Theor. Appl. Genet. 59, 373-379 (1981)

Gene Number Estimation When Multiplicative Genetic Effects are Assumed - Growth in Flour Beetles and Mice*

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Summary. Estimation of the number of segregating genes affecting a quantitative trait in populations initiated from a cross of two homozygous lines is considered. Experimental data, for the trait in question, is assumed available on total response to recurrent selection initiated in the F_2 or F_3 generation, the initial additive genetic variance and the heterosis exhibited in the F_1 generation. Appropriate procedures when multiplicative genetic effects are assumed are developed and reasons for assuming multiplicative rather than additive effects are indicated. These procedures were employed to estimate the number of genes affecting pupa weight in a population of flour beetles and growth in a population of mice. Estimates were 50-60 percent smaller than those obtained using familiar estimation procedures appropriate when no epistasis is assumed. However, the estimated numbers (about 200 and 100 for pupa weight and mouse growth, respectively) were still rather large.

Key words: Gene number estimation – Multiplicative genetic effects – Gene numbers – Pupa weight – Growth of mice.

The multiple factor hypothesis concerning the genetic variation of quantitative traits had become well established by 1920 and from 1910 to the present geneticists and breeders have been actively interested in the numbers of genes that contribute to the population variances of quantitative traits. More recently, Comstock (1973, 1977, 1978) has emphasized the importance of this issue with respect to good decisions concerning effective population size in breeding programs.

The primary bases for inference concerning number of genes that affect a quantitative trait are cytogenetic or statistical. In the first case, the basis is the number of chromosome regions in which one or more genes affecting a trait can be shown to be present. In the second, the bases are genetic variance and evidence concerning the genetic extremes of the trait; the nature of gene effects is then an obvious issue.

The first statistical procedure, outlined by Castle (1921) who acknowledged advice from Sewall Wright, is widely known as the Castle-Wright formula. The numerical quantities required are estimates of (1) the genetic effect of changing the frequencies of all alleles favorable to the trait from 0.0 to 1.0 and (2) the genetic variance when allele frequencies are all equal to 0.5. Variations of the Castle-Wright procedure have been discussed by Wright (1952, 1968), Falconer (1960), Comstock (1969) and Park (1977). All of them assume that the effects of single locus genotypes are all additive, i.e., that there is no epistasis.

Data obtained in selection experiments described by Rahnefeld et al. (1963) and Enfield et al. (1966) were in some respects more compatible with the multiplicative than with the additive effect model. The estimation procedure described herein, was therefore devised and employed.

Alternatively, we could have analyzed logarithms of the original data but that would have (1) required a rather large amount of work that was avoided by using statistics already computed from the non-transformed data and (2) entailed the assumption that non-genetic, as well as genetic, effects were multiplicative.

In addition to setting out the theory base for the estimation procedure when multiplicative genetic effects are assumed, this paper will compare estimates by different procedures using parameter estimates obtained in the selection experiments referred to above.

* Scientific Journal Series, Minnesota Agriculture Experimental Station. Work supported by the National Science Foundation Grant No. G-1238, the Minnesota Agricultural Experiment Station and by Public Health Service Grant No. 16074

0040/5752/81/0059/0373/$ 1.40

The Experimental Data

As described by Rahnefeld et al (1963) and Enfield et al. (1966) our data were obtained as follows. Two long inbred lines were crossed. The performance of the F_1 was compared with that of the parent lines. F_1 individuals were mated inter se to provide an F_2 and random F_2 individuals were mated to produce the F_3 generation. Thereafter selection among individuals was practiced in each generation, the selected animals being animals mated randomly (except for avoidance of full-sib matings) to produce the following generation. Selection was for high pupa weight in the case of flour beetles and high post-weaning (18-42 day) weight gain in the case of mice and was continued until it had become clear that plateaus had been reached.

Non-additive genetic effects were indicated by the following consequences of the recurrent selection.

