

THE RESPONSE TO ARTIFICIAL SELECTION DUE TO AUTOSOMAL GENES OF LARGE EFFECT

I. CHANGES IN GENE FREQUENCY AT AN ADDITIVE LOCUS

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Summary

In this series of papers, it is proposed to examine the theoretical consequences of the segregation of genes of large effect in populations under artificial selection. The problem of assigning selective values to the genotypes at such a locus is discussed in this paper, and the behaviour in large populations of an additive autosomal gene with two alleles is examined in detail.

A description is given of the effects of selection for genes of large effect on three observable phenomena, viz. (1) the ratio of realized to predicted response and its dependence on the intensity of selection imposed, (2) the asymmetry of response to be expected in two-way selection experiments, and (3) changes in the magnitude of the total additive genetic variance.

It is concluded that under selection of low intensity, the segregation of a small number of genes of large effect is unlikely to lead to appreciable departure from the predicted rate of response in either the positive or negative directions, or to conspicuous changes in phenotypic variance, over a five-generation period. Under selection of high intensity on the other hand, one can consider the possibility of such loci contributing up to 5% of the additive genetic variance present in the base population, without leading to dramatic changes in variance under short-term selection. Loci of proportionate effect in the neighbourhood of 1.0 may then give rise to pronounced asymmetry and to conspicuous departures from predicted rates of response.

I. INTRODUCTION

The response of a quantitative character to artificial selection over a short period of generations can readily be predicted from an analysis of the initial population, provided the system concerned satisfies certain conditions. Apart from problems associated with the choice of an appropriate scale of measurement, the main elements of modern selection theory which limit its application are the following: (1) the base population is assumed to be in equilibrium under random mating; (2) the total genotypic variance is assumed to be due to the segregation of many genes, each of small effect; and (3) any changes in genotypic frequencies due to natural selection are assumed to be negligible.

In an unselected population satisfying these requirements, a study of the correlations among relatives is sufficient to indicate the nature of the phenotypic variance displayed. If the genotypic variance is additive, and maternal effects are unimportant, estimates of heritability derived from the parent-offspring correlation, from the half-sib correlation, and from the full-sib correlation have the same expectation. In the

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presence of variation due to dominance, the heritability estimates derived from the parent-offspring correlation and the half-sib correlation have the same expectation, but that derived from the correlation among full-sibs is biased. If additive \times additive interactions between loci are important, only the parent-offspring estimate of heritability can be accepted as a satisfactory basis for prediction (Griffing 1960).

Laboratory experiments may play an important role in the comparison of predicted and realized responses to artificial selection, and in the critical study of observed discrepancies. Outstanding in this regard are the experiments conducted by Clayton, Morris, and Robertson (1957) and by Clayton and Robertson (1957) with abdominal hair number in *Drosophila*. Estimates of the heritability of this character derived from parent-offspring, half-sib, and full-sib correlations were in excellent agreement in their population, indicating that the genotypic variance was almost entirely additive. In subpopulations sampled from the equilibrium base population, the responses to selection over five generations were in fair agreement with prediction, but some aspects of the behaviour of the lines were not in accordance with simple theory. The responses to selection for reduced hair number were less than predicted, due to a decline in the magnitude of the additive genetic variance within two or three generations. It is possible that this phenomenon was due to the fixation of a single gene of fairly large effect, though there was no proof of this suggestion. The ratio of realized to predicted response was also observed to be related to the intensity of selection imposed, being greatest in lines subject to selection at an intensity of 20%, and least in those selected at an intensity of 80%.

More recent experiments with sternopleural hair number in *Drosophila* conducted by Thoday and Boam (1961) and Spickett (1963) have led to the identification of three loci, each of quite large effect, which have been concerned in the response to selection for increased hair number. In view of these experimental observations, the theoretical consequences of the segregation of genes of large effect in populations under artificial selection require detailed examination. Falconer (1954) has previously discussed the asymmetry in response to be expected in two-way selection experiments if loci of large effect are involved. In the present paper, the problem of assigning selective values to the genotypes at such a locus is discussed, and the behaviour in large populations of an additive autosomal gene with two alleles is examined in detail.

II. SELECTIVE VALUES UNDER ARTIFICIAL SELECTION

If the effect of a gene is small relative to the prevailing phenotypic standard deviation, the selective values of genotypes at the locus can be expressed as linear functions of their mean values for the quantitative character under selection (Kimura 1958; Griffing 1960). However, this approximation cannot be expected to hold for genes of larger effect, and in this section we shall attempt to define the limits beyond which its application may be misleading.

