

# Effects on phenotypic variability of directional selection arising through genetic differences in residual variability

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## Summary

In standard models of quantitative traits, genotypes are assumed to differ in mean but not variance of the trait. Here we consider directional selection for a quantitative trait for which genotypes also confer differences in variability, viewed either as differences in residual phenotypic variance when individual loci are concerned or as differences in environmental variability when the whole genome is considered. At an individual locus with additive effects, the selective value of the increasing allele is given by  $ia/\sigma + \frac{1}{2}ixb/\sigma^2$ , where  $i$  is the selection intensity,  $x$  is the standardized truncation point,  $\sigma^2$  is the phenotypic variance, and  $a/\sigma$  and  $b/\sigma^2$  are the standardized differences in mean and variance respectively between genotypes at the locus. Assuming additive effects on mean and variance across loci, the response to selection on phenotype in mean is  $i\sigma_{Am}^2/\sigma + \frac{1}{2}ixcov_{Amv}/\sigma^2$  and in variance is  $icov_{Amv}/\sigma + \frac{1}{2}ix\sigma_{Av}^2/\sigma^2$ , where  $\sigma_{Am}^2$  is the (usual) additive genetic variance of effects of genes on the mean,  $\sigma_{Av}^2$  is the corresponding additive genetic variance of their effects on the variance, and  $cov_{Amv}$  is the additive genetic covariance of their effects. Changes in variance also have to be corrected for any changes due to gene frequency change and for the Bulmer effect, and relevant formulae are given. It is shown that effects on variance are likely to be greatest when selection is intense and when selection is on individual phenotype or within family deviation rather than on family mean performance. The evidence for and implications of such variability in variance are discussed.

## 1. Introduction

In a standard model of a quantitative trait, it is assumed that the genotypes at loci that affect the trait differ in their mean performance (Bulmer, 1980; Falconer & Mackay, 1996; Lynch & Walsh, 1988). For example, in the notation of Falconer & Mackay (1996), at a locus with two alleles,  $A_1$  and  $A_2$ , the genotypes  $A_1A_1$ ,  $A_1A_2$  and  $A_2A_2$  have means (ignoring a constant) of  $a$ ,  $d$  and  $-a$ , respectively. In the infinitesimal model, all genes are assumed to act additively ( $d=0$ ) and to be of small effect, such that the population can be described solely in terms of its mean and (additive) genetic variance,  $V_A$ . In these and more general multi-locus models, it is also assumed that the environmental variance is the same for any genotype. When a single locus is considered, the variance of phenotypes of each genotype, which comprises both genetic variance at other loci and the environmental variance, is

also assumed to be constant. (Formally this requires linkage equilibrium, for otherwise the residual genetic variance may be heterogeneous.) If necessary, data may be transformed, for example by taking logarithms, in order to effect this homogeneity of variance or at least reduce heterogeneity.

In the standard model differences in genetic and hence phenotypic variance found within any environment between populations or which are induced by forces such as selection or migration arise from differences between genotypes in mean phenotypic or genotypic value. At individual loci they depend on quantities such as  $\sum_i \sum_j p_i p_j g_{ij}^2 - (\sum_i \sum_j p_i p_j g_{ij})^2$ , where  $p_i$  and  $g_{ij}$  are allele frequencies and genotypic values, respectively, and at multiple loci on correlations between frequencies at different loci due to linkage disequilibrium (e.g. induced by migration or the Bulmer effect). They do not arise because of any difference between genotypes in their environmental or residual variance. Differences in variance in such models may

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be incorporated as scale effects, where the variance is a simple function of the mean, or as environmental effects, where the environmental variance is assumed to depend on environmental group (Falconer & Mackay, 1996, ch. 17; Lynch & Walsh, 1998, ch. 11). Similarly they can arise as a consequence of ‘canalization’ (Rendel, 1967) or of ‘genetic assimilation’ (Waddington, 1957), where the genetic and phenotypic variances are some function of background genotype or environment. The variance is then assumed to be a function of the mean rather than of individual genotype.

The *a priori* reasons for assuming homogeneity of environmental variance are simple convenience and the paucity of data to assume otherwise. SanCristobal-Gaudy *et al.* (1998) reviewed some of the evidence for heterogeneity; this includes, for example, the *Ubx* locus in *Drosophila*. Further evidence comes from the comparison of inbreds and outbreds, where inbreds may show inflated environmental variance (Lerner, 1954); although the phenotypic variances may be similar despite the very different levels of genetic variance (see Falconer & Mackay, p. 267; Hill & Bünger, 2004). Extreme selected lines may show much higher levels of variation than can be explained by scale effects (see e.g. Falconer & Mackay, 1996, p. 221). For example, Clayton & Robertson (1957) found that the phenotypic variance was higher in both low and high selected lines of *Drosophila* than in the unselected base population. In a thorough analysis of alternative models, Sorensen & Waagepetersen (2003) have shown there is substantial variability among genotypes in residual variance (i.e. after removing other identifiable effects) for litter size in pigs. Unpublished data of T. F. C. Mackay and colleagues (personal communication) show substantial variation in within-line variability (expressed as the coefficient of variation) in abdominal bristle number among chromosome substitution lines in *Drosophila melanogaster*. Information will come in due course from analyses of genes or quantitative trait loci where both means and variances can be computed for each variant.

Levels of environmental or phenotypic variability are important topics: for example, in animal or plant improvement it may be important to reduce variation to obtain a more homogeneous product; and in natural populations, the evolutionary forces that determine the observed levels of variability are important questions. As discussed by Hill & Bünger (2004), why, for example, is the coefficient of variation of juvenile body weight about 10% in a wide range of species, and what controls the level? Selection must be acting on the variance *per se*, it cannot just be a consequence of variability in genotypic means.

Previous analyses using models in which the assumptions of homogeneity of phenotypic, residual

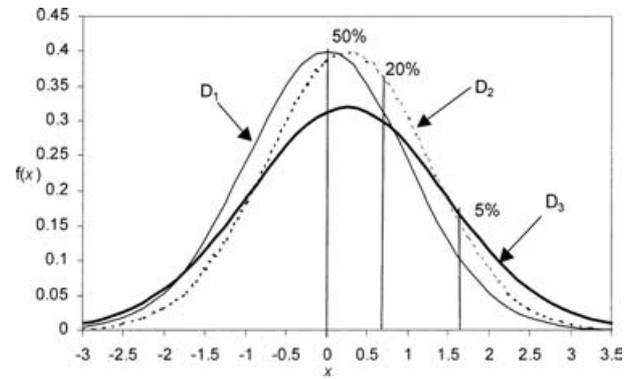


Fig. 1. Example of truncation for three arbitrary genotypes differing in mean and residual standard deviation:  $D_1 \approx N(0, 1)$ ,  $D_2 \approx N(0.25, 1)$ ,  $D_3 \approx N(0.25, 1.25)$ . The vertical bars represent the truncation points for selecting 50%, 20% and 5% of type  $D_1$ . Note that as selection becomes more intense, a relatively higher proportion of  $D_3$  would be selected.