(1) In both experiments the total response to selection was greater than the original average for the selected trait (Table 1). This indicates either non-additive genetic effects or alternatively, if effects are additive, that individuals homozygous for large proportions of the unfavorable alleles do not survive or do not reproduce.

(2) Additive genetic variance increased through one-half or more of the time required to reach plateaus. This was indicated in both experiments by constant or increasing responses per generation of selection through many generations despite concurrent increases in phenotypic variance. It was confirmed in the flour beetle experiment by the averages of statistical estimates of the additive genetic variance. In successive 36 generation intervals those estimates were 21,947; 34,678 and 36,715. These trends as the frequencies of favorable alleles were increased from 0.5 (the necessary initial values in a population from the cross of two pure lines) could result from gradual dissipation of an original excess of repulsion phase linkage disequilibrium or from dominance of unfavorable alleles instead of from epistasis. However, dominance of unfavorable alleles was contraindicated by the observation of some heterosis in the F_1 generation (Table 1).

While the results listed above are doubtful in the absence of epistasis, they are, as shown later, expected concommitants of the multiplicative model.

Table 1 lists the parameter estimates from our experimental data that were used in computing the gene number estimates reported in Table 2. The parameters are symbolized as follows both in Table 1 and elsewhere in the manuscript.

σ^2_{go} = the additive genetic variance in a linkage equilibrium population in which allele frequencies are 0.5 for all genes that were heterozygous in the F_1,

$\bar{Y}_o$ = the genotypic mean of such a population (it was estimated, of course, in terms of F_2 and F_3 performance),

$\bar{Y}_m$ = the genotypic mean of a population in which the favorable allele is homozygous for all genes that were heterozygous in the F_1,

$\bar{F}_1$, $\bar{P}_1$ and $\bar{P}_2$ = the mean performance of the F_1 and parent lines 1 and 2, respectively,

Table 1. Parameter estimates (the measurement units were micrograms for pupa weight and grams for weight gain)

Trait	Parameter[a]	Population[b]	Estimate	
Pupa weight (flour beetles)	$\bar{Y}_o$	S_1	2459	2436
		S_2	2412	
	$\bar{Y}_m$	S_1	5745	5640
		S_2	5537	
		H_1	5952	5909
		H_2	5866	
	σ^2_{go}			13,360
	H_a			251
	H_m			1.12
Weight gain (mice)	$\bar{Y}_o$			11.00
	$\bar{Y}_m$			22.60
	σ^2_{go}			0.33–0.48
	H_a			1.80
	H_m			1.20

[a] The meanings of symbols in this column are provided in the first paragraph of 'The experimental data'

[b] S_1 and S_2 were replicate populations initiated from the same F_2 population. H_1 and H_2 were replicate populations initiated from the F_1 of the cross between S_1 and S_2 made after 72 generations of selection in S_1 and S_2

Table 2. Gene number estimates

Assumptions	Pupa weight (Flour beetles)		Weight gain (Mice)	
	$\hat{\bar{Y}}_m = 5640$	$\hat{\bar{Y}}_m = 5909$	$\hat{\sigma}^2_{go} = 0.33$	$\hat{\sigma}^2_{go} = 0.48$
No epistasis	415	485	237	163
No epistasis, no dominance	384	451	204	140
Mult. genetic effects	180	197	119	81
Mult. genetic effects, $m_1 = (m_2 + 1)/2$	158	175	96	67
Mult. genetic effects, $m_2 = m_1^2$	157	174	95	66

$H_a = \bar{F}_1 - (\bar{P}_1 + \bar{P}_2)/2$, and
$H_m = \bar{F}_1/\sqrt{\bar{P}_1\bar{P}_2}$.

