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Genetic analysis of environmental variation

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Summary

Environmental variation (V_E) in a quantitative trait – variation in phenotype that cannot be explained by genetic variation or identifiable genetic differences – can be regarded as being under some degree of genetic control. Such variation may be either between repeated expressions of the same trait within individuals (e.g. for bilateral traits), in the phenotype of different individuals, where variation within families may differ, or in both components. We consider alternative models for defining the distribution of phenotypes to include a component due to heterogeneity of V_E. We review evidence for the presence of genetic variation in V_E and estimates of its magnitude. Typically the heritability of V_E is under 10%, but its genetic coefficient of variation is typically 20% or more. We consider experimental designs appropriate for estimating genetic variance in V_E and review alternative methods of estimation. We consider the effects of stabilizing and directional selection on V_E and review both the forces that might be maintaining levels of V_E and heritability found in populations. We also evaluate the opportunities for reducing V_E in breeding programmes. Although empirical and theoretical studies have increased our understanding of genetic control of environmental variance, many issues remain unresolved.

1. Introduction

The phenotypic variation (V_P) in quantitative traits comprises genetic and non-genetic components, plus possible interactions and covariances between them (Falconer & Mackay, 1996; Lynch & Walsh, 1998). The proportion of each component differs markedly among traits, although the proportion that is genetic is typically highest for traits related to morphology (e.g. mature size and conformation) and lowest for traits more closely related to fitness (e.g. litter size). For any type of trait, however, the values are typically quite similar among species.

The genotypic variance, V_G, is usually partitioned into additive genetic (V_A) and non-additive components, and the parameter most often used to compare the magnitudes of genetic and phenotypic variance is the narrow sense heritability ($h^2 = V_A/V_P$), because it is easiest to estimate from information on relatives and is used in prediction of progeny performance. In practice, however, it can be difficult to distinguish between non-additive genetic and environmental variance without the use of clones or inbred lines, as both are components of within-family variance. An alternative measure of the phenotypic variability is the coefficient of variation ($CV = \sqrt{V_P}/\mu$), which facilitates comparisons among traits and species, and the coefficient of evolvability ($CV_A = \sqrt{V_A}/\mu$) defines its additive genetic component (Houle, 1992).

Variation in quantitative traits is ubiquitous, and there has been extensive analysis and discussion as to what maintains genetic variation. This requires some balance between the input from mutation and loss by drift and by most, if not all, selective forces acting directly on the trait itself or through pleiotropic effects. There is not yet, however, an unequivocal conclusion as to how the typical levels of genetic variance are maintained (e.g. Bürger, 2000; Johnson & Barton, 2005; Zhang & Hill, 2005*a*; Hill, 2010).

Much less attention has been paid to factors accounting for the magnitude of the V_P, V_E or the CV. The CV is typically smaller for morphological traits

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(e.g. adult size) than for traits related to reproductive fitness (e.g. litter size and egg number). These quantities are not functions of the genetic variance, although typically the CV and heritability are negatively correlated. Understanding the forces that determine the magnitude of the non-genetic component of phenotypic variance is a broad question in evolutionary biology.

Thus, we wish to know how selection and other evolutionary forces are likely to influence V_E, both the variance observable among repeated records on the same individual (expressed as what is often termed 'fluctuating asymmetry' (FA)) and that between individuals. Selective forces may include stabilizing selection, which is likely to reduce variation and environmental heterogeneity in time and space, which might increase variation as individuals have to be plastic to cope successfully with varying resources.

A related topic, but which we will not pursue here, is that of canalization in its specific sense of reduced variation found for a particular phenotype (Waddington, 1942; Rendel *et al.* 1966), which has been subject to theoretical analysis in recent years by Wagner *et al.* (1997), Gavrilets & Hastings (1994) and others. Here we concentrate on the more general nature of V_E found over any range of genotypic or phenotypic mean.

The level of variation is also of importance in agricultural production because product consistency is desirable in growing, processing and consumption of foods. While it may be possible to avoid genetic variation by the use of inbred lines or their crosses, the non-genetic component cannot be avoided. Hence, there has been research recently in animal breeding on the extent to which variation can be reduced by selection so as to improve homogeneity, with the potential additional benefit of increasing accuracy of selection.

In this review we are concerned with the variation among or within individuals maintained in the same environment. A rather different but related topic is that of 'robustness' or sensitivity, which describes the extent to which the mean phenotype changes according to the environment. Differences among genotypes in such robustness give rise to genotype × environment interaction, but we shall not discuss these further in this review and focus on analyses within an identifiable (macro-) environment. Individuals within such an environment will each experience their own micro-environment, but these environmental differences are not identified. Differences among genotypes in V_E may therefore reflect, at least in part, their differing sensitivity to micro-environmental factors (e.g. Falconer & Mackay, 1996).

The approach used to analyse and understand the magnitude of the environmental variance (or of the CV or CV_E) is to consider it as a trait in its own right. For traits that are expressed or recorded only once in an individual's lifetime, there is only one environmental component, E, that can be considered. If there are two or more records, for example, of bristles on opposite sides of a fly or of piglet weight within a litter, this can be partitioned into two components, the general or permanent environment effect, E_g and that specific to individual records, E_s (Falconer & Mackay, 1996). In principle, there can be genetic variation in both components, but it may not be possible to separate them. An indicator of robustness and of fitness, widely used in evolutionary studies, is FA (Van Valen, 1962), which is a measure of individual asymmetry in bilateral traits that are symmetric at the population level, for example, features of a fly's wing or a human face and is measured as the variance in E_s. In this review, we shall concentrate primarily on the variation among individuals; reviews on FA have been published elsewhere (e.g. Leamy & Klingenberg, 2005).

Since the genotype for the magnitude of environmental variation can be regarded as a quantitative trait, it is assumed to be determined by the actions and interactions of multiple genes. Much of the standard methodology of quantitative genetics can then be invoked. We do, however, have to recognize that the variances are unlikely to be normally (Gaussian) distributed, that there are inevitable problems of scale when considering the correlation or covariance of trait mean and variance and that natural selection acts on the individual phenotype, not on the 'variation trait'.

Here we review the current state of knowledge of inheritance of environmental variance. We start by discussing quantitative genetic and statistical modelling of V_E, methods of analysis and experimental designs for estimating the genetic variance in V_E, and estimates which have been obtained of its magnitude. We subsequently consider the dynamics: the influences of artificial and of natural selection on V_E and the evolutionary forces that determine the levels of heritability in natural and domesticated populations. We conclude with uncertainties and questions to be answered in the future.

2. Quantitative genetic models

(i) *Alternative models*

In standard quantitative genetic models, the variation in phenotype given genotype, $\mathrm{Var}(P|G)$, or V_E, is assumed to be constant. When different genotypes differ in their environmental variance, we can postulate that some genes affect the phenotype and others affect the environmental variance or both, such that $\mathrm{Var}(P|G)$ depends on genotype. We can then define genotypic effects on both the mean and the variance. For simplicity and practicality of estimation, these are

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typically restricted to additive genetic effects. Different mathematical functions have been proposed to model the effect of genes on environmental variance, and here we discuss and compare their mathematical and statistical properties and their utility for predicting response to selection. We start with models assuming a single observation on an individual, and then extend the principles to include repeated observations on an individual.

In the *additive model*, the genetic component for variance is modelled as an additive effect on the environment variance (Hill & Zhang, 2004; Mulder *et al*., 2007):

$$P=\mu+A_{\mathrm{m}}+\chi\sqrt{\sigma^2_{\mathrm{E}}+A_{\mathrm{v}}}, \quad (1)$$

where μ and σ^2_{E} are, respectively, the mean trait value and the mean environmental variance of the population, A_{m} and A_{v} are, respectively, the additive genetic effects for the mean and environmental variance and χ is a standard normal deviate, $N(0,1)$, for the environmental effect. The additive genetic effects for individuals are assumed to follow a bivariate normal distribution, where $\sigma^2_{A_{\mathrm{m}}}$, $\sigma^2_{A_{\mathrm{v}}}$, $cov_{A_{\mathrm{mv}}}=\mathrm{cov}(A_{\mathrm{m}},A_{\mathrm{v}})=r_{\mathrm{A}}\sigma_{A_{\mathrm{m}}}\sigma_{A_{\mathrm{v}}}$ and r_{A} are the additive genetic variances, covariance and correlation of A_{m} and A_{v}, respectively. Covariances among individuals are additionally defined by the additive genetic relationship matrix. Note that $\sqrt{\sigma^2_{\mathrm{E}}+A_{\mathrm{v}}}$ is defined only if $\sigma^2_{\mathrm{E}}+A_{\mathrm{v}}>0$, and so the model breaks down if $\sigma^2_{A_{\mathrm{v}}}$ is very high. The model can easily be extended to include systematic environmental sources of heterogeneity of environmental variance such as herd effects. Random non-systematic environmental effects on the environmental variance are observed as sampling effects, but are not explicit in the quantitative genetic model.

In the *standard deviation model*, the genetic component for variance is modelled as an additive effect on the environmental standard deviation (Garcia *et al*., 2009):

$$P=\mu+A_{\mathrm{m}}+\chi(\sigma_{\mathrm{E}}+A_{\mathrm{v,SD}}). \quad (2)$$

It is very similar to model (1) and has the same limitation in being defined only when $\sigma_{\mathrm{E}}+A_{\mathrm{v,SD}}>0$. The magnitudes of $\sigma^2_{A_{\mathrm{v}}}$ differ between the models, however.