(i.e. phenotypic given genotype at one locus) and environmental variance are relaxed have analysed stabilizing selection on phenotype (Gavrilets & Hastings, 1994; Wagner *et al.*, 1997) or a more complex artificial selection scheme, aimed at changing the level of variability (SanCristobal-Gaudy *et al.*, 1998). In this paper we shall consider the correlated effects of directional selection on phenotype on the underlying variability, expanding on some preliminary results (Hill, 2002)

## 2. Single-locus model

### (i) Selective value

Consider genotypic values at an arbitrary locus A, at which genotypes affect both the mean and residual variance of a quantitative trait. Residual variances are assumed to be normally distributed, although formally the distributions are mixtures of normals as summation is made over possible genotypes, such that  $A_i A_j$  individuals, for example, have phenotypic distribution  $N(\mu_{ij}, \sigma_{ij}^2)$ . Assume the overall mean is  $\mu$  and the phenotypic variance is  $\sigma^2$  and further that, despite the heterogeneity of variance, the overall distribution is well approximated by a normal distribution. Assume the population is large and a proportion  $p$  of the population is selected on phenotype using truncation selection and mated at random;  $p$  is also the probability of selection of a random individual with phenotypes distributed as  $N(\mu, \sigma^2)$ . Fig. 1 illustrates the selection for three genotypes differing in mean and/or in residual variance. It shows in particular that, although  $D_2$  and  $D_3$  (arbitrary genotypic distributions) have the same mean,  $D_3$  has an increased probability of selection, particularly if a small proportion of the overall population is selected. Haldane (1930) noted this dependency on both mean and

Table 1. Proportion selected ( $p$ ), selection intensity ( $i$ ) and selection coefficient for variance term ( $\frac{1}{2}ix$ ) in a very large population

$p$	0.80	0.60	0.50	0.40	0.20	0.10	0.05	0.02	0.01	0.005	0.002	0.001
$i$	0.35	0.64	0.80	0.97	1.40	1.75	2.06	2.42	2.66	2.89	3.17	3.37
$\frac{1}{2}ix$	-0.15	-0.08	0.00	0.12	0.59	1.12	1.70	2.49	3.12	3.72	4.56	5.20

variability of performance, and computed probabilities of selection as a function of both. Other, related derivations of the probability of selection in terms of differences in mean have been given elsewhere (e.g. Latter, 1965; Kimura & Crow, 1978; Falconer & Mackay, 1996).

Assume that  $A_iA_j$  individuals are distributed with mean and variance  $\mu_{ij} = \mu + a$ ,  $\sigma_{ij}^2 = \sigma^2 + b$ , i.e. as  $N(\mu + a, \sigma^2 + b)$ . Using a Taylor series expansion, the probability of selection of individuals of this genotype is, if only linear terms are included,

$$P(a, b) = p + a\partial p/\partial a|_{a,b=0} + b\partial p/\partial b|_{a,b=0} + \dots \quad (1)$$

$$= p + za/\sigma + \frac{1}{2}xzb/\sigma^2 + \dots \quad (2)$$

where  $x$  and  $z$  are, respectively, the abscissa (truncation point) and the ordinate of the standardized normal distribution for a proportion  $p$  selected. In the previous note (Hill, 2002), the heterogeneity of variance was expressed in terms of differences in standard deviation, whereas here it is expressed as differences of variances to utilize their additive properties. Wagner *et al.* (1997) and SanCristobal-Gaudy *et al.* (1998) use a multiplicative rather than additive model for the differences in variances, which can have benefits in subsequent parametrization.

Further terms in the expansion of (1) are given in the Appendix. In particular the second-order term in effects on the mean leads to an additional term  $+\frac{1}{2}xza^2/\sigma^2$  in (2) (see also Latter, 1965). As we are concerned here with the effects of genes which influence the variability we assume that terms in  $a^2/\sigma^2$  and terms of higher order than  $1/\sigma^2$  can be ignored relative to  $a/\sigma$  and  $b/\sigma^2$ . This assumption holds, for example, with simple multiplicative scaling effects where  $k = \sigma/\mu$  is the coefficient of variation: then  $b/\sigma^2 = (d\sigma^2/d\sigma)ka/\sigma^2 = 2ka/\sigma$ , approximately, and higher-order terms become trivial if  $a/\sigma$  is small.

The selection intensity (selection differential in standard units) is given by  $i = z/p$  for this distribution. Hence, the probability of selection or fitness of individuals of a genotype that increases the mean by  $a/\sigma$  and the variance by  $b/\sigma^2$ , relative to that of a random individual, is given by

$$P(a, b)/p = 1 + ia/\sigma + \frac{1}{2}ixb/\sigma^2. \quad (3)$$

The term  $ia/\sigma$  in (3) is the standard coefficient for truncation selection (see Falconer & Mackay, 1996),

and the second is the additional term that accounts for heterogeneity in variance (Hill, 2002). Thus, as Haldane (1930) noted, the probability of selection of the genotype with higher mean is increased relatively more under intense selection if the genotype also confers more variability; whereas under weak selection increased variability reduces its advantage. Equivalently, the selective value (increment in relative fitness) of the genotype is given by

$$s(a, b) = P(a, b)/p - 1 = ia/\sigma + \frac{1}{2}ixb/\sigma^2. \quad (4)$$

The value of  $x$  increases monotonically with  $p$ , and for  $p = 0.5$ ,  $x = 0$ . Values of  $p$  and corresponding values of  $i$  and  $\frac{1}{2}ix$  are given in Table 1, indicating how the latter becomes relatively more important with increasing intensity of selection, such that genotypes conferring high variability become relatively more favoured as the intensity of selection rises. With very weak selection, such genotypes are at a selective disadvantage.

(ii) *Bi-allelic locus with additive effects*

We utilize for reference the notation of Falconer & Mackay (1996), where  $q$  refers to the frequency of the selectively disadvantaged allele,  $s$  to the difference in fitness and  $2a$  the difference in mean phenotype between homozygotes. Let us assume that the phenotypic distributions of  $A_1A_1$  individuals have  $a$  units higher mean and  $b$  units higher residual variance than  $A_1A_2$  individuals, and  $2a$  and  $2b$  respectively higher than  $A_2A_2$  individuals. Further, let us assume there is random mating and Hardy–Weinberg equilibrium. Hence the selective value of the  $A_1$  gene ( $A_1A_1 - A_2A_2$  difference in Falconer & Mackay, 1996) is

$$s = 2(ia/\sigma + \frac{1}{2}ixb/\sigma^2). \quad (5)$$

(iii) *Changes in gene frequency and population mean*

The change in the frequency ( $q$ ) of the  $A_2$  allele from one generation of selection is given by

$$\Delta q = -sq(1 - q)/2 = -q(1 - q)(ia/\sigma + \frac{1}{2}ixb/\sigma^2). \quad (6)$$

The mean phenotype is given by a constant term  $+a(1 - 2q)$  under random mating and Hardy–Weinberg

equilibrium (Falconer & Mackay, 1966) and that in variance similarly by a constant term  $+b(1-2q)$ . Hence  $d\mu/dq = -2a$ , for example, and the change in population mean due to the change in gene frequency is

$$\Delta\mu = (d\mu/dq)\Delta q = -2a\Delta q = 2q(1-q)(ia^2/\sigma + \frac{1}{2}ixab/\sigma^2); \tag{7}$$

and the consequent change in variance due to the heterogeneous variance is

$$\Delta V = (dV/dq)\Delta q = -2b\Delta q = 2q(1-q)(iab/\sigma + \frac{1}{2}ixb^2/\sigma^2). \tag{8}$$

There is, of course, an additional change in genetic and thus phenotypic variance due to genotype frequency change affecting the variation among means of each genotype. This is given by

$$2a^2[(q + \Delta q)(1 - q - \Delta q) - q(1 - q)] \approx 2\Delta q(1 - 2q)a^2 \tag{9}$$

if terms in  $(\Delta q)^2$  are ignored. The relative size of the variance changes due to ‘indirect’ (variance among genotypes) and ‘direct’ changes in variance (variance within genotypes) from (8) and (9), respectively, is therefore  $-(1-2q)(a/\sigma)^2/(b/\sigma^2)$ , i.e. proportional to the ratio of squared standardized effect of the gene on the trait and standardized effect on the variance; but the indirect change is negligible at intermediate gene frequencies. (The multi-locus ‘Bulmer effect’ on variance has been ignored here, but is included later.)

