17

Short-term Changes in the Variance: 2. Changes in the Environmental Variance

It is the purpose of this short communication to suggest that recent views on the nature of the developmental process make it easier to understand how the genotypes of evolving organisms can respond to the environment in a more co-ordinated fashion — Waddington (1942)

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Our assumption to this point has been that the environmental variation is homoscedastic (constant across genotypes), and hence not subject to modification by selection. However, a fairly universal (and very striking) observation is that most traits show at least some genetic variation in an outbred population. One can imagine that sensitivity to the environment, as measured by the environmental variance, is such a trait (Waddington 1957, Hill 2007), and thus can potentially respond to selection. If true, selection for (or against) extreme individuals, such as directional and disruptive selection for the former and stabilizing selection for the later, may also result in selection for increased (or decreased) values of σ^2_E in addition to the changes in σ^2_A discussed in Chapter 16. There are also settings that favor *direct* selection on σ^2_E, such as breeding for more uniformity in an agricultural or laboratory trait. There can also be fitness consequences for uniformity in domesticated populations. For example, pre-weaning survival increases as the within-litter variance (a function of σ^2_E) in weight decreases in both pigs (Milligan et al. 2002) and rabbits (Garreau et al. 2008). Direct selection on σ^2_E likely occurs in natural populations, such as selection on the within-plant variation in flowering time (Devaus and Lande 2009). Finally, Gibson (2009) and Feinberg and Irizarry (2010) have argued that selection on the inherent stochasticity of developmental systems may play an important role in our understanding of human diseases. All of these considerations have spurred an interest in selection response in σ^2_E (reviewed by Hill and Mulder 2010).

One technical comment before proceeding is that simple scale effects can also result in a change in the variance — if the coefficient of variation of a trait remains constant as its mean changes, then its variance must also change as well. As discussed in LW Chapter 11, a suitable transformation (such as working with the log of the trait value) often removes these scale effects and we assume this has been done previous to any analysis.

BACKGROUND: HERITABLE VARIATION IN σ^2_E

Scales of Environmental Sensitivity

The environment an organism experiences can be partitioned into many different scales of resolution, but operationally we are usually concerned with just two: features shared by all individuals in some common setting (macroenvironments) and features unique to each individual (microenvironments). Sensitivity (i.e., differential performance) of genotypes over any of these scales indicates genotype $\times$ environmental interactions (LW Chapter 22). Volume 3 examines selection response in the presence of G $\times$ E over macro-scale differences (such as different growing regions for a crop or different hostplants for an insect), by treating the trait value in each macroenvironment as a correlated character (Falconer 1952). A related

topic are **norm of reactions**, performance curves as one tunes a particular environmental value (such as temperature). The analysis of response for such **function-valued traits** is also deferred until our final volume.

Our focus here is on sensitivity to microenvironmental variation, which itself can occur over several different scales. The most fundamental is **developmental noise**, which can be measured by differences in the trait values of homologous structures within an individual, such as the amount of **fluctuating asymmetry** (differences in trait values on the left and right side of bilaterally-symmetric organisms, LW Chapter 11; see also Leamy and Klingenberg 2005, Dongen 2006, Graham et al. 2010). Presumably this within-individual variation reflects "noise" in the developmental process — variation in the end product of the same genotype in the same environment. A related measure of microenvironmental variation is the variance in the repeated performance (records) of an individual over time, such offspring size in different litters. This repeated-measures design assumes all records from a single individual contain a permanent environmental effect (Chapters 13, 19). While this is constant within the repeated records from an individual, it differs across individuals, offering another level of microenvironmental variation. While environmental variation at all three of these scales contributes to σ^2_E, it is possible that different pathways may be involved in environmental sensitivity at each scale.

Environmental vs. Genetic Canalization

The idea that genotypes may vary in their microenvironmental sensitivity has a fairly rich history, dating back to Waddington's (1942) notion of **canalization** (Schmalhausen's 1949 **autoregulation**) — developmental buffering against small perturbations (be they environmental or genetic), so that a wide range of genotypes and environments end up at essentially the same developmental end-product. He also stressed that canalization is an *evolved system* (Waddington 1957, 1959), and hence to some extend is a selectable trait. Part of Waddington's concern was sensitivity to the environment, with genotypes that show **environmental canalization** (or **environmental robustness**) having lower environmental variances. However, Waddington was also concerned with the fact that a particular genotype may find itself in a variety of different *genetic* environments and that genotypes may also differ in their sensitivities to these backgrounds. **Genetic canalization** (or **genetic robustness**) is the stability of a particular genotype when placed in a variety of different genetic backgrounds, and is a function of epistasis between a genotype of interest and the universe of genetic backgrounds in which it may find itself. These two measures of sensitivity can be easily confounded, yet they are fundamentally different. Environmental robustness does not necessarily imply genetic robustness, and vise-versa. As reviewed in Flatt (2005) and Hansen (2006), the conditions for the evolution of genetic canalization (an overall reduction in the sensitivity of a random genotype to its genetic background) are much more restrictive (in part because the target background is itself continually evolving).

Using an appropriate design, the genetic and environmental sensitivities for a particular genotype can be separated. Under a repeated-measures design, the genetic background remains constant and the residual variance is due entirely to environmental sensitivity (plus measurement error). A second (but obviously more restrictive) design is the use of a series of inbred lines. For a particular genotype of interest (such as a marker locus tagging a QTL), the *between-line* trait variance of a genotype across a series of lines (and hence different genetic backgrounds) is a measure of its genetic sensitivity, while the *within*-line variance of the target genotype is a measure of its environmental sensitivity.

