NATURAL SELECTION FOR AN INTERMEDIATE OPTIMUM

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Summary

Natural selection against extreme metric deviation is a process which is known to lead to the elimination of genetic variability in the particular quantitative character concerned. Recurrent mutation at loci affecting the character will be expected to oppose this tendency to genetic fixation, and the resulting equilibrium situation is discussed in detail in this paper.

The equilibrium genetic variance due to a given locus is shown to be a function only of the mutation rate at that locus, being independent of the magnitude of the average effect of the gene concerned. From the analysis it appears that recurrent mutation, in the face of natural selection favouring phenotypic intermediates, can account for only a small proportion of the genetic variance commonly found in natural populations, underlining the probable importance of heterozygote superiority in fitness as a mechanism conserving genetic variability.

The behaviour of the equilibrium population under artificial selection for extreme expression of the trait is discussed: the consequences of the model are found to be quantitatively similar to those expected on the basis of Lerner's model of genetic homeostasis.

I. INTRODUCTION

Of the many problems confronting the student of evolution, one of the most interesting to those concerned with plant and animal improvement is the persistence of additive genetic variation for individual quantitative characters in natural populations. Abundant evidence of the existence of such genetic variation has been accumulated for an array of species, and it is the rule rather than the exception that artificial selection is able to bring about pronounced changes in the means of individual characters over only a small number of generations. Haldane (1954a) has discussed the factors known to be responsible for the retention of genetic variation in natural populations, including spatial and temporal clines, heterosis at individual loci, and the conflict between mutation and selection. The relative importance of these factors in maintaining variation for specific quantitative characters is, however, only very imperfectly understood.

It is clear that the concept of adaptive significance cannot be applied to isolated quantitative characteristics other than tentatively, for we must always bear in mind that it is the phenotype as an integrated whole which is the subject of natural selection. Nevertheless, we must suppose that for each metric character there exists an optimum value, related to the prevailing genotypic and external environment, and that the mean of a population under natural selection will have moved to approximate to this optimum by the time genetic equilibrium is reached.

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Fisher (1930) has shown that the action of natural selection in discriminating against those individuals which deviate from the optimum in the particular character concerned is such as to lead to the elimination of genetic variability rather than its preservation, and Robertson (1956) has contrasted this situation with that in which extreme deviants are unfit because of their greater degree of homozygosity than individuals approximating to the population mean (Lerner 1954). Robertson has shown the latter model to lead to useful predictions for artificial selection imposed on the population: "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."

It is the purpose of this paper to consider in more detail the model of selection against metric deviation, with a view to setting out the expected consequences of the model under the influence of artificial selection.

II. NATURE OF THE GENETIC EQUILIBRIUM

Let us suppose, following Haldane (1954b), that the decline in reproductive fitness with deviation $x$ from the population mean of a given metric character is a continuous function of the form

$$1 - \exp(-\frac{1}{2}x^2/\sigma_f^2).$$

The scale constant $\sigma_f^2$ is obviously related to the intensity of natural selection for the optimum value, being small if selection permits only those individuals close to the mean to reproduce, and large if a greater degree of latitude is tolerated. One of the most pertinent comparisons one would wish to make in a situation to which this model applied is that of the relative magnitude of $\sigma_f^2$ and $\sigma_p^2$, the total phenotypic variance shown by the character under study. Haldane has in fact defined the intensity of selection for a normally distributed character to be the natural logarithm of the ratio of the phenotypic standard deviation prior to selection to that after selection, which comes out to be

$$I = \frac{1}{2} \log_6[1+(\sigma_p^2/\sigma_f^2)], \quad \ldots \ldots \ldots \ldots \ldots (1)$$

which equals $\frac{1}{2}\sigma_p^2/\sigma_f^2$ for low intensities of selection.

Robertson (1956) has set out in full the derivation of an expression for the change in gene frequency per generation at an individual locus with additive effects on a normally distributed metric character, other effects of the locus being assumed to have no appreciable influence on reproductive fitness. If the difference in average metric value between the two alternative homozygotes at the locus is denoted by $a$, the change in gene frequency per generation under natural selection is given by

$$\delta q = a^2pq(q-p)/8\sigma^2,$$

where $\sigma^2 = \sigma_p^2 + \sigma_f^2$, and $p = 1-q$. The sign of $\delta q$ depends only on that of $(q-p)$;
if $q$ is less than $p$, $\delta q$ will be negative and the value of $q$ reduced each generation to an extent depending on the value of $a$, measuring the effect of this locus on the metric character. If $q$ is greater than $p$, the effect of natural selection for the intermediate optimum will further increase $q$ each generation. Gene frequencies in the population will therefore tend to zero or unity.