(iv) *Dominance*

In the above it has been assumed that the gene has additive effects on both the mean and variance. If there is any dominance, whether partial, full or indeed over-dominance for either or both parameters (equality is not required), then equivalent formulae for non-additive genes can be used, with  $a$  replaced by  $\alpha = a - d(1 - 2q)$ , the average effect of the gene substitution on the mean (from Falconer & Mackay, 1996), where  $d$  is the dominance deviation, and equivalently  $b$  by  $\beta$  as the average effect of the gene substitution on the variance. Hence  $s = 2(ia/\sigma + \frac{1}{2}ix\beta/\sigma^2)$  from (5),  $dV/dq = -2\beta\Delta q$  and formulae for changes in mean and variance are obvious: (7) and (8) generalize to  $\Delta\mu = 2q(1-q)(ia^2/\sigma + \frac{1}{2}ix\alpha\beta/\sigma^2)$  and  $\Delta V = 2q(1-q)(i\alpha\beta/\sigma + \frac{1}{2}ix\beta^2/\sigma^2)$ .

(v) *Fixation probability of a mutant; long-term selection*

In a finite population of effective size  $N_e$  the fixation probability,  $u$ , of a mutant gene with additive effects is

given by  $u = s$  for  $s > 1/N_e$  (Kimura, 1964), with  $s = 2(ia/\sigma + \frac{1}{2}ixb/\sigma^2)$  from (5) in this model. For  $|s| < 1/N_e$ ,  $u = s/2 + 1/2N_e$ , approximately (Hill, 1982), otherwise  $u = 0$ . Hence a gene that increases the variance has a higher probability that it will survive (Fig. 1) and ultimately be fixed in the population if selection is intense. Predictions of long-term selection response and limits as functions of gene effects could also be made based on results of Robertson (1960), but we shall not pursue this here. The present analysis merely illustrates the problem of making long-term predictions because potential changes in variance due to selection have to be accommodated.

3. **Multi-locus models**

(i) *Non-epistatic model*

To extend the analysis to multiple loci let us assume that effects of different loci on the mean and on the variance are additive, i.e. there are no epistatic effects. SanCristobal-Gaudy *et al.* (1998), however, assumed additivity of the logarithm of the variance, which leads to more tractable distributional properties (Foulley & Quaas, 1995) and management of scale effects, but may or may not be a better biological model. Hence the distribution of phenotypes for an individual with genotype  $A_{hi}A_{hj}$  at locus  $h$  is  $N(\mu + \sum_h(\alpha_{hi} + \alpha_{hj} + \delta_{hij}), \sigma_E^2 + \sum_h(\beta_{hi} + \beta_{hj} + \varepsilon_{hij}))$  where, respectively,  $\mu$  and  $\sigma_E^2$  denote the genotypic mean and environmental variance,  $\alpha_{hi}$  and  $\delta_{hij}$ , average and dominance effects at locus  $h$  on the mean and  $\beta_{hi}$  and  $\varepsilon_{hij}$  its corresponding average and dominance effects on the phenotypic variance. With the assumption of additive gene action across loci, the selective values and changes in frequency of individual genes are as in the previous calculations (Eqns 4 and 6), where  $\sigma^2$  formally refers to the sum of the environmental variance and the genetic variance attributed to all other loci. We assume that the contribution of any individual locus to the mean or variance of the variance is small, and hence assume  $\sigma^2$  equals the phenotypic variance. Let  $\sigma_{Am}^2 = \sum_h \sum_i q_{hi} \alpha_{hi}^2$  denote the usual additive genetic variance (in terms of effects of genes on the mean, usually written  $\sigma_A^2$  or  $V_A$ ), and similarly let  $\sigma_{Av}^2 = \sum_h \sum_i q_{hi} \beta_{hi}^2$  and  $cov_{Amv} = \sum_h \sum_i q_{hi} \alpha_{hi} \beta_{hi}$  denote, respectively, the additive genetic variance in the variance and in the covariance between effects on mean and variance. Extending (7) and (8), where it is noted that, for example,  $2q(1-q)\beta^2$  is the contribution to  $\sigma_{Av}^2$  from that locus:

$$\Delta\mu = i\sigma_{Am}^2/\sigma + \frac{1}{2}ixcov_{Amv}/\sigma^2 \tag{10}$$

and

$$\Delta V = icov_{Amv}/\sigma + \frac{1}{2}ix\sigma_{Av}^2/\sigma^2. \tag{11}$$

Equations (10) and (11) apply whether or not genes are of large effect, except that higher-order terms from (1) and the indirect effects of gene frequency change on the variance (9) are ignored. The results include the infinitesimal model in which it is assumed that all of the very many unlinked loci affecting the trait are additive within and between loci and have an infinitesimally small effect on both the mean and the variance. Hence a non-trivial response, in terms of standard deviations ( $\Delta\mu/\sigma$ ) or heritability, implies that the sum over loci,  $\sum_h$ , to give the total variance,  $\sigma_{Am}^2/\sigma^2 = \sum_h 2q_h(1-q_h)(a_h/\sigma)^2$ , is finite, where  $a_h$  denotes the gene effect at locus  $h$  on the mean. Similarly, a non-trivial proportional change in variance,  $\Delta V/\sigma^2$ , implies that  $\sigma_{Av}^2/\sigma^4 = \sum_h 2q_h(1-q_h)(b_h/\sigma^2)^2$  is finite.

(ii) *Scale*

As noted by Hill (2002), if the differences in variance can be assumed to be due solely to scale, appropriate results are obtained. Thus if there are multiplicative effects such that  $\sigma = k\mu$ , and there are no other differences among genotypes in the variance they contribute, a small increment  $a$  in genotypic mean contributes an increment in standard deviation of  $ka$  and in variance of  $b = (d\sigma^2/d\sigma)ka = 2k\sigma a$  at any locus (see also Section 2(i) above). Hence  $cov_{Amv} = 2k\sigma\sigma_{Am}^2$ ,  $\sigma_{Av}^2 = 4k^2\sigma^2\sigma_{Am}^2$ , and from (10) and (11)

$$\Delta\mu = i\sigma_{Am}^2/\sigma + ixk\sigma_{Am}^2/\sigma$$

and

$$\Delta V = 2ik\sigma_{Am}^2 + 2ixk^2\sigma_{Am}^2 = 2k\sigma\Delta\mu,$$

i.e. the change in variance is proportional to the change in mean,  $\Delta V/\Delta\mu = 2k\sigma$ , and the coefficient of variation is unchanged. Clearly, if a scale transform such as the logarithmic can substantially reduce the relationship between mean and variability of the population, then it seems appropriate to do so, and then define terms such as  $b$ ,  $cov_{Amv}$  and  $\sigma_{Av}^2$  for the log-transformed data.

