Theor. Appl. Genet. 59, 251-263 (1981)

Forging Links Between Population and Quantitative Genetics

R. Frankham and R.K. Nurthen
School of Biological Sciences, Macquarie University, North Ryde, New South Wales (Australia)

Summary. An initially rare allele with a large effect on a quantitative character is expected to exhibit the following behaviour in artificial selection lines:

1. It should change in frequency, or be lost by chance, at rates predictable from the effects of the allele on the quantitative character and the selection regime imposed.

2. At the phenotypic level the behaviour of the allele should cause (a) asymmetrical responses to bidirectional selection, (b) variation among replicate lines in response to selection corresponding to the behaviour of the allele in individual lines, (c) changes in heritability in lines in which the allele increases in frequency and (d) selection response compatible with the effects of the allele.

This paper reports an experimental evaluation of these predictions utilizing a rare allele of large effect (sm^{lab}) detected in a sample of the Canberra outbred population of *Drosophila melanogaster* at a frequency of 1/120. Homosygosity for this allele reduced abdominal bristle number by more than 50%, altered the abdominal bristle pattern and reversed the sexual dimorphism for abdominal bristle number. Experiments were done to characterise sm^{lab} and all evidence indicates that it is a single allele with a very large effect.

Bidirectional selection for abdominal bristle number was carried out in three high and three low lines from this sample of the Canberra population. The sm^{lab} allele rose in frequency and went to fixation in two of the low lines (in 10 generations) but was lost from the third. These times to fixation were slower than the expectations derived from computer simulations of the behaviour of such an allele but this can be attributed to the lower fitness of sm^{lab} homozygotes. The proportions of lines with the allele fixed or lost were compatible with expectations. At the phenotypic level, the behavior of sm^{lab} had the expected consequences, namely, (i) asymmetrical responses to bidirectional selection, (ii) variation in response among replicate low lines corresponding to the behaviour of sm^{lab}, (iii) changes in heritabilities in the lines in which sm^{lab} went to fixation, and (iv) selection responses compatible with the effects of the allele.

A test for rare alleles of large effect was proposed, based on the expected pattern of change in heritability under artificial selection. This test was applied to the high selection lines but no evidence was found for important effects due to rare alleles of large effect increasing abdominal bristle number, a conclusion consistent with other independent evidence.

This work provides experimental corroboration of the links between population genetics and quantitative genetics.

Key words: *Drosophila melanogaster* – Rare allele – Dynamic behaviour – Asymmetrical selection response – Changes in heritability

Introduction

In his classic paper Fisher (1918) interpreted 'the well established results of biometry in accordance with the Mendelian scheme of inheritance'. This paper and the one of Wright (1921) provide the main theoretical cornerstones on which quantitative genetics rests, as they provide the rationale for predicting and interpreting phenotypic relationships for quantitative characters on the basis of the multiple factor hypothesis. Around the same time these two authors (Fisher 1930; Wright 1931) along with Haldane (1932) were also laying the theoretical foundations of population genetics. However, Milkman (1978) lamented the tenuous nature of links between population and quantitative genetics 'despite their common origin and common goal of defining and relating genotypic variation and phenotypic variation' in his review of the 'Proceedings of the International Conference on Quantitative Genetics' (Pollak et al. 1977).

0040-5752/81/0059/0251/$ 2.60

Population genetics deals with alleles and works towards total phenotypic definition (see Crow and Kimura 1970), while quantitative genetics has a large body of theory (see Falconer 1960; Mather and Jinks 1971; Pollak et al. 1977), dealing mainly with means, variances, correlations and regressions. However, quantitative genetic theory is based on the multiple factor hypothesis, namely, that the genetic variation for quantitative characters is controlled by the segregation of multiple Mendelian loci, called polygenic loci or quantitative trait loci (Thompson and Thoday 1974; Thoday 1977). Most of this theory is based on the assumption that the number of quantitative trait loci is large and their individual effects small and indistinguishable. There is considerable evidence confirming the general Mendelian nature of quantitative trait loci, especially from F_2 segregation of differences between inbred lines for quantitative traits (e.g. East 1916), for linkage of quantitative trait loci to known loci (e.g. Sax 1923) and for a chromosomal location for almost all quantitative trait loci (e.g. Mather and Harrison 1949; Robertson and Reeve 1953). As well, a number of quantitative trait loci are reputed to have been mapped (see Thompson and Thoday 1979) but the precise interpretation of this work remains controversial (Robertson 1966; Piper 1971; McMillan and Robertson 1974). Under selection it is assumed that gene frequencies change at segregating quantitative trait loci and that alleles behave as predicted by population genetic theory (Wright 1969), but this has not been tested experimentally. The main basis of practical applications of quantitative genetics in plant and animal breeding is the equation predicting response (ΔG) to artificial selection namely $\Delta G = ih^2$, where i is the selection differential and h^2 the heritability. Clearly this equation predicts symmetrical responses to selection in opposite directions. However, this equation may yield poor predictions if a gene of large effect is segregating (Latter 1965). A rare allele with a large effect on a quantitative character is expected to exhibit the following behaviour in artificial selection lines of finite size:

1. It should change in frequency on average if it has effects favourable to the direction of selection, but in individual lines it will either rise in frequency and go to fixation or be lost by chance (Robertson 1960). Both the rate of change in frequency and probability of chance loss should be predictable from the effects of the allele and the selection regime used (selection intensity and population size).

2. At the phenotypic level there should be changes corresponding to changes in the frequency of the allele, namely, asymmetrical responses to bidirectional selection, variation in response among replicate selection lines, changes in heritability in lines in which the allele rises in frequency and goes to fixation and the magnitude of changes should be compatible with the effects of the allele (Latter 1965).

In spite of the existence of the huge body of quantitative genetic theory and its enormous practical importance, there has been no experimental study in any species of the dynamic behaviour of a quantitative trait locus under artificial selection and its quantitative genetic consequences. Such evaluations of our assumptions and predictions are essential if the science of quantitative genetics is to advance (Popper 1972) e.g. if we are to discover whether quantitative inheritance has characteristics not predicted by Mendelian inheritance, as the unexpected results of Durrant (1974) and Beardmore et al. (1975) and Beardmore and Shami (1976) suggest.

The experimental conditions necessary to establish the links between population and quantitative genetics are:

1. To have identifiable alleles at a *single* quantitative trait locus such that the frequencies of the alleles can be followed.

2. To estimate the frequencies of the allele in the base population and compare observed changes in frequencies under a perturbation such as artificial selection, with those predicted from population genetic theory.

3. To estimate the effects of the genotypes at the locus in question on a quantitative character.

4. To compare the observed effects of changing the frequencies of the alleles on phenotypic parameters such as means, variances, correlations and regressions for the quantitative character with those predicted from quantitative genetic theory.

No study of which we are aware meets all the criteria. However, genes of large effect have been recognised and some aspects of their behaviour studied by various authors including Warwick and Lewis (1954), Fowler and Edwards (1961), McBride and Robertson (1963), Marlowe (1964), Hollingdale (1971) and most extensively by Costantino et al. (1967).

The purposes of this contribution are to provide an experimental evaluation of the behaviour of a rare allele of large effect under selection in relation to both its population genetics and the quantitative genetic consequences of that behaviour. We document both fixation and chance loss of a rare favourable allele in finite sized selection lines as predicted by Robertson (1960) and show that the dynamic behaviour of this allele is consistent with population genetic theory. As well, we demonstrate corresponding quantitative genetic consequences, namely, asymmetrical responses to bidirectional selection and rapid changes in heritability under selection.