Opposing this tendency to genetic fixation there will only be recurrent mutation at loci affecting the character, and in a natural population we can expect the two sets of opposing forces to have resulted in an array of stable gene frequencies. Assuming forward and back mutation rates at the given locus to be of the same order, we may express the equilibrium situation algebraically by the relation

$$a^2pq(q-p)/8\sigma^2 = \mu(q-p), \quad \text{............... (2)}$$

where the rate of mutation is denoted by $\mu$. It is easily shown that the genetic variance due to this locus is $\frac{1}{2}a^2pq$, which at equilibrium is equal to $4\mu\sigma^2$. Inequality of the forward and back mutation rates at the locus will have little effect on this deduction, provided $\mu$ is taken to refer to the mutation rate from the more frequent to the less frequent allele. It is important to stress that, under the assumptions stated, the equilibrium genetic variance contributed by a single locus is a function only of mutation rate, and is independent of the magnitude of the average effect of the gene concerned.

### III. Genetic Variance due to Recurrent Mutation

Let us now consider whether genetic equilibrium due solely to the conflict between mutation pressures and natural selection against phenotypic deviants can account for the amount of genetic variability commonly encountered in natural populations. For a character showing only additive genetic variation, the heritability ($h^2$) is defined to be the ratio of the total genetic variance to the phenotypic variance in the population concerned, and it is not uncommon to find heritability values as high as $\frac{1}{2}$.

According to the model we are considering, the total genetic variance at equilibrium is $4N\overline{\mu}\sigma^2$, where $N$ is the number of loci affecting the metric trait, and $\overline{\mu}$ is the mean mutation rate at these loci. The equilibrium heritability is therefore given by

$$h^2 = 4N\overline{\mu}[1+(\sigma_f^2/\sigma_p^2)].$$

We have no experimental evidence to indicate a likely value for the mean rate of mutation at individual loci affecting quantitative characters, but work with major genes in higher organisms would lead us to suggest a value for $\overline{\mu}$ of approximately $10^{-5}$.

In terms of the intensity of natural selection ($I$) the equilibrium heritability can be written (from (1))

$$h^2 = 4N\overline{\mu}[1+(1/2I)]$$

$$= 2N\overline{\mu}/I$$

approximately, provided the intensity of natural selection is low. To explain a
heritability value of $\frac{1}{2}$ for a quantitative character we should therefore have to postulate an intensity of natural selection as low as say 1 per cent., with 250 genes segregating for the character. In view of the fact that the contribution of each locus to the total genetic variance is independent of the magnitude of its effect on the measured character, we might for some characters (e.g. body size) accept this number of genes as a possible figure. In general, however, it seems unlikely that the mechanism we are considering could of itself be responsible for the maintenance of the genetic variability shown by characters of high heritability.

IV. Effects of Artificial Selection and Relaxation

Under individual selection for extreme expression of an additive genetic character, the change in gene frequency per generation at a given locus is expected to be

$$\delta q = (\mu/2\sigma_p)pq,$$

where $i$ measures the intensity of extreme selection (Haldane 1930). At equilibrium, according to the model we are considering, the value of $pq$ is $8\mu\sigma^2/a^2$ from (2), so that the change in gene frequency per generation in the early stages of selection is expected to be

$$\delta q = 4i\mu\sigma^2/a\sigma_p.$$

The change in gene frequency is therefore least for those loci with large effect on the character, and vice versa. However, the change in mean per generation due to a single locus is given by $a\delta q$, which is independent of $a$, so that the contribution of each locus to the advance in the mean under artificial selection is dependent only on the rate of mutation at that locus.

The decline in fitness with selection is readily predicted on the basis of the model we have set up: after a shift in the population mean of $x_0$, the mean fitness of the selected population in its natural environment is given by

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

$$= (\sigma_f/\sigma) \exp\left[ -\frac{1}{2} \frac{x_0^2}{\sigma^2} \right].$$

The equilibrium population ($x_0 = 0$) has average fitness $\sigma_f/\sigma$, so that the fitness of the selected population relative to that of the equilibrium population is

$$\exp\left[ -\frac{1}{2} \frac{x_0^2}{\sigma^2} \right]. \quad \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots (3)$$

We can also predict accurately the behaviour of the selected population on the relaxation of artificial selection. Let us suppose that at a particular locus the equilibrium gene frequencies $p$, $q$ have been changed to $p^*$, $q^*$ corresponding to an overall change in the population mean of $x_0$. The average fitness values of the subpopulations corresponding to the three alternative genotypes $A_1A_1$, $A_1A_2$, $A_2A_2$ are, from (3),

$$\exp\left[ -\frac{1}{2} \left( x_0 - ap^*/\sigma \right)^2 \right] : \exp\left[ -\frac{1}{2} \left[ x_0 + \alpha(q^* - \frac{1}{2})/\sigma \right]^2 \right] : \exp\left[ -\frac{1}{2} \left( x_0 + aq^*/\sigma \right)^2 \right],$$