(iii) *Recurrent selection, the infinitesimal model and the Bulmer effect*

Truncation selection induces negative gametic (linkage) disequilibrium between increasing alleles at different loci, which in turn leads to a reduction in genetic variance (the Bulmer effect). Recurrence formulae that do not involve gene frequency changes can be derived under the assumption of the infinitesimal model, in which cases all changes are due to the generation of disequilibrium. These formulae are derived in the Appendix; regrettably they are not neat! For example the recurrence equation for the additive genetic variance (in the mean) is as follows, from

appendix equation (A6):

$$\begin{aligned} \sigma_{Am,t+1}^2 &= \frac{1}{2}\sigma_{Am,0}^2 + \frac{1}{2}[\sigma_{Am,t}^2 - i(i-x)(\sigma_{Am,t}^2/\sigma_t) \\ &\quad + \frac{1}{2}ixcov_{Amv,t}/\sigma_t^2] - i(\sigma_{Am,t}^2 cov_{Amv,t})/\sigma_t^3 \\ &\quad - \frac{3}{4}ix(cov_{Amv,t}^2/\sigma_t^4), \end{aligned} \tag{12}$$

where, for example,  $\sigma_{Am,t}^2$  is the variance at generation  $t$  and  $\sigma_{Am,0}^2$  is that in the base population. This reduces to  $\sigma_{Am,t+1}^2 = \frac{1}{2}\sigma_{Am,0}^2 + \frac{1}{2}\{\sigma_{Am,t}^2 - i(i-x)(\sigma_{Am,t}^2/\sigma_t)^2\}$  in the standard model where genetic variance in variability is assumed to be absent. Recurrence formulae for  $cov_{Amv,t}$  and  $\sigma_{Av,t}^2$  follow by extension of the analysis in the Appendix:

$$\begin{aligned} cov_{Amv,t+1} &= \frac{1}{2}cov_{Am,0} + \frac{1}{2}[cov_{Amv,t} - i(i-x) \\ &\quad \times (\sigma_{Am,t}^2/\sigma_t + \frac{1}{2}ixcov_{Amv,t}/\sigma_t^2) \\ &\quad \times (cov_{Amv,t}^2/\sigma_t + \frac{1}{2}ix\sigma_{Av,t}^2/\sigma_t^2) \\ &\quad - \frac{1}{2}i(\sigma_{Am,t}^2\sigma_{Av,t}^2 + cov_{Amv,t}^2)/\sigma_t^3 \\ &\quad - \frac{3}{4}ix(cov_{Amv,t}\sigma_{Av,t}^2/\sigma_t^4)], \end{aligned} \tag{13}$$

$$\begin{aligned} \sigma_{Av,t+1}^2 &= \frac{1}{2}\sigma_{Av,0}^2 + \frac{1}{2}[\sigma_{Av,t}^2 - i(i-x)(cov_{Amv,t}/\sigma_t) \\ &\quad + \frac{1}{2}ix\sigma_{Av,t}^2/\sigma_t^2] - i(cov_{Amv,t}\sigma_{Av,t}^2)/\sigma_t^3 \\ &\quad - \frac{3}{4}ix(\sigma_{Av,t}^2/\sigma_t^4). \end{aligned} \tag{14}$$

If selection ceases, the changes in variances due to the gametic disequilibrium return asymptotically to those in the initial population, whereas those due to the (infinitesimally small) changes in gene frequency are permanent.

A particular complication is that as the phenotypic variance is changed by selection, so also is the heritability. If additive variance does not increase in proportion, there is therefore a bigger reduction in heritability and thus response; the phenotypic standard deviation is rising, however, which may compensate at least in part. Equilibrium may not, therefore be reached in this and other cases when the phenotypic variance changes as a direct consequence of selection, as will be illustrated in numerical examples. This contrasts with the usual analysis for the infinitesimal model when equilibrium is approached asymptotically, but when most change in variance occurs in the first two or so generations and is solely a consequence of the gametic disequilibrium induced by the selection.

**4. Selection other than on simple phenotype**

(i) *Within- and between-family selection*

The foregoing analysis deals solely with mass selection. More generally we need to consider selection with different weights given to individual and

relatives' performance, as is normal practice in genetic improvement programmes for livestock. It is simplest first to consider two special cases – selection within families and selection between families – which point towards the general solution. (We assume the multi-locus case and, where appropriate, the infinitesimal model.) The results can be derived either by considering the selective value of individual genes or by using a variance component argument for a continuous trait. The former seems simpler and is used here. Consider the single-locus model used previously and a mating  $A_1A_2 \times A_2A_2$ , such that one-half the  $n$  offspring are expected to inherit the  $A_1$  allele and have increased mean and variance by  $a$  and  $b$  units respectively. Let  $\sigma_B^2$  and  $\sigma_W^2$  denote the between- and within-family variances respectively, which typically can be partitioned as  $\sigma_B^2 = \frac{1}{2}\sigma_{Am}^2 + \sigma_C^2$ , where  $\sigma_C^2$  is the common environment of full sibs, and  $\sigma_W^2 = \frac{1}{2}\sigma_{Am}^2 + \sigma_E^2$ , where  $\sigma_E^2$  is the within-family error variance, such that  $\sigma_C^2 + \sigma_E^2 = \sigma^2 - \sigma_{Am}^2$ . The variance of mean performance of a full-sib family of  $n$  individuals is  $\sigma_B^2 + \sigma_W^2/n$ .

(a) Selection within families

Offspring inheriting the  $A_1$  gene are expected to have  $\frac{1}{2}a$  higher mean and  $\frac{1}{2}b$  higher variance than their sibs. Hence, from (4) their relative probability of selection is increased by

$$s_W(a, b) = \frac{1}{2}(ia/\sigma_W + \frac{1}{2}ixb/\sigma_W^2). \tag{15}$$

Except that their effects are scaled proportional to the within-family rather than phenotypic variance, genes directly influencing variability therefore have a similar relative impact on changes in parameters for within-family as for mass selection.

(b) Selection between families

Compared with families which are bred from  $A_2A_2 \times A_2A_2$  matings, the offspring mean of  $A_1A_2 \times A_2A_2$  matings is increased by  $\frac{1}{2}a$  and, since the residual error terms are assumed to be uncorrelated within families, the variance of the family mean is increased by  $\frac{1}{2}b/n$ . Hence the relative probability of selection is increased by

$$s_B(a, b) = \frac{1}{2}\{ia/(\sigma_B^2 + \sigma_W^2/n)^{1/2} + \frac{1}{2}ixb/[n(\sigma_B^2 + \sigma_W^2/n)]\}. \tag{16}$$

Relative to its effect on the mean, the gene therefore has a  $1/n$  proportionately smaller effect on the variance. Hence it is clear that family selection, or indeed other schemes whereby selection is placed on the means of groups of relatives, puts relatively much less direct selection pressure on the variance than do schemes based on individual selection such as mass or

within-family selection, particularly when family sizes are large. Analogously, sib selection in animal breeding or kin selection in natural populations will be increasingly less affected by heterogeneity of variance as survival of the individual depends on the performance of increasing number of sibs.

(c) Index and BLUP selection

Index and BLUP selection comprise weightings to the individual's own and to relatives' performance, with more to the former when heritability is high. Hence the impact of differences in variance will usually be smaller than for mass selection, particularly if the heritability is small.

(ii) Selection intensity in small population

The preceding formulae (in terms of  $i$  and  $ix$ ) apply to the case of selection from a large population. If selection is within families, it is almost certain to be from a limited number of individuals, certainly for mammals. To check on the relation between probability of selection and difference in variance, Monte Carlo simulation was used. (Numerical integration of order statistics could be used, but is inefficient for large  $n$ .) For a family of  $n$  individuals,  $n$  independent  $N(0, 1)$  observations  $x_j$  were sampled and the phenotype of one of these was scaled as  $x_1' = x_1(1 + b) + a$ . As the case of selection of only one individual is of most relevance for within-family selection, the probability  $p_1$  that this individual ranked highest was computed. Results are expressed as, for example,  $(p_1 - 1/n)n/b$ , the increase in selective value per unit increase in  $b$ , which for an infinitely large population is  $ix/2$ , comparable to  $i$  for  $a$ . Results are given in Table 2. It is seen that just as the selection intensity term  $i$  is reduced for given proportion selected in a small population, so is  $\frac{1}{2}ix$ , but proportionately rather more. Even so, as this case of selecting one individual from a group is the most extreme situation, it seems there is no need to evaluate different formulae to cater specifically for groups of small size assuming relevant correction is made where necessary.

