

THE STABILITY OF EQUILIBRIA UNDER SELECTION

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I. INTRODUCTION

THERE has been considerable recent interest in the existence of stable equilibria under selection as a possible means of maintaining genetic variability. Most work has been confined to the two-locus case (see, for example, the literature cited by Gale and Kearsley, 1968). The purpose of this paper is to develop a general theory applicable to a metric character determined by a relatively large number of loci, so that the effect of any particular locus is relatively small. This problem was first considered by Fisher (1930) and Haldane (1932), and was later investigated in more detail by Robertson (1956); it will be seen, however, that the results of these authors must be modified in one important respect, and that they can also be considerably extended. The effect of linkage disequilibrium will be ignored in the present paper, but it is believed that the results obtained here will be essentially correct under the rather weak selective pressures likely to be found under natural conditions.

2. THE EFFECT OF SELECTION

Suppose that there are two alleles, A_1 and A_2 , at a particular locus, with gene frequencies p and q , and with genetic effects on some metric character as set out in table 1. The quantity D represents the degree and direction

TABLE 1

The genetic effect at a particular locus

Genotype	A_1A_1	A_1A_2	A_2A_2
Frequency	p^2	$2pq$	q^2
Effect	$-a$	aD	a
Deviation from mean = d	$-2aq(1+pD)$	$a[(p-q)+D(1-2pq)]$	$2ap(1-qD)$

of dominance; when $D = 0$ there is no dominance, when $0 < |D| < 1$ partial dominance, when $|D| = 1$ complete dominance, and when $|D| > 1$ overdominance. The contribution from this locus to the genetic variance is proportional to a^2 , and it will be assumed that a^2 is sufficiently small compared with the total phenotypic variance, V , that higher powers of a can be ignored.

Let us now consider the effect on this particular locus of an arbitrary fitness function such that the fitness of an individual with phenotypic value y is $w(y)$. Consider a group of individuals with a specified genotype at this locus, and consequently with mean $M+d$, where M is the population mean and d is the appropriate deviation from the mean shown in the last row of table 1. If the density function in this specified group is $f(y-d)$, then the

average fitness of this group relative to a group with the same distribution but with $d = 0$ is

$$\text{Relative fitness} = \int f(y-d)w(y)dy / \int f(y)w(y)dy. \quad (1)$$

To sufficient accuracy we may take f as the density function for the whole population, since the effect of the small decrease in the variance caused by fixing the genotype at a particular locus will almost disappear in the above ratio. Furthermore, if we expand $f(y-d)$ in a Taylor series about $d=0$, we find that the selection pressure, s , against this genotype, defined as $1 - \text{Relative fitness}$, is

$$s = Ad - \frac{1}{2}Bd^2 + o(d^2) \quad (2)$$

where

$$\begin{aligned} A &= \int f'(y)w(y)dy / \int f(y)w(y)dy \\ B &= \int f''(y)w(y)dy / \int f(y)w(y)dy. \end{aligned} \quad (3)$$

Let us now consider the effect of selection on the gene frequency at this locus. If the selection pressures against the three genotypes are s_{11} , s_{12} and s_{22} respectively, then the change in p as a result of one generation of selection is, to order a^2 ,

$$\Delta p = pq[-s_{11}p + s_{12}(p-q) + s_{22}q]. \quad (4)$$

Evaluating the selection pressures from Equation 2 and substituting the appropriate values of d from table 1, we find that

$$\Delta p = pq\{Aa[1 + (p-q)D] - \frac{1}{2}Ba^2[(p-q)(1 + (p-q)D)^2 - 4pqD]\}. \quad (5)$$

At equilibrium Δp must be zero, so that the expression in curly brackets must be zero for a non-trivial equilibrium.

