Evolution, 45(3), 1991, pp. 622–629

THE GENETIC INTERPRETATION OF INBREEDING DEPRESSION AND OUTBREEDING DEPRESSION

MICHAEL LYNCH
Department of Biology, University of Oregon, Eugene, OR 97403 USA

Abstract.—Inbreeding with close relatives and outbreeding with members of distant populations can both result in deleterious shifts in the means of fitness-related characters, most likely for very different reasons. Such processes often occur simultaneously and have important implications for the evolution of mating systems, dispersal strategies, and speciation. They are also relevant to the design of breeding strategies for captive populations of endangered species. A general expression is presented for the expected phenotype of an individual under the joint influence of inbreeding and crossbreeding. This expression is a simple function of the inbreeding coefficient, of source and hybridity indices of crossbreeding, and of specific forms of gene action. Application of the model may be of use in identifying the mechanistic bases for a number of evolutionary phenomena such as the shift from outbreeding enhancement to outbreeding depression that occurs with population divergence.

Key words.—Inbreeding depression, outbreeding depression.

Received April 2, 1990. Accepted August 13, 1990.

Two topics of fundamental importance to many areas in evolutionary biology are the consequences of inbreeding within populations and of outcrossing between populations. With almost no exception, empirical studies indicate that inbreeding causes a shift in mean phenotypes in a direction that causes a reduction in fitness (Wright, 1977; Shields, 1982; Charlesworth and Charlesworth, 1987; Ralls et al., 1988; Lynch, 1989). On the other hand, crossbreeding between populations often has positive effects on fitness-related traits (Darwin, 1877; Sheridan, 1981; Turton, 1981; Sprague, 1983; Levin, 1984). It is frequently argued that this response to outcrossing is simply the recovery from inbreeding depression that is expected to result from random genetic drift in isolated populations. One problem with this argument is that outcrossing does not always enhance fitness. Crosses between different species usually lead to substantial or complete inviability or infertility in the F_1 or F_2 generations (Barton and Hewitt, 1981; Templeton, 1981; Coyne and Orr, 1989), and significant outbreeding depression is sometimes observed in crosses between distant populations of the same species (Dobzhansky, 1948; Geiger, 1988; Waser and Price, 1989).

This nonlinear response to the degree of outcrossing suggests there is a fundamental change in the predominant gene interactions as mates become more and more distantly related, and has led to the suggestion that there is an optimal degree of outbreeding (Price and Waser, 1979; Shields, 1982; Bateson, 1983; Waser and Price, 1983). Dominance is generally believed to be the primary agent of inbreeding depression (Crow, 1948, 1952; Lande and Schemske, 1985; Charlesworth and Charlesworth, 1987). On the other hand, the decline in fitness under outcrossing is usually attributed to a breakup of coadapted gene complexes or favorable epistatic relationships (Mayr, 1963; Shields, 1982; Templeton, 1987). Thus, in proceding from theories of inbreeding depression to those of outbreeding depression, there is a shift in emphasis from interactions within loci to interactions between loci.

Unfortunately, this dichotomy is not so clearcut. For example, although it has received little attention from empiricists, epistasis can contribute to inbreeding depression (Kempthorne, 1957; Bulmer, 1980; Hill, 1982). Moreover, the possibility that overdominance between alleles of closely related species gradually yields to underdominance between those of distantly related species cannot be ruled out currently on theoretical or empirical grounds. To complicate matters, individuals can be simultaneously inbred within loci and crossbred between loci (Shields, 1983; Templeton and Read, 1983, 1984).

This paper is an attempt to put the concepts of inbreeding depression, outbreeding enhancement, and outbreeding depression in a unifying framework and to provide a methodological basis for evaluating the genetic bases of these phenomena. Most of the mathematical details are left out as these are developed rigorously in the seminal papers of Cockerham (1954) and Kempthorne (1954). Full credit should go to Cockerham (1980), Mather and Jinks (1982), and Hill (1982), who developed the line-cross theory from which I have drawn heavily. The major technical innovation of this paper is the development of a simple generalization that accounts for the joint operation of inbreeding and outcrossing and that allows the resultant changes in mean phenotypes to be interpreted in terms of conventional genetic concepts.

