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Some genetic tests on asymmetry of sternopleural chaeta number in *Drosophila*

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INTRODUCTION

The variance of a quantitative character in individuals of a single genotype, reared in a given set or range of environmental conditions, is often taken as a measure of the developmental stability of the genotype. Broadly speaking, this variance is the sum of two components: (1) the direct effect of differences betweeen the environments of different individuals—the environmental variance proper, and (2) the effects of local accidents of development, originating perhaps largely at the molecular level, which prevent the perfect replication of the same phenotype even under identical environmental conditions. This variance has been given several names, including 'chance or stochastic variability' (Reeve & Robertson, 1953*b*), 'developmental error' (Clayton *et al.*, 1957), 'developmental noise' (Waddington, Graber & Woolf, 1957), or, when calculated from the uncorrelated variations among two or more elements repeated on the same individual, the 'independent variance'(Reeve & Robertson, 1954). None of these terms is entirely satisfactory, and I shall refer simply to the 'chance variance', except when another term seems more apt.

Whilst it might be supposed that the first, or true environmental, component is generally by far the most important, this is certainly not always the case. Thus Wright (1952), studying the amount of white in the coat of guinea-pigs, concluded that 86% of the total variance of an inbred strain must be attributed to local accidents of development. This proportion was, in fact, the total variance within litters, which could not be due to environmental differences between litter-mates, since there was no correlation between the amounts of white on different regions of the coat of the same animal more than a short distance apart.

Essentially the same approach was used by Reeve & Robertson (1954) in analysing the variation in the number of chaetae on the abdominal sternites of *Drosophila melanogaster* in inbred lines and crosses. Segments 3–5 were counted in males and 3–6 in females, and virtually no correlated variation was found between the numbers of hairs on the different segments, when flies of a single genotype were reared under fairly standard conditions without overcrowding. We concluded that, under these conditions, there was almost no environmental variance proper in hair number, but a large 'chance' component was present, with a coefficient of variation of about 8% per segment, which was probably caused mainly by a lack of precision

in the processes of morphogenesis responsible for chaeta formation. In addition, true environmental variation could be induced by crowding or otherwise varying the environment, and this caused highly correlated variations on the different segments.

This case evidently provides a striking parallel with that of the amount of white in the guinea-pig's coat, referred to above, and very similar results were found for variation in the number of ovarioles in the left and right ovaries of *Drosophila melanogaster* by Robertson (1957). There are typically about twenty ovarioles in each ovary, and crosses between several inbred lines gave a variance per ovary with an average coefficient of variation, for flies reared on the usual fairly standard diet, of about 8%. Approximately 90% of this variance was the result of uncorrelated variations in the two ovaries, and so comes within our category of 'chance' variance. We may note in passing the curious fact that sternites with twenty chaetae and ovaries with twenty ovarioles show almost the same variance due to chance effects, but whether this reflects any fundamental similarity in the causal factors underlying the variation it is not easy to decide.

As a contrast to these cases with the non-genetic variance mainly due to chance effects, wing length in *Drosophila* was found to have an environmental variance of which only about 13% could be attributed to differences in length of the two wings, equivalent to a coefficient of variation of about 0·5% (Reeve & Robertson, 1953*a*). Again, of the environmental variation in body-size, roughly half is due to variations in wing and thorax length which are uncorrelated with each other; this sets an upper limit of about 50% to the chance component for body-size in *D. melanogaster*, reared under the usual standard conditions (Reeve & Robertson, 1953*b*).

The total amount of non-genetic variance is certainly under partial genetic control, since heterozygotes are generally more stable than homozygotes for many quantitative characters, at least in the case of normally outbreeding organisms; and the question naturally arises whether this genetic variation in phenotypic stability affects only the environmental variance proper, or also the chance variance. Reeve & Robertson (1954) found no decrease in the variance of sternite chaeta number in *D. melanogaster*, when inbred lines were intercrossed, and they concluded that the chance variance of this character was not subject to appreciable genetic control. In keeping with this result is the fact that Mr B. J. Harrison selected for twenty generations in an attempt to increase and decrease, respectively, the difference in the number of hairs on the fourth and fifth abdominal sternites, without making any progress (private communication and Harrison, 1954).

As another example, Reeve & Robertson (1953*b*) found virtually no decrease in the uncorrelated fraction of the variance of wing length and thorax length when pure lines were intercrossed, although the correlated variances dropped to less than half.

On the other hand, Mather (1953) crossed two inbred lines of *D. melanogaster*, and found that the mean amount of bilateral asymmetry in the number of sternopleural chaetae was much lower in the F_1 and F_2 than in the parent lines.

Moreover, he was able to raise and lower the amount of asymmetry in a striking manner by selecting from the F_2 of the cross.

We thus appear to have a rather puzzling contrast in the genetic behaviour of two characters, both consisting of the number of chaetae on particular regions of the integument of the same organism, so that we might, on the face of it, expect them to show rather similar responses when inbreds are crossed or when selection is carried out. A number of experiments have been undertaken with the hope of analysing this difference in more detail, and will be described below. These included tests of the amount of genetic variance for sternopleural asymmetry in three wild stocks, and comparison of the changes in variance of the two characters when homozygous lines are intercrossed.

Several wild stocks of *D. melanogaster*, or lines derived from them, were used in these tests, and are listed below with their code letters. They have all been kept in this laboratory in mass culture, for varying periods, and have been shown by various tests to contain plenty of genetic variance for different characters. They are:

Pobla da Lillet	(PdL)	Pacific	
São Paulo	(SP)	Renfrew	(Re)
Crianlarich	(Crian)	Edinburgh	(WE)

GENETIC VARIANCE OF STERNOPLEURAL ASYMMETRY IN WILD STOCKS

The idea put forward by Mather, that the chance variability in sternopleural hair number, as measured by the mean amount of difference between right and left sides, is under genetic control, is a novel one; and it seemed to be of particular interest to test whether there is any appreciable amount of genetic variance for this character in wild stocks. To do this, a progeny test was made on the PdL wild stock, and selection for increased and decreased asymmetry was carried out on the Crian and SP stocks.

For the progeny test, forty pair-matings were made between flies 3–4 days old, chosen at random from the PdL stock. Each pair was allowed to lay eggs for 24 hr. in a 3×1 in. vial containing the usual cornmeal-molasses medium, and then transferred to a fresh vial. Cultures from eggs laid on 3 successive days were raised at 25° C., and the numbers of sternopleural hairs on the two sides were counted on all male and female progeny which survived long enough for the rather laborious work to be completed. All counts were made by the author.