The estimates of $\bar{Y}_m$ in the case of flour beetles were averages of pupa weight in cycles 111-130 of the experiment. The estimate of $\bar{Y}_m$ for mice was the average 18-40 day weight gain during cycles 47-60 of the mouse experiment. In both species the populations had apparently plateaued prior to the period used to measure $\bar{Y}_m$. In the case of the beetles additive variance had not been exhausted and thus $\bar{Y}_m$ was underestimated. The estimate of σ^2_{go} for pupa weight was an average of estimates based on sire components of variance and parent-offspring regressions using data from the S_1, the S_2 and replicate control populations in the first 12 cycles of the experiment. There were 72 full-sib families (two by each of 36 male parents) in each of the four populations in each generation. Sire components, parent-offspring regressions and realized heritabilities were used to establish the range of σ^2_{go} in the mouse experiment. Data from the first 18 generations were employed. The highest of the estimates cited by Comstock (1969) was not employed because it was obtained from results in generations 28-36 when additive genetic variance had obviously increased.

Theory Base for the Multiplicative Model

Assume two alleles per segregating locus (because our concern is with populations generated from the cross of two pure lines) and let

- G_{ik} symbolize genotype for the i-th gene where k (= 0, 1 or 2) is the number of favorable alleles in that single-locus genotype.
- m_{ik} be the multiplicative effect of G_{ik},
- f_{ik} be the frequency of G_{ik} and
- K be a row vector that specifies the number of favorable alleles for each of *n* genes in any total genotype.

Then, using K as a subscript to specify individual total genotypes,

$$Y_K = \alpha \prod_i m_{ik} \tag{1}$$

where $\prod_i m_{ik}$ signifies the product of the entire series of m's (m_{1k} through m_{nk}, the values of k for successive genes being given by K), $m_{i0} = 1.0$ for all genes and α is the value of the genotype that is homozygous for the unfavorable allele of all genes that were heterozygous in the F_1 and the same as the parent lines for all other genes.

Assuming no correlations of genotypes between loci (linkage equilibrium), the frequency distribution of total genotypes is given by expansion of the product

$$\prod_i (f_{i2} G_{i2} + f_{i1} G_{i1} + f_{i0} G_{i0})$$

and substituting m's for G's, remembering that $m_{i0} = 1.0$ for all loci,

$$\bar{Y} = \prod_i (f_{i2} m_{i2} + f_{i1} m_{i1} + f_{i0}) \tag{2}$$

where $\bar{Y}$ is the population mean of genotypic values.

To obtain the additive genetic variance contributed by any single gene, say the j-th, we require

- $\overline{BB}_j$ = the average value of all genotypes that are homozygous (BB) for the favorable allele of the j-th gene.
- $\overline{Bb}_j$ = the average value of all genotypes that are Bb for the j-th gene and
- $\overline{bb}_j$ = the average value of all genotypes that are homozygous for the unfavorable allele of the j-th gene.

From Eqs. (1) and (2) it is apparent that

$$\left.\begin{aligned} \overline{BB}_j &= m_{j2} Z_j \alpha \\ \overline{Bb}_j &= m_{j1} Z_j \alpha \\ \text{and} \\ \overline{bb}_j &= m_{j0} Z_j \alpha = Z_j \alpha \end{aligned}\right\} \tag{3}$$

where

$$Z_j = \prod_{i \neq j} (f_{i2} m_{i2} + f_{i1} m_{i1} + f_{i0} m_{i0}) \tag{4}$$

Here $\prod_{i \neq j}$ signifies the product of the whole series of values except the one for the j-th gene itself. Then using symbols defined by Comstock and Robinson (1948) and remembering that $m_{i0} = 1.0$

$$u_j = 1/2(\overline{BB}_j - \overline{bb}_j) = 1/2(m_{j2} - 1)Z_j\alpha$$

$$a_j = (2\overline{Bb}_j - \overline{BB}_j - \overline{bb}_j)/(\overline{BB}_j - \overline{bb}_j)$$

$$= (2m_{j1} - m_{j2} - 1)/(m_{j2} - 1)$$

and

$$\sigma^2_g = \sum_j \sigma^2_{gj} = \sum_j 2q_j(1 - q_j)[1 + (1 - 2q_j)a_j]^2 u_j^2$$

$$= \sum_j 2q_j(1 - q_j)[m_{j1} - 1 - q_j(2m_{j1} - m_{j2} - 1)]^2 Z_j^2 \alpha^2 \tag{5}$$

Here j is used to identify gene because Z_j is defined for the j-th (not the i-th) gene and q_j is the frequency of the favorable allele of the j-th gene.