The selective value of a genotype is defined to be the relative probability that an individual so constituted will be included in the selected set of breeding individuals. Let us suppose variation in the metric character to be distributed with zero mean and variance σ_*^2 , of which σ^2 is normally distributed and due to causes

other than segregation at the locus concerned. Under individual selection involving truncation at the value x_0 , the relative selective value of a genotype with mean d is proportional to

$$\begin{aligned}\Pr(x > x_0) &= (2\pi\sigma^2)^{-\frac{1}{2}} \int_{x_0}^{+\infty} \exp[-\tfrac{1}{2}(x-d)^2/\sigma^2] dx \\ &= (2\pi\sigma^2)^{-\frac{1}{2}} \exp[-\tfrac{1}{2}(d/\sigma)^2] \int_{x_0}^{+\infty} \exp[-\tfrac{1}{2}(x^2-2xd)/\sigma^2] dx.\end{aligned}$$

If we let

$$P = (2\pi\sigma^2)^{-\frac{1}{2}} \int_{x_0}^{+\infty} \exp[-\tfrac{1}{2}(x/\sigma)^2] dx,$$

$$z_0 = (2\pi)^{-\frac{1}{2}} \exp[-\tfrac{1}{2}(x_0/\sigma)^2],$$

and

$$\bar{i} = z_0/P,$$

then it can readily be shown that

$$\Pr(x > x_0)/P = [A + \bar{i}C(d/\sigma)] \exp[-\tfrac{1}{2}(d/\sigma)^2],$$

where

$$A = 1 + \sum_{n=1}^{\infty} \left[\frac{(d/\sigma)^{2n} 2^n \Gamma(n + \tfrac{1}{2})}{\pi^{\frac{1}{2}} \Gamma(2n+1)} \right],$$

$$C = \sum_{n=0}^{\infty} [(d/\sigma)^{n-1} u_n/n!],$$

and

$$u_0 = 0,$$

$$u_1 = 1,$$

$$u_n = [(x_0/\sigma)^{n-1} + (n-1)u_{n-2}] \text{ for } n > 1.$$

Making use of the fact that

$$\Gamma(2n+1) = \Gamma(n+1)\Gamma(n+\tfrac{1}{2})2^{2n}\pi^{-\frac{1}{2}},$$

it is simple to show that

$$A = \exp[\tfrac{1}{2}(d/\sigma)^2].$$

Whence

$$\Pr(x > x_0)/P = 1 + \bar{i}(d/\sigma)C \exp[-\tfrac{1}{2}(d/\sigma)^2].$$

For genes of small effect it is usual to take the selective value to be a linear function of the corresponding genotypic value, i.e. as $1 + \bar{i}(d/\sigma)$. From the general

expression given above it can be seen that this approximation involves an error whose magnitude depends on three parameters: (i) \bar{i} , the standardized selection differential; (ii) d/σ , the relevant maximum of which is the "proportionate effect" of the locus (Falconer 1960), unless overdominance prevails; and (iii) σ/σ_* , the ratio of the residual phenotypic standard deviation to the total.

Let us consider the effects of the first two of these three factors. In Figure 1 the ratio

$$\phi_0 = \frac{1 + \bar{i}(d/\sigma)}{\Pr(x > x_0)/P}$$

is plotted against values of d/σ for each of a selected set of values of P . The errors involved in the linear approximation are minimal in the vicinity of $P = 0.5-0.6$ and near $P = 1.0$. They rise to a local maximum at a P value in the region of 0.8 and

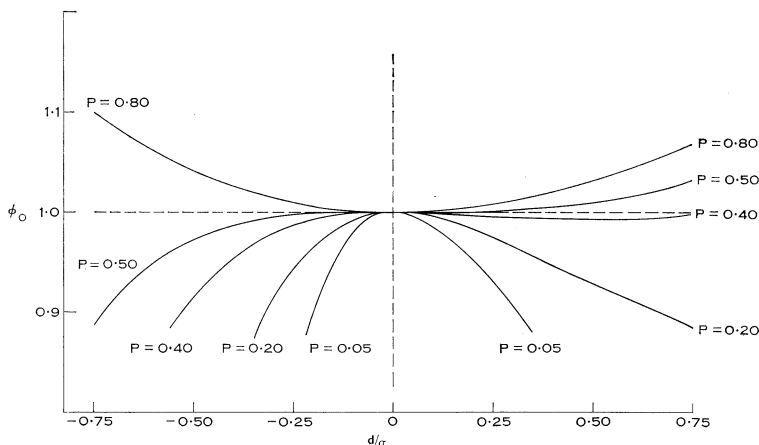


Fig. 1.—The selective value of a genotype given by the first-order approximation $1 + \bar{i}d/\sigma$, expressed as a proportion ϕ_0 of the value obtained from normal tables. P denotes the intensity of artificial selection involved.

increase very rapidly as P becomes less than 0.2. It is apparent from the figure that linear selective values are inadequate for the study of loci of proportionate effect as great as 0.5, unless the intensity of selection is restricted to values of P greater than 0.40.

