

Population structure in artificial selection: studies with *Drosophila melanogaster*

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SUMMARY

The effect of sub-dividing a population during selection was studied by selecting downwards for sternopleural bristles in *Drosophila melanogaster*. The four structures used all involved the selection of 40 individuals out of 200 measured in each sex. The alternatives were:

- (i) one large line with the same selection procedure in all generations,
- (ii) eight small lines with the same procedure in all generations,
- (iii) the 'single cycle' structure in which large lines derived from crosses between selected small lines at either the sixth or twelfth generation, and,
- (iv) the 'repeated cycle' structure in which the best five small lines were mixed at the sixth generation of selection to produce a new set of small lines on which the procedure was repeated for a total of three cycles.

Of the first two methods, the large line had a higher final response than did any of the small lines. The latter, selected with an intensity of 5 out of 25 in each sex, had lower average final response than had a similar group of lines selected from the same base population with the lower intensity of 10/25. The results showed no clear effect of the sub-division of the population, followed by selection between lines, though they were in general agreement with theoretical expectations. Several second chromosome recessive lethals were found at high frequencies in different selected lines. One of these, found in eight of the lines, had an effect on bristles in the heterozygote of about 1.5 phenotypic standard deviations. The evidence strongly suggests a pleiotropic effect on bristle score.

1. INTRODUCTION

Population structures involving sub-division into several lines and selection within and between them, followed by intercrossing, may allow more rapid improvement than is possible from selection within a single population under several genetic situations. Wright has often emphasized the advantages of structures of this type when selecting for epistatic combinations in a cross-fertilizing species. Particularly, if multiple 'peaks' of desirability in relation to gene frequencies exist, drift and local shifting of the peaks may allow the population as a

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whole to move to higher peaks after crossing (Wright, 1951). However, the consequences of a particular breeding structure will be different for loci with different types of gene action.

Epistatic relationships may arise in the interaction between natural and artificial selection. Variation between replicate lines in the changes in fitness associated with selection appears to be common in *Drosophila* experiments (Latter & Robertson, 1962; Latter, 1966; Rathie & Barker, 1968). Frankham, Jones & Barker (1968) concluded that although many genes were potentially capable of influencing bristle numbers, probably only a few were responsible for selection response in any single line. If interactions are important for the primary character or in its relationship with fitness, greater selection advance might be attained by the use of a structured population, in Wright's sense, even for apparently simple characters for which most of the variation is initially additive.

The experiment to be described was carried out to investigate the effect of population structure, in particular the consequences of selection between sublines, on the progress from selection for a single character in *Drosophila melanogaster*. It is similar in some ways to a preliminary experiment reported by Hill (1963). Different procedures were then compared, given certain fixed facilities – in this case the number of flies scored per generation. The same selection intensity was used in all lines. At the same time as the experimental work, the effect of population structure was also evaluated by computer simulation (Madelena & Hill, 1972) and those aspects of the results relevant to the present paper are dealt with later.

2. MATERIALS AND METHODS

The selection lines were started from the Kaduna base population (Clayton & Robertson, 1957) and were selected for a reduced number of sternopleural bristles at 25°. All lines were mass mated in bottles.

An essential aspect of the experiments was the comparison of different methods of utilizing the same facilities, here defined as the total number of individuals, 400, measured each generation. The selection intensity was in all cases one out of five so that the total of 400 was either devoted to one 'large' line, the parents being divided over eight bottles with a selection pressure of 40/200 in each sex or, on the other hand, eight 'small' lines, each kept in a single bottle with a selection pressure of 5/25 in each sex. All large lines were given the symbol *L* with additional figures to indicate their exact origin. The basic design of the experiments is indicated in Fig. 1. They started with a single large line, *L*, and a set of small lines numbered 1–8, in which selection was continued until there was little further response. All times quoted are in generations from the start of these lines.

The set of small lines served as a base for the examination of the effect of selection between lines. This was in two parts.

(i) *Single cycle between-line selection*

Large lines were made by combining selected small lines, both at generation 6 and at generation 12. At each occasion, large lines were made from the best 2, the best 5 and by combining all the small lines respectively. $L/5.12$ then comes from a cross between the best 5 lines at generation 12. Crosses were made in such a way as to ensure equal representation from the founder lines and selection was continued during crossing. The inter-crossing was then in all cases complete after 3 generations. After generation 22, the number of flies measured in each sex was reduced to 50 from which 10 were selected.

