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The effect of suppressing crossing-over on the response to selection in *Drosophila melanogaster*

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SUMMARY

A selection experiment for sternopleural bristles in *Drosophila melanogaster* was undertaken to measure the effect of suppressing crossing-over on chromosomes II and III using the inversions Curly and Moiré marked with a dominant gene, which severely reduce crossing-over. In one set of lines selected wild-type males were mated to selected females, heterozygous for *Cy* and *Mé*, and in a parallel set selected males carrying the inversions were mated to selected wild-type females. Because there is no crossing-over in the males in this species, crossing-over is much reduced in the first set and is at its usual level in the second. The effect of the selection was measured on flies which did not carry the inversions. The suppression of crossing-over reduced the advance at the limit by $28 \pm 8\%$ for selection upwards and by $22 \pm 7\%$ for selection downwards. The segregation ratios of the inversions were observed throughout the experiment. At the end, the proportion of wild-type flies emerging was not different in the two sets of lines. The results are consistent with an assumption of initial linkage equilibrium between loci affecting sternopleural bristles in the base population.

1. INTRODUCTION

Although linkage has quite justifiably been used to explain some aspects of selection experiments for quantitative characters, such as a sudden response to selection after a period of quiescence, there is little direct evidence as to the effect on selection response of altering the amount of crossing-over in experiments designed specifically for the purpose. At the same time, existing theories of quantitative selection have been unable to deal with linkage and have had to assume independent segregation of loci affecting the character under selection. In recent years, this gap has been to some extent filled, at least under conditions of initial linkage equilibrium between the loci concerned (Latter, 1966; Hill & Robertson, 1966; Robertson, 1970). Mather (1943) has emphasized the importance of linkage in artificial selection and has suggested that natural selection for an intermediate optimum will cause linkage disequilibrium in such a way as to reduce the amount of genetic variation immediately responsive to selection.

In the present paper we shall present evidence on the response to selection for

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sternopleural bristles under normal conditions of crossing-over and when crossing-over is almost completely suppressed on the two large autosomes in *Drosophila melanogaster*. Other factors which may affect the outcome are balanced as far as is possible. In the interpretation of the results we shall then be mainly concerned with the comparison of the observed effects with those expected theoretically on the assumption of linkage equilibrium.

2. MATERIAL AND METHODS

(i) *The experimental design*

The essential aspect of the design, which is illustrated in Fig. 1, is that there are two sets of lines identical in genetic make-up and selection procedure, except that in one set there is the normal amount of crossing-over whereas in the other recombination is almost completely suppressed. This is achieved by the use of chromosomes carrying both a dominant marker and an inversion which suppresses crossing-over in the female. All marked chromosomes of a particular type descend from one individual chromosome and therefore do not contribute to the genetic

'Suppressed' lines		'Normal' lines	
$\male\male$	$\female\female$	$\male\male$	$\female\female$
$+/+,\ +/+$	$\times\ Cy/+,\ Mé/+$	$Cy/+,\ Mé/+$	$\times\ +/+,\ +/+$
$+/+,\ +/+$	$\times\ Cy/+,\ Mé/+$	$Cy/+,\ Mé/+$	$\times\ +/+,\ +/+$

Fig. 1. The parental genotypes in the two sets of lines. The ten most extreme $\male$ and $\female$ for sternopleural bristle score were selected each generation from 25 measured in each sex. The responses to selection given in Figs. 2–5 are the means of wild-type male and female progeny.

variation between individuals. In each replicate the wild-type chromosomes are a random sample from a standard random-breeding population. In the 'normal' lines, in which the male parents carry the two marker chromosomes and the females are wild type, there will be the usual amount of crossing-over in females. In the 'suppressed' lines, in which the male parents are wild type and the females carry the marked chromosomes, there will be as usual no crossing-over in males, but in females the crossing-over on the two main autosomes, which make up some 80 % of the total map length in this species, will be considerably reduced. There may be some increase in crossing-over on the X chromosome in the 'suppressed' lines, a known effect of multiple inversion heterozygosity on the autosomes (Schultz & Redfield, 1951).

The marker chromosomes used were taken from stocks available in this laboratory. The Cy second chromosome has inversions on both arms and contains the recessive gene *purple* between the two. The $Mé$ third chromosome also has inversions in both arms and contains the recessive gene *claret* at the extreme right end. Some preliminary experiments were done with the well-known Ubx^{130} third chromosome, which proved unsuitable. It was difficult to identify the marker gene in lines

with a low bristle mean, and the inversion proved of little value in suppressing crossing-over in the presence of the Cy chromosome (see MacIntyre & Wright, 1966). All wild-type chromosomes were taken from our standard Kaduna population, which has been kept in population cages here for some 20 years.

Selection was carried out for number of sternopleural bristles in bottle cultures at 25 °C, and the 10 extreme flies out of 25 measured in each sex were selected each generation. As four different genotypes emerge every generation, periodical observations were made of segregation ratios and of the bristle scores in the four types. The experiment was carried out in two phases. The first, by A. R., involved selection downwards with five replicates in each set for 20 generations. In the second, by C. P. M., selection was in both up and down directions, again with five replicates in each set, for 17 generations.

(ii) *The problem of scale*

Before presenting the results, some consideration must be given to the problem of scale. In any experiment involving considerable changes due to selection, perhaps in opposite directions, it is important that comparisons are made on the most

Table 1. *The mean bristles scores of males having 'high' and 'low' X chromosomes in different backgrounds*

(The figures in the last column have a standard error of 0·03.)