In dealing with genes of larger effect, a second term should therefore be included in approximations to the selective values. The relationship

$$w = 1 + \bar{i}(d/\sigma)[1 + \frac{1}{2}dx_0/\sigma^2] \quad (1)$$

involves minimal errors in the vicinity of $P = 0.2$ and near $P = 1.0$. The errors rise to a local maximum at P values of the order of 0.4–0.5, and increase very rapidly as P becomes less than 0.05 (Fig. 2).

With this approximation it is possible to consider loci of proportionate effect as large as 0.50 under a wide range of selection intensities down to $P = 0.10$, without involving errors greater than 10% in the selective values. For an additive gene,

the change in gene frequency calculated on the basis of equation (1) will then be subject to an error less than $\pm 2\%$. With a selection intensity of $P = 0.20$ the range may be extended to include genes of proportionate effect equal to 1.0 without exceeding these limits. Since selection intensities in the vicinity of 20% are frequently adopted in work with mice, *Tribolium*, and *Drosophila*, the selective values given by equation (1) are ideal for the simulation of selection response under laboratory conditions.

The remaining source of error, viz. that due to the difference between σ_* and σ , turns out to be unimportant by comparison. For an additive locus with two alleles the maximum contribution to the genotypic variance is $a^2/8$, where a/σ is the proportionate effect of the locus, and this maximum is reached at intermediate gene frequencies where the effects of the other sources of error are at a minimum.

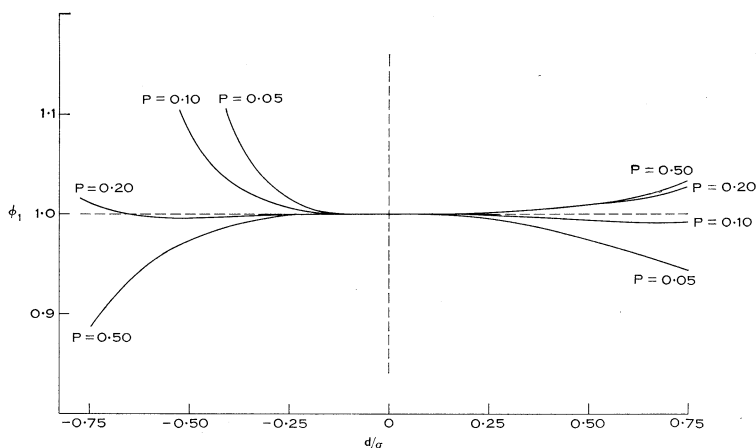


Fig. 2.—The selective value of a genotype given by the second-order approximation in equation (1), expressed as a proportion ϕ_1 of the value obtained from normal tables.

At a selection intensity of 80%, the change in gene frequency at an additive locus calculated from equation (1) consistently overestimates the true value by up to 1.9% for $a/\sigma \leq 0.5$, and by up to 7.4% for $a/\sigma \leq 1.0$. The corresponding errors at a selection intensity of 40% are up to 1.0% for $a/\sigma \leq 0.5$, and up to 4.0% for $a/\sigma \leq 1.0$.

At a selection intensity of 20% the calculated change in gene frequency is subject to an error less than $\pm 0.5\%$ for $a/\sigma \leq 0.5$, and less than $\pm 2.0\%$ for $a/\sigma \leq 1.0$. At 10% selection intensity the calculated values consistently underestimate the true values by up to 1.6% for $a/\sigma \leq 0.5$, and by up to 6.2% for $a/\sigma \leq 1.0$.

III. THE IMMEDIATE RESPONSE TO SELECTION

Consider the response to artificial selection due to a single major gene whose effect is independent of the background genotype. Let the set of possible alleles at the locus be represented by A_i with frequencies p_i , where $i = 1, 2, \dots, m$, and let

d_{ij} denote the mean value of the genotype $A_i A_j$ such that $\sum_{i,j} p_i p_j d_{ij} = 0$. Under individual selection the selective value of the genotype $A_i A_j$ may be taken to be

$$w_{ij}^* = 1 + i(d_{ij}/\sigma)[1 + \frac{1}{2}d_{ij}x_0/\sigma^2]$$

from equation (1), and the mean selective value, \bar{w} , is therefore

$$\begin{aligned}\bar{w} &= \sum_{i,j} p_i p_j w_{ij}^* \\ &= 1 + \frac{1}{2}i(x_0/\sigma)(\sigma_G^2/\sigma^2),\end{aligned}$$

