

The genetic correlation between characters maintained by selection, linkage and inbreeding

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SUMMARY

Mutation is modelled in two quantitative characters under separate genetic control in a large population. A bivariate pattern of selection acts to correlate the characters and, without pleiotropy, their genetic correlation is due entirely to linkage disequilibrium. Data on spontaneous mutation, the effective number of genes, and the intensity of natural selection on quantitative characters are used to evaluate the models. It is concluded that, even when selection favors a high correlation between the characters, with random mating and no linkage between loci influencing different traits the genetic correlation between characters is likely to be small in magnitude. A genetic correlation of large magnitude can be maintained only if the loci influencing different characters are tightly linked, or there is a high level of inbreeding in the population created by frequent mating between closely related individuals.

1. INTRODUCTION

Genetic correlations between quantitative (polygenic) characters are one of the major determinants of the rate and direction of evolution of the average phenotype in a population in response to multivariate patterns of natural selection. Denoting the characters of the population z_1, \dots, z_n in the form of a column vector, \mathbf{z} , and assuming that the distribution of phenotypes in the population is multivariate normal in each generation before selection, the change in the mean phenotypes produced by one generation of selection is $\Delta\bar{\mathbf{z}} = \mathbf{G}\beta$. The additive genetic variance-covariance matrix of the characters, \mathbf{G} , can be estimated from the phenotypic correlations between the characters in related individuals, or from artificial selection experiments (Falconer, 1981). The selection gradient, β , is a vector of forces of directional selection acting directly on the characters (Lande, 1979; Lande & Arnold, 1983). Evolution of the vector of mean phenotypes, $\bar{\mathbf{z}}$, does not generally occur in the direction of the selection gradient, but is modified by the pattern of additive genetic variances and correlations of the characters. It is therefore of interest to model deterministic mechanisms maintaining genetic correlations between characters within a large population.

Two deterministic mechanisms contributing to genetic correlations between characters are pleiotropic (manifold) effects of genes and linkage disequilibrium

(nonrandom associations of alleles) between loci affecting different characters (Falconer, 1981). Lande (1980*a*) derived a model for the evolution of \mathbf{G} , but only analysed genetic correlations between characters maintained by pleiotropic mutations. The present paper investigates the genetic correlation between characters which can be maintained in the absence of pleiotropy by linkage disequilibrium alone, due to selection, linkage and inbreeding in a large population.

Multilocus theory indicates that when selection is weak and linkage is not very tight, linkage disequilibrium should be negligible in a large population with approximately random mating (Wright, 1969, ch. 4). Substantial correlations between alleles at functionally related (epistatically selected) gene loci can be maintained without pleiotropy by tight linkage or high levels of inbreeding (Lewontin, 1974; Holden, 1982). Here we consider inbreeding in a large (effectively infinite) population produced by mating between related individuals, rather than inbreeding caused by finite population size.

To analyse the potential role of linkage disequilibrium in creating genetic correlations between quantitative (polygenic) characters, models are formulated here of two characters under separate genetic control, but which through a functional relationship are selected to be correlated. It is confirmed that without linkage or pleiotropy the genetic correlation maintained between functionally related characters is small in a random mating population under weak selection. An approximate formula is also derived for the maximum genetic correlation due to linkage disequilibrium which can be maintained by selection with tight linkage or a high level of inbreeding.

2. MODELS

The models concern two quantitative traits which are separately under stabilizing selection, but are also selected to covary. The characters, y and z , are assumed to follow a bivariate normal distribution, and the fitness of individuals with phenotype (y, z) is described by a Gaussian function with the optimal values (θ_y, θ_z) ,

$$W(y, z) = \exp \left\{ -\frac{1}{2}(y - \theta_y, z - \theta_z) \mathbf{W}^{-1}(y - \theta_y, z - \theta_z)^T \right\} \quad (1)$$

in which the superscript T indicates matrix transposition. Under weak selection the fitness function is approximately quadratic around the optimum phenotype, and when the mean phenotype of the population is near the optimum the diagonal entries in the symmetric matrix $-\mathbf{W}^{-1}$ approximate the strength of stabilizing selection acting directly on each character, whereas the offdiagonal entries approximate the strength of selection acting to correlate the characters (Lande & Arnold, 1983).

