The Effect of Neutral Nonadditive Gene Action on the Quantitative Index of Population Divergence

Carlos López-Fanjul,*,[1] Almudena Fernández† and Miguel A. Toro†

Departamento de Genética, Facultad de Ciencias Biológicas, Universidad Complutense, 28040 Madrid, Spain and †Departamento de Mejora Genética Animal, SGIT-INIA, 28040 Madrid, Spain

Manuscript received July 17, 2002
Accepted for publication April 10, 2003

ABSTRACT

For neutral additive genes, the quantitative index of population divergence (Q_{ST}) is equivalent to Wright's fixation index (F_{ST}). Thus, divergent or convergent selection is usually invoked, respectively, as a cause of the observed increase ($Q_{ST} > F_{ST}$) or decrease ($Q_{ST} < F_{ST}$) of Q_{ST} from its neutral expectation ($Q_{ST} = F_{ST}$). However, neutral nonadditive gene action can mimic the additive expectations under selection. We have studied theoretically the effect of consecutive population bottlenecks on the difference $F_{ST} - Q_{ST}$ for two neutral biallelic epistatic loci, covering all types of marginal gene action. With simple dominance, $Q_{ST} < F_{ST}$ for only low to moderate frequencies of the recessive alleles; otherwise, $Q_{ST} > F_{ST}$. Additional epistasis extends the condition $Q_{ST} < F_{ST}$ to a broader range of frequencies. Irrespective of the type of nonadditive action, $Q_{ST} < F_{ST}$ generally implies an increase of both the within-line additive variance after bottlenecks over its ancestral value (V_A) and the between-line variance over its additive expectation ($2F_{ST}V_A$). Thus, both the redistribution of the genetic variance after bottlenecks and the $F_{ST} - Q_{ST}$ value are governed largely by the marginal properties of single loci. The results indicate that the use of the $F_{ST} - Q_{ST}$ criterion to investigate the relative importance of drift and selection in population differentiation should be restricted to pure additive traits.

ASSESSING the relative contributions of natural selection and genetic drift to population differentiation for quantitative traits is an important issue, in both evolutionary and conservation genetics (Wright 1978; Endler 1986). In the absence of selection, inbreeding affects all genes to the same average degree, and the effect of the breeding structure on population divergence can be described by Wright's among-population fixation index F_{ST}. In parallel, a dimensionless measure of the quantitative genetic variance among populations (termed Q_{ST} by Spitze 1993) can be defined as $Q_{ST} = V_b/(V_b + 2V_w)$, where V_b and V_w are, respectively, the between- and the additive within-population components of the genetic variance for the trait considered. For neutral genes, with additive action between and within loci, it is expected that $V_b = 2F_{ST}V_A$ and $V_w = (1 - F_{ST})V_A$, where V_A is the ancestral additive genetic variance (Wright 1951). In this situation, Q_{ST} is the neutral quantitative analog of F_{ST}. This result holds quite generally, regardless of the model of population structure (Whitlock 1999). The computation of the expected divergence of population means due to drift requires the estimation of generally unknown parameters, such as the rate of mutation, the time since divergence, and the effective population size (Lande 1977). However, for a given set of populations, an F_{ST} estimate can be obtained from marker loci, assumed to be neutral, and it can be used as the null expectation that can be compared to the corresponding Q_{ST} estimate for a quantitative trait, assumed to be additive. Thus, divergent or convergent selection may be invoked, respectively, as a cause of the observed increase ($Q_{ST} > F_{ST}$) or decrease ($Q_{ST} < F_{ST}$) of Q_{ST} from its neutral expectation ($Q_{ST} = F_{ST}$).

Experimentally, this approach has been used in many studies (see Merilä and Crnokrak 2001 and McKay and Latta 2002 for reviews). In most instances, the errors in the estimation of F_{ST} and Q_{ST} were large, resulting in nonsignificant pairwise comparisons of these estimates. Nevertheless, a meta-analysis carried out by Merilä and Crnokrak (2001) indicated that Q_{ST} was generally larger than F_{ST}, and this result was interpreted in the sense that a considerable part of the observed population divergence for quantitative traits should be attributed to differential selection pressures imposed by local environmental conditions.

Notwithstanding, the correspondence between Q_{ST} and F_{ST} depends crucially on the assumption of pure additive gene action. This may not be an important restriction to the study of morphological traits, typically showing substantial additive genetic variation and little or no inbreeding depression, but will markedly affect that of life-history traits, usually exhibiting larger levels of nonadditive variance and, correspondingly, higher inbreeding depression (Crnokrak and Roff 1995; DeRose and Roff 1999). In the absence of selection, it has been

[1]*Corresponding author:* Departamento de Genética, Facultad de Ciencias Biológicas, Universidad Complutense, 28040 Madrid, Spain. E-mail: clfanjul@bio.ucm.es

shown theoretically that inbreeding can change the magnitude of the contribution of dominant and/or epistatic loci to the values of V_b and V_w, relative to their additive expectations (Robertson 1952; Goodnight 1988; Willis and Orr 1993; Cheverud and Routman 1996; López-Fanjul *et al.* 1999, 2000, 2002). In parallel, increases of the additive variance with inbreeding have been reported for viability in *Drosophila melanogaster* (López-Fanjul and Villaverde 1989; García *et al.* 1994) and *Tribolium castaneum* (Fernández *et al.* 1995) and for morphological and behavioral traits in the housefly (reviewed by Meffert 2000). Thus, nonadditive gene action can potentially modify the expected additive relationship between F_{ST} and Q_{ST}.