The *exponential model* (SanCristobal-Gaudy *et al*., 1998) is multiplicative on the level of the environmental effect, but additive on the level of the natural logarithm of the variance scale

$$P=\mu+A_{\mathrm{m}}+\chi\exp\left[\tfrac{1}{2}(\log(\sigma^2_{\mathrm{e}})+A_{\mathrm{v,exp}})\right]. \quad (3)$$

Modelling variances on the log scale is convenient because the log of a variance estimate tends to a normal distribution when the degrees of freedom are large. Modelling the log of variances has been applied in structural models to account for heterogeneity of variance between experimental units or farms (e.g. Foulley & Quaas, 1995; Foulley *et al*., 1998) and for genetic heterogeneity of environmental variance (SanCristobal-Gaudy *et al*., 1998; Sorensen & Waagepetersen, 2003).

In the *reaction norm model*, the genetic component of variance is additive on the level of the reaction norm (Gavrilets & Hastings, 1994; Gimelfarb, 1994; Wagner *et al*., 1997; Wu & O'Malley, 1998):

$$P=\mu+A_{\mathrm{m}}+\gamma\, e=\mu+A_{\mathrm{m}}+(\beta+A_{\mathrm{v,RN}})e, \quad (4)$$

where γ is the multiplication factor, with mean β and e is the unscaled environmental effect. It is equivalent to the linear reaction norm model (Finlay & Wilkinson, 1963), but the unscaled environmental effect is used instead of an environmental descriptive parameter.

(ii) *Comparison of models*

When the models are compared in terms of their expectations and variances (Table 1), the standard deviation and the reaction norm models are equivalent and can be re-parameterized from one to the other. The average environmental variance is a function of $\sigma^2_{A_{\mathrm{v}}}$ for the standard deviation model, the exponential model and the reaction norm model, but not for the additive model. Additive genetic values, A_{v}, can be converted from the standard deviation, exponential and reaction norm model to the additive model (Table 2) by equating the second central moments of the environmental effects and similarly those for additive genetic variances, $\sigma^2_{A_{\mathrm{v}}}$, by equating their fourth central moments.

The expectation of the environmental variance given A_{v} is linear for the additive model, but shows some non-linearity (concave upwards) for the other models, starting to become substantial when $|A_{\mathrm{v}}|>2\mathrm{SD}$; the curvilinearity increases with increasing $\sigma^2_{A_{\mathrm{v}}}$. The departure from the additive model is greatest for the exponential model.

(iii) *Extension to repeated observations on an individual*

As there may be genetic variation in environmental variation both within and between individuals, we extend the additive model for repeated observations using the additive model, but the principles are straightforward to extend to the other models.

Repeated observations lead to covariances between environmental effects. To account for these, the environmental effects can be expressed as a sum of permanent environmental effects, common to all records of the individual (Falconer & Mackay, 1996), and specific environmental effects $P_{ij}=\mu+A_{\mathrm{m},i}+PE_{\mathrm{m},i}+E_{ij}$. Analyses of genetic heterogeneity of

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Table 1. *Expectation of environmental effect and environmental variance with additive models on variance and standard deviation, exponential and reaction norm models on variance* (*modified from Walsh & Lynch, 2010*)

Model[a]	Var(E)	E	var(E)|A_v	$E(\text{var}(E)) = \overline{\sigma^2_E}$
Additive	σ^2_E	$\sqrt{(\sigma^2_E + A_v)}\chi$	$\sigma^2_E + A_v$	σ^2_E
Standard deviation	$\sigma^2_{e,SD}$	$(\sigma_{e,SD} + A_{v,SD})\chi$	$\sigma^2_{e,SD} + 2A_{v,SD}\sigma_{e,SD} + A^2_{v,SD}$	$\sigma^2_{e,SD} + \sigma^2_{A_v,SD}$
Exponential	$\sigma^2_{e,exp}$	$\exp(\frac{1}{2}A_{v,exp})e_{exp}$	$\exp(A_{v,exp})\sigma^2_{e,exp}$	$\exp(\frac{1}{2}\sigma^2_{A_{v,exp}})\sigma^2_{e,exp}$
Reaction norm	$\sigma^2_{e,RN}$	$(\beta + A_{v,RN})e_{RN}$	$(\beta + A_{v,RN})^2\sigma^2_{e,RN}$	$(\beta^2 + \sigma^2_{A_v,RN})\sigma^2_{e,RN}$

[a] A_v is the additive genetic effect for environmental variance, E is the environmental effect, χ is standard normal deviate, e_{exp} and e_{RN} are the unscaled environmental effects for exponential and reaction norm models and β is the average reaction norm = 1.

Table 2. *Conversion of breeding values* (A_v) *and its genetic variance of* ($\sigma^2_{A_v}$) *from standard deviation, exponential and reaction norm models to the additive model* (*based on Mulder* et al.*, 2007*)

Model	Breeding value	Var(E)	A_v in additive model	Var(A_v) in additive model
Additive	A_v	σ^2_E	A_v	$\sigma^2_{A_v}$
Standard deviation	$A_{v,SD}$	$\sigma^2_{e,SD}$	$A_v = \sigma^2_{e,SD} + \sigma^2_{A_{v,SD}} - \sigma^2_E + 2A_{v,SD}\sigma_{e,SD}$	$\sigma^2_{A_v} = 4\sigma^2_{A_{v,SD}}\sigma^2_{e,SD}$
Exponential	$A_{v,exp}$	$\sigma^2_{e,exp}$	$A_v = \sigma^2_{e,exp}\exp(A_{v,exp}) - \sigma^2_E$	$\sigma^2_{A_v} = \sigma^4_{e,exp}\exp(2\sigma^2_{A_{v,exp}}) - \sigma^4_E$
Multiplicative ($\beta = 1$)	$A_{v,RN}$	$\sigma^2_{e,RN}$	$A_v = \sigma^2_{e,RN} + \sigma^2_{A_{v,RN}} - \sigma^2_E + 2A_{v,RN}\sigma_{e,RN}$	$\sigma^2_{A_v} = 4\sigma^2_{A_{v,RN}}\sigma^4_{e,RN}$

variance have so far included only one of these effects, but any of the fuller models can be obtained by extending eqns (1–4), assuming that both general and specific environmental effects are under genetic control. For the additive model, from (1):

$$P_{ij} = \mu + A_{m,i} + \chi_{PE,i}\sqrt{\sigma^2_{PE} + A_{v,PE,i}} + \chi_{E,ij}\sqrt{\sigma^2_E + PE_{v,i} + A_{v,E,i}}, \quad (5)$$

where definitions are extensions of those given previously and $\chi_{PE,i}$ and $\chi_{E,ij}$ are $N(0,1)$. The additive genetic effects $A_{m,i}$, $A_{v,PE,i}$ and $A_{v,E,i}$ are assumed to be trivariate normal and the permanent environmental effects $PE_{m,i}$ and $PE_{v,i}$ to be bivariate normal, each with corresponding variances and covariances.

The model is highly parameterized and needs very good designs if all parameters are to be estimated. In principle it postulates that the repeatability of a trait is genetically determined, by genetic variance not only of specific environmental effects, but also of permanent environmentally effects. These genetic effects on the permanent and specific environment effects may be highly correlated, as both depend on the individual's ability to respond to environmental conditions. The estimation of $\sigma^2_{A_v,PE}$ requires family relationships, whereas $\sigma^2_{A_v,E}$ can be estimated based on both repeated observations on the individual itself and family relationships. Analysis of the power to estimate all parameters and development of statistical methods need further research.

3. Statistical analysis of large populations

Several methods have been proposed for estimating genetic heterogeneity in V_E. As the between-individual environmental variance can never be estimated directly unless clones or MZ twins are used, some measure of residual variance or squared residuals is modelled in order to estimate (additive) genetic variance in V_E.

The simplest type of analysis in segregating populations uses the within-family variances to estimate directly the genetic variance in V_E (e.g. Rowe *et al.*, 2006; Ordas *et al.*, 2008), i.e. by restricted maximum likelihood (REML) or least squares. In this analysis, the strong assumption is made that there are no systematic environmental effects that influence the within-family variance, although heterogeneity of environmental or residual variance has been observed in many situations. The method used by Rowe *et al.* (2006) gave upwardly biased estimates of genetic variance in V_E of broiler body weights in the data of Mulder *et al.* (2009), as the records spanned a long time period. More advanced methods have been developed that are aimed at reducing such bias (e.g. SanCristobal-Gaudy *et al.*, 1998, 2001; Sorensen & Waagepetersen, 2003; Mulder *et al.*, 2009; Rönnegård *et al.*, 2010).

SanCristobal-Gaudy *et al.* (1998, 2001) developed an EM–REML algorithm using expectation-maximisation and incorporating a structural model on the residual variance. In a structural model, fixed and random effects for both the mean and the log of

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the residual variance are fitted simultaneously, allowing for covariance structures between random effects on mean and on residual variance. To obtain solutions they used an iterative system because analytical integrals of some expressions were not available. Other simpler REML applications make use of a two-step approach, fitting a model on the phenotype in the first step and a model in which the (transformed) squared residuals are used as proxies for squared environmental effects in the second step. There are two main problems with using squared residuals, however: the residual is a mixture of true environmental effects and unexplained other effects; and if residuals are truly normally distributed, their squares are χ^2 distributed, violating the normality assumptions when the squared residuals are analysed as a trait.

