DIRECT RESPONSE TO SELECTION FOR POSTWEANING GAIN IN THE RAT¹

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ABSTRACT

The effectiveness of selection for 3-9-week gain was examined in a population of rats with a history of past selection for high 3-9-week gain. Lines were selected for high (U line) and low (D line) 3-9-week gain with two replicates of each line. Two randomly selected lines were also kept, one originating from the same base population as the two selected lines (R line) and the other originating from a population that had been randomly mated for the previous 27 generations (C line). Two replicates of each of these lines were kept. After seven generations of selection, a randomly selected line (relaxed line) was formed from each of the two upward- and each of the two downward-selected lines. Results have been presented for 13 generations of selection. The environmental trend for 3-9-week gain, as indicated by the randomly selected R and C lines, was consistently negative in all four lines. Realized heritabilities calculated by deviating the response to selection from the trend in the R or C lines resulted in non-significantly higher values in the D lines than the U lines. Six generations of relaxation of selection indicated no effect of natural selection in the U lines or the D lines. The relative magnitude of the drift, error and common environmental variances were estimated by the methods given by HILL (1971). The estimates of these parameters then led to calculation of the degree of bias in the sampling variances of the realized heritability estimates. As was predicted by HILL (1971), estimates of the variance of realized heritabilities obtained by using standard regression techniques were less than those obtained using HILL's formulae. The results are discussed in relation to other similar studies with rats and mice.

SELECTION for weight or weight gain has been studied by a number of workers using the laboratory mouse as the experimental animal. ROBERTS (1965) reviewed this work with particular attention to the contributions of these studies to animal breeding research. These studies have provided valuable experimental information on selection response and selection theory.

In contrast to the laboratory mouse, the laboratory rat is a mammal which has been used by only a few workers to investigate selection response for weight or weight gain (PARK *et al.* 1966; BAILEY *et al.* 1970; ROUBICEK and RAY 1971).

The objective of this study was to investigate response to selection for post-

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weaning gain in a population of rats with a history of past selection for the same trait. The extent to which these results are in agreement with results obtained from selection with other laboratory species, particularly the mouse, will provide a broader base for generalization of selection theory to domestic animals. This paper reports the direct response to selection for both high and low postweaning gain, with particular emphasis on methods of estimation of the sampling variance of realized heritability estimates.

MATERIALS AND METHODS

The animals used in this selection experiment came from a line of rats previously selected for increased postweaning gain from 3 to 9 weeks of age on a standard diet (about 22% protein fed *ad libitum*) as part of a genotype-environment interaction study (PARK *et al.* 1966). The foundation stock for the first study was formed by crossing four highly inbred lines of rats. Details of the origin of these inbred lines and of the crossing procedure are given by PARK *et al.* (1966). After 16 generations of mass selection the line was maintained by random selection (relaxed selection) for 10 generations (FFR line) before the present study was undertaken.

Six lines were formed from the FFR line at generation 27. Two lines were selected for increased 3-9-week gain (U lines), two lines for decreased 3-9-week gain (D lines), and two lines for continued random selection (R lines). Throughout the previous 26 generations a control line, which had originated from the original four-way cross, had been maintained by random selection. From this population two control lines (C lines) were formed in generation 27 and were continued as randomly selected lines. For the purposes of this report generation 27 has been called generation 0. Eighteen single-pair matings were made in each of these lines up to generation 7. Four additional lines were formed in generation 7. From each of the two U lines one relaxed line was formed (UR lines), with selection at random, and one relaxed line was also formed from each of the D lines (DR lines). This increase in number of lines at generation 7 necessitated a reduction in the number of pairs of rats mated per line from 18 to 15 pairs.

Selection was on the basis of individual postweaning gain from 3 to 9 weeks of age. Either 15 or 18 rats (about 45% to 55% of the population), with the highest or lowest gain in each sex, were selected in each generation for single-pair matings in each selection line. The C and R lines were selected at random within sexes and then single-pair mated. In all lines, selection was carried out in the first litters with the restriction that no more than two individuals of each sex be selected from each family. This restriction was an attempt to keep inbreeding to a minimum. Males and females were mated monogamously and at random with the restriction, also to avoid inbreeding, that if possible, no pair should have any grandparents in common. In generation 11 the selection procedure was modified to select 7 males and 14 females in each line. One male was then mated to two females with the same restrictions as above. This mating procedure was an attempt to estimate the sire and dam components of variance from a hierarchical analysis of variance. Due to poor fertility in this mating, the limited data obtained did not yield any meaningful results.

The litter size was reduced or increased (by transfer from litters born the same day and if possible from the same line) to six at one day after birth with a sex ratio as close as possible to 3 males and 3 females. Rats transferred into a litter to make it up to six were discarded at weaning. The young were weaned at 3 weeks of age, at which time all lines were randomly assigned to cages on a within-sex basis, with six rats per cage. The restriction was made that no more than two rats from any one family should be reared in the same cage. The data collected each generation were: litter size at birth, litter weight at 2 weeks of age, individual weights at 3, 6, and 9 weeks of age, and the proportion of females pupping out of the total number exposed to males. Males were left with the females for a 3-week mating period.

