	47	48	42	54	51	46	50	56
S	CV	7·1	7·5	7·1	5·9	7·9	7·2	7·4	7·2	7·7	6·7	6·2	6·4	7·3	7·4	7·3
	A/T	45	50	49	51	58	48	46	50	49	43	52	40	52	55	47

D^- Generations		30	31	32	33	34	35	36	37	38	39	40	41	42	43	44
D^-	CV	7·0	7·5	7·9	9·6	8·0	8·1	8·5	7·9	7·3	8·8	8·4	8·4	7·7	7·8	8·0
	A/T	50	58	57	52	53	50	57	61	65	63	58	66	67	48	58
D^+	CV	9·6	8·3	6·9	6·1	7·8	8·2	8·6	7·5	8·8	8·1	9·5	9·1	9·6	8·8	10·9
	A/T	47	49	41	40	55	52	47	51	49	50	54	54	49	54	62
S	CV	6·6	6·8	5·9	6·6	6·8	6·6	6·9	6·7	7·2	6·4	6·3	7·3	6·5	7·7	6·3
	A/T	51	47	45	46	56	47	49	48	45	49	50	46	49	53	55

Note.—This table and figure 1 have been completed to the time of going to press. Other tables and computations do not include the most recent generations.

(iii) The S line

The mean of this line, initially a little over 18 chaetæ, declined slowly, as is to be expected since the parents in each generation averaged 17·5 chaetæ. Variance and asymmetry suggest little, if any, significant change though variance declined a little.

4. COEFFICIENTS OF VARIATION

The differences of mean chaeta number distinguishing D^- and the other lines, and at times distinguishing D^+ and S, make it difficult to interpret comparisons of the variances of these lines. Coefficients of variation are often used in such situations, though coefficients of variation involve assumptions about the relation between variance and mean which are difficult to justify. Despite the problems to which these assumptions give rise, it seems worth comparing the lines in this way and table 2 lists the coefficients. There is no evidence of change

of the coefficient of variation of D^-. On the other hand there is evidence of a rise with generations in D^+ and a fall in S. The regression of coefficient of variation on generations for D^+ is positive and just significant ($t_{(28)} = 2{\cdot}03$, $P \simeq 0{\cdot}05$) and that for S is negative and significant ($t_{(28)} = 2{\cdot}48$, $P \simeq 0{\cdot}02$). The two regression lines meet at generation 0. Table 3 gives the results of a joint analysis of variance for these two lines, showing that the joint regression is not significant, the two regressions are significantly different, and D^+ has a significantly higher mean than S. D^+ disruptive selection has raised, and stabilising selection has lowered the coefficient of variation.

If we accept coefficients of variation as meaningful, we must conclude that D^+ disruptive selection has raised and stabilising selection has lowered variance. D^- selection has failed to raise coefficient of

TABLE 3

Analysis of variance of coefficients of variation for the D^+ and S lines

Source	*n*	Mean Square	P
Joint Regression on Generations.	1	16·1580	$\simeq 0{\cdot}5$
Difference between Regressions .	1	355·4631	$< 0{\cdot}01$
Difference between Means. .	1	968·0166	Small
Error	56	42·1597	...

variation, though it has raised mean and uncorrected variance. It is of course quite likely that the relation of variance to mean differs in different lines, and that the negative result for D^- is not real.

5. COEFFICIENTS OF ASYMMETRY

Sternopleural asymmetry is a partial measure of the stability of development (Thoday, 1958*b*), but, like variance, it may also be related to mean (Mather, 1953*b*) so that comparison of the asymmetry of lines whose means are different is problematical. The base stock, " Dronfield," used for these experiments is the same as that used for those described in Thoday (1958*b*), in which what may be called a coefficient of asymmetry was used to correct for the scaling problem. This was calculated by dividing mean asymmetry (A) by mean chaeta-number (T). Those experiments provided evidence that the correction was satisfactory for this stock and it therefore seems justifiable to use it here. Table 2 lists the A/T values (multiplied by 1,000 for convenience). There is clearly no evidence of change of A/T in D^+ or S or of difference between them in this respect. A/T has, however, risen in D^-. Its initial value ($\times$ 1,000) is of the order of 50 and is the same as that for D^+ and S and for the Dronfield stock when the experiments described in Thoday (1958*b*) were begun. This seems a stable and characteristic value of A/T in this stock in our culture conditions.