Autosomal background	Source of X chromosome		Difference	
	High	Low	Absolute	Log $(S-4)$
A	9·49	7·75	1·74	0·381
B	13·34	10·84	2·50	0·312
C	22·72	16·36	6·36	0·415
D	34·87	24·84	10·03	0·393
E	47·80	32·80	15·00	0·419

suitable scale. As theoretical discussions tend to be in terms of changes of gene frequency, the most suitable metric would be a linear one with respect to gene frequency, a condition difficult to satisfy directly. We may substitute an alternative one at the chromosome level—a satisfactory scale is one on which the effect of a given chromosomal substitution is independent of the position on the scale. We cannot here give full justification for the proposed metric, log $(S-4)$, where S is the mean sternopleural bristle score, but Table 1, taken in part from the work of Dr J. H. Louw, is given in illustration of its validity. It gives the mean scores of two groups of males, having 'low' and 'high' X chromosomes respectively, in a series of autosomal backgrounds taken in part from high and low lines. In A, the lowest background, the effect of the X chromosome substitution is 1·74 bristles whereas in the highest, E, it is 15. However, the transformed measurements show that on the scale of log $(S-4)$, the effect is almost independent of the background.

3. RESULTS

(i) *The response to selection*

The mean bristle score of wild-type individuals of both sexes is given in Figs. 2–5. In the first experiment selection was carried out downwards for 20 generations, by which time all lines had ceased to respond. No points are given before the 5th generation as only from then were wild-type flies scored of the sex not required for
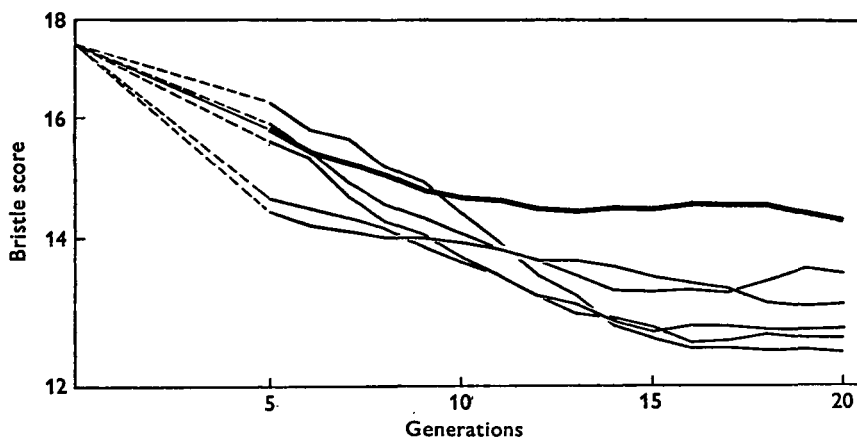

Fig. 2. Five-generation moving average score in the 'normal' lines in the first experiment. The heavy line gives the mean of all 'suppressed' lines.
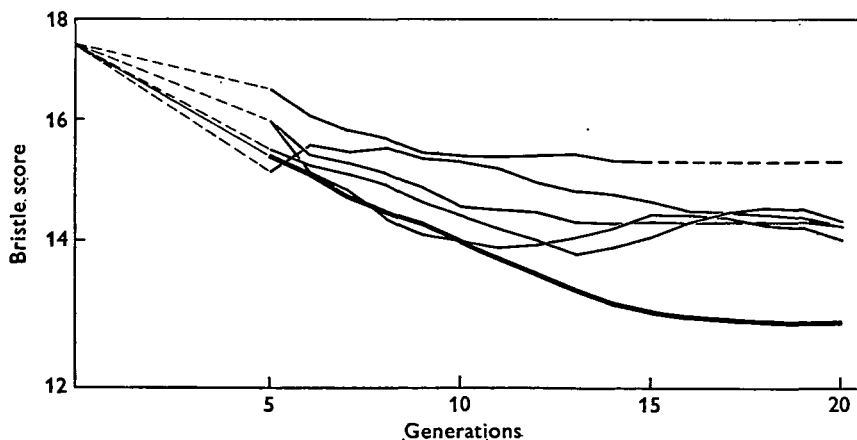

Fig. 3. Five-generation moving average score of the 'suppressed' lines in the first experiment. The heavy line gives the mean of all 'normal' lines.

selection. To reduce confusion from criss-crossing of lines, we have plotted the moving averages over five generations. The scale of log (bristle score − 4) has been used in the figures.

In interpreting the results we must take into account particular occurrences in some lines. In one of the suppressed set in the first experiment, for instance, flies