TABLE 1
Average selection differentials per generation for 3-9-week gain for male and female rats from generation 27 to 37*

Line	Selection differential		Weighted† selection differential		Expected§ selection differential		Actual¶ selection differential	
	♂	♀	Av.†	Av.†	♂	♀	♂	♀
U1	13.2 (2.0)	7.9 (1.3)	10.6 (1.4)	10.7 (1.6)	0.68 (0.07)	0.69 (0.08)	0.57 (0.09)	0.58 (0.08)
U2	10.7 (2.0)	6.4 (1.1)	8.6 (1.4)	8.9 (1.3)	0.62 (0.10)	0.65 (0.09)	0.53 (0.09)	0.56 (0.09)
D1	-11.0 (1.6)	-6.9 (0.9)	-8.9 (1.2)	-8.4 (1.3)	0.49 (0.08)	0.73 (0.08)	0.64 (0.09)	0.61 (0.07)
D2	-12.9 (1.4)	-6.6 (0.5)	-9.9 (0.9)	-9.9 (0.8)	0.58 (0.06)	0.73 (0.08)	0.78 (0.07)	0.57 (0.06)
R1	-2.1 (1.3)	0.0 (0.4)	-1.0 (0.6)	-0.6 (1.0)	—	—	-0.90 (0.05)	0.0 (0.01)
R2	0.8 (1.0)	-0.1 (0.5)	0.4 (0.6)	1.1 (1.0)	—	—	0.04 (0.03)	0.01 (0.03)
C1	0.5 (1.0)	-0.3 (0.6)	0.1 (0.6)	-0.1 (0.8)	—	—	0.02 (0.04)	0.0 (0.03)
C2	0.4 (0.7)	0.0 (0.7)	0.2 (0.5)	0.2 (0.9)	—	—	0.03 (0.02)	-0.02 (0.03)

* Figures in parentheses are standard deviations of the mean. All values in grams except the last six columns.

† Average of the two sexes.

‡ Selection differential weighted by the numbers of progeny alive at 9 weeks of age.

§ Taken from Table 2 in *Manual of Procedures in Quantitative Genetics* (BECKER 1967). Selection differentials in standard deviation units. Based on the selection intensity which averaged about 50%.

¶ Selection differentials in standard deviation units.

RESULTS

Selection differentials: Average selection differentials per generation from generation 0 to 10 are presented in Table 1. In the selected lines (the U and D lines) the absolute selection differentials applied were larger in males than in females. This was a function of the larger variance of 3–9-week gain in males than in females. The selection differentials actually applied in standard deviation units were about the same in males and females. The selection differentials in the randomly selected lines (the R and C lines) were expected to be zero and the selection differentials actually applied in these lines were not significantly different from zero. In the U1 and U2 lines the expected and observed standardized selection differentials were not significantly different. But in the D1 and D2 lines the observed selection differentials applied were less than expected in females and more in males, suggesting that the distribution of 3–9-week gains in the survivors of these lines may not have conformed to a normal distribution.

In all lines the absolute selection differential and the selection differential weighted by the number of progeny alive at 9 weeks of age were in good agreement. Thus there was no evidence of any positive association between 3–9-week gain of the parents and their productivity (number of young raised to 9 weeks of age). Although litter size was standardized to six at one day after birth, selection differentials, weighted by the number of progeny alive at birth, were also calculated, but are not shown in Table 1 since they were similar to the weighted values shown. Thus there was no evidence for any differential fertility between different phenotypes for weight gain. 'Natural' selection (FALCONER 1960a), evaluated by the difference between absolute and weighted selection differentials, was not of importance in any of the lines in this study.

The number of males selected in each line in generation 11 was halved so that selection differentials for males were about twice that of females. For this reason these values were not averaged with the previous generations. In generation 12 there was a larger proportion than usual of mated pairs not pupping in the U, D and R lines. In both the males and females in the D2 line and in the males in the R2 line there was some evidence of natural selection acting. This evidence was that rats that actually produced progeny in these lines were the heavier rats of those selected. That is, the weighted selection differentials were greater than the selection differentials originally applied.

Response to selection: The response to selection for 3–9-week gain is shown graphically for all lines in Figure 1. The positions of the lines in generation 12 from the highest to the lowest gain are: U1, U2, R1, R2, C2, C1, D1, D2. Disregarding the C and R lines, there was a significantly greater response to selection downward than upward.

The regressions of population means (unweighted means of both sexes) for 3–9-week gain on generation number over generations 0 to 12 were $1.59 \pm .49$ in the U1 line, $1.07 \pm .51$ in the U2 line, $-2.83 \pm .53$ in the D1 line, and $-3.75 \pm .52$ in the D2 line. Similar regressions for the R1, R2, C1 and C2 lines were: $-.74 \pm .46$, $-.52 \pm .45$, $-1.24 \pm .40$ and $-.52 \pm .49$, respectively. Although

FIGURE 1.—Unweighted means of the sexes for 3-9-week gain for all lines plotted against generation number.

there was a consistent decline in generation means in both R and both C lines, this decline was significantly different from zero in the C1 line only ($P < 0.01$). FISHER (1938) presents a method which may be used to test whether these four independent estimates of the trend in the generation means in the R and C lines indicate an overall significant trend. Applying this test it was found that the probability of all four of these trends downward occurring by chance was less than 0.05. The control lines could have shown this negative trend due to genetic drift combined with genotype by environment interactions. But the similarity of the trend in both lines suggests that some sort of systematic environmental effects were primarily responsible. Similar deductions also apply to the two relaxed lines except that, because of the past history of selection for large 3-9-week gain in these lines, they could also be declining due to the effects of natural selection acting on phenotypes which have been produced by this artificial selection or because of an "epistatic decay" effect (GRIFFING 1960). But the consistency of the fluctuations of the mean 3-9-week gain from generation to generation for all lines (selected and randomly bred) would seem to support the view that these were systematic environmental effects.

