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HOMEOSTASIS IN A SELECTION EXPERIMENT

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In his stimulating book, Lerner (1954) argues that *Genetic Homeostasis* (the tendency of populations of outbreeding species to resist the effects of artificial selection) arises because selection brings about inferior *Developmental Homeostasis* (canalisation of individual development). He argues, from the frequently observed inferior developmental homeostasis of homozygotes, that in these species good control of development depends on heterozygosity as such. Selection necessarily involves inbreeding and must therefore reduce the heterozygosity of the population and hence produce impaired developmental homeostasis. Natural selection will therefore operate in favour of heterozygosity and resist the artificial selection. In due course the selection pressures will balance and the artificial selection will cease to be effective.

This thesis supposes that the three following hypotheses are generally applicable to artificially selected populations. First, artificial selection must produce deterioration of developmental homeostasis. Second, this poor homeostasis must be the result of decreased heterozygosity. Third, the poor homeostasis must limit significantly the rate of response to artificial selection. The experiment to be reported here bears on the first two of these hypotheses.

1. THE MEASURE OF DEVELOPMENTAL HOMEOSTASIS

The kinds of quantity that may be taken as indicating the degree that development is under control have been discussed elsewhere (Thoday, 1953, 1956), and reasons have been given for preferring measures of within-individual variation to measures of between-individual variation. In selection experiments, since their whole success depends upon genetic heterogeneity, between-individual variance can only provide a measure of developmental homeostasis if the proportion of total variance that is genetic can be accurately estimated : a measure of within-individual variation is therefore peculiarly appropriate. The convenient character first studied by Mather (1953*a*), bilateral asymmetry of sternopleural chaeta-number in *Drosophila melanogaster*, has therefore been used in this work.

The choice of this character was based in the first place on the reasonable supposition that in a well-canalised individual the end-results of development on the two sides of the fly are likely to be very similar, whereas in a poorly-canalised individual any tendency

for development of the two sides to diverge will be inadequately buffered (Mather, 1953*a*). Such theoretical considerations alone will not convince everyone, and the author has heard doubts of the value of sternopleural asymmetry as a character, and even doubts of the value of using chaeta number as a character in any experiment in quantitative genetics. These doubts seem to be based on a feeling that chaeta number is a trivial character of little, if any, adaptive significance.

There can, however, be no doubt that chaeta number has adaptive

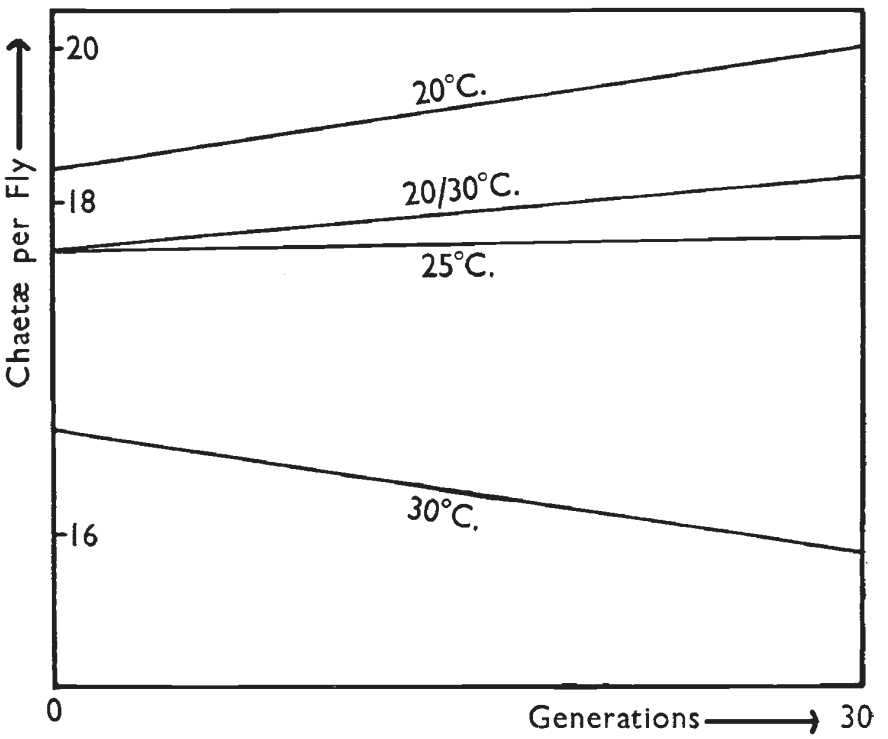

FIG. 1.—The regression lines of sternopleural chaeta number on generations in populations adapting to different environments. Each line is obtained from 3 populations each started from an F_1 cross between the inbred lines Oregon and Samarkand. (Log scale). From Beardmore (1956).

significance, for it is affected by *natural* selection. On general grounds alone this is clear : different species of *Drosophila*, and different populations of a species have different characteristic chaeta numbers, and the variance of chaeta number is very much less than the potential genetic variance can be shown to be by appropriate selection experiments (*e.g.* Sismanides, 1942 ; Mather and Harrison, 1949 ; Rasmusson, 1955). These facts must imply a history of effective stabilising selection (Mather, 1953*b*).