As when no epistasis is assumed, genetic effects are assumed equal for all genes for the purposes of gene number estimation. Then, from Eq. (1)

$$\bar{Y}_m = \alpha m_2^n \tag{6}$$

and from Eq. (2), remembering that $\bar{Y}_o$ is defined for a population in which allele frequencies at segregating loci are 0.5 so that f_{i2}, f_{i1} and f_{i0} are 1/4, 1/2 and 1/4, respectively,

$$\bar{Y}_o = \alpha\left[\frac{m_2 + 2m_1 + 1}{4}\right]^n \quad (7)$$

Next, from Eq. (4) and (5) and the fact that σ^2_{go} is defined for a population in which allele frequencies at segregating loci are 0.5,

$$\sigma^2_{go} = \frac{n}{2}\left[\frac{m_2 - 1}{2}\right]^2\left[\frac{m_2 + 2m_1 + 1}{4}\right]^{2(n-1)}\alpha^2 \quad (8)$$

It remains to obtain an expression for H_m. Because all gene loci at which different alleles are homozygous in the pure line parents will be heterozygous in the F_1 generation, we have from Eq. (1)

$$\bar{F}_1 = \alpha m_1^n$$

Going on to the quantity $\bar{P}_1\bar{P}_2$, if n_1 genes are homozygous for the favorable allele in line 1 and n_2 in line 2,

$$n_1 + n_2 = n$$

$$\bar{P}_1 = \alpha(m_2)^{n_1} \quad \bar{P}_2 = \alpha(m_2)^{n_2}$$

and

$$\bar{P}_1\bar{P}_2 = \alpha^2 m_2^n.$$

It follows that

$$H_m = \bar{F}_1/\sqrt{\bar{P}_1\bar{P}_2} = (m_1/m_2)^n \quad (9)$$

Estimation Procedures

Multiplicative Genetic Effects

Substituting numerical estimates of $\bar{Y}_o$, $\bar{Y}_m$, σ^2_{go} and H_m in Eqs. (6)-(9) yields four equations in four unknowns but α appears only in Eqs. (6), (7) and (8) and cancels out of the following ratios. From Eqs. (6) and (7)

$$\frac{\bar{Y}_m}{\bar{Y}_o} = \left[\frac{4m_2}{m_2 + 2m_1 + 1}\right]^n \quad (10)$$

and from Eqs. (7) and (8)

$$\frac{\sigma^2_{go}}{\bar{Y}^2_o} = 2n\left[\frac{m_2 - 1}{m_2 + 2m_1 + 1}\right]^2 \quad (11)$$

leaving three equations, (9), (10) and (11), to be solved for m_2, m_1 and n.

If a satisfactory estimate of H_m is not available but there is reason to believe that there was essentially no heterosis exhibited in the F_1, either of the following assumptions concerning the relative sizes of m_2 and m_1 may be adequate for reducing the unknowns in Eqs. (10) and (11) from three to two. Assuming no dominance, by the criterion that $\overline{Bb_j} = 1/2(\overline{BB_j} + \overline{bb_j})$, we have from Eqs. (3) that $m_1 = (m_2 + 1)/2$. Substituting this value of m_1 in eqs. (10) and (11)

$$\frac{\bar{Y}_m}{\bar{Y}_o} = \left[\frac{2m_2}{m_2 + 1}\right]^n \quad (12)$$

and

$$\frac{\sigma^2_{go}}{\bar{Y}^2_o} = \frac{n}{2}\left[\frac{m_2 - 1}{m_2 + 1}\right]^2 \quad (13)$$