In this article, we have investigated theoretically the effect of successive population bottlenecks on the difference $F_{ST} - Q_{ST}$ for two-locus neutral epistatic systems, covering all possible types of marginal gene action at the single-locus level (excluding overdominance). Our approach follows that of Robertson (1952), where the expected values of the derived within-line additive variance and the between-line variance, after consecutive bottlenecks of size N, are obtained from the expressions giving the corresponding ancestral values in an infinite population at equilibrium and the moments of the allele frequency distribution in populations of size N with binomial sampling. Explicit equations in terms of the genetic effects and allele frequencies derived by López-Fanjul *et al.* (2002) have been used, allowing the specification of the necessary conditions to observe a departure of Q_{ST} from the pertinent F_{ST} value.

THE MODEL

We consider the model developed by López-Fanjul *et al.* (2002), where the variation is due to segregation at two neutral independent loci ($i = 1, 2$) at Hardy-Weinberg equilibrium. At each locus there are two alleles, with frequencies p_i and q_i ($=1 - p_i$). Both loci have equal homozygous effect ($s/2$), showing any degree of dominance in the absence of epistasis ($h_i = 0, ½$, or 1 for complete recessive, additive, or complete dominance action, respectively). This basic gene action can be viewed as that shown by single loci segregating against a fixed genetic background. Epistasis has been imposed on that basic system, and it is represented by a factor k affecting the genotypic value of the double homozygote for the negative allele at each locus ($k < 2$, $k > 2$, or $k = 2$ for diminishing, reinforcing, or no epistasis, respectively). A full specification of the genotypic values is given in Table 1. At the ith locus, the marginal average effect of gene substitution (α_i), the marginal genotypic value of the heterozygote (δ_i, expressed as deviation from the midhomozygote value), and the marginal degree of dominance (γ_i) are given by

TABLE 1

Genotypic values for the neutral two-locus epistatic system

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	1	$1 - sh_1$	$1 - s$
B_1B_2	$1 - sh_2$	$1 - s(h_1 + h_2)$	$1 - s(1 + h_2)$
B_2B_2	$1 - s$	$1 - s(1 + h_1)$	$1 - ks$

$s/2$ ($s > 0$) and h_i ($0 \le h_i \le 1$) are, respectively, the basic homozygous effect at each locus and the basic coefficient of dominance at the ith locus, and k ($k \neq 2$) is the epistatic factor.

$$\alpha_i = s[h_i + (1 - 2h_i)q_i + (k - 2)q_iq_j^2], \quad (1)$$

$$\delta_i = s[(1 - 2h_i) + (k - 2)q_j^2]/2, \quad (2)$$

$$\gamma_i = h_i/[1 + (k - 2)q_j^2]. \quad (3)$$

Thus, epistasis ($k \neq 2$) modifies the basic properties of single loci, as α_i, δ_i, and γ_i become dependent on the allelic frequencies at the other locus (q_j); *i.e.*, they are contingent on the genetic background. For a given k value, the basic (h_i) and the marginal (γ_i) degrees of dominance become closer to each other as q_j decreases. On the other hand, γ_i approaches zero (complete recessivity) as k and q_j increase.

In an infinitely large panmictic population, expressions for the mean (ancestral mean M) and the additive component of the genetic variance (ancestral additive variance V_A) can be obtained from Table 1, as

$$M = 1 - 2s\Sigma h_iq_i - s\Sigma(1 - 2h_i)q_i^2 + (k - 2)q_1^2q_2^2, \quad (4)$$

$$V_A = \Sigma\alpha_i^2H_i, \quad (5)$$

where H_i is the ancestral heterozygosity at the ith locus ($H_i = 2p_iq_i$). These expressions are polynomial functions of p_i^m ($i = 1, 2$; $m = 1$–4) and their expected values at equilibrium, after t consecutive bottlenecks of N randomly sampled parents each (derived mean M_t^* and additive variance V_{At}^*), can readily be deduced by substituting p_i^m in Equations 4 and 5 by the corresponding exact mth moment of the allelic frequency distribution with binomial sampling, given by Crow and Kimura (1970, p. 335). In parallel, the between-line variance $V(M_t)$ after t consecutive bottlenecks can be derived by taking variances in Equation 4, the resulting expression being also a function of the first four moments of the allelic frequency distribution at each locus. As these moments can also be written in terms of the inbreeding coefficient after t generations (F_t), expressions for M_t^*, V_{At}^*, and $V(M_t)$ also apply when bottleneck sizes are not constant from generation to generation. Those expressions (given by López-Fanjul *et al.* 2002) are analytically unmanageable, but numerical solutions can be calculated for any combination of allele frequencies, as well as the corresponding value of the quantitative index of population divergence $Q_t = V(M_t)/(V(M_t) + 2V_{At}^*)$ (see next section). In the following, the notations F_t, Q_t,

$V(M_t)$, and V_{At}* are kept for the two-locus system and the subdivided population studied, but F_{ST}, Q_{ST}, V_b, and V_w are used, respectively, with reference to the whole set of loci affecting a metric trait and the relevant population structure.