The accuracy of squared residuals (i.e. correlation between squared environmental effects and squared residuals) is a function of the accuracy of the estimated effects (i.e. correlation between true and estimated effects) and is reflected in the so-called hat-matrix of the mixed model equations, for which diagonal elements are called 'leverages' (Hoaglin & Welsch, 1978). The hat-matrix describes the influence each observed value has on each fitted value and the leverage describes the influence each observed value has on the fitted value for that same observation (Hoaglin & Welsch, 1978). This idea of accounting for leverages is implemented in the double hierarchical generalized linear model (DHGLM) (Rönnegård *et al*., 2010), where the squared residuals are assumed to be gamma distributed, the residual variance is fitted using a generalized linear model (GLM) with gamma-distributed residuals to resolve the non-normality problem and the algorithm iterates between a model on the phenotype and a model on the residual variance. The DHGLM algorithm can be implemented in ASREML (Gilmour *et al.,* 2006), but estimation of the genetic correlation between effects for mean and residual variance is not possible with the current algorithm (Rönnegård *et al*., 2010). Although less appealing in theory than GLM, the non-normality of squared residuals can be resolved by appropriate transformations (Mulder *et al*., 2009).

An alternative way to model genetic heterogeneity of residual variance is to use structural modelling of variances in a Bayesian framework (Sorensen & Waagepetersen, 2003; Sorensen, 2009) and Markov chain Monte Carlo (MCMC) sampling to estimate all the parameters, both on phenotype and residual variance. Complex sampling algorithms (e.g. mixtures of Gibbs sampling and Metropolis–Hastings or Langevin–Hastings algorithms) are necessary in order to estimate all parameters because full conditional distributions are not of standard form, and some approximations may be used to increase efficiency and reduce computing time (Waagepetersen *et al*., 2008). Even so, computing time may prohibit the use of these highly dimensional models on extremely large data sets. Although a potential downside of the Bayesian approach is its dependence on priors and prior distributions, results are not strongly dependent on them (Sorensen & Waagepetersen, 2003; Ibáñez-Escriche *et al*., 2008*a*).

In the Bayesian approach, all parameters can be estimated in all designs, posterior intervals give information about the precision and model selection criteria such as the deviance information criterion and Bayes factors can be used to compare the fit of different models (Sorensen & Waagepetersen, 2003). In the computationally much less demanding REML framework, methods of comparison are less developed and there is not yet a well-established way to estimate the genetic correlation between the additive genetic effects on mean and V_E.

The Bayesian methodology has been used in a number of studies to estimate the genetic variation in V_E (Table 3) and a software package is now freely available (Ibáñez-Escriche *et al*., 2010). Some published studies using both REML and Bayesian methods on the same data have given similar estimates of genetic variance in V_E (Rönnegård *et al*., 2010; Wolc *et al*., 2009) and others quite different estimates (Gutierrez *et al*., 2006). A more formal comparison on simulated and on real data using cross-validation is recommended for repeated observations on the same individual or with large family groups.

One of the main dilemmas in estimating genetic variation in V_E is that these highly dimensional models may pick up some confounding effects. Perhaps most importantly, skew and kurtosis in the data may lead to biased estimates. Therefore, Box–Cox transformation has been proposed to transform the data and can have a substantial effect on estimates of the genetic variance in V_E and the genetic correlation between mean and V_E (Yang *et al*., 2010). Another solution might be to use residuals with a Student's *t*-distribution, which are more robust to their non-normality (Rosa *et al*., 2003; Cardoso *et al*., 2005).

There are some important assumptions in many of these analyses. The first is that there is no confounding of environmental variance with non-additive genetic components. These are overtly confounded in simple analyses such as those in which heterogeneity of variance within half-sib families is undertaken. In other more sophisticated methods such as fitting a structural model, there again can be confounding because covariances of relatives include both additive genetic and other genetic variance components. The particular concern is that there are individual genes or quantitative trait loci (QTL) segregating with individually large effect on the trait. Although these may lead to heterogeneity of within-family variance, Rowe

Table 3. *Published estimates of heritability* ($h_v^2 = \sigma_{A_v}^2/(2\sigma_P^4 + 3\sigma_{A_v}^2)$), *genetic coefficients of variation* ($GCV_E = \sigma_{A_v}/\sigma_E^2$) *and genetic correlation* ($r_{A_{mv}}$) *between additive genetic effects for mean and environmental variance*. (– *no estimate published*)

Source	Trait	Method[a]	h_v^2	*GCV*	$r_{A_{mv}}$
SanCristobal-Gaudy *et al.* (1998)	Fat/protein ratio milk goats	REML	0·000	0·00	–
	pH muscle pigs	REML	0·039	0·40	0·79
SanCristobal-Gaudy *et al.* (2001)	Litter size sheep	REML	0·048	0·51	0·19
Sorensen & Waagepetersen (2003)	Litter size pigs	MCMC	0·026	0·31	−0·62
Ros *et al.* (2004)	Body weight snails	MCMC	0·017	0·58	−0·81
Rowe *et al.* (2006)	Body weight broiler males, females	ANOVA	0·029, 0·031	0·30, 0·32	−0·17, −0·11
Gutierrez *et al.* (2006)	Litter size, litter weight mice	MCMC	0·048, 0·039	0·44, 0·37	−0·93, −0·81
	Birth weight mice	MCMC	0·208	1·21	0·97
Ibáñez-Escriche *et al.* (2008*a*)	Body weight 21d, 42d old mice	MCMC	0·006	0·36	−0·31
	Weight gain mice	MCMC	0·018	0·47	−0·19
Ibáñez-Escriche *et al.* (2008*b*)	Litter size rabbits	MCMC	0·045	0·42	−0·74
Ibáñez-Escriche *et al.* (2008*c*)	Slaughter weight pigs	MCMC	0·011	0·34	−0·07
Garreau *et al.* (2008)	Birth weight rabbits	REML	0·013	0·25	–
Ordas *et al.* (2008)	Plant height, ear height maize	ANOVA	–	0·24, 0·19	–
	Tassel length, days to flowering maize	ANOVA	–	0·15, 0·21	–
Wolc *et al.* (2009)	Body weight broiler males, females	REML	0·030, 0·038	0·32, 0·37	−0·23, −0·27
	Conformation score broiler males, females	REML	0·023, 0·032	0·25, 0·31	0·40, 0·33
Mulder *et al.* (2009)	Body weight broiler males, females	REML	0·046, 0·047	0·49, 0·57	−0·45, −0·41
Yang *et al.* (2010)	Litter size rabbits, pigs[b] (no Box–Cox)	MCMC	0·041, 0·021	0·37, 0·27	−0·73, −0·64
	Litter size rabbits, pigs[b] (+ Box–Cox)	MCMC	0·017, 0·012	0·24, 0·19	0·28, 0·70

[a] Methods classified into ANOVA, REML and MCMC. Within the REML methods in particular there are substantial differences in procedures applied (see text).
[b] Before and after Box–Cox transformation of data.

et al. (2006) concluded that it could not explain the amount of heterogeneity found in their study. In general, however, all methods rely to some extent on the infinitesimal model and normality assumptions and all methods may be biased if these are violated.

4. Empirical evidence for genetic variation in environmental variance

(i) *Direct estimates of* V_E

Inbred lines (Whitlock & Fowler, 1999; Sorensen *et al.*, 2007) and chromosome substitution lines (Mackay & Lyman, 2005) have provided direct evidence of overall genetic variation in V_E in *Drosophila melanogaster*. The differences in V_E for bristle number observed by Mackay and Lyman, for example, cannot be accounted for solely by scale transformation. Individual genes associated with differences in V_E or CV_E have also been identified, e.g. the *Dopa decarboxylase* (*Ddc*) gene in *D. melanogaster* was shown to cause differences of up to 5% between homozygotes in CV_E of abdominal bristle number (Mackay & Lyman, 2005). There are widely accepted differences in environmental variability between inbred lines and their hybrid crosses (Lerner, 1954; Falconer & Mackay, 1996; Lynch & Walsh, 1998). At a more basic level, genetic differences in variability of gene expression differences among cells have been observed (Ansel *et al.*, 2008), which may in turn provide insight into the magnitude of differences found at the level of the observable trait.

(ii) *Estimates in large segregating populations*

In the last ten years many estimates of genetic variance in V_E between individuals have been published, predominately of body weight or litter traits. Table 3 updates that of Mulder *et al.* (2007) and shows estimates of heritability (h_v^2), genetic coefficient of variation (GCV_E; note also that $GCV_E^2 \approx \sigma_{A_v,\exp}^2$) based on the linear model and genetic correlations ($r_{A_{mv}}$) between the additive genetic effects for mean and V_E. With one exception (Gutierrez *et al.*, 2006, for body weight in mice), estimates of h_v^2 range between 0·0 and 0·05 and those for GCV_E between 0·0 and 0·60, albeit

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with some consistency, and median values are 3 and 30 %, respectively. Estimates of $r_{A_{mv}}$ take up the whole parameter space between $-1{\cdot}0$ and $1{\cdot}0$, but tend to be negative for the body weight traits. Estimates are based on different models (see above) and data structures, however, and the studies using MCMC all have quite large 95 %-posterior intervals. In addition, Yang *et al.* (2010) showed that Box–Cox transformation of litter size data of pigs and rabbits reduced h_v^2 by, respectively, 45 and 51 % and $r_{A_{mv}}$ changed sign.