To interpret the significance of the coefficients A and B defined in Equation 3 let us suppose that the phenotype is normally distributed with mean M and variance V . Then

$$\begin{aligned} f'(y) &= -\frac{(y-M)}{V}f(y) \\ f''(y) &= \left[-\frac{1}{V} + \frac{(y-M)^2}{V^2}\right]f(y). \end{aligned} \quad (6)$$

Furthermore, the distribution of the phenotype *after* the operation of selection is $f(y)w(y) / \int f(y)w(y)dy$. If the mean and variance after the operation of selection are $M+DM$ and $V+DV$ respectively, it follows that

$$\begin{aligned} A &= -DM/V \\ B &= (DV+DM^2)/V^2. \end{aligned} \quad (7)$$

At equilibrium DM must be approximately zero, so that B is approximately DV/V^2 . Now stabilising selection tends to reduce the phenotypic variance and will therefore be associated with a negative value of DV and hence of B , while disruptive selection tends to increase the phenotypic variance and will therefore be associated with positive values of DV and B . It will be seen in the next section that the conditions for the stability of an equilibrium depend essentially on the sign of B and hence on the type of selection in operation.

Since DM and consequently A must be small at equilibrium it might be thought that A could be ignored. This would not be valid, however, unless Aa were small compared with Ba^2 , that is to say unless A were small compared with a . This assumption cannot be made for the following reasons: (1) The result that $A = -DM/V$ is only true exactly under normality. (2) The result that $DM = 0$ at equilibrium only holds exactly when the regression of offspring on parent is linear; non-linearity may be introduced by dominance or by skewness in the distribution of environmental deviations. (3) Even if it were true that $A = 0$ at equilibrium, it would be necessary to take account of small changes in A resulting from small departures from equilibrium in order to study the stability of the equilibrium. Previous investigations by Fisher (1930), Haldane (1932) and Robertson (1956) have assumed that the selection pressure is proportional to d^2 and have thus implicitly ignored the coefficient A .

3. THE STABILITY OF EQUILIBRIA

Loci with equal effects without dominance

We consider first the simplest case of N loci each with the same effect, without dominance. If the gene frequency at the i th locus is p_i the genetic variance is $h^2V = 2a^2\Sigma p_iq_i$, where h^2 is the heritability; the remaining variance is assumed to be due to independent environmental effects. The change in the i th gene frequency as the result of selection is, from Equation 5 with $D = 0$,

$$\Delta p_i = p_iq_i\{Aa - \frac{1}{2}Ba^2(p_i - q_i)\}. \quad (8)$$

At equilibrium we must have $\Delta p_i = 0$, so that, unless $p_i = 0$ or 1, the equilibrium gene frequency, P , must be the same at all loci and must satisfy the equation

$$A - \frac{1}{2}Ba(P - Q) = 0. \quad (9)$$

To investigate the stability of this equilibrium suppose that it is subjected to a small perturbation so that $p_i = P + e_i$. Then in the next generation $e_i^* = e_i + \Delta p_i$; to order a^2 , Δp_i is given by

$$\Delta p_i = PQ \left\{ a \frac{dA}{dM} \Delta M - a^2 B e_i \right\} \quad (10)$$

where $\Delta M = -2a\Sigma e_j$ is the change in the mean due to the perturbation. Furthermore, since $\partial f / \partial M = -\partial f / \partial y = -f'$, it follows from the definitions of A and B in equation 3 that

$$\frac{dA}{dM} = -B + A^2 \doteq -B. \quad (11)$$

Hence, to order a^2 ,

$$e_i^* = e_i + \frac{h^2VB}{N} \left\{ \Sigma e_j - \frac{1}{2}e_i \right\}. \quad (12)$$

If \mathbf{e} is the column vector of the e_i 's then

$$\mathbf{e}^* = \mathbf{C}\mathbf{e} \quad (13)$$

where the matrix \mathbf{C} has diagonal elements $1 + \frac{1}{2}Bh^2V/N$ and off-diagonal elements Bh^2V/N .