The value has, however, risen in the D⁻ line. The regression on generations is positive and significant ($t_{(40)} = 4{\cdot}7$, P small). It seems likely, however, that the rise has not been consistent, but that it is entirely attributable to two periods in the history of the line, one at about generation 11 and the other at about generation 36. Table 4 gives the analysis of variance of D⁻ A/T for generations 0-41, the generations being combined into seven blocks of 6 generations each. Two of the six degrees of freedom for blocks of generations absorb all the significant variance. These two degrees of freedom correspond to the divisions between generations 11 and 12 and between generations 35 and 36. The first rise is that evident in fig. 1 and coincides with the first sharp rise of mean chaeta-number. Here selection of higher chaeta-number genes may have caused a deterioration of developmental stability as it did in the lines described in Thoday (1958*b*).

TABLE 4

Analysis of variance of A/T for the D⁻ line, generations 0-41 (Six-generation blocks)

Source	*n*	Mean Square	P
Blocks 1 + 2 v. rest . . .	1	310·2880	<0·001
Block 7 v. rest	1	246·5334	<0·001
Residual blocks . . .	4	6·0208	...
7 six-generation blocks . .	6	96·8175	<0·001
Within blocks (Error) . .	35	12·8048	...

The second rise, at generation 36, occurred in a period of stable mean and presumably reflects a direct response of developmental stability to disruptive selection.

The indications would seem to be that disruptive selection can pick out genotypes that decrease developmental stability, but that the resulting effect is slight and is rarely permanent. Of the rises in asymmetry and A/T that occurred in D⁻, only the two discussed above were sustained. Others occurred, notably at generations 17, 22 and 31, but each was followed by a fall as if natural selection were subsequently eliminating them. It must be concluded that stability of development as measured can respond but responded little to the types of selection used here. There is certainly no evidence of steady deterioration in both the D lines or of improvement in S.

It may seem that the rises in A/T which did occur in the D⁻ line should be reflected in the variances or coefficients of variation. The correlation between coefficient of variation and A/T for the D⁻ line is positive but very insignificant, so that there is no evidence of such reflection. Correlations between asymmetry and variance can occur (Thoday, 1955; Beardmore, unpub.) and might be expected to be evident in these data. That they cannot be detected may indicate that other more important causes of variation of variance are operating.

6. FERTILITY

The data available provide two measures of the fertility of the lines. Records have been kept of the cultures that failed in each generation, and of the number of flies collected in the culture used to assay each female line (except on the 8 occasions when all 4 single-pair cultures of a female sub-line failed and the mass cultures had to be used).

The failure rates are (per culture) 0·187 for D^-, 0·184 for D^+ and 0·254 for S. There is no evidence of difference between coincident generations of D^- and D^+ in this respect, and there is no evidence of a consistent trend of failure rate in D^- as the experiment progressed. The difference between S and D^+, however, is significant (100 failures

TABLE 5

The number of single-pair cultures that failed.
(From 16 cultures set up per line per generation)