It can be shown (López-Fanjul *et al.* 2002) that the change in mean after t bottlenecks is always negative for basic recessive gene action (complete or incomplete, $0 \leq h_i < \frac{1}{2}$) and reinforcing epistasis ($k > 2$) or no epistasis ($k = 2$). Nevertheless, diminishing epistasis ($k < 2$) and/or basic dominance (incomplete or complete, $\frac{1}{2} < h_i \leq 1$) result in an unrealistic enhancement of the mean with inbreeding and, therefore, they are not considered further.

For pure additive action it is expected that $Q_t = F_t$, as $V_{At}^* = (1 - F_t)V_A$ and $V(M_t) = 2F_tV_A$ (Wright 1951). For additive-by-additive epistasis, $Q_t < F_t$ for $F_t < 1$ (Whitlock 1999) as $V_{At}^* = (1 - F_t)V_A + 4F_t(1 - F_t)V_{AA}$ and $V(M_t) = 2F_tV_A + 4F_t^2V_{AA}$, where V_{AA} is the additive-by-additive variance component (Goodnight 1988). With dominance (with or without epistasis) equations giving V_{At}^* and $V(M_t)$ cannot be written in terms of summary statistics, as in the previous cases, but as complex functions of the allele frequencies and effects at each locus and the pertinent epistatic factor (Robertson 1952; Willis and Orr 1993; López-Fanjul *et al.* 1999, 2000, 2002). However, for nonepistatic complete recessive action ($h_i = 0$, $k = 2$), some further insight on the redistribution of the genetic variance induced by bottlenecks and, consequently, on the relationship between Q_t and F_t, can be achieved as follows.

In general, from Equation 5, the expected additive variance after bottlenecks can be given as

$$V_{At}^* = \Sigma\ \mathrm{cov}(\alpha_i^2, H_i) + \Sigma E(H_i)E(\alpha_i^2)$$
$$= \Sigma\ \mathrm{cov}(\alpha_i^2, H_i) + (1 - F_t)\Sigma H_i(V(\alpha_i) + \alpha_{it}^{*2}) \quad (6)$$

(López-Fanjul *et al.* 2002), where $E(H_i) = (1 - F_t)H_i$, and α_{it}* and $V(\alpha_i)$ are, respectively, the derived marginal average effect of gene substitution at the ith locus after t bottlenecks and its variance, which can be deduced by taking expectations or variances, respectively, in Equation 1. Equation 6 shows that any excess of V_{At}^* over its ancestral value can be assigned to the spatial and temporal changes in α_i (represented by $V(\alpha_i)$ and α_{it}*, respectively), which are both induced by drift, as well as to the covariance term, which depends on the ancestral properties of dominant loci [$\Sigma\ \mathrm{cov}(\alpha_i^2, H_i) = 0$ for pure additive or additive-by-additive gene action]. Of course, dominance may be basic ($0 \leq h_i < \frac{1}{2}$) or marginal ($h_i = \frac{1}{2}$, $k > 2$). For nonepistatic complete recessives ($h_i = 0$, $k = 2$), $\alpha_{it}^* = \alpha_i$, $V(\alpha_i) = F_ts^2H_i/2$, and $\Sigma\ \mathrm{cov}(\alpha_i^2, H_i) > 0$. Thus,

$$V_{At}^* = \Sigma\ \mathrm{cov}(\alpha_i^2, H_i) + (1 - F_t)(V_A + 2F_tV_D), \quad (7)$$

where V_D is the dominance component of the ancestral genetic variance, $V_D = \Sigma\delta_i^2H_i^2 = \Sigma s^2H_i^2/4$ (from Equation 2). Equation 7 shows that V_{At}^* always exceeds its additive expectation, *i.e.*, $V_{At}^* > (1 - F_t)V_A$. Furthermore, as $\Sigma\ \mathrm{cov}(\alpha_i^2, H_i) > 0$, the condition $V_{At}^* > V_A$ can be given as $V_A < 2(1 - F_t)V_D$, implying $q_i < (1 - F_t)/(2 - F_t)$, *i.e.*, $q_i < \frac{1}{2}$. These results also apply for incomplete recessives ($0 < h_i < \frac{1}{2}$).

