Genet. Res., Camb. (1966), **8**, *pp.* 347–360
With 3 text-figures
Printed in Great Britain

The limits to artificial selection for body weight in the mouse

I. THE LIMITS ATTAINED IN EARLIER EXPERIMENTS

By R. C. ROBERTS

A.R.C. Unit of Animal Genetics, Institute of Animal Genetics, Edinburgh, 9

(*Received* 21 *June* 1966)

1. INTRODUCTION

The expected pattern of response to artificial selection is well known—progress is made at an ever diminishing rate as the limit is approached asymptotically. Though deviations from this general form are frequently encountered in practice, as discussed by Falconer (1955), ultimately a stage is reached after which no further progress is made. This limit to selection will inevitably be met when all the alleles affecting the trait have been fixed in the population; in biometrical terms, the genetic variance will then have been exhausted. But the limit may be reached well before the point when the genetic variance is exhausted, and despite the fact that some loci are not fixed, selection may fail to change the mean value of the population any further. Such a contingency may arise if the selection favours individuals that are heterozygous at some loci, of if natural selection opposes the direction of the artificial selection.

In view of such uncertainties about the nature of the limit to selection, predictions about the length of time taken to reach the limit, and its ultimate level, become hazardous. Reviewing some experimental evidence from mice and *Drosophila*, Falconer (1960*a*) suggests that the response may be expected to continue for some twenty or thirty generations, producing a total divergence between strains selected for high and low expressions of the trait of the order of fifteen to thirty times the additive genetic standard deviation in the initial population, or ten to twenty times the phenotypic standard deviation. In a theoretical treatment of the subject, Robertson (1960) formulates his conclusions in terms of the effective population size, N. Robertson confirms Dempster's (1955) derivation that the total advance should equal $2N$ times the gain in the first generation, provided that the rate of fixation is low and provided also that the genes act additively. If dominance is involved, the total advance may be well in excess of this amount. Robertson shows also that half of the total gain should be achieved in not more than $1{\cdot}4N$ generations for genes that act additively, though the figure may rise to $2N$ generations for rare recessives. If the half-life of the selection process falls short of $1{\cdot}4N$ generations, Robertson suggests that the majority of alleles favourable to the direction of the selection will have been fixed in the population.

An important concept involved in a discussion of selection limits is this chance fixation of some unfavourable alleles in a selected line even though selection is directed against them. The probability that this may occur will obviously depend on the population size, and also on the selective advantage of the gene, or the intensity of selection in a quantitative situation. Kimura's (1957) treatment of chance fixation is extended by Robertson to show that the expected limit to selection based on individual measurements is a function only of the product Ni (where i is the intensity of selection, measured as the selection differential in phenotypic standard deviation units). As Ni increases, the probability diminishes that the less favourable allele at a locus is fixed during the course of selection.

A limitation on Robertson's theoretical treatment is that it is developed entirely in terms of the exhaustion of additive genetic variance. The study of selection limits is therefore still largely confined to the experimental investigation of particular cases. The present series of papers will report some long-term experiments on the limits to artificial selection for body weight in the mouse. This first paper reviews the limits attained in earlier selection programmes in this laboratory. Later papers will examine more closely the genetic nature of the limits, and will describe methods whereby further progress might be made.

2. MATERIAL AVAILABLE FOR STUDY

Seven selected strains of mice—four large and three small ones—were available for study in this laboratory. As far as can be judged, each strain had been selected to its limit for body weight, either high or low as the case may be. The designation of these strains, the number of generations of selection they had undergone prior to this study, and references to their original sources are all shown in Table 1. Briefly,

Table 1. *Strains selected to the limit for body weight*

Line	Generation reached prior to present study	Character selected	Reference
RCL	36	High 6-week weight	Falconer & King, 1953
NF	52	High 6-week weight	Falconer, 1953
CFL	31	High growth, 3–6 weeks	Falconer, 1960*b*
CRL	31	High growth, 3–6 weeks	Falconer, 1960*b*
MS	38	Low 6-week weight	MacArthur, 1949; King, 1950
NS	42	Low 6-week weight	Falconer, 1953
CFS	31	Low growth, 3–6 weeks	Falconer, 1960*b*

the origin of the various strains was as follows. *RCL* stemmed originally from a cross between Goodale's (1938, 1941) and MacArthur's (1944, 1949) large strains. The *NF* and *NS* strains both derived from a four-way cross of inbred lines. *CFL* and *CFS* were selected from a heterogeneous outbred base population, but one which contained *RCL* and had also some overlap with the *N* strains; *CRL* had an identical origin but was selected on a low plane of nutrition. *MS* stands for 'MacArthur's

Small', but is a slight misnomer. Dr MacArthur supplied nine males to this laboratory in 1948. These were crossed with females of three inbred strains. Some of the original males were available for three further backcrosses, though these matings were supplemented with some intercrosses. The result was a population 87% of whose genes derived from the original MacArthur strain, which formed a base population for further selection for small size.