To evaluate the response to selection in the U and D lines, adjusted for this negative "environmental trend," analysis of variance of the data plotted in Figure 1 is presented in Table 2. These data are also shown graphically in Figures 2 and 3, where the response to selection for all lines is shown as a deviation from the mean of the R lines. The component of most interest in this analysis is the generation by line interaction term which was partitioned into the 3 degrees of

TABLE 2

Analysis of variance of the response to selection for 3-9-week gain (grams)†

Source	df	M.S.
Lines (L)‡ A	1	8493**
B	1	166
C	1	249
Replicates (R)/L	4	178
Generations (G) Regression	1	1076
Residual	11	250
G × L Regression‡ A	1	3896**
B	1	15
C	1	20
Residual	33	16
G × R/L Regression	4	39*
Residual	44	12
Deviation from Line Regressions§	44	74

* $P < 0.05$.** $P < 0.01$.

† Mean of the two sexes analyzed.

‡ Orthogonal comparisons: A Up minus Down.

B Relaxed minus Control.

C (Up + Down) minus (Relaxed + Control).

§ G × L residual (33 df) plus G residual (11 df).

FIGURE 2.—Unweighted means of the sexes for 3-9-week gain for the selected lines (generations 27-39) and the relaxed lines (formed in generation 34) as a deviation from the mean of the two control lines plotted against generation number.

FIGURE 3.—Unweighted means of the sexes for 3-9-week gain for the U, R and D lines averaged over replicates and as a deviation from the mean of the two control lines plotted against generation number.

freedom due to regression and the residual. The 3 degrees of freedom due to regression can then be partitioned into 3 orthogonal comparisons, as shown in Table 2. There was a significant difference between the up and down regressions, as would be expected since the regression coefficients are opposite in sign. There was not a significant difference between the relaxed and control regression coefficients. The last orthogonal comparison ($U + D$ minus $R + C$) is a measure of the degree of asymmetry in the response to selection after accounting for the trend in the R and C lines. This term was not significant. Also of interest is the extent of variation between replicates within each line. This can be investigated by dividing the generation by replicate within-line component of variance into that due to regression and the residual. A significant term due to regression was found. The difference between the two replicate regression coefficients and the associated standard error can be calculated for each line. These differences were $0.52 \pm .29$ for the up line, $0.92 \pm .49$ for the down line, $0.22 \pm .26$ for the relaxed line and $0.72 \pm .32$ for the control line. The difference between the control replicates was significant at the 5% level, while the differences between the up replicates and between the down replicates were both significant at the 10% level. This variation between replicates within each line could be due to random drift as well as sampling variation from unknown environmental sources. The magnitude of the random drift in this study will be investigated in more detail in a later section. Since there was significantly more variation about the line regressions than between replicate regressions within

lines, the former was used as the error term to test the three orthogonal comparisons among line regressions. However the result would have been the same regardless of which term was used as error. The mean difference between lines could also be divided into 3 orthogonal comparisons where the appropriate error term was the variation between replicate means within lines. As might be expected from the plots of data in Figures 2 and 3, the only significant difference of the comparisons made was between the up and down lines.

Realized heritability estimates and their sampling variance: The realized heritabilities have been estimated in this study by fitting a linear regression to generation means and cumulative selection differentials (b_c) over generations 1 to 12. It has been pointed out by FALCONER (1953) and HILL (1971) that with genetic sampling (drift) the variance of the population mean increases each generation, and these means become correlated. In standard regression analysis the observations are assumed to have equal variance and be uncorrelated so that the estimates of variance of realized heritabilities obtained by using standard regression techniques are biased downwards.

HILL (1972a,b) has discussed methods of estimation of realized heritabilities from selection experiments. The model used by HILL is based on several assumptions. A basic assumption is that the genetic and environmental variance and covariances remain constant during the selection program. This should be true if the experiment is of short duration, the final inbreeding level (F) is small, and the quantitative trait under selection is not determined by genes with very large effect. Although the first two of these conditions probably do not hold in this study and nothing is known about the third condition, it is still of considerable interest to test HILL's models on these experimental data.

HILL considered several designs of a selection experiment. These were divergent selection—that is, selection in two lines in the opposite direction for the same trait—and selection in a single direction with and without a control line.

The results obtained by HILL (1972a,b) can be summarized as follows: Three simple linear regression estimators of realized heritability and a maximum likelihood estimator were compared. The three linear estimators were: regression of generation means of selected lines or the deviations of these between up and down lines or from control lines on cumulative selection differential (b_c); regression of individual generation response on selection differential (b_l); and the ratio of total response to total selection differential (b_R). The most efficient estimator was defined by HILL as the estimator with minimum variance. The best estimator under most circumstances was b_c , but it was often only a little better than the simplest estimator, b_R . Standard methods of calculating the variance of these linear estimators were shown to be biased downward. Almost unbiased methods of estimating the variance from experimental data were given for all designs of selection experiments considered by HILL.

In light of these theoretical results the formulae derived by HILL (1972a,b) were applied to these data. In this study the main interest was in estimating the relative magnitude of the drift variance (σ_d^2), the error variance (σ_e^2), the com-

mon environment variance (σ_e^2), and the magnitude of the bias of the sampling variances of the realized heritability estimates.

