THE EFFECT OF SELECTION AGAINST EXTREME DEVIANTS BASED ON DEVIATION OR ON HOMOZYGOSIS

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(With Two Text-figures)

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The theoretical investigations presented in this paper were suggested in the course of an experiment on the genetical control of environmental variability (Falconer & Robertson, 1956) which involved the mating of animals close to the population mean for body size in one line and in the other line of animals from opposite extremes. It was realized that the result of the mating system (in effect, a type of assortative mating) on gene frequencies was not known. Generalization of the solution to include a gradual decline in selective advantage with metric deviation meant that we were discussing a problem of evolutionary importance, i.e. 'stabilizing selection' in which the extreme deviants have fewer offspring than do intermediates. This particular model, in which the population mean has always the highest fitness (although it may change from its original value in the course of selection) and in which the fitness is causally related to the metric deviation, proved in fact to lead to fixation of genes as did selection for a constant value of the character. This naturally led to an analysis of the alternative model of stabilizing selection in which the extreme deviants are less fit not because they are extremes but because they are more homozygous than intermediates. This model has been put forward by Lerner in his book *Genetic Homeostasis* (1954), and is here termed the homoeostatic model.

The genetic consequence of selection for and against metric deviation

During some experiments involving assortative mating for a metric character, it appeared that no theoretical analysis had been made of the genetic consequences of the mating system used. Wright (1921), in his classical series of papers, discusses the mating system in which the correlation between phenotypes of mates was $+1$ or -1. Both systems involved the mating of all members of the population, so that animals close to the population mean in the character concerned would be mated together in both. In the experiments referred to, we were investigating the long-term effects of (*a*) restricting parents to those close to the population mean, (*b*) mating together animals from different extremes, which might be called compensatory mating.

We shall first discuss the situations in which animals lying in a small range about the population mean are chosen. The first case is that of an autosomal gene in which the heterozygote lies exactly halfway between the two homozygotes for the metric character, which can be represented diagrammatically as follows:

Genotype	A_1A_1	A_1A_2	A_2A_2
Frequency	p^2	$2pq$	q^2
Average value	0	$\frac{1}{2}a$	a

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If, as a result of selection, the relative chances of individuals of the three genotypes being chosen as parents is $1-s_1$, 1 and $1-s_2$ respectively, the change in gene frequency Δq can be shown to be $pq(s_1 p - s_2 q)$.

Suppose that, apart from that due to segregation at this locus, there is additional variance σ^2 normally distributed. Each of the three genotypes will then generate a subpopulation about its respective mean and the overall population mean will be aq. If we select the parents of the next generation from near the population mean then the relative probabilities of members of the three genotypes being chosen are

$$\exp\left(-\frac{a^2q^2}{2\sigma^2}\right), \quad \exp\left(-\frac{a^2(q-\frac{1}{2})^2}{2\sigma^2}\right) \quad \text{and} \quad \exp\left(-\frac{a^2p^2}{2\sigma^2}\right).$$

We have
$$1-s_1 = \exp\left(-\frac{a^2q^2}{2\sigma^2}+\frac{a^2(q-\frac{1}{2})^2}{2\sigma^2}\right)$$
$$= \exp\left(-\frac{a^2}{2\sigma^2}(q^2-(q-\tfrac{1}{2})^2)\right),$$

giving
$$s_1 = \frac{a^2}{2\sigma^2}(q-\tfrac{1}{4}) \quad \text{if } a/\sigma \text{ is small,}$$

and by a similar argument
$$s_2 = \frac{a^2}{2\sigma^2}(p-\tfrac{1}{4}).$$

Thus
$$\Delta q = \frac{a^2}{2\sigma^2}[p(q-\tfrac{1}{4})-q(p-\tfrac{1}{4})]$$
$$= \frac{a^2pq(q-p)}{8\sigma^2}.$$

Within the range $\frac{1}{2} \leqslant q \leqslant \frac{3}{4}$, the heterozygote will be preferred over either homozygote, but the change in q will depend on the sign of $q-p$. If $q > \frac{1}{2}$, then q will increase, and if $q < \frac{1}{2}$, it will decrease. The effect of continued selection of the population mean is thus to send gene frequencies to 0 or 1 with a position of metastable equilibrium at $q = \frac{1}{2}$. The process is thus not one leading to the maintenance of genetic variation in the population but leads instead to its extinction by fixation.