In parallel, the between-line variance can be written as

$$V(M_t) = \mu_4 - F_tV_A - F_t^2V_D,$$

where $\mu_4 = s^2\Sigma[E(q_i^4) - q_i^4] > 0$. Thus, $V(M_t)$ equals only its additive expectation ($2F_tV_A$) for $\mu_4 = 3F_tV_A + F_t^2V_D$. Moreover, Q_t will be larger than F_t if $\mu_4 < 3F_tV_A + 5F_t^2V_D$ and smaller otherwise, these conditions being slightly more restrictive than those for $V(M_t) \neq 2F_tV_A$, unless F_t is large [*e.g.*, $V(M_t) > 2F_tV_A$ for $\mu_4 > 3F_tV_A + F_t^2V_D$].

Summarizing, for neutral loci and nonadditive gene action (dominant and/or epistatic), Q_t will generally depart from F_t, except in the particular case of $V(M_t) = 2F_tV_{At}^*/(1 - F_t)$.

NUMERICAL EVALUATION

Three representative cases were studied, with additive ($h_i = \frac{1}{2}$) or recessive ($h_i = 0$) basic gene action at both loci ($s = 0.1$) and strong reinforcing epistasis ($k = 6$) or with recessive nonepistatic action ($h_i = 0$, $k = 2$). For each case, surfaces were represented (Figure 1), giving the values of the following contrasts after one bottleneck ($N = 2$, $F_1 = 0.25$) for all possible combinations of allele frequencies at both loci: (1) the ratio of derived to ancestral additive components of variance V_{A1}^*/V_A, (2) the ratio of the between-line variance to its expected value for additive gene action $V(M_1)/2F_1V_A$, and (3) the difference $F_1 - Q_1$ between the inbreeding coefficient and the quantitative index of population divergence. With different basic gene action at each locus and epistasis, intermediate results were obtained (not shown).

For complete recessive nonepistatic action, $Q_1 < F_1$ for only low to moderate frequencies of the recessive allele at both loci (or for the recessive allele fixed in one locus and segregating at low frequency in the other); otherwise, $Q_1 > F_1$. The absolute value of the difference $F_1 - Q_1$ increased as the corresponding allele frequencies became more extreme. With additional epistasis, the condition $Q_1 < F_1$ holds for a much broader range of allele frequencies, and $Q_1 > F_1$ for only high frequencies of the recessive allele at both loci (or for the dominant allele fixed in one locus and the recessive one segregating at high frequency in the other). This situation is similar to that obtained with basic additive action and epistasis but, for low frequencies of both negative alleles, the excess of F_1 over Q_1 was, comparatively, much reduced. As shown by Equation 3, this can be ascribed to the marginal degrees of dominance (γ_i) becoming closer to the basic ones ($h_i = \frac{1}{2}$) as the frequencies of both negative alleles diminish. However, that excess was