The conclusion based on these general considerations is supported by the behaviour of sternopleural chaeta number in populations of *Drosophila melanogaster* studied by Beardmore (1956) who has kindly

permitted me to outline them. Beardmore established three populations in each of four environmental conditions, 20° C., 25° C., 30° C. and an incubator in which the mean temperature is 25° C., but in which there is a smooth diurnal temperature cycle from 20° midnight to 30° C. midday. All the populations were maintained by, as far as possible, a three-weekly transfer of ten pairs of flies and had been started from the same cross between two lines, Oregon and Samarkand, both long inbred at 25°. (Great difficulty was experienced in maintaining the 30° populations, and their incubator was at first left at 28° and only gradually raised to 30°. They have not yet adapted to 30° and, periodically, resort has to be made to insurance cultures kept for one generation at 25° to prevent them dying out.)

TABLE 1

Significance of changes of chaeta number in adapting populations

(*From Beardmore, 1956*)

Environment	Joint regression	Sign of *b*	Differences between three replicate populations	
			Difference of regressions	Difference of means
20° C.	$t_{(54)} = 3{\cdot}366$ P. $\simeq 0{\cdot}001$	+	P. large	P. large
25° C.	$t_{(60)} = 2{\cdot}407$ P. $< 0{\cdot}02$	+	P. $< 0{\cdot}05$	P. $< 0{\cdot}001$
30° C.*	$t_{(42)} = 2{\cdot}789$ P. $< 0{\cdot}01$	−	P. large	P. $\simeq 0{\cdot}01$
F. 20°/30° C.	$t_{(66)} = 2{\cdot}811$ P. $< 0{\cdot}01$	+	P. large	P. $< 0{\cdot}01$

* See footnote to Table 2.

Fig. 1 illustrates the results. The first point of note is that adaptation to the new environments does involve changes of chaeta number. The regressions of chaeta number on generations are significant (table 1), and the slopes are greater in the new environments than in the old. Further, in the old environment the regressions of replicate populations are not consistent, whereas in the new environments they are.

The second point is that the directions of change in 20° and 30° differ, which can only be taken as evidence that it is a good thing for flies developing at 20° to have more chaetæ, and a good thing for those developing at 30° to have less chaetæ. In other words, chaeta number measures something of adaptive significance.

A third point is of the greatest importance. It is well known (Plunkett, 1927) that *Drosophila* cultured at higher temperatures produce fewer chaetæ than those cultured at lower temperatures. This environmental effect is the reason for the differing chaeta numbers of the flies at the start of Beardmore's experiments (fig. 1).

Without Beardmore's results, interpretation of this phenotypic effect of the environment would be difficult. It might on the one hand be held that the environmentally caused modification of chaeta

number arose through poor canalisation of individual development. On the other hand it might be held that the modification of chaeta number arises because the individual is capable of adapting its development so as to produce a phenotype approaching the optimum required in the environment in which development takes place. This is the standard problem, discussed by Thoday (1953), of determining whether inter-individual variation is evidence of good or bad developmental homeostasis. Beardmore's results seem to settle the question for this character, this environmental variable and these flies. The genetic changes in his 20° and 30° populations augment the standard effects of the environment. It follows that the individual fly modifies its development *adaptively* in producing more chaetæ in lower temperatures and fewer chaetæ at higher temperatures.

TABLE 2

Significance of changes of asymmetry in adapting populations
(From Beardmore, 1956)

Environment	Joint regression	Sign of *b*	Differences between three replicate populations	
			Difference of regressions	Difference of means
20° C.	$t_{(54)} = 1{\cdot}887$ P. $<0{\cdot}1$	−	P. large	P. large
25° C.	$t_{(60)} = 0{\cdot}008$ P. large	+	P. large	P. large
30° C. *	$t_{(42)} = 2{\cdot}530$ P. $<0{\cdot}02$	−	P. large	P. $<0{\cdot}2>0{\cdot}05$
F. 20°/30° C.	$t_{(66)} = 2{\cdot}989$ P. $<0{\cdot}01$	−	P. large	P. $\simeq 0{\cdot}05$

* The 30° regressions ignore the data obtained before the incubator had been raised to 30° C.

It cannot, of course, be argued from this that higher variance of chaeta number is always to be taken as a measure of higher developmental homeostasis. There is in fact evidence (Thoday, 1956) that high within-culture non-genetic variance is sometimes evidence of low developmental homeostasis (see also Lewontin, 1956), which merely serves to underline the value of measures of within-individual variance such as have been used by Mather (1950, 1953*a*), Jinks and Mather (1955), Paxman (1956), Thoday (1953, 1956), and Tebb and Thoday (1954).