It has been suggested that homozygotes are in general more variable in their expression than heterozygotes (see Lerner, 1954). The calculation was therefore repeated, but the variance of heterozygotes was taken as k times that of homozygotes. We then find

$$\Delta q = \frac{a^2pq(q-p)[\frac{1}{4}+(k-1)pq]}{2k\sigma^2}.$$

The expression $\frac{1}{4}+(k-1)pq$ is always positive unless $k=0$ and $p=q=\frac{1}{2}$. The process will again lead to fixation with a metastable equilibrium at $q=\frac{1}{2}$.

It may be objected that, from the evolutionary point of view, the results of continued selection for the population mean, even though that mean changes, are not of great interest, because in wild populations it is a certain fixed value which has the highest fitness. It seemed necessary to consider this situation in some detail. Consider first a single gene segregating against a constant background, with additive action. Returning to the earlier analysis, we found that on selection for the population mean the selective disadvantage, relative to the heterozygote, was $\frac{a^2(q-\frac{1}{4})}{2\sigma^2}$ and $\frac{a^2(p-\frac{1}{4})}{2\sigma^2}$ for A_1A_1 and A_2A_2

respectively. If that absolute value were continuously selected for, then a new equilibrium would be reached at

$$\hat{q} = \frac{s_1}{s_1 + s_2}$$

$$= \frac{q - \frac{1}{4}}{(p - \frac{1}{4}) + (q - \frac{1}{4})}$$

$$= 2q - \tfrac{1}{2},$$

or

$$\hat{q} - \tfrac{1}{2} = 2(q - \tfrac{1}{2}). \qquad (1)$$

Expressing this in terms of the measured character, this means that the new population mean is twice the distance from the mean value of the heterozygote, $a(\hat{q} - \frac{1}{2})$, as was the selected value from the heterozygote mean $a(q - \frac{1}{2})$. This turns out to be generally true—that if only one gene is segregating, then selection for a given value will not bring the population mean to that value but either lead to fixation (if the selected value is closer to one of the homozygote means than it is to the heterozygote mean) or to an equilibrium such that the selected value is half-way between the heterozygote mean and the new population mean.

But, if there are many genes segregating in the population with different values of a, this equilibrium process cannot at the same time apply to all of them. As the effect is proportional to a^2, it will change first of all the frequency of the gene with the largest effect. Concentrating on this gene, the first step can be illustrated in stages I and II of Fig. 1, in which the population mean has changed so that the major gene is in equilibrium.

But now genes with smaller effects, or perhaps new mutants, whose effect is in the direction of the selected value will tend to be fixed. The population mean will thus move back towards the selected value and with it will move the mean values of the three genotypes for the major gene-pair (stage III). The equilibrium for this gene will then be disturbed, and this will adjust itself by going further to fixation (stage IV). Another repetition of this process and the major gene will have reached fixation. Thus the end-result will be a population whose mean is at the selected value but with fixation at all such loci (stage VII).

This is in essence the same problem as that discussed by Wright (1935), although the approach is different. Equation (1) in this paper in fact corresponds to Wright's equation (9) (p. 259). The final conclusions of the analysis are the same in both cases.

In the case of a recessive gene, the situation is more immediately obvious. We have only two subpopulations, and the more frequent one will have its mean closer to the population mean and will therefore be more often chosen as parent. We find

$$\Delta q = \frac{a^2 p q^2 (2q^2 - 1)}{2\sigma^2}$$

with metastability at $q = 1/\sqrt{2}$. We have again the result that continued selection of the metric intermediate will lead to fixation at loci concerned with that character. Similar reasoning applies to selection for a fixed value.

These results can be generalized to the case in which fitness declines continuously as the deviation of an animal from the population mean increases. Haldane (1953) used for this decline the function $\exp(-x^2/2\sigma_2^2)$, where x is the deviation in the character concerned from the population mean. This has the merit of leading to algebraic simplicity. It turns

out that the previous formulae apply with the substitution of $\sigma^2+\sigma_2^2$ for σ^2. If σ_2^2 is small, indicating choice of parents close to the mean, we get the previous results. If σ_2^2 is large, indicating only a slight decrease of fitness as x increases, the change of gene frequency is less.