In every case, the selection was within litters, to avoid some of the complications due to maternal effects in the interpretation of the results. The character selected was either the body weight of the mouse at 6 weeks of age or else the growth between 3 and 6 weeks. These two characters are scarcely distinguishable in terms of the ranking of the mice on the two measurements (Falconer, 1955), which enables us to discuss both sets of experiments within the same framework. The limits reached are examined empirically and in terms of Robertson's theory, with its extension by Hill (1965) and Hill and Robertson (1966).

3. RESULTS AND DISCUSSION

(i) *Empirical observations*

A summary of the responses to selection of the seven strains available in the laboratory is given in Figs. 1, 2 and 3. The mean weights are plotted against the number of generations of selection; in the present context, this is the most meaningful way to examine the results. The present analysis is confined to the limits ultimately reached. We are not concerned here with the patterns of the response nor with other features discussed in the original publications. However, some points that have arisen since those publications are relevant to the present discussion. Figure 1 is straightforward, but Fig. 2 presents a complication. There was a decline in weight of the *CFL* line between generation 19 and generation 27, and no ready explanation is available. It is too great to dismiss as an accident of sampling, and as the other two selected lines in the same figure were mated contemporaneously with *CFL*, a general environmental trend cannot be invoked. For whatever reason, the outcome was that the *CFL* ultimately reached a level not much above its origin. However, the decline in the *CFL* line assumes less significance when compared to the precipitous fall in weight of the *RCL* line, shown in Fig. 3. Between generations 19 and 24, the mean weight dropped by no less than 16 g., despite continued selection for large size. Although there was some recovery in later generations, the *RCL* line never again achieved its previous high weights, and provides a second instance of a selected line ending up more or less where it began. Newman (1960) investigated the rise and fall of the *RCL* line in some detail. He carefully excluded the possibility of an accidental outcross to a smaller line and, by comparing expected and realized selection differentials, he failed to establish that there was any natural selection against large size over this period. In fact, the magnitude of the decline is not amenable to any reasonable genetic interpretation, and Newman was forced to postulate the imposition of some environmental stress, possibly an unidentified pathogen, that was highly specific to the *RCL* line. Nevertheless, whatever the

cause, a genetic change of an unfavourable kind was brought about, otherwise the line should ultimately recover its previous level. From Fig. 3, it can be seen that the supposition of eventual recovery would, at best, invite scepticism.

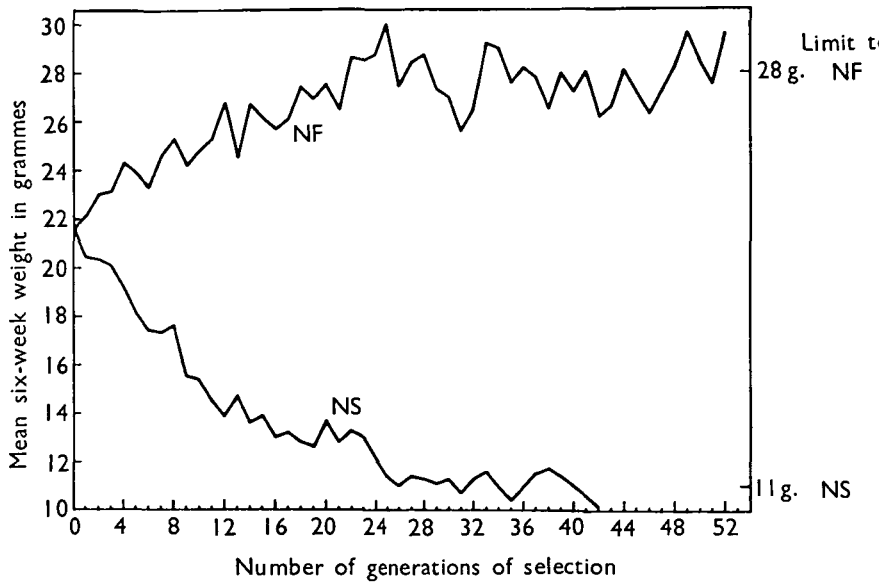

Fig. 1. Responses to selection for body weight. The limits attained in selected lines first reported by Falconer (1953).