A Genetic Interpretation of Mean Phenotypes

As a point of departure, consider two parental populations (P_1 and P_2) with an arbitrary genetic distance. So that differences in mean phenotypes can be interpreted as consequences of shifts in the genetic background, these and all subsequent populations derived from them are assumed to be raised and evaluated in a common environment. Whether this is a source environment or an environment unique to both parental species, the interpretation of results from the genetic analysis should be confined to be experimental setting until the possibility of genotype × environment interaction can be ruled out. It is also assumed that the two source populations are in gametic-phase equilibrium, that the major constituent loci for the characters of interest are unlinked, and that within a class of individuals there is no variance in pedigree structure. The following theory is restricted to autosomal loci with additive, dominance, and two-locus epistatic gene action, but extension to sex-linked loci and higher level interactions is straightforward. No assumptions are made us to the number of alleles per locus.

Under the above conditions, an F_2 population (obtained by random crossing of the P_1 and P_2 and subsequently random mating within the F_1) should be in Hardy–Weinberg equilibrium both within and between loci for genes derived within and between source populations. Thus, it is logical to treat the F_2 as the reference population. Its mean phenotype is represented as μ_0, and all of the average effects of various types of gene action are defined to be zero in the F_2 background.

For crossbred populations, it is useful to define two summary coefficients that describe the genetic composition from the standpoint of the two parental sources. Let m and f represent a mother and a father, and p_m and p_f be the fractions of their autosomal genes that descended from the P_1 population. The expected fraction of P_1 genes in the offspring of m and f is then $S = (p_m + p_f)/2$. The source index $\theta_s = 2S - 1$ provides a linear scale that ranges from -1 when all of an individual's genes derive from the P_2 population to $+1$ when they all derive from the P_1 population. The probability that an individual has one P_1 gene and one P_2 gene at a locus is $H = p_m(1 - p_f) + p_f(1 - p_m)$. The hybridity index, $\theta_H = 2H - 1$, ranges from -1 when the individual contains genes from only one source to $+1$ when the individual is crossbred at every locus.

In statistical genetics, the effects of various types of gene action are defined in a hierarchical fashion, the additive effects first being extracted to account for as much of the genetic variance as possible, the dominance effects accounting for nonlinear interactions within loci and describing as much of the remaining variance as possible, the additive × additive effects coming in next, and so on (Fisher, 1918; Cockerham, 1954; Kempthorne, 1954). The focus here is on the summed effects for all loci, which will be called crossbreeding effects. These are equivalent to Hill's (1982) composite effects. Additive and dominance effects are denoted by α and δ, respectively. The number of loci involved in a particular type of effect are denoted by a numerical subscript and an × indicates that a contrast is being made between source genes. Thus, $\alpha_{1\times}$ is the mean additive crossbreeding effect, $\delta_{1\times}$ the mean dominance crossbreeding effect, and $\alpha_{2\times}$, $(\alpha_1\delta_1)_\times$, and $\delta_{2\times}$ are the mean crossbreeding effects for additive × additive, additive × dominance, and dominance ×

dominance epistasis. The magnitude of these effects is a function of the contrasts in gene frequencies and effects in the two source populations.

With this notation in hand, a general expression for the expected phenotype of any crossbred (but noninbred) individual is

$$\mu = \mu_0 + \theta_s\alpha_{1\times} + \theta_H\,\delta_{1x} + \theta_s^2\alpha_{2\times} + \theta_s\theta_H(\alpha_1\delta_1)_\times + \theta_H^2\delta_{2\times} + \cdots \quad (1)$$

Note that the coefficients for the crossbreeding effects are of the form $\theta_S^i\theta_H^j$ where i and j refer to the number of additive and dominance effects involved. For example, the term for additive × additive × dominance epistasis would be $\theta_S^2\theta_H(\alpha_2\delta_1)_\times$. Equation (1) is much easier to use than the table of coefficients and contrasts in Hill (1982) and gives the same results.