Example 17.1 Fraser and Schadt (2010) considered expression (mRNA) levels for thousands

of genes over a series of 19 mouse inbred lines. Within each line, roughly 20 individuals were scored at $\sim$ 160,000 markers. For a given trait (the expression level at a specified gene), the within-line variation was contrasted between the two alternative genotypes at each marker. Since there is essentially no genetic variation within an inbred line, a significant differences in the within-line variance over marker genotypes indicates linkage to a QTL influencing environmental robustness (differences in σ_E^2). Conversely, a significant difference in the dispersion of the mean values of the marker genotypes *across* inbred lines indicates that the marker is linked to a QTL influencing genetic robustness. Using this approach, these authors found QTLs for both types of robustness. QTLs for environmental robustness were largely trans-acting and sex-specific (different QTLs in the two sexes). In contrast, QTLs for genetic robustness were often cis-acting and were not sex-specific. There was no overlap between the two classes of QTLs. More generally, most settings lack this strict control over genetic background and thus any measure of residual variance confounds these two sources. Our assumption below is that any heritable variation in the residual variance is due to environmental sensitivity, which does not rule out nonadditive variation in the residual variance from genetic and/or environmental sensitivity.

Evidence for Heritable Variation in Environmental Variance

The observation that different genotypes may have different environmental variances is not new. Robertson and Reeve (1952) and Lerner (1954) noted that inbred lines often have large environmental variances relative to their outbred counterparts (see Whitlock and Fowler 1999 for a recent example). This led Lerner to propose that **genetic homeostasis** (developmental buffering across environments) was facilitated by heterozygosity, with environment sensitivity (σ_E^2) increasing with homozygosity. Consistent with this suggestion is the observation that developmental noise (measured by the amount of fluctuating asymmetry) often decreases with increasing levels of protein (i.e., isozyme) heterozygosity (reviewed in Mitton and Grant 1984, Livshits and Kobyliansky 1985, Zouros and Foltz 1987, Chakraborty 1987, Britten 1996, Vøllestad et al. 1999), a point we return to shortly.

Direct evidence for genetic variation in σ_E^2 is provided by comparing inbred lines. Mackay and Lyman (2005) observed different amounts of environmental variation for bristle number across inbred lines of *Drosophila* from a common source population. Similar findings were seen for four maize traits over a series of recombinant inbred lines by Ordas et al. (2008). While these studies provide direct evidence for *genetic* variation in σ_E^2, our concern is with *heritable* variation — additive genetic variation in the trait that can respond to selection. There is direct evidence for heritable variation at the level of developmental noise in that traits usually respond to selection to either increase or decrease the amount of fluctuating asymmetry (LW Chapter 11). However, this is only one potential component of the microenvironmental variance, so just what evidence is there for a heritable component of σ_E^2 in general?

Indirect support comes from observations of heritable variation of the within-family variance in livestock traits. Van Vleck (1968) and Clay et al. (1979) observed significant sire differences in the variation in milk yield in dairy cattle across half-sib families, while Rowe et al. (2006) found significant sire variation in the within-family residual variance for 35-day body weight in broiler chickens. While variation between sires is consistent with a heritable component for within-family variances, it can also arise from genetic segregation. In particular, heteroscadisticity of family variances is a classic (but weak) test for the presence of a major gene, with parents heterozygous for the major allele having sibs a larger within-family variance than homozygous parents. (LW Chapter 13).

A more recent line of evidence comes from a significantly improved fit of statistical models assuming a heritable component of the residual variance (and hence a correlation in σ_E^2 among relatives) over those that assume no such heritable variation. Such an improved

fit has been seen for fecundity in sheep (SanCristobal-Gaudy et al. 2001), body weight in the snail *Helix aspersa* (Ros et al. 2004), and litter size in pigs (Sorensen and Waagepetersen 2003), with additional examples listed in Table 17.2. The caveat with these results is the concern that violations of the underling statistical models may lead to an incorrect suggestion that such genetic variation exists when in fact it is absent. Indeed, Yang et al. (2011) showed that these analyses are strongly biased by the presence of skew in the data, as the presence of heritable variation in σ^2_E is also manifested as skew (Ros et al. 2004). These authors simultaneously fit a model along with a general Box-Cox transformation (LW Chapter 11) of their data to remove any intrinsic skewness. Evidence for genetic variance in σ^2_E was reduced in some cases after accounting for skew, while in others it was strengthened. The bottom line is that there does appear to be real evidence for heritable variation from the analysis of these models, but estimating some of its features (in particular the correlation between breeding values for trait means and residual variances) is very delicate.

The final line of evidence is the mapping of genes involved in either canalization or trait variances. The classic example of the former is the heat shock protein HSP90, which has been shown to buffer both genetic and environmental effects (reviewed in Sangster et al. 2008). The latter are QTLs associated with trait variances (denoted **vQTLs** by Rönnegård and Valdar 2011). While early QTL mapping projects noted that some marker genotypes differed in their trait variances as well as their means (e.g., Edwards et al. 1987), the formal development of specific methods to map such QTLs is rather recent (Ordas et al. 2008; Paré et al. 2010; Struchlain et al. 2010; Visscher and Posthuma 2010; Rönnegård and Valdar 2011, 2012; Jimenez-Gomes et al. 2011; Hothorn et al. 2012; Shen et al. 2012). While these studies have found a number of candidate regions, as with between-sire differences in family variances, they reflect differences in the *residual* (as opposed to strictly the *environmental*) variance for marker genotypes, and hence can arise from differences in sensitivity to genetic background. Indeed, Paré et al. (2010) and Deng and Paré (2011) have suggested using variance heterogeneity across markers as a preliminary scan for potentially epistatic loci.

Collectively, these observations suggest that heritable variation in the environmental variation likely exists for many traits, and that selection on the phenotypic variance can result in a response in part due to changes in the overall environmental variance of the population. Consistent with the view, recall that changes in σ^2_E were seen in several of the stabilizing/disruptive selection experiments reviewed in Chapter 16.