Studies are not included in Table 3 if published results were insufficient to compute h_v^2 and GCV_E. In these the heritability reported for within-litter variability of birth weight generally lies in the range 0·06–0·11 (Damgaard *et al.*, 2003; Wittenburg *et al.*, 2008; Canario *et al.,* 2010). In some older studies, ANOVA techniques were used to analyse within-family variances of dairy bulls with large offspring groups, and substantial differences between sires were found (Van Vleck, 1968; Clay *et al.*, 1979).

There is substantial literature and discussion on estimates of genetic parameters for FA, which are *de facto* repeat records with only two observations. The data come particularly from Drosophila and humans (Møller & Thornhill, 1997; Gangestad & Thornhill, 1999; Fuller & Houle, 2003; Leamy & Klingenberg, 2005). The general finding is that heritability estimates are low and averaging about 0·03 (Fuller & Houle, 2003), but depend to some extent on the trait and on the statistical methodology used. By aggregating traits on each side of the body, for example physical dimensions in humans, Johnson *et al.* (2008) show that heritabilities over 0·25 can be obtained.

(iii) *Results from selection experiments*

Other evidence for the existence of genetic variation in V_E comes from selection experiments, but changes in genetic and environmental variances are often confounded and results are not clear cut. No significant changes in phenotypic variance of body size of mice were found by Falconer & Robertson (1956) who selected mice with either the largest deviations or the smallest deviations from their litter-mean. Following canalizing selection in both *D. melanogaster* (Rendel *et al.*, 1966) and *Tribolium castaneum* (Kaufman *et al.*, 1977) substantial decreases in phenotypic variance were obtained, both V_G and V_E decreasing in the latter. Disruptive selection in *D. melano*gaster led to increases in V_G and V_E in one experiment (Scharloo *et al.* 1972), but only in V_G in another (Sorensen & Hill, 1983), and there were substantial changes in phenotypic variance following selection on higher and lower within-family variance in *Tribolium* (Cardin & Minvielle, 1986). Although phenotypic variance can change greatly in directional selection experiments (Clayton & Robertson, 1957; Falconer & Mackay, 1996), these changes are further confounded by scale effects.

A few selection experiments have been conducted to reduce phenotypic variance by selecting on estimated breeding value (EBV) for environmental variance. No response to divergent selection in pigs on EBV for V_E in pH was observed by Larzul *et al.* (2006), but EBVs were based on only four progeny and had low accuracy. In experiments with rabbits, divergent selection was practised for eight generations on within-litter variability in birth weight (Garreau *et al.*, 2008; Bodin *et al.*, 2010) and for high or low variability in litter size for three generations in another population (Argente *et al.*, 2010). Although a substantial response was obtained in the first generation in both experiments, only after generation 5 was further response achieved in the experiment of Bodin *et al.* (2010) and little further response was obtained by Argente *et al.* (2010).

(iv) *Conclusion*

There are data from genetically homogeneous populations showing genetic variation in V_E. From the published results on analyses of large outbred populations and selection experiments, it can be concluded that there is much empirical evidence for the existence of additive genetic variation in V_E, although appropriate modelling of genetic heterogeneity of environmental variance remains a challenging area. The results from the selection experiments are not convincing, but changes in variance in the expected direction seem to be observed in the majority. There may, however, be some publication bias.

5. Experimental design for estimating genetic parameters

In laboratory- and population-based studies where new information has to be collected in order to obtain estimates of parameters such as the variance or QTL effects for genetic heterogeneity of V_E, designs can be optimized and the minimal experimental size determined. For field data already collected, there is little opportunity to influence design, but the expected sampling errors of estimates and power of detection can determine whether it is worthwhile doing any analysis. It is assumed that the basic observations X are normally distributed, and also, where necessary, that the distributions among groups of log variance estimates are also normally distributed.

(i) *Estimating QTL or other fixed effects*

For comparing two groups each with n observations, and assuming only V_E is unaccounted for, the sampling error of the difference in means is $2V_E/n$ and

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of (natural) log variance $4/n$. Hence, roughly twice as many observations are required to detect a proportional effect on variance of the same size as an effect on mean expressed in SD units. For example, if the sample size is 1000 and there is a real 10% proportionate difference (b) in variance, $b/\mathrm{SE}(b) \sim 1{\cdot}6$ and the power to detect the difference would be low. More records are needed if degrees of freedom are lost through fixed effects and/or if genetic variance in addition to V_E is included in the error variance. Yang (2010) considered detection of QTL in an association study more formally but, as she assumed the variance in one of the groups was known without error, sampling variances were half the above.

The analysis was further developed by Visscher & Posthuma (2010) for a linear regression of (mean or) variances of genotype (scored 1, 2, 3), with estimation of V_P and V_E from sets of either unrelated individuals or identical twin pairs. They argue that, as genome-wide association studies rarely find loci accounting for over 1% of variation in mean human height, effects on V_E are also likely to be small. As tiny type-I errors are needed in whole genome investigations, very large samples will be needed, e.g. over 10 000 individuals or monozygotic (MZ) twin pairs (over all genotypes) to detect a QTL with an effect of 10% on the variance. They further show that, if the QTL affects only V_E, identical twin pairs give a more efficient design than unrelated individuals. Even though power is low, seeking QTL affecting variance is a cheap by-product of studying genome-wide associations for trait mean.

(ii) *Estimation of components of variance*

To study the inheritance of V_E, measures of variance on relatives are needed. The more highly related they are, the smaller is the sampling variance of the estimates, but the greater is the risk of confounding by environmental covariances. If interest is in estimating the genotypic rather than the additive genetic variance, and if they are available, clones or highly inbred/isogenic lines are most efficient. Otherwise family studies are needed, and design considerations are similar to those for estimating the usual genetic variances (i.e. σ^2_{Am}).

For simplicity consider a one-way classification with n individuals, each with single records; if repeat records are being analysed, a further nested effect is needed. Results initially derived for an additive model (Hill, 2004), are simpler to optimize using the exponential variance model. If $z_i = \log[\sum_j (X_{ij} - \bar{X}_i)^2/(n-1)]$ in group i, z_i has an approximate normal distribution with variance $2/(n-1) + \gamma^2$, where γ^2 is the CV^2 of the variance within groups. For large n and m (needed for useful estimates) and $\gamma^2 \to 0$, it can be shown that $\mathrm{SE}(\hat{\gamma}) \sim [\sqrt{(8/m)}]/n$ and is increased by a factor $1/R$ to estimate 'heritability' if family members have relationship R. For example, with 100 half-sib families each of size 20, $\mathrm{SE}(\hat{\gamma}^2) \sim 0{\cdot}014$, so a much larger experiment would be needed to get much power to detect $\sigma^2_{A_v} > 0$, if the true value of γ^2 is small (see also Mulder, 2007). The SE would be halved by a doubling of family size or by a fourfold increase in the number of families. The optimum family size, $2/\gamma^2$ for a specified total number recorded, is large because the genetic variance in V_E is generally low, just as for estimating the usual heritability of a very lowly heritable trait (Robertson, 1959; Falconer & Mackay, 1996).

(iii) *Selection experiments*

As selection intensities for disruptive selection can be higher than for stabilizing selection, the former is likely to provide a more powerful test of whether $\sigma^2_{A_v} > 0$, but analysis is complicated by changes in genetic variance due to gametic disequilibrium. For a trait recorded only once on each individual, selection has to be practised among families and so, to maintain large-enough families to practise accurate selection with adequate effective population size, selection intensity has to be low. Power calculations for short-term experiments to detect between individual variance in V_E show that such experiments may be feasible, but need large resources (Mulder, 2007).

If, however, the trait of interest is variance among repeated observations on each individual, truncation selection can be practised on within-individual variance among n records. Ibáñez-Escriche *et al.* (2008*b*) consider the optimization and concluded that such a selection experiment to estimate the genetic variance in V_{Ew} would also have to be large, particularly when n is small (e.g. $n = 2$, for bilateral traits).

In principle, information on the between individual heterogeneity can come from data on traditional mass selection experiments to increase or decrease the mean. In practice, however, analysis and interpretation of data to reveal the genetic variance in heterogeneity is complicated by potential changes in genetic variance caused by selection, which are predictable under infinitesimal model assumptions, but not otherwise (Hill & Zhang, 2004; Mulder, 2007; Mulder *et al.*, 2008).