At the other extreme, we can consider a population that is potentially inbred but not crossbred. Let the random-mating population have a mean phenotype equal to μ', with all average effects being equal to zero. Inbreeding causes an increase in homozygosity, but without selection does not induce a change in gene frequencies. Thus, the average additive and additive × additive effects are not modified by inbreeding. Let f be the inbreeding coefficient, i.e., the probability that two alleles at a locus are identical by descent, and let δ_1^1 be the expected change in the mean caused by dominance effects under complete inbreeding. (The subscript 1 again indicates that single-locus effects are under consideration, while the superscript indicates the presence of inbreeding at single loci). The shift in the mean caused by dominance is then $f\delta_1^1$. For pairs of loci, the probability of joint inbreeding is f^2, whereas the probability of being inbred at one but not the other locus is $2f(1-f)$. Both situations can cause a shift in the mean through their influence on the average dominance × dominance effect—$f^2\,\delta_2^2$ in the first case, $2f(1-f)\delta_2^1$ in the second. (The superscript on δ again denotes the number of interacting loci that are inbred.) Finally, the average additive × dominance effect is altered under inbreeding by an amount $f(\alpha_1\delta_1)^1$.

Summing up terms, the mean phenotype of an inbred population can be written

$$\mu = \mu' + f[\delta_1^1 + 2\,\delta_2^1 + (\alpha_1\delta_1)^1] + f^2(\delta_2^2 - 2\delta_2^1) \quad (2a)$$

which abbreviates to

$$\mu = \mu' + f\,\delta_1 + f^2\delta_2 + \cdots \quad (2b)$$

(Anderson and Kempthorne, 1954; Bulmer, 1980). This shows that dominance, additive × dominance, and dominance × dominance effects can all contribute to inbreeding depression, although these effects are not entirely separable. Thus, the mean is a simple quadratic function of the inbreeding coefficient (assuming higher order epistatic effects are of negligible importance), where δ_1 and δ_2 represent the composite linear and quadratic effects of inbreeding.

Finally, we consider the joint consequences of crossbreeding and inbreeding. This introduces the need to discriminate between the probability of identity by descent of alleles through parental populations 1 and 2. We let these probabilities be f_1 and f_2, respectively, where $f_1 + f_2 \leq 1$ is the total inbreeding coefficient. The two composite inbreeding effects for population k are denoted $\delta_{1(k)}$ and $\delta_{2(k)}$.

Five additional crossbreeding terms also arise. For the additive × dominance effects, we must account for the possibility that the two alleles at one locus are identical by descent through population 1 or 2 while a random gene at a second locus is from the opposite population. The sums of these effects for all gene combinations are denoted $(\alpha_1\delta_1)_{(1)}$ and $(\alpha_1\delta_1)_{(2)}$, respectively. For the dominance × dominance effects, we account for the possibility that either or both loci are inbred by the terms $\delta_{2\times(1)}$, $\delta_{2\times(2)}$, and $\delta_{2\times(1,2)}$.

Weighting these five types of interactions by their probabilities of occurrence and including the inbreeding terms, Equation (1) generalizes to

$$\begin{aligned}\mu = \mu_0 &+ \theta_S\alpha_{1\times} + (\theta_H\delta_{1\times} + f_1\delta_{11} + f_1\delta_{12}) \\ &+ \theta_S^2\alpha_{2\times} \\ &+ [\theta_S\theta_H(\alpha_1\delta_1)_\times + (1-\theta_S) \\ &\quad \cdot f_1(\alpha_1\delta_1)_{(1)} + (1+\theta_S)f_2(\alpha_1\delta_1)_{(2)}] \\ &+ \Bigg[\theta_H^2\delta_{2\times} + f_1^2\delta_{21} + f_2^2\delta_{22} \\ &\quad + \frac{\theta_H+1}{2}(f_1\delta_{2\times(1)} + f_2\delta_{2\times(2)}) \\ &\quad + 2f_1f_2\delta_{2\times(1,2)}\Bigg] + \cdots \end{aligned} \quad (3)$$

TABLE 1. Coefficients for the line mean components in Equation (3) under various types of mating. For the cases with inbreeding, it is assumed that no inbreeding has occurred prior to the specified mating.