where σ_G^2 is the genotypic variance contributed by the A locus. The relative selective value of $A_i A_j$ is therefore

$$w_{ij} = w_{ij}^*/\bar{w}. \quad (2)$$

The frequency of the genotype $A_i A_j$ following selection is $p_i p_j w_{ij}$, so that the frequency of the allele A_i in the progeny of selected parents is

$$\begin{aligned}p'_i &= \sum_j p_i p_j w_{ij} \\ &= (p_i/\bar{w})[1 + i(\alpha_i/\sigma) + \frac{1}{2}i(x_0/\sigma)(\kappa_i/\sigma^2)],\end{aligned}$$

where α_i is the additive effect of the allele A_i , and

$$\kappa_i = \sum_j p_j d_{ij}^2.$$

The change in gene frequency in one generation is then

$$\Delta p_i = i(p_i/\bar{w})[(\alpha_i/\sigma) + \frac{1}{2}(x_0/\sigma)(\kappa_i - \sigma_G^2)/\sigma^2]. \quad (3)$$

For an additive locus with two alleles and proportionate effect a/σ , the change in the frequency of the favoured allele A_2 in one generation is

$$\Delta p_2 = s p_2(1-p_2)[1 + \frac{1}{2}r(1-2p_2)]/[1 + r s p_2(1-p_2)], \quad (4)$$

where $s = \frac{1}{2}i(a/\sigma)$, and $r = \frac{1}{2}a x_0/\sigma^2$. If the initial frequency of A_2 is denoted by π_0 , the potential response under artificial selection is $a(1-\pi_0)$, and a proportion Q of this potential response corresponds to a realized frequency π_n given by

$$\pi_n = \pi_0 + Q(1-\pi_0) = Q + \pi_0(1-Q).$$

The number of generations of selection required to effect this change in frequency can be estimated to be

$$\begin{aligned}n &= \int_{\pi_0}^{\pi_n} (\Delta p_2)^{-1} dp_2 \\ &= [F(\pi_n) - F(\pi_0)]/s(1 - \frac{1}{4}r^2)\end{aligned} \quad (5)$$

where

$$F(x) = (1 - \frac{1}{2}r)\ln x - (1 + \frac{1}{2}r)\ln(1-x) + [r - s(1 - \frac{1}{4}r^2)]\ln[1 + \frac{1}{2}r(1-2x)].$$

Comparison of Realized and Predicted Response

The change in gene frequency at an additive locus of small effect is

$$\Delta p_2 = sp_2(1-p_2), \quad (6)$$

and the immediate response to selection due to the locus is then a simple function of its additive genetic variance. From equation (4) it follows that the change in gene frequency at a locus of larger effect will be a fraction

$$\theta_1 = [1 + \frac{1}{2}r(1-2p_2)]/[1 + rsp_2(1-p_2)] \quad (7)$$

of that predicted on the basis of its contribution to the additive genetic variance. The ratio can be seen to depend on the prevailing gene frequency, and also on the proportionate effect of the locus and the intensity of selection involved.

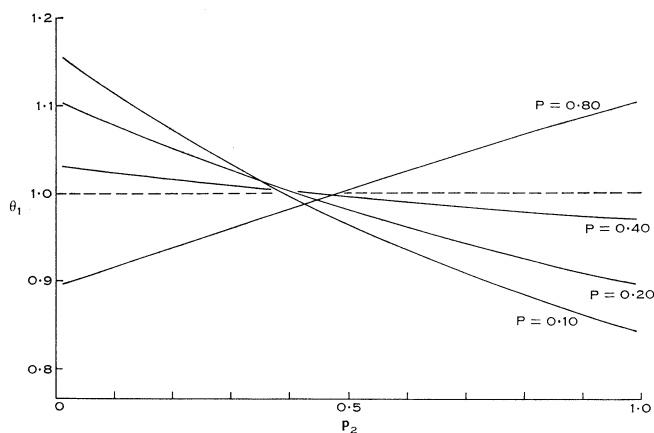


Fig. 3.—The immediate response to selection due to an additive locus of proportionate effect 0.5, expressed as a proportion θ_1 of that predicted on the basis of its contribution to the additive genetic variance. The frequency of the favoured allele in the population is denoted by p_2 .