Experiment 1: Discovery and Effects of a Rare Allele of Large Effect

Three high (H1, H2, H3) and three low (L1, L2, L3) abdominal bristle selection lines plus six control lines (C1-C6) were founded from the progeny of 30 single pair matings of the Canberra outbred stock (Latter 1964) of *Drosophila melanogaster* into which the fourth chromosome recessive spa^{pol} had been substituted. The selection lines were founded by taking one pair of progeny from each of the 30 single pair matings for each pair of lines (H1 and L1; H2 and L2; H3 and L3). These progeny were scored (generation zero) and ten pairs of high progeny and ten pairs of low progeny selected as the parents of generation one for the respective high and low lines. Selection was for the number of bristles on two abdominal segments (fifth and sixth in females and fourth and fifth in males), 10 pairs of flies being selected from 30 pairs scored per

generation. For convenience scoring was done in groups of 15 flies per sex with the five most extreme flies per group being selected. The controls were founded by sampling one fly from the progeny of each of 20 of the single pair matings and were subsequently maintained with 10 pairs of parents per generation. Each line was maintained in one bottle with media and other conditions similar to those described previously (Frankham et al. 1968a). In addition to the above lines, whose behaviour is described later, 40 bottlenecked selection lines were founded, two from each of twenty of the above mentioned single pair matings (see Frankham 1980). It was in generation one progeny of a pair of these lines that flies exhibiting extremely low abdominal bristle number were detected and used to found a stock (these bottlenecked lines are not considered further in this paper). This low bristle effect was inherited as if controlled by a single autosomal Mendelian recessive allele in crosses between this stock and C6. We designated this allele sm^{lab} for reasons given later. The F_2 males and females were scored for two segment abdominal bristle number and individually progeny tested for the sm^{lab} allele. Three features of the results (Fig. 1) were notable. Firstly, the sm^{lab}/sm^{lab} homozygotes had a greatly reduced abdominal bristle number and did not overlap the distributions for $sm^{lab}/+$ and $+/+$ individuals. Secondly,

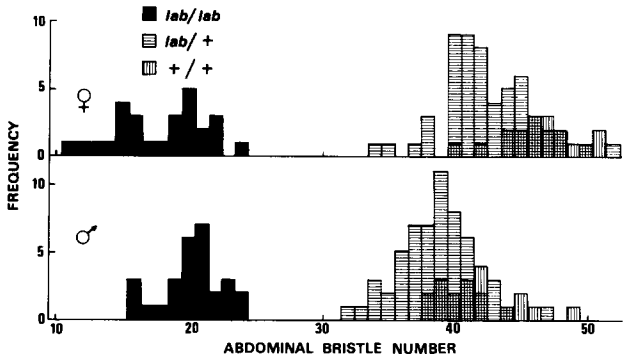

Fig. 1. Abdominal bristle number distributions in females and males for the sm^{lab}/sm^{lab}, $sm^{lab}/+$ and $+/+$ genotypes in F_2's between the sm^{lab} stock and a + control stock

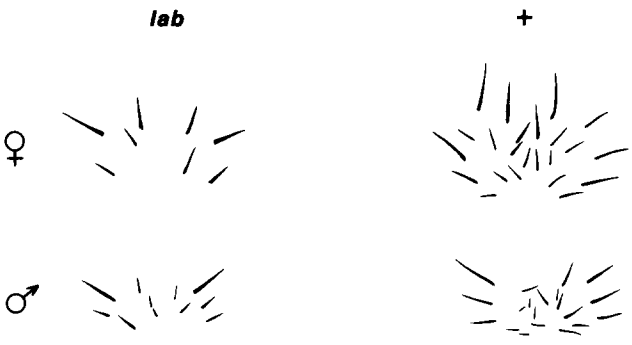

Fig. 2. Pattern of abdominal bristles in sm^{lab}/sm^{lab} and $+/+$ flies

the $sm^{lab}/+$ distributions overlapped those for $+/+$, but had slightly lower means (42.45 versus 46.44 in females and 38.64 versus 41.74 in males, respectively). Consequently sm^{lab} is largely but not completely recessive. Thirdly, the sexual dimorphism in sm^{lab}/sm^{lab} was reversed over that normally found, with sm^{lab}/sm^{lab} males having a higher mean than sm^{lab}/sm^{lab} females, while $+/+$ males had a lower mean than $+/+$ females (as is characteristic of this species).

The sm^{lab}/sm^{lab} individuals were also observed to have an altered abdominal bristle pattern (Fig. 2), the reduction in bristle number being more extreme on the anterior and midline portions of the abdominal segment, rather than being a generalized reduction on all sections of the segment. Such a pattern is to be expected from Claxton's (1974) analyses of bristle density distributions in wild type flies.

Observations of sm^{lab}/sm^{lab} flies revealed no obvious effects of this genotype apart from those on abdominal bristles (Frankham, unpublished).

Experiment 2: Mapping the sm^{lab} Gene

In light of the ambiguity concerning claims for mapping of alleles with large effects on quantitative characters, an intensive effort was made to map sm^{lab} and to determine whether it was due to a single locus or to multiple loci. Firstly, the sm^{lab} gene was shown to be located on chromosome 2 by a crossing program involving dominant markers. Secondly, the gene was mapped within chromosome 2 using an *al dp b pr Bl c px sp/In (2LR) SM1, al*^{2} *Cy sp*^{2} stock (all mutant and deletion stocks used are described by Lindsley and Grell 1968). Virgin sm^{lab}/sm^{lab} females were crossed to males of this stock, virgin *Bl* female progeny backcrossed to males of this stock, and individual *Bl* male progeny carrying parental or recombinant chromosomes progeny tested by mating to sm^{lab} females. Three pairs of progeny of the appropriate genotype were scored in each of the test crosses. The results (Fig. 3a) clearly indicate that sm^{lab} is located in the *c-px* (75.5-100.5) interval. Of the recombinants in this *c-px* region, 5 were to the left of sm^{lab} and 2 to the right of it. To more precisely map sm^{lab}, females of genotype *c + px sp/+* sm^{lab} *+ +* were crossed to *al dp b pr Bl c px sp/Cy* males, and *Bl* male progeny test crossed to sm^{lab} females. These results (Fig. 3b) confirm that sm^{lab} lies between *c* and *px*. In this series of crosses 20 crossovers were between *c* and sm^{lab}, and 11 between sm^{lab} and *px*, an overall total of 25 and 13, respectively, in these two regions. Consequently the map position of sm^{lab} is 2-91.95 ± 1.92. No recombinants with intermediate means were found in these experiments. Further experiments established that sm^{lab} did not lie in the regions of the *Df(2R)*

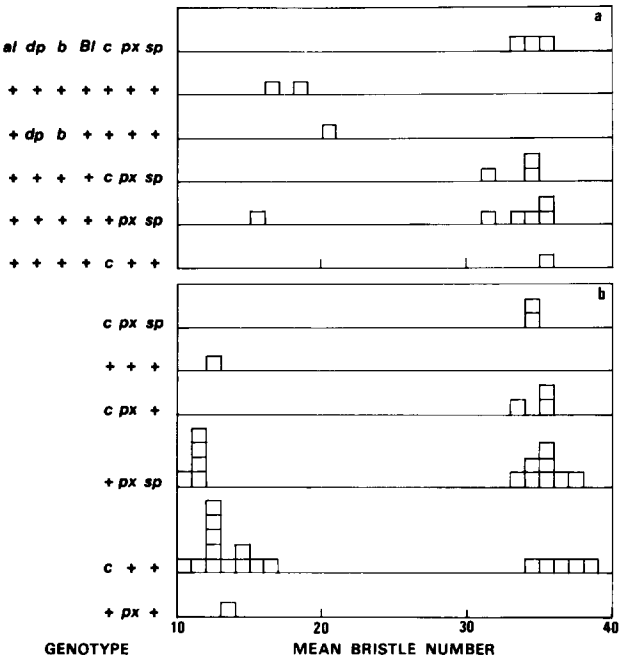

Fig. 3a and b. Chromosome mapping of sm^{lab}. Mean abdominal bristle number of test cross progeny carrying the designated chromosome and a sm^{lab} chromosome. Each square represents the mean attributable to a single parental or recombinant chromosome.

vg^B (49D3-4; 50A2-3), $Df(2R)\,vg^C$ (49B2-3; 49E7-F1), or $Df(2R)bw^5$ (59D10-E1; 59E4-F1) deletions. The map position of the allele is not in the region of any of these deletions but they help test for multilocus effects because of their proximity. A further mapping experiment showed sm^{lab} to lie between *wt* (2-82) and *px* (2-100.5). Finally, crosses to a *sm px pd/Cy* stock showed sm^{lab} to be an allele at the *smooth* locus (2-91.5). The *smooth* phenotype is described as follows 'abdomen partially denuded of bristles and shrunken, wings usually warped and semi-erect, acrostitial hairs disarranged, tendency for erect postscutellars, male genitalia often disturbed, anal protuberances of female bent down, viability 30% wild type and both sexes entirely sterile' (Lindsley and Grell 1968). The allele we have discovered has normal fertility and low abdominal bristle number but none of the other features of *smooth* so it is clearly a new allele at that locus, which we have designated sm^{lab}. Tests were also made for recombination between *sm* and sm^{lab} and yielded two wild type recombinants out of 7354 progeny examined.