5. Numerical results: simulation check

(i) Monte Carlo simulation method

To check both the formulae for the infinitesimal model (Eqns 12–14) and the degree of fit of the equations derived in the text and Appendix, Monte Carlo simulation of directional selection was undertaken using a finite-locus model. The model was, however, designed to be close to the infinitesimal model approximation and so no test was made of the infinitesimal model *per se*. Eight hundred unlinked bi-allelic loci were simulated with additive effects on

Table 2. Selection of the most extreme individual from a group of size  $n$ . The coefficients  $i$  and  $\frac{1}{2}ix$  are the coefficients of  $a$  and  $b$ , respectively, with the standard error of their estimates, obtained by Monte Carlo simulation each with  $10^6$  replicates

$n$	2	3	5	10	20	40	100
$i^*$	0.56 ± 0.01	0.86 ± 0.01	1.20 ± 0.01	1.58 ± 0.02	1.98 ± 0.03	2.26 ± 0.04	2.69 ± 0.07
$\frac{1}{2}ix$	0	0.12 ± 0.01	0.39 ± 0.01	0.87 ± 0.02	1.42 ± 0.03	1.94 ± 0.04	2.79 ± 0.07
$i + \frac{1}{2}ix$	0.56 ± 0.01	0.97 ± 0.01	1.58 ± 0.01	2.39 ± 0.02	3.37 ± 0.03	4.30 ± 0.04	5.67 ± 0.07

\* Model simulated (parameters  $a, b$ ):  $i$  (0.05, 0),  $\frac{1}{2}ix$  (0, 0.05),  $i + \frac{1}{2}ix$  (0.05, 0.05).

the mean and variance within and between loci, i.e. no dominance or epistasis. Each allele had initial frequency of 0.5, so as to minimize the change in variance due to change in gene frequency. As far as possible consistent with the parameters simulated, gene effects were the same at each locus. Allele  $A_i$  at locus  $i$  had effect  $a_i$  on the mean and  $b_i$  on the variance, and the initial environmental variance was 1.0. Hence, for example, to simulate  $\sigma_{Am}^2 = 0.5$ , i.e. an initial heritability of 1/3, the allelic effect at each locus was  $a_i = 0.025\sqrt{2}$ , giving  $\sigma_{Am}^2 = 800 \times 2q(1-q)a_i^2 = 0.5$ . Then, for example: (a) to simulate  $\sigma_{Av}^2 = cov_{Amv} = 0$ ,  $b_i = 0$  at each locus; (b) to simulate  $\sigma_{Av}^2 = 0.25$  and  $cov_{Amv} = 0$ ,  $b_i = 0.025$  for  $i = 1$  to 400 and  $b_i = -0.025$  for  $i = 401$  to 800; (c) to simulate  $\sigma_{Av}^2 = 0.25$  and  $cov_{Amv} = 0.187 = 0.25/\sqrt{2}$ , a correlation of 0.5 between effects on the mean and variance,  $b_i = 0.025$  for  $i = 1$  to 600 and  $b_i = -0.025$  for  $i = 601$  to 800. An alternative simulation was also used as a check of robustness for  $\sigma_{Am}^2 = 0.5$ ,  $\sigma_{Av}^2 = 0.25$ ,  $cov_{Amv} = 0$ : for  $i = 1$  to 400,  $a_i = 0.05$ ,  $b_i = 0$  and for  $i = 401$  to 800,  $a_i = 0$ ,  $b_i = 0.025\sqrt{2}$ ; but short-term results were little affected.

#### (ii) Comparison of simulation and infinitesimal model approximation

For the infinitesimal model approximation, calculations were undertaken using (12–14). Some examples are given in Fig. 2 for 5 generations of selection using both methods. This short period was used because subsequently gene frequency and hence variance changes become appreciable, such that the simulation becomes a poor check of the infinitesimal model calculations. Simulation was undertaken with 100 replicates, using a monoecious population with 100 selected out of either 400 ( $p = 0.25$ ) or 1000 ( $p = 0.1$ ) recorded. The agreement is generally seen to be quite good, even though large heritabilities, values of  $\sigma_{Av}^2$  and correlations between mean and variance effects are used. The poorest fit is found when the covariance  $cov_{Amv}$  is negative; this is the situation where heritability can increase, perhaps quickly, because the environmental variance may be falling as a consequence of the selection on the mean. The simulations do indicate that the infinitesimal approximations given in

the Appendix are correctly computed; but note the good fit here has no wider implication as the simulation model was chosen to be that best approximated by the infinitesimal model.

## 6. Numerical results: patterns of change

Examples of predicted responses in mean and changes in variances based on the infinitesimal model are given in Tables 3–6, the number of relevant parameters that change precluding simple visual representation. For reference, in all parameter sets the environmental variance in the base population ( $\sigma_{E0}^2$ ) is set equal to 1.0.

Consider firstly Table 3, which shows the influence of the magnitude of  $\sigma_{Av}^2$  for a proportion selected of  $p = 10\%$ , an initial value of  $\sigma_{Am}^2 = 0.5$  (i.e.  $h^2 = 1/3$  and  $\sigma_p^2 = 1.5$ ) and no correlation of effects on mean and variance ( $cov_{Amv} = 0$ ). For  $\sigma_{Av}^2 = 0$ , the results are the standard values for the infinitesimal model with these initial variances, with a decline in heritability and phenotypic variance arising due to the Bulmer effect that quickly reach an asymptote (in the absence of linkage, as here). The pattern changes more as higher initial values of  $\sigma_{Av}^2$  are taken; but even for the lowest non-zero value (0.0625) of  $\sigma_{Av}^2$ , the phenotypic variance increases above its initial value after four generations, while the heritability falls further than when  $\sigma_{Av}^2 = 0$ , and consequently response in the mean is predicted to be smaller. The environmental variance changes substantially over generations, increasing by over 20% after 4 generations when  $\sigma_{Av}^2 = 0.125$ . There is only a small impact on the change in mean performance, however. Note also that  $\sigma_{Am}^2$ ,  $\sigma_{Av}^2$  and  $cov_{Amv}$  decline a little from their initial values as a consequence of the Bulmer effect, which implies that a small negative correlation between genetic effects on the mean and variance is generated (i.e.  $cov_{Amv} < 0$  for  $t > 0$ ). Whilst in Table 3 comparisons are made among values of  $\sigma_{Av}^2$  for given initial  $\sigma_{Am}^2$ , in Table 4 the same value of  $\sigma_{Av}^2$  (0.125) is used for a range of values of  $\sigma_{Am}^2$ . The impact of  $\sigma_{Av}^2$  on the phenotypic variance, for example, is seen to be greater in absolute terms, and much greater in proportional terms, when  $\sigma_{Am}^2$  is small.