Altogether, counts were made on thirty-one families in males and thirty in females which provided at least two cultures, with an average of 15·3 males and 16·3 females per culture, and 43·5 and 45·1 per family.

The simplest measure of asymmetry is the absolute difference in hair number on the two sides, $|L-R|$ taken regardless of sign, where L and R are the numbers of left and right sternopleurals. This may be compared with the total count $(L+R)$. After fitting constants for day differences because of the variable number of flies per culture, the progeny variances are separated into the mean squares between

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days, between families, between cultures within families and within cultures. Since the last two items were in no case significantly different they have been pooled, and the results for both $|L-R|$ and $(L+R)$ are given in Table 1.

Table 1. *Progeny test on sternopleural sums and differences*

	Degrees of freedom		Mean Squares			
			$L+R$		$\|L-R\|$	
	♂♂	♀♀	♂♂	♀♀	♂♂	♀♀
Between days	2	2	55·4*	50·0*	0·32	0·68
Between families	30	29	18·30*	22·52*	1·33*	0·90
Within families	1316	1321	2·72	2·99	0·71	0·81
Heritability %			23·5	25·3	4·0	0·5

* P less than 0·01

Taking first the variance in total count $(L+R)$, we notice a significant difference between days, due to the fact that the third day, with averages of 17·7 in males and 19·1 in females, had 0·6 hairs less than the first 2 days, whose mean counts were almost identical. Both sexes gave a highly significant variance between families, equivalent to a heritability of 23–25% when this is calculated in the usual way, as the ratio of the component of variance between families to the sum of the components within and between families. Clearly there is plenty of genetic variance for total count in the stock.

In the case of asymmetry, there was no day effect, and the variance between families was greater than that within families in both sexes, and significantly so (at the 1% level) in males. This suggests that there is a small amount of genetic variability for asymmetry in the stock. The heritability is estimated as 4% in males and 0·5% in females, and on pooling these figures we estimate the genetic variance as about 2% of the phenotypic variance. We should, therefore, expect to make some slight progress on selecting to increase or decrease the level of asymmetry.

In the two selection experiments, twelve males and twelve females were used as parents each generation. These were mass-mated and their eggs cultured (70 per vial) in vials of the usual cornmeal-molasses medium at 25° C. All the flies emerging in three vials were scored, and the extreme four males and four females from each vial were selected as parents and mass-mated for the next generation. This meant that usually 15 to 20% of the flies examined were selected.

In the first experiment, with the Crianlarich wild stock, one line was selected for the greatest absolute value of $L-R$, and the other for the smallest difference between L and R, regardless of the total number of sternopleurals present. The results are shown to the left in Fig. 1, in which $(+)$ and $(-)$ indicate the lines selected for increased and decreased asymmetry. The top graph shows the changes in mean asymmetry, the middle graph the changes in mean total count, and the bottom graph the changes in the standard deviation of total count.

Both lines were continued for four generations, and moved steadily apart in all three indices. Then the (−) line was discontinued, and four generations later unselected controls (*C*), taken off the mass stock each generation but raised in the same way as the selected lines, were put up concurrently with the (+) line. The experiment was terminated after thirteen generations, and the graphs show the average levels of (+) and controls for each index, over the six generations when they were run together.

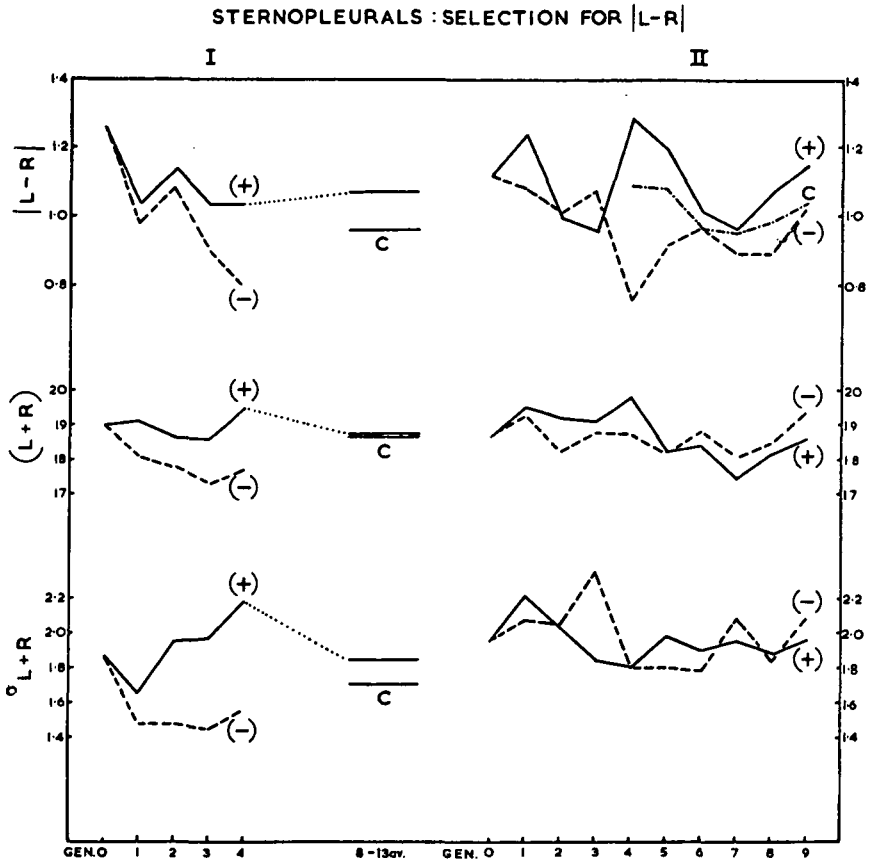

Fig. 1. Selection for increased sternopleural asymmetry (+) and decreased asymmetry (−) in two wild stocks. I: first experiment, on the Crianlarich stock. II: second experiment, on the SP stock. *C* indicates unselected control stock.

The trends in asymmetry are a little difficult to interpret in view of the high level at generation 0, which may possibly have been caused by some undetected environmental factor. Changes in asymmetry were certainly induced by selection, and the impression given by the graph is that the (−) made more progress than the (+) line. The latter had evidently made some progress by the end of the experiment, but there is little doubt that selection for decreased asymmetry had been effective in the (−) line. The changes in asymmetry were accompanied by parallel

changes in total count, leading to a mean difference of nearly 2 hairs at generation 4, but this is hardly sufficient to explain the change in asymmetry as a scale effect. Rather dramatic changes in the same sense also occurred in the standard deviation of total count, so that the (−) line became both less asymmetrical and less variable in total count than the (+) line.