MODELING GENETIC VARATION IN σ^2_E

A variety of statistical models have been proposed to account for heritable transmission of at least part of the environmental variance. The starting point for each is that the phenotypic value of an individual of genotype i can be written as

$$z_i = \mu + G_i + E, \quad \text{where} \quad E \sim (0, \sigma^2_i) \tag{17.1a}$$

The notation $x \sim (\mu, \sigma^2)$ denotes that x comes from a distribution with mean μ and variance σ^2. For ease of development, we generally assume that the trait is entirely additive so that $G = A_m$, the breeding value for the mean. Taking the expectation (to avoid confusion, we use roman E for expectation and italic E for environmental values), the population environmental variance is the average of the σ^2_i,

$$\sigma^2_E = \mathrm{E}[\,\sigma^2_i\,] \tag{17.1b}$$

If working with a series of pure lines, one can estimate σ^2_i directly. The more interesting (and difficult) problem arises when considering an outbred population. In this case we have to deal with both estimation and the vexing issue of modeling transmission. Models allowing

for heterogeneity of environmental variance were introduced in the 1990's (e.g., Foulley et al. 1992, Foulley and Quaas 1995, Cullis et al. 1996), but these ignored the question of selection (and evolution) of the environmental variance itself. The first formal analyses of the evolution of the environmental variance were population-genetic models by Gavrilets and Hastings (1994) and Wagner et al. (1997), and breeding-value based models by SanCristobal-Gaudy et al. (1998).

The Multiplicative Model

Gavrilets and Hastings (1994) assumed some underlying environmental value e (such as temperature), with different genotypes having different sensitivity γ_i, so that

$$E = \gamma_i\, e, \quad \text{where} \quad e \sim (0, \sigma_e^2) \tag{17.2a}$$

This **multiplicative model** is simply the joint regression model for genotype-environment interactions (LW Equation 22.13b; Volume 3), and was also used by Wagner et al. (1997). Under Equation 17.2a, the conditional environmental variance (given the genotypic value and its environmental sensitivity) is

$$\sigma^2[E \,|\, G, \gamma_i] = \gamma_i^2 \sigma_e^2 \tag{17.2b}$$

As shown in Example 17.2 (below), taking the expected value over $\gamma \sim (\mu_\gamma, \sigma_\gamma^2)$ gives the unconditional environmental variance as

$$\sigma_E^2 = \left(\mu_\gamma^2 + \sigma_\gamma^2\right) \sigma_e^2 \tag{17.2c}$$

Under the multiplicative model, the environmental variance for the population decreases by selecting μ_γ to zero and/or by decreasing the variance σ_γ^2. The problematic issue here is modeling the change in the distribution of the genotypic-specific sensitivities γ. The simplest approach is to assume the environmental sensitivity γ is an entirely additive quantitative trait, so that $\gamma = A_v$, namely the breeding value for the environmental variance.

Equation 17.2c lead Gavrilets and Hasting to comment on the relationship between developmental noise and heterozygosity mentioned previously. Lerner assumed this was causative — higher levels of heterozygosity resulted in decreased environmental variance. However, Gavrilets and Hastings noted that when $\mu_\gamma^2 = 0$, as might occur with selection to decrease σ_E^2, then the environmental variance is proportional to the additive genetic variance $\sigma_\gamma^2 = \sigma_{A_v}^2$. Recalling a result from Chakraborty (1987), namely that for an additive trait, the genetic variance is a decreasing function of the number of heterozygous loci, they note that the correlation between heterozygosity and σ_E^2 simply falls out as a consequence of their model, rather than from any functional relationship between the two. Conversely, if Lerner was correct and the relationship between σ_E^2 and heterozygosity is indeed casual, Zhivotovsky and Feldman (1992) note that if σ_E^2 is a decreasing function of heterozygosity, the equilibrium mean value of a trait under stabilizing selection may not coincide with its optimal fitness value.

If we allow for dominance in the quantitative-trait formulation of γ, we now have $\gamma = A_v + D_v$, where the dominance value D_v is *not* transmitted from parent to offspring. Further, by construction D_v has a mean value of zero and under the infinitesimal model, the dominance variance is not changed by selection (Chapter 15). Under this extension, the mean environmental variance becomes

$$\sigma_E^2 = \left(\mu_{A_v}^2 + \sigma_{A_v}^2\right) \sigma_e^2 + \sigma_{D_v}^2\, \sigma_e^2 \tag{17.2d}$$

While selection can reduce the first component (either by driving the mean breeding value to zero and/or reducing $\sigma_{A_v}^2$ by generating negative disequilibrium), the component involving

non-additive variance remains unchanged. Hence, implicit in assuming a breeding value for this model (or any of the others discussed below) is that any non-transmissible genetic variation in σ^2_E remains unchanged by selection. Genetic variation in σ^2_E, by itself, is not sufficient for a selection response, as the later requires that at least part of this variation must be transmissible under the breeding scheme used.

The Exponential Model

While we have presented the multiplicative model within a breeding-value framework, this was not explicitly done by Gavrilets and Hastings (1994), who (coming from a population-genetics background) were more concerned with evolution of the environmental variance than estimating A_v. Conversely, SanCristobal-Gaudy et al. (1998), coming from an animal breeding background, were more concerned with estimation. They did so by modeling E using an **exponential model**,

$$E = \exp\left(\frac{A_v}{2}\right) \cdot e, \quad \text{where} \quad e \sim N(0, \sigma^2_e) \quad \text{and} \quad A_v \sim N(\mu_{A_v}, \sigma^2_{A_v}) \tag{17.3a}$$

The connection with the multiplicative model follows by noting for small $|x|$ that $e^x \simeq 1 + x$, so that $E \simeq (1 + A_v/2) \cdot e$ for small $|A_V|$. By assuming normality and independence (of e, A_v, and A_m), SanCristobal-Gaudy et al. (1998) obtain likelihood estimators for the breeding values for the environmental variance (A_v) and trait mean (A_m). They explicitly considered estimation under either a sire design (using half sib values to estimate A_v and A_m of the parent) or using a repeatability model (Chapters 13, 19) where repeated measurements on a single individual and its relatives are used to estimate breeding values for σ^2_E. SanCristobal-Gaudy et al. (2001) extend this approach to threshold traits (in particular, litter size). Bayesian estimators under this model were developed by Sorensen and Waagepetersen (2003) and Ros et al. (2004).