D^- Generations	D^-	D^+	S
0-10	18	...	...
11-21	46	40	48
22-32	42	37	43
33-43	19	23	43

out of 528 cultures in D^+, 134 out of 528 in S, $\chi^2_{(1)} = 6{\cdot}3465$ $P<0{\cdot}02$) and there is evidence suggesting that this difference has increased with generations. (Comparing the lines in the first 11 generations $\chi^2_{(1)} = 0{\cdot}9697$, $P>0{\cdot}3$, the second 11 generations $\chi^2_{(1)} = 0{\cdot}5823$, $P>0{\cdot}3$ and in the third 11 generations $\chi^2_{(1)} = 7{\cdot}4592$, $P<0{\cdot}01$, though the lines × generations χ^2 is not quite significant.) If this increase of difference between the lines is real it is a little difficult to interpret, for it occurs, not as increase in the number of failures in S, but as decrease of failures in D^+ (table 5). The only firm conclusion we can draw, therefore, is that failures are more frequent in the S line than the others. However, the D^- data would suggest that culture conditions or the handling of the flies has varied, thus masking deterioration of fertility in S and giving a spurious improvement in D^+. That S has in fact deteriorated is clear from other evidence (see below).

The data for productivity are more informative, despite the large error such data have. The total flies recorded for D^+ and S (the two strictly comparable lines) are summarised in table 6. Table 7 presents the results of an analysis of variance of the D^+ and S productivities. It seems clear that productivity has declined significantly in both lines, that it has declined more in S than D^+, and that S is very much less productive than D^+. D^- figures are similar to those for D^+. That fertility declines with selection is well known (Mather and Harrison, 1949), but it seems surprising that stabilising selection should be the

more effective in producing such a decline in the present experiments. Quite apart from these data, handling the lines themselves gives a strong impression that the S line has become very poor indeed. Its

TABLE 6

Mean numbers of flies collected per culture in D+ and S

Generations	D−	S
First 8 . . .	154	134
Second 8 . .	128	91
Third 8 . .	103	76
Fourth 8 . .	122	77
Total . .	*127*	*95*

lack of vigour is similar to that of a poor inbred line or a newly-plateaued selection line and suggests that stabilising selection in conjunction with small population size may have led to increasing homozygosity and consequent unbalance.

TABLE 7

Analysis of variance of productivities of cultures: D+ and S

Source	*n*	Mean Square	P
Lines	1	63409	Small
Generation Blocks . . .	3	39833	Small
Lines × Generation Blocks . .	3	2758	<0·001
Residual Generations . . .	28	6011	Small
Cultures, etc. (Error) . . .	219	389	...

7. RESPONSIVENESS TO DIRECTIONAL SELECTION

It is clear that, though it provides positive clues in the D+ line and perhaps in S, variance cannot be relied upon in a negative sense as an indicator of the effects of disruptive or stabilising selection. There are too many factors that may cause it to change and some of them at least (*e.g.* inbreeding in the S line) may act to change variance in directions opposite to those in which the artificial selection might be expected to change it.

Such difficulties were anticipated when the experiments were initiated and it was planned to test the lines, using divergent directional selection experiments, to determine how much free genetic variation they possessed. Such tests have been carried out on D− at generations 21, 27 and 32; on D+ at generations 13 and 23 and 34 (= D− 22, 32 and 43); and on S at generations 11, 12, 17 and 22 (= D− 21, 22, 27 and 32).

The results are presented in fig. 2 in which the rates of divergence of High and Low line means are plotted. Results are also given in

