ANALYSIS OF QUANTITATIVE INHERITANCE OF BODY SIZE IN MICE. II. GENE ACTION AND SEGREGATION[1]

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FISHER (1918), WRIGHT (1935) and KEMPTHORNE (1954) showed that variation and correlation between relatives ascribable to additive effects, dominance and interaction of the genes can be partitioned. Methods of estimation of the effective number of factors have been given by FISHER, IMMER and TEDIN (1932), WRIGHT (1934, 1950), CASTLE (1921) and MATHER (1949).

In mice, BUTLER (1952) has made five crosses between strains different in body size. He found that the F_1 and F_2 means were half way between those of the parents. backcross means were half way between that of the F_1 hybrid and that of the pure-strain parent. As expected, the variances of the parental strains and the F_1 hybrids were similar; however, the variance of the F_2 was no larger than that of the F_1.

In the present study the genetic component of the quantitative variability of body size in mice has been analyzed. Among the matters that have been considered were number of loci or at least effectively independent blocks of loci, the degree of dominance among the loci, the distribution of gene effects, and the amount of environmental contributions to the total variation.

BREEDING PLANS

The Large and Small strains of mice were used as the parental stocks. Their historical developments have been previously reported. There were 12 cross-bred types used: two F_1, two F_2 and eight first-backcross generations. The type and number of matings, average litter sizes and designations for each of the different types of matings are given in table 1. Throughout this paper "subgroup" refers to all the females or males under each different type of mating and "genotypic group" refers to all the individuals within each pure strain or hybrid, i.e. P_L, P_S, F_1, F_2, B_L and B_S.

Maternal influence within each hybrid group was balanced by making reciprocal matings between the two parental genotypes. For instance the F_1 hybrids were produced by two different types of matings, L $\times$ S and S $\times$ L. Other hybrids were similarly produced. Maternal effects will still exist between crosses, and will be considered at length below. Inbreeding was avoided as much as possible in the production of the F_2 and backcross mice. There were no matings closer than second cousins or single first cousins. Therefore the effects of inbreeding were trivial and no correction is needed.

Prolificness varied between mice of different genetic constitutions. The hybrid mouse was a better reproducer than the pure-strain mouse. This is evidenced by large litters in the F_2 generation and in those backcross mice with the F_1 hybrid as the

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TABLE 1

The type and total number of matings, with the average size of litters in each type of mating

To produce	Type of mating	Total no. matings	No. of litters	Lit. avg.	Size range
Large	L × L	9	22	6.0	1–10
Small	S × S	7	19	4.5	2–7
F_1	L × S	6	14	4.6	1–9
	S × L	10	24	5.5	1–8
F_2	$(L \times S)^2$	4	17	10.9	4–16
	$(S \times L)^2$	4	16	11.6	9–15
B_L	SL × L	2	9	5.8	2–10
	LS × L	2	9	10.2	8–14
	L × SL	2	5	8.0	5–12
	L × LS	2	5	8.0	4–10
B_S	SL × S	1	4	9.5	8–10
	LS × S	2	5	8.5	2–12
	S × SL	4	10	5.7	3–8
	S × LS	3	11	5.2	3–9

maternal parent (table 1). The F_1 mothers also had very short intervals between litters. Practically all the F_2 and some of the backcross animals came from early litters of their parents, while the F_1 and the pure-strain animals studied were produced throughout the life history of their parents. In order to give the young equal suckling opportunity, a maximum of 8 young were kept in a litter.

RESULTS AND ANALYSIS

A total of 801 mice were included in this study. The number of animals, means, variances, and coefficients of variation of body weight for each pure strain and each subgroup are given in table 2. The distributions of body weight for each genotypic group are illustrated in figure 1.

The average body weight of males was greater than that of females in each subgroup of mice. In order to circumvent the complications of sex differences and unequal sex ratios, a subgroup mean for 60-day weight was taken to be the unweighted average of the mean weights of the male and female mice in the subgroup. Similarly, since the number of mice in each subgroup varied, the mean body weight of each hybrid group has been computed by averaging all the unweighted subgroup means. The same procedure has been employed for combining the variances and the coefficients of variation.

Before presenting the results of the biometrical analysis, it seems necessary to consider the effects of litter size, age of the mother and maternal influence. We shall first examine the maternal influence. As each hybrid was produced by mothers of different strains, maternal effect between strains, if different, would contribute unequally to the means of the different hybrids. It appeared that F_1 hybrid mothers had more augmenting influence to the young than purebred mothers and similarly the Large mother had more augmenting influence to the young than the Small mother.