Given A_v, the conditional distribution of the environmental variance becomes

$$\sigma^2(E \mid A_v) = \sigma^2_e \exp(A_v), \tag{17.3b}$$

which follows by recalling $(e^a)^2 = e^{2a}$. Hence, the environmental variance is a constant (σ^2_e) multiplied by a scaling factor that is a function of the breeding value A_v for the environmental variance. Decreasing A_v results in an individual with reduced environmental sensitivity (reduced σ^2_E). The constant σ^2_e can be interpreted as the environmental variance for an individual with an environmental breeding value of zero. The exponential model is also called the **log-additive model**, as the breeding value is additive on the log of the variance scale,

$$\ln\left[\sigma^2(E \mid A_v)\right] = \ln\left(\sigma^2_e\right) + A_v, \tag{17.3c}$$

As detailed in Example 17.2, the expectation of Equation 17.3b (over the population distribution of A_v values) gives the mean environmental variance as

$$\sigma^2_E = \sigma^2_e \, \exp\left(\mu_{A_v} + \sigma^2_{A_v}/2\right) \tag{17.3d}$$

Equation 17.3d shows that either decreasing the mean breeding value μ_{A_v}, or its additive variance $\sigma^2_{A_v}$, decreases the environmental variance. Comparison of Equations 17.2c and 17.3d shows one subtle difference between the multiplicative and exponential models. Under the former, the minimal population environmental variance occurs when $\mu_{A_v} = 0$, with any deviation from this increasing the average environmental variance in the population. By contrast, under the exponential model, decreasing μ_{A_v} always decreases the average value of σ^2_E in the population. Thus, under the exponential model, σ^2_E can be selected to be arbitrary

small, while under the multiplicative model, it has a lower bound set by $\sigma^2_{A_v}$ (and more generally by the dominance variance as well, see Equation 17.2d).

The Additive Model

Our last formulation for modeling genetic variation in E was suggested by Hill and Zhang (2004) and Mulder et al. (2007),

$$E = U \cdot \sqrt{\sigma^2_e + A_v}, \quad \text{where} \quad U \sim N(0,1) \quad \text{and} \quad A_v \sim N(\mu_{A_v}, \sigma^2_{A_v}) \tag{17.4a}$$

This is the **additive model**, as the environmental variance for an individual with breeding value A_v is simply

$$\sigma^2(E \mid A_v) = \sigma^2_e + A_v, \tag{17.4b}$$

with the constraint on the breeding value that $\sigma^2_e + A_v > 0$. The additive model is a *local* analysis around the current mean, as selection to decrease A_v can eventually result in this constraint being violated, generating a negative variance. Under the additive model, the mean population value for the environmental variance is simply

$$\sigma^2_E = \mathrm{E}\left(\sigma^2_e + A_v\right) = \sigma^2_e + \mu_{A_v} \tag{17.4c}$$

Unlike the multiplicative and exponential models, changes in σ^2_E under the additive model depend only on changes in the mean breeding value, and not its variance (Table 17.1).

Table 17.1. Models for heritable variation in the environmental value E. The basic model is $z = \mu + A_m + E$, where z is the trait value and $A_m \sim N(\mu_{A_m}, \sigma^2_{A_m})$ the breeding value for z. The table gives the assumed form of E for different models as a function of the breeding value in variance $A_v \sim N(\mu_{A_v}, \sigma^2_{A_v})$, some intrinsic environmental value $e \sim N(0, \sigma^2_e)$, and the unit normal $U \sim N(0,1)$.

Model	E	$\sigma^2(E \mid A_v)$	$\sigma^2(E) = \mathrm{E}\left[\sigma^2(E \mid A_v)\right]$
Multiplicative	$A_v \cdot e$	$A_v^2\,\sigma^2_e$	$\left(\mu^2_{A_v} + \sigma^2_{A_v}\right)\sigma^2_e$
Exponential (or log-additive)	$\exp\left(A_v/2\right) \cdot e$	$\sigma^2_e \exp\left(A_v\right)$	$\sigma^2_e\,\exp\left(\mu_{A_v} + \sigma^2_{A_v}/2\right)$
Additive	$\sqrt{A_v + \sigma^2_e} \cdot U$	$A_v + \sigma^2_e$	$\mu_{A_v} + \sigma^2_e$

The additive model has the advantage of being much more tractable, but the disadvantage that it breaks down when the breeding value becomes sufficiently negative ($A_v < -\sigma^2_e$). In contrast, the exponential model has additivity on the log of the variance scale, which is a nice statistical feature, as log variances are approximately normally-distributed (Box 1953, Layard 1973). Mulder et al. (2007) discuss additional connections between the additive and exponential models, while Hill and Mulder (2010) review the different estimation methods.

Example 17.2. Here we derive the unconditional variances for the models summarized in Table 17.1. Consider the multiplicative model first, where

$$\sigma^2_E = \mathrm{E}[\,\gamma^2\sigma^2_e\,] = \sigma^2_e\,\mathrm{E}[\,\gamma^2\,]$$

Recalling that $\mathrm{E}[\,x^2\,] = \mu^2_x + \sigma^2_x$,

$$\sigma^2_E = \sigma^2_e\,\mathrm{E}[\,\gamma^2\,] = \sigma^2_e\left(\sigma^2_\gamma + \mu^2_\gamma\right)$$

Now consider the exponential model (Equation 17.3a). By construction both E and e have expected value zero, so that the variances of E and e are simply the expected values of E^2 and e^2,

$$\sigma_E^2 = \mathrm{E}\left[\left(e \cdot \exp\{A_v/2\}\right)^2\right] = \sigma_e^2\,\mathrm{E}\left[\left(\exp\{A_v/2\}\right)^2\right] = \sigma_e^2\,\mathrm{E}\left[\exp\left(A_v\right)\right],$$

where the expected value is taken with respect to the distribution of breeding values A_v. The last expectation is computed by noting for a normal x with mean μ and variance σ^2, that $\mathrm{E}[e^x] = \exp(\mu + \sigma^2/2)$, which follows using the standard expression for the moment generating function $\mathrm{E}(e^{tx})$ upon setting $t = 1$ (Johnson and Kotz 1970a). Since we assumed $A_v \sim N(\mu_{A_v}, \sigma^2_{A_v})$, the average environmental variance for the population becomes

$$\sigma_E^2 = \sigma_e^2\,\exp\left(\mu_{A_v} + \frac{\sigma^2_{A_v}}{2}\right).$$

Table 17.2. Estimates of the heritability h_v^2 and evolvability $CV_{A_v} = \sigma_{A_v}/\sigma_E^2$ (Equation 13.22b) of the environmental variance, as well as the additive-genetic correlation ρ between A_m and A_v. For some of Yang et al. (2011) results, BC denotes a Box-Cox transformation was simultaneously fitted with the model, while their results without this notation indicate this transformation was not used. In part, from Mulder et al. (2007) and Hill and Mulder (2010).