Beardmore's results show that sternopleural number is of adaptive importance, a fact of significance for our argument. If this were not so, it would be less easy to suppose that sternopleural asymmetry might be of importance. His results also provide direct evidence that sternopleural asymmetry is a character of adaptive significance. Table 2 demonstrates the significance of changes in sternopleural asymmetry in his adapting populations. Asymmetry was measured by summing the differences of chaeta number between the two sides of a standard number of flies, a measure differing from that used by

Mather (1953*a*), but the same as that used by Tebb and Thoday (1954). There is no indication of regression on generations in the 25° populations. Each of the other populations (in new environments) shows a negative regression of asymmetry on generation and this is significant in the F. 20/30° and in the 30° populations. The regression in the 20° populations is not quite significant, but that this regression should be the least significant is to be expected, since 20° seems to be as good an environment as 25° for Oregon/Samarkand F_1 flies (Thoday, 1953). Furthermore, the rise in chaeta number in the 20° populations might be expected to raise asymmetry as a result of the scaling phenomenon referred to below, and this would mask any improvement of symmetry that was occurring. This same scaling problem somewhat weakens the evidence provided by the 30° populations whose chaeta number decreased. It cannot, however, affect conclusions based on the fluctuating environment populations, so that the overall result is clear : sternopleural asymmetry decreased as the populations adapted to particular new conditions. It must be concluded that natural selection promoted sternopleural symmetry, which, therefore, is of adaptive significance. The same conclusion follows from the experimental results of Tebb and Thoday (1954).

It would in fact be very surprising if bilateral symmetry of chaeta number were not of adaptive significance, since chaeta number must measure some of the attributes of a particular set of differentiation fields, and hence numerical symmetry must be a partial measure of the similarity of the comparable differentiation fields on the two sides of the fly.

A further point arises concerning the relevance of sternopleural asymmetry as a measure of homeostasis. Mather (1953*a*) argued that asymmetry is not so much a result of variation of external environment, but a consequence of internal " accidents of development ". Similar arguments have been used by Reeve and Robertson (1954) concerning abdominal chaetæ and Waddington, Graber and Woolf (1957), who refer to asymmetry as developmental "noise". Our own results (Thoday, 1956 ; Tebb and Thoday, 1954 ; Beardmore, 1956) clearly show that major changes of external environment can affect sternopleural asymmetry, but this does not mean that the divergence of the two sides in development is initiated by a difference of the external environment of the two sides : accidents of development may be more frequent or less well buffered in an unfavourable environment. It is quite probable that we are, in fact, dealing with accidents of development, but this has little, if any, bearing on the validity of sternopleural asymmetry as a measure of the competence of developmental control. Just as a " good " genotype will buffer the individual against undesirable effects of external variables, so a " good " genotype will lead to fewer accidents of development and better buffering of the individual against the effects of such accidents as do occur.

2. SCALING PROBLEMS

One disadvantage of sternopleural asymmetry is that it presents problems of scaling when it is desired to use it for the comparison of two populations whose mean sternopleural chaeta numbers differ. Mather (1953*a*) found that there was sometimes no relationship between asymmetry and total sternopleural chaeta number, but that in other types of fly there was a positive relationship. The control lines used in the present experiment show a highly significant positive relationship (calculation by Beardmore, 1956). The experiment involves lines selected for sternopleural chaeta number and some scaling correction is therefore required. The correction used by Thoday (1956), which involves dividing summed asymmetry by total chaeta number, seems to be satisfactory for the population used here since it gives comparable results for high and low selection lines. Asymmetry results are therefore presented as A/T, that is, the summed differences between the two sides of a set of flies (sign ignored) divided by their total chaeta number.

3. MATERIAL AND METHODS

The experiments began with a wild stock (" Dronfield ") of *D. melanogaster*, derived from the progeny of a single inseminated female captured near Sheffield. Since its capture the stock had been maintained for six months by standard culture at 25° C., 4 pairs of flies being transferred each generation. This stock was then split into two lines, I and II, and in the next generation 4 single-pair cultures labelled *a*, *b*, *c* and *d* were set up from each. Assay and selection for number of sternopleural chaetæ began with the progeny of these eight pairs.

Assay of any line in any generation involved counting the sternopleural chaetæ on each side of 20 females and 20 males from each of four single-pair cultures except in generation O in which 24 of each sex were counted. In this generation the first four were used to establish control lines. From the remainder, the four with highest chaeta numbers were used to establish high selection lines and the four with lowest chaeta numbers were used to establish low lines.

Thus in generation O the following flies were selected from line I : 4 random females and 4 random males from each culture *a* to *d* ; the 4 highest flies of each sex numbered 1 to 4 from each of the four cultures and the 4 lowest flies likewise. These groups of flies were used to establish lines I C, I H, I L.