Relationship	θ_S	θ_H	f_1	f_2
Outcrossing, no inbreeding				
P_1	1	−1	0	0
P_2	−1	−1	0	0
F_1	0	1	0	0
F_n ($n \geq 2$)	0	0	0	0
B_1	1/2	0	0	0
B_2	−1/2	0	0	0
Outcrossing, inbreeding				
P_1 parent × F_1 offspring	1/2	0	1/4	0
P_2 parent × F_1 offspring	−1/2	0	0	1/4
F_1 parent × F_2 offspring	0	0	1/8	1/8
F_n full-sib mating ($n \geq 1$)	0	0	1/8	1/8
B_1 full-sib mating	1/2	−1/4	3/16	1/16
B_2 full-sib mating	−1/2	−1/4	1/16	3/16
F_n selfing ($n \geq 1$)	0	$(1/2)^{n-1} - 1$	$[1 - (1/2)^n]/2$	$[1 - (1/2)^n]/2$
B_1 selfing	1/2	−1/2	3/8	1/8
B_2 selfing	−1/2	−1/2	1/8	3/8
P_1 uncle × F_1 niece	1/2	0	1/8	0
P_2 uncle × F_1 niece	−1/2	0	0	1/8
F_1 uncle × F_2 niece	0	0	1/16	1/16
F_2 first cousins	0	0	1/32	1/32
F_3 second cousins	0	0	1/128	1/128
Inbreeding, no outcrossing (source population 1)				
Parent × offspring	1	−1	1/4	0
Full-sib mating	1	−1	1/4	0
Selfing	1	−1	1/2	0
Uncle–niece	1	−1	1/8	0
First cousins	1	−1	1/16	0
Second cousins	1	−1	1/64	0

This formula gives the expected mean phenotype of a cohort of individuals with properties θ_s, θ_H, f_1, and f_2. Individual phenotypes will deviate from this expectation as a consequence of segregation and environmental effects. Table 1 summarizes the coefficients for progeny derived from several types of outcrossing and inbreeding.

DISCUSSION

The inbreeding and crossbreeding effects defined above can provide some insight into the genetic basis of interdemic differentiation and the mechanisms responsible for the phenotypic response to inbreeding and outbreeding. Consider, for example, the crosses between two populations (without inbreeding, and ignoring epistasis involving more than pairs of loci). From Table 1, the expected phenotypes for the midparent (mean of P_1 and P_2), F_1, and F_2 individuals are $\mu_0 - \delta_{1\times} + \alpha_{2\times} + \delta_{2\times}$, $\mu_0 + \delta_{1\times} + \delta_{2\times}$, and μ_0, respectively. Thus, outcrossing enhancement in the F_1 can be caused by dominance of favorable genes isolated in the two parental populations ($\delta_{1\times} > 0$), or by the existence of favorable additive × additive epistatic interactions between genes from different sources ($\alpha_{2\times} < 0$), or both. (It may be a bit bothersome that positive $\alpha_{2\times}$ implies a breakdown of coadapted gene complexes on outcrossing, but it should be kept in mind that the coefficient θ_S^2 approaches a maximum value of 1 as a population becomes more purebred.) Generally, it is believed that isolated populations evolve coadapted complexes of genes with favorable epistatic effects ($\alpha_{2\times} > 0$). If so, then the loss of favorable additive × additive epistasis would have to exceed twice the benefit from the between-population dominance ($\alpha_{2\times} < 2\delta_{1\times}$) for the F_1 population to exhibit a decline in fitness relative to the midparent value. Since F_2 individuals have only half the between-source heterozygosity as F_1 individuals, a further decline in per-

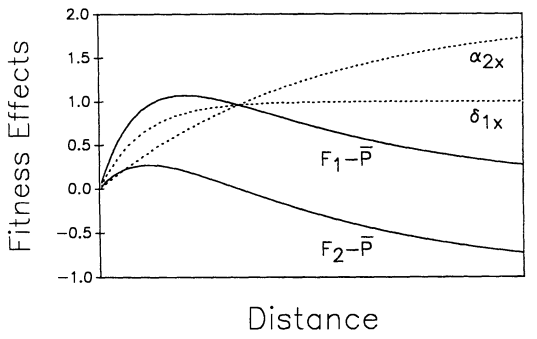

FIG. 1. A hypothetical example in which dominance and additive × additive crossbreeding effects increase hyperbolically with geographic distance between mates. The consequences for mean fitness in F_1 and F_2 descendents relative to mean fitness in the mates are evaluated by use of Equation (1), such that the $F_1 - \bar{P}$ difference is $2\sigma_{1x} - \alpha_{2x}$ and the $F_2 - \bar{P}$ difference is $\delta_{1x} - \alpha_{2x}$.

formance is expected in the F_2 generation unless there is highly favorable between-source dominance × dominance epistasis ($\delta_{2x} < -\delta_{1x}$).