Both characters are influenced by a number of mutable loci, labelled $1, \dots, n$ for trait y and $n+1, \dots, m$ for trait z , and all of their genetic variance and covariance is assumed to be additive. At the i th locus mutation occurs to a wide range of possible allelic effects on the character it influences, such that each allele produces the same distribution of mutational changes, and there is a constant input, u_i , of genetic variance each generation (Kimura, 1965; Lande, 1975). To account for high total mutation rates observed in quantitative characters, in excess

of 10^{-2} per gamete per generation for morphological traits in maize (Sprague, Russell & Penny, 1960; Russell, Sprague & Penny, 1963) and mice (Hoi-Sen, 1972), high per locus mutation rates are assumed to occur at a moderate number of gene loci (including the effects of transposable elements and unequal recombination between tandem duplications). Further supposing that selection on the characters is weak, the distribution of allelic effects on the characters in gametes can be approximated as multivariate normal (cf. Fleming, 1979; Turelli, 1984).

The covariance of allelic effects at loci i and j within gametes is written as C_{ij} . In a large population with inbreeding due to mating between relatives there is an average correlation between the effects of genes on any character in uniting gametes denoted as f (Wright, 1969, ch. 7), and more generally the covariance between the effects of alleles from different gametes within zygotes at loci i and j is fC_{ij} (Lande, 1977). The total genetic variances, G_{yy} and G_{zz} , and the total genetic covariance, G_{yz} , of the characters can be expressed as

$$\begin{aligned} G_{yy} &= 2 \sum_{i=1}^n C_{iy} \quad \text{where} \quad C_{iy} = (1+f) \sum_{j=1}^n C_{ij} \\ G_{zz} &= 2 \sum_{i=n+1}^m C_{iz} \quad \text{where} \quad C_{iz} = (1+f) \sum_{j=n+1}^m C_{ij} \end{aligned} \quad (2)$$

and

$$G_{yz} = 2 \sum_{i=n+1}^m C_{iy} = 2 \sum_{i=1}^n C_{iz}.$$

The recombination rate between loci i and j is signified by r_{ij} , with $r_{ii} = 0$. Environmental effects on the characters are also incorporated, with no genotype-environment interaction or correlation, so that the phenotypic variance-covariance matrix, \mathbf{P} , is a sum of the genetic and environmental variance-covariance matrices, $\mathbf{P} = \mathbf{G} + \mathbf{E}$.

The dynamical equations describing the evolution of the genetic variances and covariances of allelic effects can be derived by considering the multiple regressions of the effects of alleles at each locus on both of the characters (Lande, 1977, 1980*a*),

$$\Delta C_{ij} = -(C_{iy} \ C_{iz})(\mathbf{W} + \mathbf{P})^{-1}(C_{jy} \ C_{jz})^T - (1-f)r_{ij}C_{ij} + \delta_{ij}u_i, \quad (3)$$

where $\delta_{ij} = 1$ if $i = j$ and zero otherwise. Assuming that selection on the genetic variance of any linear combination of the characters is weak, $\mathbf{W} + \mathbf{P}$ is nearly equal to $\tilde{\mathbf{W}} = \mathbf{W} + \mathbf{E}$ (Lande, 1980*a*).