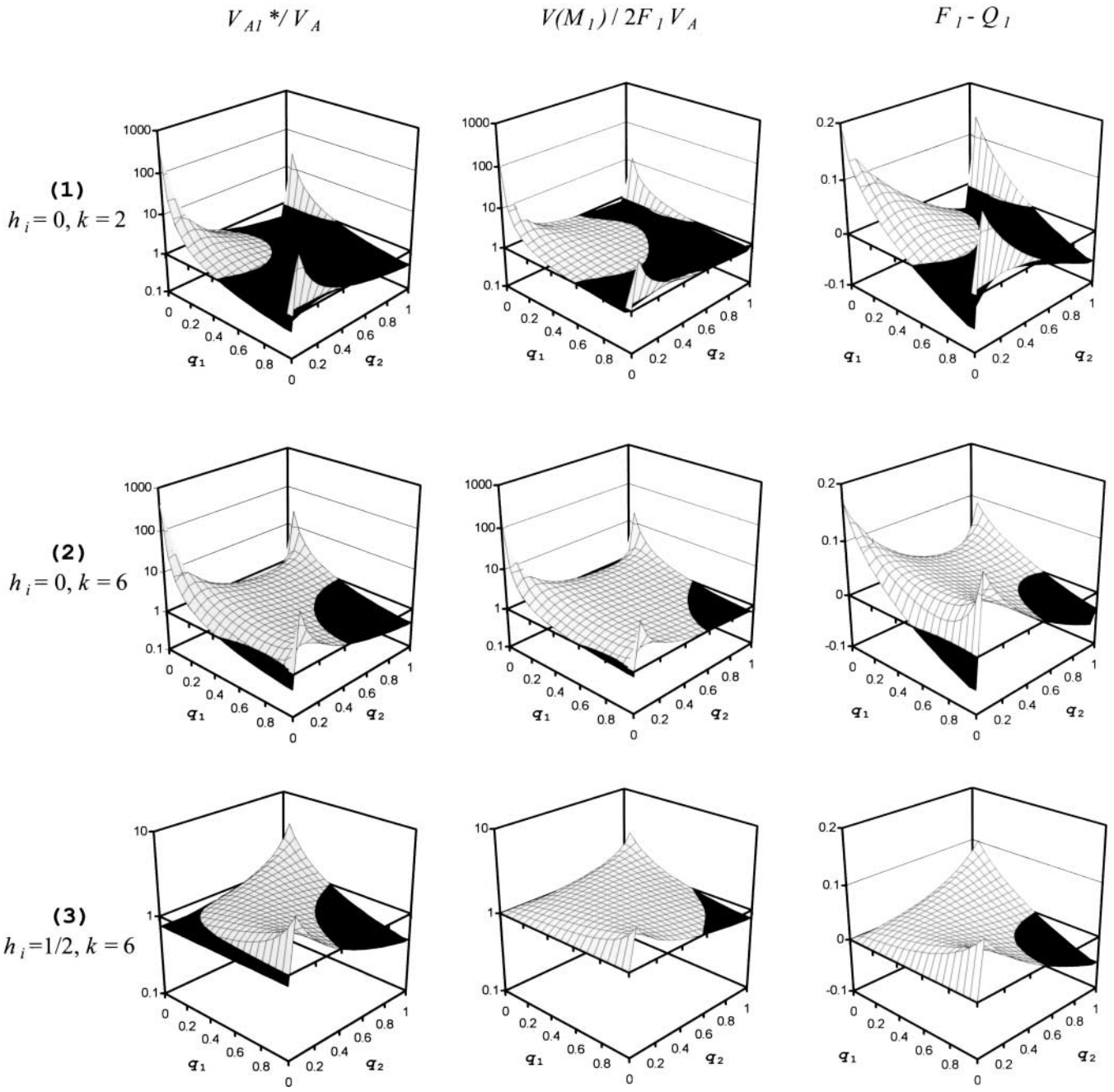

FIGURE 1.—Ratio of derived to ancestral additive components of variance V_{A1}^*/V_A (log scale), ratio of the between-line variance to its additive expectation $V(M_1)/2F_1V_A$ (log scale), and difference $F_1 - Q_1$ between the inbreeding coefficient and the quantitative index of population divergence, after one bottleneck ($N = 2$, $F_1 = 1/4$), for (1) nonepistatic complete recessive action at both loci ($h_i = 0$, $k = 2$), (2) basic complete recessive action at both loci and reinforcing epistasis ($h_i = 0$, $k = 6$), and (3) basic additive action at both loci and reinforcing epistasis ($h_i = 1/2$, $k = 6$). Darker zones correspond to ratios smaller than one or to negative $F_1 - Q_1$ values.

preserved when the negative allele is fixed in one locus and segregates at low frequency in the other as, in this case, the marginal degree of dominance of this second locus approaches zero (*i.e.*, the locus becomes increasingly recessive). These results apply to populations subjected to a single bottleneck of any size, albeit the absolute value of $F_1 - Q_1$ decreased as the size of the bottleneck increased. With basic recessive action, increasing values of the epistatic factor k did not affect much the absolute value of the contrast (not shown) as, in this case, the basic and marginal degrees of dominance are the same. However, with epistasis and basic additive action, that absolute value was positively correlated with k, as the marginal degree of dominance tends

to zero for increasing k values. Of course, for basic additive action without epistasis $F_1 = Q_1$.

As shown in Figure 1, $Q_1 < F_1$ holds approximately for the whole range of allele frequencies implying both $V(M_1) > 2F_1V_A$ and $V_{A1}^* > V_A$, irrespective of the type of basic gene action, and the reverse was also true. These conditions also hold after consecutive bottlenecks, but the absolute value of $F_t - Q_t$ initially increases with the number of bottlenecks until a maximum is reached for F_t close to 0.5 and then subsequently decreases to zero (not shown). These changes have also been described by Robertson (1952) for nonepistatic recessives at low frequency. Summarizing, with epistasis, $Q_t < F_t$ for all combinations of allele frequencies at both loci, excepting for high frequencies of the negative (recessive) alleles. Without epistasis, however, $Q_t < F_t$ for only low to moderate frequencies of those alleles.

DISCUSSION

We have shown that the Q_t value generated by neutral dominant and/or epistatic loci, after t consecutive population bottlenecks, will always be larger or smaller than its additive expectation F_t, with the trivial exception determined by those particular combinations of allele frequencies fixing the boundary lines between the positive and negative regions of the $F_t - Q_t$ surface. Therefore, the use of the $F_t - Q_t$ difference as a criterion to investigate the relative importance of genetic drift and natural selection in population differentiation is restricted to pure additive traits, as nonadditive action at neutral loci can mimic the expectations for additive loci under divergent ($Q_t > F_t$) or convergent selection ($Q_t < F_t$). Moreover, for nonneutral nonadditive loci, selection will also affect (positively or negatively) the $F_t - Q_t$ value and this additional effect could even change the expected sign of that difference under neutrality.