At a selection intensity of 50% the value of r is zero, and θ_1 is therefore unity for all values of p_2 . At low selection intensities, i.e. $P > 0.50$, r is negative and θ_1 tends to the value $1 + \frac{1}{2}r(1-2p_2)$ as P tends to 1.0. The discrepancy between realized and predicted response will then be greatest at extreme gene frequencies, and will be close to zero at $p_2 = 0.5$. When the frequency of the favoured allele A_2 is low, the value of θ_1 is close to $1 + \frac{1}{2}r$, so that the realized response in the first generation falls short of that predicted. At the other extreme the ratio of realized to predicted response approaches $1 - \frac{1}{2}r$.

With higher intensities of selection corresponding to $P < 0.50$, the value of r is positive. At extreme gene frequencies the denominator in equation (7) is close to

unity, so that θ_1 approximates $1 + \frac{1}{2}r$ when p_2 is small, and approaches $1 - \frac{1}{2}r$ as p_2 tends to unity. The realized response due to an additive locus with the favoured allele initially at low frequency will then exceed the response expected on the basis of its contribution to the additive genetic variance, and conversely for loci with the favoured allele already at high frequency. Values of θ_1 corresponding to selection intensities of 80, 40, 20, and 10% are plotted in Figure 3 for a locus of proportionate effect equal to 0.5.

The ratio of realized to predicted response for an additive locus of proportionate effect equal to 1.0 is plotted in Figure 4 for the same range of selection intensities as in Figure 3. However, for this graph the precise ratio (θ_2) has been obtained from tables of the normal distribution.

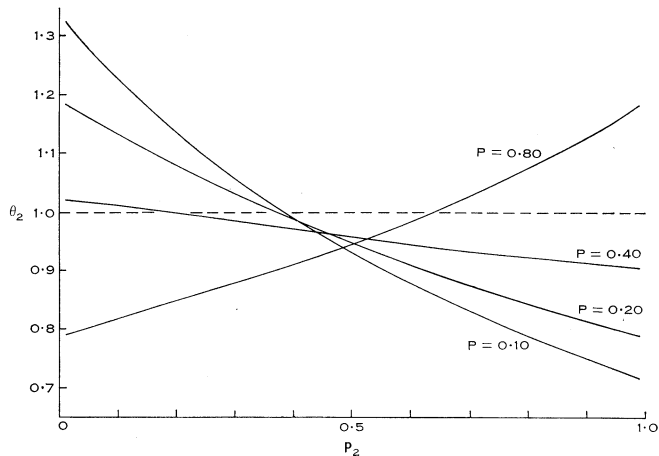


Fig. 4.—The immediate response to selection due to an additive locus of proportionate effect 1.0, expressed as a proportion θ_2 of that predicted on the basis of its contribution to the additive genetic variance.

IV. THE SHORT-TERM RESPONSE TO SELECTION

We have so far been concerned only with the immediate response to selection due to genes of large effect, and its correspondence with response predicted from a prior analysis of the base population. However, it is quite clear that the realized response over a longer period of five or ten generations will not bear the same relationship to predicted response, because of appreciable changes in gene frequencies and associated parameters over such a period of generations.

Tables 1 and 2 summarize the accumulated changes in gene frequency over periods of five and ten generations, given by repeated application of equation (4), for selection intensities of 80, 40, 20, and 10%. The calculations have been made for additive loci of proportionate effect equal to 1.00, 0.50, and 0.25, with the favoured allele at initial frequencies ranging from 0.05 to 0.95. Also given in the tables is the ratio of realized response to that predicted on the basis of the contribution of the locus to the additive genetic variance in the base population. A plot of this

ratio is given in Figure 5 for a locus of proportionate effect equal to 0.5, following selection over a period of five generations.

TABLE 1

SHORT-TERM RESPONSE OF AN ADDITIVE GENE TO SELECTION OF LOW INTENSITY

Proportionate Effect	Initial Gene Frequency	Accumulated Change in Gene Frequency		Ratio of Realized to Expected Response	
		5 Generations	10 Generations	5 Generations	10 Generations
(a) $P = 0.80$					
1.00	0.05	0.044	0.123	1.055	1.481
	0.25	0.175	0.396	1.069	1.206
	0.50	0.220	0.381	1.004	0.871
	0.75	0.148	0.215	0.901	0.655
	0.95	0.034	0.045	0.816	0.542
0.50	0.05	0.022	0.052	1.045	1.255
	0.25	0.085	0.184	1.033	1.125
	0.50	0.110	0.212	1.002	0.970
	0.75	0.079	0.137	0.960	0.837
	0.95	0.019	0.031	0.921	0.749
0.25	0.05	0.011	0.024	1.027	1.129
	0.25	0.042	0.088	1.017	1.067
	0.50	0.055	0.109	1.001	0.993
	0.75	0.040	0.076	0.981	0.923
	0.95	0.010	0.018	0.964	0.872
(b) $P = 0.40$					
1.00	0.05	0.260	0.791	2.271	3.449
	0.25	0.536	0.735	1.184	0.811
	0.50	0.434	0.496	0.718	0.411
	0.75	0.231	0.249	0.510	0.275
	0.95	0.047	0.050	0.413	0.217
0.50	0.05	0.090	0.289	1.563	2.518
	0.25	0.270	0.539	1.192	1.190
	0.50	0.275	0.426	0.910	0.706
	0.75	0.166	0.226	0.732	0.499
	0.95	0.036	0.046	0.631	0.404
0.25	0.05	0.036	0.094	1.257	1.646
	0.25	0.126	0.274	1.116	1.209
	0.50	0.147	0.272	0.976	0.902
	0.75	0.098	0.162	0.866	0.718
	0.95	0.023	0.035	0.793	0.616