homozygous for the mutant *claret*, which is in the *Mé* chromosome, were first seen in the 15th generation (after the line had apparently reached its limit of selection), and after this they continued to appear although none were selected as parents. At the same time the line began to respond to selection again. We propose to include this line in the overall means after the 15th generation with the score it then had.
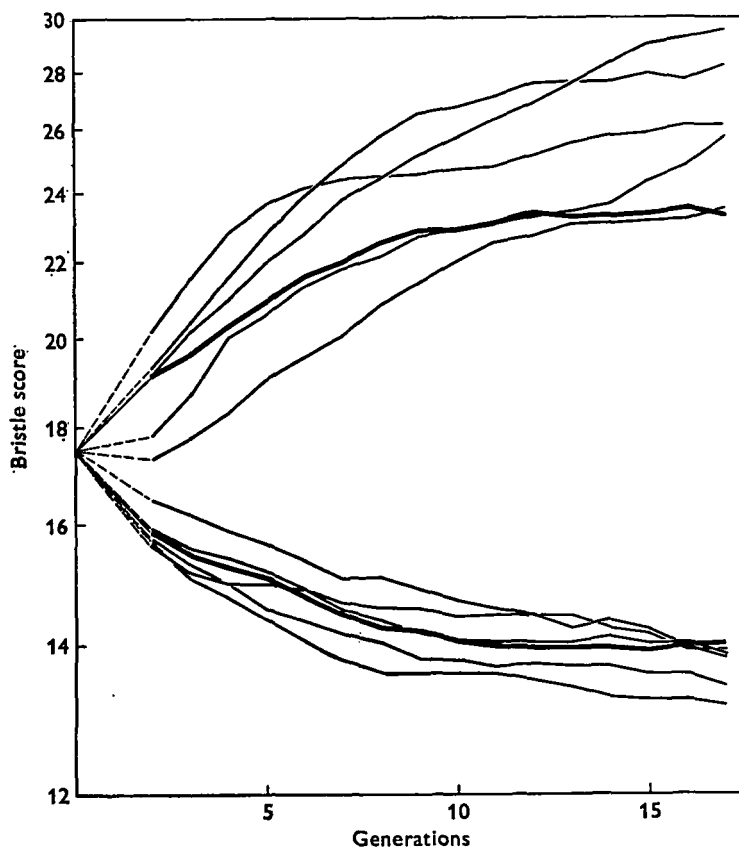

Fig. 4. Five-generation moving average score of the 'normal' lines in the second experiment. The heavy lines give the mean of all 'suppressed' lines in a given direction of selection.

In the second experiment, in which selection ceased at the 17th generation, one of the high suppressed lines was unfortunately lost at the 12th generation, but, again, as it had responded little to selection in the last three generations we propose to include it as though it had reached its final limit.

As, in the early generations, selection operates on the existing variation in the population, it is to be expected that the initial response will be the same in the two sets, and this is seen to be so. However, the subsequent effect of crossing-over on response is not large. In the first experiment, in which there was only downward selection, the sets overlapped until the 11th generation. In the second the sets overlapped even at the end in both directions. There was considerable variation

between replicates, the coefficient of variation of advance at the limit being 20 % downwards and 22 % upwards. From the graphs, it seems probable that some of the 'normal' lines being selected upwards were still responding when selection ceased.
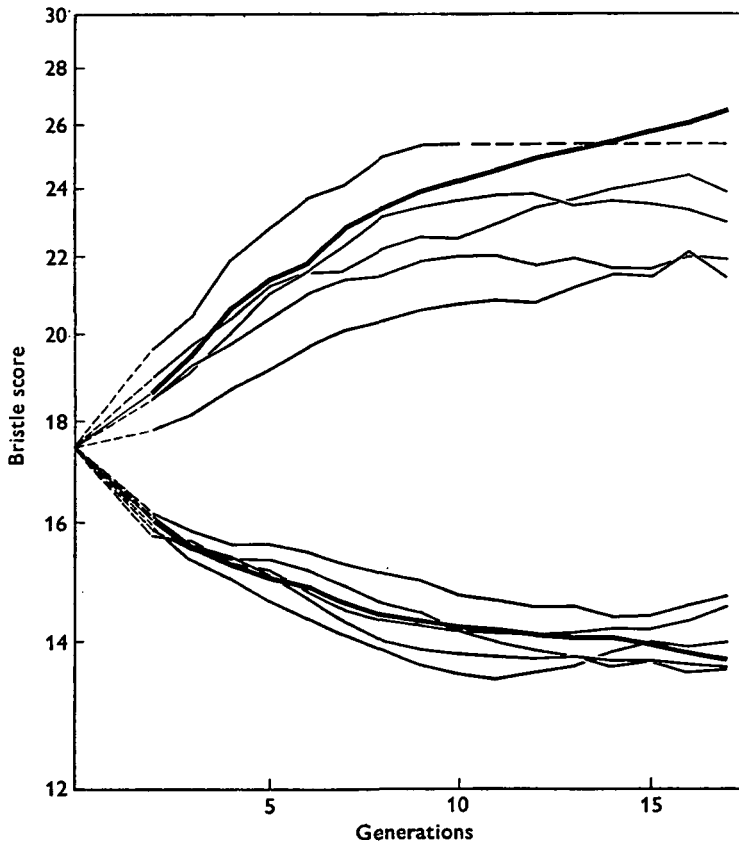

Fig. 5. Five-generation moving average score of the 'suppressed' lines in the second experiment. The heavy lines give the mean of all 'normal' lines in a given direction of selection.

(ii) *The efficiency of the cross-over suppression*

Both the *Cy* and *Mé* chromosomes contain inversions in both arms. The former contains the mutant *pr* between the two inversions and the latter the mutant *ca* at the extreme right end. Crossing-over was measured using the 'all-*Bl*' stock for the second chromosome and a '*rucuca*' stock, from which the *ca* had been removed, for the third (Lindsley & Grell, 1967, p. 413). The double heterozygote females containing both *Cy* and *Mé* chromosomes as well as one of the two chromosomes marked with recessives were mated to the corresponding homozygous recessive stock and cross-overs scored. The gene *pr* is in the 'all' stock, so that it could not be used. The results are summarized in Table 2. The *Mé* chromosome with only one cross-over, at the left end, suppresses recombination very efficiently. The *Cy* chromosome is less satisfactory. Two per cent of chromosomes contain cross-overs,

and of these nine are single, with interchange of whole arms, and three are double with interchange of genes in the section between the inversions. More important, as we shall see later, 1 % of the *Cy* chromosomes have lost the inversion from the right arm with a consequent loss of efficiency in cross-over suppression in subsequent generations.