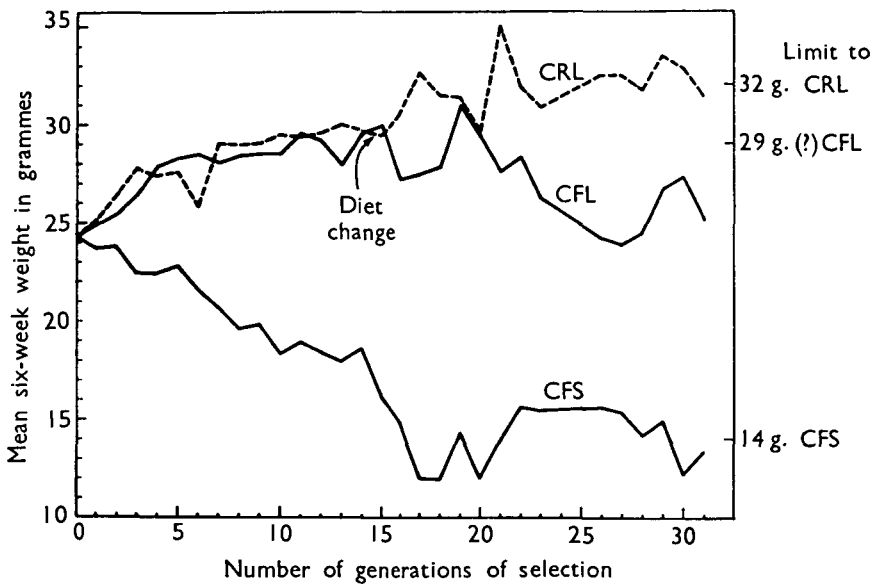

Fig. 2. Responses to selection for growth. The limits attained in selected lines first reported by Falconer (1960*b*). *CRL* was selected on a restricted diet for fourteen generations, but the weights shown were for animals measured on a normal diet. Only the criterion of selection changed at the point marked 'diet change'.

https://doi.org/10.1017/S001667230001020X Published online by Cambridge University Press

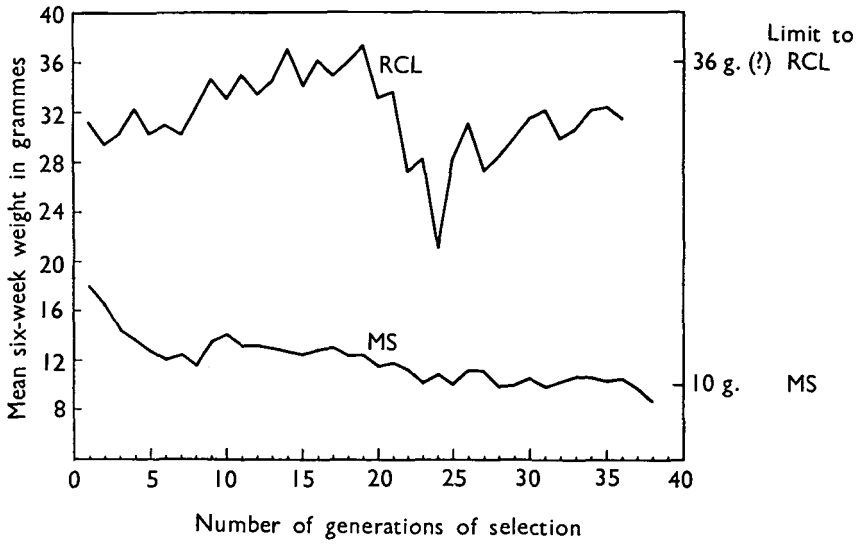

Fig. 3. Responses to selection for body weight. Upper graph: the limit attained in selected line first reported by Falconer & King (1953). Lower graph: the limit attained in selected line first reported by MacArthur (1944, 1949) and reconstructed by King (1950).