6. Effects of selection on environmental variance

Selection changes gene frequencies and hence the population mean and the genetic variance. Selection can also influence the magnitude of non-genetic components of phenotypic variance if these are at least partially under genetic control and genes responsible are segregating in the population. In the evolutionary literature, following Bull (1987), much of the interest has been on studying the extent to which stabilizing

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Box 1. *Some formulae for predicting response to selection in mean, μ and environmental variance, V_E*

Changes due to a gene with effect a on mean and b on V_E as a function of relative fitness $w/\bar{w}$ and magnitude of mutation effects

$$\Delta\mu = \mathrm{cov}(w/\bar{w},\ a) + \Delta_u\mu \text{ and } \Delta V_E = \mathrm{cov}(w/\bar{w},\ b)\ + \Delta_u V_E. \tag{B1}$$

Under *stabilizing selection* with optimum Θ and strength V_S, relative fitness is

$$w/\bar{w} \approx \text{const} + (\Theta-\mu)a/V_S + \tfrac{1}{2}[((\Theta-\mu)^2 - V_S)(b+a^2)]/V_S^2. \tag{B2}$$

Assuming a normal distribution of a and b,

$$\begin{aligned}\Delta\mu &\approx (\Theta-\mu)\sigma^2_{A_m}/V_S + \tfrac{1}{2}[(\Theta-\mu)^2 - V_S]\mathrm{cov}_{A_{mv}}/{V_S}^2 + \Delta_u\mu,\\ \Delta V_E &\approx (\Theta-\mu)\mathrm{cov}_{A_{mv}}/V_S + \tfrac{1}{2}[(\Theta-\mu)^2 - V_S]\sigma^2_{A_v}/{V_S}^2 + \Delta_u V_E.\end{aligned} \tag{B3}$$

For *truncation selection* of a proportion p, with i the corresponding selection intensity and x the standardized truncation point, relative fitness is

$$w/\bar{w} \approx \text{const.} + ia/\sqrt{V_P} + \tfrac{1}{2}ix(b+a^2)/V_P. \tag{B4}$$

The predicted changes in μ and V_E are, ignoring mutation,

$$\begin{aligned}\Delta\mu &\approx i\sigma^2_{A_m}/\sqrt{V_p} + \tfrac{1}{2}ix\,\mathrm{cov}_{A_{mv}}/V_P \quad \text{and}\\ \Delta V_E &\approx i\mathrm{cov}_{A_{mv}}/\sqrt{V_p} + \tfrac{1}{2}ix\sigma^2_{A_v}/V_P.\end{aligned} \tag{B5}$$

Here cov(P, P^2) is ignored; otherwise more complicated formulae apply (Mulder *et al.*, 2007).

For *n-repeat records* on each individual with truncation selection on $I = \log[\Sigma_j(X_{ij}-\bar{X}_i)^2/(n-1)]$, predictions in terms of I are:

$$\begin{aligned}&\mathrm{Var}(I) = [2/(n-1) + \sigma^2_{A_{v,\,exp}}],\ \mathrm{cov}(I, A_v) = \sigma^2_{A_{v,\,exp}},\ \text{and hence}\\ &\mathrm{R}(\sigma_{A^*}{}^2) \sim i\sigma^2_{A_{v,\,exp}}/\sqrt{[2/(n-1) + \sigma^2_{A_{v,\,exp}}]}\ .\end{aligned} \tag{B6}$$

See Ibáñez-Escriche *et al.* 2008*b*) for more accurate formulae if $\sigma^2_{A_{v,\,exp}}$ is not small.

selection might reduce the environmental variance and on other factors, such as the ability to cope with changing environments, which might favour increasing variance (e.g. Zhang & Hill, 2005*b*). In the breeding literature emphasis has been on how quickly V_E could be reduced by artificial selection (SanCristobal-Gaudy *et al.* 1998; Mulder *et al.*, 2007; 2008; Ibáñez-Escriche *et al.*, 2008*a*, *b*) and on the correlated response in V_E with directional selection on phenotype (Hill & Zhang, 2004; Mulder *et al.*, 2007). Here, we deal with theory that has been undertaken both at the level of individual genotypes and using the infinitesimal model. In addition we quantify how response to selection with artificial selection can be increased using family information or repeated observations, but defer fuller discussion of the evolution of V_E to the subsequent section.

Rather than review the development of the methodology we utilize a recent generalization (Zhang & Hill, 2010) based on the Price (1970) equation. Relevant formulae are summarized in Box 1 eqs (B1–B6). A genotype is assumed to have an effect a on mean phenotype, i.e. on genotypic value G and corresponding effect b on environmental variance, Var($G|E$). From the Price equation, the expected genetic changes in trait mean $\Delta\mu$ and environmental variance ΔV_E between generations due to selection are given by the covariance of genotypic value and relative fitness, with the addition of other segregation effects, restricted here to those from mutation (eqn. B1 in Box 1).

(i) *Stabilizing selection*

Stabilizing selection in a natural population towards an optimum Θ is usually modelled as a nor-optimal fitness function (i.e. with shape that of a normal distribution), with 'variance' ω^2 about the optimum (i.e. ω^2 is small when selection is strong) (Bürger, 2000). Selection strength then depends on $V_S = \omega^2 + V_E$ (eqns. B2 and B3). If the population is at or near the optimum, genotypes causing an increase in V_E are at a selective disadvantage. The strength is reduced if the population mean departs from the optimum, but if the mean is far from the optimum, genes increasing phenotypic variance and V_E could be at a selective advantage (Slatkin & Lande, 1976; Bull, 1987). The former would pertain if the environment

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and optimum remain fairly constant, the latter if it shows trends or fluctuates. The same patterns in selective advantage for optimum traits can be achieved by deriving economic values for mean and variance (Mulder *et al.*, 2008).

Providing the position of the optimum remains constant, the trait mean converges at or close to the optimum, although it can be displaced somewhat by mutation and by a covariance of gene effects on mean and variance. The environmental variance declines to zero as long as there is genetic variance affecting V_E, i.e. $\sigma^2_{A_v} > 0$ and there is no increase in V_E from mutation (Bull, 1987; Zhang & Hill, 2005*b*, 2010).

Disruptive selection where intermediates are at a disadvantage will have opposite effects to those of stabilizing selection near what is then an unstable optimum, but as the population departs from the optimum the population will increasingly behave as for directional selection.

(ii) *Truncation selection*

The impact of directional selection on both phenotypic mean and V_E is quite different from that of stabilizing selection acting on fitness (Hill & Zhang, 2004; Zhang & Hill, 2010). If there is no genetic covariance between the effects of genes on mean and V_E, i.e. $\mathrm{cov}_{A_{mv}} = 0$, response in the mean is given by the breeders' equation, $R = h^2 S$. If $\sigma^2_{A_v} > 0$, selection also increases V_E if selection is intense (< 50 % selected), and the responses in mean and variance are both influenced if effects are correlated ($|\mathrm{cov}_{A_{mv}}| > 0$). Thus, under intense truncation selection whereby extreme individuals are favoured, V_E is predicted to increase if it varies genetically (eqns. B4 and B5). Scale effects complicate interpretation.

These arguments can also be shown under multiple locus models, but a full multi-generation analysis requires that changes in the components such as $\sigma^2_{A_v}$ be computed. This can be done under infinitesimal model assumptions, i.e. to account for reduction in $\sigma^2_{A_v}$ due to gametic phase disequilibrium ('Bulmer effect') (Hill & Zhang, 2004), but otherwise it depends on knowledge of individual gene effects.

If selection is weak and gene effects are additive the responses to multi-locus selection can be predicted adequately from eqn (B5), where terms such as $\mathrm{cov}_{A_{mv}}$ and $\sigma^2_{A_v}$ now refer to sums over loci. With intense artificial selection on mean or variance complications arise because, if there is heterogeneity of environmental variance, the regression of breeding value (A_m) on phenotype (P) is no longer linear (Mulder *et al.*, 2007). As extreme scoring individuals are more likely to come from high variance families, this regression is slightly sigmoid. Hence, P and P^2 can be regarded as two traits in a bivariate selection index and response in mean and variance predicted more accurately.

Table 4. *Approximate accuracy r_A of predicted breeding value $\hat{A}_v$ for V_E using family information*

	h^2_v	0·005			0·05		
Relatives	n	1	10	100	1	10	100
Clones		0·071	0·219	0·58	0·224	0·59	0·92
Full-sibs		0·035	0·111	0·32	0·112	0·32	0·60
Half-sibs		0·018	0·056	0·17	0·056	0·17	0·37
Half-sib progeny		0·035	0·111	0·33	0·112	0·33	0·75

$r_{A_v} = \rho_b h_v \sqrt{\{n/[1+\rho_w(n-1)h^2_v]}$, for n phenotypic records, and additive (unless clones) genetic relationships, ρ_b between the evaluated animal and the group of relatives and ρ_w among individuals within the group (based on Mulder *et al.* 2007).

Predictions for response to stabilizing selection in a breeding programme carried out by truncation of extremes can be predicted similarly from the reduction in selection differential.

Family information can be utilized in animal and plant breeding to increase the accuracy of selection decisions. As prediction of breeding values for environmental variance (A_v) can be regarded as predictions for a trait with a low heritability, records on large numbers of relatives are needed to get high accuracy. Selection index theory can be used to predict the accuracy of $\hat{A}_v$ based on family size and relationship (Mulder *et al.*, 2007, 2008), and examples are given in Table 4. Observations on clones, feasible in some plant species, are most effective in realizing high accuracy. Half-sib progeny can provide higher accuracy than sibs, and so progeny testing may be more efficient than sib-testing schemes in reducing V_E by selection (Mulder *et al.*, 2008).