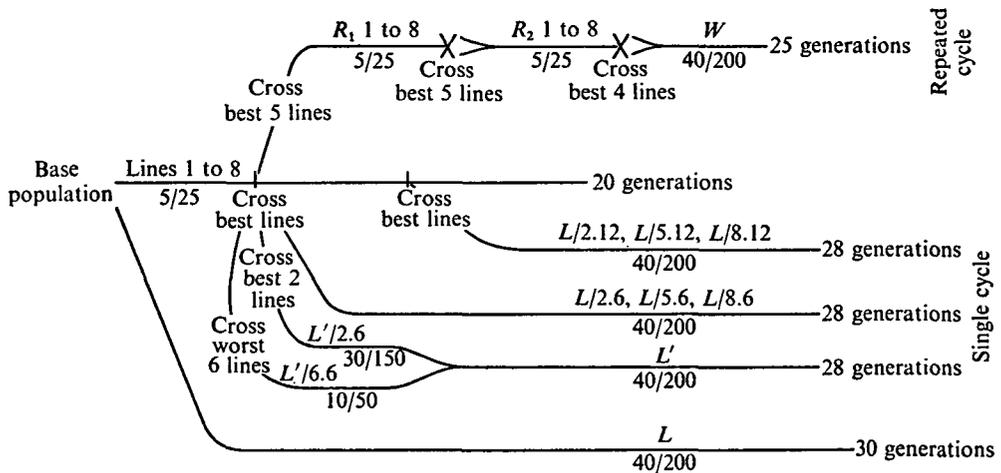


Fig. 1. The structure of the experiments. 5/25 indicates that 5 individuals were selected from 25 in each sex.

(ii) *Repeated cycle between-line selection*

From a cross of the best 5 small lines at generation 6 (from which line $L/5.6$ comes) a further set of 8 small lines were started (R_1). From this set, the process was repeated at generation 15 to give R_2 . At generation 21, the poorest 4 were discarded and the remainder combined to give line W .

The only deviation from this plan was the large line L' (an attempt to get the best of both worlds), formed by crossing selected lines $L'/2.6$ and $L'/6.6$ derived respectively from, first, the best 2 small lines at generation 6 and, secondly, the worst 6. The results from this line will not be discussed in detail except where they throw some light on the behaviour of the other lines.

3. RESULTS

Single populations

The heritability of sternopleural bristle number in the base population was estimated from the regression of offspring on mid-parent value using assortative

mating. Two progeny of each sex were measured from 85 matings giving an estimate of 0.39 ± 0.05 . From the variance between the two sides of individual flies, it was estimated that developmental error specific to each side contributed $47 \pm 2\%$ of the variance in total score. The mean score in males was 17.08 with a standard deviation of 1.88 and in females 17.67 with a standard deviation of 1.85.

The results for the small first cycle lines and for the large line *L* are shown in Fig. 2 where five-generation running averages are plotted. Population size affected response even in the early generations, and after the 5th generation the large line had a larger response than any of the small ones. These showed the usual dispersion with more change of ranking than has been found in other similar experiments. For instance, when the lines were crossed at generation 6, line 1 was second in response whereas at generation 12 it was seventh, having responded by only 0.3 bristles in the previous six generations. The phenotypic variance and the realized heritability both dropped rapidly on selection. The values averaged over intervals

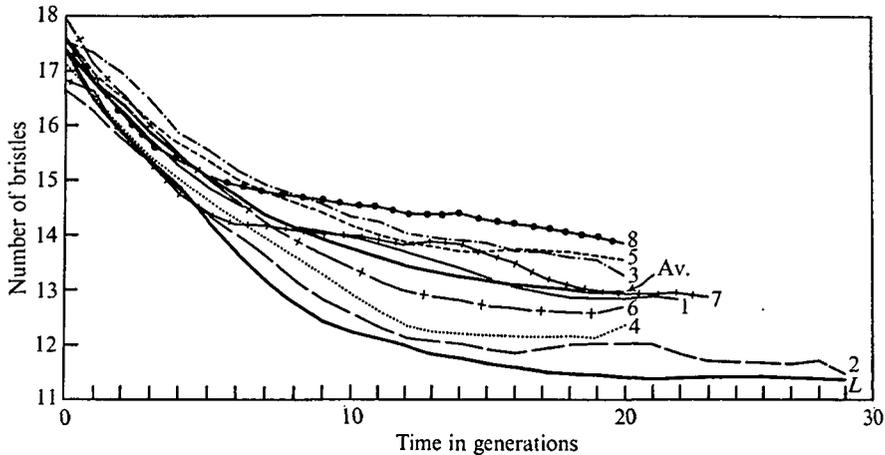


Fig. 2. The single populations. Lines 1-8 selected 5/25. *L* selected 40/200.