The second experiment was made on the SP wild stock, and this time controls were maintained from the start and were scored each generation. The results of the nine generations of selection in this experiment are shown in the right-hand graphs of Fig. 1.

In the first three generations little progress was apparent, since the (+) line was no more asymmetrical than the (−) line, but from generation 4 onwards $|L-R|$ was always greater in the (+) line, although the deviation between the two lines was never as large afterwards as it was at generation 4. A transient effect, either genetic or environmental, must have been responsible for this trend. The line of the controls (C) is only plotted from generation 4 onwards, and clearly runs in between the two selected lines. This means that selection was able both to increase and decrease the amount of asymmetry in the parent wild stock, and supports our tentative conclusion from the previous experiment.

The two lower graphs indicate that, in this experiment, the changes in asymmetry produced no correlated changes in total count or its variance. The (+) line had a slightly larger total count than the (−) line up to generation 5 and a smaller count afterwards, while no definite trend appears in its standard deviation. The control line is not plotted for these indices, since its values intermingle with those of the two selected lines in both cases.

Both selection experiments, then, give a clear indication that the level of bilateral asymmetry of the sternopleurals can be both increased and decreased in a wild stock by selection, and these changes are not necessarily accompanied by change in the total count or its variance.

Each selection experiment can be made to provide a rough estimate of the genetic variance in the parent wild stock, calculated as the fraction of the total selection pressure applied which is converted into genetic progress. This fraction is known, perhaps a little ambiguously, as the 'realized heritability' (Falconer, 1954), and has the practical disadvantage that it often varies a good deal with the number of generations of selection included. Where there are rather marked fluctuations from generation to generation in total progress, due possibly to evanescent environmental effects, a good compromise is to assume a linear rate of progress, so that the mean of all the differences between the two lines—or between one line and its control—can be taken as the result of half the overall selection pressure applied.

We have applied this method to the first four generations of selection in the first experiment and the full nine generations in the second. In the latter, the progress of each line is compared with the controls. The results are summarized, and compared with the corresponding figure from the progeny test, in Table 2.

The progeny test gave a figure of about 2%, while the estimates of heritability obtained from the two selection experiments are 2·5% for the Crian and 1·3% for the SP lines. The last figure is the average of 1·6% for (+) selection and 1·0% for (−) selection. In general, therefore, the estimates from the three stocks are in

Table 2. *Heritability of sternopleural asymmetry*

	Average $\lvert L-R \rvert$ per generation		
Selection in:	Selection differential	Advance	Heritability %
SP Stock (+)	1·33	0·021	1·58
(−)	0·97	0·010	1·05
Total	2·30	0·031	1·32
Crian stock: total	2·46	0·062	2·52
Progeny test on PdL stock			1·98

remarkably good agreement, and suggest that in typical wild stocks some 2–3% of the phenotypic variance in asymmetry is genetic.

It is of interest to compare our rates of progress with those obtained by Mather (1953) on selecting from the F_2 of a cross between two inbred lines. Mather measured asymmetry by the mean square difference, $V = (L-R)^2/n$, where n is the number of flies scored; and Table 3 gives V for the first five generations in our two selection experiments.

Table 3. *Mean square differences in selection experiments*

	First experiment on Crian			Second experiment on SP		
	(+)	(−)	Divergence	(+)	(−)	Divergence
Gen. 0	2·64	2·64	0·0	2·14	2·14	0·0
1	1·86	1·63	0·23	2·50	1·94	0·56
2	2·04	1·92	0·12	1·87	1·73	0·14
3	1·74	1·50	0·24	1·63	1·91	−0·28
4	1·78	1·14	0·64	2·35	1·05	1·30
5	1·76	—	—	2·37	1·59	0·78

On selecting the extreme 10% each generation, Mather was able in a few generations to establish a (−) line with V about 1·0 and a (+) line with V 2·5 or more, so that the total divergence in V was at least 1·5 units. Our own progress, selecting the extreme 15–20% of the population, appears to have been rather less dramatic than this, since V in the (+) and (−) lines only diverged by 0·6 unit after four generations of selection in the Crian stock, and fell away again after reaching a divergence of 1·3 units at generation 4 in the SP stock. This suggests that the F_2 of the two inbred lines crossed by Mather had rather more genetic variance

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in asymmetry, in a form readily available for selection, than the two wild stocks.

A particularly important point is that both series of selection experiments are consistent in demonstrating that asymmetry can be reduced well below the level of wild stocks or heterozygous genotypes by direct selection. This point will be discussed later.

One difficulty in interpreting the graphs needs further comment: mean asymmetry shows striking fluctuations from one generation to the next, in both experiments. In the first test, for example, $|L-R|$ starts at 1·26 and falls to 1·03 and 0·98 in the (+) and (−) lines in the next generation, although the total count remains almost constant. This drop is as large as the final divergence between the two lines of 0·25 unit. The parallel fluctuations of the two lines in this experiment strongly suggest the effect of some environmental factor, changing from one generation to another; but it must be admitted that to accept this hypothesis blurs the distinction between environmental and 'chance' variability, since it suggests that the latter can be strikingly modified by undetected changes in culture conditions, which we attempted to keep constant. It is, perhaps, just possible that the change between generations 0 and 1 reflects a change in genetic equilibrium when the stock was transferred from bottle culture to vials.

Equally striking fluctuations, though not always parallel, occurred in the second experiment, particularly over generations 4–6. Possibly one of the genes specifically affecting bristle variance, which turned up in the SP inbred lines to be described later, and so were probably also present in the wild stock, contributed to some of these fluctuations, but we have no further evidence on this point. What is clear, however, is that the changes in absolute level of asymmetry from one generation to the next cannot be taken as a direct measure of the effects of selection, and we must base our conclusions on comparisons between lines reared together.

In the next section we shall examine the behaviour of the sternopleural variances in crosses between inbred or otherwise homozygous lines, in comparison with the variances of the sternite counts.

THE EFFECTS OF INTERCROSSING HOMOZYGOUS LINES

As we noted earlier, published data suggest that the variances of sternopleural and sternite chaeta number behave differently when inbred lines are intercrossed; but a larger body of evidence is needed on this point, since the former character was only examined in a single cross. Further data have now been collected, and their analysis will be summarized below.