Alternatively, following Charles and Smith (1939) in assuming that individual gene effects (not just the single-locus genotype effects) are multiplicative makes $m_2 = m_1^2$. Substituting accordingly in Eqs. (10) and (11), yields

$$\frac{\bar{Y}_m}{\bar{Y}_o} = \left[\frac{2m_1}{m_1 + 1}\right]^{2n} \quad (14)$$

and

$$\frac{\sigma^2_{go}}{\bar{Y}^2_o} = 2n\left[\frac{m_1 - 1}{m_1 + 1}\right]^2 \quad (15)$$

Exact simultaneous solutions of these non-linear expressions cannot be obtained. However, approximate solutions, as good as desired, can be produced quite easily by successive approximation. We proceeded as follows in solving Eqs. (9), (10) and (11) for m_2, m_1 and n. From Eq. (10)

$$n = \frac{\ln(\bar{Y}_m/\bar{Y}_o)}{\ln[4m_2/(m_2 + 2m_1 + 1)]} \quad (10a)$$

Using our estimates of $\bar{Y}_m$ and $\bar{Y}_o$ and trial values of m_2 and m_1, a provisional value of n was obtained from Eq. (10a). This value of n along with the trial values of m_2 and m_1 was then substituted in Eq. (9) to determine whether the H_m value obtained was close to our experimental estimate. If not, the trial value of m_1 was changed, new values of n and H_m obtained from Eqs. (10a) and (9) and the process repeated until the H_m value found was sufficiently close to our experimental estimate. At that point values of m_1 and n had been found that, together with the first trial value of m_2, would explain our estimates of $\bar{Y}_m/\bar{Y}_o$ and H_m. These values were then substituted in Eq. (11) to determine whether our estimate of $\sigma^2_{go}/\bar{Y}^2_o$ would also be reasonable well satisfied. Of course it would be remarkable if that were accomplished in the first trial. If not, the next step was to repeat the entire process with a new trial value of m_2 until a set of values for m_2, m_1 and n was found that provided a good fit, by Eqs. (9), (10) and (11), to all of the experimental estimates. The n-

value of this set was, of course, the one accepted as the proper estimate.

Procedures are similar when only Eqs. (12) and (13), or Eqs. (14) or (15), are used because one of the assumptions described above has been made concerning the relative magnitudes of m_2 and m_1. Of course, in either case, the approximation process requires less time because there are only two equations to be satisfied.

No epistasis

When no epistasis was assumed the n was estimated in the usual ways. When, ignoring the observed heterosis, no dominance was also assumed, the estimation formula was

$$\hat{n} = (\hat{\bar{Y}}_m - \hat{\bar{Y}}_o)^2/2\hat{\sigma}^2_{go} \quad (16)$$

as outlined by Comstock (1969) and Park (1977). When dominance was not excluded, the formula employed was

$$\hat{n} = (\hat{\bar{Y}}_m - \hat{\bar{Y}}_o + \hat{H}_a/2)^2/2\hat{\sigma}^2_{go} \quad (17)$$

as indicated by Comstock (1969). In Eqs. (16) and (17) a caret is employed to indicate estimates.

The Estimates

Gene number estimates obtained using quantities shown in Table 1 are listed, according to trait and assumptions employed, in Table 2. As indicated in the table two estimates of $\bar{Y}_m$ (the ones provided by the S and H populations, respectively) were employed in the case of pupa weight. The estimate provided by the H population is considered more appropriate because the larger $\bar{Y}_m$ is probably due to favorable alleles that had been lost from either S_1 or S_2 but were present in the H populations following the initiation of H_1 and H_2 from the $S_1 \times S_2$ cross. In the case of growth in mice, for which the estimate of σ^2_{go} was less precise, results were obtained using estimates at the extremes of the range within which the true value of σ^2_{go} was believed to be contained.