Most studies of the consequences of outcrossing have confined the analysis to the F_1 generation. Figure 1 illustrates some of the difficulties with that approach. In this simple hypothetical example, additive × additive interactions are assumed to be the only epistatic effects. Dominance of favorable genes (δ_{1x}) increases rapidly to a maximum with physical distance between mates. The break-up of coadapted gene complexes (α_{2x}) has consequences that build up more slowly with distance, but eventually they become more substantial than the advantages of dominance. However, since α_{2x} is always less than $2\delta_{1x}$, F_1 progeny of distant parents always have enhanced fitness relative to progeny of contiguous parents. Although there is an optimal outcrossing distance, this is not transmitted to the next generation. Due to the loss of favorable epistasis, there is only a slight enhancement of fitness for F_2 progeny derived from parents separated by a relatively short distance, and for all greater distances F_2 progeny actually have depressed fitness relative to the native population. Thus, the advantages of outcrossing revealed in the F_1 individuals can be completely reversed in the following generation.

As emphasized by Templeton and Read (1984), there are many practical situations in which inbreeding and crossbreeding occur simultaneously. This can cause problems, for example, in captive breeding programs involving individuals of mixed ancestry when one is attempting to evaluate whether an observed decline in fitness is caused by initial outcrossing of individuals from different subpopulations, subsequent inbreeding, or both. To separate these factors, Templeton and Read (1984) developed a model in which the two determinants of an individual's fitness were its inbreeding coefficient and the hybridity of its *parents*. Inbreeding depression was taken to be a linear function of f. Such treatment ignores the potential contribution of epistasis to inbreeding depression, but may be adequate since in most cases the regression of mean phenotype on f is very close to linear (Lynch and Walsh, in prep). However, Templeton and Read's (1984) treatment of cross-population epistasis is less satisfactory. First, such effects are not simply linear functions of hybridity. Depending on the nature of the epistatic interaction, they depend on θ_S^2, $\theta_S\theta_H$, and/or θ_H^2. Second, although the additive × dominance and dominance × dominance effects depend on an *individual's* hybridity, none of the effects is a consequence of the hybridity of its *parents*.

The full model given by Equation (3) indicates that a genetic interpretation of the joint influence of inbreeding and outcrossing on phenotypic expression is quite complex if there is any epistasis. Since Equation (3) contains 15 unknowns, individuals with at least 15 types of ancestry need to be evaluated in order to obtain the complete set of parameter estimates. The situation is rendered even more complex when one considers that the inbreeding effects are actually linear functions of several more fundamental composite effects, as shown above for δ_1 and δ_2 and further discussed by Cockerham (1980). It should also be kept in mind that Equation (3) applies to ideal experimental populations consisting of individuals with identical pedigree structure. Natural and/or captive populations will usually consist of individuals that vary with respect to θ_S, θ_H, and/or f, and that may also be hybrid with

respect to more than two parental sources. This can only further complicate the genetic interpretation of crossbred/inbred performance.

For experimental situations in which the number of equations is exactly equal to the number of unknowns, estimates of the parameters for Equation (3) can be obtained by the solution of the set of simultaneous equations. This, however, constrains the predicted line means to equal the observed means so the goodness-of-fit of the model cannot be evaluated. Significance testing requires that there be more classes of individuals than unknowns. If this can be accomplished, the entire set of data can be subjected to weighted least-squares analysis (Cavalli, 1952; Hayman, 1960) or to more recent estimation procedures (Henderson, 1984; Kennedy and Sorensen, 1988; Gianola et al., 1986). Exploratory analyses with these procedures can be used to eliminate nonsignificant terms from the full model. There may also be situations in which the general model can be reduced on biological grounds. For example, if it is known in advance that the response to inbreeding is linear and not significantly different between two parental populations, then the two linear inbreeding effects ($\delta_{1(1)}$ and $\delta_{1(2)}$) can be set equal to each other, and the quadratic inbreeding effects ($\delta_{2(1)}$ and $\delta_{2(2)}$) set equal to zero.