TABLE 2

The means ($\bar{x}$), variances (s^2) and coefficients of variation (C) of 60-day body weight in each subgroup of mice

Genotype		No. of animals	$\bar{x}$	s_l^{2*}	s_i^{2**}	s_t^{2***}	$C_l{}^*$	$C_i{}^{**}$	$C_t{}^{***}$
P_L	(L × L) ♀	20	33.23	8.36	1.86	10.22	.0870	.0411	.0962
	(L × L) ♂	45	41.48	8.36	5.97	14.33	.0697	.0588	.0912
P_S	(S × S) ♀	20	12.84	1.35	0.26	1.61	.0906	.0397	.0988
	(S × S) ♂	21	14.37	3.05	0.63	3.68	.1223	.0553	.1335
	Total	106							
F_1	(L × S) ♀	30	25.23	8.18	.98	9.16	.1134	.0392	.1200
	(L × S) ♂	35	29.08	7.37	1.92	9.29	.0934	.0476	.1048
	(S × L) ♀	53	22.13	1.98	.96	2.94	.0636	.0442	.0775
	(S × L) ♂	43	26.80	4.33	1.24	5.57	.0776	.0415	.0881
	Total	161							
F_2	(S × L)² ♀	55	25.00	0	5.66	5.56	0	.0952	.0952
	(S × L)² ♂	58	30.72	1.63	9.89	11.52	.0415	.1024	.1105
	(L × S)² ♀	52	24.57	1.73	5.26	6.99	.0539	.0937	.1076
	(L × S)² ♂	51	28.54	0	9.46	9.46	0	.1077	.1077
	Total	216							
B_L	(S × L)L ♀	58	29.16	2.44	3.69	6.43	.0535	.0659	.0849
	(L × S)L ♀								
	(S × L)L ♂	56	36.25	5.52	5.48	11.0	.0648	.0646	.0915
	(L × S)L ♂								
	L(S × L) ♀	26	28.41	0	7.73	7.73	0	.0979	.0979
	L(L × S) ♀								
	L(S × L) ♂	24	34.20	8.63	9.88	18.51	.0858	.0919	.1258
	L(L × S) ♂								
	Total	164							
B_S	(S × L)S ♀	23	19.68	8.83	4.07	12.90	.1503	.1023	.1825
	(L × S)S ♀								
	(S × L)S ♂	36	22.60	5.31	6.82	12.13	.1023	.1156	.1541
	(L × S)S ♂								
	S(L × S) ♀	41	18.10	.97	2.64	3.61	.0545	.0898	.1050
	S(S × L) ♀								
	S(S × L) ♂	54	21.28	1.88	3.27	5.15	.0646	.0852	.1066
	S(L × S) ♂								
	Total	154							