The case of divergent selection is considered first. HILL (1972a) pointed out that if a selection experiment has been replicated several times, the best estimate of the variance of the average realized heritability will be the variance between replicates. In this study there are only two lines selected upward and two selected downward so that replicate variation in this case is based on too few degrees of freedom to be reliable. But a method was given by HILL (1972a) for obtaining an estimate of the variance of the realized heritability ($V(b)$) that is much less biased than the estimate obtained from usual regression analysis ($U(b)$). In order to estimate the parameters shown in Table 3, the responses and selection differentials for each pair of up- and down-selected lines were averaged and the divergent response and the selection differentials then calculated on this basis. The estimates of the phenotypic variance ($\hat{\sigma}^2$) for 3-9-week gain were obtained by pooling all variance estimates on a within-generation and within-line basis. The $\hat{\sigma}^2$ for males is based on 1486 degrees of freedom, while the $\hat{\sigma}^2$ for females is based on 1527 degrees of freedom. The $\hat{\sigma}^2$'s for males and females were heterogeneous so estimates of parameters based on the male and female data pooled were not calculated. All parameter estimates shown in Table 3 were calculated by the methods given by HILL (1972a) and the numbers of his formulae are shown in the table. The drift variance was found to be about one-half of the error variance in this analysis. It should be noted that when divergent selection is considered or when response is measured as a divergence from a control line, common

TABLE 3

*Estimates of realized heritability, drift and error variances and the sampling variances of the realized heritability estimates based on divergent selection for 3-9-week gain (grams)**

Item	Males		Females	
	b_G	b_R	b_G	b_R
$\hat{h}^2$	0.21	0.21	0.29	0.35
$\hat{\sigma}^2$	524.47	524.47	152.78	152.78
$\hat{\sigma}_a^2$ (3)	12.03	11.86	4.51	5.32
$\hat{\sigma}_e^2$ (4)	25.76	25.95	6.81	6.21
$U(b)^\dagger$ (17)	36	—	44	—
$\hat{V}(b)^\dagger$ (8,11)	173	162	247	261
$\hat{\sigma}_a^2/\hat{\sigma}_e^2$	0.467	0.457	0.662	0.857
$U(b)/\hat{V}(b)$	0.208	—	0.178	—

* All symbols used in this table are defined in the text and the numbers in parentheses in the item column refer to the formulae derived by HILL (1972a).

† These values must be multiplied by 10^{-5} .

environmental effects are eliminated. This should be reflected in a lower estimate of error variance in these types of analyses than when no control lines are kept and selection is in one direction only. From Table 3 it can be seen that $U(b_c)$ was one-fifth of $\hat{V}(b_c)$. There was little difference between $\hat{V}(b_c)$ and $\hat{V}(b_r)$.

HILL (1972b) considered the situation in which no control line was kept to measure environmental effects common to all individuals in the selected line and their influence on the estimate of response and its variance: To obtain unbiased estimates of realized heritability in this situation, it must be assumed that there is no directional trend in the environment. The analysis of the responses in the control lines in this study showed that there had been a systematic decline in the environment over the period of selection considered here. HILL's formulae were applied to these data even though this assumption was untenable. The results obtained are shown in Table 4. The estimates of the phenotypic variance ($\hat{\sigma}^2$) were obtained by pooling all estimates on a within-generation basis; the degrees of freedom for each estimate are shown. The error variance is considerably higher than that shown in Table 3 due to the common environment component, which was about 80% of $\hat{\sigma}^2$. It was found that the assumption of equal selection differentials, made by HILL to simplify some of his derivations, can be justified by these data since the approximate and more precise estimates of both

TABLE 4

*Estimates of realized heritability, drift, error and common variances and the sampling variances of the realized heritability estimates based on selection in one direction for 3-9-week gain (grams) assuming no environmental trend**

Item	Males				Females			
	U1	U2	D1	D2	U1	U2	D1	D2
b_c (5)	0.12	0.08	0.35	0.33	0.22	0.21	0.31	0.45
$\hat{\sigma}^2$	591.25	487.78	541.15	481.89	201.05	140.57	125.01	146.11
df	362	351	365	408	378	357	408	384
$\hat{\sigma}_d^2$ (1)	4.00	2.25	9.49	7.86	2.35	1.59	1.94	3.06
$\hat{\sigma}_e^2$ (16)	53.56	105.45	87.17	58.34	29.88	24.27	18.10	12.46
$\hat{\sigma}_e^2 \ddagger$	53.84	105.52	87.68	58.58	29.98	24.35	18.10	12.54
$\hat{\sigma}_c^2$ (17)	36.78	90.50	75.83	49.11	25.13	20.69	15.63	10.02
$U(b_c) \dagger$ (11)	160	377	486	188	303	404	241	193
$\hat{V}(b_c) \dagger$ (14)	328	499	1214	536	644	788	614	785
$\hat{V}(b_c) \dagger$ (15)	315	501	1255	544	624	813	662	875
$\hat{\sigma}_d^2/\hat{\sigma}_e^2$	0.075	0.021	0.109	0.135	0.078	0.066	0.107	0.245
$\hat{\sigma}_c^2/\hat{\sigma}_e^2$	0.687	0.858	0.869	0.842	0.841	0.852	0.864	0.805
$U(b_c)/\hat{V}(b_c)$	0.488	0.756	0.400	0.351	0.471	0.513	0.393	0.246

* All symbols used in this table are defined in the text; the numbers in parentheses in the item column refer to the formulae derived by HILL (1972b).