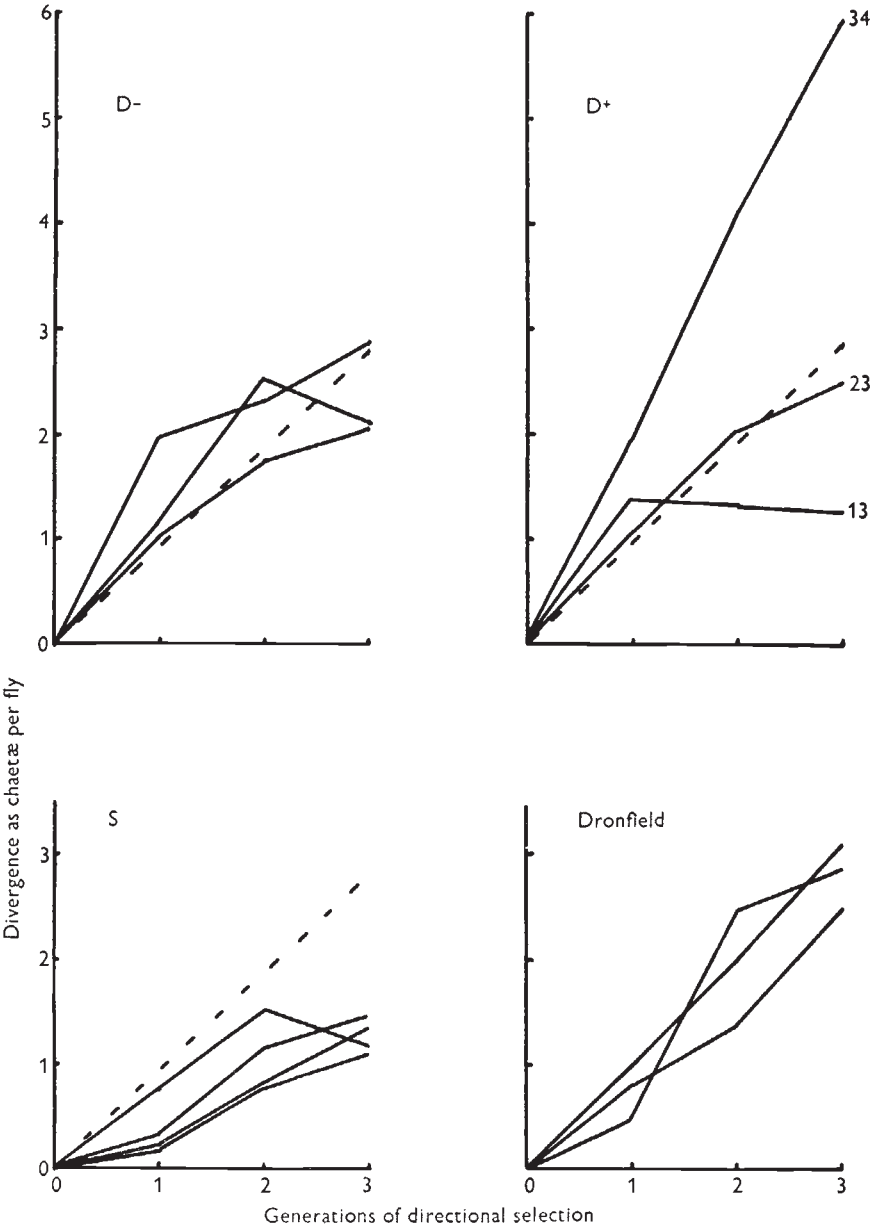

FIG. 2.—Results of divergent-directional selection tests on the lines and on the base stock (Dronfield) from which they were derived. Each solid curve represents the difference, in chaetæ per fly, between a high and a low selection line. The broken line represents the mean result of the three tests on the base stock. The generations in which D^+ was tested are indicated and are those plotted with D^- 22, 32 and 43 in Figure 1.

this figure for comparable tests of the wild Dronfield stock from which all the lines derive. Two of these are taken from the data of Thoday

(1958*b*), and the third was carried out two and a half years later (coincidentally with the tests on generation 27 D⁻ and 17 S). The agreement between these three testifies to the stability of this stock.

It is clear from the results of these tests that the D⁻ line and the S line differ. They were in fact already different when first tested and there is no evidence of subsequent further change. The D⁻ line is responsive to selection, and the S line is much less so. The S line is less responsive to selection than the Dronfield stock from which it came. The D⁻ line seems to respond more than the Dronfield stock to one generation of selection, but thereafter its response decreases so that after three generations of directional selection it has diverged no more and perhaps less than the stock.