* l = between litters. ** i = within litters. *** t = total

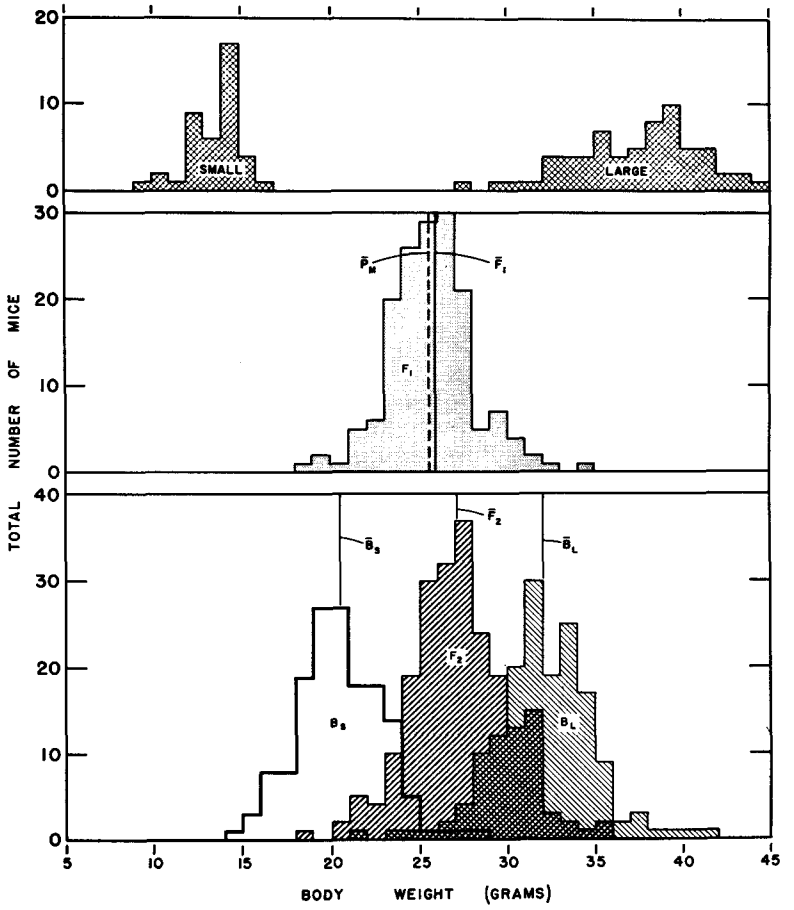

FIGURE 1.—A graph showing the distributions of 60-day mouse body weight of the pure strains, Large and Small, and the hybrids, F_1, F_2, B_L and B_S. It was constructed by superposing all subgroups within each genotype so that all the subgroup means are lying on their general mean.

The average sizes of litters from matings producing pure-strain and F_1 hybrid offspring were similar, i.e. 4.5 to 6.0 (table 1). The average sizes of litters in matings producing the F_2 generation were 10.9 and 11.6. The sizes of litters in the backcross generations were intermediate between the two extremes, 5.2 to 10.2. Since body weight at 60 days of age may be influenced by size of litter the observed mean body weight in the F_1 hybrids would be overestimations, and the mean body weights in the F_2 would be underestimations. Effect of parental age may tend to offset the bias due to litter size since F_2 mice were produced during the first part of the productive age of their parents and the pure strains and F_1 mice were produced throughout the life history of their parents. The method of computing multiple regression coefficients has been often employed to correct for such effects (EATON 1954). However, it could not be satisfactorily applied to the present data because the sample sizes were too small to consider each subgroup separately. On the other hand, the differences be-

tween the subgroups in the mean body weight and pattern of reproduction of their parents would make the computed coefficients of the pooled sample meaningless. It is generally considered that the preweaning environment of either first litter or late litters in mice is less favorable than that of the middle litters. Therefore, in the pure-strains and F_1 hybrids, mice of the late litters may have the tendency to reduce the mean body weight and, in turn, result in an underestimation. Nevertheless, errors in estimation of body weight introduced from such sources are difficult to evaluate.

With regard to the effects of litter size, mother's age and certain maternal influences upon body-weight variances in the different subgroups, it is thought that variations from these sources exist mainly between litters rather than within litters. By removing the between-litter variation from the total variation, effects from such sources can be eliminated. Therefore, the method of analysis of variance has been employed to separate the variations between litters and within litters. The variance due to litter, s_l^2, and the variance due to individuals within litter, s_i^2, as well as the corresponding coefficients of variation, C_l, C_i, for all the subgroups have been computed (table 2).

The variances and coefficients of variation due to litter vary among subgroups within the Small strain, F_1 and backcross generations. If each genotypic group as a whole is considered, the F_2 hybrids give the lowest values. From the analysis of variance it has also been shown that the variation due to litter in the F_2 hybrids was nonsignificant while that in the parental strains and the F_1 hybrid was significant ($P < .01$). As the 8 different backcross subgroups show two are nonsignificant, two are significant at the 5% probability level and four are significant at the 1% probability level. Although some sampling errors due to smaller number of individuals contained in certain subgroups may be unduly large, the results seem, in general, to indicate the lack of consistency of environments provided by the mothers and the differences in litter sizes between the pure strains and the F_1 hybrids. As was expected, variation from such sources was larger in those subgroups whose parent, particularly the maternal one, belonged to a pure strain. Variations due to such unevenly distributed environmental sources have been found to differ among genotypic groups or their subgroups. These variations must be removed in order to arrive at a genetic analysis of these genotypic groups.

Having removed variations caused by factors that were unequally distributed among the parental strains and hybrids, e.g. variation due to litter, the residual within-litter variation within the different genotypic groups would measure the amount of variation attributable to different genotypes under similar environmental influences. This may be expressed by the within-litter variance, s_i^2. It is noticed that the values of the within-litter variances of the subgroups within the same genotype are more similar than the average values between genotypes.

WRIGHT (1952) has given the formulae for estimating the mean and variance on the logarithmic scale from the actual mean and coefficient of variation.

$$\overline{log_{10}\, x} = log_{10}\, \bar{x} - \tfrac{1}{2} log_{10}\, (1 + C^2)$$
$$s^2_{log_{10} x} = .43431\ log_{10}\, (1 + C^2)$$

By applying the above formulae the logarithmic values of both means and variances have been obtained (table 3).