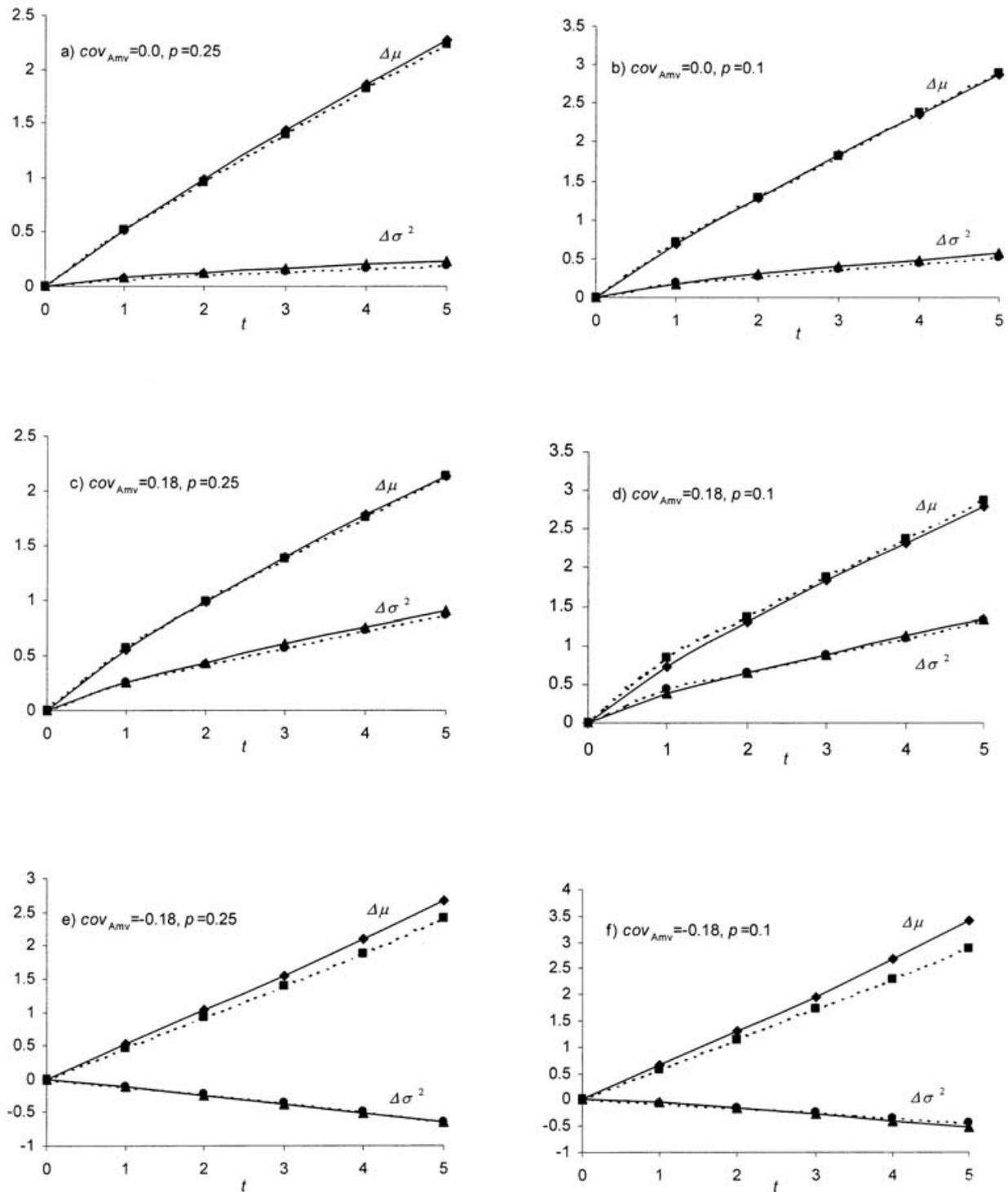


Fig. 2. Comparisons of multi-locus simulated (continuous line) and infinitesimal model theoretical (dashed line) predictions of change in mean ( $\Delta\mu$ ) and phenotypic variance ( $\Delta\sigma^2$ ) for the same initial environmental variance,  $\sigma_E^2=1$ , additive genetic variance on the mean,  $\sigma_{Am}^2=0.5$ , and on variance  $\sigma_{Av}^2=0.25$ , and differing values of additive genetic covariance ( $cov_{Amv}$ ), and of proportion selected ( $p$ ).

The influence of selection intensity is considered in Table 5, again for the case of  $cov_{Amv}=0$  initially. In these examples, the relative values of the importance of selection on variance to that on mean in the first generation ( $ix/2$  to  $i$ : see (4)), takes values of approximately  $-1/3, 0, 1/3, 2/3$  and  $1$  for  $p=0.75, 0.5,$

$0.15, 0.1$  and  $0.02$ , respectively. Selection has to be relatively strong for the changes in phenotypic variance to be substantial, not least to overcome the impact of the Bulmer effect in producing a negative covariance of effects on mean and variance. But for the most intense selection, environmental

Table 3. Changes in parameters with directional selection in the infinitesimal model: effects of magnitude of the genetic variance in residual variance

<i>t</i>	$\Delta\mu$	$\Delta\sigma_E^2$	$\sigma_{Am}^2$	$cov_{Amv}$	$\sigma_{Av}^2$	$\sigma_P^2$	$h^2$
Selection practised: $p=0.1, i=1.755, x=1.282$							
0	0.000	0.000	0.500	0.000	0.000	1.500	0.333
1	0.716	0.000	0.431	0.000	0.000	1.431	0.301
2	1.349	0.000	0.412	0.000	0.000	1.412	0.292
4	2.557	0.000	0.404	0.000	0.000	1.404	0.288
8	4.950	0.000	0.404	0.000	0.000	1.404	0.288
0	0.000	0.000	0.500	0.000	0.062	1.500	0.333
1	0.716	0.047	0.431	-0.012	0.061	1.478	0.292
2	1.329	0.076	0.417	-0.014	0.060	1.493	0.279
4	2.498	0.124	0.415	-0.015	0.060	1.539	0.270
8	4.783	0.215	0.418	-0.014	0.061	1.633	0.256
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.716	0.094	0.431	-0.024	0.118	1.525	0.283
2	1.311	0.147	0.422	-0.027	0.117	1.569	0.269
4	2.447	0.237	0.423	-0.027	0.118	1.660	0.255
8	4.648	0.408	0.427	-0.024	0.119	1.835	0.233
0	0.000	0.000	0.500	0.000	0.250	1.500	0.333
1	0.716	0.187	0.431	-0.048	0.222	1.618	0.266
2	1.277	0.276	0.431	-0.048	0.224	1.707	0.253
4	2.363	0.439	0.434	-0.045	0.227	1.873	0.232
8	4.437	0.749	0.439	-0.038	0.232	2.188	0.201

*t*, generations;  $\Delta\mu$ , response in population mean to generation *t*;  $\Delta\sigma_E^2$ , response in residual variance at linkage equilibrium to generation *t*;  $\sigma_{Am}^2$ ,  $\sigma_{Av}^2$  and  $cov_{Amv}$  are, respectively, additive genetic variance, additive genetic variance in residual variance, and covariance between them;  $\sigma_P^2$ , phenotypic variance;  $h^2$ , heritability; *p*, proportion selected; *i*, selection intensity; *x*, truncation point.

variance is seen to increase by nearly 50% after 4 generations.

In Table 6 the influence of the magnitude of the covariance between additive effects on the mean and variance is considered for the same initial values of  $\sigma_{Am}^2$  and  $\sigma_{Av}^2$ . The sign of  $cov_{Amv}$  has a major impact. If it is positive the environmental variance rises more rapidly, and the heritability consequently falls, such that response in the population mean is reduced. If it is negative, however, the environmental variance falls and consequently the heritability rises increasingly rapidly, with the impact on the variance becoming sufficiently large that the model breaks down ( $\sigma_E^2 < 0$  for  $t > 9$  with initial  $cov_{Amv} = -0.125$  in this example). These pairs of results with the same values of initial  $|cov_{Amv}|$  (e.g.  $cov_{Amv} = 0.0625$  and  $-0.0625$ ) can be viewed as those for lines in a bi-directional selection experiment: results for  $cov_{Amv} > 0$  can be regarded as those for the high selection line, and those for  $cov_{Amv} < 0$  as those for the low selection line, except that the sign of the change in the population mean has to be reversed. Asymmetry of response is therefore expected if  $cov_{Amv}$  is not zero, with more rapid response in the direction in which environmental

Table 4. Changes in parameters with directional selection in the infinitesimal model: effects of magnitude of the genetic variance