Multiple objectives feature if, for example, amount and consistency of product at the farm and/or consumer level are desirable, including, for example, robustness to environmental fluctuation. Selection for reduced variance is therefore of interest for traits with an optimum, and more generally there is a non-linear profit equation (Mulder *et al.*, 2008). To bring the mean closer to the optimum and decrease the variance around it, selection both on mean and variance is needed. SanCristobal-Gaudy *et al.* (1998) derived an appropriate quadratic index, although a linearized selection index with updated weights can bring the mean to the optimum more rapidly (Mulder *et al.*, 2008).

Repeated records allow individual animals to have a direct measure of within-individual variation in the trait (V_{Es}). The analysis therefore differs from that above which is based on one record per individual. If selection operates on the variation among the n observations on each individual, a simple prediction is

that the response in variance will equal the product of selection differential on variance and its 'heritability' as a function of the number of records (eqn. B6, from SanCristobal-Gaudy *et al.*, 1998; Ibáñez-Escriche *et al.*, 2008*b*).

The more general case of a repeated trait such as the distribution of flowering time among florets of a plant, where natural selection may operate within and between plants, is considered by Deveaux & Lande (2010). The effects of artificial selection for the similar situation, e.g. egg weight of birds where homogeneity among both individual eggs within birds and average egg size between birds may be desirable, have not been worked out.

7. Factors affecting the magnitude of V_E

The presence of genetic variance for a trait requires that genes with influence on the trait are segregating in the population. In contrast, the presence of V_E does not require segregation and in that sense is more like the population mean. If no mutations occur that influence V_E then obviously it will fix at a constant level, but there is plenty of evidence for genetic variation in V_E (Table 3) and, by inference, mutations that affect V_E. Therefore, we need to consider what determines the levels maintained. We review what forces may be acting and discuss some of the models, but recognize that the analysis is far from being conclusive: indeed, this is hardly surprising as our real understanding is weak of why trait means take the values they do, and is poorer for why genetic variance and V_E take the values they do. It should be emphasized that we are considering just the magnitude of V_E expressed by quantitative traits in segregating populations and are not concerned with major transitions or with, for example, evolution of canalization to a specific phenotype.

Stabilizing selection in a constant environment where extreme organisms are at a disadvantage provides selective pressure to reduce V_E in all traits (Slatkin & Lande, 1976; Bull, 1987; Box 1), and there is no reason to assume that the nor-optimal model would lead to different general conclusions than others in which extremes are at a disadvantage. Hence, stabilizing selection acts like directional selection downwards on V_E among individuals. Similarly, any selection against variation within individuals, e.g. FA, whether it is stabilizing selection on individual records or selection against asymmetry among trait expressions, similarly leads to downward selection pressure. The theoretical problem is basically, therefore, to establish why V_E does not decline towards zero and is maintained at values typical for the trait. We distinguish between potential extrinsic opposing forces, such as variability in the optimum phenotype among generations or niches (Bull, 1987), and intrinsic forces such as those associated with costs of regulating the phenotype.

(i) *Extrinsic factors*

Environmental heterogeneity. There is extensive discussion on the impact of environmental heterogeneity in the evolution of plasticity and maintenance of genetic variation, but rather little on its influence on the maintenance of V_E, although variation in plasticity to local heterogeneity would appear in analyses as V_E. Bull (1987), in a pioneering study, proposes a model whereby stabilizing selection operates within the environment (Box 1), but with Θ_t, the position of the optimum at generation t, varying among generations. If Θ_t is constant, the population mean stabilizes at the optimum and there is consistent selection to reduce V_E towards 0. If the position of the optimum varies, however, the expected fitness of a genotype k with mean μ_k and environmental variance V_{Ek} is then also a function of V_{Ek} at generation t. The optimum genotype maximizes the expectation of this quantity over generations. If μ_k has a constant mean and the optima Θ_t are uncorrelated over generations, the presence of genetic variation in V_{Ek} leads to an optimum at $V_E = \pi^2 - \omega^2$, where π^2 is the variance of μ_k and must exceed ω^2 (Bull, 1987). If the fluctuation in the mean is large, the optimum V_E is greater than 0, but this is a very stringent requirement. Even at what are generally regarded as typical values of ω^2 of at least 20 (but see Kingsolver *et al.*, 2001, indicating higher values), this implies that the position of the optimum has a variation across generations in excess of 20 phenotypic standard deviations.

Fluctuations in the width of the selection profile, i.e. in ω_k^2, can reduce this stringency a little, however, dependent on the correlation of mean and width of the fitness profile (Zhang & Hill, 2005*b*). Nevertheless, simple fluctuations in the position of the optimum or width of the fitness profile do not seem sufficient forces on their own to maintain V_E.

In the presence of heterogeneity in the environment, V_E may reflect plastic responses to this heterogeneity in addition to intrinsic factors such as developmental noise. Zhang (2005) shows that plasticity can be adaptive if a correlation can be established between the optimal phenotype and environmental quality if it varies over time or space. The consequent increase in evolved plasticity induces increases in the V_E of the trait. While the sum of spatial and temporal variation needs to be larger than the observed V_E, which is a stringent requirement, variation in environmental quality can be much less than V_E. Some of these issues have been further explored subsequently (Zhang, 2006). The inter-relationship between parameters such as heterogeneity of environment in time and space and rates of migration are complicated, although the

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magnitude of V_G maintained is much less sensitive to them than is V_E. Even so, there are circumstances with high levels of environmental variability that can lead to reductions in V_E.

Competition within species. Competition between individuals for resources, e.g. seeds as food for birds, would appear to favour high V_E in, say, bill size in that it increases differences between them and thereby reduces direct competition. Although under strong assumptions such a model can lead to increases in V_G in the presence of stabilizing selection, it has little impact on maintaining V_E because competing genotypes diverge and stabilizing selection still acts within each (Zhang & Hill, 2007).

Interactions among species. A specific example is considered by Deveaux & Lande (2010) who model the variation in flowering time of an insect-pollinated plant species for which there are two levels of variation, between individual flowers within one plant and that between plants. They show that selective forces may act to increase (environmental) variation in flowering time within plants, in particular if there is a limitation in pollinator availability at any one time and a temporal autocorrelation of individual pollinator visitation. Such a model might apply in other organisms in which the phenotype is repeated at different times or in different locations, but not for bilateral traits.

Conclusion. None of the above models lead to an equilibrium in V_E at observed levels except for special situations (e.g. flowering time) without very stringent requirements on the parameters, such as the magnitude of variation in the optimum genotype.

(ii) *Intrinsic factors*

Cost of uniformity. If the same genes are assumed to be expressed on bilaterally repeated traits, then variation in a trait between sides can be regarded as developmental noise. This is, presumably, under some degree of selective control: in *Drosophila*, for example, the CV within individuals for wing size is much smaller than that of sternopleural bristle number. While stabilizing selection would be expected to reduce the V_{Es}, one can reasonably assume it is stronger for maintaining symmetry of wings than of bristles. It does not address what magnitude is maintained. One simple model is that there is a cost to the organism associated with reducing variability, an 'engineering cost' of control of the trait or homeostasis in Lerner's (1954) terms.

The same cost argument pertains in principle to reducing V_E between individuals for a trait such as body size. Zhang & Hill (2005*b*) applied a rather arbitrary cost function of $\exp(C/V_E)$, which increases as V_E decreases, such that fitness with stabilizing selection is proportional to $\exp(C/V_E)\exp[-\frac{1}{2}(X-\Theta)^2/\omega^2]$. The model predicts a stable equilibrium at $V_E \sim \sqrt{(2C\omega^2)}$, with quite a small accompanying loss of mean fitness (selection load) compared to an equilibrium at $V_E = 0$. The equilibrium in the CV and, for repeated traits, an equilibrium point in within-individual V_E can be computed similarly. The model is appealing but direct evidence, such as observations showing the energetic cost of developmental stability, is lacking.

Mutation effects on V_E. Mutation influences the genotypic mean and can also affect the variance, typically upwards, by more than can be explained by a simple scale effect. The *scute* gene in *Drosophila* is an example, albeit associated with canalizing effects (Rendel *et al*., 1966). If the mutations have symmetrically distributed effects on V_E, i.e. are equally likely to increase or decrease it, they merely provide fuel for V_E to evolve and are unlikely to affect equilibrium points. If, however, mutants tend to increase V_E, i.e. to reduce developmental control, equilibria can be obtained (Zhang & Hill, 2008). These depend on the mean effect of mutations on V_E, on the relation between effects of mutation on the mean and the variance and on the fitness function. As the mutation rate affects both the amount of genetic variance maintained and the amount of environmental variance, it leads to stable values of the heritability, for which we know of no other model.

A basic model with stabilizing selection which yields analytic solutions is to assume that mutant effects a on the mean are normally distributed $N(0, \varepsilon_a^2)$, and so a^2 is gamma distributed with shape parameter 1/2, and effects b on V_E are independently gamma (½) distributed with variance ε_b^2. Equilibria are obtained for $\sigma^2_{A_m}$ and $\sigma^2_{A_v}$ and consequently for heritability, at $h^2 = \varepsilon_a/(\varepsilon_a + \sqrt{\varepsilon_b})$ (Zhang & Hill, 2008). For h^2 in the range 0·1–0·5, ε_b has to lie in the range ε_a^2 to almost $81\varepsilon_a^2$, implying that mutants must have as large or greater effects on V_E as on the trait itself. Evidence for the effects of mutations on V_E of quantitative traits is limited, but there is some from mutation accumulation experiments that show a net increase in variance (Fry *et al*., 1995; Baer, 2008). Even so, the magnitude of mutational increase in V_E needed seems so large that, judging by this simplistic model, a mutation–selection balance is no more than a partial candidate for explaining the levels of V_E or heritability.