Each such line was set up by mating the female a_1 to male b_1, a_2 to b_2, a_3 to b_3, a_4 to b_4, b_1 to c_1, c_1 to d_1 and d_1 to a_1 and so on, providing 16 single-pair cultures. Culture $a_1 \times b_1$ was labelled a_1 and provided this was successful a_2, a_3 and a_4 were discarded. If a_1 failed, a_2 was used. If a_1 and a_2 failed, a_3 was used, etc. (An additional mass culture (4 random pairs) was also set up to insure against loss of all four single-pair cultures. Resort to this culture was only necessary on four occasions, that is for 4 of the 244 cultures assayed.) The progeny of the successful culture were assayed and selected and the next generation set up as before except that the mating system was changed to $a \times c$, $b \times d$, $c \times a$, $d \times b$. In the following generation the mating was $a \times d$, $b \times a$, $c \times b$, $d \times c$, and in the following the first mating system was repeated. Thus the four single pairs used in each generation are maintained as one population and the labels *a*, *b*, *c* and *d* merely designate female lines.

In the control lines the first 4 flies of each sex that were counted from each culture were labelled 1 to 4 and used. In the selection lines the " best " 4 were used. " Best " was defined as, *e.g.* in a high line, the fly with the most sternopleural chaetæ,

but, if choice were necessary, the most symmetrical fly was used, that is, that with the most nearly equal numbers of chaetæ on its two sides.

In addition to the lines, F_1 cultures were also obtained in most generations from crosses between I C and II C, I H and II H, I L and II L and between High and Low lines. Each F_1 assay involved 20 flies of each sex from each of 4 single-pair cultures, two of each reciprocal cross. In the H×L F_1s the four cultures were of

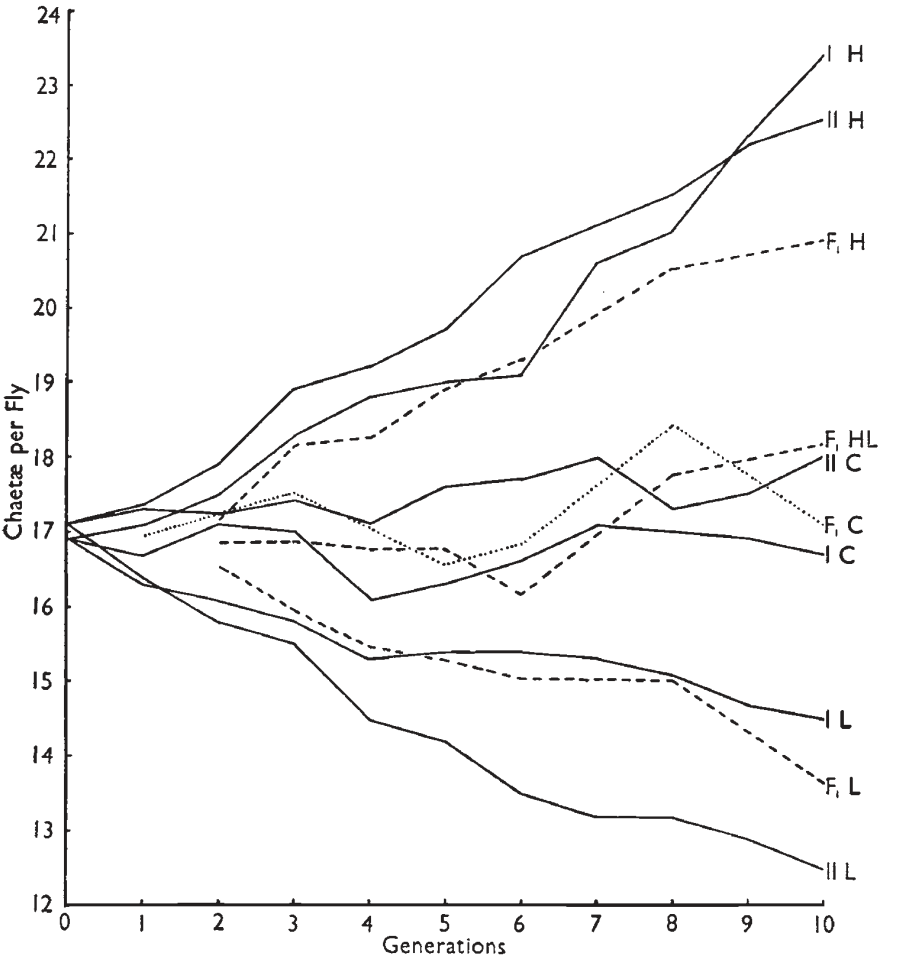

FIG. 2.—Mean sternopleural chaeta number in the lines and their F_1 crosses. Solid curves, the lines. Broken curves, the F_1s between selected lines. Dotted, the F_1s between the control lines. (The F_1s are plotted with the generation with which they were cultured.)