For nonadditive gene action, previous theoretical work concerned with the divergence between F_t and Q_t was restricted to the neutral additive-by-additive model, where $Q_t < F_t$ for $F_t < 1$ (Whitlock 1999). However, the effect of dominance (with or without epistasis) can qualitatively alter that result, as Q_t may be smaller or larger than F_t, depending on the relevant allele frequencies. With simple dominance, $Q_t < F_t$ for only low to moderate frequencies of the recessive alleles, but additional epistasis extends that condition to higher values of the frequencies of the negative (recessive) alleles at one of the loci involved (but not at both). Irrespective of the type of gene action considered, we have also shown that $Q_t < F_t$ generally implies an increase of the within-line additive variance after bottlenecks ($V_{At}^* > V_A$), as well as an excess of the between-line variance over its additive expectation ($V(M_t) > 2F_tV_A$). Thus, both the redistribution of the genetic variance after bottlenecks and the value of $F_t - Q_t$ are governed largely by the marginal properties of single loci, epistasis acting only as a modulating factor (López-Fanjul *et al.* 1999, 2000, 2002).

So far, this discussion has been limited to investigating the consequences of population bottlenecks on the $F_t - Q_t$ difference generated by two-locus nonadditive neutral systems. An extension of these results to the whole set of loci determining the additive variance of a quantitative trait will, in principle, require a complete specification of their genotypic effects and allele frequencies, as the contribution of loci with the same type of gene action to the total $F_{ST} - Q_{ST}$ value can even be of different sign, depending on their respective allele frequencies. Generalizations into multilocus systems can be made only if individual loci show the same type of gene action and segregate with similar frequencies. Only in this situation do our theoretical results provide a framework within which some experimental data can be interpreted. The following discussion is restricted to *D. melanogaster* and *T. castaneum*, where detailed genetic information on relevant traits is available.

At one extreme of the spectrum, we have traits such as abdominal bristle number or wing size and shape characteristics of the wing. In natural populations of Drosophila, very little or no inbreeding depression has been detected for those characters and their between- and within-line additive variances after bottlenecks very closely approached the expectations under the pure additive model (López-Fanjul *et al.* 1989; Whitlock and Fowler 1999). In parallel, spontaneous mutations affecting bristle number, wing length, and wing width occur at a low rate and have a relatively large average homozygous effect (García-Dorado *et al.* 1999). Furthermore, those mutations with an effect smaller than one-half phenotypic standard deviation of the pertinent trait were predominantly additive and quasi-neutral (Santiago *et al.* 1992; López and López-Fanjul 1993; Merchante *et al.* 1995). Thus, a large fraction of the corresponding genetic variance in natural populations will be contributed by a small number of quasi-neutral additive loci segregating at intermediate frequencies (Robertson 1967; Gallego and López-Fanjul 1983). At the other end of the spectrum, we consider viability in natural populations of Drosophila and Tribolium. After bottlenecks, viability showed strong inbreeding depression and its within-line additive variance significantly increased above the ancestral value (López-Fanjul and Villaverde 1989; García *et al.* 1994; Fernández *et al.* 1995). Therefore, much of the genetic variance of the trait should be due to partially (or totally) recessive deleterious alleles segregating at low frequencies. In Drosophila, most newly arisen mutations affecting viability had, on the average, a relatively large homozygous disadvantage and their gene action was close to recessive (García-Dorado *et al.* 1999; García-Dorado and Caballero 2000; Chavarrías *et al.* 2001). Using mutational information, Wang *et al.* (1998) have been

TABLE 2

F_{ST} and Q_{ST} estimates after experimental bottlenecks

Species and traits	V_b^f	V_w^g	F_{ST}	Q_{ST}
	Drosophila			
Wing area[a]	0.000502	0.000691	0.25	0.27
Angle 5-7-4[a]	0.000462	0.000594	0.25	0.28
Angle 8-7-6[a]	0.001270	0.001600	0.25	0.28
Angle 2-9-3[a]	0.000043	0.000060	0.25	0.26
Angle 2-1-5[a]	0.000088	0.000132	0.25	0.25
Angle 2-3-5[a]	0.000290	0.000372	0.25	0.28
Abdominal bristles[b]	5.22	2.50	0.50	0.51
Early viability[c]	40.00	98.10	0.25	0.17
Early viability[d]	56.90	134.18	0.25	0.17
Early viability[d]	75.88	150.72	0.50	0.20
	Tribolium			
Early viability[e]	3.86	14.79	0.25	0.11
Late viability[e]	2.95	8.28	0.25	0.15

Estimates of the between- (V_b) and the additive within- (V_w) line components of variance after one or three consecutive bottlenecks ($N = 2$) and the corresponding F_{ST} and Q_{ST} values for morphological traits and viability in *Drosophila melanogaster* and *Tribolium castaneum*.

[a] Whitlock and Fowler (1999) and unpublished data.

[b] López-Fanjul *et al.* (1989).

[c] López-Fanjul and Villaverde (1989).

[d] García *et al.* (1994).

[e] Fernández *et al.* (1995).

[f] All estimates were corrected for common environmental effects by subtracting the corresponding V_b at generation 0.

[g] Estimates from mother-daughter regression analysis (reference in *a*) or realized heritability after one generation of artificial selection (references in *b*–*e*).

able to show that the inbreeding depression and the increase in the additive variance of viability following bottlenecks can be ascribed mainly to a rise in the frequency of lethals and partially recessive mutations of large deleterious effects.