The estimates shown are similar, but not identical, in magnitude to the comparable estimates reported by Enfield (1973, 1974) and by Comstock (1969, 1973). They differ partly because slightly different estimates of $\bar{Y}_o$ or σ^2_{go} (judged more appropriate) have been used in this case and partly because total response to selection had not been completely realized at the time of the earlier reports.

It is apparent from the last two rows of Table 2 that when heterosis is assumed absent or very small, the choice between the two assumptions regarding the relative size of m_2 and m_1 is of no practical consequence. The estimates of m_2, m_1 and α that accompanied the gene number estimates when heterosis were taken into account were as follows.

	Pupa weight (flour beetles)		Weight gain (mice)	
	$\hat{\bar{Y}}_m = 5640$	$\hat{\bar{Y}}_m = 5909$	$\hat{\sigma}^2_{go} = 0.33$	$\hat{\sigma}^2_{go} = 0.48$
m_2	1.01	1.0096	1.0136	1.02
m_1	1.00562	1.00536	1.0082	1.012
α	941	900	4.53	4.54

The estimates of α were available from Eq. (6) once the estimates of m_2 and n had been obtained. Note that the estimate of α is, in terms of the multiplicative model, the estimate of the plateau that would have been reached in response to recurrent downward selection and that this is greater than zero even though response to upward selection was greater than the initial average.

Discussion

The effect on gene number estimates of assuming multiplicative rather than additive effects of single locus genotypes is substantial (Table 2). It resulted in 50-60 percent decreases in the estimates obtained in this study. This was obviously to be expected because, assuming $m_{i2} > m_{i1} > m_{i0}$, the average multiplicative effect of single-locus genotypes, $\bar{m}_i = f_{i2}m_{i2} + f_{i1}m_{i1} + f_{io}m_{i0}$, increases as the frequency of the favorable allele increases so that bb and Bb genotypes are replaced by BB genotypes. A consequence is positive interaction among the effects of increases in frequencies of favorable alleles so that the total effect of making favorable alleles homozygous is greater than the sum of their effect reflected in the additive genetic variance when all allele frequencies are 0.5. This is in contrast to the situation when there is no epistasis and u-values (average effects of substituting favorable for unfavorable alleles in genotypes) are not functions of allele frequencies at other genes.

The progressive increase in $\bar{m}_i$ as q_i increases is responsible also for the increase, for some time, in additive genetic variance in response to selection (for large values of the trait) that is initiated when allele frequencies are near 0.5. Because Z_j, the product of all $\bar{m}$'s except that for the j-th locus, see Eq. (4), is increased progressively as the q's approach 1.0, it is apparent from Eq. (5) that additive genetic variance will increase until the q's are large enough so that further increases in them will cause decreases in the values of $q(1-q)$ that are sufficient to more than offset the increases in the Z^2's. It is quite easily shown by substitution in Eqs. (4) and (5) that additive genetic variance can continue to increase until allele frequencies have become relatively large. Assume, for example,

(1) Hardy-Weinberg frequencies of genotypes for all genes

(2) No variation among genes in either m_2 or m_1 (remember that $m_0 = 1.0$)

(3) That allele frequencies increase at the same rate for all genes so that q, though changing, does not become variable among genes and

(4) That the values of n, m_2 and m_1 are those estimated for mouse growth ($n = 81$, $m_2 = 1.02$, $m_1 = 1.012$) when $\hat{\sigma}^2_{go} = 0.48$ was employed.

Then σ^2_{go} continues to increase until the q's exceed 0.8.