A number of lines were available which had been prepared by introducing third chromosomes, picked at random from the Renfrew wild stock, in homozygous phase into an unrelated inbred line (WE 3), in such a way that the other chromosomes of this line remained homozygous. These lines were prepared for another purpose, and their method of preparation will be described elsewhere. Although

they differed only in their third chromosomes, there were marked differences among them in such characters as body-size and the numbers of sternite and sternopleural hairs.

Eight of the lines which showed no signs of visible mutations on their third chromosomes were selected and cultured at the same time as eight intercrosses between them, eggs being cultured on the usual medium at 25° C., with seventy eggs per vial so as to avoid overcrowding. Thorax length was measured on forty females, while the sternopleurals and the hairs on sternites 3 to 5 were counted on thirty males of each mating. The behaviour of the mean and variance of each character, averaged over the heterozygotes and over their mid-parents, is given in Table 4, together with the average percentage change from homozygote to heterozygote.

For the sternopleurals, we have their sum (s), and its variance (σ_s^2), and the mean asymmetry $d = |L-R|$ and mean square asymmetry $Av(d^2)$, calculated as the mean value of d^2. This is identical with Mather's V.

In the case of the abdominal sternite hairs, we have the sum of segments 3 to 5 (s), the variance of this sum (σ_s^2), and the sum of the independent variances on the three segments (σ_d^2), which is calculated so as to be directly comparable with the mean square asymmetry of the sternopleurals. For this purpose we suppose that the variance of each segment is made up of a fraction common to all segments (σ_c^2) and an independent fraction (σ_i^2), and that these fractions are the same for each segment. The two components are then estimated from the observed variances as follows (cf. Reeve & Robertson, 1954):

$$\begin{aligned} V(\Sigma) &= 9\sigma_c^2 + 3\sigma_i^2, & V(\Sigma) - \Sigma(V) &= 6\sigma_c^2, \\ \Sigma(V) &= 3\sigma_c^2 + 3\sigma_i^2, & 3\Sigma(V) - V(\Sigma) &= 6\sigma_i^2, \end{aligned}$$

where $V(\Sigma)$ is the variance of the sum of the counts on the three segments, and $\Sigma(V)$ is the sum of the separate segment variances. Our index σ_d^2 is then calculated as $\frac{1}{2}[3\Sigma(V) - V(\Sigma)]$, and provides an estimate of $3\sigma_i^2$, or the sum of the independent variances of the three segments.

Applying this method to the sternopleurals, it is easy to see that

$$\begin{aligned} \sigma_s^2 &= 4\sigma_c^2 + 2\sigma_i^2, \\ Av(d^2) &= 2\sigma_i^2. \end{aligned}$$

It will be noted that the mean square asymmetry measures the amount of independent variance in the two groups of sternopleurals, and in the same way σ_d^2 for the sternites may be taken as a measure of the amount of antero-posterior asymmetry among the sternites, after adjustment for differences in their mean counts.

Finally, we have the mean and variance of thorax length. Thorax length shows the familiar result that mean size is about 2% larger and the variance about 32% less in the heterozygotes than in the parent lines. The total sternopleural count is a little lower (2·6%) and its variance is 7·5% higher in the crosses, though

neither of these changes is statistically significant. But both the mean asymmetry ($-13{\cdot}5\%$) and the mean square asymmetry ($-18{\cdot}0\%$) are significantly reduced in the crosses, and the latter figure is remarkably close to the $17{\cdot}4\%$ decline in mean square asymmetry obtained by Mather (loc. cit.) on crossing an Oregon and a Samarkand inbred line together. His figures are given in the furthest right-hand column of Table 4.

Table 4. *Average indices of eight homozygous lines and eight intercrosses (Re in WE 3)*

	Sternopleurals				
	s	σ_s^2	d	$Av(d^2)$	$Av(d^2)$ (Mather)
Homozygotes	17·46	1·45	1·108	1·99	2·22
Heterozygotes	17·00	1·56	0·958	1·63	1·84
Per cent change	−2·6	+7·5	−13·5	−18·0	−17·4

	Abdominal sternites 3–5			Thorax length (1/100 mm.)	
	s	σ_s^2	σ_d^2	Mean	σ^2
Homozygotes	59·38	8·70	7·24	105·0	2·09
Heterozygotes	59·21	8·76	7·68	107·1	1·43
Per cent change	−0·3	+0·7	+6·1	+2·1	−31·6

In contrast to these results, the number of hairs on the abdominal sternites shows no appreciable change in mean or variance ($-0{\cdot}3$ and $+0{\cdot}7\%$ respectively), while the independent variance is higher, if anything, in the crosses than in the parent lines, the net change being $+6\%$. Clearly in this set of crosses the amount of bilateral asymmetry of the sternopleurals was substantially reduced, but no parallel reduction occurred in the corresponding antero-posterior asymmetry between adjacent sternite counts, so that the difference in behaviour of the two groups of bristles seems well established.

A further interesting point is that the variance of total count is less than the mean square difference for the sternopleurals, at least in the homozygotes, so that the variance common to the two sides (σ_c^2) is negative, or, in other words, there is a negative correlation between the two sides. This is about $-0{\cdot}15$ in the homozygotes, but virtually disappears in the crosses ($-0{\cdot}02$), because of the reduction in mean square difference.

These results, taken together with the data published previously, seem perfectly clear, but some further tests, made on another set of homozygous lines and on a set of inbred lines, obscured the clarity of the picture because of the presence of what appeared to be specific genes affecting bristle number and variance in the lines tested.

First, a set of homozygous lines similar to those discussed above was created by making third chromosomes of the SP wild stock homozygous in the genetic background of the WE 3 inbred line. Of the eight lines fully tested, four were found to be homozygous for an allele of the third-chromosome recessive gene polychaetoid (*pyd*). Yet more surprising, the other four lines all carried another third-chromosome recessive effect, which will be referred to as 'sternopleural gaps' (*stg*). This was probably a single gene effect, though not established as such, and caused gaps to appear in the row of sternopleural hairs on one or both sides, at least partly by replacing individual hairs by sockets without hairs.

The means and variances of sternopleural and sternite counts for the two groups of lines and some intercrosses are shown in Table 5, taken from a test made in the same way as before. In the top line we have the average indices of the eight Renfrew lines from Table 4, for comparison. Below are the averages for the four polychaetoid lines and the four lines showing sternopleural gaps.