TABLE 3

Means and variance of body weight of mice in each genotype on logarithmic and actual scales

Genotype	$\bar{x}$ obs.	$\bar{x}$ corr.	$\bar{x}$ theo.	s^2	$\overline{logx}$ obs.	$\overline{logx}$ corr.	$\overline{logx}$ theo.	s^2_{logx}	Correction factors
P_L	37.35	35.98		3.92	1.56778	1.54121		.00049	$-x$ 0
P_S	13.61	13.61		0.46	1.13004	1.13004		.00044	0 0
P_M	25.48	24.80		2.18	1.34891	1.23562		.00047	$-\frac{1}{2}x$ 0
F_1	25.82	25.01		1.28	1.40754	1.39425		.00036	$-\frac{1}{2}x$ 0
F_2	27.10	25.10	24.95	7.57	1.43175	1.39499	1.36493	.00191	$-\frac{1}{2}x$ $-y$
B_L	31.59	30.77	30.50	6.70	1.50067	1.46900	1.46773	.00125	$-\frac{3}{4}x$ $-\frac{1}{2}y$
B_S	19.72	19.36	19.31	4.21	1.30419	1.28581	1.26214	.00184	$-\frac{1}{4}x$ $-\frac{1}{2}y$

x = correction for large dam. y = correction for crossbred vs. inbred dam.

The two sources of maternal effect, the differences between the Large dam and Small dam and the differences between the crossbred and inbred dams, need to be corrected before considering the means of the different genotypic groups. A generalized correction factor of each for the means is derived according to WRIGHT (personal communication):

$$x = (L \times S) - (S \times L)$$
$$-x = (F_1 \times L) - (L \times F_1) - (F_1 \times S) + (S \times F_1)$$
$$2y = (F_1 \times L) - (L \times F_1) + (F_1 \times S) - (S \times F_1)$$

where x is the correction factor which converts the Large dam to the Small dam basis and y that which converts the crossbred dam to the inbred dam basis. The following values were obtained according to the above equations:

$$x = 1.37 \text{ (actual scale)}, .02657 \text{ (log scale)}$$
$$y = 1.42 \text{ (actual scale)}, .02347 \text{ (log scale)}$$

The necessary corrections are listed in the last column of table 3. The observed, corrected and theoretical means, and the within litter variances in the different genotypic groups are given in the same table. The mean of the F_1 hybrids is close to the midparent value and the means of the backcross fall between the mean of the F_1 and that of their respective parental strain. It is observed that the corrected means are in better agreement with the theoretical means on the actual scale than on the logarithmic scale. The variance of the F_2 hybrids gives the highest value, the backcross hybrids the intermediate values, and the F_1 and the parental strains the lowest values. These orders of both means and variances are as expected.

TESTS OF THE SCALE

The choice of an adequate scale is important for the analysis of quantitative variability. The best scale for the purpose of such an analysis is one on which the effects of factors (genetic and environmental) are as nearly additive as possible. The logarithms of measurements of organisms are often used in statistical studies based on the hypothesis that the growth factors tend to contribute constant percentage increments (POWERS 1942) or to act on a geometric scheme. It appears to be necessary to

compare the fitness of the two different scales, actual gram weight and logarithmic gram weight, to the present data.

On an adequate scale for the theoretical means for each of the hybrids, the following equations according to WRIGHT (1952) will hold:

$$\bar{F}_2 = \tfrac{1}{2}(\bar{P}_M + \bar{F}_1)$$
$$\bar{B}_L = \tfrac{1}{2}(\bar{P}_L + \bar{F}_1)$$
$$\bar{B}_S = \tfrac{1}{2}(\bar{P}_S + \bar{F}_1)$$

where the subscript M denotes mid-parent. Several statistics which may be used for testing the adequacy of a scale of measurement with respect to additivity when the two pure strains, F_1 and F_2 and the backcrosses are available have been given by MATHER (1949):

$$A = 2\bar{B}_L - \bar{P}_L - \bar{F}_1 \qquad s_A^2 = (4s_{B_L}^2 + s_{P_L}^2 + s_{F_1}^2)$$
$$B = 2\bar{B}_S - \bar{P}_S - \bar{F}_1 \qquad s_B^2 = (4s_{B_S}^2 + s_{P_S}^2 + s_{F_1}^2)$$
$$C = 4\bar{F}_2 - 2\bar{F}_1 - \bar{P}_L - \bar{P}_S \qquad s_C^2 = (16s_{F_2}^2 + 4s_{F_1}^2 + s_{P_L}^2 + s_{P_S}^2)$$