Table 2 shows the between- and the additive within-line components of the genetic variance after one or three consecutive bottlenecks ($N = 2$) and the corresponding F_{ST} and Q_{ST} values, for seven morphological traits in Drosophila (wing area, five angles whose vertices are defined by the intersections of the veins of the wing, and abdominal bristle number) and viability in Drosophila and Tribolium. As expected, F_{ST} and Q_{ST} were very close for all morphological traits (average $F_{ST} - Q_{ST} = -0.018$, range -0.03–0) and, for viability, F_{ST} was considerably larger than Q_{ST} in all cases (average $F_{ST} - Q_{ST} = 0.14$, range 0.08–0.30). It must be stressed that, in the experiments reviewed, all lines have been maintained under the same environmental conditions and have been subjected to a small number of bottlenecks (typically one). Thus, the effect of selection can be assumed to be small and the contrasting behavior of the $F_{ST} - Q_{ST}$ value for morphological traits and viability can be ascribed essentially to the changes induced by a known bout of random drift in sets of loci differing in their predominant type of gene action. In other words, the results in Table 2 can be taken as an experimental check of the validity of our theoretical predictions.

Incomplete information on the genetic properties of the traits studied makes the interpretation of the $F_{ST} - Q_{ST}$ difference more problematic. Estimates of F_{ST} (from molecular markers) and Q_{ST} (for different quantitative traits) have been reported for sets of populations in a variety of plant and animal species (reviewed by Merilä and Crnokrak 2001 and McKay and Latta 2002). For most traits Q_{ST} was larger than F_{ST}, this result being interpreted as a consequence of differential population adaptation to local conditions. The most common experimental design included populations from different geographic origins, each of them subdivided into families (typically full-sib families) and a number of individuals assayed per family, all of them maintained under the same environmental conditions. Here we are not concerned with the validity of inferring the population structure from the marker's information, but we consider only those potential biases resulting from the treatment of quantitative data (detailed by Merilä and Crnokrak 2001). Following standard ANOVA procedures, the total variance for each trait was partitioned into sources arising from variation between populations, between families, within populations, and within families. In general, the genetic architecture of the traits assayed was unknown and, therefore, the estimates of the additive within-line variance obtained from full-sib analysis could be biased upward, as they may include fractions of the dominance and epistatic components of variance, as well as twice the environmental component of variance common to family members (including maternal effects). Biases due to nonadditive gene action will be more likely for life-history traits, which generally show higher levels of dominance variance than morphological traits show. Furthermore, estimates of the between-population variance could also be inflated to an unknown amount, due to common environmental effects (maternal and nonmaternal) that have not been experimentally removed. Even in a pure neutral additive situation, with biased estimates of the between- and within-line variances due to common environment only, $V_b = 2F_{ST}(1 + a)V_A$, $V_w = (1 - F_{ST})(1 + b)V_A$, and $Q_{ST} = (1 + a)F_{ST}/[(1 + a)F_{ST} + (1 + b)(1 - F_{ST})]$. Therefore, the neutral expectation $Q_{ST} = F_{ST}$ will hold only when the magnitude of both biases is the same ($a = b$), and $a > b$ or $a < b$ will, respectively, mimic the expectation under divergent ($Q_{ST} > F_{ST}$) or convergent selection ($Q_{ST} < F_{ST}$). In parallel, as shown by our theoretical analysis, nonadditive action of neutral quantitative loci could also distort the expected additive relationship between F_{ST} and Q_{ST}, even if the estimates of Q_{ST} are free from environmental biases.

Summarizing, the sign of the difference $F_{ST} - Q_{ST}$ will be indicative of selection for only those traits whose

genetic variance is mostly (or totally) generated by segregation at pure additive loci. Although these traits are commonly assumed to be quasi-neutral, the $F_{ST} - Q_{ST}$ criterion may be useful to establish the validity of this hypothesis.

We thank Michael Whitlock and Kevin Fowler for kindly allowing us to use their unpublished estimates of variance components for Drosophila wing traits. This study was supported by grant PB98-0814-C03-01 from the Ministerio de Educación y Cultura and RZ01-028-C2-1 from Instituto Nacional de Investigaciones Agrarias.

LITERATURE CITED

Chavarrías, D., C. López-Fanjul and A. García-Dorado, 2001 The rate of mutation and the homozygous and heterozygous mutational effects for competitive viability: a long-term experiment with *Drosophila melanogaster*. Genetics **158:** 681–693.

Cheverud, J. M., and E. J. Routman, 1996 Epistasis as a source of increased additive genetic variance at population bottlenecks. Evolution **50:** 1042–1051.

Crnokrak, P., and D. A. Roff, 1995 Dominance variance: associations with selection and fitness. Heredity **75:** 530–540.

Crow, J. F., and M. Kimura, 1970 *An Introduction to Population Genetics Theory*. Harper & Row, New York.