of 5 generations are given in Table 1. It will be seen that the variance in the large line was at the end very much larger than the average value for the small lines. One of the latter, line 2, which showed the greatest overall response, had a variance of the same order as that of the large line. Subsequent analysis showed that both were segregating for a recessive lethal which reduced bristle score in the heterozygote by 1.8 bristles.

The rate of approach to the final selection limit may be measured by the half-life of the selection process, the number of generations necessary for half the final advance to be achieved. For this to be meaningful it should be measured on a scale on which the effects of genetic substitution are approximately additive. Earlier work has shown that a transformation of $\log(S - 4)$, where S is the mean score, is reasonable for this character (McPhee & Robertson, 1970). On this scale the small lines had an average half-life of 4.6 generations whereas that of the large line

was very little greater at 5.3. At the 20th generation, the mean of the 8 small lines was 12.98 bristles. It is interesting that in previous work (see McPhee & Robertson, 1970) 8 lines had been selected downwards from the base population with an intensity of 10/25 and that their mean score at the limit was 12.08 bristles. This is a practical example of a situation in which a lower intensity of selection from a given total number of individuals measured produces a higher final response, as predicted by theory (Robertson, 1960).

The single cycle structure

As was noted earlier, the ranking of the small lines changed between the 6th and 12th generations, the two occasions on which they were crossed. Five-generation running averages for the large lines formed at generation 6 are shown in Fig. 3,

Table 1. Phenotypic variance and realized heritability in the initial lines

Gen.	1	2	3	4	5	6	7	8	<i>L</i>	Average of small lines excluding (2)
Phenotypic variance										
0	1.76	3.41	3.67	2.19	3.35	5.32	5.45	3.16	3.19	3.56
1-4	2.17	1.66	2.33	1.99	2.58	1.90	1.79	2.11	1.92	2.02
5-8	1.15	1.25	1.45	1.38	1.27	1.23	1.20	1.28	2.31	1.28
9-20	1.09	2.41	1.10	1.15	0.96	1.13	0.96	1.09	2.33	1.07
Realized heritability ($\times 100$)										
0-5	29	23	20	29	24	32	29	33	32	28
5-10	7	27	5	20	14	28	17	3	27	13
10-15	10	2	6	15	10	10	-6	10	9	8
15-20	7	-5	5	1	-1	4	13	8	1	5

together with the mean performance of *L*, and the scores of the separate small lines at the 6th generation are indicated on the left of the figure. The cross of the lowest two small lines, *L*/2.6, started at a lower value and had a higher initial rate of response than both *L*/5.6 and *L*/8.6. However, it did not reach the level of *L* until the 12th generation and had similar values afterwards, though *L*/2.6 was generally somewhat lower. After a slow initial response, the other two crosses gradually approached the level of *L* though even in the final generations their means were somewhat above it. The variance of *L*/2.6 increased after generation 9 to the level characteristic of *L* and small line 2 and it was subsequently found to be segregating for the lethal common to these. The lethal was not found in the other two crosses made from the 6th generation.

The figure also shows the results from the modified single cycle structure, *L'*, in which it had been hoped to achieve an increased response by gradually feeding into the cross of the best two small lines any genes from the remaining lines which it might not contain. Several more or less arbitrary decisions had to be made with respect to the allocation of facilities to the original cross lines, the importance of which it is difficult to guess. *L'*/2.6 was similar to *L*/2.6 except for an initial delay

but, after the injection of some genes into it from $L'/6.6$, it responded rapidly and was below $L/2.6$ after the 10th generation. It too carried the lethal found in L and 2.

The results from the crosses made at generation 12 are shown in Fig. 4. The small lines had by this time already realized more than 90% of their final advance. The 3 large lines produced by crossing were in the order expected from their parental small lines in the early generations and all responded rapidly to further selection. $L/2.12$ quickly passed L though it made little progress in the final 10 generations of selection. Both $L/5.12$ and $L/8.12$ made very rapid initial response and the former, after slowing down somewhat, showed a period of increased response after the 23rd generation to finish well below L . All three of the large lines derived from crosses made at the 12th generation contained the lethal found in L , presumably having derived it from line 2.