Species	Trait	h_v^2	CV_{A_v}	ρ	Reference
Pig (*Sus*)	Meat pH	0.039	0.40	0.79	SanCristobal-Gaudy et al. (1998)
	Litter size	0.026	0.31	−0.62	Sorensen & Waagepetersen (2003)
		0.021	0.27	−0.64	Yang et al. (2011)
		0.012	0.19	0.70	Yang et al. (2011), BC
	Weight	0.011	0.34	−0.07	Ibáñez-Escriche et al. (2008c)
Sheep (*Ovis*)	Litter size	0.048	0.51	0.19	SanCristobal-Gaudy et al. (2001)
Snail (*Helix*)	Body weight	0.017	0.58	−0.81	Ros et al. (2004)
Chicken	Body weight	0.029	0.30	−0.17	Rowe et al. (2006)
(*Gallus*)	(male)	0.046	0.49	−0.45	Mulder et al. (2009)
		0.030	0.32	−0.23	Wolc et al. (2009)
	Body weight	0.031	0.32	−0.11	Rowe et al. (2006)
	(female)	0.047	0.57	−0.41	Mulder et al. (2009)
		0.038	0.37	−0.27	Wolc et al. (2009)
Rabbit (*Lepus*)	Litter Size	0.045	0.42	−0.74	Ibáñez-Escriche et al. (2008b)
		0.041	0.37	−0.73	Yang et al. (2011)
		0.017	0.24	0.28	Yang et al. (2011), BC
	Birth weight	0.013	0.25	—	Garreau et al. (2008)
Mouse (*Mus*)	Litter size	0.048	0.44	−0.93	Gutierrez et al. (2006)
	Litter weight	0.039	0.37	−0.81	Gutierrez et al. (2006)
	Birth weight	0.208	1.21	0.97	Gutierrez et al. (2006)
	Body weight	0.006	0.36	−0.31	Ibáñez-Escriche et al. (2008a)
	Weight gain	0.018	0.47	−0.19	Ibáñez-Escriche et al. (2008a)
Average		0.038	0.41	−0.24	

h_v^2, the Heritability of the Environmental Variance

Mulder et al. (2007) suggest a definition for the heritability of the environmental variance as the slope of the regression of the breeding value of an individual on its phenotype. Under the additive model framework (Equation 17.4), they show that A_v is a linear function of the square z^2 of phenotypic value. From regression theory (LW Chapter 3), the slope of the regression of A_v on z^2 is simply their covariance divided by the variance of the predictor variable,

$$h_v^2 = \frac{\sigma(A_v, z^2)}{\sigma^2\left(z^2\right)} \tag{17.5a}$$

By definition, $\sigma(A_v, z^2) = \sigma(A_v, A_v) = \sigma_{A_v}^2$, while (assuming z is normally distributed) $\sigma^2(z^2) = 2\sigma_z^4 + 3\sigma_{A_v}^2$. This gives the heritability as

$$h_v^2 = \frac{\sigma_{A_v}^2}{2\sigma_z^4 + 3\sigma_{A_v}^2} \tag{17.5b}$$

Table 17.2 reviews estimates of h_v^2 from the literature. The listed studies vary in which model (Table 17.1) was used for the heritable transmission of σ_E^2, with the additive variance for σ_E^2 extracted from each and used in Equation 17.5b.

Note that the estimated heritabilities are low, typically less that five percent. However, also note that the evolvability is large. Although selection may be difficult (given the low heritability), there is much variation to exploit, as a high evolvability implies that significant proportional change in the trait value can be achieved. (Chapter 13). The average estimated value of CV_{A_v} in Table 17.2 is roughly 0.4, for a squared value of 0.16. Recall from Chapter 13 that the metric $I_{A_v} = CV_{A_v}^2$ gives of the expected amount of response given a standard unit of selection (Equation 13.22c). Thus, a total unit amount of selection on the environmental value is expected to change its mean value by 16%. The fragility of these models can be seen by comparing the estimated additive-genetic correlation ρ in the two litter size studies (Yang et al. 2011). For pigs, untransformed data gave $\rho = -0.64$, which changes to $\rho = 0.70$ when a Box-Cox transformation was used. For rabbits, ρ changes from -0.73 to 0.28.

SELECTION ON σ_E^2

The response in σ_E^2 is a function of two issues: the nature of transmission and the nature of selection. We first discuss transmission: how a change in the mean value of A_v translates into a change in σ_E^2 in the next generation. As might be expected from the above discussion, the results depend on which of the models given in Table 17.1 is used. Second, how does selection act to change the distribution of A_v? Three general pathways are available. The first is direct selection on A_v generated by selection on the phenotypic value z of a trait. Second, natural or artificial selection can be based on direct expression of σ_E^2 in an individual through repeated measurements, selecting for individuals with a larger (or smaller) range in these records.

The final route is through a correlated response (Equation 13.26c), with selection on z resulting in selection on the breeding value A_m for the trait, which in turn is correlated with A_v. The machinery of multivariate selection is needed to consider the totality of response in such cases, so we focus solely here on the direct response (i.e., assume a zero correlation), deferring the general case until Volume 3. However, a few brief comments on the nature of this correlation are in order. If the coefficient of variation σ_z/μ_z is to remain roughly constant under selection, we expect A_m and A_v to be positively correlated, with larger breeding values for the trait resulting in larger environmental variances. While most estimated corrrelations are negative (Table 17.2), there are reasons these should be viewed with caution. Current

statistical models assume no intrinsic skew in the data other than that generated by any correlation between A_m and A_v. If skew is present for other reasons, this can significantly bias estimates (Ros et al. 2004). For example, Yang et al. (2011) obtained highly negative estimates for litter size in pigs and rabbits using untransformed data ($\rho = -0.64$ and -0.73), but these estimates changed sign (to 0.70 and 0.28, respectively) when the data were transformed.