Two of the D⁺ line tests were made at unfortunate times. The first test at generation 13 was made before variance had begun to rise in the line. It gave results in the first generation of directional selection comparable with those of the D⁻ line, but there was no further response. It was not possible to arrange to test it again until shortly *after* the error in selection had been made. It then (generation D⁺ 23 = D⁻ 32) responded exactly as the base stock. Bearing in mind that the selection error in D⁺ 21 (= D⁻ 30) had lowered the mean-square of this line from about 2·5 to about 1·5, this response is remarkable. D⁺ was tested again at generation 34 (= D⁻ 43) after it had regained a higher variance. At this test it proved most responsive, and there seems no doubt that it is now much more responsive than the base stock from which it was derived.

Together these tests make it quite clear that the D lines contain more effective genetic variation than the S line. They are genetically more flexible. There is also a suggestion that the genetic variation in the D⁻ line is more readily exploited by one generation of selection than is that in the Dronfield wild stock, and there is no doubt that disruptive selection has made the D⁺ line considerably more responsive than the stock.

These results may be used to provide estimates of heritability (realised heritability) from the formula $h^2 = \frac{d\mathrm{O}}{d\mathrm{P}}$ (where dO is the difference between the high and low line means after 1 generation of selection and dP is the difference between the selected parents used to produce the two lines). The formula is equivalent to $h^2 = \Delta \mathrm{P}/_i$ (Lerner 1950).

The combined results for the first generations of all the divergent directional selection tests give $h^2 = 0{\cdot}29$ for D⁻, 0·26 for D⁺, 0·15 for the base stock, and 0·09 for S. Heritability estimates obtained from the progeny tests of D⁻ and S figured in Thoday (1958*a*, fig. 3) are 0·20 for D⁻ and 0·05 for S, and are in reasonable agreement with those above.

8. DISCUSSION

Natural populations of outbreeding species are genetically diverse (*e.g.* Dobzhansky, 1955) and the causes and maintenance of this diversity present problems of great importance in the study of evolution. This genetic diversity is, in some materials at least, so great that we can speak of genetic individuality. Its study is therefore also of general philosophic importance, especially as man himself is one of the species in which (apart from identical twins) each individual is genetically unique (Medawar, 1957).

Systems that promote outbreeding help to maintain such genetic diversity. Indeed we regard the maintenance of diversity as the main function of outbreeding systems and of all the relevant aspects of genetic systems that promote heterozygosity and segregation (Darlington, 1939). But outbreeding systems cannot of themselves maintain gene frequencies indefinitely, and it is necessary to postulate selective forces that will do so. The same selective forces may be supposed responsible for the maintenance of the genetic systems themselves.

Three such selective forces have been proposed. The first is long-term selection for adaptability or genetic flexibility (*e.g.* Darlington, 1939; Mather, 1943; Thoday, 1953). Organisms have evolved in a changing environment, and selection must have, in the long run, eliminated those forms which did not maintain sufficient genetic flexibility. At the same time, short-term selection promotes genetic stability, so that high mutation rates which would permit genetic flexibility only at the expense of stability are inadequate. Heterozygous systems permit both stability and flexibility, so that stable heterozygous systems and the genetic diversity they bring about would result. Such long-term selection seems sufficient explanation to some but others doubt whether the selective forces could be adequate to account for the prevalence of outbreeding systems or the degree of diversity in contemporary populations. This quantitative objection may be valid, though it is difficult to assess, for selection against genetic inflexibility must in the long run be absolute, and the capacity of pathogens for rapid evolution implies that the long run may be shorter than we think. Nevertheless it does seem probable that other factors must be involved.