For simplicity, certain symmetry assumptions are now introduced so that the two characters are equally variable and equally heritable, and each locus contributes the same amount of genetic variance to the character it influences. Specifically, let

$$\mathbf{W} = \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix} \omega^2 \quad \text{and} \quad \mathbf{E} = \begin{pmatrix} 1 & \epsilon \\ \epsilon & 1 \end{pmatrix} \sigma_\epsilon^2 \quad (4a)$$

so that $\tilde{\mathbf{W}}$ can be written in the same symmetrical form as \mathbf{W} but with

$$\tilde{\omega}^2 = \omega^2 + \sigma_\epsilon^2 \quad \text{and} \quad \tilde{\rho} = (\rho\omega^2 + \epsilon\sigma_\epsilon^2)/(\omega^2 + \sigma_\epsilon^2). \quad (4b)$$

These parameters describe the shape of the fitness surface acting on the genotypic

(or breeding) values of the characters, which is of the same form as in equation (1) but with $\bar{\mathbf{W}}$ in place of \mathbf{W} and breeding values instead of phenotypes (Lande, 1979, 1980a). Note that an environmental correlation between the characters ($\epsilon \neq 0$) produces selection for the breeding values to be correlated ($\tilde{\rho} \neq 0$) even in the absence of selection acting to correlate the phenotypes ($\rho = 0$).

It is also assumed that both characters are influenced by the same number of equally mutable loci, so that $m = 2n$ and $u_i = u$ for all i . If the pattern of recombination and the system of mating also promote an equal contribution of genetic variance from each locus, we can set

$$C_{iy} = C_{jz} = c \quad \text{and} \quad C_{jy} = C_{iz} = b \quad (4c)$$

for $i = \{1, \dots, n\}$ and $j = \{n+1, \dots, 2n\}$, so that

$$G_{yy} = G_{zz} = 2nc, \quad G_{yz} = 2nb \quad (4d)$$

and the genetic correlation between the characters is $\gamma = b/c$.

The assumption of weak selection on the breeding values of any linear combination of the characters entails that the eigenvalues of the matrix $\mathbf{G}\bar{\mathbf{W}}^{-1}$ must be much less than unity (Lande, 1980a). Under the symmetry assumptions above, \mathbf{G} and $\bar{\mathbf{W}}$ have the same eigenvectors (with slopes $+1$ and -1), hence the eigenvalues of $\mathbf{G}\bar{\mathbf{W}}^{-1}$ are equal to those of \mathbf{G} each divided by the eigenvalue of $\bar{\mathbf{W}}$ corresponding to the same eigenvector. The conditions for weak selection are thus found to be

$$\frac{(1+\gamma)2nc}{(1+\tilde{\rho})\tilde{\omega}^2} \ll 1 \quad \text{and} \quad \frac{(1-\gamma)2nc}{(1-\tilde{\rho})\tilde{\omega}^2} \ll 1, \quad (5)$$

which together imply $2nc \ll \tilde{\omega}^2$. In the present models with no pleiotropy it can be anticipated (and it is confirmed below) that the genetic correlation between the characters will always have a magnitude smaller than the 'correlation' in the fitness surface acting on the genotypic values of the characters, $|\gamma| < |\tilde{\rho}|$.

The genetic correlation between the characters maintained in different situations consistent with the above symmetry conditions can be examined using the equilibrium equations

$$-\{[c^2 + b^2 - 2\tilde{\rho}bc]/(1 - \tilde{\rho}^2)\tilde{\omega}^2\} - (1-f)r_{ij}C_{ij} + \delta_{ij}u = 0 \quad (6a)$$

for loci i and j affecting the same character, and

$$-\{[2bc - \tilde{\rho}(c^2 + b^2)]/(1 - \tilde{\rho}^2)\tilde{\omega}^2\} - (1-f)r_{ij}C_{ij} = 0 \quad (6b)$$

for loci i and j affecting different characters.