At each of the selection intensities, the ratio of realized to expected response over a five-generation period is always greater than unity for loci of proportionate effect between 0.1 and 1.0, provided the frequency of the favoured allele is initially less than 0.20. The ratio is always less than unity for initial frequencies above 0.50.

At the lowest intensity of selection, i.e. $P = 0.80$, the agreement between realized and expected response over a five-generation period is excellent, except for loci of proportionate effect close to 1.0 with the favoured allele at initial frequencies above

TABLE 2
SHORT-TERM RESPONSE OF AN ADDITIVE GENE TO SELECTION OF HIGH INTENSITY

Proportionate Effect	Initial Gene Frequency	Accumulated Change in Gene Frequency		Ratio of Realized to Expected Response	
		5 Generations	10 Generations	5 Generations	10 Generations
(a) $P = 0.20$					
1.00	0.05	0.506	0.931	3.047	2.800
	0.25	0.663	0.748	1.011	0.570
	0.50	0.475	0.499	0.543	0.286
	0.75	0.243	0.250	0.370	0.190
	0.95	0.049	0.050	0.295	0.150
0.50	0.05	0.166	0.552	1.992	3.319
	0.25	0.399	0.669	1.217	1.019
	0.50	0.355	0.474	0.812	0.542
	0.75	0.199	0.242	0.607	0.368
	0.95	0.042	0.049	0.505	0.293
0.25	0.05	0.060	0.174	1.432	2.094
	0.25	0.191	0.404	1.166	1.233
	0.50	0.206	0.354	0.944	0.810
	0.75	0.130	0.197	0.792	0.602
	0.95	0.029	0.041	0.701	0.499
(b) $P = 0.10$					
1.00	0.05	0.681	0.946	3.267	2.268
	0.25	0.705	0.749	0.857	0.456
	0.50	0.487	0.500	0.444	0.228
	0.75	0.246	0.250	0.299	0.152
	0.95	0.049	0.050	0.237	0.120
0.50	0.05	0.246	0.733	2.359	3.519
	0.25	0.489	0.714	1.190	0.868
	0.50	0.400	0.489	0.730	0.446
	0.75	0.216	0.246	0.525	0.300
	0.95	0.045	0.049	0.429	0.237
0.25	0.05	0.083	0.259	1.588	2.488
	0.25	0.246	0.497	1.196	1.208
	0.50	0.250	0.401	0.912	0.732
	0.75	0.151	0.216	0.736	0.524
	0.95	0.033	0.044	0.637	0.427

0.75. At the highest selection intensity of 10%, the response over a five-generation period due to loci with extreme initial gene frequencies is markedly different from that predicted, even when the proportionate effect is as low as 0.25. The phenomenon

of a striking relationship between the ratio of realized to expected response, and the selection intensity imposed, may then quite possibly be attributable to genes of this order of effect.

Asymmetry of Response

Asymmetry is one of the most conspicuous features of the response to selection due to additive genes of large effect. It has already been seen that the response in the first generation will be asymmetrical unless the selection intensity is in the vicinity of 50% or the initial gene frequency is 0.5 (Fig. 4). At high selection intensities ($P = 0.10$) the degree of asymmetry in the response shown by genes at extreme

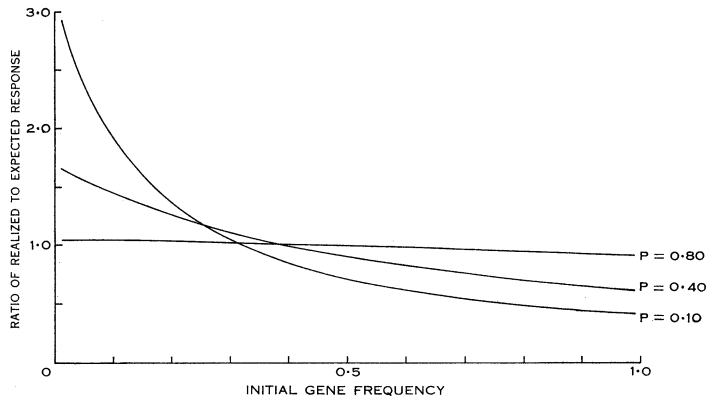


Fig. 5.—The response to selection over a five-generation period due to an additive locus of proportionate effect 0.5, expressed as a proportion of that predicted on the basis of its initial contribution to the additive genetic variance.