The effect of inversion heterozygosis of the autosomes on the crossing-over on the *X* chromosome was investigated using the multiple recessive stock *scar*. Crossing-over was increased but not greatly. There was an average of 0·71 cross-overs in each *X* chromosome derived from females heterozygous for *Cy* and *Mé*, compared to 0·66 in their absence. The increase only reached statistical significance for the extreme right end of the chromosome where it was around 70 %.

Table 2. *Cross-overs in segregation from* Cy Mé *double heterozygotes, tested against*
al dp b pr Bl c px sp *and* ru h th st cu sr e, *respectively*

(The *Mé* chromosome contains the gene *ca* to the right of *e*.)

	Chromosome	
	II	III
Non-crossovers	416	604
Cross-overs	4 *Cy b-sp*	1 *ru Mé ca*
	2 *al-Bl px sp*	
	1 *al-pr c-sp*	
	2 *al-pr*	
Total	425	605

There are two kinds of internal checks on the efficiency of the cross-over suppressors. The first is provided by the recessive markers which they contain. These were looked at in the second experiment. It was found that the mutant *pr* had been lost from all *Cy* chromosomes in the third replicate of the high suppressed line. On the other hand, the mutant *ca* was found to be present in all the *Mé* chromosomes in all lines.

Information of a different kind comes from the bristle scores of individuals carrying the marker chromosomes *Cy* and *Mé*. Both these chromosomes reduce bristle score slightly on substitution into the unselected population. As, in the second experiment, all four genotypes were scored in every generation, the effect of substituting a wild-type chromosome for a marker chromosome in the selected line could be followed continuously. This might be expected to go up in high lines and down in low. The trends of the substitutions of the marked third chromosomes were in agreement with expectation, but there were discrepancies in the effect of the marked second chromosomes in the suppressed high lines. There the effect of the substitution increased up to generation 10 (though not so much as in the 'normal' lines) but then declined so that at the 17th generation it had become negative. This would happen if there had been crossing-over in the second chromosome and genes from the selected wild-type chromosomes had been substituted into the marked one. Examination of the replicates separately showed that the effect of the

substitution had declined in three of them and not in the other two. The marker chromosome initially contained inversions in both arms, the *Cy* phenotype being associated with that in the left. These results would suggest that in some of the high suppressed lines the complete right arm of the second marked chromosome had been lost by crossing-over. The effect of this on the selection limit is difficult to predict.

The effect of selection on the marker chromosomes themselves was measured by substituting them into a standard inbred background. For this, the extreme low line, DF, selected from the base population (A in Table 1), was used and the results for the second experiment are summarized in Table 3. As the chromosomes in the 'normal' lines have been kept entirely in males, the results from these can be taken as referring to the chromosomes at the start of the selection experiment. It will be

Table 3. *The mean absolute bristle score of marker chromosome heterozygotes on substitution into the homozygous tester line DF at the end of selection in the second experiment*

(Each mean has a standard error of 0·14.)

	Marker chromosome	
Selection regime	*Cy*	*Mé*
Low normal	8·46	9·84
Low suppressed	8·36	9·89
High normal	8·14	9·94
High suppressed	8·89	9·87

remembered that, apart from mutation, all marker chromosomes are genetically identical, so that if they are kept in males, they cannot be modified by selection. There is no evidence that the marker third chromosome has been affected. However, the second chromosome in the 'suppressed' high lines gives a significantly higher bristle score than that from the other three sets. This is in agreement with the other evidence that in these lines some high bristle genes had been inserted into the marked second chromosome. It is quite possible that crossing-over on the second chromosome would only be important in the high lines. The *Cy* chromosome reduces bristle score in the initial population and, if this effect is due to genes on the right arm, chromosomes which have lost this arm will have no advantage in selection downwards. Unfortunately all the lines had been discarded before it was realized that an examination of the salivary chromosomes would have been informative.

(iii) *Viability in the selected lines*

The segregation ratios of the marker chromosomes were recorded at various times during selection. In the first experiment 100 females were examined from each of the selected lines from generations 10–14, as well as in the initial population. In the second, 125 males and females were examined at generations 0, 7 and 8, and 16 and 17. The results were expressed as the viabilities of the wild-type individuals compared to heterozygotes for the marker chromosome. The results for the final generations as well as for the base population are presented schematically in