The picture that emerges from all this is that, at the limit, lines of mice selected for large size tend to be rather unstable. At the very least, we cannot regard the attainment of a steady state at the limit as an inviolable rule. Even the *NF* line, which shows the clearest pattern, is inclined to oscillate rather violently between higher and lower weights, although over a longer period no discernible trend is apparent. This is also a feature of one of the small lines (*CFS*). For this reason, it becomes extremely difficult to decide what mean weight we are prepared to regard as 'the limit', and quite impossible to decide at what exact point in time this limit was reached. As a rough guide, some weights have been marked on the right-hand sides of Figs. 1, 2 and 3, showing the approximate limits reached. The weights shown were derived quite subjectively, by averaging to the nearest gramme the mean weight over the period during which the line concerned was at its highest or lowest, as appropriate, and showed no obvious trend. It is fortunate perhaps that for present purposes, any more precise estimates would have served no purpose. The question marks after the limits shown for *RCL* and *CFL* are there for reasons that are all too obvious; the limits marked correspond to what looked like the limit before these lines declined.

In similar fashion, the time taken to reach the limit has been taken rather arbitrarily as the generation that first exceeded the level of the limit. If we think of the hypothetical smooth curve approaching an asymptote, it can be appreciated that accidents of sampling will tend to make the criterion an underestimate of the number of generations required. However, in the absence of a clear alternative, we shall accept this estimate, bearing in mind that it is probably biased downward.

The level of the limit in absolute terms is less interesting than the magnitude of

the response in terms of the variance in the base population before any selection was practised. The most informative way of looking at the response is in 'standard units', i.e. as multiples of the original standard deviation. Falconer (1955) gives the requisite information for the *NF* and *NS* lines; the phenotypic standard deviation was 1·9 g., while the additive genetic standard deviation was 0·9 g. The corresponding figures for the *C* stocks were 2·3 g. and 1·3 g.; these values were calculated from data on the base population kindly provided for me by Dr Falconer.

The results derived by these admittedly somewhat crude methods are presented in Table 2. The *RCL* and *MS* lines, by the nature of their origin, mentioned earlier, represent a situation totally different from the other five lines. Their mean levels

Table 2. *Limits reached by selected lines of mice*

Line	Limit in grammes	Generations to reach limit	Response		
			Grammes	$/\sigma_P$	$/\sigma_A$
RCL	36	14	4·8	—	—
NF	28	22	6·4	3·4	7·1
CFL	29	11	4·7	2·0	3·6
CRL	32	17	7·7	3·3	5·9
MS	10	28	8·0	—	—
NS	11	26	10·6	5·6	11·8
CFS	14	17	10·3	4·5	7·9

The last two columns evaluate the response as multiples of σ_P and σ_A respectively, where σ_P is the phenotypic standard deviation in the base population, and σ_A is the additive genetic standard deviation.

are presented for comparison with the other lines with a shorter history of selection, but beyond that they cannot be discussed in the same context. The apparent response of the *MS* is false in any event; most of it occurred during the first few generations and represents the repeated backcrosses after an outcross as mentioned previously.

Table 2 permits some empirical statements about the limit to artificial selection for body weight in the mouse at 6 weeks of age. It is emphasized that this is a well-defined character and that the experiments were all conducted in the same laboratory over much the same period of time. The outcome was that superficially, different experiments were in broad qualitative agreement with each other. Some large mice were developed that had mean weights in the region of 30 g., while the small mice ceased to respond around 12 g., give or take a gramme or two at both levels. Yet, when these separate lines are examined more closely in terms of the limits reached, some important differences emerge. Firstly, the response may continue for anything, it seems, between ten and thirty generations. On a temporal scale, this represents for the mouse a range from, at best, 2 years to, at worst, 8 years. Translating the result to domestic livestock, where the generation interval may well exceed 2 years, this range assumes far greater importance. It becomes desirable, therefore, to scan the base populations for reliable correlates of the duration of the

response, and to evaluate the effects of such correlates on the limit ultimately reached. Unfortunately, excluding the irrelevant cases of *RCL* and *MS*, the lines discussed here were derived from two base populations only, and correlations based on only two points do not engender much faith. But for what they are worth, the following observations can be made from Table 3, which derives largely from the

Table 3. *Duration of response in relation to variances in base populations*

Lines	Generations to reach limits	Base population			Response	
		σ_P	σ_A	h^2	$/\sigma_P$	$/\sigma_A$
C	15	2·3	1·3	0·31	3·3	5·8
N	24	1·9	0·9	0·22	4·5	9·5