<i>t</i>	$\Delta\mu$	$\Delta\sigma_E^2$	$\sigma_{Am}^2$	$cov_{Amv}$	$\sigma_{Av}^2$	$\sigma_P^2$	$h^2$
Selection practised: $p=0.1, i=1.755, x=1.282$							
0	0.000	0.000	1.000	0.000	0.125	2.000	0.500
1	1.241	0.070	0.792	-0.031	0.121	1.863	0.425
2	2.241	0.103	0.770	-0.036	0.121	1.873	0.411
4	4.164	0.155	0.770	-0.036	0.121	1.925	0.400
8	7.951	0.254	0.776	-0.034	0.121	2.030	0.382
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.716	0.094	0.431	-0.024	0.118	1.525	0.283
2	1.311	0.147	0.422	-0.027	0.117	1.569	0.269
4	2.447	0.237	0.423	-0.027	0.118	1.660	0.255
8	4.648	0.408	0.427	-0.024	0.119	1.835	0.233
0	0.000	0.000	0.250	0.000	0.125	1.250	0.200
1	0.250	0.112	0.229	-0.016	0.115	1.342	0.171
2	0.727	0.185	0.227	-0.018	0.114	1.411	0.160
4	1.361	0.311	0.227	-0.017	0.115	1.538	0.147
8	2.568	0.544	0.229	-0.015	0.117	1.772	0.129

Definitions as in Table 3.

variance is reduced; for example if  $cov_{Amv} = 0.0625$ , the expected response upwards after 8 generations is 4.53 and downwards is 4.82 (parameters and results in Table 6).

### 7. Discussion

A critical question is whether these formulae and computations have any practical value in the real world, or are merely theoretical games, as would be the case if, in fact, there is no genetic variance in the residual variance (i.e.  $\sigma_{Av}^2 = 0$ ). Firstly, there is no *a priori* reason to suppose that there is *no* heterogeneity in environmental variance or residual phenotypic variance given genotype at a particular locus. Indeed it is a convenience in statistics to assume homogeneity, for example in enabling use of the analysis of variance and in reducing numbers of parameters to be fitted; for discussion see Foulley & Quaas (1995). When the assumption has actually been tested heterogeneity has often been found among environmental groupings and may be substantial, for example in variation among herds in the phenotypic variance of milk yield in dairy cattle within herds (Brotherstone & Hill, 1986). Heterogeneity is, however, commonly assumed in analysis of, for example, binomially distributed data or body size data, and a transformation used to induce homogeneity. Secondly, while there is a remarkable homogeneity of variance of some traits, for example when expressed as CV in juvenile body weight of selected lines of mice (Hill & Bünger, 2004), there are other situations where that is not the case, for example in selected lines of *Drosophila*

Table 5. Changes in parameters with directional selection in the infinitesimal model: effects of selection intensity

<i>t</i>	$\Delta\mu$	$\Delta\sigma_E^2$	$\sigma_{Am}^2$	$cov_{Amv}$	$\sigma_{Av}^2$	$\sigma_P^2$	$h^2$
Selection practised: $p=0.75, i=0.424, x=-0.674$							
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.173	-0.012	0.461	-0.001	0.126	1.449	0.318
2	0.336	-0.025	0.446	-0.002	0.126	1.422	0.314
4	0.652	-0.051	0.438	-0.002	0.126	1.387	0.316
8	1.287	-0.106	0.435	-0.002	0.126	1.328	0.327
Selection practised: $p=0.50, i=0.798, x=0.000$							
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.326	0.000	0.447	-0.007	0.125	1.447	0.309
2	0.622	-0.005	0.430	-0.009	0.125	1.426	0.302
4	1.195	-0.017	0.423	-0.010	0.125	1.405	0.301
8	2.335	-0.046	0.421	-0.011	0.126	1.375	0.306
Selection practised: $p=0.25, i=1.271, x=0.674$							
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.519	0.036	0.437	-0.015	0.122	1.472	0.297
2	0.972	0.055	0.422	-0.019	0.122	1.478	0.286
4	1.839	0.085	0.419	-0.020	0.122	1.504	0.278
8	3.543	0.141	0.421	-0.019	0.122	1.561	0.269
Selection practised: $p=0.10, i=1.755, x=1.282$							
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.716	0.094	0.431	-0.024	0.118	1.525	0.283
2	1.311	0.147	0.422	-0.027	0.117	1.569	0.269
4	2.447	0.237	0.423	-0.027	0.118	1.660	0.255
8	4.648	0.408	0.427	-0.024	0.119	1.835	0.233
Selection practised: $p=0.02, i=2.421, x=2.054$							
0	0.000	0.000	0.500	0.000	0.125	1.500	0.333
1	0.988	0.207	0.426	-0.036	0.109	1.633	0.261
2	1.740	0.304	0.428	-0.035	0.110	1.733	0.261
4	3.203	0.491	0.432	-0.032	0.112	1.923	0.224
8	5.989	0.842	0.437	-0.026	0.115	2.279	0.192

Definitions as in Table 3.

(Clayton & Robertson, 1957). Canalization (Rendel, 1967) is a description of heterogeneity of variance associated with level of the mean, but not as a simple transformation. Variation in phenotypic plasticity, for example among varieties of cereals, in response to environmental differences (see e.g. de Jong & Bijma, 2002, for a review) implies genetic differences in environmental variances. Comparisons of variation between individuals of inbred lines and their F1 crosses typically show lower variance in the hybrid (for examples, see Falconer & Mackay, 1996, p. 268), which led to Lerner's (1954) theory of genetic homeostasis. A more relevant example to this study is that of Sorenensen & Waagepetersen (2003), who found variation in breeding values for residual variance in litter size of pigs for a large data set, which could not be explained simply by the non-normal distribution of that trait. SanCristobal-Gaudy *et al.* (1998) gave evidence for such heterogeneity in two small data sets of goat milk composition and muscle pH in piglets. Other examples include heterogeneity among

Table 6. Changes in parameters with directional selection in the infinitesimal model: effects of magnitude of the genetic covariance

<i>t</i>	$\Delta\mu$	$\Delta\sigma_E^2$	$\sigma_{Am}^2$	$cov_{Amv}$	$\sigma_{Av}^2$	$\sigma_P^2$	$h^2$
Selection practised: $p=0.1, i=1.755, x=1.282$							
0	0.000	0.000	0.500	0.125	0.125	1.500	0.333
1	0.810	0.273	0.376	0.071	0.094	1.649	0.228
2	1.372	0.439	0.383	0.074	0.103	1.822	0.210
4	2.445	0.755	0.396	0.081	0.107	2.152	0.184
8	4.446	1.349	0.416	0.091	0.111	2.764	0.150
0	0.000	0.000	0.500	0.063	0.125	1.500	0.333
1	0.763	0.183	0.405	0.025	0.111	1.588	0.255
2	1.345	0.296	0.402	0.024	0.111	1.699	0.237
4	2.448	0.505	0.409	0.027	0.113	1.914	0.214
8	4.532	0.899	0.420	0.034	0.115	2.320	0.181
0	0.000	0.000	0.500	-0.000	0.125	1.500	0.333
1	0.716	0.094	0.431	-0.024	0.118	1.525	0.283
2	1.311	0.147	0.422	-0.027	0.117	1.569	0.269
4	2.447	0.237	0.423	-0.027	0.118	1.660	0.255
8	4.648	0.408	0.427	-0.024	0.119	1.835	0.233
0	0.000	0.000	0.500	-0.063	0.125	1.500	0.333
1	0.670	0.004	0.453	-0.076	0.123	1.457	0.311
2	1.270	-0.011	0.443	-0.080	0.123	1.432	0.309
4	2.443	-0.053	0.440	-0.082	0.123	1.386	0.317
8	4.822	-0.143	0.439	-0.084	0.122	1.295	0.339
0	0.000	0.000	0.500	-0.125	0.125	1.500	0.333
1	0.623	-0.085	0.472	-0.131	0.126	1.386	0.340
2	1.220	-0.178	0.463	-0.134	0.126	1.285	0.361
4	2.435	-0.374	0.461	-0.138	0.126	1.087	0.424
8	5.125	-0.795	0.472	-0.151	0.125	0.677	0.697

Definitions as in Table 3.

chromosome substitution lines in *Drosophila* (T. F. C. Mackay, personal communication). Whilst stabilizing selection can lead to reduction in variance (see summary by SanCristobal-Gaudy *et al.*, 1998), reductions due to changes due to variation in mean between genotypes and to variation within genotypes are confounded; indeed some degree of such confounding is inevitable in most experiments.