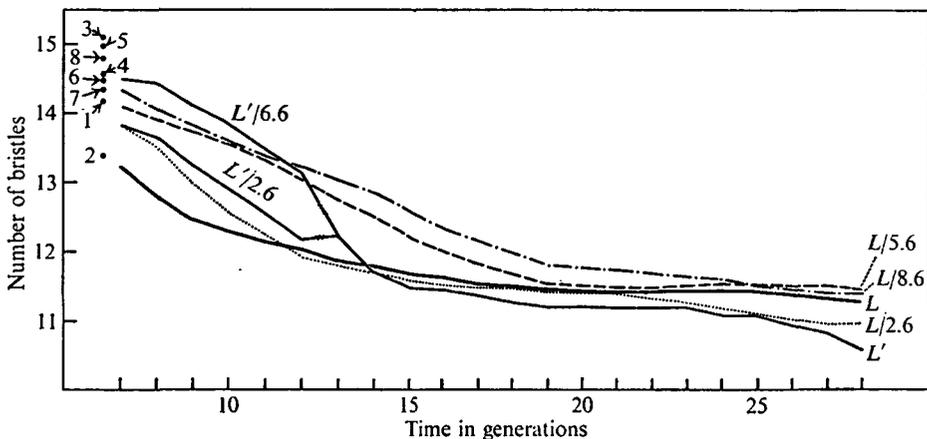


Fig. 3. The large lines derived from crosses between the small lines at the sixth generation, compared to line L .

The repeated cycle structure

The means of the lines in the repeated cycle structure are shown in Fig. 5 where, because of the short period of sub-division, 3-generation running averages are plotted. The lines connecting the groups of replicates in different cycles give the average during the period necessary to complete the crossing. After the sub-division at the start of the second cycle, the replicates spread out rapidly and two were clearly below L . The best five were crossed again at generation 15 using a similar procedure to that at generation 6 and here a rapid response was observed to the selection practised during crossing, presumably because of the considerable variation between the parental lines. When the new set of small lines, R_2 , were formed, the mean performance was well below L and below the level of the best two replicates in the previous cycle. However response to selection within lines was small during this cycle and four, which had responded in the wrong direction, were discontinued after 3 generations. The remainder were crossed for generations 25 and

26 and two further generations of mass selection were carried out. There was again selection response during crossing and the final average at generation 28 (when the line was still responding) was about 10 bristles, much lower than the mean of L and practically the same as $L/5.12$. The lethal with a large effect on bristle score in the heterozygote was also found in this line.

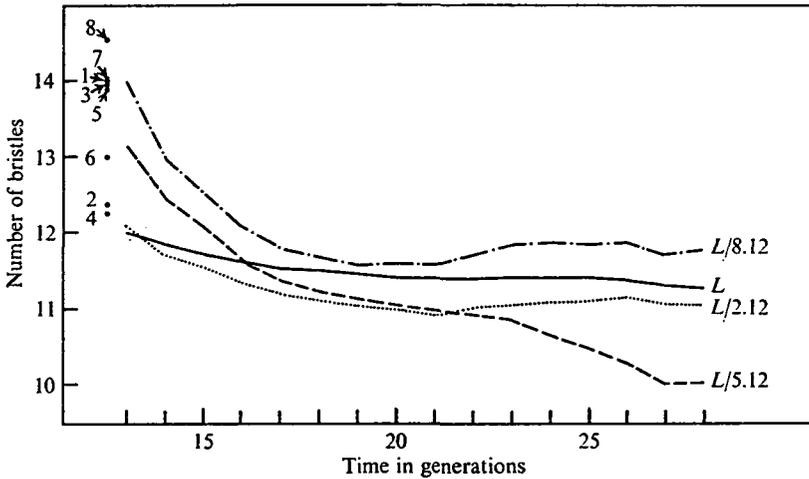


Fig. 4. The large lines derived from crosses between the small lines at the twelfth generation, compared to line L .