Transmission: Translating the Response in A_v into Response in σ^2_E

A number of authors have modeled the response in the phenotypic variance when there are heritable differences in environmental sensitivity (Gavrilets and Hastings 1994; Wagner et al. 1997; SanCristobal-Gaudy et al. 1998, 2001; Sorensen and Waagepetersen 2003; Ros et al. 2004; Hill and Zhang 2004; Mulder et al. 2007, 2008). A critical step in each of these models is treating phenotypic value and residual variance as two separate (and potentially correlated) traits, both with heritable (i.e., additive-genetic) variation. While some models (Gavrilets and Hastings 1994, Wagner et al. 1997, Hill and Zhang 2004) are based on strict population-genetic analysis (following the change in individual allele frequencies), most are based on schemes that assign breeding values to the heritable component of σ^2_E (Table 17.1). Under the infinitesimal model, the expected breeding value in the offspring is simply the mean breeding values of its parents (Chapter 13), while changes in the variance in breeding values from parent to offspring follow from Equation 16.8b. Using the expressions given Table 17.1 allows us to map changes in μ_{A_v}, the mean breeding value for environmental sensitivity, into changes in σ^2_E. The simplest case is the additive model (Equation 17.4b). Let the response R_{A_v} denote the change in the mean breeding value of the selected parents from the mean breeding value of the entire population. The resulting change in σ^2_E becomes

$$\begin{aligned}\Delta\sigma^2_E(t) &= \sigma^2_E(t+1) - \sigma^2_E(t) = \left[\, \mu_{A_v}(t+1) + \sigma^2_e \,\right] - \left[\, \mu_{A_v}(t) + \sigma^2_e \,\right] \\ &= \mu_{A_v}(t) + R_{A_v}(t) - \mu_{A_v}(t) = R_{A_v}(t) \end{aligned} \tag{17.6a}$$

The response a bit more complex under the multiplicative and exponential models, as the mean population value σ^2_E for the environmental variance is a non-linear function of the mean (and variance) of the A_v. Assume no change in the additive variance of environmental sensitivities following selection. Under the multiplicative model (Equation 17.2a), the change in σ^2_E given a change in breeding values becomes

$$\begin{aligned}\Delta\sigma^2_E(t) &= \left(\left[\, \mu_{A_v}(t) + R_{A_v}(t) \,\right]^2 + \sigma^2_{A_v} \right) \sigma^2_e - \left(\mu^2_{A_v}(t) + \sigma^2_{A_v} \right) \sigma^2_e \\ &= \left[\, 2\mu_{A_v}(t) R_{A_v}(t) + R^2_{A_v}(t) \,\right] \sigma^2_e \end{aligned} \tag{17.6b}$$

Change in the variance in breeding value in the parents can similarly be accounted for by using Equation 16.8b. Under the exponential model, again assuming no change in $\sigma^2_{A_v}$,

$$\begin{aligned}\Delta\sigma^2_E(t) &= \sigma^2_e \, \exp\left[\mu_{A_v}(t) + R_{A_v}(t) + \sigma^2_{A_v}/2\right] - \sigma^2_e \, \exp\left[\mu_{A_v}(t) + \sigma^2_{A_v}/2\right] \\ &= \sigma^2_e \, \exp\left[\mu_{A_v}(t) + \sigma^2_{A_v}/2\right] \left(\exp\left[R_{A_v}(t)\right] - 1\right) \\ &= \sigma^2_E(t) \cdot \left(\exp[\, R_{A_v}(t)\,] - 1\,\right) \end{aligned} \tag{17.6c}$$

These expressions translate a response R_{A_v} into the expected change in σ^2_E. We consider two different setting by which such a responsecan occur: as a consequence of direct selection on phenotypic value z and as the result of direct selection on σ^2_E itself.

Response From Stabilizing Selection on Phenotypic Value z

We have previously suggested that selection either for, or against, extreme individuals may also result in some selection for genotypes with higher or lower environmental variances.

We formalize this by considering how selection on a phenotypic value z maps into selection on A_m and A_v. First consider a quadratic fitness model of stabilizing selection. Here, the expected fitness of an individual with phenotypic value z is

$$W(z) = 1 - s(z-\theta)^2, \tag{17.7a}$$

where θ is the optimal trait value and s the strength of stabilizing selection. This is a weak selection model, as $W \geq 0$ only for sufficiently small s relative to the total variance of z. Note that if we take $s < 0$, Equation 17.7a becomes a model of (weak) disruptive selection. Gavrilets and Hastings (1994) examined how this phenotypic fitness function translates into selection on (A_m, A_v) under the multiplicative model. To do so, replace z by $A_m + A_v e$ and take the expectation over e. Noting that $\mathrm{E}[e] = 0$, $\mathrm{E}[e^2] = \sigma_e^2$, the expected fitness as a function of A_m and A_v becomes

$$\begin{aligned} W(A_m, A_v) &= 1 - s\,\mathrm{E}_e\left[\,(A_m + A_v\,e - \theta)^2\right] \\ &= 1 - s\left[\,(A_m-\theta)^2 + 2(A_m-\theta)A_v\mathrm{E}_e\left[\,e\,\right] + A_v^2\,\mathrm{E}_e\left(e^2\right)\right] \\ &= 1 - s\left[\,(A_m-\theta)^2 + A_v^2\,\sigma_e^2\right] \end{aligned} \tag{17.7b}$$

Similar fitnesses arise under the guassian model of weak stabilizing selection (Equation 16.17), see Hill and Mulder (2010), but also see Example 17.3. Equation 17.7b shows that phenotypic stabilizing selection favors A_v values near zero, decreasing σ_E^2. There are two important consequences of this. First, the reduction in phenotypic variance can be significantly greater than predicted from the simple reduction in the additive variance from the Bulmer effect (Chapter 16). Second, there can be cases where the heritability will *increase* under stabilizing selection. Since both additive and environmental variances are decreased, if the decrease in environmental variance is sufficiently greater, h^2 increases. Results for quadratic disruptive selection follow by changing the sign on s, resulting in selection to increase A_v.