Where A, B, and C are quantities denoting the discrepancies of the observed means according to the theoretical equations and S_A, S_B, and S_C are the respective standard errors. Tests of significance may be carried by the customary methods. If the scale is adequate these quantities will each equal zero within the limits of their standard errors. The results of the three tests for the adequacy of the actual scale and the logarithm scale are:

	$A \pm s_A$	$B \pm s_B$	$C \pm s_C$
Actual weight	.55 ± 1.59	.10 ± 1.20	.79 ± 1.97
Logarithmic weight	.0025 ± .0192	.0473 ± .0266	.1202 ± .0322

The above results seem to indicate that the actual scale is superior than the logarithmic scale. However, this test is merely based on the comparison between the

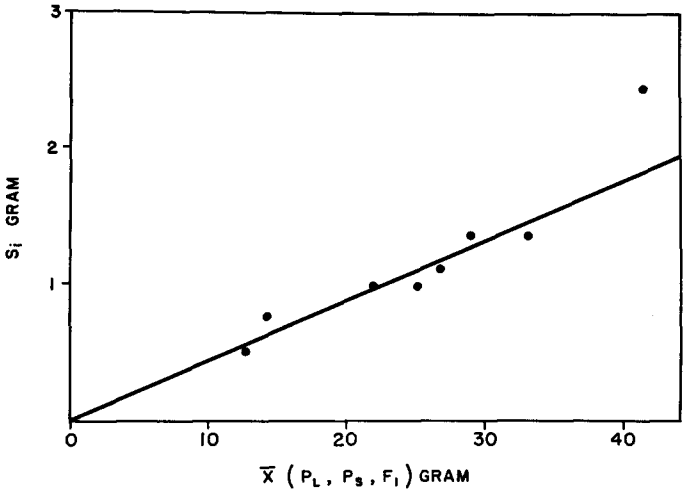

FIGURE 2a.—A plot of the standard deviation within litter against the mean body weight in each subgroup of the Large, Small and F_1 hybrid. It shows that the standard deviation increases proportionally to the mean.

means of the different groups of mice. Some tests based on the other statistics have to be considered.

One test is the comparison of standard deviations with their respective means of the genetically constant populations. If the standard deviation increases with increase of the mean, multiplicative gene action and/or environment genic interaction are suggested. In these data, the standard deviations of the F_1 hybrid and parental subgroups are approximately proportional to their means (fig. 2a). Consequently the coefficients of variation are about the same size allowing for random deviation (fig. 2b).

One could also use the standard deviations and the means of the backcrosses, both B_L and B_S, if there were no dominance. Although this test was not as indicative

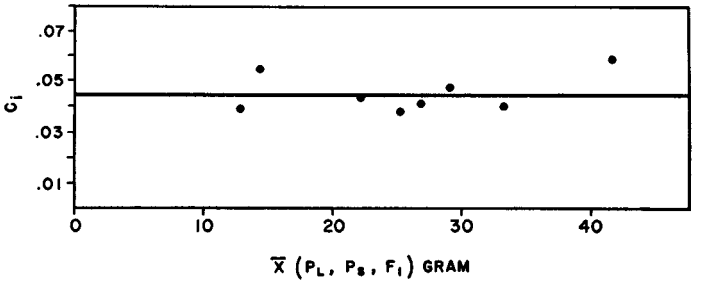

FIGURE 2b.—A plot of the coefficient of variation against the mean body weight in each subgroup of the Large, Small and F_1 hybrid. It shows that the coefficients vary randomly about their mean

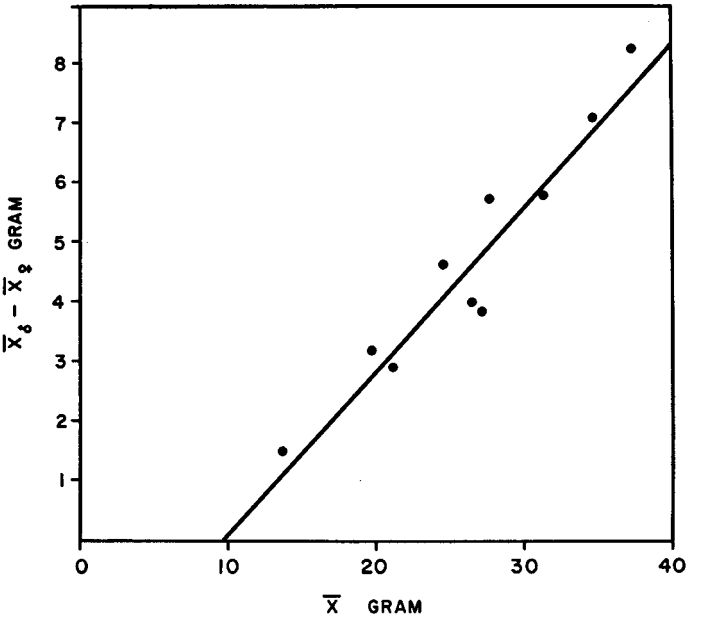

FIGURE 3a.—A plot of sex difference against the mean in gram body weight in each subgroup of the Large, Small and F_1 hybrid. The regression coefficient of sex difference on the mean in gram body weight is .28. The regression line intercepts the x-axis at about the 10 gram point.