As noted above, the model provides a potential tool for interpreting the phenotypic consequences of crossing populations that have been isolated for different periods of time or that are located at various positions across a landscape. A comparison of the composite effects within and between source populations may be useful in evaluating whether there is a fundamental change in the ways genes interact as they diverge in evolutionary time. For example, if deleterious genes are unconditionally recessive, either partially or entirely, then $\delta_{1\times}$, $\delta_{1(1)}$, and $\delta_{1(2)}$ should all be positive regardless of the evolutionary distance between hybridizing populations or species. Such an analysis would require that the appropriate crosses be carried out between demes at various points along the temporal or ecological gradient, which would be a lot of work.

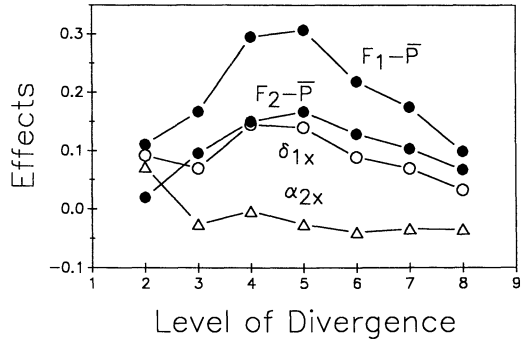

FIG. 2. Heterosis of grain yield (difference between F_1 and midparent means) in various crosses of maize grown in a common environment. The hypothesized dominance and additive × additive composite effects were computed as described in the text. The data from each of the seven experiments were standardized to have F_2 means equal to one. Data from Moll et al. (1965). Note that $F_1 - \bar{P} = 2\delta_{1\times} - \alpha_{2\times}$.

However, if the primary interest is in the consequences of interdemic crosses, inbreeding generations do not need to be carried out, as seen in the following example.

Moll et al. (1965) produced F_1 and F_2 generations from crosses between several pairs of maize populations with varying degrees of genetic divergence "based on ancestral relationships and differences in adaptation." All crosses exhibited F_1 hybrid superiority with respect to grain yield, but this was most pronounced in crosses involving populations with intermediate levels of divergence (Fig. 2). As a possible interpretation of this pattern, suppose that all forms of epistasis except additive × additive are of negligible importance, as in Figure 1. The expected midparent, F_1, and F_2 generation mean phenotypes can then be represented as $\mu_0 - \delta_{1\times} + \alpha_{2\times}$, $\mu_0 + \delta_{1\times}$, and μ_0. Substituting the observed means (represented by $\bar{z}$) for their expected values, the dominance and additive × additive crossbreeding effects can then be estimated with the linear functions

$$\hat{\delta}_{1\times} = \bar{z}(F_1) - \bar{z}(F_2)$$
$$\hat{\alpha}_{2\times} = \bar{z}(F_1) - 2\bar{z}(F_2) + \bar{z}(\bar{P})$$

The solutions are plotted in the figure. Assuming the genetic model is correct, it appears that the net dominance effects between the two parental lines have a favorable

influence on grain yield at all levels of genetic divergence but that the magnitude of this effect is maximized at an intermediate genetic distance. Except at the lowest level of divergence, $\alpha_{2\times}$ is negative. This suggests that pairs of (nonallelic) genes from distant populations have favorable epistatic effects on grain yield, contrary to the expectation that local populations harbor coadapted gene complexes.

To further evaluate the adequacy of this genetic interpretation, additional generation means (such as backcrosses) would have to be available so that the significance of the model and of other composite effects could be determined. The standard errors of the composite effect estimates can be computed from linear functions of the sampling variances of the means. For example, for the preceding equations, $SE(\hat{\delta}_{1\times}) = \{Var[\bar{z}(F_1)] + Var[\bar{z}(F_2)]\}^{1/2}$ and $SE(\hat{\alpha}_{2\times}) = \{Var[\bar{z}(F_1)] + 4Var[\bar{z}(F_2)] + Var(\bar{P})\}^{1/2}$.

If this type of analysis were extended to multiple environments, it would be possible to evaluate how the crossbreeding effects can be modified by a change in the environmental background. It is well known that the magnitude of inbreeding depression and outbreeding enhancement depends on habitat quality (Barlow, 1981; Levin and Bulinska-Radomska, 1988; Schmitt and Ehrhardt, 1990), but little is known about the genetic basis of such environmental dependence.