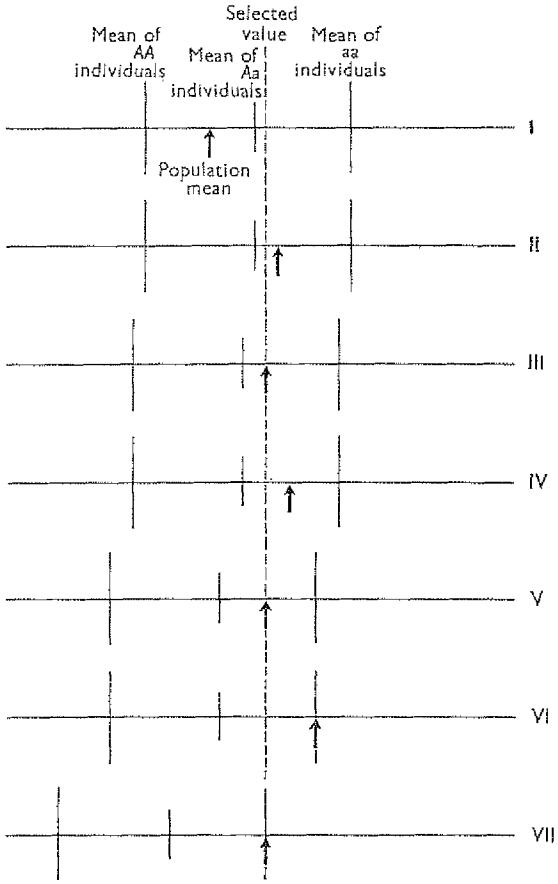

Fig. 1. Fixation of a major gene during the selection of a constant value of the character.

We have found that selection of parents close to the population mean leads to gene fixation. It follows that the mating of extreme deviants will lead to a stable situation with intermediate gene frequencies. This has been pointed out by Moree (1953) in the case of a recessive gene with a major effect. In a character distributed continuously, we can investigate this effect using the model used previously. The relative probabilities of the three genotypes A_1A_1, A_1A_2, A_2A_2 lying in the range x to $x+dx$ are

$$\exp\left(-\frac{(x-aq)^2}{2\sigma^2}\right), \quad \exp\left(-\frac{(x-a(q-\tfrac{1}{2}))^2}{2\sigma^2}\right), \quad \exp\left(-\frac{(x+ap)^2}{2\sigma^2}\right),$$

and similar expressions apply to the range $-x$ to $-x-dx$. For A_1A_1, the joint probability in the two intervals is

$$\exp\left(-\frac{(x-aq)^2}{2\sigma^2}\right)+\exp\left(-\frac{(-x-aq)^2}{2\sigma^2}\right).$$

By Maclaurin's theorem, we have

$$\tfrac{1}{2}(f(x+h)+f(x-h))=f(x)+\frac{h^2}{2}f''(x)+\text{terms in } h^4, \text{ etc.}$$

The probability of choice of A_1A_1 will then be proportional to

$$\exp\left(-\frac{x^2}{2\sigma^2}\right)+\frac{(aq)^2}{2}\frac{d^2}{dx^2}\left[\exp\left(-\frac{x^2}{2\sigma^2}\right)\right]=\exp\left(-\frac{x^2}{2\sigma^2}\right)\left(1+K\frac{a^2q^2}{2}\right),$$

where

$$K=\frac{x^2}{\sigma^4}-\frac{1}{\sigma^2},$$

with similar expressions for A_1A_2 and A_2A_2. Then

$$1-s_1=\frac{1+K\dfrac{a^2q^2}{2}}{1+K\dfrac{a^2(q-\frac{1}{2})^2}{2}}$$

$$=1+\frac{Ka^2(q-\frac{1}{2})}{2}+\text{terms in } K^2, \text{ etc.}$$

Similarly

$$1-s_2=1+\frac{Ka^2(p-\frac{1}{2})}{2}.$$

Thus

$$\Delta q=pq(s_1p-s_2q)$$

$$=\frac{Ka^2pq(p-q)}{8}.$$

Thus the sign of Δq will depend on the sign of K. If $|x|$ is less than σ, K is negative and the process leads to fixation. At more extreme values of x, K is positive and the changes in q will lead to stability at intermediate frequencies.