as the one above, the standard deviations within litter were found approximately proportional to their means.

Another test is the relation of constant factors to the scale. In this case, the difference in body weight between sexes in each subgroup is unique and can be applied effectively. It was found the larger the body size the greater the sex difference in body weight; that is, the difference is proportional to the mean in each subgroup (fig. 3a). This is a third bit of evidence which suggests multiplicative gene action. From the results of the different tests and previous investigations, it is felt that, although the actual scale appeared to fit the means better, the logarithmic scale is more adequate when all evidence is considered. Therefore, in the following analyses, only the means and variances on the logarithmic scale are considered.

PARTITION OF VARIANCE AND ESTIMATION OF SEGREGATING UNITS

Several statistics concerning the various proportions of genetic and environmental variances were given by FISHER, *et al.* (1931) and WRIGHT (1952) on the assumption that non-additive interactions have been eliminated by use of an adequate scale. The following equations are based on the symbols adopted by WRIGHT.

$$\begin{aligned} \sigma_P^2 &= \sigma_{F_1}^2 = \sigma_e^2 \\ \sigma_{F_2}^2 &= \sigma_g^2 + \sigma_d^2 + \sigma_e^2 \\ \sigma_{B_1}^2 + \sigma_{B_2}^2 &= \sigma_g^2 + 2\sigma_d^2 + 2\sigma_e^2 \end{aligned}$$

The genetic variance may be analyzed into an additive component, σ_g^2, due to the difference between the homozygotes of each pair of genes; and a genetic dominance component, σ_d^2, due to the difference between the heterozygote and the mid-parent of each pair of genes. The relative proportion of σ_g^2 and σ_d^2 is different between the F_2 and backcross hybrids. The environmental variance σ_e^2, can be estimated by the variance within the pure strain or the F_1 hybrid. Using the variance of only the F_1 hybrid would have the advantage of eliminating any bias due to inadequate scaling, but any error due to genetic homeostasis will be introduced. Consequently, the average of the variances of the parental strains and the F_1 hybrid may be a better estimate of σ_e^2 than one based on either parental strain or F_1 hybrid alone. On the within litter basis it was found to be .00041. Using the computed variances from the different genotypic populations, it is possible to solve the following equations simultaneously, thereby obtaining the estimates of the different genetic components.

$$\sigma_g^2 = 2\sigma_{F_2}^2 - (\sigma_{B_L}^2 + \sigma_{B_S}^2) \quad (1a) \qquad 2\sigma_g^2 = \sigma_{F2}^2 + \sigma_{B_L}^2 + \sigma_{B_S}^2 - 3\sigma_e^2 \quad (2)$$

$$\sigma_d^2 = \sigma_{F_2}^2 - (\sigma_g^2 + \sigma_e^2) \quad (1b)$$

Equations (1a) and (1b) can be used to separate dominance component from additive genetic variance, however, they magnify sampling error, whereas equation (2) incorporates the dominance component with the additive genetic variance but does not introduce a greater sampling error. The computed values of the additive genetic variance was .00189 from equation (2) and .00073 from equation (1a) and of the dominance variance was .00077 from equation (1b). The additive genetic variance .00189 estimated from equation (2) is considered to be a better estimate. The reason will be discussed later.

A formula for estimating the minimum number of segregating units, $R^2/8s_g^2$, was

TABLE 4

Estimates of the number of segregating units which distinguish the Large and Small strains with respect to body size and the interpretations of the segregating index

Segregating index	Equal effect		Geometric series		Maximum amount possible to one locus
	N	$2G_A/R$	C	$2G_A/R$	
11	11	2.03	.83	3.80	6.76

given by CASTLE (1921) (modified by WRIGHT). It is assumed that each parental strain of mouse, Large and Small, has its own set of genes having a constant effect on body size. The Small strain contributes no plus genes for body size except those that may already be present in the Large. The reciprocal situation is assumed to be equally true. Then the amount of difference in body weight, R, between the Large and Small strains could be ascribed to the blocks of genes segregating freely in the F_2 generation. Applying the computed additive genetic variance, .00189, the minimum number of segregating units was estimated at 11, using the logarithmic scale.