Table 5. *Characteristics of* (*SP in WE 3*) *lines compared with* (*Re in WE 3*) *lines*

	Sternopleurals			Sternite counts		
	s	σ_s^2	$Av(d^2)$	s	σ_s^2	σ_d^2
Re in WE 3 averages (8 lines)	17·5	1·45	1·99	59·4	8·7	7·2
SP line averages						
4 *pyd* lines	20·8	2·92	2·78	60·3	13·4	11·7
4 *stg* lines	17·0	3·96	3·80	55·8	12·1	7·0
5 crosses	17·3	2·09	1·71	59·2	10·2	8·4
Per cent change	−8	−39	−48	+2	−20	−11

The *pyd* lines had, on the average, about four more sternopleural and four more sternite hairs than the *stg* lines, but the latter had some 30% higher sternopleural variances (3·96 against 2·92 for σ_s^2, and 3·80 compared with 2·78 for $Av(d^2)$). Both series had much higher variances than the corresponding Renfrew-line averages of 1·45 and 1·99. Both SP series also had increased variances for total sternite count (13·4 and 12·1 compared with 8·7), while the *pyd* lines had an increased independent variance for the sternite hairs. Thus in general the counts were more variable and the asymmetry greater in the SP lines.

A set of five crosses between SP lines such that *pyd* or *stg* or both were heterozygous but neither was homozygous are summarized in the fourth line of the table, and the percentage changes in their indices, compared with the average of the *pyd* and *stg* lines, are given in the last line. These crosses agree remarkably well in their indices with the crosses between the Renfrew lines of Table 4, so evidently neither gene has an appreciable effect on variance or asymmetry when heterozygous. The result is that the crosses show reductions of some 40–50% below the parent values in the variance and mean square asymmetry of the sternopleurals, while less drastic but still appreciable reductions occur in the corresponding sternite variances.

Some crosses were also made between SP lines carrying the same gene, and these had just as much variance and asymmetry as the parent lines, suggesting that the increased variances in these lines were due to the *pyd* and *stg* genes themselves, rather than to the overall homozygosity of the third chromosome. It is also of interest that one of the 'sternopleural gap' lines had four flies, out of the thirty examined, with differences of 5, 6, 7 and 8 hairs between the two sides, against a mean sternopleural count of 8·6 hairs per side. The resulting mean asymmetry was 2·13 and the mean square asymmetry 8·7, values enormously greater than have been recorded before.

In a final test, four inbred lines from the Pacific wild stock and six intercrosses were cultured in the usual way, and forty to eighty flies of each sex per mating were scored for sternopleurals, the variable numbers arising because of variable fertility in the different lines. In addition, samples of each line and cross were reared in sterile cultures on 50% concentration of synthetic medium C of Sang (1956). This reduced diet has the effect of reducing body-size (thorax length) by about 12%. The cultures of this test were all prepared by my colleague Dr F. W. Robertson for other purposes, and I am indebted to him for making the flies available to me. Males only from the synthetic-medium cultures were scored for sternopleurals.

The test on the full diet is analysed in Table 6, where the two sexes are treated separately. In males, the results differ strikingly from the earlier tests (Tables 4

Table 6. *Sternopleural indices in Pacific inbreds and F_1's: normal diet*

Averages of six crosses among four inbred lines

Males	s	σ_s^2	d	$Av(d^2)$
Mid-parent mean	18·54	4·79	1·216	2·71
F_1 mean	17·53	3·70	1·313	2·86
Per cent change	−5·4	−22·7*	+8·0	+5·6
Females				
Mid-parent mean	18·18	3·88	1·378	3·03
F_1 mean	17·78	2·80	1·230	2·61
Per cent change	−2·2	−2·1	−10·7†	−14·0

* P less than 0·001. † P less than 0·05.

and 5), since the F_1's show a sharp drop of 22·7% in the variance of total count, and yet have actually an increase in mean asymmetry (d) which is almost statistically significant. The females, on the other hand, behave much as the Renfrew series of Table 4, since the level of asymmetry declines significantly while there is little or no change in total count or its variance. So the curious fact emerges that the males show an increase and the females a decrease in sternopleural asymmetry, when the Pacific inbred lines are intercrossed.

It is possible that here again we have the intervention of one or more genes with specific effects on bristle number and variance, since a variable tendency was noticed for certain bristle abnormalities to occur in the four Pacific inbred lines used and in the intercrosses between them. These took the form of missing dorso-central or scutellar bristles, the bristle being represented only by its socket, or of extra scutellar bristles. As an example, in one of the inbred lines, twenty-seven females possessed, between them, 1 extra scutellar bristle, 34 scutellar sockets without bristles, and 43 missing dorso-central bristles.

These abnormalities occurred with varying frequency, usually higher in females than in males, in all the intercrosses, and also in the Pacific wild stock, so it appears that a genetic condition present in the wild stock was fixed in all the four inbred lines. This is particularly surprising, since the wild stock originated from a large sample of wild flies and has been kept in a large mass culture since. Further genetic analysis is obviously desirable, but is likely to be difficult because of the variable and rather low frequency of manifestation of the effect.

The point of main interest in the present context is that one or more genes affecting the regularity of the bristle patterns are present in the inbred lines of the Pacific stock as in the SP lines, and that in both series they appear to cause a greatly increased variance of total sternopleural count, and also an increased asymmetry as measured by $Av(d^2)$. Intercrosses which leave the genes responsible for these effects homozygous produce little or no reduction in variance and asymmetry.

Some sternopleural indices for the different series are gathered together in Table 7, and compared with those of the PdL wild stock, obtained from the

Table 7. *Sternopleural indices in different lines and crosses*

	s	σ_s^2	$Av(d^2)$ $=2\sigma_i^2$	$2\sigma_e^2$	r_{LR}
Renfrew lines (males)					
Homozygotes	17·5	1·45	1·99	(−0·27)	−0·16
Heterozygotes	17·0	1·56	1·63	(−0·04)	−0·02
SP lines (males)					
Pyd	20·8	2·92	2·78	0·07	+0·02
Stg	17·0	3·96	3·80	0·08	+0·02
Intercrosses	17·3	2·09	1·71	0·19	+0·10
Pacific lines					
Inbred males	18·5	4·79	2·71	1·04	+0·28
F_1 males	17·5	3·70	2·86	0·42	+0·13
Inbred females	18·2	3·88	3·03	0·42	+0·12
F_1 females	17·8	3·80	2·61	0·60	+0·19
PdL wild stock					
Males	18·1	2·72	1·69	0·52	+0·23
Females	19·5	2·99	1·84	0·58	+0·24

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progeny test. Besides the total count (s) and its variance, and the mean square asymmetry (which also estimates $2\sigma_i^2$), we give the corresponding variance due to correlated variations on the two sides ($2\sigma_c^2$) and the correlation between the two sides, which may be estimated as $\sigma_c^2/(\sigma_i^2+\sigma_c^2)$.