Turning now to the selection of all animals lying outside a fixed value of x, i.e. $|x|>x_0$, we have the following expression for the probability of A_1A_1 animals being chosen:

$$\frac{1}{\sqrt{(2\pi)}\sigma}\left[\int_{-\infty}^{-x_0}\exp\left(-\frac{(x-aq)^2}{2\sigma^2}\right)dx+\int_{x_0}^{\infty}\exp\left(-\frac{(x-aq)^2}{2\sigma^2}\right)dx\right]$$

$$=\frac{1}{\sqrt{(2\pi)}\sigma}\left[\int_{x_0}^{\infty}\exp\left(-\frac{(-x-aq)^2}{2\sigma^2}\right)dx+\int_{x_0}^{\infty}\exp\left(-\frac{(x-aq)^2}{2\sigma^2}\right)dx\right]$$

$$=\frac{1}{\sqrt{(2\pi)}\sigma}\left[\int_{x_0-aq}^{\infty}\exp\left(-\frac{x^2}{2\sigma^2}\right)dx+\int_{x_0+aq}^{\infty}\exp\left(-\frac{x^2}{2\sigma^2}\right)dx\right],$$

which is again in the form $f(x+h)+f(x-h)$. In this case

$$f''(x_0)=\frac{x_0}{\sqrt{(2\pi)}\sigma^3}\exp\left(-\frac{x_0^2}{2\sigma^2}\right)=\frac{x_0z}{\sigma^3},$$

where z is the ordinate of the normal curve at the point x_0/σ. We may similarly write v for the proportion of the normal curve lying outside x_0/σ. Then the chance of A_1A_1 animals being chosen is

$$2v+\frac{a^2x_0zq^2}{\sigma^3},$$

with similar expressions for

$$A_1A_2\colon\ 2v+\frac{a^2x_0z(q-\frac{1}{2})^2}{\sigma^3}$$

and

$$A_2A_2\colon\ 2v+\frac{a^2x_0zp^2}{\sigma^3}.$$

Thus

$$s_1=\frac{a^2x_0z}{2\sigma^3v}\,(q^2-(q-\tfrac{1}{2})^2)$$

$$=\frac{a^2x_0\bar{\imath}(q-\frac{1}{4})}{2\sigma^3},$$

where $\bar{\imath}$ is the selection intensity in standard units (see Lerner, 1950, p. 147).

Similarly

$$s_2=\frac{a^2x_0\bar{\imath}(p-\frac{1}{4})}{2\sigma^3},$$

so that

$$\Delta q=\frac{a^2x_0\bar{\imath}pq(p-q)}{8\sigma^3}.$$

As would be expected, Δq is zero when x is zero and the whole population is selected, but is otherwise of the same sign as $p-q$ and will therefore lead to intermediate gene frequencies. Similar arguments apply to recessive genes.

The magnitude of these changes will depend on the values of a, the effect of the gene concerned. It will be noted that the change in gene frequency was in all cases proportional to a^2, whereas it can easily be shown (following Haldane, 1927) that the change in frequency of an additive gene in one-way selection is $\frac{\bar{\imath}a}{2\sigma}pq$ per generation. If we represent the selective advantage of the gene, $\bar{\imath}a/2\sigma$, by s, then the change of gene frequency on the mating of the extremes of the same proportions will be of the order of that in one-way selection with selective advantage approximately $\frac{1}{2}s^2$. Falconer (1953) has suggested that in his mouse selection work, values of a/σ of the neighbourhood of 0·4 for several of the more important genes could account for his results. If we take a value of $q=0{\cdot}75$ for convenience, then the effect of mating together animals at the population mean is an increase of q by 0·002 per generation.

Table 1

Extreme proportions selected (%)	Δq
50	−0
25	−0·0016
10	−0·0042
5	−0·0063
1	−0·0115

The effect of extreme mating is of course dependent on the proportion chosen, and Table 1 shows the change in q for various proportions selected. The 5% figure, for instance, means that the top 5% were mated to the bottom 5%.

In a situation with many alleles at a locus, it is difficult to predict precisely what will happen. It seems probable that both types of selection will lead to an immediate decrease in the number of alleles segregating, selection of intermediates by an increase in the frequencies of alleles in the middle of the range of alleles and selection of extremes by an increase in the alleles with extreme effects. The effect on variance will be the same as in the two-allele case.

In the time scale of most laboratory experiments, these changes are small and would not be expected to alter materially the genetic situation in such a population. However, on the evolutionary time scale, changes of such a magnitude would be of importance. It must be emphasized that in this model we have been dealing with genes whose effect on reproductive fitness is solely through the metric character concerned. It has been suggested that the reproductive superiority of intermediate phenotypes which has been observed in many cases (see Lerner, 1954) is an important factor leading to the preservation of genetic variability within a population. However, the present investigation shows that such selection, if due to the character itself, would lead to genetic fixation. It follows that the superiority of fitness of the intermediate may not be causal in the sense that fitness is determined by the phenotype for that character. Other genetic mechanisms, such as the general superiority of heterozygotes in fitness over homozygotes, can also lead to this decrease of fitness of the extremes. This alternative model for the situation will be discussed in the second half of the paper.