There are many possible interpretations with regard to the distribution of the genic effects. It may be assumed that their effects are equal among the different pairs of alleles, or their maximum effects are attributed to a single pair of alleles or thirdly that the effects of the different pairs of alleles are decreasing geometrically from a leading locus. The equations for computing the contribution from one pair of alleles according to the different interpretations has been given by WRIGHT (1952). The computed values for the effect of various combinations of pairs of alleles upon the body weight within each of the three possible interpretations have been given in table 4.

DISCUSSION

Scale

The choice of an appropriate scale is the fundamental step in the analysis of polygenic variation since the description of a body of data or a comparison of two or more bodies of data are dependent on the scale used in measurement. We cannot assume without evidence that a scale adequate to represent the variation of a character in one population under one certain kind of environment will be as adequate to represent the variation of the same character under another different environment. Nor could we assume without evidence that the same scale would suffice for the same character for different genotypes. It is certainly not possible to assign an *a priori* scale to express variation in a continuously varying character with our present knowledge of the complexities of gene action. It is essential, therefore, to devise and test some scale, which is thought possible to fit the data at hand.

There are many different types of transformations of actual measurements that are adaptable to characters with different underlying causes (WRIGHT 1952). Both MACARTHUR and FALCONER have favored the logarithmic scale for body weight in mice. Use of the logarithmic scale in this body of data can be further justified by a comparison of s^2 and $s^2_{\log x}$ between the different genotypic groups (table 3). On an adequate scale, the variances of the isogenic lines theoretically should be equal. In

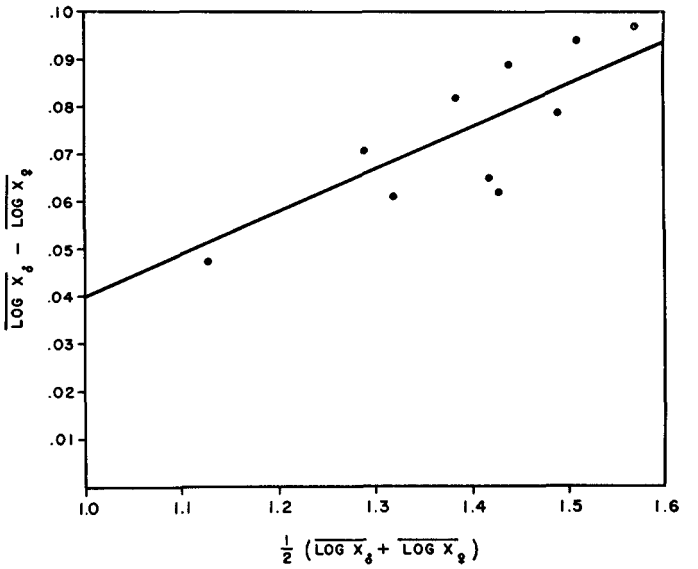

FIGURE 3b.—Illustrating, on the logarithmic scale, the sex difference in body weight in relation to the mean body weight in each subgroup of the Large, Small and F_1 hybrid. It shows that a slight regression appears still to exist.

these data on the logarithmic scale, the variances of P_L and P_S were quite similar, while on the actual scale the variance of P_L was about 9 times larger than that of the P_S. In addition, the variance of the F_1 hybrid on the logarithmic scale was shown to be closer to the parental strains than on the actual scale. The slightly lowered value of the F_1 hybrid could be attributed to genetic homeostasis of hybridization. The other noticeable difference between the two scales, is the interchange of the relative order of magnitude of the variances in the backcrosses. That is $s^2_{P_L} > s^2_{P_S}$ on the actual scale, while $s^2_{P_L} < s^2_{P_S}$ on the logarithmic scale. This does not imply necessarily that the logarithmic scale is superior to the actual scale. It indicates, however, a practical difference between the two scales when applied to the same data, and reflects the importance of choosing the appropriate scale.

In figure 3a, the regression line of sex difference on mean body weight intercepts the x-axis at about the 10 gram point, and the same regression line on the logarithmic scale is not parallel to the x-axis (fig. 3b). These results seem to indicate that log x-transformation probably does not go far enough, and log (x − 10) transformation would be more adequate.