Figs. 6–8. In the first experiment the relative viabilities of the wild-type individuals have declined in both sets of lines. The one notable exception is the second replicate in the 'normal' set which had a ratio of wild-type to *Mé* chromosomes of 2·7:1. Leaving this aberrant line out of account, there is no clear difference between the two sets.
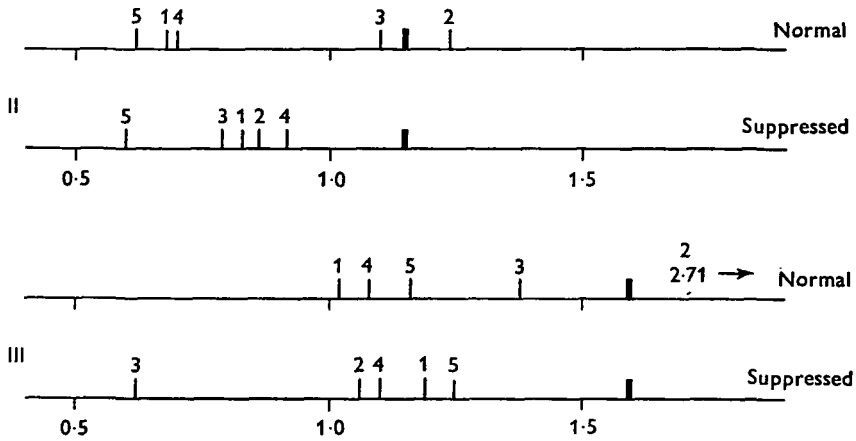

Fig. 6. Relative viabilities measured by the ratio of numbers of wild-type flies to marker heterozygotes for the second and third chromosomes in generations 10–14 in the first experiment. The heavy lines give the value at the start of selection, the separate replicates are labelled 1–5.
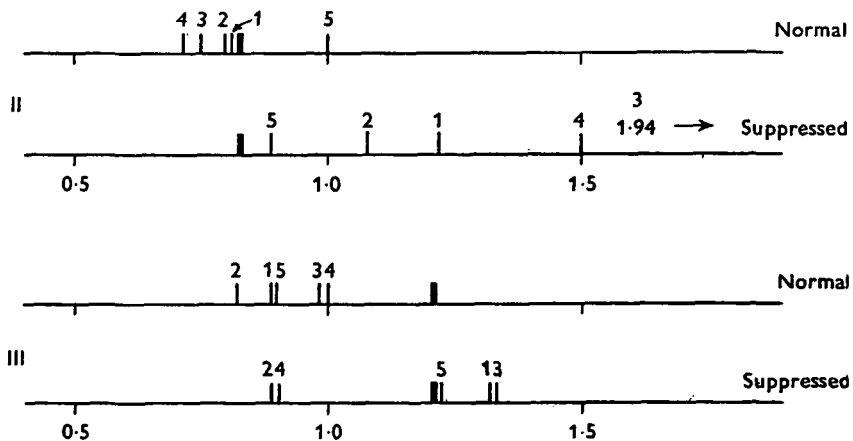

Fig. 7. Relative viabilities measured by the ratio of numbers of wild-type flies to marker heterozygotes in the low lines at generations 16 and 17 of the second experiment. The heavy lines give the values at the start of selection, the separate replicates are labelled 1–5.

In the second experiment selection has had little overall effect on the relative viability of wild-type individuals in either set of lines. There is again an aberrant line showing a very high proportion of flies with two wild-type second chromosomes. There has been some decrease in the relative viabilities on the third chromosome, but, this has not been greater in the 'suppressed' than in the 'normal' lines.

The consequences of the selection for bristles leading to homozygosity can be predicted to some extent on the assumption that any recessive lethals have no effect on bristle score in the heterozygote. The viability of wild-type flies will decline as sections of the chromosomes become homozygous because of selection for the bristle genes they contain. Temin (1966) has shown that, in a wild population of *D. melanogaster*, two-thirds of the reduction in viability of 0·40 caused by making second chromosomes homozygous is due to lethal homozygotes. Concentrating on this class, tests on our base population show about 20 % of second chromosomes and 30 % of third chromosomes are lethal when homozygous. In the 'normal' lines there would be an opportunity for the genes affecting bristles to become separated
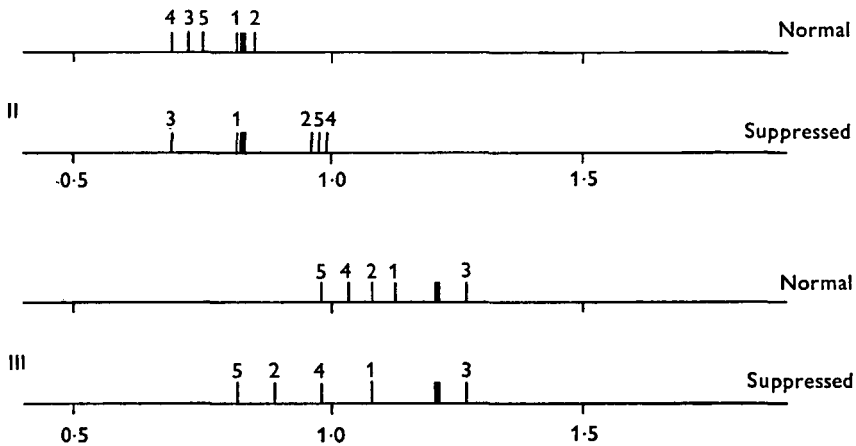

Fig. 8. Relative viabilities measured by the ratio of numbers of wild-type flies to marker heterozygotes on the second and third chromosomes in the high lines at generations 16 and 17 in the second experiment. The heavy lines give the values at the start of selection, the separate replicates are labelled 1–5.

from those affecting viability, with a consequent increase in both bristle score and fitness. If, in a 'suppressed' line, chromosomes carrying lethals are selected because they also contain genes affecting bristles, the viability index would be reduced. However, the average effect should not be large. If the best chromosome for bristle genes in a suppressed line contained a lethal, it would remain balanced against the second best, which might or might not itself contain a different lethal. On the third chromosome the *a priori* probability of a lethal/non-lethal balance is 0·21 with a consequent loss in viability of wild-type flies of 0·25. The probability of both chromosomes carrying lethals is 0·09 with an expected loss in viability of 0·50. Thus the overall expected loss in viability in the suppressed lines due to a balance of lethal genes in selected chromosomes is of the order of 10 %. If we assume a frequency of lethal genes on the second chromosome of 20 %, the expected loss in viability is 6 %.