Experiment 3: Dynamic Behaviour of sm^{lab} Under Artificial Selection

The sm^{lab} allele is expected to increase in frequency in low abdominal bristle selection lines as it has a large effect on that character. We were able to study its dynamic behaviour in the three low abdominal bristle selection lines (L1, L2, L3) founded from the sample of the Canberra outbred population containing the sm^{lab} allele at a frequency of 1/120.

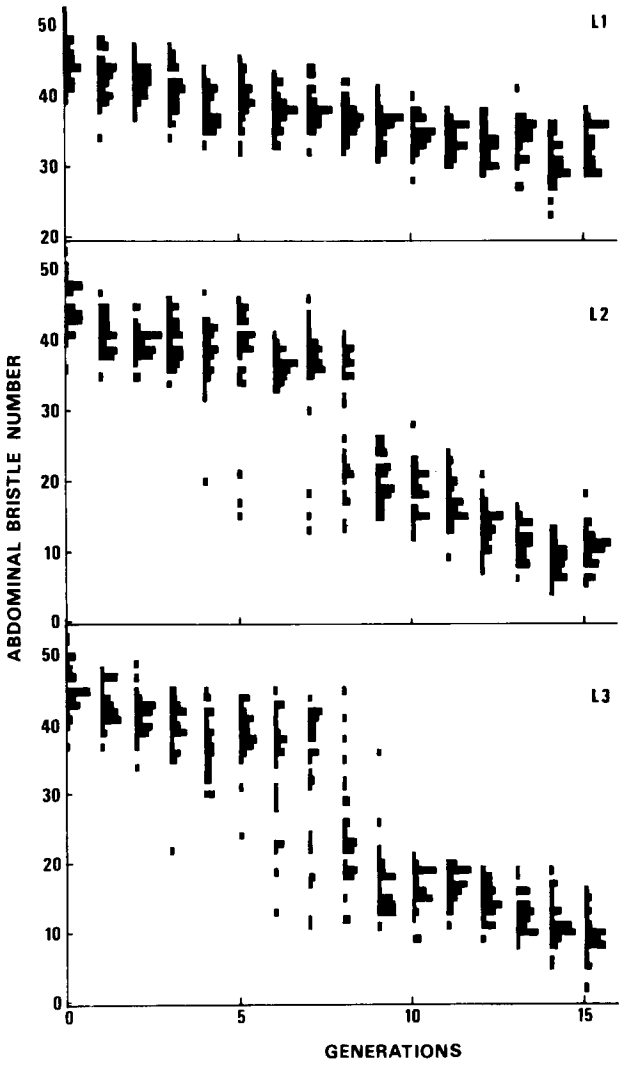

Fig. 4. Distributions of abdominal bristle number of females in three low selection lines over 15 generations of selection. The lower portions of the distributions in L2 and L3 represent sm^{lab} homozygotes. The sm^{lab} allele went to fixation in L2 and L3 but not in L1

The frequency of sm^{lab} homozygotes can be assessed from the abdominal bristle number distribution. This is shown for females of the three low lines in Fig. 4. From these distributions it is clear that the sm^{lab} allele rose in frequency and went to fixation in lines L2 and L3 but not in line L1. These conclusions have been confirmed by test crossing the lines to the sm^{lab} stock. The first presumed sm^{lab}/sm^{lab} homozygotes were noted in L2 at generation 1 (a male with 26 bristles), in L3 at generation 3 (a female with 22 bristles), but none were detected in L1. In L2 and

L3 there were sporadic but increasingly frequent occurrences of sm^{lab}/sm^{lab} individuals till generation 5 or 6, followed by a very rapid increase in sm^{lab} frequency culminating in its fixation probably at generation 10 in both L2 and L3. The sm^{lab} gene is clearly largely responsible for the large difference in response of L1 versus L2 and L3. In quantitative terms the responses in L2 and L3 as a deviation from the controls should be equal to or greater than the known effects of the sm^{lab} homozygotes and the difference in response between L1 versus L2 and L3 should also be of a similar magnitude. The responses to G.10 in L2 and L3 were 0.35 and 0.38, respectively, versus an initial effect of sm^{lab} of 0.35 (all as means of males and females on the log (1 + bristle number) scale) confirming the former prediction. The differences in response of L1 versus L2 and L1 versus L3 were 0.25 and 0.27, respectively, somewhat less than the effect of sm^{lab} of 0.35. This discrepancy may be due to the generation of linkage disequilibrium under selection in lines L2 and L3 i.e. negative linkage disequilibrium between sm^{lab} and other second chromosome genes affecting abdominal bristle number.

Experiment 4: Monte Carlo Simulation of the Dynamic Behaviour of sm^{lab} Under Artificial Selection

To evaluate the population genetic behaviour of sm^{lab} it is necessary to use Monte Carlo simulation to generate the predictions as the available equations are either deterministic or only valid for genes of small effect. The use of a deterministic equation to predict the behaviour of a largely recessive allele in finite sized selection lines is likely to be rather misleading. To generate predictions we have used the GSD-1 computer program (Fraser et al. 1965) with genotypic values and variance derived from the data in Figure 1. (transformed to the $\log_{10}$ (1 + bristle number) scale). The simulations were run with a population size of 20 parents, a selection intensity of 33 1/3%, a single locus with two alleles, genotypic values for the three genotypes of 0, 1.8 and 2.0, and an environmental standard deviation of 0.2455. The simulation programme commenced with a generation without selection so that the starting allele frequencies used (1/120 or 1/40) are not particularly informative. Runs used were those with one or two heterozygous parents chosen in generation 1 (see below). The distributions of times to fixation, for lines which eventually went to fixation, are given in Table 1. The time to fixation for lines with two heterozygous individuals in the parents of generation one was markedly less than that for the lines with one heterozygous parent at this stage so these are presented separately in the Table. The values of 10 generations to fixation observed in L2 and L3 lie within the range of these computer generated predictions. However, the observation of a presumed sm^{lab} homozygote in L2 at generation 1 indicates that it had two heterozygous individuals among the parents of generation 1. Consequently, its time to fixation is slower than predicted (see lowest line in Table 1). The generations to fixation in L3 is also in the upper end of the distribution for lines with 1 heterozygous individual in the generation 1 parents. Consequently, the times to fixation must be considered to be slower than expected.