† These values must be multiplied by 10^{-5} .

‡ The shortcut method of estimation as given by HILL (1972b).

$\hat{\sigma}_e^2$ and $\hat{V}(b_c)$ were similar. This is of some interest since there was quite a high variation in selection differentials in these data due to severe disease problems in some generations. In this case it was found that $U(b_c)$ was usually less than one-half of the value of $\hat{V}(b_c)$.

HILL (1972b) also considered the error structure of the realized heritability estimate when a control population is maintained concurrently with the population undergoing selection. Assuming that there is no interaction between the environment and the control and selected lines' performance, common environmental effects will be eliminated when response to the selection is expressed as a deviation from a control line. HILL considers two types of random-breeding control lines: (a) where the control and the selected line are taken from the same base population at generation zero, so the initial mean is known without error; (b) where they have a different base and there is error of estimation of the initial mean.

The C lines in this study fall into category (b), although they did have the same origin as the selected lines originally—that is, 27 generations previous to the start of this selection. The R lines fall into category (a), since the R, U and D lines were formed from the same population in generation 26 and then selection began in generation 27. In case (a) the regression of cumulative response on selection differential can be forced through the origin, which will be zero. As HILL pointed out, with a reasonably large number of generations of selection (t) and $\sigma_d^2 > 0$, there is very little difference between the efficiency of this estimator of b_c and the efficiency of the estimator obtained without forcing the regression through the origin. In fact with t equal to 13 generations and σ_d^2 one-half of σ_e^2 , which is approximately the case in these data when σ_e^2 is eliminated, then $V(b_c)$ was similar by both methods of calculation. Thus when realized heritabilities were calculated by deviating the U and D lines' responses from the trend in the R lines, the estimates were not forced through the origin.

Using the $\hat{\sigma}_e^2$ given in Table 4, estimates of σ_e^2 , σ_d^2 and $V(b_c)$ were calculated from both the control and relaxed lines. Results are presented in Tables 5 and 6, respectively.

In Tables 5 and 6 the ratio of $\hat{\sigma}_d^2$ to $\hat{\sigma}_e^2$ averaged about 0.5 but ranged from .21 to .71. The ratio of $U(b_c)$ to $\hat{V}(b_c)$ averaged less than 0.2 in both tables and ranged from 0.09 to 0.50.

The realized heritability estimates presented in Tables 3, 4, 5, and 6 indicate that selection has been effective in both the up and down lines. The marked asymmetric response apparent in Table 4 (greater response downward than upward), when ignoring the negative environmental trend in the C and the R lines, was much reduced when realized heritabilities were calculated as a deviation from the C or R lines (Tables 5 and 6). The degree of asymmetry in the realized heritability estimates in any of these tables cannot be established as statistically significant when the standard errors based on $U(b_c)$ are considered. Similarly, the higher realized heritabilities in females than males observed in most lines were not statistically significant.

TABLE 5

*Estimates of realized heritability, drift and error variances and the sampling variances of the realized heritability estimates based on selection in one direction for 3-9-week gain (grams) as a deviation from the control lines**

Item	Males				Females			
	U1	U2	D1	D2	U1	U2	D1	D2
b_c	0.20	0.17	0.25	0.25	0.30	0.32	0.21	0.34
$\hat{\sigma}_a^2$ (18)	12.71	9.06	14.13	12.59	6.12	4.51	2.81	4.92
$\hat{\sigma}_e^2$ (18)	30.41	25.50	27.06	24.09	9.76	6.75	6.39	6.93
$\hat{\sigma}_a^2/\hat{\sigma}_e^2$	0.418	0.355	0.522	0.523	0.258	0.668	0.439	0.709
$U(b_c)^\dagger$	76	142	181	97	160	294	98	137
$\hat{V}(b_c)^\dagger$ (7)	653	615	1294	664	1039	1265	651	1010
$U(b_c)/\hat{V}(b_c)$	0.116	0.231	0.140	0.146	0.154	0.232	0.151	0.136

* All symbols used in this table are defined in the text; the numbers in parentheses in the item column refer to the formulae derived by HILL (1972b).

† These values must be multiplied by 10^{-5} .

Relaxation of selection: CLAYTON, MORRIS and ROBERTSON (1957) stated that "The behavior of selected lines on the cessation of selection is of interest from two points of view: It gives a measure of the natural selection which is opposing the artificial selection and is therefore relevant to the problem of asymmetrical response; and, if done in the early generations before the fixation of many segregating genes has taken place, shows the strength of the evolutionary forces holding the mean in its original position." In this study relaxed lines were formed from each selection line in generation 7.