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where \( q \) is the frequency of the \( A_1 \) allele. To a first approximation these fitness values are as \( 1 : 1 - s : 1 - 2s \), where \( s = ax_0/2\sigma^2 \). Hence the change in gene frequency under relaxation of selection is expected to be, per generation,

\[
\delta q^* = \frac{ax_0}{2\sigma^2} p^* q^*.
\]

The effect of natural selection on the relaxed population can be compared with that of artificial back selection of intensity \( i \), which would lead to a change in gene frequency of \( (ia/2\sigma_p)p^*q^* \), assuming \( \sigma_p^2 \) to have been little altered in the course of selection. The effects of natural selection can then be seen to be equivalent to artificial back selection of intensity \( x_0\sigma_p/\sigma^2 \). Assuming the overall heritability of the character to have remained unchanged over the original period of artificial selection (a reasonable assumption in the light of experimental evidence for periods of up to 10 generations of moderately intense selection), the actual change in the mean of the selected population on relaxation in the first generation is given by

\[
i h^2 \sigma_p = h^2 x_0 \sigma_p^2/\sigma^2
\]

towards the mean of the unselected population; i.e. a proportion \( h^2 \sigma_p^2/\sigma^2 \) of the progress previously made.

V. DISCUSSION

The genetic variability displayed by quantitative characteristics in natural populations of cross-breeding species must in the main be preserved by three types of mechanism. We may expect that there will be some loci affecting the particular metric character concerned which have no influence on reproductive fitness other than that due to the causal relation between fitness and metric deviation. It is almost certain that, in addition, natural selection will favour the heterozygous genotypes at some loci at the expense of the homozygous, resulting in stable intermediate gene frequencies. And, finally, it is possible that some of the genetic variation shown by a given quantitative character is promoted by loci at which deleterious recessive alleles are maintained by recurrent mutation.

As a result of the preceding analysis, we are in a position to compare the effects of loci of the first two categories when artificial selection is imposed on the population. Robertson (1956) has shown that if all the genetic variation shown by an additive character is due to loci showing heterozygote superiority in fitness, a change in the mean of the population of \( x_0 \) under artificial selection can be expected to lead to a decline in the relative fitness of the population of \( S^2 x_0^2/2h^2 \sigma_p^2 \). In this expression, \( S \) is a constant called the homeostatic strength of the character concerned, and is related to the mean fitness of homozygotes compared with that of heterozygotes at the individual loci. On relaxation of selection, the return of the mean in one generation is expected to be a proportion \( S \) of the progress originally made.

We have shown in the present paper that if all loci affecting an additive genetic character influence fitness solely through their effects on the character
itself, the decline in fitness with artificial selection is expected to be \(1 - \exp[-\frac{1}{2}(x_0/\sigma)^2]\). Provided that artificial selection has not been pushed too far, and that the intensity of natural selection against phenotypic extremes is low, this expression is roughly equal to \(x_0^2/2\sigma^2\). On relaxation of selection, the change in the mean of the selected population in the first generation is expected to be a proportion \(h^2\sigma_p^2/\sigma^2\) of the progress previously made.

Both models therefore lead to the same pattern of behaviour under artificial selection and relaxation. The decline in the relative fitness of the population (which can be measured satisfactorily in *Drosophila melanogaster* by competition with marked laboratory stocks) is expected to be \(x_0^2/2h^2\sigma_p^2\) times the proportion of the response to selection which is lost after one generation of relaxation, irrespective of the relative importance of the two types of mechanism in maintaining the equilibrium genetic variation. The change in population mean on relaxation of selection is a function both of the homeostatic strength of the character, and of the intensity of natural selection against extreme metric deviation, but the two components cannot be separated.

Waddington (1957) has stressed the importance of distinguishing between these two aspects of the relationship between a quantitative character and natural selection. He has referred to the "true" and "spurious" fitness cross sections of the character in a natural population, corresponding to the model of selection against metric deviation and the homeostatic model respectively. The experimental approach which comes closest to making this distinction possible seems to be a comparison of the effects of relaxation of artificial selection under natural conditions on the one hand, and under controlled environmental conditions on the other. For many characters, one may perhaps attribute the difference in behaviour in the two situations to the effects of natural selection against extreme metric deviation.

### VI. References


**Lerner, I. M. (1954).**—"Genetic Homeostasis." (Oliver and Boyd: London.)