The stability of the equilibrium depends on the latent roots of the matrix \mathbf{C} ; if the dominant latent root is less than 1 in absolute value the equilibrium is stable, otherwise it is unstable. It is not difficult to show that the matrix has two latent roots,

$$\begin{aligned}\lambda_1 &= 1 - \frac{1}{2}Bh^2V/N \\ \lambda_2 &= 1 + Bh^2V \left(1 - \frac{1}{2N}\right)\end{aligned}\quad (14)$$

the first latent root having multiplicity $(N-1)$ and the second being a single root. Thus whatever the sign of B one or other of the two roots must be greater than 1, and so the equilibrium is unstable under any form of selection, either stabilising selection (B negative) or disruptive selection (B positive). This is in disagreement with the results of Robertson (1956) who concluded that disruptive selection leads to a stable equilibrium in the absence of dominance.

To investigate further the reason for instability in these two cases let us write $\bar{e} = \sum e_i/N$, $\delta_i = (e_i - \bar{e})$. It follows from Equation 12 that

$$\begin{aligned}\bar{e}^* &= \lambda_2 \bar{e} \\ \delta_i^* &= \lambda_1 \delta_i.\end{aligned}\quad (15)$$

If B is negative (stabilising selection) λ_1 will be greater than 1 and λ_2 less than 1; hence \bar{e} will tend to zero, so that the average gene frequency which determines the mean of the distribution will tend to revert to its equilibrium value, but the δ_i 's will diverge, so that the individual gene frequencies will tend to fixation at 0 or 1. On the other hand, if B is positive (disruptive selection), λ_2 will be greater than 1 so that \bar{e} will diverge, but λ_1 will be less than 1 so that the δ_i 's will tend to zero; hence the gene frequencies will all tend to have the same value but they will move away together from the position of unstable equilibrium. This conclusion makes sense if we think of disruptive selection as being caused by selection for two widely separated optimal values with an equilibrium value in between them; the system will tend to move away towards one or other of the optimal values until a situation of stabilising selection is reached.

Loci with equal effects with dominance

Let us now consider the case of N loci each with the same effect but with coefficient of dominance D as defined in table 1. Proceeding in the same way as before, we find that if the system is displaced slightly from its equilibrium position, then in the next generation

$$e_i^* = e_i + \frac{h^2VB}{N} \{\sum e_j - \alpha e_i\} \quad (16)$$

where

$$\alpha = \frac{1}{2}[1 + 8D^2PQ - D^2]/[1 + (P - Q)D]^2 \quad (17)$$

and where $h^2V = 2NPQa^2[1 + (P - Q)D]^2$ is the additive genetic variance.

The matrix \mathbf{C} which defines stability has diagonal elements $1 + (1 - \alpha)Bh^2V/N$ and off-diagonal elements Bh^2V/N . Its latent roots are

$$\begin{aligned}\lambda_1 &= 1 - \alpha Bh^2V/N \\ \lambda_2 &= 1 + Bh^2V \left(1 - \frac{\alpha}{N}\right)\end{aligned}\quad (18)$$

with multiplicities $(N-1)$ and 1 respectively.

If B is negative (stabilising selection) the condition for stability is that α is negative. This condition is fulfilled if *either* $(P-Q)$ and D have the same sign and $8PQ < (D^2-1)/D^2$ or $(P-Q)$ and D have opposite signs and $(D^2-1)/D^2 < 8PQ < 2(D^2-1)/D^2$. Thus there cannot be stability unless there is overdominance, and the region of stability increases with the amount of overdominance. For example, if there is a small amount of overdominance so that $D = 1 + \varepsilon$, where ε is a small positive quantity, the regions of stability are $P > 1 - \frac{1}{4}\varepsilon$ and $\frac{1}{4}\varepsilon < P < \frac{1}{2}\varepsilon$. If $D = +2$, the regions of stability are $P > 0.9$ and $0.1 < P < 0.25$. When D becomes very large the regions of stability become $P > 0.85$ and $0.15 < P < 0.5$. (For $D < -1$ the above results remain valid if Q is substituted for P .)