The data from these relaxed lines are plotted in Figures 2 and 3. The genera-

TABLE 6

*Estimates of realized heritability, drift and error variances and the sampling variances of the realized heritability estimates based on selection in one direction for 3-9-week gain (grams) as a deviation from the relaxed lines**

Item	Males				Females			
	U1	U2	D1	D2	U1	U2	D1	D2
b_c	0.14	0.10	0.33	0.31	0.31	0.33	0.18	0.31
$\hat{\sigma}_a^2$ (18)	9.19	5.53	17.80	15.07	6.29	4.62	2.44	4.57
$\hat{\sigma}_e^2$ (18)	31.42	26.48	25.82	23.27	9.71	6.71	6.50	7.06
$\hat{\sigma}_a^2/\hat{\sigma}_e^2$	0.292	0.209	0.689	0.648	0.648	0.689	0.375	0.647
$U(b_c)^\dagger$	85	205	276	111	63	119	52	342
$\hat{V}(b_c)^\dagger$ (7)	497	413	1589	776	1064	1293	576	1031
$U(b_c)/\hat{V}(b_c)$	0.171	0.496	0.174	0.143	0.059	0.092	0.090	0.332

* All symbols used in this table are defined in the text; the numbers in parentheses in the item column refer to the formulae derived by HILL (1972b).

† These values must be multiplied by 10^{-5} .

tion means for these lines were regressed on generation number over generations 7 to 12, inclusive. None of these regression coefficients were significantly different from zero. On the basis of this somewhat limited period of relaxation of selection it seems that many of the genes controlling 3–9-week gain in this population of rats have little effect on natural fitness. However, this conclusion must also be interpreted in the context of the observation that the FFR line had already regressed from its initial level of about 18 grams above the control in generation 16 to about 5 grams above the control in generation 27 when this selection study began (Figure 3). The average of the two randomly bred lines (R1 and R2) formed from the FFR line showed no statistically significant regression to the control line level over the period from generation 0 to 12 of this study. These data are shown in Figure 3. This emphasizes the fact that conclusions concerning the nature and strength of natural selection forces may be markedly affected by the length of the period of relaxation of selection.

Inbreeding: The base population for this study was one which had been under selection for a number of generations previously but was originally formed from a cross of four inbred lines (PARK *et al.* 1966). There is an expectation of 25% homozygosity in the base population within which selection started (FALCONER 1960a). Inbreeding was computed from generation 0 to 17 for the full fed (FF) selected line and the control line, using the “co-ancestry” technique (FALCONER 1960a). By generation 17 the average inbreeding coefficient (F) was 0.17 in the FF line and 0.16 in the control line. Pedigree information was not available for all of the next ten generations of relaxed selection. The assumption was made that the inbreeding continued to increase at about 1% per generation. The inbreeding at generation 0 of this study would then be about 52%. This would be made up of the original 25% from the base population plus the additional 27% accumulated over 27 generations. Thus the base population for this study was rather highly inbred. Inbreeding was also computed over generations 0 to 11 of this study.

The inbreeding continued to increase at about 1% per generation in the control lines. In all other lines the increase in inbreeding was about 1.5% per generation. It has been pointed out (HILL, personal communication) that since a base of $F = 0$ was assumed at generation 27, then the actual rate of inbreeding over the succeeding generations should be roughly halved to allow for the initial value of about 50%. The inbreeding estimates obtained from this pedigree analysis can be compared to that expected based on the effective population size (N_e) (FALCONER 1960a).

Thus with 15 pairs of parents the rate of inbreeding increase (ΔF) is estimated to be 1.7%. When efforts are made to insure that each family is represented by one male and one female in the next generation, then the effective population size is doubled and ΔF is halved (FALCONER 1960a). A ΔF value of 0.85% is close to the 0.5% value actually calculated in the two control lines. It thus seems that the efforts to avoid inbreeding, by the restrictions that no more than two individuals of each sex be selected from each family and by avoiding mating individuals with grandparents in common, was successful.

In the selected lines ΔF may be increased due to the fact that each pair of parents will not have an equal chance of contributing to the next generation (GOWE, ROBERTSON and LATTER 1959). Thus any differences among the parents in fertility or between-family differences in survival to age at selection will result in an increase in the variance of progeny per parent and to a decrease in the effective number of parents. This effect was minimized to some extent by standardizing litter size at birth and through the restrictions on inbreeding. However, in the lines under selection, complete families are more likely to be eliminated in the selection process at 9 weeks of age and this would decrease the effective population size. The magnitude of this effect was not calculated in this study but could be the cause of the higher inbreeding in the U and D lines than in the C lines. The similar and higher ΔF in the R, U and D lines could also be due to the higher proportion of parents failing to pup in these lines (these data will be shown in a subsequent paper) compared to the C lines.

A commonly observed consequence of an increase in inbreeding is the reduction in mean phenotypic values of some characteristics, especially those closely related to fitness. Inbreeding depression was investigated in this study by regressing weights at different ages and 3-9-week gain on the inbreeding coefficient on a within-generation basis (Table 7). None of these regression coefficients was significant, but the consistency of negative values in the replicates of the relaxed and control lines of each of the traits, even though not independent, points to inbreeding depression.