Conclusion. The models that appear to have most promise are those in which a cost is attached to homogeneity, and are plausible in that if a more intense selection is applied to inequality of wing size than to bristles, the latter would show relatively higher within-individual variance, as is indeed the case. These are compatible with stabilizing selection, but other forms of selection have not been investigated in this context. Our understanding of why variances and heritabilities take the levels they do is at best, however, superficial.

8. Concluding remarks

While we have attempted to assess some of the current state of knowledge, we see there are many uncertainties and questions still to be answered. We emphasize a few which we consider as most important:

(i) Estimates of the magnitude of genetic variance in V_E in segregating populations are potentially biased upwards by factors such as non-normality of data, confounding with fixed effects, confounding with non-additive sources of genetic variance such as epistasis and simple errors in data. The magnitude of such biases remains to be assessed.

(ii) There is no consistent choice of the statistical model, e.g. between the exponential and the additive model of variance partition. The importance in practice for estimation of parameters and predictions of breeding values for V_E has not been fully evaluated, and might lead to choice of a more uniform approach.

(iii) The magnitude of parameter estimates indicates that there are substantial opportunities to change the magnitude of V_E by selection, but the possible biases noted in (i) show that, for example, cross-validation in breeding programmes is needed.

(iv) Current models to explain the levels of V_E and heritability of traits maintained in nature are both simplistic and inadequate, but it will be difficult to obtain sufficient information on selective forces and parameters to improve our understanding forward.

(v) The level of understanding of the genetic basis of V_E is poor, for example, the extent to which it is related to and can be explained by biological phenomena such as epigenetic and other non-Mendelian variation, to plasticity in response to micro-environment and between- and within-individual variation.

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References

Ansel, J., Bottin, H., Rodriguez-Beltran, C., Damon, C., Nagarajan, M., Fehrmann, S., Francois, J. & Yueot, G. (2008). Cell-to-cell stochastic variation in gene expression is a complex genetic trait. *Public Library of Science Genetics* **4**, e1000049.

Argente, M. J., Garcia, M. L., Muelas, R., Santacreu, M. A. & Blasco, A. (2010). Preliminary results in a divergent selection experiment on variance for litter size in rabbits. In *Proceedings of the 9th World Congress on Genetics Applied to Livestock Production*, Leipzig, Germany. Communication 0526.

Baer, C. F. (2008). Quantifying the de-canalizing effects of spontaneous mutations in rhabditid nematodes. *American Naturalist* **172**, 272–281.

Bodin, L., Bolet, G., Garcia, M., Garreau, H., Larzul, C. & David, I. (2010). Robustesse et canalisation: vision de généticiens. *INRA Production Animales* **23**, 11–22.

Bürger, R. (2000). *The Mathematical Theory of Selection, Recombination, and Mutation*. New York: Wiley.

Bull, J. J. (1987). Evolution of phenotypic variance. *Evolution* **41**, 303–315.

Canario, L., Lundgren, H., Haandlykken, M. & Rydhmer, L. (2010). Genetics of growth in piglets and the association with homogeneity of body weight within litters. *Journal of Animal Science* **88**, 1240–1247.

Cardin, S. & Minvielle, F. (1986). Selection on phenotypic variation of pupa weight in *Tribolium castaneum*. *Canadian Journal of Genetics and Cytology* **28**, 856–861.

Cardoso, F. F., Rosa, G. J. M. & Tempelman, R. J. (2005). Multiple-breed genetic inference using heavy-tailed structural models for heterogeneous residual variances. *Journal of Animal Science* **83**, 1766–1779.

Clay, J. S., Vinson, W. E. & White, J. M. (1979). Heterogeneity of daughter variances of sires for milk yield. *Journal of Dairy Science* **62**, 985–989.

Clayton, G. A. & Robertson, A. (1957). An experimental check on quantitative genetic theory. 2. The long-term effects of selection. *Journal of Genetics* **55**, 152–170.

Damgaard, L. H., Rydhmer, L., Løvendahl, P. & Grandinson, K. (2003). Genetic parameters for within-litter variation in piglet birth weight and change in within-litter variation during suckling. *Journal of Animal Science* **81**, 604–610.

Deveaux, C. & Lande, R. (2010). Selection on variance in flowering time within and among individuals. *Evolution* **64**, 1311–1320.

Falconer, D. S. & Mackay, T. F. C. (1996). *Introduction to Quantitative Genetics*, 4th edn. Essex: Pearson Education Limited.

Falconer, D. S. & Robertson, A. (1956). Selection for environmental variability of body size in mice. *Zeitschrift fur Inductive Abstammungs- and Vererbungslehre* **87**, 385–391.

Finlay, K. W. & Wilkinson, G. N. (1963). The analysis of adaptation in a plant breeding programme. *Australian Journal of Agricultural Research* **14**, 742–754.

Foulley, J. L. & Quaas, R. L. (1995). Heterogeneous variances in Gaussian linear mixed models. *Genetics, Selection, Evolution* **26**, 117–136.

Foulley, J. L., Quaas, R. L. & Thaon d'Arnoldi, C. (1998). A link function approach to heterogeneous variance components, *Genetics, Selection, Evolution* **30**, 27–43.

Fry, J. D., deRonde, K. A. & Mackay, T. F. C. (1995). Polygenic mutation in *Drosophila melanogaster*: genetic analysis of selection lines. *Genetics* **139**, 1293–1307.

Fuller, R. C. & Houle, D. (2003). Inheritance of developmental instability. In *Developmental Instability: Causes and Consequences* (ed. M. Polak), pp. 157–183. Cambridge: Cambridge University Press.

Gangestad, S. W. & Thornhill, R. (1999). Individual differences in developmental precision and fluctuating asymmetry: a model and its implications. *Journal of Evolutionary Biology* **12**, 402–416.

Garcia, M., David, I., Garreau, H., Ibañez-Escriche, N., Mallard, J., Masson, J. P., Pommeret, D., Robert-Granié, C. & Bodin, L. (2009). Comparisons of three models for canalising selection or genetic robustness. In *60th Annual Meeting of European Association for Animal*

Production, Barcelona, Spain, August 2009, Abstracts, p. 599.

Garreau, H., Bolet, G., Larzul, C., Robert-Granie, C., Saleil, G., SanCristobal, M. & Bodin, L. (2008). Results of four generations of a canalising selection for rabbit birth weight. *Livestock Science* **119**, 55–62.

Gavrilets, S. & Hastings, A. (1994). A quantitative-genetic model for selection on developmental noise. *Evolution* **48**, 1478–1486.

Gilmour, A. R., Gogel, B. J., Cullis, B. R. & Thompson, R. (2006). *ASREML User Guide Release 2.0*. Hemel Hempstead: VSN International.

Gimelfarb, A. (1994). Additive–multiplicative approximation of genotype–environment interaction. *Genetics* **138**, 1339–1349.

Gutierrez, J. P. Nieto, B., Piqueras, P., Ibáñez, N., & Salgado, C. (2006). Genetic parameters for canalisation analysis of litter size and litter weight traits at birth in mice. *Genetics, Selection, Evolution* **38**, 445–462.

Hill, W. G. (2004). Heterogeneity of genetic and environmental variance of quantitative traits. *Journal of the Indian Society of Agricultural Statistics* **57**, 49–63.

Hill, W. G. (2010). Understanding and using quantitative genetic variation. *Philosophical Transactions of the Royal Society B* **365**, 73–85.

Hill, W. G. & Zhang, X.-S. (2004). Effects on phenotypic variability of directional selection arising through genetic differences in residual variability. *Genetical Research* **83**, 121–132 (Erratum 83, 160).

Hoaglin, D. C. & Welsch, R. E. (1978). The hat matrix in regression and ANOVA. *American Statistician* **32**, 17–22.

Houle, D. (1992). Comparing evolvability and variability of quantitative traits. *Genetics* **130**, 195–204.

Ibáñez-Escriche, N., Garcia, M. & Sorensen, D. (2010). GSEVM v.2: MCMC software to analyze genetically structured environmental variance models. *Journal of Animal Breeding and Genetics* **127**, 249–251.

Ibáñez-Escriche, N., Moreno, A., Nieto, B., Piquears, P., Salgado, C. & Gutierrez, J. P. (2008*a*). Genetic parameters related to environmental variability of weight traits in a selection experiment for weight gain in mice; signs of correlated canalised response. *Genetics, Selection, Evolution* **40**, 279–293.

Ibáñez-Escriche, N., Sorensen, D., Waagepetersen, R. & Blasco, A. (2008*b*). Selection for environmental variance: a statistical analysis and power calculations to detect response. *Genetics* **180**, 2209–2226.

Ibáñez-Escriche, N., Varona, L., Sorensen, D. & Noquera, J. L. (2008*c*). A study of heterogeneity of environmental variance for slaughter weight in pigs. *Animal* **2**, 19–26.