The second selective force is selection for heterozygotes. Here it is supposed that heterozygosity *per se* has some intrinsic virtue, in providing a more complex and versatile physiology. This must derive from inter-allelic interactions, or otherwise duplication could permit both alleles to become homozygous. There is evidence suggesting that such heterozygous advantage may occur, though it is always difficult to be sure what " allele " means in this context. The most cogent evidence is that of Allison (1955) and Hunt and Ingram (1958) concerning sickle-cell anaemia and the chemical structure of the haemoglobins. Here, however, there seems no good reason for invoking inter-allelic interaction. The evidence rather indicates

independent action of the two alleles and there seems no reason why duplication should not ultimately occur and produce a homozygous individual capable of producing haemoglobin A and one or both the alternatives. On the whole there seems little reason for supposing that heterozygosity had any primitive advantage (Thoday, 1955). Though some results (e.g. Wallace and Vetukhiv, 1955) are difficult to explain, it seems unlikely that superior fitness of heterozygotes can be the prime cause of heterozygosity. The success of haploid and inbreeding species argues strongly against heterozygosity having any essential virtue other than as the prerequisite of segregation as Mather has made clear (*e.g.* Jinks and Mather, 1955).

The third type of selective force (Levene, 1953; Moree, 1953; da Cuhna and Dobzhansky, 1954; Mather, 1955*a*; Li, 1955; Robertson, 1956; Thoday, 1956) is one which may be supposed to operate in the short run to maintain the frequencies of heterozygotes. This is continued selection for actual phenotypic (especially physiological) diversity. Most populations occupy quite heterogeneous environments and are therefore exposed to disruptive selection. Their environments are also subject to cyclic changes so that the populations will also be exposed to cyclic selection which is likely to have similar effects. Robertson (1956) has shown theoretically that disruptive selection (D^- in type) would be expected to maintain gene frequencies and that stabilising selection would be expected to lead to fixation. The present experiments show that this result is borne out in practice. Further, the D^+ line, which represents a situation likely to occur in nature more often than disruptive selection with negative assortative mating, shows that disruptive selection can actually increase the effective variation within a population. The experiments therefore demonstrate that heterogeneity of the environment can in practice promote genetic diversity, as well as maintaining such diversity, and provide evidence favouring the view that disruptive selection is an important cause of the genetic diversity which we find in populations in nature.

9. SUMMARY

1. Three lines, each derived from the same base stock of wild *D. melanogaster*, have been maintained under different systems of selection for sternopleural chaeta-number. One (D^-) was maintained under disruptive selection with negative assortative mating, one (D^+) under disruptive selection with positive assortative mating, and the third (S) under stabilising selection.

2. D^- selection resulted in an increase of mean chaeta-number, some deterioration of developmental stability (homeostasis) as measured by sternopleural asymmetry, but little if any change of variance that could not be attributed to the correlation of variance and mean.

3. D^+ selection resulted in an increase of variance.

4. S selection resulted in a decrease of variance and a decline of vigour.

5. The D lines were more responsive to directional selection than the S line.

6. The D^+ line has become more responsive to directional selection than the base stock from which it was derived. The S line is less responsive than the base stock.

7. Estimates of realised heritability are D^- 0·29, D^+ 0·26, the base stock 0·15, and S 0·09. The D^+ estimate is minimal as two of the three tests on which it is based were carried out at unfavourable times in the history of the line.

8. It is concluded that disruptive selection can promote and stabilising selection can decrease genetic flexibility, and, therefore, that heterogeneity of habitat may be an important cause of genetic diversity in natural populations.

Acknowledgments.—I am indebted to Mr T. B. Boam for assistance and to the Agricultural Research Council for a grant which has aided this work.

10. REFERENCES

ALLISON, A. C. 1955. Aspects of polymorphism in Man. *Cold Spr. Hbr. Symp. Quant. Biol.*, *20*, 239-255.

DARLINGTON, C. D. 1939. *The Evolution of Genetic Systems.* Cambridge.

DA CUHNA, A. B., AND DOBZHANSKY, TH. 1954. A further study of chromosomal polymorphism of *D. willistoni* in its relation to the environment. *Evolution*, *8*, 119-134.