initial gene frequencies is greatly accentuated after five generations of selection, due to accompanying changes in the magnitude of the additive genetic variance, whereas at low selection intensities ($P = 0.80$) these changes are such as to reverse the initial direction of the genetic asymmetry.

As a measure of the *degree of asymmetry* it is proposed to use the ratio of the difference in response in the positive and negative directions, to the sum of the two responses. If we denote the responses to selection in the two directions by ΔG_H and ΔG_L , then the degree of asymmetry in response is defined to be

$$S = [\Delta G_H - \Delta G_L] / [\Delta G_H + \Delta G_L]. \quad (8)$$

This parameter will then be zero in the case of a symmetrical response, and will lie in the range $-1, +1$. Values of S after one, five, and ten generations of selection are given in Table 3 for selection intensities of 80, 20, and 10%, and for initial gene frequencies of 0.01, 0.10, and 0.25. The values of S for an initial gene frequency of 0.5 are zero, and those for frequencies initially greater than 0.5 are equal in magnitude, but of opposite sign, to those given for the complementary gene frequency, $1 - p_2$.

V. DISCUSSION

The effects of the segregation of additive genes of large effect in a population under artificial selection have been examined in terms of two observable phenomena, viz. (i) the ratio of realized to predicted response and its dependence on the intensity

TABLE 3

ASYMMETRY OF RESPONSE AS A FUNCTION OF THE PROPORTIONATE EFFECT AND INITIAL FREQUENCY OF AN ADDITIVE GENE, AND THE INTENSITY OF SELECTION

Proportionate Effect	Initial Gene Frequency	Asymmetry of Response		
		1 Generation	5 Generations	10 Generations
(a) $P = 0.80$				
1.00	0.01	-0.199	0.133	0.485
	0.10	-0.161	0.120	0.432
	0.25	-0.099	0.085	0.296
0.50	0.01	-0.103	0.068	0.271
	0.10	-0.084	0.057	0.227
	0.25	-0.052	0.037	0.146
0.25	0.01	-0.052	0.034	0.140
	0.10	-0.042	0.028	0.115
	0.25	-0.026	0.018	0.072
(b) $P = 0.20$				
1.00	0.01	0.199	0.892	0.977
	0.10	0.162	0.736	0.799
	0.25	0.100	0.464	0.499
0.50	0.01	0.103	0.647	0.908
	0.10	0.084	0.531	0.747
	0.25	0.053	0.334	0.469
0.25	0.01	0.052	0.373	0.669
	0.10	0.042	0.305	0.548
	0.25	0.026	0.191	0.344
(c) $P = 0.10$				
1.00	0.01	0.297	0.939	0.979
	0.10	0.241	0.770	0.800
	0.25	0.149	0.483	0.500
0.50	0.01	0.157	0.752	0.949
	0.10	0.128	0.617	0.778
	0.25	0.080	0.387	0.487
0.25	0.01	0.079	0.465	0.769
	0.10	0.064	0.380	0.630
	0.25	0.040	0.238	0.395

of selection imposed, and (ii) the asymmetry of response to be expected in two-way selection experiments. It is important also to discuss the concomitant changes in the

magnitude of the additive genetic variance, and to determine to what extent these aspects of behaviour under selection are interrelated.

(a) Selection of Low Intensity

At a selection intensity of 80%, it has been shown that the immediate response to selection is asymmetrical for genes initially at either very low or very high frequency, the measure of asymmetry defined in equation (8) being negative for loci at which the "plus" allele is at low frequency, and positive for those loci at which the "minus" allele is at low frequency. Subsequent changes in the magnitude of the additive genetic variance are such that the accumulated response over a five-generation period shows a reversal of the direction of the initial asymmetry (Table 3). However, the degree of asymmetry involved does not become appreciable until after ten generations, and then only for loci of proportionate effect greater than 0.5.

When subject to selection at an intensity of 80%, loci of proportionate effect in the range 0.5–1.0 with the plus allele initially at *low* frequency, give a realized response in the first generation which is 10–20% *less* in the positive direction and 10–20% *greater* in the negative direction than that predicted. However, the accumulated response in the positive direction over a five-generation period shows excellent agreement with prediction, while that in the negative direction may fall short of the predicted response by up to 20% for loci of proportionate effect close to 1.0.