Variance

To remove the variation between litters would undoubtedly tend to reduce some of the environmental variation which may be unequally distributed through the different populations. Sources contributing to such variation, in addition of the measurable factors, such as litter size and age of the mother, could involve any permanent or temporary irregularities of the mother such as chronic disease or short period of physiologic disturbance. The latter may retard the growth of the young,

remain undetected and hence be non-correctable, by the method of regression coefficient. The method of analysis of variance has the advantage that variation from such undetectable sources are incorporated into the between-litter variation. Only a very small portion of genetic variation is involved in the litter variation. Its effect relative to the total genetic variation could be considered practically negligible.

However, the variation between litter constituted a large proportion of the total variation. This variance has to be restored if we want to consider the over-all environmental contribution to the total variability. The average of the total variances of the subgroups in the F_1 hybrids and the pure strains may be considered as a good estimate of the over-all environmental variance. It was obtained to be .00198. Thus the environmental variation within litter contributed only about one fifth of the total environmental variation.

Whether or not dominance played an important role in this cross between mouse strains deserves consideration. According to equations (1a) and (1b), the dominance variance was estimated to be .00077 and the additive variance to be .00073. The dominance variance was even slightly higher than the additive genetic component. From the previous observations (CHAI 1956), the means of body weight of the F_1 hybrids were about the same as the means of the mid-parents. If dominance existed, it would be equally distributed between parental strains; then, and only then such a comparatively large component of dominance variance could be explained. If such a situation exists, the means of the B_L and B_S in the present study should be closer to the means of their pure parental strains than to the mean of the F_1 hybrid. On the contrary, the backcross means, although both shifted very slightly to large size, were about the same as the mid-values of the parental groups. Therefore, we very much suspect that the relatively large value of the dominance variance obtained was mainly due to magnification of sampling error. Thus both estimates of dominance variance and additive genetic variance from equations (1a) and (1b) are considered unacceptable. The main contribution to the genetic variance are most likely the genes giving only additive effects. Therefore the amount of dominance variance incorporated into the additive genetic variance (.00189) according to equation (2), if any, is assumed to be negligible.

Segregating units

The number of loci for size inheritance would be underestimated if linkage among them existed. However, it would be impossible to detect linkages without second backcross or F_3 generations. If the genes concerned in the present cross have no lethal or semi-lethal effect, linkage would not affect the frequencies with which the allelomorphs of each gene are recovered in the segregating generations. On an adequate scale, linkage can have no effect on the mean measurements of the segregating generation. It, however, shows its effect in the second degree statistics, the variance. At the present stage of our knowledge it would be safe to consider the value N as a *segregating index* as suggested by WRIGHT. It measures the freely segregating units, instead of all segregating factors. Each unit would be assumed to have at least one locus modifying body size. The computed segregating units, approximately 11, seems not unreasonable in comparison with minimal number of 19 factors in FALCONER'S experiment and 54 factors in MACARTHUR'S experiment as estimated by FALCONER (1953).

One might ask if there is a major locus which modifies body size on either plus or minus direction. In view of the fairly symmetrical distributions of the hybrids, such a possibility would be practically eliminated. The data do not permit a choice between the alternatives, equal effect and effect in geometric series. Still another possibility exists, that is the gene effects are so different and so irregular that they would be difficult to describe mathematically. According to FALCONER'S selection experiment the rate of progress in each generation appeared fairly even. This may suggest a possibility of equal gene effects. Mice in the present experiment were genetically so different from FALCONER'S that without further experimentation similar interpretation would hardly be justified.

One powerful method for determining the relative effects of genes on body size is to make repeated backcrosses using a marker gene closely linked to one for body size. Because the character of body size is polygenic, relatively small effects could be produced by one or two gene substitutions. The detection of such a marker gene would not be an easy task.

SUMMARY

A study of the genetics of body size in mice by crossing Large and Small strains of mice to produce F_1, F_2 and backcross generations has been made.

An analysis of the means and variances of 60-day body weight in the different genotypic groups of mice has been carried out. Means of F_2 and backcross generations were slightly above their respective theoretical values. The F_1 and F_2 means were halfway between the parents and the backcross means were halfway between the respective parents. The variance of the F_2 hybrids was the largest, the first backcross generations the next and the average of the variances of F_1 hybrids and the Large and Small strains were the smallest.

The effective size genes involved in this cross have been found to act additively on a logarithmic scale rather than arithmetic scale. The computed value of additive genetic variance was .00189 and of the environmental variance within litter was .00041. The overall environmental variance was .00198. The dominance effect contributed to the total variability, if any, was considered to be trivial.

The minimum number of segregating units has been estimated at 11. Each segregating unit has been assumed to include at least one locus modifying body size. The possible interpretation of distribution of genic effect was proposed.

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