DISCUSSION

Selection in rats for both high and low postweaning gain, from 3 to 9 weeks of age, was effective in this study. Realized heritability estimates obtained in this study can be compared with other similar selection studies with rats. PARK *et al.* (1966) found that selection for high 3-9-week gain on a standard diet fed *ad libitum* over 16 generations gave a realized heritability estimate of 0.11. Com-

TABLE 7
*Regression of weights (grams) on inbreeding (%F) within generations 30 to 38**

Line	df	3-week weight	6-week weight	9-week weight	3-9 week gain
U1	578	0.46 $\pm$.29	0.81 $\pm$ 1.05	2.38 $\pm$ 2.04	1.89 $\pm$ 1.95
U2	566	-.60 $\pm$.33	-.51 $\pm$ 1.09	-.02 $\pm$ 2.12	0.59 $\pm$ 2.01
D1	600	0.29 $\pm$.19	-.48 $\pm$ 0.74	-.55 $\pm$ 1.51	-.84 $\pm$ 1.44
D2	618	-.16 $\pm$.18	0.14 $\pm$ 0.70	-1.40 $\pm$ 1.40	-1.27 $\pm$ 1.28
R1	546	0.06 $\pm$.18	-.35 $\pm$ 0.67	-.18 $\pm$ 1.38	-.25 $\pm$ 1.34
R2	535	-.46 $\pm$.24	-.63 $\pm$ 0.89	-1.58 $\pm$ 1.80	-1.12 $\pm$ 1.71
C1	688	-.70 $\pm$.26	-1.10 $\pm$ 0.88	-1.00 $\pm$ 1.90	-.35 $\pm$ 1.82
C2	684	0.25 $\pm$.25	0.67 $\pm$ 0.88	-.31 $\pm$ 1.78	-.55 $\pm$ 1.70
Pooled†	4868	-.16 $\pm$.07	-.31 $\pm$ 0.25	-.85 $\pm$ 0.50	-.70 $\pm$ 0.48

* Pooled within generations.

† Pooled within lines.

parable estimates from this study, ignoring any trend in the R and C lines, were 0.16 and 0.12 for the U1 and U2 lines, respectively. This comparison is of interest since the rats used in this study were derived from the same line of rats selected by PARK *et al.* (1966). From this comparison of selection response upward and the fact that divergent response to selection was evident, it can be concluded that neither the history of past selection in this line of rats nor the fairly high inbreeding coefficient (about 50%) which occurred as a result of this selection in a closed line had affected the genetic variation available for selection.

BAILEY *et al.* (1970) selected for high 4–10-week gain in two replicate lines of rats on a standard diet fed *ad libitum* and obtained realized heritabilities over 5 generations of 0.38 and 0.32. Comparable estimates in this study over 12 generations of selection, taking into consideration the trends in the R and C lines, were 0.24 and 0.23. It is worth noting that when realized heritabilities were calculated for the U lines over the first six generations of this study, as was done by BAKER and CHAPMAN (1969), it was found that selection resulted in a small and non-significant increase in 3–9-week gain. This result is quite different from that obtained by BAILEY *et al.* (1970), who obtained an immediate response to selection. ROUBICEK and RAY (1971) selected for high and low 3–13-week gain in rats at both 22° and 35° for 10 generations. At 22° realized heritabilities, based on the assumption of no directional trend in the control line, were 0.19 for positive selection and 0.44 for negative selection and 0.31 for the divergence between these two lines. In the present study, when the negative trends in the C and R lines have been accounted for, realized heritabilities of 0.24 and 0.23, respectively, were obtained in the U lines and 0.24 and 0.30, respectively, in the D lines. The value calculated from the divergence of the up and down lines was 0.25.

These results with rats can also be compared with similar types of studies with mice. A large number of studies involving selection for weight or weight gain have now been reported and most of these have been reviewed and summarized by ROBERTS (1965) and by BAKER (1971). Although these studies employed different base populations for selection, selected for different criteria of growth, and employed a variety of selection procedures, some consistent results are beginning to appear. In general it is quite clear that much of the variation in body weight of the mouse has an additive genetic source. This is in agreement with the selection studies with rats. Comparison of realized heritabilities between studies can be complicated by the number of generations of selection. But it is possible to summarize selection studies in which selection has been practiced for approximately equal numbers of generations. A good estimate of the total genetic variation available for selection is the realized heritability calculated from the divergence between high and low selected lines. The average of four such values, reported by MCARTHUR (1949), FALCONER (1953, 1955), FALCONER (1960b) and LEGATES (1969), was 0.25 with a range of 0.17 to 0.33. These estimates were based on at least 13 generations of selection under a standard diet. These results are in good agreement with comparable estimates in rat selection studies of 0.25 found in this study and 0.31 reported by ROUBICEK and RAY (1971).

Asymmetry of response is a fairly regular occurrence in two-way selection experiments. It can only be firmly established when random-bred controls are maintained. Of six studies of lines of mice selected for high and low weight or high and low weight gain for 12 or more generations on a standard diet, five (FALCONER 1953, 1955; SUTHERLAND, BIONDINI and HAVERLAND 1968; LEGATES 1969) showed greater response in the downward than in the upward direction. Averages for realized heritabilities in these five sets of lines were 0.20 upward and 0.63 downward. Calculations were based on the assumption that no environmental trend was indicated by the control lines which were kept; or, in LEGATES' case, response was actually expressed as a deviation from the control values. The other study (DALTON 1967) showed about equal responses in the two directions. The magnitude of this asymmetrical response in the realized heritabilities in mouse studies was similar to that reported by ROUBICEK and RAY (1971) in rats—viz., 0.19 upward *versus* 0.44 downward. The results in the present study, obtained by taking an unweighted mean of the values in Tables 5 and 6 (0.23 upward and 0.27 downward), did not show a statistically significant difference.

It has been found that asymmetry of response may change during selection. For example, FALCONER (1960b) found that on his standard diet, for about the first five generations, realizing heritabilities were about 0.70 for selection upward and 0.20 for selection downward. Thereafter they were 0.12 upward and 0.45 downward. There was some evidence for a similar type of change in this study, although in this case just the magnitude of the asymmetry of response was concerned. Over the first six generations of selection there was no detectable response to selection upward and rapid response to selection downward. For the next seven generations response upward was obtained, while response downward was reduced slightly.