(iv) *The effect of selection on the* X *and fourth chromosomes*

As there is other evidence from extreme selected lines that genes affecting this character were present in the base population on both the first and fourth chromosomes, the contributions to the selection response from these chromosomes were measured in the different lines. The marked second and third chromosomes were used to cross the first and fourth chromosomes into the DF low line, which contains a fourth chromosome with a recessive effect on bristle score. There proved to have been no selection response on the fourth chromosome. This is perhaps not surprising as the fourth chromosome in the DF line is the only one we know to have an effect on bristles. X chromosomes from the low lines gave a significantly lower bristle score in males than those from either the unselected population or the high lines, though the difference was small (0.36 ± 0.07 bristles). Within directions of selection, the difference between X chromosomes from the 'normal and 'suppressed' sets was not significant.

4. DISCUSSION

Over the past decade in this laboratory, eight wild-type lines drawn from the Kaduna base population have been selected for increase and decrease in number of sternopleural bristles, with the same intensity of selection and population size as used here. The mean responses of these at the limit, indicated by the words 'neither sex', are given in Table 4, together with those for the lines selected in the presence of marker chromosomes in the present experiment.

Table 4. *The mean advance at the end of selection on the observed scale and on the transformed scale of log* $(S - 4)$

(The lines indicated as 'neither sex' are from previous selection experiments from the same base population with the same number of parents and selection intensity.)

Inversions present in:	Direction of selection	No. of replicates	Mean advance at the limit	
			Observed scale	Transformed scale
Males	Up	5	$+9.1$	0.231 ± 0.017
Females	Up	5	$+5.9$	0.166 ± 0.014
Neither sex	Up	8	$+14.4$	0.309 ± 0.027
Males	Down	10	-4.4	-0.162 ± 0.010
Females	Down	10	-3.2	-0.134 ± 0.009
Neither sex	Down	8	-5.4	-0.224 ± 0.027

It has been shown (Robertson, 1970) that, on a scale of measurement of the character which is linear with respect to gene frequencies and such that gene action is additive, an upper bound to the selection advance at the limit is given by the response in the first generation multiplied by twice the effective population size. In considering the advance at the limit with marker chromosomes in selected males compared with that when selection is applied to wild-type flies of both sexes, we may deal with these two factors separately.

(1) The response in the first generation may be written as iV_a/σ, where i is the

selection intensity in standard units, V_a is the additive genetic variance of the character and σ its phenotypic standard deviation. Consider the response on the two autosomes when selection is applied to marker heterozygotes of both sexes. The above equation will then apply to the change in mean of the heterozygotes, though the additive genetic variance will be half that in wild-type flies and the phenotypic standard deviation will be slightly reduced because the marker chromosomes are genetically invariant. But the response to selection measured in wild-type flies will be twice that in the heterozygote, so that the effect of the presence of the marker chromosomes will be solely due to the reduction of the phenotypic standard deviation. We reach the surprising conclusion that the effect of selecting in the presence of invariant marker chromosomes is to increase the response. If we assume that one-third of the phenotypic variance is due to the two large autosomes, the presence of marked inversions on both will reduce the phenotypic variance by one-sixth and its standard deviation by one-twelfth or 8 %. In our case the wild-type chromosomes in the heterozygotes are only one-third of the total in the line, so that the effect will be only 3 %.

(2) A reduction in the effective population size in the selection process. Instead of sampling 40 wild-type autosomes in each generation, we are only selecting 30 since one sex contributes only ten. The effective population size is thus reduced by 25 %. The joint effect of these two factors taken together would therefore be a reduction in advance of up to 22 %.

As mentioned earlier, we have evidence that the scale of $\log (S-4)$ is more meaningful than the absolute scale. On this scale the advance with the marker chromosomes in the males, relative to that in their absence, is 0.75 ± 0.09 upwards and 0.72 ± 0.10 downwards, an effect very close to the upper bound calculated above. The ratio of advance when recombination is suppressed to that with marker chromosomes in males is 0.72 ± 0.08 for upward selection and 0.78 ± 0.07 for selection downwards. The former figure is probably an overestimate of the true value as some lines in the 'normal' set may not have reached their limit.

It may be objected that the estimate of the effect of suppressing crossing-over is in some doubt because of the inefficiency of cross-over suppression on the second chromosome. In this population the third chromosome usually contributes rather more to selection response in this character than does the second (Osman & Robertson, 1968).

As all four genotypes were scored for bristles in the second experiment, it was possible to estimate the change produced by selection in the third chromosome by comparing scores on $M\acute{e}/+$ and $+/+$ flies. In the lines selected upwards the changes were 0.075 and 0.047 units on the transformed scale for the normal and suppressed lines, respectively—a ratio of 0.63. In the lines selected downwards the values were 0.040 and 0.036 respectively—a ratio of 0.90.