Johnson, T. & Barton, N. H. (2005). Theoretical models of selection and mutation on quantitative traits. *Philosophical Transactions of the Royal Society B* **360**, 1411–1425.

Johnson, W., Gangestad, S. W., Segal, N. L. & Bouchard, T. J. Jr (2008). Heritability of fluctuating asymmetry in a human twin sample: the effect of trait aggregation. *American Journal of Human Biology* **20**, 651–658.

Kaufman, P. K., Enfield, F. D. & Comstock, R. E. (1977). Stabilizing selection for pupa weight in *Tribolium castaneum*. *Genetics* **87**, 327–341.

Kingsolver, J. G., Hoekstra, H. E., Hoekstra, J. M., Berrigan, D., Vignieri, S. N., Hill, C. E., Hoang, A., Gibert, P. & Beerli, P. (2001). The strength of phenotypic selection in natural populations. *American Naturalist* **157**, 245–261.

Larzul, C., Le Roy, P., Tribout, T., Gogue, J. & SanCristobal, M. (2006). Canalizing selection on ultimate PH in pigs: consequences on meat quality. In *Proceedings of the 8th World Congress on Genetics Applied to Livestock Production*, Belo Horizonte, Brasil. Communication 13–09.

Leamy, L. J. & Klingenberg, C. P. (2005). The genetics and evolution of fluctuating asymmetry. *Annual Review of Ecology, Evolution, and Systematics* **36**, 1–21.

Lerner, I. M. (1954). *Genetic Homeostasis*. Edinburgh, UK: Oliver & Boyd.

Lynch, M. & Walsh, B. (1998). *Genetics and Analysis of Quantitative Traits*. Sunderland, MA: Sinauer Associates.

Mackay, T. F. C. & Lyman, R. F. (2005). Drosophila bristles and the nature of quantitative genetic variation. *Philosophical Transactions of the Royal Society B* **360**, 1513–1527.

Møller, A. P. & Thornhill, R. (1997). A meta-analysis of the heritability of developmental stability. *Journal of Evolutionary Biology* **10**, 1–16.

Mulder, H. A. (2007). Methods to optimize livestock breeding programs with genotype by environment interaction and genetic heterogeneity of environmental variance. PhD thesis, Wageningen University, The Netherlands.

Mulder, H. A., Bijma, P. & Hill, W. G. (2007). Prediction of breeding values and selection responses with genetic heterogeneity of environmental variance. *Genetics* **175**, 1895–1910.

Mulder, H. A., Bijma, P. & Hill, W. G. (2008). Selection for uniformity in livestock by exploiting genetic heterogeneity of residual variance. *Genetics, Selection, Evolution* **40**, 37–59.

Mulder, H. A., Hill, W. G., Vereijken, A. & Veerkamp, R. F. (2009). Estimation of genetic variation in residual variance in female and male broilers. *Animal* **3**, 1673–1680.

Ordas, B., Malvar, R. A. & Hill, W. G. (2008). Genetic variation and quantitative trait loci associated with developmental stability and the environmental correlations between traits in maize. *Genetical Research* **90**, 385–395.

Price, G. R. (1970). Selection and covariance. *Nature* **227**, 520–521.

Rendel, J. M., Sheldon, B. L. & Finlay, D. E. (1966). Selection for canalization of the *scute* phenotype. II. *American Naturalist* **100**, 13–31.

Robertson, A. (1959). Experimental design in the evaluation of genetic parameters. *Biometrics* **15**, 219–226.

Rönnegård, L., Felleki, M., Fikse, F., Mulder, H. A. & Strandberg, E. (2010). Genetic heterogeneity of residual variance – estimation of variance components using double hierarchical generalized linear models. *Genetics, Selection, Evolution* **42**, 8.

Ros, M., Sorensen, D., Waagepetersen, R., Dupont-Nivet, M., SanCristobal, M., Bonnet, J. C. & Mallard, J. (2004). Evidence for genetic control of adult weight plasticity in the snail *Helix aspersa*. *Genetics* **168**, 2089–2097.

Rosa, G. J. M., Padovani, C. R. & Gianola, D. (2003). Robust linear mixed models with normal/independent distributions and Bayesian MCMC implementation. *Biometrical Journal* **45**, 573–590.

Rowe, S. J., White, I. M. S., Avendano, S. & Hill, W. G. (2006). Genetic heterogeneity of residual variance in broiler chickens. *Genetics, Selection, Evolution* **38**, 617–635.

SanCristobal-Gaudy, M., Bodin, L., Elsen, J. M. & Chevalet, C. (2001). Genetic components of litter size variability in sheep. *Genetics, Selection, Evolution* **33**, 249–271.

SanCristobal-Gaudy, M., Elsen, J.-M., Bodin, L. & Chevalet, C. (1998). Prediction of the response to selection for canalization of a continuous trait in animal breeding. *Genetics, Selection, Evolution* **39**, 423–451.

Scharloo, W., Zweep, A., Schuitema, K. A. & Wijnstra, J. G. (1972). Stabilizing and disruptive selection on a mutant character in *Drosophila*. IV. Selection on sensitivity to temperature. *Genetics* **71**, 551–566.

Slatkin, M. & Lande, R. (1976). Niche width in a fluctuating environment – density independent model. *American Naturalist* **110**, 31–55.

Sorensen, A. C., Kristensen, T. N., Loeschcke, V., Ibáñez, N. & Sorensen, D. (2007). Genetically controlled environmental variance for sternopleural bristles in *Drosophila melanogaster* – an experimental test of a heterogeneous variance model. *Acta Agriculturae Scandinavica, Section A, Animal Science* **57**, 196–201.

Sorensen, D. A. (2009). Developments in statistical analysis in quantitative genetics. *Genetica* **136**, 319–332.

Sorensen, D. A. & Hill, W. G. (1983). Effects of disruptive selection on genetic variance. *Theoretical and Applied Genetics* **65**, 173–180.

Sorensen, D. & Waagepetersen, R. (2003). Normal linear models with genetically structured residual variance heterogeneity: a case study. *Genetical Research* **82**, 207–222.

Van Valen, L. (1962). A study of fluctuating asymmetry. *Evolution* **16**, 125–142.

Van Vleck, L. D. (1968). Variation of milk records within paternal-sib groups. *Journal of Dairy Science* **51**, 1465–1470.

Visscher, P. M. & Posthuma, D. (2010). Statistical power to detect genetic loci affecting environmental sensitivity. *Behavior Genetics* **40**, 728–733.

Waagepetersen, R., Ibáñez-Escriche, N. & Sorensen, D. (2008). A comparison of strategies for Markov chain Monte Carlo computation in quantitative genetics. *Genetics, Selection, Evolution* **40**, 161–176.

Waddington, C. H. (1942). Canalization of development and the inheritance of acquired characters. *Nature* **150**, 563–565.

Wagner, G. P., Booth, G. & Bagheri-Chaichian, H. (1997). A population genetic theory of *canalization*. *Evolution* **51**, 329–347.

Walsh, B. & Lynch, M. (2010). *Evolution and Selection of Quantitative Traits: I. Foundations*. Available at http://nitro.biosci.arizona.edu/zbook/NewVolume_2/newvol2.html, Chapter 13.

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

Wittenburg, D., Guiard, V., Teuscher, F. & Reinsch, N. (2008). Comparison of statistical models to analyse the genetic effect on within-litter variance in pigs. *Animal* **2**, 1559–1568.

Wolc, A., White, I. M. S., Avendano, S. & Hill, W. G. (2009). Genetic variability in residual variation of body weight and conformation scores in broiler chickens. *Poultry Science* **88**, 1156–1161.

Wu, R. L. & O'Malley, D. M. (1998). Nonlinear genotypic response to macro- and micro-environments. *Theoretical and Applied Genetics* **96**, 669–675.

Yang, Y. (2010) The genetics of environmental variation. PhD thesis, Aarhus University, Denmark.

Yang, Y., Christensen, O. & Sorensen, D. A. (2010). Analysis of a genetically structured variance heterogeneity model using the Box–Cox transformation. *Genetics Research* (in press).

Zhang, X.-S. (2005). Evolution and maintenance of the environmental component of the phenotypic variance: benefit of plastic traits under changing environments. *American Naturalist* **166**, 569–580.

Zhang, X.-S. (2006). The phenotypic variance within plastic traits under migration–mutation–selection balance. *Evolution* **60**, 1125–1136.

Zhang, X.-S. & Hill, W. G. (2005*a*). Genetic variability under mutation selection balance. *Trends in Ecology and Evolution* **20**, 468–470.

Zhang, X.-S. & Hill, W. G. (2005*b*). Evolution of the environmental component of the phenotypic variance: stabilizing selection in changing environments and the homogeneity cost. *Evolution* **59**, 1237–1244.

Zhang, X.-S. & Hill, W. G. (2007). Competition can maintain genetic but not environmental variance in the presence of stabilizing selection. *Evolution* **61**, 1532–1545.

Zhang, X.-S. & Hill, W. G. (2008). Mutation–selection balance for environmental variance. *American Naturalist* **171**, 394–399.

Zhang, X.-S. & Hill, W. G. (2010). Change and maintenance of variation in quantitative traits in the context of the Price equation. *Theoretical Population Biology* **77**, 14–22.