Because gene number estimates are substantially lower when multiplicative, rather than additive, effects are assumed the choice of model is not trivial. Two reasons, (1) total response to upward selection in excess of average performance when allele frequencies are 0.5 and (2) an increase in additive genetic variance through a considerable portion of the time required to reach a plateau in response to upward selection, have been given for choosing the multiplicative model. The first of these is not thoroughly compelling because individuals homozygous for large numbers of unfavorable alleles may either not survive or not reproduce. The second appears a more compelling reason. When there is reason to believe that, on average, dominance is not in the direction of the unfavorable alleles, the only explanation for such an increase in additive variance given additive gene effects would be a substantial initial excess of repulsion phase linkage disequilibrium, a state for which no good argument can be made on probabilistic grounds even when the performance of the two parent inbreds is nearly equal. Published experimental evidence is understandably meagre. However, Moll et al. (1964) report estimates of the magnitudes, at the F_2 and later (F_8 and F_{12}) stages, of the genetic variance in Design III experiments that would be affected in the same way by linkage disequilibrium as additive genetic variance. Because their experiments involved no selection, and hence minimal decreases in $q(1 - q)$, dissipation of repulsion phase disequilibrium would have had maximum opportunity to cause increase in the genetic variance in question. However, decreases were more frequent than increases and statistically significant increases were observed in only one of the seven traits of maize that were studied. All things considered, it appears that the multiplicative model should certainly receive attention when, as in our experiments, both phenomena discussed in this paragraph are encountered.

Wright (1952, 1968) pointed out that if gene effects, though additive, are variable in magnitude, the number estimate obtained using the Castle-Wright formula is biased downward. For this and other reasons he chose to refer to the quantity estimated as the 'segregation ratio'. Comstock (1969) noted that if all else were as assumed in the procedure that is appropriate when there is no epistasis, the quantity estimated is $n/(1 + \sigma^2_u/\bar{u}^2)$ where σ^2_u and $\bar{u}$ are the variance and mean, respectively of the u-values of genes affecting the trait. We have no comparable general expression for the bias due to variation of m-values among loci when multiplicative effects are present and the estimation method described in this paper is employed. However, we have by numerical examination found that the result again is downward bias.

The estimates in Table 2 indicate that the magnitude of heterosis exhibited in the F_1 generation should be taken into account if an adequate estimate of it is available. It provides a non-arbitrary basis for assessing the size of m_1 relative to that of m_2. With respect to both traits for which results are presented herein, the gene number estimate was somewhat larger when the evidence concerning heterosis was employed even though the amounts of heterosis were rather small.

It is interesting that, in the case of mouse growth, the relative effect of using different estimates of σ^2_{go} was the same for all methods employed. It is obvious that this should be so for estimates provided by Eqs. (16) and (17). It is not so obvious (to us, at least) that the effect should have been the same when multiplicative effects were assumed.

Our gene number estimates for mouse growth are much larger than those reported by Roberts (1966). The theory base for his estimates assumed no epistasis. Our estimates assuming no epistasis varied from 140 to 237, his varied from 2 to 20. Roberts used theory by Hill and Robertson (1966) to estimate $2Niu/\sigma$ from the 'half-life' of response to recurrent selection. Here N = effective population size, i = the selection differential per generation, σ = the phenotypic standard deviation of the trait and u has the meaning used elsewhere in this manuscript. Figure 11 of Hill and Robertson (1966) shows the relations among half-life measured in terms of N, $2Niu/\sigma$ and initial frequency of the favorable allele. It provides a basis for estimating $2u/\sigma$ when N, half-life and initial allele frequencies are known. Then estimates of $2u/\sigma$ and heritability enable estimation of gene number (subject to assumptions that include additivity of gene effects, independent assortment and the same u-values for all genes). We applied the method described and used by Roberts and obtained estimates in the range, 145-200, depending on the heritability estimate employed. These are in line with other estimates (163 and 237) obtained when additivity was assumed. Half-life as a multiple of N was similar (0.45N) in our experiment to those reported by Roberts. However, because N was considerably larger in our experiment, our estimate of $2u/\sigma$ was smaller (0.087) than those he obtained. Why his estimates of the proportionate effects ($2u/\sigma$) of genes were from 4 to 10 times as large as ours is not easily explained. There is no obvious reason why large-effect genes should have been segregating in the populations from which his

data were obtained and not in ours. Because effective population size was only about 35 percent as large in his populations as in ours there was probably more linkage disequilibrium (see Hill and Robertson 1968) and while that would probably shorten half-life, thereby increasing the estimates of proportionate effects, it is far from obvious that the impact would be enough to account for the large difference between estimates from his data and ours.