Example 17.3. The quadratic fitness function (Equation 17.7a) is a model for weak stabilizing selection, as it can generate negative (and hence undefined) fitness values when selection is sufficiently strong. A completely general model of stabilizing selection without this constraint is normalizing selection (Equation 16.17), where θ denotes the optimal phenotypic value and ω^2 the strength of selection around this optimum. Devaus and Lande (2009) use this fitness function in their study of selection on the flower-timing variance within an individual. They assumed the additive model for genetic variation in σ_e^2 (Equation 17.4c) and that repeated expressions z of the trait from an individual with breeding values A_m (for the trait) and A_v (for σ_E^2) were drawn from a normal, so that

$$p(z \mid A_m, A_v) = \frac{1}{\sqrt{2\pi(\sigma_e^2 + A_v)}} \exp\left(-\frac{(z-A_m)^2}{2(\sigma_e^2 + A_v)}\right).$$

Integration of $W(A_m, A_v) = \int W(z)\, p(z \mid A_m, A_v)\, dz$ yields

$$W(A_m, A_v) = \sqrt{\frac{\omega^2}{\omega^2 + \sigma_e^2 + A_v}}\, \exp\left(-\frac{(A_m-\theta)^2}{2(\omega^2 + \sigma_e^2 + A_v)}\right) \tag{17.8}$$

When $A_m \simeq \theta$, the exponential term is near one (as its numerator is near zero), so that fitness is largely driven by the square root term. As was the case for weak quadratic selection, fitness

increases as A_v decreases. The more interesting case is when the population is far from the equilibrium, so that $|\, A_m - \theta \,| \gg 1$, and the numerator in the exponential term is large. In this case, fitness can be improved by *increasingly* the value of A_v, reducing the magnitude of the exponential term. Thus, as also noted by Lande (1980) and Bull (1987), stabilizing selection can actually favor an *increase* in σ_e^2 when the population is far from its optimal, as the larger variance increases the chance that some phenotypes are near θ.

Response From Directional Selection on z

Now consider directional selection. Assuming the multiplicative model and a simple linear fitness function

$$W(z) = 1 + sz, \tag{17.9a}$$

Gavrilets and Hastings found that

$$W(A_m, A_v) = 1 - s\mathrm{E}_e(A_m + eA_v) = 1 - sA_m + A_v\mathrm{E}_e(e) = 1 - sA_m \tag{17.9b}$$

Under this setting, there is no direct selection on A_v. A rather different outcome was noted by both Hill and Zhang (2004) and Mulder et al. (2007) for truncation selection on a normally-distributed trait. As a measure of fitness, Hill and Zhang considered the probabilty $P(a, b)$ that a genotype with mean effect $\mu + a$ and variance effect $\sigma^2 + b$ is selected by using a Taylor series approximation for the probability that such a genotype exceeds the truncation threshold when a fraction p are saved and $z \sim N(\mu, \sigma^2)$. Keeping only first-order terms in a and b recovers

$$\frac{P(a,b)}{p} \simeq 1 + a\frac{\overline{\imath}}{\sigma_z} + \frac{b}{2}\,\frac{\overline{\imath}\; x_{[1-p]}}{\sigma_z^2} \tag{17.10a}$$

Here $\overline{\imath}$ is the selection intensity (Equation 14.3a), and $x_{[1-p]}$ satisfies $\Pr(U \geq x_{[1-p]}) = p$ where $U \sim N(0,1)$. Thus, truncation selection generates selection pressure $\overline{\imath}$ on A_m and selection pressure $\overline{\imath}\, x_{[1-p]}$ on A_v. When A_m and A_v are uncorrelated, the expected response in the trait mean is just our standard result from Chapter 13 (Equation 13.6b),

$$R_{A_m} = h_m^2\, \overline{\imath}\, \sigma_z \tag{17.10b}$$

Under the additive model for the environmental variance, Hill and Zhang found the response in the mean breeding value for the envrionmental variance is

$$R_{A_v} = h_v^2\; \overline{\imath}\; x_{[1-p]}\, \sigma_z^2, \tag{17.10c}$$

which is also the response in σ_E^2 (Equation 17.6a). Equation 17.10a assumes the population distribution of the trait value z is approximately normal, which breaks down at extreme trait values when there is heritable variation in σ_E^2 (as z is no longer normally distributed but rather a weighted mixture of normals). Hence, for strong selection these results are biased.

Example 17.4. Consider a trait with $\sigma_z^2 = 100$, $h_m^2 = 0.3$, and $h_v^2 = 0.03$ (a typical value from Table 17.2). Assume the additive model for the environmental variance. What is the expected response in the mean and σ_E^2 following a single generation of truncation selection with $p = 0.1$? First note that that under these assumptions $h_m^2\sigma_z = h_v^2\sigma_z^2 = 3$, so that the differences in response are due to differences in the strength of selection (Equations 17.10b versus 17.10c), not the genetic variances of these traits.

Noting that $\Pr(U > 1.282) = 0.1$, we have $x_{[1-0.1]} = 1.282$ and $\overline{\imath} = \varphi(1.282)/0.1 = 1.755$, with Equations 17.10b and c giving

$$R_{A_m} = 0.3 \cdot 1.755 \cdot 10 = 5.265, \quad \text{and} \quad R_{A_v} = 0.03 \cdot 1.755 \cdot 1.282 \cdot 100 = 6.750,$$

so that a single generation of selection increases the mean by 5.3 and the environmental variance by 6.75. Using these same parameter values, the Bulmer equation (Equation 16.12d) gives the change in $\sigma^2_{A_m}$ after one generation of selection as $d = -3.74$, for (ignoring changes in σ^2_E) a phenotypic variance of 96.26 and a heritability of (30-3.74)/(100-3.74) = 0.27. Accounting for changes in σ^2_E gives phenotypic variance as 100-3.74+6.75 = 103.1 and heritability (30-3.74)/103.1 = 0.25. Since the response in the trait mean is given by $R(t) = h^2(t)\,\overline{\imath}\,\sigma_z(t)$, the decrease in h^2 is somewhat offset by the increase in the phenotypic variance. The response in the trait mean in generation two is $0.27 \cdot 1.77 \cdot \sqrt{96.26} = 4.69$ ignoring the change in σ^2_E and $0.25 \cdot 1.77 \cdot \sqrt{103.1} = 4.49$ including it.