The following cases postulate certain patterns of recombination between loci influencing different characters, but in each case loci influencing the same character are allowed to have any positive recombination rates. Comparing the diagonal equations (with $i = j$) and the offdiagonal equations (with $i \neq j$) in (6a) it can be seen that

$$C_{ij} = -u/(1-f)r_{ij} \quad (7a)$$

for loci i and j influencing the same character. Then from (2) and (4c) the variance of allelic effects at each locus is

$$C_{ii} = \begin{cases} \frac{c}{1+f} + \frac{u}{1-f} \sum_{\substack{j=1 \\ j \neq i}}^n \frac{1}{r_{ij}} & \text{for } i = 1, \dots, n \\ \frac{c}{1+f} + \frac{u}{1-f} \sum_{\substack{j=n+1 \\ j \neq i}}^m \frac{1}{r_{ij}} & \text{for } i = n+1, \dots, 2n. \end{cases} \quad (7b)$$

Using the diagonal equation in (6a) to substitute for $c^2 + b^2$ in (6b) yields

$$(2bc/\bar{\omega}^2) - \tilde{\rho}u + (1-f)r_{ij}C_{ij} = 0 \quad (8)$$

for loci i and j influencing different characters. We now proceed to examine different cases which produce the minimum and maximum genetic correlation between the characters.

In the absence of pleiotropy, the genetic correlation between the characters is due entirely to linkage disequilibrium created by epistatic selection acting to correlate the characters. From (4), (6) and (7) it can be seen that the equilibrium genetic variances and covariance of the characters do not depend on the recombination rates between loci influencing the same trait. However, it will be shown that when selection favors a high genetic correlation between the characters ($|\tilde{\rho}| \rightarrow 1$) the equilibrium genetic covariance depends strongly on the inbreeding coefficient of the population and the recombination rates between loci influencing different characters. The minimum genetic correlation between the characters should occur when there is no linkage between genes influencing different traits, and no inbreeding in the population ($f = 0$). The maximum genetic correlation between characters should occur with tight linkage between loci influencing different characters and/or a high level of inbreeding in the population.

Minimum genetic correlation. Suppose that there is free recombination between loci affecting different traits, and that the inbreeding coefficient of the population is low, so that $r_{ij} = \frac{1}{2}$ and $f \ll 1$ in equation (8). Then because each locus contributes equally to the total genetic variance of a character, $b = (1+f)nC_{ij}$ for all loci i and j influencing different characters. Substituting for C_{ij} in terms of b in (8), and employing the assumption of weak selection ($2nc \ll \bar{\omega}^2$) produces the approximation

$$b = 2nu\tilde{\rho}(1+f)/(1-f). \quad (9a)$$

The diagonal equation of (6a) is then quadratic in c and has the solution

$$c = \sqrt{[(1-\tilde{\rho}^2)(\bar{\omega}^2u - b^2)] + \tilde{\rho}b}. \quad (9b)$$

Thus with loose linkage between loci influencing different traits, and a low inbreeding coefficient in the population, the genetic correlation between the characters, $\gamma = b/c$, depends not only on the 'correlation' in the fitness surface acting on the genotypic values of the characters ($\tilde{\rho}$), but also on the general intensity of stabilizing selection ($\bar{\omega}^2$) and the number and mutability of the genes influencing the characters.

For a numerical example, choosing parameters of the model to be representative of data from observations and experiments on quantitative traits, let the effective number of loci for each character be $n = 10$ (Wright, 1968, ch. 15; Falconer, 1981, ch. 12; Lande, 1981), and let $u = 5 \times 10^{-5} \sigma_e^2$ so that in units of the environmental variance the total mutability of each character is $2nu/\sigma_e^2 = 10^{-3}$ (Lande, 1975; Hill, 1982). Setting $\tilde{\omega}^2/\sigma_e^2 = 100$ and supposing that there is selection for the characters to be highly correlated, $\tilde{\rho} = 0.9$, implies that $b = 9 \times 10^{-4}$ and $c = 3.16 \times 10^{-2}$. Thus, using (4d), the heritability of each of the characters (the proportion of the total phenotypic variance due to additive gene effects) is $h^2 = 0.39$, and their genetic correlation is $\gamma = 0.028$. These parameters satisfy the conditions for weak selection in (5) and are consistent with apparent selective mortalities of a few percent from observations on single characters (Haldane, 1954; Johnson, 1976, ch. 7).