These results may have some relevance to practical breeding. The maintenance of phenotypic variability in morphological characters to which considerable attention is paid by breeders is striking. This may perhaps be due to the tendency to correct faults in an animal by a compensatory mating to an animal deviating in the opposite way. If this practice is at all widespread in the top pedigree herds, the resulting stabilization of the genetic situation might account for the maintenance of the observed variation.

The homoeostatic model

In a general discussion of the lower fitness of extreme deviants and other related phenomena, Lerner (1954) put forward the following thesis: 'The inheritance of metric traits may be considered, at least operationally, to be based on additively acting polygenic systems while the totality of traits determining reproductive capacity and expressed as a single value (fitness) exhibits overdominance.' The treatment given here is in essence a generalization of that given by Lerner (1954, pp. 86–92).

For a single gene, we may picture the situation as follows:

Genotype	A_1A_1	A_1A_2	A_2A_2
Frequency	p^2	$2pq$	q^2
Metric character	$-\frac{1}{2}a$	0	$+\frac{1}{2}a$
Fitness	$1-s_1$	1	$1-s_2$

The differences between the values of s_1 and s_2 from those in the previous sections must be emphasized. Here we are discussing natural selection on the genotypes themselves, whereas formerly the selection was the result of the phenotypic value of the

animal for the metric character. If there is a stable situation, we will h
We have the relationships

$$S = S(p+q)$$

$$= (s_1 + s_2)pq,$$

and

$$S = \frac{s_1 p \times s_2 q}{(s_1 + s_2)pq}$$

$$= \frac{s_1 s_2}{s_1 + s_2}.$$

The latter expression is that usually given for the fitness of the equilibrium population relative to that of the heterozygote. At equilibrium, consider the relative proportion of the three genotypes at the point x, relative to the mean value of the heterozygote $A_1 A_2$.

We have for $A_1 A_1$

$$f(x)(1 - \alpha + \beta + \text{second-order terms})$$

for $A_1 A_2$ $\qquad f(x)$

and $A_2 A_2$ $\qquad f(x)\,(1 + \alpha + \beta + \text{second-order terms}),$

where $f(x) = \frac{1}{\sqrt{(2\pi)}\sigma} \exp\left(-\frac{x^2}{2\sigma^2}\right)$, σ^2 is the remainder of the variance apart from that due to this particular gene, $\alpha = \frac{ax}{2\sigma^2}$ and $\beta = \left(\frac{x^2}{\sigma^4} - \frac{1}{\sigma^2}\right)\frac{a^2}{8}$, by the application of Maclaurin's theorem. Thus for the fitness at x we have

$$\frac{p^2(1-\alpha+\beta)\,(1-s_1) + q^2(1+\alpha+\beta)\,(1-s_2) + 2pq}{p^2(1-\alpha+\beta) + 2pq + q^2(1+\alpha+\beta)}$$

$$= 1 - \frac{s_1 p^2 + s_2 q^2 + \alpha(s_2 q^2 - s_1 p^2) + \beta(s_1 p^2 + s_2 q^2)}{1 + \alpha(q^2 - p^2) + \beta(q^2 + p^2)} \qquad (2)$$

$$= 1 - \frac{S + \alpha S(q-p) + \beta S}{1 + \alpha(q-p) + \beta(q^2+p^2)}$$

$$= 1 - S(1 + \beta . 2pq) \text{ approximately}$$

$$= 1 - S - S\frac{a^2}{8}\left(\frac{x^2}{\sigma_4} - \frac{1}{\sigma^2}\right) 2pq$$

$$= 1 - S\left(1 - \frac{a^2 pq}{4\sigma^2}\right) - \frac{Sa^2 pq}{4\sigma^4} x^2. \qquad (3)$$