σ_P and σ_A are defined in legend of Table 2. h^2 is the heritability $= \sigma_A^2/\sigma_P^2$.

arithmetical means of some quantities presented in Table 2, and the information given previously about the base populations. The *C* lines reached the limit in less time than the *N* lines, and the base population of the *C* lines showed larger variances and a higher heritability. Since such a population would be preferred for selection purposes anyway, there is no incompatibility of objectives on this score. However, by virtue of the longer time taken to reach the limit, the final response of the *N* lines was just as impressive as that of the *C* lines, suggesting that their lower genetic variance had somehow been utilized more effectively. The material on which these observations are based is too tenuous to warrant further speculation, especially as other variables affect the limit attained. But it may serve to focus attention on the kind of information that is required.

A final point on the duration of the response is that no differences appear between large and small mice in this respect. The differences that were observed seem to be associated entirely with features of the base populations.

In terms of the variances in the base populations, it appears from Table 2 that the final response may amount to between two and six times the phenotypic standard deviation, and anything between three and twelve times the additive genetic standard deviation. These values were calculated for the response in one direction only. For the total divergence in two-day selection, values for corresponding high and low lines should be added together. When this is done, it puts the *C* lines, especially, slightly lower than the bottom of the range suggested by Falconer, quoted earlier.

The results obtained from the selection experiments discussed in this section must now be examined against the theoretical considerations outlined earlier.

(ii) *Theoretical considerations*

The theory of limits (Robertson, 1960; Hill, 1965; Hill & Robertson, 1966) outlined earlier frames its conclusions in terms of the effective size (N) of the population. We must therefore estimate the effective sizes of the populations under discussion.

The number of matings used to propagate the stocks during selection was not constant from generation to generation. Some of the variation was deliberate, as different numbers of mice were required for different phases of the experiments. Most of the variation, however, was attributable to some sterility, which is a common feature of all selected stocks. The procedure under such circumstances is quite straightforward. The effective number is given by the harmonic mean of the number of individuals that contributed to the succeeding generation. The results for the seven lines are shown in Table 4.

Table 4. *Half-life of selection responses*

Line	Effective number N	Half-life (generations)	Values of $Ni\alpha$ $p=0{\cdot}5$	0·25	0·1
RCL	19·0	$9=0{\cdot}47N$	—	—	—
NF	14·5	$8=0{\cdot}55N$	6	8	(10)
CFL	15·8	$4=0{\cdot}25N$	10	14	20
CRL	16·8	$7=0{\cdot}42N$	7	9	12
MS	19·5	$4=0{\cdot}21N$	—	—	—
NS	14·6	$9=0{\cdot}62N$	4	5	(8)
CFS	18·8	$10=0{\cdot}53N$	5	7	10

p is the frequency in the base populations of genes favourable to the direction of the selection. Values of 0·1 were not possible for the *NF* and *NS* lines, from the method of their construction.

It was mentioned earlier that the method of selection adopted was in all cases within families. It is well known that in idealized populations, this practice ought to double the effective number; each family contributes two individuals as parents for the next generation, which reduces to zero the variance between families in their contribution. However, mouse stocks always show some sterility, and to obtain the requisite number of matings, some families (and especially the larger ones) will contribute more than two individuals as parents for the next generation. It becomes imperative then to determine how these complications should be accommodated to estimate the effective number. The proper approach under such circumstances is to compute from pedigrees the inbreeding coefficient accumulated during the selection. If the inbreeding coefficient after t generations is F_t, then the formula

$$F_t = 1-\left(1-\frac{1}{2N}\right)^t$$

can be solved to give the effective number, N. I am indebted to Dr D. S. Falconer for kindly providing me with some inbreeding coefficients he had calculated for the *NF* and *NS* stocks. The effective numbers, as established by this accurate method, compare with the estimates from the harmonic mean over the same period as follows:

Stock	Generations	Effective number from inbreeding coefficients	Harmonic mean
NF	26	14·9	13·1
NS	22	14·3	13·6

https://doi.org/10.1017/S001667230001020X Published online by Cambridge University Press

It is seen that the harmonic mean provides an estimate that is only slightly lower than the accurate calculation, whereas in idealized populations one should be half the other. This does not imply that the within-family method of selection did not increase the effective number over what it would have been with, say, mass selection. Without regard to the representation of as many families as possible, variation in fertility and viability leads to an effective number much lower than the supposed number of parents.