The second point to consider is the probability of loss of the sm^{lab} allele. It is not possible to obtain this probability from the available diffusion equation formula as it is only valid for small selective values (Crow and Kimura 1970). The allele may be lost in the initial sampling of the foundation stock, or it may be lost subsequently in the selection lines. The selection lines were founded by sampling one pair of flies from the progeny of each of thirty single pair matings. One of these single pair matings had sm^{lab} at a frequency of $\frac{1}{4}$ so their progeny must have been $\frac{1}{2}$ $sm^{lab}/+$: $\frac{1}{2}$ $+/+$. Consequently, the probability that the allele was missed in the initial sampling was $(\frac{1}{2})^2 = \frac{1}{4}$ and the probability of sampling one and two heterozygotes, $\frac{1}{2}$, and $\frac{1}{4}$, respectively. The probability that the allele was lost after having been included in the initial sample of 30 pairs can only be obtained indirectly from the simulations as they commenced with a generation of no selection. Of the 110 simulated runs with one heterozygous parent chosen after this generation of zero selection (see Table 1), 25 subsequently lost the favourable allele, while only two of the 52 runs with two heterozygous parents at this stage

Table 1. Results of Monte Carlo simulations of the behaviour of sm^{lab}

Numbers of heterozygotes in parents of generation 1	Generations to fixation									Total number fixed	Total number losses
	5	6	7	8	9	10	11	12	13		
1	0.012	0.165	0.259	0.247	0.153	0.082	0.059	0.012	0.012	85	25
2	0.080	0.320	0.240	0.180	0.160	0.02				50	2

subsequently lost the allele. The other probability required is the probability that a heterozygote for sm^{lab}, once included in the initial sampling, is selected in the initial generation. We have computed this as the probability that a standard normally distributed heterozygote (mean 0.82) exceeds the fifth order statistic (mean 0.516) out of a sample of 15 from a standard normal curve. This probability is 0.62. If two heterozygotes are sampled the probabilities that both, one or zero are selected in the first generation are 0.38, 0.47 and 0.14, respectively.

On combining these probabilities, the probability that sm^{lab} is lost at some stage is 0.58, and that it is fixed is 0.42. Consequently, the probability of observing two lines with fixation and one with loss is 0.31. Clearly our results do not deviate significantly from expectations for such a small number of lines.

Experiment 5: Asymmetrical Responses to Selection due to a Rare Allele of Large Effect

Asymmetrical response to bidirectional selection is to be expected in abdominal bristle selection lines founded from the sample of the Canberra population containing sm^{lab} at a frequency of 1/120.

The response to selection in the three high and three low abdominal bristle selection lines plus their controls (described under Experiment 1), are presented in Fig. 5. All results are presented on the scale of $\log_{10}$ (1 + bristle number). The logarithmic scale removes the correlation between mean and environmental variance evident on the bristle number scale (Frankham 1977 and unpublished) and puts male and female genetic differences on an equal (rather than a proportional) scale (Frankham 1977). McPhee and Robertson (1970) have used a related scale for sternopleural bristle number based on related considerations. Unity is added to the score to allow analysis of observations of zero bristles. Generation 0 and the means (average of males and females) of each subsequent five generation period are plotted for each of the selection lines and the mean of the control lines. Two features of the response were notable. Firstly, there was a large asymmetry in the response to selection, low lines responding more than the high lines. This asymmetry was evident even in the early generations of selection. Secondly, there was a very large difference in response among low lines but very similar response in all three high lines. Both these features can be attributed to the behaviour of the sm^{lab} allele.

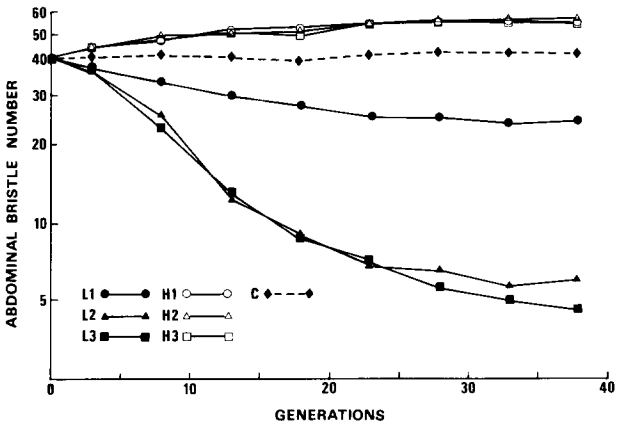

Fig. 5. Mean abdominal bristle number in the high and low selection lines and the controls

The sm^{lab} allele does not appear to be solely responsible for the asymmetry of selection response, as L1, from which it is absent, also gave approximately twice as much response as the high lines (this conclusion depends on the validity of the scale transformation). Even in the case of L2 and L3, the sm^{lab} allele was fixed by generation 10 and less than half of their responses can be attributed to the known effect of this gene.

Causes of asymmetry, other than genetic asymmetries were not responsible for the observed asymmetry in response. Falconer (1960, 1977) has discussed the following possible causes of asymmetrical selection response.

1. Asymmetrical selection differentials due to natural selection, to fertility changes or to scale effects.
2. Genetic asymmetry due to either directional dominance and/or directional gene frequencies.
3. Selection for heterozygotes in one direction but not the other.
4. Inbreeding depression
5. Asymmetrical maternal effects, and
6. Genetic drift.

An initially rare allele of large effect may cause asymmetry in short term selection response (Latter 1965). This contrasts with the effects of directional dominance and directional gene frequencies (for genes of small effect) which result in asymmetrical response only in the long term (Falconer 1960).

For abdominal bristle number, the character of interest in these studies, the causes of asymmetry (other than genetic asymmetry) can be estimated or eliminated from consideration. Firstly, the question of an adequate scale has been considered by Frankham (1977). Secondly, no directional maternal effects have been found for this character in this population (Frankham 1974). Thirdly, the genes affecting this character in this population are approxi-

Table 2. Cumulative selection differential (Σi) over the first three generations of selection in the selection lines (on the $\log_{10}$ (1 + bristle number) scale)

Line	Σi	Line	Σi
H1	0.197	L1	0.183
H2	0.227	L2	0.189
H3	0.184	L3	0.201

mately additive on average on a logarithmic scale (Frankham unpublished). Fourthly, selection differentials in the two directions were very similar in the high and low lines over the first three generations of selection (Table 2). Not surprisingly the selection differentials in L2 and L3 did increase during the period of rapid rise in frequency of sm^{lab} (generations 6-10) but returned to normal thereafter. Directional changes in reproductive fitness (number of progeny emerging per generation) were observed, the fitness of the low lines declining more than that of the high lines. This change is in the opposite direction to that necessary to contribute to the observed asymmetry. Selection for heterozygotes in one direction but not in the other does not appear to have occurred as there was no substantial regression on relaxation of selection in any of the lines (Table 3). There are certainly no grounds for suspecting the presence of lethals with large effects on bristle number in any of the lines. Apart from the lack of substantial regression on relaxation, the broad sense heritabilities (see Experiment 6 for method of estimation and standard errors) in the selection lines were not elevated in comparison to those in the controls (Table 4), nor was there any evidence of bimodality in the phenotypic distributions in the lines after generation 10. All these features have previously been found in lines containing high frequency lethals with large effects on the selected character (Frankham et al. 1968b). Consequently, the observed asymmetry in response can be attributed to genetic asymmetry.

Experiment 6: Changes in Heritability in Selection Lines Due to Rare Alleles of Large Effect

As an initially rare allele of large effect increases in frequency under selection it is expected to lead to an increase in heritability (Latter 1965). The heritability should later decline as the allele of large effect approaches fixation. This effect arises from the relation between allele frequency and the contribution of a locus to the heritability (Table 5). The relations between allele frequency and genetic variation for additive, dominant, overdominant and recessive alleles are plotted in Figure 8.1 of Falconer (1960, p. 137). Consequently, the heritabilities are expected to have changed in lines L2 and L3 in which the sm^{lab} allele rose in frequency from a low frequency and

Table 3. Regression on relaxation from selection

Line	Means[a]	
	Selection Lines[b]	Relaxed Lines[c]
H1	56.16	56.25
H2	58.18	57.60
H3	54.62	54.20
L1	23.89	26.28
L2	5.84	5.31
L3	3.92	4.44
Mean C	42.84	42.93

[a] Calculated on the $\log_{10}$ (1 + bristle number) scale and detransformed
[b] Mean of both sexes for generations 40 to 44
[c] Scored after relaxation for nine generations

Table 4. Average heritabilities (broad sense) over generations 36–40 in the selection lines and controls

Line	h^2	Line	h^2	Line	h^2
H1	0.13	L1	0.24	C1	0.36
H2	0.15	L2	0.20	C2	0.26
H3	0.25	L3	0.21	C3	0.25
				C4	0.39
				C5	0.35
				C6	0.42
Mean C					0.34

Table 5. Effect of a locus on the broad-sense heritability (h^2)

	Genotypes		
	A_1A_1	A_1A_2	A_2A_2
Frequencies	p^2	2pq	q^2
Effects	a	d	−a

Heritability due to a specific locus (h^{*2}) is

$$h^{*2} = \frac{2pq\,[a + d\,(q-p)]^2 + (2pqd)^2}{\sigma_P^2} = \frac{\sigma_{G*}^2}{\sigma_P^2}$$

Where σ_{G*}^2 = total genotypic variance contributed by the locus

and σ_P^2 = phenotypic variance = $\sigma_{G*}^2 + \sigma_R^2$

and σ_R^2 = $\sigma_{GR}^2 + \sigma_E^2$

where σ_R^2 = Residual variance, σ_E^2 the environmental variance and σ_{GR}^2 the residual genetic variance due to other loci.