Maximum genetic correlation due to linkage. Suppose that pairs of loci influencing different characters are completely linked, but that loci influencing the same character are not linked, and the average inbreeding coefficient in the population is low, so that $r_{i\ n+i} = 0$ for all i and r_{ij} is near $1/2$ for all other pairs of loci. Then from (8) with $j = n + i$

$$b = \tilde{\rho}\tilde{\omega}^2u/2c \tag{10a}$$

and substituting this in the diagonal equation in (6a) yields a quartic equation for c ,

$$c^4 - \tilde{\omega}^2uc^2 + \frac{1}{4}\tilde{\rho}^2\tilde{\omega}^4u^2 = 0$$

which has the solution

$$c = \sqrt{[(1 + \sqrt{(1 - \tilde{\rho}^2)})\tilde{\omega}^2u/2]}. \tag{10b}$$

This is the only feasible solution corresponding to a positive definite genetic variance-covariance matrix for the characters (with positive variances and a genetic correlation between $+1$ and -1),

$$\gamma = \tilde{\rho}/(1 + \sqrt{(1 - \tilde{\rho}^2)}). \tag{10c}$$

From (8) it can also be seen in this case that because $r_{ij}C_{ij} = r_{kl}C_{kl}$ for loci i and j (and k and l) influencing different traits, the only pairs of loci contributing to the correlation between the characters are the tightly linked pairs i and $n + i$,

$$C_{i\ n+i} = 0 \quad \text{for } j \neq i \tag{11a}$$

and hence

$$(1 + f)C_{i\ n+i} = b \quad \text{for } i = \{1, \dots, n\}. \tag{11b}$$

Thus the correlation between the effects of alleles within gametes at a tightly linked pair of loci influencing different characters, which are isolated on the linkage map from other such pairs of loci, may be almost as large as the genetic correlation between the characters.

In this model the only linkage disequilibrium for genes in different linkage groups occurs between effects of alleles at loci influencing the same character, which does not alter the equilibrium genetic variances or the covariance of the characters. This observation suggests that in a random mating population the impact of tight linkage on the genetic correlations between characters can be analysed using

models of pleiotropic mutations (Lande, 1980*a*). When loci influencing a set of characters are organized into tightly linked groups between which there is free recombination, this is nearly equivalent to a lesser number of loci with pleiotropic effects. Let \mathbf{U}_i be the net variance-covariance matrix of mutational changes in the effects on the characters of alleles at all loci in the i th linkage group, and let \mathbf{W} denote the matrix describing the shape of the Gaussian fitness function acting on the breeding values in the population. The variance-covariance matrix of effects on the characters by combinations of alleles in the i th linkage group maintained by mutation in a randomly mating population is approximately

$$\mathbf{C}_{ii} = \mathbf{W}^{\frac{1}{2}} \sqrt{(\mathbf{W}^{-\frac{1}{2}} \mathbf{U}_i \mathbf{W}^{-\frac{1}{2}})} \mathbf{W}^{\frac{1}{2}} \quad (12)$$

(which was misprinted in formula (21*c*) of Lande, 1980*a*). The matrix square roots in (12) are taken to be positive definite.

If there are n linkage groups which each contribute an equal mutational input, u , to the variance of each character, but nothing to their covariance, then $\mathbf{U}_i = u\mathbf{I}$ for all i (where \mathbf{I} is the identity matrix), and the total genetic variance-covariance matrix of the characters can be simply approximated as $\mathbf{G} = 2nu^{\frac{1}{2}}\mathbf{W}^{\frac{1}{2}}$, ignoring linkage disequilibrium between the linkage groups. In the case of two characters, with \mathbf{W} as specified by (4*a*) and (4*b*), the genetic variance of each trait is found to be

$$2nc = n\sqrt{(u\omega^2)} [\sqrt{(1 + \tilde{\rho})} + \sqrt{(1 - \tilde{\rho})}] \quad (13a)$$

and their genetic covariance is

$$2nb = n\sqrt{(u\omega^2)} [\sqrt{(1 + \tilde{\rho})} - \sqrt{(1 - \tilde{\rho})}]. \quad (13b)$$

Squaring the bracketed quantity in (13*a*) and taking its square root confirms (10*b*). The product bc computed from these formulae agrees with (10*a*).