As the N stocks did not appear to differ much from the others with respect to fertility and ease of maintenance, we shall accept the harmonic mean of the number of parents as being a sufficiently accurate estimate of the effective number for all the stocks. It is possibly a slight underestimate of the true value, but any error that may be involved is not sufficient to affect grossly any conclusions that we may draw.

We shall now examine the half-life of the selection response in terms of the effective population size. The half-life was estimated in a manner identical to that explained in connexion with the total response. In this case, the half-life was taken as the generation whose mean first exceeded one-half of the total response. Again, this will tend to underestimate the true value. The results, tabulated in Table 4, reveal that half of the response was obtained in most cases by about $\frac{1}{2}N$ generations, whereas the value expected when the chance of fixing an unfavourable allele is not high varies at most from N to $2N$ generations, as shown by Robertson (1960). The implication of this low value of half-life, in the context of a study of selection limits, is that all of the alleles favourable to the direction of the selection should have been fixed. Should it turn out that a less favourable allele has been fixed, then the disparity between the value of $\frac{1}{2}N$ and the range quoted by Robertson is such that we may safely infer that some process other than fixation is operative in the determination of the limit reached.

The values obtained for the half-life of the selection process lead directly to two other estimates that are of some consequence in quantitative genetics. The first reflects the order of magnitude of the effect of the individual genes involved in the response to the selection. The second provides some estimate of the number of 'loci' or effective factors which are concerned in the process. This number of course estimates only those loci which happen to be segregating in that particular population. Though these estimates are by their nature imprecise, they cover an area where but little knowledge is available, especially for mammals.

The procedure for estimating the gene effects and the number of loci is most easily derived as follows. It can be shown (Robertson, 1960, as developed by Hill, 1965) that a half-life of a given magnitude corresponds to a limited range of values of $Ni\alpha$. N, the effective population size, has been discussed already; i is the intensity of selection, and tabulated values in terms of the proportion of animals selected are widely available; α is the average proportionate effect of the genes:

$$\alpha = \frac{a}{\sigma_P}$$

https://doi.org/10.1017/S001667230001020X Published online by Cambridge University Press

where a is defined as the difference in value between the two homozygotes, and σ_P is the phenotypic standard deviation.

Now, the exact value of $Ni\alpha$ corresponding to a certain half-life depends somewhat on the gene frequencies in the base population. Some graphs are provided by Hill & Robertson (1966), and by interpolation, values corresponding to the appropriate half-life and specified gene frequencies may be obtained. Such values, for gene frequencies of 0·5, 0·25 and 0·1 in the base populations, are entered in Table 4. The *RCL* and *MS* lines are ignored since their previous history excludes them from being subjected to the present treatment. The values for the *NF* and *NS* lines corresponding to a gene frequency of 0·1 are entered in parentheses, since frequencies lower than 0·25 were impossible in this stock from the method of its construction.

Thus, having estimated $Ni\alpha$, we may now derive α, since N and i are observable quantities. N is given in Table 4, and i for the selected lines described here was always close to 1·0. This value was ascribed to all lines, being quite accurate enough for present purposes. However, the value of α so obtained must be adjusted to allow for the fact that the selection was, in all cases, based on deviations from the means of full-sib families. The selection therefore operated on only half of the additive genetic variance in the population, and the corresponding phenotypic variance is that within families (σ_w^2). The definition of α must therefore be modified appropriately:

$$\alpha = \frac{a}{2\sigma_w}$$

Since we still want to derive the proportionate effect of the genes on a population basis, let

$$k = \frac{\sigma_w}{\sigma_P}$$

Then, the proportionate effect of the genes (a/σ_P) is given by:

$$\frac{a}{\sigma_P} = 2k\alpha$$

Values of k were calculated for the base populations from data kindly supplied by Dr D. S. Falconer. These were employed to estimate the proportionate effects.