Literature

Castle, W.E. (1921): An improved method of estimating the number of genetic factors concerned in cases of blending inheritance. Science 54, 223

Charles, D.R; Smith, H.H. (1939): Distinguishing between two types of gene action in quantitative inheritance. Genetics 24, 34-48

Comstock, R.E.; Robinson, H.F. (1948): The components of genetic variance in populations of bi-parental progenies and their use in estimating the average degree of dominance. Biometrics 4, 254-266

Comstock, R.E. (1969): Number of genes affecting growth in mice. Genetic Lectures (Oregon State University) 1, 137-148

Comstock, R.E. (1973): Growth in mice. Genetics 74, 51

Comstock, R.E. (1974): Consequences of genetic linkage. Proc. 1st World Congress on Genetics Applied to Livestock Production. 1, 353-363

Comstock, R.E. (1977): Quantitative genetics and the design of breeding programs. In: Proc. International Conference on Quantitative Genetics (eds.: Pollak, E.; Kempthorne, O.; Bailey, T.B.), pp. 705-718. Ames, Iowa: The Iowa State University Press

Comstock, R.E. (1978): Quantitative genetics in maize breeding. In: Maize Breeding and Genetics (ed.: Walden, D.B.), pp. 191-205. New York-Chichester-Brisbane-Toronto: John Wiley and Sons

Enfield, F.D.; Comstock, R.E.; Braskerud, O. (1966): Selection for pupa weight in *Tribolium Castaneum*. I. Parameters in base populations. Genetics 54, 523-533

Enfield, F.D. (1973): Long term selection for pupa weight in *Tribolium*: gene action and gene numbers. Genetics 74(2, part 2), s72

Enfield, F.D. (1974): Recurrent selection and response plateaus. Proc. 1st World Congress on Genetics Applied to Livestock Production. 1, 365-371

Falconer, D.S. (1960): Introduction to Quantitative Genetics. New York: The Ronald Press Company

Hill, W.G.; Robertson, A. (1966): The effect of linkage on artificial selection. Genet. Res. 8, 269-294

Hill, W.G.; Robertson, A. (1968): Linkage disequilibrium in finite populations. Theoret. Appl. Genet. 38, 226-231

Moll, R.H.; Lindsey, M.F.; Robinson, H.F. (1964): Estimates of genetic variances and level of dominance in maize. Genetics 49, 411-423

Park, Y.C. (1977): Theory for the number of genes affecting quantitative characters I. Estimation of and variance of the estimation of gene numbers for quantitative traits controlled by additive genes having equal effect. Theoret. Appl. Genet. 50, 153-161

Rahnefeld, G.W.; Boylan, W.J.; Comstock, R.E.; Singh, M. (1963): Mass selection for post-weaning growth in mice. Genetics 48, 1567-1583

Roberts, R.C. (1966): The limits of artificial selection for body weight in mouse I. The limits attained in earlier experiments. Genet. Res. 8, 347-360

Wright, S. (1952): The genetics of quantitative variability. In: Quantitative Inheritance, pp. 5-41. Agric. Res. Council, London: Her Majesty's Stationery Office

Wright, S. (1968): Evolution and the Genetics of Populations. I. Genetic and Biometric Foundations. Chicago and London: The University of Chicago Press

Received December 18, 1980
Communicated by R.C. Lewontin

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