Rathie & Barker (1968) have recently considered the effect of intermittent generations without selection for abdominal bristles in *D. melanogaster*. They report that 'all intermittent selection treatments gave similar amounts of response per generation of actual selection to those of the relevant continuous selection treat-

ments'. Nevertheless, 'fitness declined more under continuous than under intermittent selection'. In such an experiment the amount of crossing-over per generation of selection is increased at the expense of an increase in the amount of genetic drift (unless the number of parents in the additional generations is very large) and in the effect of any natural selection opposing artificial selection. They conclude that 'any increase in response in our intermittent selection lines due to recombination among purely bristle-affecting genes must have been very small'.

A general theoretical approach to the effect of linkage in selection if gene action is entirely additive has recently been published (Robertson, 1970) which is relevant to the present results. It is based upon the assumption that, as the number of loci affecting the character on a chromosome increases, the initial distribution of chromosomal effects approaches normality. In the absence of crossing-over, selection operates on whole chromosomes as units and, if gene action is additive, can be described solely in terms of the total genetic variance controlled by the chromosome independently of the number of loci and the frequency of the desirable alleles. The process is then entirely determined by the population size, N, the intensity of selection, i, and the heritability attributable to the chromosome, h^{*2}. It can be shown further that the pattern of change is determined by the product Nih^*, and that the time scale of the change is proportional to N. Since the normal distribution is symmetrical, the response to selection in opposite directions is expected to be symmetrical in the absence of crossing-over. As Nih^* increases, it was shown that the expected advance at the limit is in the neighbourhood of three times the initial genetic standard deviation attributable to this chromosome and that the half-life of the selection process is approximately $2/ih^*$ generations. If there is crossing-over, the parameters l, n and q (the length of the chromosome, the number of loci and the initial frequency of the preferred allele respectively) enter into the predictions, the first always appearing as Nl, and there is no longer any expectation of symmetry.

What are the expected values of these parameter combinations in the present case? The effective population size will be reduced from the actual number of 20 by two factors. The first is the known and inevitable effect of variations in fertility between individual parents, and the second comes from the fact that the invariant marker chromosomes make up one-quarter of the autosomal complement. Following Crow & Morton (1955), we shall assume that the first factor reduces effective population size in *D. melanogaster* to two-thirds of the actual value. The joint effect will then be a reduction of the effective population size from the actual number of 20 to 10. The selection intensity, i, can be estimated from the amount of selection practised as being close to unity. We know that the heritability of this character in the base population is close to 0·40. If, on the evidence from other selection experiments for sternopleural bristles from this population, we assume that the X, 2nd and 3rd chromosomes contribute to the variance roughly in the proportions 1:2:3, then h^* for the second and third chromosomes is 0·37 and 0·45 respectively, giving predicted values of Nih^* of 3·7 and 4·5 for the two chromosomes. From the known lengths of these chromosomes, allowing for the absence of crossing-over in the male, l is close to 50 cMs.

In the development of the theory, the assumption was made that all loci were equivalent in their effect on the character and in their initial gene frequencies. It was found that at fixed values of the other parameters, an increase in the number of loci always increased the effect of suppressing crossing-over, if this was measured as the ratio of the advance at the limit with no crossing-over to that with the usual amount. Some consideration was also given to the consequence of variation between loci in the effect of allele substitutions, when the total genetic variance due to the
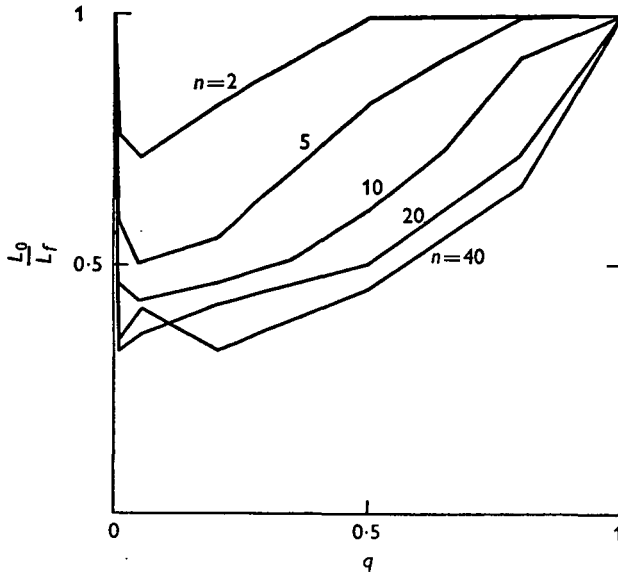

Fig. 9. The ratio of the advance at the limit with no recombination (L_0) to that with free recombination (L_f), with varying numbers of loci (n) and initial frequencies of the desirable allele (q). $Nih^* = 4$.

chromosome was kept constant. The effective number for this purpose is always less than Wright's effective number of loci (Wright, 1952), which is always less than the actual number. Wright's effective number rests in principle on the ratio of the difference between extreme selected lines to the standard deviation of the genetic variation in a population derived from them, after linkage equilibrium has been re-established. We have a strain in which the third chromosomes derive from a cross between extreme high and low chromosomes selected from this base population followed by many generations of crossing-over, while the other chromosomes are homozygous. The estimate of the genetic variance from the response to selection in this strain would suggest an effective number of loci of around ten for the third chromosome. This is in agreement with efforts to locate the relevant loci by using visible markers (J. H. Louw, personal communication). The effective number of loci on each chromosome would then certainly seem to be less than ten for our present purpose.