Maximum genetic correlation due to inbreeding. Suppose that in a large population there is a high probability of mating between closely related individuals producing an average inbreeding coefficient near unity ($f < 1$ with mutation), or that all of the loci are tightly clustered on the linkage map, $f \rightarrow 1$ or $r_{ij} \rightarrow 0$ for all $i \neq j$. Then from (8) and (6*a*) the solutions are identical to the previous case of tight linkage between pairs of loci (eqs. 10*a*, *b*, *c*). With high inbreeding or tight linkage the genetic correlation between the characters maintained at equilibrium depends only on the 'correlation' in the fitness surface acting on genotypic values ($\tilde{\rho}$).

When all of the genes are tightly linked, all n^2 pairs of loci influencing different traits contribute subequally to the genetic correlation between characters, and their average correlation is smaller in magnitude than γ/n . In this case, if the characters are polygenic ($n \gg 1$) allelic effects at each pair of loci influencing different characters are only weakly correlated although the genetic correlation between the characters may be large. It can also be shown that because the correlations between allelic effects at loci influencing the same character are all negative, their average magnitude of correlation must be less than $1/(n - 1)$ if their correlation matrix is to be positive definite (Lande, 1975). Therefore, clustering of genes influencing polygenic characters which are selected to be correlated can produce large genetic correlations between the characters, although it can not create large correlations between the effects of alleles at different loci.

For a numerical example to compare with the minimum genetic correlation achieved under free recombination and random mating, the maximum genetic correlation under tight linkage or high inbreeding with $\tilde{\rho} = 0.9$ is $\gamma = 0.627$, which is much greater than the minimum genetic correlation calculated above. With the same values of the other parameters as above, the heritability of each of the characters is $h^2 = 0.55$, which is somewhat larger than that maintained under random mating with free recombination between loci influencing different traits. Again these parameters satisfy the conditions for weak selection in (5).

Mean fitness in the population. Under random mating, or a regular system of inbreeding (Wright, 1969, ch. 7), such as where every individual mates with a sibling, the mean fitness can be calculated by assuming the characters follow a multivariate normal distribution. With a Gaussian fitness function as in equation (1), the mean fitness is

$$\bar{W} = \sqrt{(|\mathbf{W}| |\bar{\mathbf{W}} + \mathbf{G}|^{-1})} \exp \left\{ -\frac{1}{2} (\bar{y} - \theta_y, \bar{z} - \theta_z) (\bar{\mathbf{W}} + \mathbf{G})^{-1} (\bar{y} - \theta_y, \bar{z} - \theta_z)^T \right\} \quad (14a)$$

(Lande, 1979). When the mean phenotypes are at equilibrium this gives the proportionality

$$\bar{W} \propto 1/\sqrt{(|\mathbf{I} + \mathbf{G}\bar{\mathbf{W}}^{-1}|)}. \quad (14b)$$

Making use of the simplifying assumptions above for \mathbf{G} and $\bar{\mathbf{W}}$, these matrices have the same eigenvectors (with slopes $+1$ and -1), and the determinant of $\mathbf{I} + \mathbf{G}\bar{\mathbf{W}}^{-1}$ is the product of the eigenvalues,

$$1 + \frac{2nc}{\tilde{\omega}^2} \left(\frac{1+\gamma}{1+\tilde{\rho}} \right) \quad \text{and} \quad 1 + \frac{2nc}{\tilde{\omega}^2} \left(\frac{1-\gamma}{1-\tilde{\rho}} \right).$$