4 crosses, I H×II L, II L×I H, II H×I L and I L×II H. Parents for F_1 cultures were chosen at random.

All cultures were set up in standard half-pint milk bottles with standard corn-meal black-treacle agar medium, inoculated with live baker's yeast. Counts and matings were made on Tuesdays and Wednesdays, the mating pairs being placed in 2×1 in. tubes. The cultures were set up on Saturday (having been poured on Thursday and yeasted Friday), and the parents were removed on Tuesday. Emergence of adults began the following Monday and the flies were sexed and separated morning and evening until and including Thursday, by which time

emergence was usually complete. The flies were preserved until Tuesday for counting. This routine means keeping the flies for some time and forces a three-week generation, but it is simple to manage and usually permits collection of all the progeny before selection, a matter that may be of some importance (*cf.* Durrant, 1955).

4. RESULTS

Fig. 2 shows that the response to selection in the four selection lines was good, and that the control lines, though differing somewhat, remained fairly steadily near their original chaeta numbers.

Table 3 gives the A/T figures, multiplied by 1000 for convenience, for each of the six lines, and for each of the four F_1s which are classed with the generations with which they were grown.

TABLE 3

A/T × 1000 for the lines and their F_1 crosses

Generation :	0	1	2	3	4	5	6	7	8	9	10
I Control . .	52	56	53	46	58	50	53	52	46	50	53
II Control . .	49	49	55	54	58	62	53	54	56	50	51
F_1 . . .	...	50	57	58	48	55	53	...	54	...	60
I High . .	...	47	59	60	51	50	58	62	53	58	59
II High . .	...	50	54	62	62	54	62	61	63	57	66
F_1 . . .	...	...	50	57	62	58	57	...	48	...	56
I Low . .	...	55	48	53	56	57	57	54	55	57	64
II Low . .	...	55	58	49	57	52	59	52	56	55	62
F_1 . . .	...	...	49	55	53	53	55	...	58	...	62
High/Low F_1 .	...	...	54	50	56	56	58	...	55	...	58

Fig. 3 shows A/T for the selected and the control lines and table 4 the corresponding analysis of variance. The following points emerge :

1. A/T is higher in the selection lines than in the controls.
2. There is no significant difference between mean A/T for high and low lines, indicating that A/T is a measure satisfactorily compensating for the relationship between arithmetical asymmetry and total chaeta number.
3. A/T does not vary significantly with generation in the controls, but there is a highly significant increase with generations of selection. Furthermore there is no suggestion of differences between the regression slopes of the four selection lines. Both high and low selection result in such an increase. (The regression coefficients of A/T × 1000 on generation are : I C −0·3000, II C 0·1091, I H 0·6545, II H 1·2545, I L 0·8364, II L 0·6091).

The mean bristle numbers for the F_1 cultures are illustrated in fig. 2, along with those of the lines. They are plotted with the generation with which they were cultured, not with that which provided their parents. Having due regard to the fact that the parents of the F_1 cultures were chosen at random, it seems clear that the bristle numbers of F_1 flies show little evidence of overall dominance.