This leads to an overall heritability as follows:

$$h^2 = \frac{\sigma_{G*}^2 + \sigma_{GR}^2}{\sigma_{G*}^2 + \sigma_R^2}$$

$$= \frac{\sigma_{G*}^2/\sigma_R^2 + h_R^2}{1 + \sigma_{G*}^2/\sigma_R^2}$$

where h_R^2 is the residual heritability i.e. the heritability excluding contributions from the above locus.

went to fixation. No such changes are expected in L1 (from which sm^{lab} was lost) or in the controls.

Estimates of heritabilities in these lines were obtained from the phenotypic correlations (r_P) between bristle number on adjacent segments of the same fly. This correlation is made up as follows:

$$r_P = h_1\, h_2\, r_G + r_E \sqrt{(1 - h_1^2)(1 - h_2^2)}$$

(modified from Falconer 1960) where h_1^2 and h_2^2 are the broad sense heritabilities for the two traits and r_G and r_E are the total hereditary and environmental correlations, respectively. As the environmental correlation is effectively zero and the total hereditary correlation effectively unity in this population (Sheridan et al. 1968), this phenotypic correlation provides an estimate of broad sense heritability for one segment abdominal bristle number (see Reeve and Robertson 1954; Frankham et al. 1968b for more details of this procedure). These correlations were calculated on data transformed to the scale of $\log_{10}$ (1 + bristle number). Expected standard errors of the plotted points (correlations) after transformation to z are $1/(n-3)^{\frac{1}{2}}$ (Snedecor and Cochran 1967) and are ± 0.061 for the selection lines and ± 0.049 for the mean of the controls.

In both L2 and L3 the sm^{lab} allele rose slowly in frequency in the early generations of selection but rose rapidly in frequency from generation 5 to fixation by generation 10 as gauged from the bristle number distributions given in Experiment 3. Consequently, the heritability in both these lines is expected to rise to a maximum between generations 5 and 9 and subsequently return to normal by generation 10. L2 and L3 both exhibited changes in heritability of the predicted form (Fig. 6), the heritability rising to a maximum in the generation 5-9 period and subsequently dropping in the generation 10-14 period. No such changes were evident in L1 (from which sm^{lab} was absent) or the controls. There was a slight decline in heritabilities in the controls over this period,

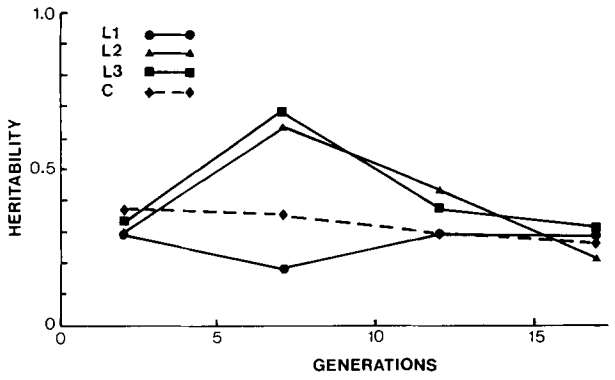

Fig. 6. Changes in heritabilities during selection in lines L2 and L3 corresponding to changes in the frequency of sm^{lab}

most probably due to genetic drift. It is possible to estimate the maximum expected contribution of the sm^{lab} allele to the heritability using the equation given in Table 5. Values of a, d, h_R^2 and σ_R^2 for one segment abdominal bristle number on the transformed scale were obtained from the original data used to construct Fig. 1. These values were 0.198, 0.115, 0.36 and 0.00365 for females and 0.148, 0.115, 0.36 and 0.00179 for males, respectively. The maximum broad sense heritability in a population containing this allele is expected to be 0.94 at a frequency of 0.696 for the allele. The maximum observed heritabilities of 0.87 and 0.86 in L2 and L3 at generation 7 were close to this expected maximum, especially when it is remembered that the gene frequencies in the selection lines are unlikely to attain the precise value necessary to yield the maximum heritability.

Further evidence for the predicted changes in heritability due to changes in the frequency of an initially rare allele (a new 'mutant') of large effect come from an independent set of selection lines in which *bb* alleles arose, rose in frequency and went to fixation. Selection lines were founded from a base stock with a homozygous X chromosome and a low residual level of autosomal genetic variation. These lines were maintained by selecting the 10 extreme pairs from 30 pairs scored each generation. In two out of three low abdominal bristle selection lines (LA, LC) there were large rapid bursts of selection response in females, but not in males, due to the occurrence and selection to fixation of *bobbed* alleles (on the X, but not the Y chromosomes). These lines were described by Frankham et al. (1978, 1980).

Heritabilities for males and females for all three low lines are plotted (10 generation averages) in Fig. 7a along with the mean heritabilities for the two sexes in the high lines. The course of change in frequency of *bb* alleles is indicated by the ratio of male to female means given in Fig. 7b. Clear changes in female but not in male heritabilities were evident in LA and LC, corresponding approximately to the changes in frequency of *bb* alleles in LA and LC. No systematic changes in heritability in either sex were evident in LB (in which *bb* alleles did not arise and rise in frequency), or in the high lines.

Experiment 7: A test For Rare Genes of Large Effect Based on Changes in Heritability Under Selection for High Abdominal Bristle Number

In the preceding experiment it has been shown that initially rare alleles of large effect cause changes in heritability under selection as they rise in frequency and go to fixation. This change in heritability can be used as the basis of a test for detecting initially rare alleles of large effect in selection lines. In theory, it should also be possible to