If B is positive (disruptive selection) the condition for stability is that $\alpha > N$. If α is fixed then the equilibrium must always become unstable as the number of loci increases, but stable equilibria may exist for moderately large values of N . For example, if $D = 1$ (complete dominance of the A_2 gene) then $\alpha = \frac{1}{2}Q/P^2$; if $N = 50$ there is stable equilibrium when $P < 0.095$, and in general the approximate condition for stability when $D = 1$ is that $P < (2N)^{-\frac{1}{2}}$. Large values of α are in general associated with a high ratio of dominance variance to additive genetic variance and hence with a low heritability.

Loci with unequal effects

In the general case when the i th locus has an effect $\pm a_i$ in the homozygotes and $a_i D_i$ in the heterozygote, the equilibrium gene frequency, P_i , which makes the expression in curly brackets in Equation 5 zero, will vary from locus to locus. If we now subject the equilibrium to a small perturbation so that $p_i = P_i + e_i$, then it can be shown by the same argument as before that in the next generation

$$e_i^* = e_i + 2P_i Q_i w_i B [\sum w_j e_j - \alpha_i w_i e_i] \quad (19)$$

where

$$w_i = a_i [1 + (P_i - Q_i) D_i] \quad (20)$$

and where α_i is defined as in Equation 17 with the appropriate subscripts. The matrix \mathbf{C} which determines stability can therefore be written down and its latent roots evaluated in any particular case, but it will be necessary to use a rather heuristic approach to arrive at an approximate general solution.

To consider the conditions for stability under stabilising selection let us suppose that two loci, which may be labelled loci 1 and 2, have the same effect so that $a_1 = a_2$, $D_1 = D_2$, $P_1 = P_2$; it follows from Equation 19 that

$$(e_1^* - e_2^*) = (e_1 - e_2)(1 - 2P_1 Q_1 w_1^2 \alpha_1 B). \quad (21)$$

If B is negative there can only be stability if α_i is negative, which is the same

condition as in the case when all loci have equal effects. From considerations of continuity it is clear that a similar condition must be satisfied if two loci have nearly the same effects. It can be concluded that an approximate condition for stability under stabilising selection is that α_i is negative at all loci, which implies overdominance at all loci.

Under disruptive selection let us consider the stability of $\Sigma w_i e_i$. It follows from Equation 19 that

$$\Sigma w_i e_i^* = \Sigma w_i e_i + B\{\Sigma w_i e_i \Sigma 2P_i Q_i w_i^2 - \Sigma w_i e_i \cdot 2P_i Q_i w_i^2 \alpha_i\}. \quad (22)$$

The quantity $2P_i Q_i w_i^2$ is the contribution of the i th locus to the additive genetic variance. If we define $\bar{\alpha}$ as a weighted average of the α_i 's, the weights being equal to $2P_i Q_i w_i^2$, and if we assume as an approximation that $w_i e_i$ is uncorrelated with $2P_i Q_i w_i^2 \alpha_i$, it follows that

$$\Sigma w_i e_i^* \doteq \Sigma w_i e_i \left\{ 1 + Bh^2 V \left(1 - \frac{\bar{\alpha}}{N} \right) \right\}. \quad (23)$$

It is therefore suggested that when B is positive an approximate criterion for stability is that $\bar{\alpha} > N$. Since large values of α_i are likely to receive rather small weights in calculating the weighted average $\bar{\alpha}$, stability is even less likely to be attained than when all loci have equal effects.

4. SUMMARY

1. The effect of selection on a locus with a small effect on a metric character is formulated in general terms for an arbitrary fitness function.

2. It is shown that equilibria for polygenic characters are usually unstable under either stabilising or disruptive selection.

3. Under stabilising selection there cannot be stability unless there is overdominance at all loci; under disruptive selection there can only be stability when the ratio of dominance to additive genetic variance is high.

5. REFERENCES

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