Autosomes have been extracted from the most extreme bristle lines selected from this population and substituted into a standard background so that their effect on

bristle score can be compared with that of a random sample of chromosomes from the base population, both as homozygotes and heterozygotes (Osman & Robertson, 1968). The bristle score of flies containing second or third chromosomes from the base population is a little lower than the average of the values for chromosomes from the high and the low lines. If we assume that the latter contain almost all the high and low alleles respectively, this would indicate an average frequency of alleles of high effect around 0·4 in the base population.

In computer simulation work in connexion with the development of the theory, runs had been made with $N = 10$ and $ih^* = 0.4$, for various numbers of equivalent loci, n, and initial frequencies of the desirable alleles, q. The main body of this material consisted of comparisons of the advance at the limit when no recombination is permitted (L_0) with that with independent segregation of all loci (L_f), and the results are summarized in Fig. 9. The ratio L_0/L_f always declines as the number

Table 5. *The ratio* ($\times 100$) *of the expected final advance on a chromosome with no recombination to that with a map length of 50 cMs with* $N = 10$, $i = 0.8$, $h^* = 0.5$ (*obtained by computer simulation*)

No. of loci	Initial frequency of desirable allele					
	0·05	0·2	0·35	0·5	0·65	0·80
5	69 ± 4	67 ± 2	77 ± 3	82 ± 2	92 ± 2	100 ± 1
10	60 ± 4	62 ± 3	63 ± 3	70 ± 2	80 ± 3	94 ± 2

Initial frequency	No. of loci				
	2	5	10	20	40
0·2	80 ± 2	67 ± 2	62 ± 3	64 ± 4	54 ± 3
0·5	100 ± 1	82 ± 2	70 ± 2	64 ± 4	61 ± 4

of loci increases but, with respect to changes in initial gene frequency, it passes through a minimum which always occurs at gene frequencies below 0·5, as can be seen from the figure. It can be shown theoretically that, as n increases, L_0/L_f tends to a limiting value independent of both n and q. A smaller number of runs were done with the loci scattered at random on a chromosome of length 50 cMs and these are given in Table 5. The results are not very different from those in Fig. 9, indicating that with this amount of crossing-over the advance is close to that with free recombination.

If the average initial frequency of the desirable allele for selection upwards is 0·4 it will be 0·6 for selection downwards. It will be seen that the effect of suppressing crossing-over should then be greater for selection upwards than for selection downwards. This we did find though the effect was not significant. It will be clear from the simulation results that the effect of suppressing crossing-over in our experiments is certainly consistent with expectations on the basis of an effective number of loci between five and ten on each chromosome with an average initial frequency of the 'high' allele of somewhat less than 0·5. One of the basic assumptions of the

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theoretical approach has been that linkage is initially at equilibrium. The results of these experiments therefore constitute some evidence that linkage equilibrium, or something very close to it, exists between the loci affecting bristles in the base population.

It was noted earlier that, in the absence of crossing-over, some prediction of the probable limits of selection could be made from a knowledge of the selection process and the effective heritability on the two separate autosomes. On the observed scale, the genetic standard deviation in the base population is approximately 1·15 bristles and on the transformed scale this equals 0·037 units. Assuming the above relative contributions of the major chromosomes to the genetic variance, the genetic standard deviations for the two autosomes are then 0·021 and 0·026 units, respectively. The advance on each chromosome is then expected to be about three times this, making a total of 0·141 units for the two. The X chromosome must be expected to contribute a little but it will be seen from Table 4 that the prediction is certainly of the right magnitude, as the observed advances with crossing-over suppressed averaged 0·162 units upwards and 0·135 units downwards. The expected half-life of the selection process would be predicted to be in the neighbourhood of five generations. The observed value on the transformed scale in the absence of crossing-over was five generations for both directions of selection.

REFERENCES

Crow, J. F. & Morton, N. E. (1955). Measurement of gene frequency drift in small populations. *Evolution* 9, 202–214.

Hill, W. G. & Robertson, A. (1966). The effect of linkage on limits to artificial selection. *Genetical Research* 8, 269–294.

Latter, B. D. H. (1966). The response to selection due to autosomal genes of large effect. *Australian Journal of Biological Sciences* 19, 131–146.

Lindsley, D. L. & Grell, E. H. (1967). Genetic variations of *Drosophila melanogaster*. *Publications: Carnegie Institution of Washington*, no. 627.

MacIntyre, R. J. & Wright, T. R. F. (1966). Recombination in FM4/+; SM1/+; Ubx[130]/+ heterozygotes. *Drosophila Information Service* 41, 141.

Mather, K. (1943). Polygenic inheritance and natural selection. *Biological Reviews* 18, 32–64.

Osman, H. S. & Robertson, A. (1968). The introduction of genetic material from inferior into superior strains. *Genetical Research* 12, 221–236.

Rathie, K. A. & Barker, J. S. F. (1968). Effectiveness of regular cycles of intermittent artificial selection for a quantitative character in *Drosophila melanogaster*. *Australian Journal of Biological Sciences* 21, 1187–1213.

Robertson, A. (1970). A theory of limits in artificial selection with many linked loci. In *Mathematical Topics in Population Genetics*, ed. K. Kojima. Berlin: Springer-Verlag.

Temin, R. G. (1966). Homozygous viability and fertility loads in *Drosophila melanogaster*. *Genetics* 53, 27–46.

Wright, S. (1952). The genetics of quantitative variability. In *Quantitative Inheritance*, pp. 5–41. Ed. E. C. R. Reeve and C. H. Waddington. London: H.M.S.O.