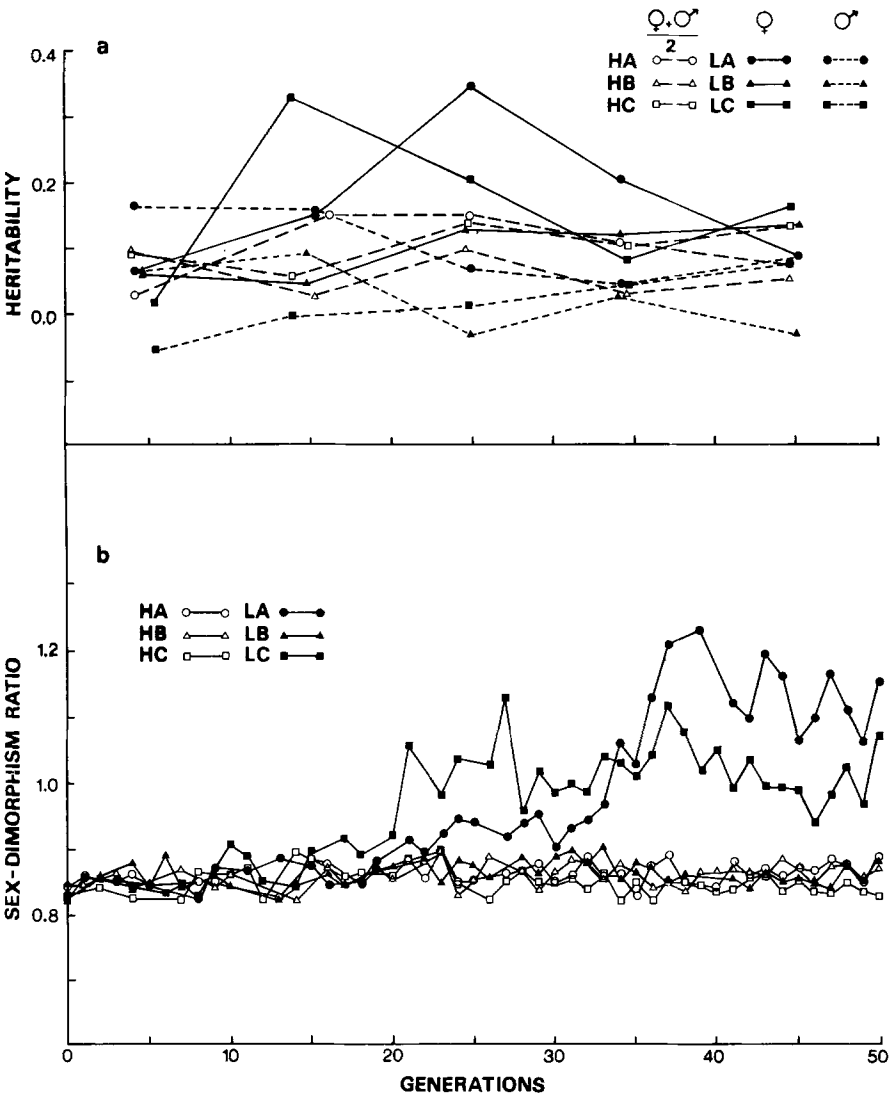

Fig. 7a and b. Changes in heritabilities during selection in females of lines LA and LC corresponding to changes in the frequency of *bb* alleles (**a**). Changes in sex-dimorphism ratio, an indicator of the frequency of *bb* alleles in LA and LC (**b**)

detect alleles of large effect initially at high frequencies from the drop in heritability under selection. In practice genetic drift and disequilibrium generated by selection (Bulmer 1976; Avery and Hill 1977) also cause heritabilities in selection lines to decrease so such observations are not particularly informative.

This test for rare alleles of large effect is applied to a separate set of selection lines, namely, the three high abdominal bristle selection lines (H1-3) from the Canberra outbred population described in Experiment 1. The broad sense heritabilities (again estimated as previously) in these three lines and the controls (same as in Experiment 6) are plotted (five generation averages) in Fig. 8. There was no evidence for changes in heritability of the type expected from initially rare alleles of large effect in any of the high selection lines. In fact, some of the heritabilities showed a

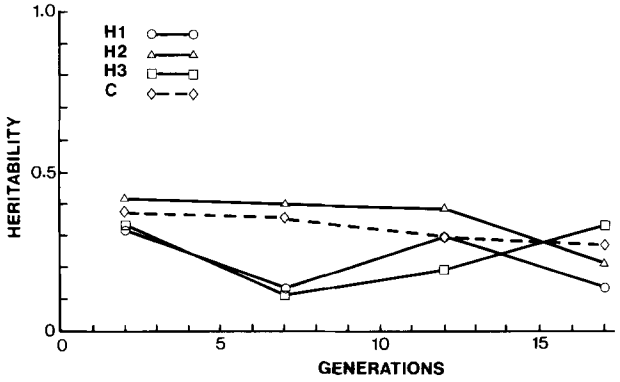

Fig. 8. Changes in heritabilities during selection in the high abdominal bristle selection lines and controls

transitory decline but we are unable to clearly delineate the reason for this.

Discussion

One important question to be considered is whether sm^{lab} is in fact a single locus effect, or one due to multiple loci. All lines of evidence point to a single gene basis for sm^{lab}. Firstly, it was discovered in an unselected population so no forces had been applied to build up multigenic linkage disequilibrium and there is no evidence for widespread linkage disequilibrium in natural populations (McPhee and Robertson 1970; Langley et al. 1978) apart from that associated with inversions. Nor was sm^{lab} associated with an inversion on the right arm of chromosome 2. Secondly, no intermediate individuals were detected in either the F_2 or in the mapping experiments where recombinants between multigenic loci might have been expected to be detected. It could be argued that intermediate types were present in the selection experiment in lines L2 and L3 (Fig. 4). However, repulsion linkage disequilibrium is expected to build up under artificial selection (Felsenstein 1965) so the comparison is not valid i.e. any chromosome carrying sm^{lab} is likely to have a strong selective advantage and be selected, especially when homozygous, irrespective of other genes being carried, while chromosomes not carrying sm^{lab} will only be selected if they are extreme in the direction of selection at other loci. Thirdly, sm^{lab} showed allelism with the *smooth* mutant. It is formally possible that sm^{lab} may be due to a multilocus deletion but its viability as a homozygote, its location in a region of haploinviability (Lindsley et al. 1972), and its low level of recombination with *sm* make this explanation untenable. The rate of recovery of wild type recombinants between *sm* and sm^{lab} (2/7354) is of the order of magnitude expected for intragenic crossing over. Thus, sm^{lab} is most probably a single allele with a very large effect.

A notable feature of the results in this paper is the dynamic behaviour of sm^{lab} under artificial selection. In two of three replicates this allele went to fixation. This is the first time such fixation has actually been followed in detail. It was possible to evaluate the observed fixation times against computer generated predictions and while the observed values lay within the range of the predicted values they were significantly slower than predicted. Three possible reasons for this exist, namely, a lower fitness for carriers of sm^{lab}, unreliability of the parameter estimates used in the simulation, and retardation of response due to the generation of repulsion linkage disequilibrium under selection (Latter 1966). Homozygotes for sm^{lab} certainly do have a lower fitness than wild type homozygotes, the mean numbers of flies emerging from 12 vials of each of these genotypes being 103.5 and 193.0, respectively. This lowered fitness is probably the main reason for the slow times to fixation of sm^{lab} in L2 and L3.

The failure of sm^{lab} to rise in frequency in L1 provides the first demonstration of the chance loss of a favourable allele under artificial selection, as predicted from the stochastic theory of the selection process (Robertson 1960). We do not know whether sm^{lab} was missed in the initial sampling of the foundation stock, or whether it was subsequently lost from L1 during selection, but in either case these are parts of the chance loss included in Robertson's (1960) theory. The proportions of lines with sm^{lab} fixed and lost are consistent with computer generated expectations, though the number of lines observed is very small.

Latter (1965) predicted that the presence of a rare allele of large effect will lead to asymmetrical responses to bidirectional selection, even in the early generations of selection. Our results clearly confirm Latter's prediction, the low lines L2 and L3 giving much more response than the high lines due largely to sm^{lab}. Other workers (see Falconer 1977) have previously observed asymmetrical responses to bidirectional selection but have not been able to clearly delineate the cause(s). Our results also confirm that chance loss of favourable alleles due to genetic drift causes differences among replicate selection lines (compare response in L1 versus that in L2 and L3).

A rare favourable allele of large effect is expected to cause changes in heritability as it rises in frequency under artificial selection (Latter 1965). As the frequency of the allele rises, the heritability is expected to rise through a maximum and subsequently drop again as the allele approaches fixation. The expected changes in heritabilities were observed in the low selection lines in which the sm^{lab} allele rose from a low frequency and went to fixation, but were not observed in L1 from which sm^{lab} was absent. In the lines in which *bb* 'mutants' arose, increased in frequency and went to fixation, approximately the expected pattern of change in heritability was also observed in females. No such changes were observed in the males of these lines (where *bb* had little effect), in line LB (from which *bb* was absent), nor in the high lines. There are indications of the same pattern of change in heritability in the work of Costantino et al. (1967), and elevated broad sense heritabilities have previously been noted in three high abdominal bristle selection lines (designated 10(10%)b, 20(20%)a and 40(10%)) with high frequency lethals presumed to have a large effect on the trait (Frankham et al. 1968b).