The fitness will thus be a maximum at the mean value of the heterozygote and will then decrease as the square of the deviation. If we sum the effect over all genes, the coefficient of the squared term will be

$$\frac{1}{4\sigma^4} \Sigma S a^2 pq.$$

The variation due to each gene is equal to $\frac{a^2pq}{2}$, so that we can write for the coefficient

$$\frac{\Sigma\frac{Sa^2pq}{2}}{\Sigma\frac{a^2pq}{2}}\times\frac{\Sigma\frac{a^2pq}{2}}{2\sigma^4}$$

$$=\tfrac{1}{2}\bar{S}\frac{\sigma_g^2}{\sigma^4}$$

$$=\frac{\bar{S}h^2}{2\sigma^2},$$

where S is the average value of S weighted according to the variance contributed by that gene, σ_g^2 is the genetic variance due to all genes and h^2 the heritability. Thus, although the position of optimum fitness may not coincide with the population mean, the decline in fitness will be proportional to the square of the deviation from the mean. It would perhaps have been better to combine the effects of the separate genes by multiplication, when we would have got an expression $\exp\left(-\frac{\bar{S}h^2x^2}{2\sigma^2}\right)$ similar to that used by Haldane. It is interesting that in obtaining this result, we have had to make no assumptions as to the effect or frequency of the genes, except that they are at equilibrium.

If the equilibrium has been altered by selection, then it is to be expected that the fitness of the population as a whole will decline. If the frequencies have been changed to $q+r$, $p-r$, then the decline in fitness due to that gene is

$$\begin{aligned}&s_1((p-r)^2-p^2)+s_2((q+r)^2-q^2)\\&=s_1(-2rp+r^2)+s_2(2qr+r^2)\\&=-2prs_1+2qrs_2+r^2(s_1+s_2)\\&=r^2(s_1+s_2).\end{aligned}$$

Now the change in gene frequency in each generation under individual selection is equal to $\frac{\bar{\imath}a}{2\sigma}pq$, assuming that the effect of natural selection in retarding artificial selection is small. So, over t generations we have for the decline in fitness $(s_1+s_2)\frac{\bar{\imath}^2a^2p^2q^2}{4\sigma^2}t^2$, ignoring changes in pq as selection proceeds.

The change in the metric character is equal to $\frac{\bar{\imath}a^2pqt}{2\sigma}$, and summing over all genes, the total change Δx is $\frac{\bar{\imath}t}{2\sigma}\Sigma pqa^2$. Thus the change in fitness $\Delta\bar{w}$ due to all genes equals

$$\frac{\bar{\imath}^2t^2}{4\sigma^2}\Sigma(s_1+s_2)a^2p^2q^2,$$

and

$$(\Delta x)^2=\frac{\bar{\imath}^2t^2}{4\sigma^2}[\Sigma a^2pq]^2.$$

Thus

$$\frac{\Delta\bar{w}}{(\Delta x)^2}=\frac{\Sigma(s_1+s_2)a^2p^2q^2}{\Sigma a^2pq}\frac{1}{\Sigma a^2pq},$$

$$\Delta\bar{w}=\frac{\bar{S}(\Delta x)^2}{2\sigma_g^2}=\frac{\bar{S}(\Delta x)^2}{2h^2\sigma^2},$$

where $\bar{w}$ is used in Wright's sense of the average fitness of the population. This may be compared to the decline in fitness of individuals at different distances from the mean in the population at equilibrium, $\frac{\bar{S}h^2x^2}{2\sigma^2}$. Thus, unless there is no non-genetic variation, the decline in fitness of the population for a given change by selection should be greater than that of individual deviants of the same magnitude in the original population. It is of interest that it is proportional to the square ratio of the change to the genetic standard deviation.

The change in the population mean also causes a radical change in the relationship of fitness to deviation within the population. Instead of a second-order relationship, we have a linear effect. This is simply illustrated by the graph (Fig. 2) showing the proportion of homozygotes at different values of x for a gene with $a/\sigma = 0{\cdot}4$. It will be seen that there is now no maximum in the population range when the gene frequency is altered even to 0·6. To generalize this, we have to go back to equation (2). We have then for the change in fitness

$$\bar{w} = 1 - \frac{s_1p^2 + s_2q^2 + \alpha(s_2q^2 - s_1p^2) + \beta(s_1p^2 + s_2q^2)}{1 + \alpha(q-p) + \beta(q^2+p^2)}$$

$$= 1 - [(s_1p^2 + s_2q^2) + \alpha(s_2q^2 - s_1p^2 - (q-p)\,(s_2q^2 + s_1p^2)) + \beta \,.\, 2pq(s_1p^2 + s_2q^2)]$$

$$= 1 - [(s_1p^2 + s_2q^2) + \alpha 2pq(s_2q - s_1p) + \beta \,.\, 2pq(s_1p^2 + s_2q^2)].$$