Finally, it should be recalled that the model presented above is derived under the assumption of negligible linkage. The results still hold in the presence of linkage provided there are no significant epistatic effects. However, in the presence of epistasis, the coefficients of the epistatic effects need to be increased to account for the fact that pairs of genes that are linked in the parental lines will tend to stay associated (in excess of expectations under free recombination). The matter is complicated by the fact that the correction factor declines with each generation of recombination and varies between pairs of loci (Mather and Jinks, 1982). However, for species with large numbers of chromosomes, most pairs of segregating loci will be on different chromosomes, so the problem of linkage may be of minor importance.

Acknowledgments

This work has been supported by NSF Grant BSR 86-00487 and PHS Grant R01 GM36827-01. Very useful comments were provided by Clark Cockerham, who in reviewing this paper pointed out the existence of his 1980 paper, which seems not to have received the attention that it deserves.

Literature Cited

Anderson, V. L., and O. Kempthorne. 1954. A model for the study of quantitative inheritance. Genetics 39:883–898.

Barlow, R. 1981. Experimental evidence for interaction between heterosis and environment in animals. Anim. Breeding Abst. 49:715–737.

Barton, N. H., and G. M. Hewitt. 1981. Hybrid zones and speciation, pp. 109–145. *In* W. R. Atchley and D. S. Woodruff (eds.), Evolution and Speciation. Essays in Honor of M. J. D. White. Cambridge Univ. Press, Cambridge, U.K.

Bateson, P. 1983. Mate Choice. Cambridge Univ. Press, Cambridge, U.K.

Bulmer, M. G. 1980. The Mathematical Theory of Quantitative Genetics. Oxford Univ. Press, N.Y.

Cavalli, L. L. 1952. An analysis of linkage in quantitative inheritance, pp. 135–144. *In* E. C. R. Reeve and C. H. Waddington (eds.), Quantitative Inheritance. His Majesty's Stationary Office, London, U.K.

Charlesworth, D., and B. Charlesworth. 1987. Inbreeding depression and its evolutionary consequences. Annu. Rev. Ecol. Syst. 18:237–268.

Cockerham, C. C. 1954. An extension of the concept of partitioning hereditary variance for analysis of covariances among relatives when epistasis is present. Genetics 39:859–882.

———. 1980. Random and fixed effects in plant genetics. Theor. Appl. Genetics 56:119–131.

Coyne, J. A., and H. A. Orr. 1989. Patterns of speciation in *Drosophila.* Evolution 43:362–381.

Crow, J. F. 1948. Alternative hypotheses of hybrid vigor. Genetics 33:477–487.

———. 1952. Dominance and overdominance, pp. 282–297. *In* J. E. Gowen (ed.), Heterosis. Iowa State College Press, Ames, IA.

Darwin, C. 1876. The Effects of Cross and Self-Fertilization in the Vegetable Kingdom. Appleton, N.Y.

Dobzhansky, T. 1948. Genetics of natural populations. XVIII. Experiments on chromosomes of *Drosophila pseudoobscura* from different geographical regions. Genetics 33:588–602.

Fisher, R. A. 1918. The correlation between relatives on the supposition of Mendelian inheritance. Trans. Royal Soc. Edinburgh 52:399–433.

Geiger, H. H. 1988. Epistasis and heterosis, pp. 395–399. *In* B. S. Weir, E. J. Eisen, M. M. Goodman, and G. Namkoong (eds.), Proceedings of the Second International Conference on Quantitative Genetics. Sinauer Associates, Sunderland, MA.

Gianola, D., J. L. Foulley, and R. L. Fernando. 1986. Prediction of breeding values when variances are not known. Génét. Sél. Evol. 18:485–498.

HAYMAN, B. I. 1960. The separation of epistatic from additive and dominance variation in generation means. Genetica 31:371–390.

HENDERSON, C. R. 1984. Applications of Linear Models in Animal Breeding. Univ. Guelph Press, Guelph.

HILL, W. G. 1982. Dominance and epistasis as components of heterosis. Z. Tierz. Züchtungsbiol. 99: 161–168.

KEMPTHORNE, O. 1954. The correlation between relatives in a random mating population. Proc. R. Soc. London Ser. B 143:103–113.

———. 1957. An Introduction to Genetic Statistics. Wiley, NY.

KENNEDY, B. W., AND D. A. SORENSEN. 1988. Properties of mixed-model methods for prediction of genetic merit, pp. 91–103. *In* B. S. Weir, E. J. Eisen, M. M. Goodman, and G. Namkoong (eds.), Proceedings of the Second International Conference on Quantitative Genetics. Sinauer Associates, Sunderland, MA.