The other significant feature of these results resides in the potential for using such changes in heritability under selection to detect the presence of initially rare genes of large effect. If such genes can be detected in practical breeding programs they can be manipulated with much

greater efficiency, especially if genetic engineering procedures come into general usage in plant and animal breeding. The potential for detecting major genes from changes in heritability is dependent on accurate estimates of heritabilities being available in selection lines. This should be possible in large breeding schemes involving artificial insemination, for large plant breeding schemes in outbreeding species and in situations where clonal material can be utilized.

The power of this method requires consideration. This has been investigated by considering examples. We have assumed that a single locus effect is only likely to be detected in practice if it results in an increase in heritability under selection of at least 0.10 or 0.25 (in absolute value). The magnitude of gene effects necessary to give such changes in heritability under selection for alleles with different initial frequencies and different residual heritabilities has been calculated (see Appendix 1 for details of the calculations) and a number of examples are presented in Table 6. In all cases it is assumed that the population is selected until the maximum increase in heritability is reached. The magnitude of the gene effects which might lead to detectable changes in heritability depends on initial allele frequency, residual heritability, degree of dominance and the increase in heritability required for detection. This method may be of assistance in the detection of rare alleles with effects of one to three residual standard deviations or greater. A number of initially rare alleles at different loci with somewhat smaller effects would, of course, be expected to lead to detectable changes in heritability under selection. In reality, the magnitude of effects required to lead to detectable changes in heritability will be greater than indicated above as the residual heritability will tend to decrease under selection due to the generation of disequilibrium (Bulmer 1976; Avery and Hill 1977) and to genetic drift and the precise value of gene frequency required to give the maximum heritability is unlikely to be attained in any generation.

Table 6. Size of gene effect ($2a/\sigma_R$) which will lead to a detectable increase in heritability under selection for different initial allele frequencies, degrees of dominance and residual heritabilities (h^2_R).

Initial frequency	Increase in h^2	Additive	Dominant	Recessive
$h^2_R = 0$				
0.01	0.10	0.97	0.70	0.67
	0.25	1.69	1.25	1.16
0.05	0.10	1.08	0.89	0.67
	0.25	2.02	2.24	1.17
$h^2_R = 0.25$				
0.01	0.10	1.14	0.83	0.78
	0.25	2.10	1.56	1.41
0.05	0.10	1.28	1.08	0.79
	0.25	2.75	$-a^a$	1.43
$h^2_R = 0.33$				
0.01	0.10	1.22	0.89	0.84
	0.25	2.30	1.73	1.54
0.05	0.10	1.38	1.18	0.84
	0.25	3.34	–	1.56
$h^2_R = 0.50$				
0.01	0.10	1.46	1.07	1.00
	0.25	3.10	2.49	2.00
0.05	0.10	1.69	1.54	1.01
	0.25	–	–	2.04

[a] No solution exists

This test has been applied to three high abdominal bristle selection lines. No evidence for the expected pattern of change in heritability under selection due to initially rare alleles of large effect was found in these lines. Consequently, rare alleles of large effect which increase abdominal bristle number are not making an important contribution to the genetic variation in the Canberra outbred population. Two other lines of evidence support this conclusion. Firstly, the long term response to bidirectional selection is asymmetrical (more in the low direction) indicating that alleles decreasing abdominal bristle number are on average rarer, or have larger effects, or both, than alleles increasing bristle number (Experiment 5). Secondly, the effects of population size bottlenecks on the long term response to selection for increased abdominal bristle number does not indicate that rare alleles increasing abdominal bristle number are an important component of the genetic variation for this character (Frankham 1980). These observations do not preclude the presence of alleles of large effect at higher frequencies.

Our results corroborate several features of the behaviour of a locus affecting a quantitative trait under artificial selection and show that it behaves as predicted by population genetic theory. We also demonstrate corresponding consequences at the quantitative genetic level, namely, asymmetrical responses to bidirectional selection even in the short term response, variation among replicate selection lines due to chance loss of this favourable allele, and changes in heritability under selection due to this rare allele of large effect. This work represents the most complete evaluation, so far, of the characteristics and behaviour of an allele affecting a quantitative character and its phenotypic consequences, but the scale of the work remains small and the power of tests against quantitative predictions weak.

Acknowledgement

We thank Ms A. Gorry for technical assistance, Mr. R.J. Oldfield for photographic assistance, Ms B. Thorn for preparing the Figures, Professor J.S.F. Barker and Dr. F. Nicholas for carrying out the computer simulations and Professor J.S.F. Barker, Dr. D.A. Briscoe, Mr. G. Daggard and Ms H.N. Frankham for their comments on the manuscript. This work was made possible by Australian Research Grants Committee and Macquarie University research grants.

Appendix 1. Calculation of size of gene effects which will lead to detectable changes in broad sense heritability under selection

Presence of a rare allele of large effect will lead to changes in both genetic variance and phenotypic variance under selection. Consequently, the ratio $2a/\sigma_P$ (all terms are as defined in Table 5) will change and thus is an unsuitable measure of size of gene effect. However, the expression $2a/\sigma_R$ is constant (provided residual variance σ_R^2 does not change due to other loci) during such changes. In most cases σ_R is very similar to σ_P in the base population. To examine the changes in broad sense heritability it is most convenient to express the heritability due to a specific locus (h^{*2}) in the following form:

$$h^{*2} = \sigma_G^2{}^*/\sigma_R^2 \times (1 + \sigma_G^2{}^*/\sigma_R^2)$$

and the overall heritability (h^2) as

$$h^2 = (\sigma_G^2{}^*/\sigma_R^2 + h_R^2)/(1 + \sigma_G^2{}^*/\sigma_R^2)$$

Where h_R^2 is the residual heritability (excluding the locus in question).
For an additive locus (d = 0)

$$h^2 = (2pq\,(a/\sigma_R)^2 + h_R^2)/(1 + 2pq\,(a/\sigma_R)^2)$$

and this expression has a maximum (h_{max}^2) when p = q = 0.5
The expression for a locus with complete dominance (d = a) is

$$h^2 = (4q^2(1 - q^2)(a/\sigma_R)^2 + h_R^2)/(1 + 4q^2(1 - q^2)(a/\sigma_R)^2)$$

and that for a recessive (d = −a)

$$h^2 = (4p^2(1 - p^2)(a/\sigma_R)^2 + h_R^2)/(1 + 4p^2(1 - p^2)(a/\sigma_R)^2)$$

These expressions have maxima at $p = 1 - \sqrt{\frac{1}{2}}$ and $p = \sqrt{\frac{1}{2}}$, respectively.
For alleles with initial frequencies (p_o) of 0.01 or 0.05, and initial heritability of h_I^2, we have equated the differences between h_{max}^2 and h_I^2 to either 0.10 or 0.25 and solved for $2a/\sigma_R$. This has been done for h_R^2 = 0, 0.25, 0.33 and 0.50 and the values are given in Table 6.

Literature

Avery, P.J.; Hill, W.G. (1977): Variability in genetic parameters among small populations. Genet. Res. 29, 193-213

Beardmore, J.A.; Lints, F.; Al-Baldawi, A.T.F. (1975): Parental age and heritability of sternopleural chaeta number in *Drosophila melanogaster*. Heredity 34, 71-82

Beardmore, J.A.; Shami, S.A. 1976: Parental age, genetic variation and selection. In: Population genetics and ecology (eds.: Karlin, S.; Nevo, E.), pp. 3-22. London: Acad. Press

Bulmer, M.G. (1976): The effect of selection on genetic variability: A simulation study. Genet. Res. 28, 101-117

Claxton, J.H. (1974): Some quantitative features of *Drosophila* sternite bristle patterns. Austr. J. Biol. Sci. 27, 533-543

Constantino, R.F.; Bell, A.E.; Rogler, J.C. (1967): Genetic analysis of a population of *Tribolium*. 1: Corn oil sensitivity and selection response. Heredity 22, 529-539

Crow, J.F.; Kimura, M. 1970: An Introduction to Population Genetics Theory. New York: Harper and Row

Durrant, A. (1974): The association of induced changes in flax. Heredity 32, 133-143

East, E.M. (1916): Studies on size inheritance in Nicotiana. Genetics 1, 164-176

Falconer, D.S. (1960): Introduction to Quantitative Genetics. Edinburgh: Oliver and Boyd

Falconer, D.S. (1977): Some results of the Edinburgh selection experiments with mice. In: Proc. Int. Conf. Quant. Genetics (Eds.: Pollak, E.; Kempthorne, O.; Bailey, T.B.Jr.), pp. 101-115. Ames: Iowa State Univ.