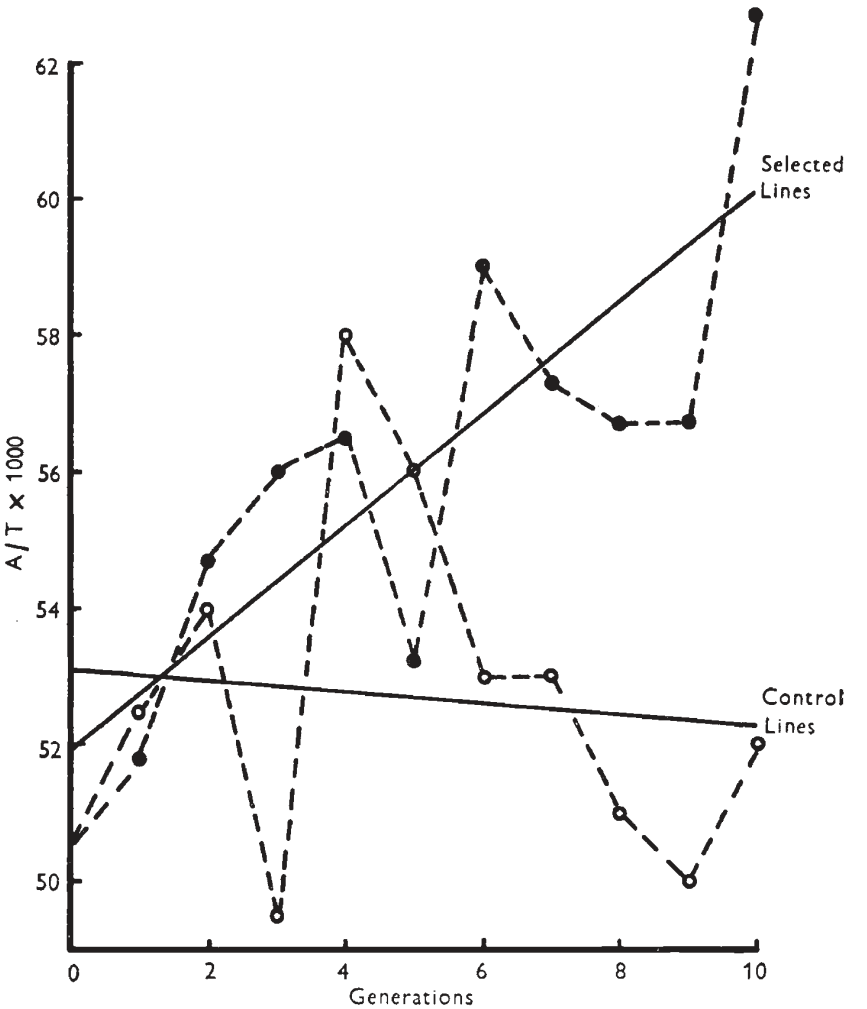

FIG. 3.—Asymmetry in the selected and control lines.

TABLE 4

Analysis of variance of A/T× 1000 for the lines

Source	Sum of squares	N	M.S.	P
Joint regression on generations .	183·4909	1	183·4909	≃0·001
Difference selected and control regressions	127·9704	1	127·9704	<0·01
Difference High and Low regressions	5·9113	1	5·9113	...
Difference selected and control means	150·6439	1	150·6439	<0·01
Difference High and Low means .	31·0834	1	31·0834	...
Residual differences between means	66·4090	3	22·1363	...
Error	866·2638	53	16·3446	...
Total . . .	1431·7727	61	...	...

Table 3 lists the A/T values for the F_1 cultures and those for the F_1s between the selected lines are illustrated in fig. 4. Table 5 gives

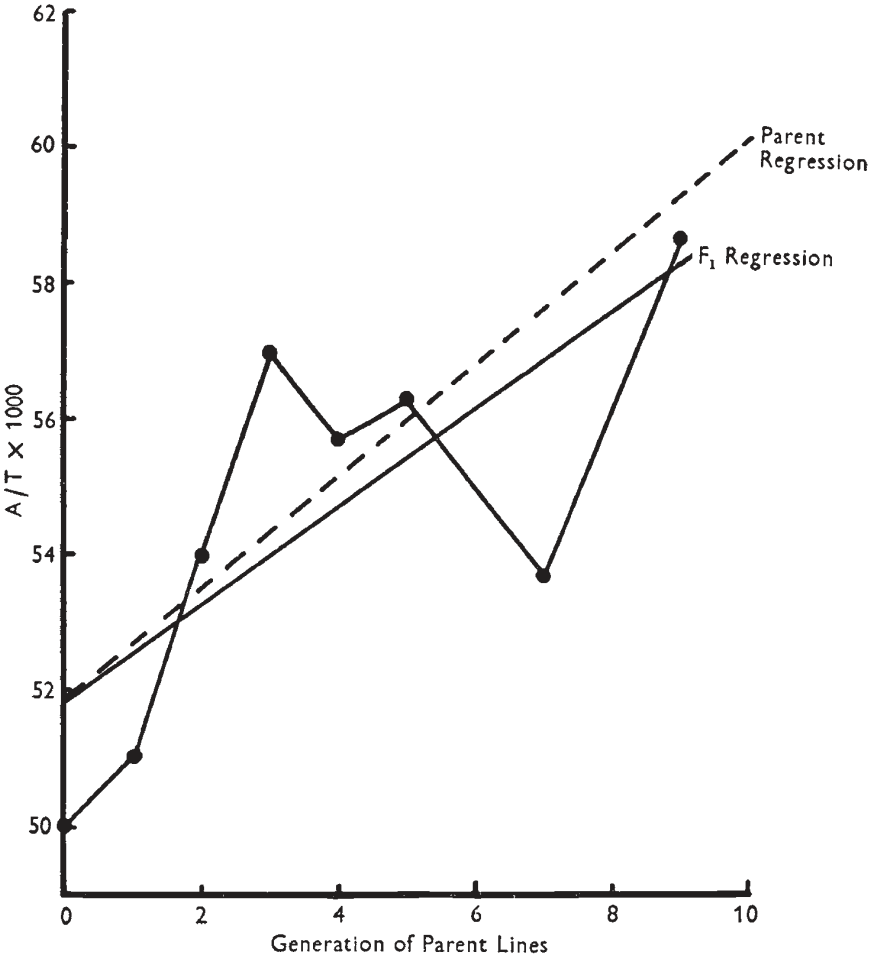

FIG. 4.—Asymmetry of the F_1s between selected lines. The regression for the selected lines is plotted as well as the F_1 joint regression. (The F_1s are plotted with the generation that provided their parents.)