The mean count is much the same in all series, apart from the three to four extra bristles in the *pyd* lines, and we do not need to consider possible corrections for scale effects. The asymmetry variance is very similar in the Renfrew crosses (1·63), SP crosses (1·71) and wild-stock males (1·69), and these figures probably represent the general level for heterozygotes with seventeen to eighteen bristles. Nevertheless, selection is apparently able to reduce the mean square asymmetry to not much above unity, without changing total count. The level of asymmetry is much higher in the Pacific lines and crosses and in the SP lines, probably because of the homozygosity of specific genes which affect the bristles and not because of the general level of homozygosity.

From the fourth column of Table 7, we see that there is a large correlated variance in the Pacific lines and crosses, but not in the SP lines, so that the fixation of particular genes affecting bristle variability may cause correlated or random fluctuations in count on the two sides. These variations are, of course, non-genetic in origin, but it is not at present clear whether they all come within our category of 'chance' variation or whether the correlated variations are the result of the Pacific-line genotypes possessing a greater sensitivity to environmental effects. What does stand out, however, is that the magnitudes of the non-genetic variances and their behaviour on crossing are very strikingly influenced by the particular lines we select.

The correlation coefficients listed in the last column of Table 7 show that a non-genetic correlation, as in the Pacific-line males, may be as high as the correlation in the wild stock, which one would suppose was entirely genetic. Evidently it would be unwise to assume that the correlated and uncorrelated fractions of the variance in total sternopleural count will necessarily divide it into the genetic and non-genetic fractions.

As a final point, Table 8 shows the effect of restricting the food intake, by using a diluted synthetic diet, on the various sternopleural indices. Data are only available for the Pacific inbred and F_1 males, and in view of their peculiarities it cannot be assumed that other lines would behave in the same way. The table gives the average mid-parent and F_1 values on normal and restricted diet, and the percentage reduction on the reduced diet, for four crosses among the four inbred lines.

Body surface area, measured by the square of thorax length, was reduced in both series by about 23%, but the other indices responded rather differently in inbreds and crosses. In fact, it appears that the total count and its variance were reduced most in the inbreds, while the two measures of asymmetry came down most in the crosses. This result is rather suggestive, and could, no doubt, be fitted in with some recent speculative deductions about the advantages in combined phenotypic stability and flexibility of heterozygotes compared with homozygotes.

Table 8. *Effect of diet on sternopleural indices*

	Pacific inbred lines and crosses: males Sternopleural indices				Thorax area
	s	σ_s^2	d	$Av(d^2)$	
Full diet					
Mid-parent	19·34	5·08	1·24	2·85	
F_1	18·38	3·78	1·34	2·93	
Restricted diet					
Mid-parent	15·75	3·78	1·15	2·34	
F_1	15·98	3·64	1·12	2·12	
Per cent reduction					
Mid-parent	18·5	25·6	7·0	17·9	23·4
F_1	13·1	4·0	16·3	27·4	22·7

Thus it might be argued that the greater reduction in asymmetry shown by the F_1's reflects their greater developmental flexibility, while their smaller change in total count and its variance reflect their greater developmental stability, compared with the inbred lines, both being aspects of the greater developmental homeostasis of the heterozygotes. Unfortunately, the argument can be inverted with equal effect, and a satisfactory interpretation must wait until we have a broader experimental and speculative basis to build on.

DISCUSSION

In discussing experiments on quantitative characters, there is a tendency, illustrated in the last paragraph, for theoretical geneticists to jump from general deductions based on evolutionary suppositions to the interpretation of the statistical indices in terms of which the behaviour of the character is expressed, without giving much attention to the possible biological attributes of the character concerned. Unfortunately these statistical parameters have a very limited power of self-expression, so that whatever theoretical constructs the experimenter starts with may easily be found to have been proved by the experimental behaviour of the parameters he calculates. Our difficulty is, of course, to determine what are the significant biological attributes of any character, from the genetical point of view, or to express them in any but rather general and ambiguous terms. Thus it is an acceptable tautology that natural selection favours maximum 'fitness', of individual or population, but very difficult to lay down what is the relation of any quantitative character to fitness. Even when it seems obvious that more of some character such as egg production is generally of selective advantage, we are far from disentangling the complex interplay of genetical and physiological correlations which obscure any simple relationship between the two.

In the case of the two bristle-count characters, our limits of plausible deduction are yet more restricted, since even their main functions are quite uncertain.

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Thoday (1958) states that the number of sternopleural chaetae must have 'adaptive significance', since different populations and species have different characteristic numbers, so that the character is affected by natural selection; but though the fact that different populations have different means must be the result of natural selection (if genetic drift is not responsible), it does not follow that these differences must have any adaptive significance in terms of the character concerned. Many genes are known to act pleiotropically, and non-adaptive changes in one character may be caused by selective forces acting on another, and causing changes in the frequencies of genes which have pleiotropic effects on both. The sternopleurals are most unlikely to have a special set of genes to themselves, with no other effects, and some of the genes which influence their number probably have also more important effects on the integument, or other tissues or organs, which need to change adaptively with change of environment. This, or mutal adjustment of gene frequencies in different genetic backgrounds, is quite sufficient to explain differences in mean count of different populations.

It still remains an open qusetion, then, whether the number of sternopleurals is an adaptive character in the sense that it matters to the individual or population whether it has one or two bristles more or less on each side, or in the sense that the optimum number of bristles is different in different environments. It is worth while looking at these bristles to see what their appearance suggests. There are, in fact, three very stable larger bristles forming a triangle at the dorsal end of the group, and a variable row of smaller ones extending ventrally, together with a sporadic occurrence of very small hairs near the large dorsal bristles. The group occupies a triangular region of hard sclerotized integument near the base of the second leg, and is surrounded by seemingly equally well sclerotized integument without bristles.