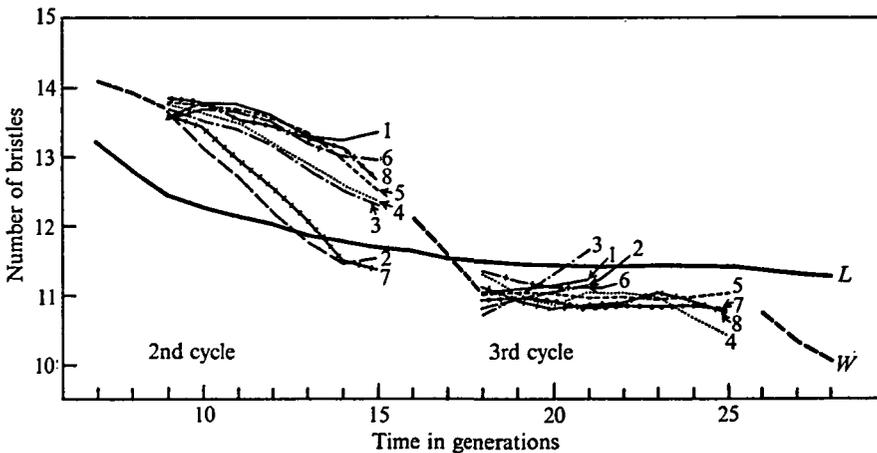


Fig. 5. The lines in the repeated cycle experiment, compared to line L .

The effects of relaxed and reversed selection

Selection was relaxed in several of the lines after nine generations of selection. The lines were then kept in bottles with a large number of parents in each generation so that the level of crowding would be fairly high. This was done with all of the first cycle small lines and the lines L , $L/2.6$, $L/5.6$, $L/8.6$. The results were con-

sistent over lines in showing little change of the mean after relaxation for eight generations. In two lines, 3 and 5, on relaxation the mean changed in the direction of original selection. These effects were apparently real and the change was maintained in subsequent generations of relaxation. The only line which showed any consistent return to the level of the base population was the line *L* which was subsequently found to contain the main lethal. On the average, the return in *L* after eight generations was 1.3 bristles, about one-quarter of the previous response. Rather surprisingly, line 2, which also carried this lethal at the end of the experiment, did not return on relaxation at generation 9, perhaps an indication that the lethal had not by then reached a high frequency.

The effect of reversed selection was more striking. This was carried out for a single generation at generations 16, 17 and 18 for the small first cycle lines with the same intensity as the forward selection. For the larger lines, very intense backward selection, 5/200, was carried out for a single generation followed by several further generations with intensity 5/25. The small first cycle lines did not show a consistent picture. For six of them, there was essentially no effect, suggesting that the genetic variance had almost been exhausted. Line 7 showed a consistent return on reverse selection, averaging 0.65 bristles in the first generation, but this was not repeated at generation 21. A consistent return was found in line 2 and line *L* in which the main lethal was present. The return over the first 3 generations averaged 1.3 bristles in line 2 and 1.82 bristles in line *L*.

The other large lines were reverse-selected at generation 20, again with very intense selection in the first generation followed by 5/25 for a further 3 generations. For the single 3rd cycle replicates, reverse selection for 3 generations with intensity 5/25 was practised from generation 22. All these lines responded to reverse selection – those containing the lethal showed a large effect in the first generation and subsequent changes were small. But the results were not consistent over lines. For instance the lines formed by crossing at generation 12 showed an average return at the 4th generation of over 3 bristles whereas in the single replicates deriving from *W* the effect was only a little over 1 bristle. The general picture then is of an immediate response to reverse selection due to the effect of the main lethal followed by smaller changes due to other loci affecting the character.

The analysis of the lethals

A lethal analysis was carried out in all lines between generations 22 and 24, using the marked autosomes SM1 for the second and *Ubx*¹³⁰ for the third chromosome. No lethals were found on the third chromosome. Selection in the large lines had then been reduced to 10/50, that in the small lines remaining at 5/25. The selected male parents were recovered and 4 second chromosomes sampled from each. The chance of a lethal carried by only one of the males not being detected is then around 1/16. Tests for allelism between lethal chromosomes were carried out, first within lines and then across lines. When the general situation had become clear, a more precise test was carried out to estimate the frequencies of the lethals in each line. 28 pairs of unselected progeny were scored in each line in generation 28

and each was classified as homozygous non-lethal or heterozygous for the lethals already detected in that line, by testing 4 chromosomes from each scored individual.

The resultant estimates of gene frequency in any line have a standard error around 0.04. This test also allows an estimate of the effect of the lethal on bristle score in the heterozygote to be obtained. The four lethals have all been mapped and their locations, which have a standard error of 2 map units, as well as their frequencies in the separate lines, are given in Table 2. It will be seen that they cover a total length of only one third of the chromosome.