DOBZHANSKY, TH. 1955. A review of some fundamental concepts and problems of population genetics. *Cold Spr. Hbr. Symp. Quant. Biol.*, *20*, 1-15.

FALCONER, D. S. 1957. Selection for phenotypic intermediates in *Drosophila*. *J. Genet.*, *55*, 551-561.

FALCONER, D. S., AND ROBERTSON, A. 1956. Selection for environmental variability of body size in mice. *Z.I.A.V.*, *87*, 385.

HUNT, J. A., AND INGRAM, V. M. 1958. Allelomorphism and the chemical difference of the human haemoglobins A, S and C. *Nature*, *181*, 1062-3.

JINKS, J. L., AND MATHER, K. 1955. Stability of development of homozygotes and heterozygotes. *Proc. Roy. Soc.* B, *143*, 561-578.

LERNER, I. M. 1950. *Population Genetics and Animal Improvement.* Cambridge.

LEVENE, H. 1953. Genetic equilibrium when more than one ecological niche is available. *Amer. Nat.*, *87*, 331-333.

LI, C. C. 1955. *Population Genetics.* Chicago.

MATHER, K. 1943. Polygenic balance and natural selection. *Biol. Rev.*, *18*, 32-64.

MATHER, K. 1953*a*. The genetical structure of populations. *Symp. Soc. Exp. Biol.*, *7*, 66-95.

MATHER, K. 1953*b*. Genetical control of stability in development. *Heredity*, *7*, 297-336.

MATHER, K. 1955*a*. Polymorphism as an outcome of disruptive selection. *Evolution*, *9*, 52-61.

MATHER, K. 1955*b*. Response to selection. *Cold Spr. Hbr. Symp. Quant. Biol.*, *20*, 158-165.

MATHER, K., AND HARRISON, B. J. 1949. The manifold effect of selection. *Heredity*, *3*, 1-52, 131-162.

MEDAWAR, P. B. 1957. *The Uniqueness of the Individual.* Methuen, London.

MOREE, R. 1953. An unexpected relation between negative assortative mating and gene frequency. *Genetics*, *38*, 677.

ROBERTSON, A. 1956. The effect of selection against extreme deviants based on deviation or on homozygosis. *J. Genet.*, *54*, 236.

SCHMALHAUSEN, I. I. 1949. *Factors of Evolution.* Blakiston, Philadelphia.
SIMPSON, G. G. 1944. *Tempo and Mode in Evolution.* Columbia, New York.
THODAY, J. M. 1953. Components of fitness. *Symp. Soc. Exp. Biol.*, *7*, 96-113.
THODAY, J. M. 1955. Balance, heterozygosity, and developmental stability. *Cold Spr. Hbr. Symp. Quant. Biol.*, *20*, 318-326.
THODAY, J. M. 1956. Population Genetics. *Nature*, *178*, 843-844.
THODAY, J. M. 1958*a*. Effects of disruptive selection : the experimental production of a polymorphic population. *Nature*, *181*, 1124-1125.
THODAY, J. M. 1958*b*. Homeostasis in a selection experiment. *Heredity*, *12*, 401-415.
THODAY, J. M. 1958*c*. The cytoplasm and quantitative variation in *Drosophila*. *Proc. Roy. Soc.* B, *148*, 352-355.
WADDINGTON, C. H. 1953. Epigenetics and evolution. *Symp. Soc. Exp. Biol.*, *7*, 186-199.
WADDINGTON, C. H. 1958. *The Strategy of the Genes.* London, Allen and Unwin.
WADDINGTON, C. H., GRABER, H., AND WOOLF, B. 1957. Isoalleles and the response to selection. *J. Genet.*, *55*, 246-250.
WALLACE, B., AND VETUKHIV, M. 1955. Adaptive organisation of the gene pools of *Drosophila* populations. *Cold Spr. Hbr. Symp. Quant. Biol.*, *20*, 303-310.