TABLE 5

Analysis of variance of F_1 $A/T \times 1000$. Selected and controls

Source	Sum of squares	N	M.S.	P
Joint regression on generations	120·8989	1	120·8989	≃0·01
Difference between selected and control regressions	1·8169	1	1·8169	...
Residual difference between regressions	42·0739	2	21·0369	...
Error	309·1791	24	12·8825	...
Total	473·9688	28	...	...

the analysis of variance of F_1 A/T. The joint regression of A/T on generation for the F_1s is significant and there is no significant difference of behaviour over the generations between the different types of F_1. However, the control F_1 regression is not by itself significant and it is lower than the joint regression for the selected F_1s. The control F_1s do not therefore provide sufficient data to be useful. The F_1s between the selected lines, on the other hand, do. It is clear (fig. 4) that the F_1s between the selected lines increase in A/T in exactly the same way as the selected lines themselves.

Now if the deterioration of the selected lines arose because of increasing homozygosity, their F_1s should show lower A/T values than the lines, unless the lines crossed to give the F_1s had identical genotypes, which is unlikely for all and impossible for the H $\times$L F_1s. It would therefore appear that increasing homozygosity in the selected lines cannot be invoked as an explanation of their increasing asymmetry.

There is, however, one possibility that might render this conclusion invalid. If asymmetry were a character *entirely* determined by maternal genotype and completely independent of the genotype of the individual in which it is measured, then the F_1s would be expected to show the same asymmetry as the parent. If this asymmetry arose from maternal homozygosity, we should then expect reduced asymmetry in F_2, for the F_2 would have heterozygous mothers. Mather (1953*a*) did in fact find some evidence that asymmetry might *in part* be determined by maternal genotype, but only *complete* maternal inheritance would invalidate the conclusion reached above. Further, 25 F_2 cultures raised from the High $\times$Low F_1 after the completion of the experiment gave A/T values identical with those of 16 contemporaneously reared F_1 cultures (A/T $\times$1000 F_1 56·3, F_2 56·0), and it seems clear that maternal inheritance cannot be important in this experiment. It must be concluded that homozygosity is not an important factor determining the observed increase of asymmetry.

5. DISCUSSION

The results presented show clearly that directional selection can cause deterioration of the systems responsible for developmental homeostasis as here measured, and to this extent they are in agreement with Lerner's thesis. They do not, however, lend any support to Lerner's hypothesis that increasing homozygosity is the cause of the deterioration.

There are two alternative explanations which may account for the increased asymmetry. The first is similar to that put forward by Mather to explain declining fertility in selection lines. Selection produces unbalance in gene complexes linked to the genes directly concerned with the character under selection and the result is impaired fertility (Mather and Harrison, 1949). The increased asymmetry may merely be another manifestation of this poor balance.

In a discussion of the results obtained part way through the present experiment, and of those obtained with some other lines, the author (Thoday, 1956), put forward a second explanation similar to that discussed by Falconer and Robertson (1956). This was that, in selecting for a given character, we may pick out from a population not only individuals whose genotypes determine directly an extreme value for that character, but also individuals whose genotypes render them exceptionally subject to modification by the environmental variation in the culture, or exceptionally incompetent at buffering the effects of internal accidents of development, or exceptionally subject to such accidents. Selection of these latter types would lead to increase of genotype-environment interaction and/or deterioration of developmental stability. That such genes exist in *Nicotiana* has been made abundantly clear by the work of Mather and his associates (Jinks and Mather, 1955 ; Paxman, 1956), and in addition Mather (1953*a*) has demonstrated that sternopleural asymmetry in *Drosophila* is itself a character responsive to artificial selection. Such genes would be selected in this experiment. Provided that the same genes, or some of the same genes, that affect inter-individual variance of sternopleural number also affect asymmetry in the same direction, the present increase of A/T in the selection lines is formally explicable on the basis of such selection.

Evidence concerning coefficients of variation in the lines of this experiment might be expected to provide relevant information. Unless new mutants arise or fixed variability becomes freed at a greater rate than the available genetic variance is used up, genetic variance must decline in lines undergoing inbreeding, such as the control lines in this experiment, and in selection lines. Phenotypic variance must therefore decline unless genotype-environment interaction and/or developmental variation caused by intrinsic accidents during development increase. Selection for increase of these will, on the other hand, arrest the decline and may even produce an increase of phenotypic variance. The final result will depend upon the relative variance arising from stability genes and additive genes at the beginning of selection.