Now, to estimate the number of loci involved in the response, we need to consider the within-family heritabilities (h_w^2), published for the N stocks by Falconer (1955) and for the C stocks by Falconer (1960*b*). Values for the high and low lines were averaged, and the average taken to apply to the base population. Each locus, in the terms outlined above and in a within-family selection programme, contributes $\frac{1}{4}a^2p(1-p)$ to the additive genetic variance, where p is the gene frequency. If we make the assumption that each of the loci involved contributes equally to the genetic variance, then

$$h_w^2 = \frac{na^2p(1-p)}{4\sigma_w^2}$$

https://doi.org/10.1017/S001667230001020X Published online by Cambridge University Press

where n is the number of loci contributing to the response. By rearranging the expression derived, we obtain

$$n = \frac{4\sigma_w^2 h_w^2}{a^2 p(1-p)}$$

$$= \frac{h_w^2}{\alpha^2 p(1-p)}$$

Since α and h_w^2 have already been determined, this enables us to estimate the number of loci by substituting various values for the initial gene frequency.

The estimates of the average proportionate effects of the genes and the number of loci concerned are shown in Table 5, for the five lines to which the procedure was

Table 5. *Proportionate effects of genes and number of loci*

		Proportionate effect (α)			Number of loci		
Line	h_w^2	$p=0{\cdot}5$	0·25	0·1	$p=0{\cdot}5$	0·25	0·1
NF	0·35	0·57	0·76	(0·95)	8	6	8
CFL	0·33	1·03	1·46	2·08	3	2	2
CRL	0·33	0·59	0·79	0·98	10	8	10
NS	0·35	0·37	0·47	(0·76)	19	16	13
CFS	0·33	0·44	0·61	0·87	18	13	13

h_w^2 is the realized heritability within litters.

applied. Over the range of gene frequencies considered, the estimated number of so-called loci does not very much, since $p(1-p)$ diminishes as α^2 increases. But above a gene frequency of 0·5, both would tend to diminish together, leading to successively lower values for the number of loci, though $Ni\alpha$ (and therefore α) does not alter much over this range.

The estimates shown in Table 5 are not given with any pretensions about their numerical accuracy. Rather, they serve as indicators of the order of magnitude of the effects with which we are dealing. By and large, however, the five lines have produced reasonably consistent answers. They seem to indicate that the average difference between the two homozygotes at a locus produces an effect usually in the region of a half to one phenotypic standard deviation, and that this corresponds to a total of up to twenty loci in the base population contributing to the response to selection. If some of the estimates of the number of loci appear to be low, it should be noted that any violation of the basic assumptions biases the estimate downwards. The fact that the lines selected for small size appear to have more loci contributing to the response does not arouse much curiosity. Directional dominance favours large size in the mouse. If selection is for the dominant genes, this leads to a shorter half-life, a higher value of $Ni\alpha$ and thus to a lower estimate of the number of genes, if other factors remain constant.

The estimates obtained of the proportionate effect of the genes and the number of loci involved perhaps serve three purposes. Firstly, they can be compared with some other meagre evidence on the same topic. For instance, Falconer (1960*a*) gives estimates derived by an alternative (though related) approach for some traits in both mice and *Drosophila*; his figures for 6-week weight in the mouse are of the same order of magnitude as the ones given here. Secondly, the estimates reveal no basic incompatibility between the parameters of the base populations and the responses actually obtained. And lastly, they lend some experimental support to the theoretical considerations developed by Robertson and by Hill.

4. CONCLUSIONS

This survey of previous selection experiments for body weight indicates to within a fairly narrow range the limits that can be expected, under the conditions of our laboratory, when selection is applied to a heterogeneous population. It seems that the upward response reaches its limit around 30 g. while the downward response ceases in the region of 12 g. or so, on average. The most extreme cases found were a high line limit of 32 g. (unless we invoke the transient glory of the *RCL* line before its mysterious decline) and a low line limit of 10 g. These figures set standards for further experimental attacks on the limits.

What is also of relevance in this context is that from theoretical considerations, we have been able to exclude almost completely the idea that the limits were set by the chance fixation of unfavourable alleles at the loci that were segregating in the base populations. Bearing in mind Robertson's (1960) derivation of the relationship between the half-life and the chance of fixation, the values observed for the half-life were sufficiently small to accommodate some margin of error in their estimation and still make the above statement valid. In other words, the selection as practised seems to have accomplished what it could reasonably be expected to accomplish, given these populations. A contribution to this end was undoubtedly the fact that the proportion of animals selected (about one-third) was close to the optimum, from the point of view of achieving the greatest possible advance. Robertson (1960) establishes that the maximum gain corresponds to a proportion selected of one-half; however, as the number of animals measured rises to 50 or so (as it did in the experiments discussed in this paper) the plot of limit against proportion selected becomes very flat topped, and the loss of potential gain by selecting only a third of the measured animals is but barely detectable. Fortuitously perhaps, the experiments discussed here seem to have featured high initial responses to selection without a sacrifice of ultimate gain, if we can safely conclude that unfavourable alleles have not been fixed. To combine these two objectives appropriately is a problem in practice, and one that has proved intractable to theoretical treatment.