If the results found in the studies reviewed here are characteristic of results of selection for growth traits in mammals, this means that actual progress in the positive direction will fall short of that predicted from the usual heritability estimates based on parent-offspring or half-sib data. Some evidence is available on this point in these data. PARK *et al.* (1966) present estimates of heritability based on the regression of 3–9-week gain of offspring on those of the parents. Regression of the offspring (male and female) on mid-parent in the FF line gave a value of $0.26 \pm .05$, while the estimate from the control rats on the full-fed environment was $0.20 \pm .12$. These regressions are direct estimates of the heritability and these estimates were greater than the realized heritability made by PARK *et al.* (1966) of 0.11, but similar to the average value of 0.23 found in the U lines in this study.

An effort has been made in this study to test some of the models involving the estimation of sampling variances of realized heritabilities presented by HILL (1971, 1972a,b) on these experimental data. The rationale for these analyses was presented in some detail when the results were presented. It should be emphasized that no attempt has been made to test HILL's models exhaustively. This would involve more than two replicates per line in a two-way selection study. A study of this kind should lead to estimation of the variances of all four esti-

mators of realized heritability considered by HILL, with the one with the smallest sampling variance being the estimator that could be recommended for use. It would then be possible to see if the result from experimental data agreed with HILL's theoretical results and also whether the variances estimated by Hill's formulae were in reasonable agreement with the more direct measures of sampling variance that would be available from the between-replicate component of variance. In addition the assumptions on which HILL's models were based could be evaluated on experimental data. Although this sort of approach is not possible with these data because of minimal replication, some useful results have been obtained. In particular, it seems clear that standard regression methods of estimating the variance of the regression of cumulative response on cumulative selection differential (b_c) yield smaller values than those calculated using the methods of estimation presented by HILL. This indicates a downward bias in the regression calculated by the standard method. When common environmental effects are removed—that is, with response measured as a divergence from a control or as divergence between high and low lines—the bias downward is about one-fifth. When common environmental effects are not removed—that is, when no control line is kept and selection is in one direction only—the downward bias is less. It is about one-half as large in these data. This result was predicted by HILL (1972b) as illustrated in his Figure 2.

The estimation of the relative magnitude of the drift, random error and common environmental variances was carried out using the methods given by HILL (1972a,b). Similar types of formulations were also presented for drift and random error variances by DICKERSON (1969) when comparing the efficiencies of different types of control schemes in selection experiments.

The magnitude of the drift variance is of particular interest since it is expected to be one of the reasons for deviation between the replicate lines. The actual degree of variation between each pair of replicate lines can be considered in a number of different ways. When analysis of variance was carried out on the generation means (average of the two sexes) for the 13 generations of selection for each pair of replicate lines, the variance between replicates was estimated as 36.6, 39.6, 24.3 and 9.3 for the U, D, C and R lines, respectively. The estimates of drift variance, calculated in this study for the U and D lines, ranged from 1.6 to 17.8, which only accounts for part of the divergence between these lines. FALCONER (1953) considered the effect of genetic drift in his selection for high and low 6-week weight in mice. His study was not replicated so drift, random error and common environmental variances were calculated from residual variances about regression lines. FALCONER concluded that drift was not important in his study and that the fluctuation of the divergence between his high and low lines was due entirely to the sampling error of the generation means. The responses to selection for the two U lines and the two D lines in this study were averaged and then calculations similar to those of FALCONER were carried out in these data. This form of analysis gave no evidence for genetic drift in the D lines but possibly some in the U lines. It is considered more reliable to estimate drift variance by the methods of HILL (1971, 1972a,b). The method of derivation of the drift

variance for a selected population is given by HILL (1971). Another approach was adopted by CLAYTON, MORRIS and ROBERTSON (1957), who selected for high and low numbers of abdominal bristles in *Drosophila melanogaster*. They calculated their expected drift variance from $2F\sigma_g^2$ (WRIGHT 1921), where σ_g^2 is the additive genetic variance. The observed variances between replicates were then calculated at a given generation. There were five lines selected at the highest intensity of selection in each of the up and down directions. By comparing the observed variances with those expected from genetic drift, it was concluded that genetic sampling could account for the divergences between the down lines but not between the up lines. An attempt was made to use the same approach in this study. The observed variances between the two U lines and the two D lines in generation 12 were higher than the expected variances based on the estimate of genetic drift of $2F\sigma_g^2$. But since each of the observed variances was only based on one degree of freedom, little weight can be put on this result.

The relative magnitudes of $\hat{\sigma}^2$, $\hat{\sigma}_c^2$, $\hat{\sigma}_e^2$, and $\hat{\sigma}_d^2$ can be of particular interest for deciding whether or not a control population should be maintained, as has been discussed by HILL (1972b). The results in this study showed that $\hat{\sigma}_c^2$ was relatively small compared with $\hat{\sigma}^2$ (about 12%) and that $\hat{\sigma}_d^2$ was about one-half $\hat{\sigma}_e^2$ after $\hat{\sigma}_c^2$ had been excluded. While the results from this one study are of little use for generalization, it will be of considerable interest to compare these results with other adequately replicated selection studies which attempt to estimate these parameters.

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