In these experiments, the variance of the control lines behaved as expected. Some of the selection lines, on the other hand, increased in variance. Furthermore, the regression slopes for coefficients of variation for the different lines fall in the same order as those for A/T, which supports the view that A/T and coefficient of variation have some common causes. The changes in variance are therefore in agreement with the hypothesis that the decline of developmental homeostasis observed in the selection lines results from the selection for low developmental stability, which in small or large degree is a necessary consequence of directional selection. This evidence is, however, of no real value, for the changes of variance are not significant and are open to other interpretations. The alternative balance

hypothesis would explain them and the freeing of fixed variability in the selection lines would also explain them.

Distinction between the balance hypothesis, and that involving direct selection of genes for poor homeostasis is, however, possible. If the deterioration of homeostasis arises as a result of the selection of unbalanced gene-complexes linked to chaeta number genes, then increase of asymmetry should be greatest when the selection of extreme chaeta number genotypes is most effective. If, on the other hand, increase of asymmetry arises because of the selection of individuals whose extreme chaeta-number is caused by poor developmental canalisation instead of an extreme chaeta-number genotype, then

TABLE 6

Correlation between increase of asymmetry and $h^2 = \Delta P/i$ *in the selected lines*

Generation	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10
A/T increase .	−4·9	11·7	1·0	−8·5	−0·5	7·3	4·0	−8·6	4·5	1·5
I H h^2 . . .	0·05	0·19	0·30	0·17	0·05	0·04	0·39	0·13	0·33	0·27
A/T increase .	1·4	4·3	7·6	0·4	−8·2	8·2	−1·1	1·4	−5·7	8·8
II H h^2 . . .	0·06	0·17	0·26	0·09	0·19	0·30	0·14	0·08	0·21	0·07
A/T increase .	3·1	0·8	4·8	3·4	−8·5	9·2	−2·7	1·2	2·0	7·1
I L h^2 . . .	0·33	0·07	0·06	0·10	−0·26	0·00	0·06	0·13	0·20	0·08
A/T increase .	6·3	7·5	−8·2	8·0	−4·8	6·6	−6·3	−3·5	−0·7	6·6
II L h^2 . . .	0·32	0·27	0·15	0·44	0·14	0·32	0·13	0·26	0·19	0·37

increase of asymmetry should be greatest when the selection of extreme chaeta-number genotypes is least effective.

Accordingly the regression of increase of asymmetry in a generation on the advance of chaeta number made in that generation, measured by the heritability formula $h^2 = \Delta P/i$ (Lerner, 1950), has been calculated (table 6).

The regression is positive and just significant ($t_{(38)} = 2{\cdot}22$, $P < 0{\cdot}05$) suggesting that the balance hypothesis is the more important, and providing no evidence that the other effect is operative. It should, however, be borne in mind that the two hypotheses are not mutually exclusive and that direct selection of instability genes may also be effective. It might even be more important than the balance effect if heritability were relatively low and response of the primary character to selection were small, as was suggested in explanation of the behaviour of the *vg* line described by Thoday (1956).

We may now suggest the following history for poor homeostasis in a longer term selection experiment. If, at the start of the experiment, the available genetic variance directly affecting the primary character is relatively high, selection will be effective in changing the mean, but development will become gradually less stable as linked gene complexes affecting stability become unbalanced. The resulting

decrease in heritability of the primary character may render more likely the direct selection of instability genes (as might occur if heritability were low at the beginning). Stability should therefore deteriorate at an increasing rate except in so far as the genetic variance of stability is used up. If, however, after a period of selection, new genetic variance directly affecting the primary character were to be produced in the line, either by mutation, recombination, or gene-interactions increasing the expressivity of existing heterozygous loci, then a new balance of selection pressures would be set that might permit rapid improvement of stability. Accelerated response to selection, or the crossing of selection lines might therefore, on these grounds, result in improvement of stability. Such was the behaviour of the *dp* line described by Thoday (1956), which showed a clear improvement in sternopleural symmetry at the same time as an accelerated response to selection. After such a response we would expect stability to begin to deteriorate once more. Whether or no the final level of instability reached might prove an effective bar to full exploitation of the genetic variance directly affecting the primary character would depend on the degree of correlation of stability with fitness in the particular population and environment. If it were an effective bar, coincident artificial selection, both for the primary character and for stability, might in the long run produce more satisfactory results than selection for the primary character alone.

6. SUMMARY

(1) It is argued from results of Beardmore that asymmetry of sternopleural chaeta number is a useful measure of developmental homeostasis.

(2) Ten generations of selection for high or low sternopleural chaeta number produced a deterioration of developmental homeostasis so measured.

(3) This decline of developmental homeostasis was not caused by increasing homozygosity, for the same deterioration was observed in crosses between the selected lines.

(4) Two alternative hypotheses are suggested. One involves direct selection of " poor-homeostasis " genes. The other involves the deteriorating balance of gene complexes linked to those directly affecting bristle number. The results indicate that the second of these is correct, but it is suggested that direct selection of instability genes may be more important when heritability is relatively low, the balance effect being more important when heritability is high enough to permit good response to selection.

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