The experiments reviewed in this paper seem to agree reasonably well with a model of selection limits based on the exhaustion of the additive genetic variance. It is emphasized however that this does not necessarily establish that model as the exclusive explanation of the phenomena. The genetic nature of the limits can be exposed to experimental investigation, as discussed in the next paper in the series.

SUMMARY

1. The results of some selection experiments for body weight in the mouse, conducted in the past in this laboratory, have been examined from the point of view of the limits ultimately reached.

2. The limits that are apparently attained do not necessarily remain stable over prolonged periods of time; two large lines showed marked decreases despite continued selection for high body weight.

3. Selection for high body weight reached a limit in the region of 30 g. at 6 weeks of age; small mice reached their limit at around 12 g.

4. The time taken to reach the limit may vary from ten to thirty generations, even for this one trait.

5. The total response for unidirectional selection was between two and six times the phenotypic standard deviation, or three to twelve times the additive genetic standard deviation.

6. Consideration of the half-life of the selection responses excluded the likelihood of the chance fixation of alleles unfavourable to the direction of selection.

7. The loci contributing to the response could each have an effect amounting to anything from one-half to one phenotypic standard deviation in the base population.

8. This indicated that up to twenty loci had contributed to the response.

9. The intensity of selection practised was close to the optimum for obtaining the maximum total response.

10. The rule of parsimony would indicate the exhaustion of the additive genetic variance as an adequate explanation of the limits attained.

I should like to acknowledge the profit and pleasure of discussions with Drs D. S. Falconer, Alan Robertson and W. G. Hill on various issues that arose during the preparation of this manuscript.

Dr Falconer kindly provided me with data to supplement his original publications. This facilitated greatly the examination of several points.

REFERENCES

Dempster, E. R. (1955). Genetic models in relation to animal breeding problems. *Biometrics*, **11**, 535–536.

Falconer, D. S. (1953). Selection for large and small size in mice. *J. Genet.* **51**, 470–501.

Falconer, D. S. (1955). Patterns of response in selection experiments with mice. *Cold Spring Harb. Symp. quant. Biol.* **20**, 178–196.

Falconer, D. S. (1960*a*). *Introduction to Quantitative Genetics*. Edinburgh and London: Oliver & Boyd, Ltd.

Falconer, D. S. (1960*b*). Selection of mice for growth on high and low planes of nutrition *Genet. Res.* **1**, 91–113.

Falconer, D. S. & King, J. W. B. (1953). A study of selection limits in the mouse. *J. Genet.* **51**, 561–581.

Goodale, H. D. (1938). A study of the inheritance of body weight in the albino mouse by selection. *J. Hered.* **29**, 101–112.

Goodale, H. D. (1941). Progress report on possibilities in progeny-test breeding. *Science, N.Y.* **94**, 442–443.

HILL, W. G. (1965). Studies on artificial selection. Ph.D. Thesis, University of Edinburgh.
HILL, W. G. & ROBERTSON, A. (1966). The effect of linkage on limits to artificial selection. *Genet. Res*, **8**, 269–294.
KIMURA, M. (1957). Some problems of stochastic processes in genetics. *Ann. math. Statist.* **28**, 882–901.
KING, J. W. B. (1950). Pygmy, a dwarfing gene in the house mouse. *J. Hered.* **41**, 249–252.
MACARTHUR, J. W. (1944). Genetics of body size and related characters. I. Selecting small and large races of the laboratory mouse. *Am. Nat.* **78**, 142–157.
MACARTHUR, J. W. (1949). Selection for small and large body size in the house mouse. *Genetics*, **34**, 194–209.
NEWMAN, J. A. (1960). Reciprocal recurrent selection for body size in the mouse. Ph.D. Thesis, University of Edinburgh.
ROBERTSON, A. (1960). A theory of limits in artificial selection. *Proc. R. Soc.* B, **153**, 234–249.