LANDE, R., AND D. W. SCHEMSKE. 1985. The evolution of self-fertilization and inbreeding depression in plants. I. Genetic models. Evolution 39:24–40.

LEVIN, D. A. 1984. Inbreeding depression and proximity-dependent crossing success in *Phlox drummondii*. Evolution 38:116–127.

LEVIN, D. A., AND Z. BULINSKA-RADOMSKA. 1988. Effects of hybridization and inbreeding on fitness in *Phlox*. Am. J. Bot. 76:1632–1639.

LYNCH, M. 1989. Design and analysis of experiments on random drift and inbreeding depression. Genetics 120:791–807.

MATHER, K., AND J. L. JINKS. 1982. Biometrical Genetics, 3rd ed. Chapman and Hall, N.Y.

MAYR, E. 1963. Animal Species and Evolution. Belknap Press, Cambridge, MA.

MOLL, R. H., J. H. LONNQUIST, J. V. FORTUNO, AND E. C. JOHNSON. 1965. The relationship of heterosis and genetic divergence in maize. Genetics 52: 139–144.

PRICE, M. V., AND N. M. WASER. 1979. Pollen dispersal and optimal outcrossing in *Delphinium nelsoni*. Nature (London) 277:294–297.

RALLS, K., J. D. BALLOU, AND A. TEMPLETON. 1988. Estimates of lethal equivalents and cost of inbreeding in mammals. Conserv. Biol. 2:185–193.

SCHMITT, J., AND D. W. EHRHARDT. 1990. Enhancement of inbreeding depression by dominance and suppression in *Impatiens capensis*. Evolution 44: 269–278.

SHERIDAN, A. K. 1981. Crossbreeding and heterosis. Anim. Breeding Abst. 49:131–144.

SHIELDS, W. M. 1982. Philopatry, Inbreeding, and the Evolution of Sex. State Univ. of New York Press, Albany, N.Y.

———. 1983. Genetic considerations in the management of the wolf and other large vertebrates: An alternative view, pp. 90–92. *In* L. Carbyn (ed.), Wolves in Canada and Alaska: Their Status, Biology, and Management. Can. Wildlife Serv. Publ. No. 45, Edmunton, Alberta.

SPRAGUE, G. F. 1983. Heterosis in maize: Theory and practice, pp. 47–70. *In* R. Frankel (ed.), Heterosis. Monog. Theor. Appl. Genetics 6. Springer-Verlag, Berlin.

TEMPLETON, A. R. 1981. Mechanisms of speciation—a population genetic approach Annu. Rev. Ecol. Syst. 12:23–48.

———. 1987. Inferences on natural population structure from genetic studies on captive mammalian populations, pp. 257–272. *In* B. D. Chepko-Sade and Z. T. Halpin (eds.), Mammalian Dispersal Patterns. Univ. Chicago Press, Chicago, IL.

TEMPLETON, A. R., AND B. READ. 1983. The elimination of inbreeding depression in a captive herd of Speke's gazelle, pp. 241–261. *In* C. M. Schonewald-Cox, S. M. Chambers, B. MacBryde, and L. Thomas (eds.), Genetics and Conservation: A Reference for Managing Wild Animal and Plant Populations. Benjamin/Cummings, Menlo Park, CA.

———. 1984. Factors eliminating inbreeding depression in a captive herd of Speke's gazelle. Zoo Biol. 3:177–199.

TURTON, J. D. 1981. Crossbreeding of dairy cattle—a selective review. Anim. Breeding Abst. 49:293–300.

WASER, N. M., AND M. V. PRICE. 1983. Optimal and actual outcrossing in plants, and the nature of plant-pollinator interaction, pp. 341–359. *In* C. E. Jones and R. J. Little (eds.), Handbook of Experimental Pollination Biology.

———. 1989. Optimal outcrossing in *Ipomopsis aggregata*: Seed set and offspring fitness. Evolution 43:1097–1109.

WRIGHT, S. 1977. Evolution and the Genetics of Populations, Vol. 3. Experimental Results and Evolutionary Deductions. Univ. Chicago Press, Chicago, IL.

Corresponding Editor: T. Mackay