Table 2. *The analysis of the lethals*

	Lethal			
	1	2	3	4
Position on second chromosome	78	73	95	66
Found in	<i>L</i> , 2, <i>L</i> /2.6, <i>L</i> /2.12, <i>L</i> /5.12, <i>L</i> /8.12, <i>L'</i> , <i>W</i>	<i>L'</i>	<i>L</i> /2.12 <i>L</i> /8.12	<i>L</i> /8.6
Mean frequency in above lines	0.33	0.32	0.16	0.22
Effect in heterozygote				
♂	-1.36 ± 0.15	-0.48 ± 0.35	0.21 ± 0.35	—
♀	-2.27 ± 0.20	-0.75 ± 0.50	0.06 ± 0.39	-0.30 ± 0.38

The overall frequency of l_1 , in all the lines in which it was observed, was very close to one-third which would be expected if all selected parents were heterozygotes. l_2 also had a frequency approaching this in the only line in which it appeared and the remaining two had lower frequencies. The lethal l_2 was detected in lines *L*/8.6 and *L*/5.12 in the preliminary analysis at generation 22 but was not found in individuals from the same lines in the more detailed analysis at generation 28. It was also possible to score chromosomes for the simultaneous presence of two lethals. In all cases the number of chromosomes containing both lethals was less than expected from the separate frequencies. The base population was screened for the presence of these lethals using a sample of approximately 100 chromosomes in each case, but none were found.

The test at generation 28 was designed to measure the effect of the lethals on bristle score, and the results are presented in Table 2. The standard error for the estimate of the effect of l_1 was of course smaller than that of the other lethals because it was present in more lines. At this level of bristle score, the residual standard deviation within genotypes is approximately 1 bristle. It will be seen that no significant effects were found for l_3 and l_4 . l_2 had an average effect of 0.6 bristles which was just significant at the 5% level whereas the main lethal l_1 reduced score in the heterozygote by 1.8. In both cases in which significance was found, the effects were greater in females as in males.

The finding of several lethals in the same region of the second chromosome in different lines is not as surprising as it might seem. In any chromosome which is transmitted from generation to generation only in heterozygotes and in which there is no crossing-over, there is no selection against recessive lethals either in the chromosome itself or in its homologue. In the present situation, all parents are heterozygotes for the main lethal, l_1 . There will then be no selection against any recessive lethal very closely linked to l_1 . Apart from genetic drift, the gene frequency at equilibrium will depend only on the effect of natural and artificial selection in heterozygotes. If there is crossing-over between the two lethals, this will tend to reduce the frequency of the second lethal. If the second lethal has any effect on the character under selection, the equilibrium frequency will be much higher in the presence of the main lethal than if the second lethal was present by itself. This would then explain

(i) the presence of lethals l_3 and l_4 at reasonable frequencies but with no effect on bristles;

(ii) the presence of l_2 in L' at a higher frequency than would be expected from its effect on bristles. Chromosomes carrying both l_1 and l_2 produced by a crossover would be at a disadvantage and were in fact never found;

(iii) the loss of l_2 from $L/8.6$ and $L/5.12$ between the critical and final analysis. Over this period, the number of parents in the large lines had been reduced from 80 to 20 and the lethal may have been lost due to sampling.

4. DISCUSSION

Before discussing responses to selection, one finding is particularly important, the presence of the lethal affecting bristle score in the heterozygote.

Such a lethal complicates the interpretation in several ways, the most important of which is perhaps the lack of generality of the results, though this is also true for any rare gene with a large effect on the selected character. Since, at equilibrium, with all selected flies heterozygotes for the lethal, two-thirds of the surviving progeny will also be heterozygotes, the expected contribution to the observed change due to selection will be about 1.2 bristles. There will however be two ways in which the response at other loci may be reduced. While the lethal is increasing rapidly in frequency, the effective population size may well be small with a consequent reduction in the genetic variance. After reaching the state in which all selected parents are lethal heterozygotes, the non-lethal homozygotes are effectively excluded from the selection process so that the effective proportion selected, with respect to other loci, is increased by one half and the effective intensity of selection correspondingly reduced.