DeRose, M. A., and D. A. Roff, 1999 A comparison of inbreeding depression in life-history and morphological traits in animals. Evolution **53:** 1288–1292.

Endler, J. A., 1986 *Natural Selection in the Wild*. Princeton University Press, Princeton, NJ.

Fernández, A., M. A. Toro and C. López-Fanjul, 1995 The effect of inbreeding on the redistribution of genetic variance of fecundity and viability in *Tribolium castaneum*. Heredity **75:** 376–381.

Gallego, A., and C. López-Fanjul, 1983 The number of loci affecting a quantitative trait in *Drosophila melanogaster* revealed by artificial selection. Genet. Res. **42:** 137–149.

García, N., C. López-Fanjul and A. García-Dorado, 1994 The genetics of viability in *Drosophila melanogaster*: effects of inbreeding and artificial selection. Evolution **48:** 1277–1285.

García-Dorado, A., and A. Caballero, 2000 On the average coefficient of dominance of deleterious spontaneous mutation. Genetics **155:** 1991–2001.

García-Dorado, A., C. López-Fanjul and A. Caballero, 1999 Properties of spontaneous mutations affecting quantitative traits. Genet. Res. **75:** 47–51.

Goodnight, C., 1988 Epistasis and the effect of founder events on the additive genetic variance. Evolution **42:** 441–454.

Lande, R., 1977 Statistical tests for natural selection on quantitative characters. Evolution **31:** 442–444.

López, M. A., and C. López-Fanjul, 1993 Spontaneous mutation for a quantitative trait in *Drosophila melanogaster*. II. Distribution of mutant effects on the trait and fitness. Genet. Res. **61:** 117–126.

López-Fanjul, C., and A. Villaverde, 1989 Inbreeding increases genetic variance for viability in *Drosophila melanogaster*. Evolution **43:** 1800–1804.

López-Fanjul, C., J. Guerra and A. García, 1989 Changes in the distribution of the genetic variance of a quantitative trait in small populations of *Drosophila melanogaster*. Genet. Sel. Evol. **21:** 159–168.

López-Fanjul, C., A. Fernández and M. A. Toro, 1999 The role of epistasis in the increase in the additive genetic variance after population bottlenecks. Genet. Res. **73:** 45–59.

López-Fanjul, C., A. Fernández and M. A. Toro, 2000 Epistasis and the conversion of non-additive to additive genetic variance at population bottlenecks. Theor. Popul. Biol. **58:** 49–59.

López-Fanjul, C., A. Fernández and M. A. Toro, 2002 The effect of epistasis on the excess of the additive and non-additive variances after population bottlenecks. Evolution **56:** 865–876.

McKay, J. K., and R. G. Latta, 2002 Adaptive population divergence: markers, QTL and traits. TREE **17:** 285–291.

Meffert, L. M., 2000 The evolutionary potential of morphology and mating behavior. The role of epistasis in bottlenecked populations, pp. 177–193 in *Epistasis and the Evolutionary Process*, edited by J. B. Wolf, E. D. Brodie and M. J. Wade. Oxford University Press, New York.

Merchante, M., A. Caballero and C. López-Fanjul, 1995 Response to selection from new mutation and effective size of partially inbred populations. II. Experiments with *Drosophila melanogaster*. Genet. Res. **66:** 227–240.

Merilä, J., and P. Crnokrak, 2001 Comparison of genetic differentiation at marker loci and quantitative traits. J. Evol. Biol. **14:** 892–903.

Robertson, A., 1952 The effect of inbreeding on the variation due to recessive genes. Genetics **37:** 189–207.

Robertson, A., 1967 The nature of quantitative genetic variation, pp. 265–280 in *Heritage From Mendel*, edited by A. Brink. University of Wisconsin Press, Madison, WI.

Santiago, E., J. Albornoz, A. Domínguez, M. A. Toro and C. López-Fanjul, 1992 The distribution of effects of spontaneous mutations on quantitative traits and fitness in *Drosophila melanogaster*. Genetics **132:** 771–781.

Spitze, K., 1993 Population structure in *Daphnia obtusa*: quantitative genetic and allozymic variation. Genetics **135:** 367–374.

Wang, J., A. Caballero, P. D. Keightley and W. G. Hill, 1998 Bottleneck effect on genetic variance: theoretical investigation of the role of dominance. Genetics **150:** 435–447.

Whitlock, M. C., 1999 Neutral additive genetic variance in a metapopulation. Genet. Res. **74:** 215–221.

Whitlock, M. C., and K. Fowler, 1999 The changes in genetic and environmental variance with inbreeding in *Drosophila melanogaster*. Genetics **152:** 345–353.

Willis, J. H., and H. A. Orr, 1993 Increased heritable variation following population bottlenecks: the role of dominance. Evolution **47:** 949–957.

Wright, S., 1951 The genetical structure of populations. Ann. Eugen. **15:** 323–354.

Wright, S., 1978 *Evolution and the Genetics of Populations: Variability Within and Among Natural Populations*, Vol. 4. University of Chicago Press, Chicago.

Communicating editor: Z-B. Zeng