Putting $p = \bar{p} - r$, $q = \bar{q} + r$, $s_1\bar{p} = s_2\bar{q} = \bar{S}$, we have

$$\bar{w} = 1 - (\overline{pq} + r^2)\,(s_1 + s_2) - \alpha \,.\, 2pqr(s_1 + s_2) - \beta \,.\, 2pq(\overline{pq} + r^2)\,(s_1 + s^2).$$

This differs from equation (2) in having a term in α and in having the coefficient of β slightly altered. Substituting $\alpha = ax/2\sigma^2$, we have

$$\left(\frac{d\bar{w}}{dx}\right)_{x=0} = -\frac{2pqr(s_1+s_2)\,a}{2\sigma^2}.$$

If the shift in the mean has been achieved by individual selection, we have as before

$$r = \frac{\bar{i}a}{2\sigma}\overline{pq}t,$$

so that summing for all genes,

$$\left(\frac{d\bar{w}}{dx}\right)_{x=0} = -\Sigma\frac{\bar{i}t}{2\sigma^3}pq\,\overline{pq}\,a^2(s_1+s_2).$$

The total change under selection Δx is given as before by

$$\Delta x = \frac{\bar{i}t}{2\sigma}\Sigma pqa^2.$$

Thus

$$\left(\frac{d\bar{w}}{dx}\right)_{x=0} = -\frac{\Delta x}{\sigma^2}\frac{\Sigma pq\,\overline{pq}(s_1+s_2)}{\Sigma pqa^2}.$$

If r is small, we may equate pq and $\overline{pq}$ giving

$$\left(\frac{d\bar{w}}{dx}\right)_{x=0} = -\frac{\bar{S}\Delta x}{\sigma^2},$$

for the change of fitness with the metric character within the population after selection has altered the average of the character by Δx.

Finally, we can predict on this model the rate of relaxation to the original mean if selection is no longer practised. The rate of change of gene frequency in the first generation Δq is equal to

$$pq(s_1 p - s_2 q) = pqr(s_1 + s_2).$$

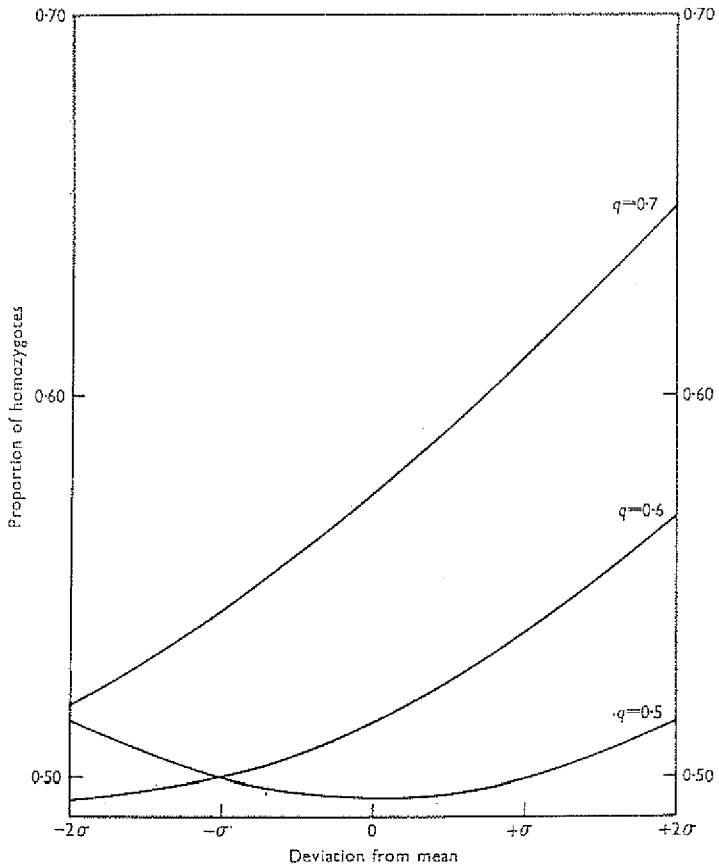

Fig. 2. The proportion of homozygotes at different distances from the population mean, computed from tables of the normal distribution ($a/\sigma = 0{\cdot}4$).