It is therefore clear that under selection of low intensity, only loci of proportionate effect as large as 1.0 are likely to contribute to conspicuous departures from the predicted pattern of response. The additive genetic variance contributed by loci of this magnitude of effect with the plus allele initially at a frequency of 0.01–0.10, will be approximately doubled under selection in the positive direction after five generations, and reduced to one-third in the same period under selection in the negative direction. The half-life of the response in the positive direction due to such loci can be calculated from equation (5) to be in the range 15–30 generations, and at this phase of the selection response their contribution to the additive genetic variance will be close to maximal. For a gene at an initial frequency of 0.01, this contribution will be roughly 25 times that in the base population, whereas a similar gene at an initial frequency of 0.10 will contribute at most 2.8 times the base population variance.

If the genotypic variance displayed by a quantitative character were due primarily to genes of this magnitude of effect, all initially with the "plus" allele at low frequency, it might well be possible to detect departures from prediction under short-term selection of low intensity. However, it is clear that a small number of genes of large effect segregating against a background provided by genes of minor effect will lead neither to appreciable departures from the predicted rate of response nor to conspicuous changes in phenotypic variance, over a five-generation period.

(b) Selection of High Intensity

The immediate response to selection of high intensity has been shown to be asymmetrical for genes at extreme initial frequencies, the direction of the asymmetry being opposite to that produced by selection of low intensity (Fig. 4). The measure

of asymmetry given by equation (8) is positive for loci at which the plus allele is initially at low frequency, and negative for those with the minus allele at low frequency. Subsequent changes in the contribution of such loci to the additive genetic variance tend to reinforce the initial asymmetry produced, and after five generations of selection at an intensity of 10%, loci of proportionate effect as low as 0.25 may give rise to markedly asymmetrical responses (Table 3).

Loci of proportionate effect in the vicinity of 1.0, with the plus allele initially at very low frequency, e.g. 0.01, lead to an extremely pronounced asymmetry of response in two-way selection experiments, the ratio of realized to predicted response in the positive direction after five generations of selection at an intensity of 10% being 7.3, and that in the negative direction being 0.23. The magnitude of the additive genetic variance due to such loci also changes dramatically over a five-generation period, the variance increasing under selection in the positive direction by a factor of 22, and decreasing under selection in the negative direction to approximately one-hundredth that in the base population.

Let us suppose 5% of the total additive genetic variance shown by a quantitative character to be due to loci with $a/\sigma = 1.0$, and $p_2 = 0.01$. The number of such loci will then be $10h^2$, where h^2 denotes the heritability of the character, so that most situations of interest will be covered if we think in terms of from 1 to 10 of these major loci. Under selection in the positive direction at an intensity of 10%, the total additive genetic variance would then be expected to increase by a factor of two by the fifth generation, and to decline to the level of the base population by the tenth generation, which represents the 95% life span of response due to the major loci. Under selection in the negative direction, the corresponding changes in variance would be of a minor order, involving a total reduction of only 5%.

In work with a character of medium to low heritability these changes in variance may well go undetected. However, the total response in the positive direction over five generations would be expected to exceed that predicted by approximately 30%, while the response in the negative direction would fall short of that predicted by only 4%.

VI. REFERENCES

- CLAYTON, G. A., MORRIS, J. A., and ROBERTSON, A. (1957).—An experimental check on quantitative genetical theory. I. Short-term responses to selection. *J. Genet.* **55**: 131–51.
- CLAYTON, G. A., and ROBERTSON, A. (1957).—An experimental check on quantitative genetical theory. II. The long-term effects of selection. *J. Genet.* **55**: 152–70.
- FALCONER, D. S. (1954).—Asymmetrical responses in selection experiments. Symposium on Genetics of Population Structure, Pavia, Italy. *Un. Int. Sci. Biol.* No. 15. pp. 16–41.
- FALCONER, D. S. (1960).—“Introduction to Quantitative Genetics.” (Oliver and Boyd: Edinburgh.)
- GRIFFING, B. (1960).—Theoretical consequences of truncation selection based on the individual phenotype. *Aust. J. Biol. Sci.* **13**: 307–43.
- KIMURA, M. (1958).—On the change of population fitness by natural selection. *Heredity* **12**: 145–67.
- SPICKETT, S. G. (1963).—Genetic and developmental studies of a quantitative character. *Nature, Lond.* **199**: 870–3.
- THODAY, J. M., and BOAM, T. B. (1961).—Regular responses to selection. I. Description of responses. *Genet. Res.* **2**: 161–76.