Now, if any of these bristles have a specific function, it is certain to be the larger and more stable ones at the dorsal end of the group; and it is quite likely that the smaller hairs are simply a by-product of the morphogenetic forces required to create the three larger bristles. If this is the case, their number would depend on the balance between forces which have other primary functions in development. Selection to alter the number of sternopleurals would eventually disturb this balance, with consequent effects on other features of development. These suggestions are, of course, speculative, and they are put forward to draw attention to a neglected aspect of the whole problem and to emphasize the danger of attaching labels with an evolutionary flavour to characters whose whole biological basis is unexplored and has been left out of account. The alternative hypothesis, that it is of adaptive significance to the fly to have one or two more or less of these small hairs, is very difficult for anyone who has gazed at them for long to believe.

A different aspect was considered by Mather (1953), who pointed out the interesting possibilities of bilateral asymmetry as a subject for genetic study. In particular, it provides a means of investigating the genotypic stabilization of developmental processes, since the two sides of an individual develop under the influence of identical sets of genes, so that differences between them must be due

to what he calls 'local upsets' in development. The level of asymmetry must reflect the degree to which the individual or genotype is able to correct such local accidents, and so measures its developmental stability. Mather chose sternopleural asymmetry because of its ease of study, and Thoday (1958) also takes up this point and argues that this character is 'a useful measure of developmental homeostasis'.

The argument implied here is the familiar one that adapted populations possess genotypes which are better 'canalized in development' (Waddington, 1953), or have more 'developmental homeostatis' (Lerner, 1954), whichever term we prefer, because of natural selection, and this makes them better able to resist the effects of environmental variables or accidents of development in establishing a constant phenotype, than are less well-adapted genotypes. Likewise, heterozygotes will have the same advantages over homozygotes in outbreeding species. The further assumption is clearly implicit in the statements of Mather and Thoday that this greater developmental stability will affect all characters, so that any bilateral character we like to study will give a measure of the same stabilizing forces.

This is, of course, a most engaging thesis, and suggests a method of getting at selective effects which cannot otherwise be investigated except in clones of identical genotype, such as inbred lines and crosses between them. Unfortunately, the experimental results so far obtained do not lend the thesis much support. Mather (1953), for instance, found a higher asymmetry in two inbred lines than in the F_1 and F_2, but selection from the F_2 reduced the level much further still; and my own selection experiments, described earlier in this paper, also show that asymmetry can be reduced well below that of a wild stock by a few generations of selection. Now one must conclude either that the (−) selected lines in these experiments have a much greater developmental homeostasis than the wild stocks or F_2 from which they originated, or that the level of asymmetry is not a measure of developmental homeostasis. The first of these conclusions defies common sense—a wild stock must surely be maintained at or near the maximum level of homeostasis by natural selection—and we are forced to conclude that the level of sternopleural asymmetry does not give us an adequate index of homeostasis, in so far as this is a general characteristic of the organism.

Crosses between inbred lines or artificially created homozygotes usually produce a reduction in asymmetry, so that the character often behaves in this respect like so many other quantitative characters in different species. This decline may, in fact, be the result of increased general developmental stability in heterozygotes; but it must be borne in mind that this is a very crude comparison, since homozygotes from an outbreeding species are genetical oddities, which would have no chance of surviving in competition with normal individuals. A good correlation between the length of chromosome homozygous and the non-genetic variance has been found for body-size and rate of egg-production in *Drosophila*, by Robertson & Reeve (1955), but it has yet to be seen whether any vestige of such a correlation occurs for asymmetry. The fact that there are very different levels of asymmetry in different homozygotes and that the level is not always reduced on crossing,

suggests that any such correlation which occurs will tend to be swamped by other effects.

In spite of these uncertainties of interpretation, it would be of interest to follow changes in asymmetry in populations subjected to various experimental treatments, such as inbreeding or selection for some character. Thoday (1958) studied the behaviour of the index: mean asymmetry divided by total count (d/s in our terminology), when total count was changed by selection, and found that his index increased with selection in both directions. This suggested the occurrence of a phenomenon which one could predict on theoretical grounds—a deterioration in homeostasis with selection. However, an awkward question of scale arises here.

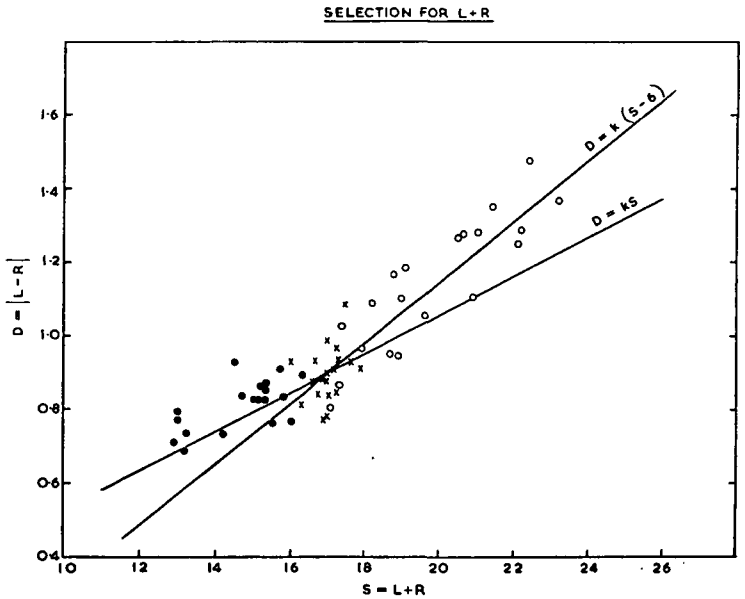

Fig. 2. Mean asymmetry (D) plotted against total sternopleural count (S) in lines selected for increased total count (rings), lines selected for decreased total count (solid circles) and control lines (crosses). Data recalculated from Thoday (1958). For each line, k is chosen to make the line pass through the mean of the control points.

Change in mean count will automatically produce a change in mean left-right asymmetry, quite apart from any change in developmental stability, and the problem is how to eliminate this scalar effect in studying the effects of selection. Thoday's choice of the index d/s is obviously unsatisfactory, since variation in count and asymmetry will depend entirely on the variation in the smaller bristles, at least in the earlier generations of selection. A much better index would be $d/(s-6)$, the denominator being the total count excluding the three stable bristles on each side.

Thoday's data on selection for high count (rings), selection for low count (solid circles) and controls (crosses) have been replotted in the form D against S, in Fig. 2, where $D = |L-R|$ and $S = (L+R)$. The figures have actually been recalculated from his Table 3 and Fig. 2, and may be taken as accurate enough for our purpose.