Felsenstein, J. (1965): The effect of linkage on directional selection. Genetics 52, 349-363

Fisher, R.A. (1918): The correlation between relatives on the supposition of Mendelian inheritance. Trans. Roy. Soc. Edinburgh 52, 399-433

Fisher, R.A. 1930: The Genetical Theory of Natural Selection. Oxford: Clarendon

Fowler, R.E.; Edwards, R.G. (1961): 'Midget', a new dwarfing gene in the house mouse dependent on a genetic background of small body size for its expression. Genet. Res. 2, 272-282

Frankham, R. (1974): The nature of quantitative genetic variation in *Drosophila*. 2: Average dominance of abdominal bristle polygenes. Austr. J. Biol. Sci. 27, 683-686

Frankham, R. (1977): The nature of quantitative genetic variation in *Drosophila*. 3: Mechanism of dosage compensation for sex-linked abdominal bristle polygenes. Genetics 85, 185-191

Frankham, R. (1980): The founder effect and response to artificial selection in *Drosophila*. In: Proc. Int. Sym. on Selection Experiments on Laboratory and Domestic Animals (ed.: Robertson, A.)

Frankham, R.; Briscoe, D.A.; Nurthen, R.K. (1978): Unequal crossing over at the rRNA locus as a source of quantitative genetic variation. Nature 272, 80-81

Frankham, R.; Briscoe, D.A.; Nurthen, R.K. (1980): Unequal crossing over at the rRNA tandon as a source of quantitative genetic variation in *Drosophila*. Genetics 95, 121-142

Frankham, R.; Jones, L.P.; Barker, J.S.F. (1968a): The effects of population size and selection intensity in selection for a quantitative character in *Drosophila*. 1: Short-term response to selection. Genet. Res. 12, 237-248

Frankham, R.; Jones, L.P.; Barker, J.S.F. (1968b): The effects of population size and selection intensity in selection for a quantitative character in *Drosophila*. 3: Analyses of the lines. Genet. Res. 12, 267-283

Fraser, A.; Miller, D.; Burnell, D. (1965): Polygenic balance. Nature 206, 114

Haldane, J.B.S. 1932: The Causes of Evolution. London: Longmans Green

Hollingdale, B. (1971): Analyses of some genes from abdominal bristle number selection lines in *Drosophila melanogaster*. Theor. Appl. Genet. 41, 292-301

Langley, C.H.; Smith, D.B.; Johnson, F.M. (1978): Analysis of linkage disequilibria between allozyme loci in natural populations of *Drosophila melanogaster*. Genet. Res. 32, 215-229

Latter, B.D.H. (1964): Selection for a threshold character in *Drosophila*. 1: An analysis of the phenotypic variance on the underlying scale. Genet. Res. 5, 198-210

Latter, B.D.H. (1965): The response to artificial selection due to autosomal genes of large effect. 1: Changes in gene frequency at an additive locus. Austr. J. Biol. Sci. 18, 585-598

Latter, B.D.H. (1966): The response to artificial selection due to autosomal genes of large effect. 3: The effects of linkage on the rate of advance and approach to fixation in finite populations. Austr. J. Biol. Sci. 19, 131-146

Lindsley, D.L.; Grell, E.H. (1968): Genetic variations of *Drosophila melanogaster*. Carnegie Inst. Wash. Publn. No. 627

Lindsley, D.L.; Sandler, L.; Baker, B.S.; Carpenter, A.T.C.; Denell, R.E.; Hall, J.C.; Jacobs, P.A.; Miklos, G.L.G.; Davis, B.K.; Gethmann, R.C.; Hardy, R.W.; Hessler, A.; Miller, S.M.; Nozawa, H.; Parry, D.M.; Gould-Somero, M. (1972): Segmental aneuploidy and the genetic gross structure of the *Drosophila* genome. Genetics 71, 157-184

Marlowe, T.J. (1964): Evidence of selection for the Snorter dwarf gene in cattle. J. Anim. Sci. 23, 454-460

Mather, K.; Harrison, B.J. (1949): The manifold effect of selection. I and II. Heredity 3, 1-52; 131-162

Mather, K.; Jinks, J.L. 1971: Biometrical Genetics (2nd ed.). London: Chapman and Hall

McBride, G.; Robertson, A. (1963): Selection using assortative mating in *Drosophila melanogaster*. Genet. Res. 4, 356-369

McMillan, I.; Robertson, A. (1974): The power of methods for the detection of major genes affecting quantitative characters. Heredity 32, 349-356

McPhee, C.P.; Robertson, A. (1970): The effect of suppressing crossing over on the response to selection in *Drosophila melanogaster*. Genet. Res. 16, 1-16

Milkman, R. (1978): Review of Proceedings of the International Conference on Quantitative Genetics. Science 200, 1261-1262

Piper, L.R. (1971): The isolation of genes underlying continuous variation. Ph.D. thesis. University of Edinburgh

Pollak, E.; Kempthorne, O.; Bailey, T.B. Jr. (eds.) (1977): Proc. Int. Conf. Quant. Genetics. Ames: Iowa State Univ.

Popper, K.R. (1972): The Logic of Scientific Discovery. London: Hutchinson

Reeve, E.C.R.; Robertson, F.W. (1954): Studies in quantitative inheritance. VI. Sternite chaeta number in *Drosophila*, a metameric quantitative character. Z. ind. Abst. Vererbungsl. 86, 269-288

Robertson, A. (1960): A theory of limits in artificial selection. Proc. Roy. Soc. (Lond.) B 153, 234-249

Robertson, A. (1966): Artificial selection in plants and animals. Proc. Roy. Soc. (Lond.) B 164, 341-349

Robertson, F.W.; Reeve, E.C.R. (1953): Studies in quantitative inheritance. IV. The effects of substituting chromosomes from different genetic backgrounds of *Drosophila melanogaster*. J. Genet. 51, 586-610

Sax, K. (1923): The association of size differences with seed-coat pattern and pigmentation in *Phaseolus vulgaris*. Genetics 8, 552-560

Sheridan, A.K.; Frankham, R.; Jones, L.P.; Rathie, K.A.; Barker, J.S.F. (1968): Partitioning of variance and estimation of genetic parameters for various bristle number characters of *Drosophila melanogaster*. Theor. Appl. Genet. 38, 179-187

Snedecor, G.W.; Cochran, W.G. 1967: Statistical Methods (6th Ed.). Ames: Iowa State Univ.

Thoday, J.M. 1977: Effects of specific genes. In: Proc. Int. Conf. Quant. Genetics pp. 141-159. Ames: Iowa State Univ.

Thompson, J.N. Jr.; Thoday, J.M. (1974): A definition and standard nomenclature for 'polygenic loci'. Heredity 33, 430-437

Thompson, J.N. Jr.; Thoday, J.M. (eds.) (1979): Quantitative Genetic Variation. New York; Acad. Press

Warwick, E.J.; Lewis, W.L. (1954): Increase in frequency of a deleterious recessive gene in mice. J. Hered. 45, 143-145

Wright, S. (1921): Systems of mating. Genetics 6, 111-178

Wright, S. (1931): Evolution in Mendelian populations. Genetics 16, 97-159

Wright, S. (1969): The theoretical course of directional selection. Amer. Nat. 103, 561-574

Received November 19, 1978
Accepted September 9, 1980
Communicated by J.S.F. Barker

Dr. R. Frankham
Mr. R.K. Nurthen
School of Biological Sciences
Macquarie University
North Ryde, New South Wales 2113 (Australia)