The total change in the mean due to all genes is equal to

$$\begin{aligned} R &= \Sigma pqr(s_1 + s_2)a \\ &= \Sigma pq \frac{\bar{\imath}a}{2\sigma} \overline{pq}\, t(s_1 + s_2)a \\ &= \Sigma \frac{\bar{\imath}a^2}{2\sigma} pq\, \overline{pq}(s_1 + s_2)t \\ &= -\sigma^2 \left(\frac{d\bar{w}}{dx}\right)_{x=0} \\ &= \bar{S}\Delta x, \end{aligned}$$

$$\frac{R}{\Delta x} = \bar{S}.$$

It will be seen that the proportion of the gain by selection which will be lost on one generation of relaxation is equal to $\bar{S}$. This factor, $\bar{S}$, which appears throughout the calculations and which is equal to the average value of S weighted according to the variance contributed at the locus concerned, may be termed the 'strength' of the homoeostasis. It is not to be expected that relaxation will continue at this rate. The total process is the sum of parts with different relaxation rates, and it might be expected that the speed of relaxation would fall off as the more rapid processes reached equilibrium and left only those proceeding more slowly. Indeed, it does not follow that the relaxation will go back to the starting point as some loci may have very small or zero S values.

We can therefore collect together the relationships derived from this model:

(*a*) in equilibrium, the fitness of individual deviants from the mean falls off as $\frac{\bar{S}h^2x^2}{2\sigma^2}$;

(*b*) after change of the mean of the character by Δx under individual selection, the relative fitness of the population will have declined by $\frac{\bar{S}(\Delta x)^2}{2h^2\sigma^2}$;

(*c*) there will then be a linear relationship between fitness and deviation from the mean, the coefficient being $-\frac{\bar{S}\Delta x}{\sigma^2}$;

(*d*) on relaxation of selection, the return in one generation will be a proportion $\bar{S}$ of the progress originally made.

DISCUSSION

From the evolutionary point of view, the most important aspect of these results is their relevance to the problem of 'stabilizing selection', the lower survival of extreme deviants. It must be emphasized that we have been analysing the consequences of two distinct models. In the first model we have assumed that the fitness is determined, as far as these genes are concerned, by the deviation of the animal from the mean in the metric character or from a fixed value. If fitness declines as the deviation increases, then it has been shown that the gene frequencies will tend to 0 or 1. In other words, if this mechanism operates in practice, it cannot be at all responsible for the maintenance of genetic variability in the population. In this model we have assumed that the deviation itself is the determinant and have worked out the genetic consequences.

In the second model we assume that the determinant is the individual properties of the individual genes and work out the consequences on the metric character. The maintenance of genetic variability is therefore one of the premises and the reduction in fitness of the extreme deviants is one of the consequences. This model, being more fundamental, is a much more fruitful one than the former and leads to several predictions of behaviour within and between populations on the basis of the 'homoeostatic strength' of the character, in its simplest manifestation the proportional return to the population equilibrium position in the first generation after selection is relaxed. These predictions could well be checked by experiment, whereas the predictive value of the first model seems to be very limited.

There is another difference in the consequences of the two models not related to our calculations. If the first model is correct, then on inbreeding to complete homozygosis the more extreme lines should be less fit than the intermediate ones. On the second model

there would be no relationship between the mean value of the line and its fitness because all lines would be equally homozygous. The simplest way to do this experimentally would be to select for several generations before inbreeding. There would then be no effect of the previous selection on the fitness of the lines at a high level of homozygosis. It may be possible by such an experiment and by measurements of the different manifestations of the homoeostasis as calculated earlier to throw some light on the basic mechanism involved.

SUMMARY

1. The genetic consequences of selection of intermediates or extremes for metric characters has been analysed. Selection of intermediates leads to fixation and selection of extremes (disassortative mating) will lead to a stable genetic situation with intermediate gene frequencies.

2. The selection of intermediates is similar to the higher natural fitness of metric intermediates often found in nature. The alternative model for the latter situation, in which the extremes have a low fitness because they are homozygotes, was also analysed. It was found that several different phenomena could be interrelated on this model—the relationship of fitness to deviation both in the equilibrium population and after artificial selection, the decline in fitness after such selection and the rate of return to the equilibrium position when selection was suspended. The constant integrating these, called the homoeostatic strength of the character, is related to the mean fitness of homozygotes compared to that of heterozygotes at the individual loci concerned.

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