Under weak selection as in (5) both of these eigenvalues are close to unity and the mean fitness is proportional to approximately

$$\bar{W} \propto 1 - \frac{2nc}{\tilde{\omega}^2} \left(\frac{1-\gamma\tilde{\rho}}{1-\tilde{\rho}^2} \right). \quad (15)$$

Evidently, an increase in the genetic correlation between the characters increases the mean fitness in the population. In view of formulae (9) and (10) high inbreeding or tight linkage produces not only an increase in the magnitude of the genetic correlation between the characters, but also to a lesser extent increases the genetic variance maintained in each character. Therefore it appears that when there is selection for the characters to be highly correlated a high level of inbreeding or tight linkage between loci influencing different traits can substantially decrease the equilibrium selective load on the population, $L = 1 - \bar{W}$.

Inbreeding depression and heterosis under stabilizing selection. In a large population with a heterogeneous system of inbreeding, such as a plant species with mixed self-fertilization and random mating, the phenotype distribution of the characters can be approximated as multivariate normal within each subset of the population in which all individuals have the same inbreeding coefficient. When self-fertilization evolves polygenically, by small steps, the critical parameter controlling the direction of selection on the selfing rate is not the change in equilibrium mean fitness in the entire population, but the relative fitnesses of selfed versus outcrossed individuals in any given generation (Lloyd, 1979; Lande & Schemske, 1984).

The genetic variance-covariance matrices of the characters within the subpopulations of selfed and outcrossed individuals are written respectively as \mathbf{G}_1 and \mathbf{G}_0 , with the corresponding mean fitnesses \bar{W}_1 and \bar{W}_0 . Since all of the genetic variances and covariance of the characters are assumed to be additive each of these subpopulations has the same mean phenotype before selection, and when the mean phenotypes are at their optima, the ratio of the mean fitnesses of individuals produced by selfing and outcrossing is

$$\bar{W}_1/\bar{W}_0 = \sqrt{(|\mathbf{I} + \mathbf{G}_0 \bar{\mathbf{W}}^{-1}|/|\mathbf{I} + \mathbf{G}_1 \bar{\mathbf{W}}^{-1}|)}.$$

Under weak selection this becomes approximately

$$\bar{W}_1/\bar{W}_0 = \sqrt{(|\mathbf{I} - (\mathbf{G}_1 - \mathbf{G}_0) \bar{\mathbf{W}}^{-1}|)}.$$

However, with mixed selfing and random mating, $\mathbf{G}_1 - \mathbf{G}_0 = \mathbf{G}/2$ where \mathbf{G} is the additive genetic variance-covariance matrix of the characters in the entire population (Wright, 1969, ch. 7; Lande & Schemske, 1984). The proportional decrease in the mean fitness of selfed individuals in comparison to outcrossed individuals is a measure of inbreeding depression, which can then be approximated as in formulae (14*b*) and (15),

$$\delta = 1 - \bar{W}_1/\bar{W}_0 = \frac{nc}{\omega^2} \left(\frac{1 - \gamma\bar{\rho}}{1 - \bar{\rho}^2} \right). \quad (16)$$

Although all of the genetic variance in the characters is assumed to be additive, stabilizing selection creates dominance and epistatic variance in fitness (Wright, 1969, ch. 16). In this model, inbreeding depression in fitness results from the greater genetic variance in the characters among inbred individuals in comparison to outbred individuals, causing the inbred individuals to deviate from the joint optimum phenotype by a greater amount on average than do the outbred individuals.

Equation (16) shows that increasing the genetic correlation between the characters decreases the inbreeding depression (or heterosis) in the population as measured by δ . In view of equations (9) and (10), when there is selection for the characters to be highly correlated, the inbreeding depression upon selfing in a predominantly outcrossing population may greatly exceed the heterosis upon outcrossing in a predominantly selfing population. This contrasts with the situation in which there is no selection for the characters to be correlated ($\bar{\rho} = 0$), for which these quantities are equal.