We should, however, discuss an alternative hypothesis – that the response in bristle score is due to a gene closely linked to the lethal. This argument becomes in the long run academic but we should at least consider whether the results suggest linkage of such closeness that the combination of lethal gene and bristle gene has a reasonable chance of breaking up within the time scale of the experi-

ment. Put more precisely, the hypothesis is that there is a rare gene in the population which reduces bristles in the heterozygote and which is associated with a closely linked lethal. From initial samples of flies in which all chromosomes carrying the bristle gene also carry the lethal, selection will lead to a balanced state with high variability. Note, however, that there would not be a higher response in this than in other replicates since now the lethal is reducing response by preventing the bristle gene being fixed. The production by recombination of chromosomes carrying the bristle gene but lacking the lethal would lead to a period of response after which the phenotypic variance would fall. In selection following a cross between a line containing the lethal complex and one homozygous for the bristle gene, the lethal would subsequently be lost. None of our observations point in the direction of this hypothesis. Of the small lines, that which made the greatest response was the one in which the lethal was segregating at the end of selection. Of large lines formed after crossing of lines containing the lethal, in five cases out of seven the lethal was still segregating at the end and those in which it was not segregating showed the least advance at the limit. Thus we have no evidence that, within the time scale of our experiments, the bristle effect ever separated from the lethal effect.

A little is known theoretically about the expectations from this kind of breeding programme. Robertson (1960) showed that, with additive gene action, if a set of lines were crossed at fixation and subsequently selected with the same overall population size, the expected advance at the limit is equal to that obtained by selecting from the base population with the same selection intensity and the larger population size. Maruyama (1969) showed that this equality of expectations also held whatever the time at which the cross was made. Thus we should expect that with additive gene action the $L/8.6$ and $L/8.12$ lines would have the same limit as L itself.

Since these experiments were started, theoretical and simulation studies carried out in this laboratory have given some further indications of theoretical expectations (Madalena & Hill, 1972). The results may be summarized briefly as follows:

(i) With additive gene action, though the expected response with a given selection intensity is higher at any time for large lines, the existence of variance in response between small lines may mean that the best of a set of small lines may exceed that of the large line for a brief period, which in our case might be expected to occur around the third or fourth generation. At the limit the large line should be expected to exceed the best of the small lines.

(ii) With additive gene action, selection between small lines followed by crossing, as in the single cycle structure, always reduces the average advance at the limit, though it may lead to an increased gain at intermediate generations. The more intense the selection between lines the greater the reduction at the limit.

(iii) These effects are greatest for loci segregating independently and are reduced as linkage between loci is tightened.

(iv) In a repeated cycle structure, selection between lines always reduces the advance at the limit. With no selection between lines, the same limit is reached as with the large line but very much more slowly.

(v) In selection for low frequency recessives or for high frequency dominants, the response in the early generations is much higher in small than in large lines. At the limit after crossing, the response is usually greater for lines whose initial history had been as a group of small lines, irrespective of the amount of selection between lines. The effect of linkage is not clear cut.

The selection advances at the limit are summarized in Fig. 6 in which those lines carrying the main lethal are indicated. Various points are of interest. The average advance at the limit of the lines selected with an intensity of 5/25 is in fact less than the average of other lines selected in this laboratory from the same population with an intensity of 10/25. It has been shown theoretically that, if

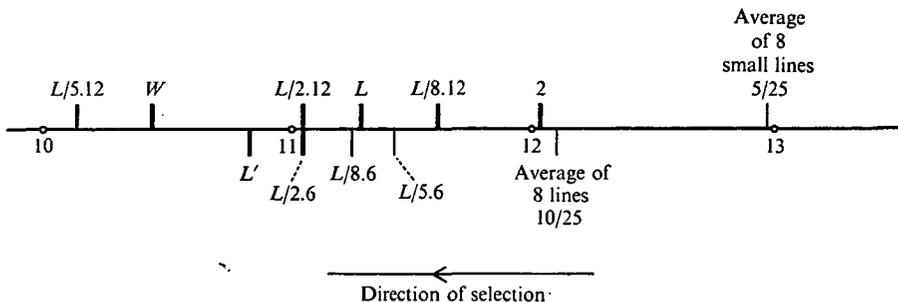


Fig. 6. The scores of the different lines at the end of selection. The point '10/25' gives the mean of 8 lines selected 10/25 from the same population. Lines indicated by a heavy stroke carried the main lethal.

selection is from a given total number of individuals measured, then for independently segregating genes the largest advance at the limit will be obtained from a proportion selected of 50% and that linkage will slightly increase this proportion. Here we have a clear instance in which the more intense selection leads to a lower response at the limit. As would be expected the large line, *L*, shows a greater advance at the limit than do the small lines though a proportion of the increase is presumably due to the effect of the main lethal. The half-life of the selection response of 5.3 generations in this line was surprisingly low, perhaps because genes with large effects were involved.