There are other potential sources of information from which estimates of the parameters of heterogeneity used in this theoretical study could be obtained, in particular large families of animals or plants from which reliable estimates of within-family variance could be obtained and hence estimates of between-family variance in that quantity. For livestock, a potential source is large half-sib families of broiler chickens, which are kept in the same environment; although progeny groups of dairy sires used in artificial insemination are also very large, they are scattered over multiple farms, reducing the power of analysis. At the single-locus level, analysis of data on distributions of the alternative phenotypes at known quantitative trait loci or genes would also provide information.

The theoretical analysis shows that there is sufficient flexibility in the model to explain why phenotypic

variances can rise, fall, or remain fairly constant (expressed as variance or CV as appropriate) under directional selection. Indeed, this flexibility is such as perhaps to hamper interpretation of data from experiments. Further, it is important in any analysis to consider correction for scale effects; we are essentially dealing here with components that can not be so explained. Perhaps the clearest prediction is that the effect of directional selection on heterogeneity is likely to be greatest when selection is intense. In experiments in mice for growth, where CVs have remained fairly constant, the fraction of animals selected is rarely much less than one-quarter. In contrast, in *Drosophila* much more intense selection can be and has been practised. Selection experiments for high and low bristle number have been conducted at different selection intensities (Clayton & Robertson, 1957; Frankham *et al.*, 1968), but variances in the different groups were not tabulated. In any case it would be necessary to compare lines after different numbers of generations but after similar changes in mean, i.e. for given selection intensity  $\times$  generation number.

To address the question of the relevance of the theory reported here, it is clear that more data on genetic variation in residual variation are necessary. We do, however, consider that it would be worthwhile to obtain information and meanwhile, in analysis of selection experiments and breeding programmes, to consider the possibility and impact of direct selection on the variance when evaluating selection responses and variability retained.

**Appendix. Prediction of the probability of selection and of induced linkage disequilibrium**

In the text (Eqn 3) the probability of selection is evaluated including only the terms in the Taylor series that are linear in  $a$  and in  $b$ . At least quadratic terms are needed to predict the magnitude of linkage (gametic) disequilibrium induced by directional selection (Bulmer effect).

Then, using the same method as for (3) and excluding cubic and higher terms,

$$\begin{aligned}
 P(a, b)/p &= 1 + ia/\sigma + \frac{1}{2}ixb/\sigma^2 + \frac{1}{2}ix(a/\sigma)^2 \\
 &+ \frac{1}{2}i(x^2 - 1)(a/\sigma)(b/\sigma^2) \\
 &+ (i/8)(x^3 - 3x)(b/\sigma^2)^2 + \dots \quad (A1)
 \end{aligned}$$

which can be rewritten

$$\begin{aligned}
 P(a, b)/p &= 1 + i(a/\sigma + \frac{1}{2}xb/\sigma^2) \\
 &+ \frac{1}{2}ix(a/\sigma + \frac{1}{2}xb/\sigma^2)^2 \\
 &- \frac{1}{2}i(a/\sigma)b/\sigma^2 - (\frac{3}{8})ix(b/\sigma^2)^2 + \dots \quad (A2)
 \end{aligned}$$

To compute the disequilibrium induced by selection in a population initially at equilibrium assuming bi-allelic loci, it is necessary to compute the value of  $D_{12} = f(A_1B_1)f(A_2B_2) - f(A_1B_2)f(A_2B_1)$ , where, for example,  $f(A_1B_1)$  is the frequency of the haplotype  $A_1B_1$  after selection, and the corresponding effects on the mean and variance of the trait are  $a_1 + a_2$  and  $b_1 + b_2$ , respectively. Excluding cubic and higher terms in  $a$  and  $b$  and extending the results of Hill & Robertson (1966), then among selected parents at loci 1 and 2

$$\begin{aligned}
 D_{12} &= [-i(i-x)(a_1/\sigma + \frac{1}{2}xb_1/\sigma^2)(a_2/\sigma + \frac{1}{2}xb_2/\sigma^2) \\
 &- \frac{1}{2}i(a_1b_2 + a_2b_1)/\sigma^3 - \frac{3}{4}ixb_1b_2/\sigma^4] \\
 &\times q_1(1 - q_1)q_2(1 - q_2). \quad (A3)
 \end{aligned}$$

Including terms contributed by disequilibrium, the additive genetic variance is given by summing over loci:

$$\sigma_{Am}^2 = \sum_j 2a_j^2q_j(1 - q_j) + \sum \sum_{j \neq k} 2a_ja_kD_{jk}. \quad (A4)$$

In the infinitesimal model negligible variance is contributed by individual loci, so the inequality in the second term can be removed. Hence, in the next generation, among selected individuals

$$\begin{aligned}
 \sigma_{Am}^2(S, 1) &= \sum_j 2a_j^2q_j(1 - q_j) \\
 &+ \sum \sum_{jk} 2a_ja_k[-i(i-x)(a_j/\sigma + \frac{1}{2}xb_j/\sigma^2) \\
 &\times (a_k/\sigma + \frac{1}{2}xb_k/\sigma^2) - \frac{1}{2}i(a_jb_k + a_kb_j)/\sigma^3 \\
 &- \frac{3}{4}ixb_jb_k/\sigma^4]q_j(1 - q_j)q_k(1 - q_k) \\
 &= \sigma_{Am}^2 - i(i-x)(\sigma_{Am}^2/\sigma + \frac{1}{2}xcov_{Amv}/\sigma^2)^2 \\
 &- i(\sigma_{Am}^2cov_{Amv})/\sigma^3 - \frac{3}{4}ix(cov_{Amv}^2/\sigma^4)]. \quad (A5)
 \end{aligned}$$

Equation (A5) reduces to  $\sigma_{Am}^2 - i(i-x)(\sigma_{Am}^2/\sigma)^2$ , the standard formula, if  $b_j = 0$  at all loci. In (A5) the first term is also proportional to the selection response in the mean, and it is tempting, for simplicity, to ignore the second and third terms in (A5), but doing so can only be justified if the terms in both  $cov_{Amv}/\sigma^2$  and  $\sigma_{Amv}^2/\sigma^4$  are negligible compared with  $\sigma_{Am}^2/\sigma$ .

The variance among selected individuals contributes to the between-family variance in the next generation, and assuming the infinitesimal model so that the variance within families remains constant at its value in the base population, the recurrence equation for variance in generation  $t + 1$  in terms of that in generation  $t$  is given by

$$\begin{aligned}
 \sigma_{Am, t+1}^2 &= \frac{1}{2}\sigma_{Am, 0}^2 + \frac{1}{2}\{\sigma_{Am, t}^2 - i(i-x)[(\sigma_{Am, t}^2/\sigma_t \\
 &+ \frac{1}{2}ixcov_{Amv, t}/\sigma_t^2]^2 - i(\sigma_{Am, t}^2cov_{Amv, t})/\sigma_t^3 \\
 &- \frac{3}{4}ix(cov_{Amv, t}^2/\sigma_t^4)]\}. \quad (A6)
 \end{aligned}$$

Equivalent recurrence formulae for  $cov_{A_{mv},t+1}$  and  $\sigma_{A_{v},t+1}^2$  in terms of quantities in the base population and at generation  $t$  follow from (A3) and extending (A4)–(A6) are given in the text (Eqns 12–14).

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