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Two lines have been drawn on the graph, both through the mean of the points for the controls. The line $D = kS$ gives the expected scalar change assuming Thoday's index D/S is the correct one, and we see that the majority of points for both up and down selection have values of D above this line. This leads to Thoday's conclusion that homeostasis deteriorated in both selection lines.

The second line is $D = k(S-6)$, and gives the expected scalar change with our more realistic index $D/(S-6)$. This line runs well below the down selection line, but runs through the middle of the points from selection for increased total count, so that with this scale we should conclude that selection for reduced count caused a rapid deterioration in homeostasis, while selection for increased count left it virtually unaffected.

No doubt we could argue, plausibly enough, that any selection which alters the co-adapted gene pool of the wild stock is bound to reduce the level of homeostasis; but since we have been forced to conclude that mean asymmetry tells us very little about the level of homeostasis, it follows that Thoday's experiment gives us no information about the effects of selection on homeostasis. Nevertheless, the scalar problem is an important one, and Thoday's approach provides a good illustration of the dangers pointed out in the first paragraph of this discussion.

Something must finally be said about the differences in behaviour of the sternopleural and sternite characters. Our results are in agreement with the previous conclusion that the variances in number of sternite bristles—both the total variance and the independent component—hardly change when homozygotes are intercrossed, with the exception of the lines homozygous for the gene *polychaetoid*, which has specific effects on the various bristle regions. Thus no question of developmental stability seems to arise here, since the homozygotes are no less stable than heterozygotes. But, in examining the two characters, sternite and sternopleural bristles, certain important differences become evident which might account for their difference in genetic behaviour.

First, as regards origin, the sternopleurals on each side are believed to develop from part of a single imaginal disc, and the discs on the two sides are certainly derived from groups of cells which separate from each other at some time during embryonic development, since the rudiments of each disc can be detected in the newly hatched larva (Auerbach, 1936). Hence separation of the cell lineages responsible for each group of sternopleurals must occur extremely early in development. Each sternite, on the other hand, is the product of two cell groups, the hypodermal histoblasts, one on each side, so that it is actually of bilateral origin. These histoblasts can first be detected in the early pupa (see discussion in Reeve & Robertson, 1954), and those on one side which contribute to the sternites of the different segments probably only separate from each other late in larval development. The bilateral origin of each sternite would eliminate any asymmetry of the type which affects the sternopleurals, and the comparatively late separation of the elements giving rise to the different sternites might limit the influence of different genotypes on the level of stability.

Second, and perhaps more important, is the fact that the sternite bristles occupy

a definite area, clearly delimited by the sternite itself, while the area occupied by the sternopleurals is somewhat variable and appears to have no clear-cut boundary. Thus, to the variation in density within a definite region, such as occurs in the sternites, is added the variation in extent of the potential bristle-forming region in the case of the sternopleurals. The latter type of variation might well be more sensitive to local conditions, and lead to the variation in bilateral asymmetry found in different genotypes.

There are good grounds, then, for maintaining the distinction between true environmental and chance variability in the case of the sternite counts, and of putting all the independent fraction of the variance in the latter class. This variability represents an aspect of developmental stability which appears to be very little affected by changing the genotype. But with the sternopleurals the distinction is not so clear, since some genotypes may produce correlated non-genetic variation on the two sides, while marked differences in asymmetry can occur between different genotypes. The nature of this variability clearly needs further study before we can decide how to classify it.

SUMMARY

1. Published data suggest that mean left-right asymmetry in number of sternopleural bristles of *D. melanogaster* declines when inbred lines are crossed, while the corresponding variance for sternite bristles remains unchanged. Some genetic tests were undertaken to analyse this difference in behaviour of the two characters.

2. A progeny test on a wild stock showed that a small amount of genetic variance in sternopleural asymmetry was present, equivalent to about 2% of the total phenotypic variance.

3. It was possible to increase and decrease the level of sternopleural asymmetry in two wild stocks by selection. These experiments gave an estimated heritability of some 2–3%, in close agreement with the progeny test. Change in asymmetry did not necessarily lead to a change in mean count.

4. Homozygous lines, consisting of individual third chromosomes from the Renfrew wild stock made homozygous in an inbred line genetic background, were intercrossed, and the average indices for a number of characters of eight intercrosses involving eight lines were compared with their mid-parent averages. Thorax length was 2% greater and its variance 32% less in the crosses; total sternopleural count and its variance did not change significantly, but the asymmetry variance declined by 18%. In contrast, the corresponding asymmetry or independent variance for numbers of sternite bristles was 6% higher in the crosses, although the total sternite count and its variance did not change. These results fit in with previous work.

5. Tests on a similar set of homozygous lines in which the third chromosomes came from the SP wild stock, and on some long inbred lines from the Pacific wild stock, gave discordant results. Of eight SP lines examined, four were homozygous

for a gene *polychaetoid*, and four were homozygous for a genetic effect causing sockets without bristles to occur among the sternopleurals. Both types had much greater sternopleural variance and asymmetry than the Renfrew lines, and both indices declined sharply in intercrosses leaving these genetic effects heterozygous, but neither declined if they were left homozygous in the crosses. Similarly high sternopleural variances were found in the Pacific lines, but only the total variance declined in males and only the asymmetry variance declined in the females, when they were intercrossed. All the four Pacific lines tested appeared to be homozygous for a genetic effect which caused a variable number of dorso-central and scutellar bristles to be replaced by sockets without bristles, and an occasional extra scutellar bristle to appear. This effect was also probably responsible for the high sternopleural variances.

6. Males of the Pacific inbred lines and intercrosses were compared when reared on the normal live medium and on a synthetic diet in reduced concentration, which reduced body-size by 23% (thorax area). The inbred lines were reduced more than the F_1's in total sternopleural count and its variance, but the F_1's were reduced more in sternopleural asymmetry, by the restricted diet.

7. The problems of interpreting these experiments, in view of our ignorance of the biological functions and attributes of the sternopleural and sternite bristles, are discussed. It is concluded that we have no basis yet for deciding whether sternopleural bristle number is of adaptive significance, but this is considered improbable.

8. The experimental evidence suggests that sternopleural asymmetry cannot be considered a measure of general developmental stability, particularly as the level of asymmetry can be reduced by selection well below that of typical wild stocks.

9. The scaling problems arising when the mean asymmetry of lines with different mean counts are to be compared, are examined, and it is suggested that the ratio of asymmetry to total count does not eliminate scale effects.

10. Developmental and anatomical differences between the sternopleural and sternite bristles suggest a possible reason why they behave differently when inbred lines are intercrossed.

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