The interpretation of the responses in the other lines is somewhat complicated by the absence of replication, unavoidable in an experiment in which the lines are so large. The large lines derived from crossing at the 6th generation were very similar in response to one another. Only one of these, *L*/2.6, contained the main lethal. There was much more variation between the lines obtained from the crosses at the 12th generation, those involving selection between lines showing a greater response than that obtained from the amalgamation of all the small lines (*L*/8.12). All the lines produced from crosses at the 12th generation carried the main lethal, whereas it had been lost from two of the similar lines from the 6th generation. This might suggest that between generations 6 and 12 the effect of the lethal on bristle score had been increased by selection on the heterozygote in small line 2

causing the accumulation of modifiers. If the lethal had such a large effect on bristle score from the start, one would expect that the gene frequency would rapidly reach the limiting value of one-third, after which the line would have a high variance. The evidence would suggest that this was not so in line 2 when it was crossed at generation 6. Its variance was then not high though it increased rapidly in the next few generations. $L/2.6$, in which the lethal was subsequently found, had a high variance in the generations immediately after crossing – $L/5.6$ and $L/8.6$, which did not contain it, both had a low variance. A possible explanation would then involve the accumulation of modifiers interacting with the lethal to decrease score in the heterozygote but not in the non-lethal homozygote. However, our analysis of the effect of the main lethal on bristle score produced no evidence that the effect was not the same in all selected lines in which it occurred, nor that it was changed by the simultaneous presence of the other lethals. It seems unlikely that the lethal was a new mutation during selection because of its independent occurrence in L and in small line 2.

The existence of recessive lethal genes in a balanced state in lines selected in *Drosophila* populations is now commonplace (Robertson & Reeve, 1952; Clayton & Robertson, 1957; Frankham *et al.* 1968; Hollingdale, 1971). Some of the problems arising are well discussed by Hollingdale. Unfortunately none of these investigations are complete in the sense that one would ideally like to know the location of the lethal and its effect on fitness and on the character under selection, not only in the selected line but also in the unselected population. In none of the above instances, including the present, has the lethal been found in the unselected population. This is not surprising since most recessive lethals will be present at low frequencies and for a limited period of time. It is possible that some lethals may reach high frequencies in finite selected populations due to close linkage with a rare allele affecting the selected character. They might then be expected to appear only transiently in the selected line, as Hollingdale has found. In the present case, there can be no doubt as to the effect of the main lethal, l_1 , on bristle score in the selected lines and that this is probably not due to linkage. But the possibility remains that the effect has been much increased by the accumulation of specific modifiers during selection.

The three lines with the largest response had quite different histories. $L/5.12$, with a final score close to 10 bristles, responded rapidly to selection after crossing and exceeded L at the 16th generation. After a period of slow response the variance increased around the 20th generation, followed by further rapid response. Line W came from an amalgamation of the lines in the repeated cycle structure. During the crossing phase after generation 15, there was a rapid response and all 8 lines were then below L . For the rest of the 3rd cycle there was little further response but after the third crossing there was again a rapid response. The third line in order of advance was the 'hybrid' line in which, after crossing at the 6th generation, most of the effort (a selection intensity of 30/150) was concentrated on the cross coming from the best two small lines while the remainder of the facilities were devoted with a selection intensity of 10/50 applied to a mixture of the remaining

6 lines. This was followed by a process of back crossing the best individuals from the second section into the first between the 12th and 15th generations. L' was then below L at the 15th generation and remained below it for the remaining 13 generations of selection.

The results of this experimental investigation are in general agreement with the theory in suggesting that selection within sub-lines in the course of a selection experiment will not necessarily lead to an increase in the advance at the limit when the gene action is mostly additive. On the whole, the response to between-line selection was somewhat greater than would have been expected on the basis of additive genetic theory, which predicts that the overall response will always be reduced. Both for crossing at the 6th and at the 12th generation, the line deriving from a cross of the best two small lines made a greater advance than that obtained by combining all the lines together. Also the line coming from the repeated cycle selection experiment had the second largest response of all the lines. Although gene action in this character is known to be mainly additive, some recessive genes have been detected and this is a possible cause of the phenomena.

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