3. DISCUSSION

For quantitative characters in a population under multivariate stabilizing selection, both the genetic and environmental components of phenotypic variation and correlation of the characters are selected to conform to the shape of the fitness surface acting on them (Schmalhausen, 1949; Waddington, 1957, 1960; Olson & Miller, 1958). Studies of variation in character complexes (other than major fitness components) usually involve sets of characters for which the genetic, environmental and phenotypic correlations tend to be similar (Bailey, 1956; Hashiguchi &

Morishima, 1969; Hegmann & DeFries, 1970; Leamy, 1977; Falconer, 1981, ch. 19). Comparative studies of variation have shown that functionally related characters, and homologous and contiguous traits, tend to be highly correlated (Darwin, 1876, pp. 346–347; Kurtén, 1953; Olson & Miller, 1958; Berg, 1960; Bader & Hall, 1960; Cheverud, 1982).

Changing regimes of selection caused by new functional constraints can alter the genetic correlation between characters either by changing the pattern of polymorphism at loci with pleiotropic effects, or by changing linkage disequilibrium between tightly linked loci. But for genes influencing quantitative characters, which usually have small effects, it is not generally possible to distinguish pleiotropy from linkage disequilibrium between tightly linked loci. Homologous and adjacent characters are genetically (and environmentally) correlated in part because they are influenced by similar processes in development, i.e. pleiotropic effects of genes.

In the absence of any selective constraint on the characters, and if there is no assortative mating involving them, a stable genetic correlation can only be attributed to pleiotropy. Homologous and contiguous characters often are functionally related, so that it is usually difficult to determine whether pleiotropic mutations are primarily responsible for the genetic correlation between traits. There are some characters with a high genetic correlation for which no special functional constraint can be postulated. For example, the high genetic correlation between homologous morphological characters in males and females of dioecious species is apparently due to pleiotropic expression of virtually the same genes influencing these traits in the two sexes (Lande, 1980*b*). Similarly, the high phenotypic correlation between the lengths of homologous bones in the wing and foot of bats, compared to that of non-homologous bones (Bader & Hall, 1960), is likely to be caused in large part by pleiotropic effects of genes in addition to an environmental correlation.

Even for homologous and contiguous characters, functional constraints are often important in maintaining high genetic and phenotypic correlations, as indicated by differences in correlation patterns among species which differ in functional relations between characters. This is especially evident in the increase in relative variability and decrease in correlation with homologous and adjacent structures shown by highly reduced characters, such as vestigial teeth (Kurtén, 1953) and reduced bones in the wing of modern bats (Bader & Hall, 1960).

In the present models genetic variability in each of the characters is maintained by mutation at multiple loci, with a wide range of possible allelic effects at each locus such that there is a constant input of new genetic variance in each character every generation. Using a polygenic mutation model of this type for a single character under stabilizing selection Lande (1977) showed that at equilibrium the genetic variance of the character is independent of the linkage map of the loci and the mating system of the population. With two characters under separate genetic control, this property appears in the present models in a more limited way: the total genetic variance and covariance of the characters do not depend on the recombination rates between loci influencing the same trait. However, when selection favors a high correlation between the characters, the genetic correlation

maintained is sensitive to the recombination rates between loci influencing different characters, and to the average inbreeding coefficient in the population.

The models demonstrate that if two characters under separate genetic control are selected to be highly correlated, in a large randomly mating population with no linkage between loci influencing different characters the genetic correlation maintained is small in magnitude. This supports the conclusion of Wright (1969, ch. 4). But tight linkage or a large average inbreeding coefficient maintains enough linkage disequilibrium to produce a large magnitude of genetic correlation between the characters, when this is favored by selection. The tighter the linkage between genes influencing different characters, and the larger the average inbreeding coefficient in the population, the more closely the genetic pattern of variation and correlation of the characters conforms to the shape of the fitness surface acting on the genotypes.

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