Now consider stronger selection, $p = 0.01$. Here $x_{[1-p]} = 2.326$ and $\overline{\imath} = 2.666$, giving

$$R_{A_m} = 0.3 \cdot 2.666 \cdot 10 = 7.998, \quad \text{and} \quad R_{A_v} = 0.03 \cdot 2.666 \cdot 2.326 \cdot 100 = 18.603$$

Relative to $p = 0.1$, this is roughly a 50% increase in the response in the mean, but a 275% increase in the response in the environmental variance. The Bulmer equation gives $d = -4.06$ for one generation of selection and a resulting heritability (ignoring any changes in σ^2_E) of 0.27. Including the change in environmental variance, the new phenotypic variance is 100-4.06+18.60 = 114.54, for a heritability of 25.94/114.54 = 0.23. As above, the actually heritability is less than predicted from the Bulmer equation, but the resulting impact on the response in the mean is again partly offset by the increase in the phenotypic variance, with the expected response in generation two of 7.06 (Bulmer) and 6.78 (Bulmer plus changes in σ^2_E).

Example 17.4 illustrates that as truncation selection becomes stronger, there is a disproportionate change in the variance relative to the mean, as selection is choosing outliers, and hence more strongly influenced by genotypes with larger variances. The effect on σ^2_E from directional selection on trait value is thus expected to be greatest under strong selection (Hill and Zhang 2004). We can quantify this using Equation 17.10a. As shown in Figure 17.1, from large p (weak selection as most of the population is saved), selection on the mean ($\overline{\imath}$) dominates. The two strengths of selection are equal around $p = 0.16$, below which selection on the variance ($\overline{\imath}\,x_{[1-p]}$) is stronger. For $p > 0.5$ (more than half the population is saved), $x_{[1-p]} < 0$ implying that weak directional selection results in a slight *decrease* in σ^2_E (Hill and Zhang 2004). The effect is largest around $p = 0.80$ (only 20 percent of the population culled) and but even here the strength of selection σ^2_E is fairly small, with $\overline{\imath}\,x = -0.3$. This slight decrease in σ^2_E under weak directional selection occurs because only low outliers are selected *against*, and such genotypes tend to have slightly higher variances.

As we have seen, there are two very different pathways, through either σ^2_A or σ^2_E, for short-term change in the phenotypic variance σ^2_z. Generation of gametic-phase disequilibrium by selection changes σ^2_A without requiring significant allele-frequency change. Likewise, the presence of heritable variation in σ^2_E can also generate a short-term response in the total variance. As noted by Bull (1987), "environmental and genetic factors may thus compete to produce a given selected level of phenotypic variance". What insight do our above results offer on which factor is more important? The general conclusion is that while the direct selection pressure on σ^2_E *often* has the same sign as the selection on σ^2_A, this is not *always* the case.

Under disruptive selection, there is direct select for positive disequilibrium (and hence an increase in σ^2_A), along with direct selection to increase σ^2_E, so that the Bulmer equation

is expected to under-predict the increase in phenotypic variance. With stabilizing selection (when the population mean is close to the optimum value), the direct selection pressures on σ^2_A and σ^2_E also align, favoring a decrease in each and again an underprediction of the total change if just the Bulmer equation is applied. However, when the current population mean is far from the optimum, there can be selection pressure to *increase* σ^2_E. The most direct conflict between these two potential components of change in the phenotypic variance occurs under directional selection. This always generates negative d and hence a reduction in the additive variance. However, under modest to strong selection, it also favors an *increase* in σ^2_E, often resulting in both an increase in the phenotypic variance and a further decrease in the heritability. The net result is that the Bulmer equation underpredicts the expected change in the mean (Example 17.4). With very modest selection (over 50% of the population saved), there is weak selection pressure for a slight *decrease* in σ^2_E. It is important to stress that all of these results only consider *direct* response in σ^2_E (i.e., we assume $\rho(A_m, A_v) = 0$). When the breeding values for the trait value and its environmental variance are negatively correlated, the sign of response on σ^2_E can depart from these predictions.

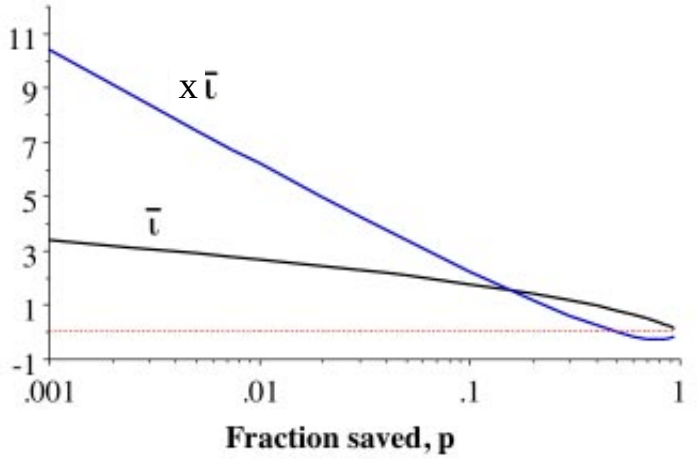

Figure 17.1. The relative strengths of selection on the mean ($\bar{\imath}$) and variance ($x\,\bar{\imath}$) under truncation selection as a function of the fraction p saved. The two strengths of selection are equal around $p = 0.16$. Note for $p > 0.5$ there is (weak) selection to *decrease* the variance, as the curve for $x\,\bar{\imath}$ dips below the dotted line indicating a value of zero.

Finally, while simple selection on z can result in direct selection on A_v, it also targets A_m as well. Through the use of an appropriate selection index, one can directly select on A_v alone (and hence directly target σ^2_E) even with only a single observation per individual. This is possible because A_m is linearly associated with z, while A_v is associated with z^2. Rescaling z to have mean zero, an index of the from $I_i = az_i + bz_i^2$ can be constructed to specifically target individuals with high (or low) A_v values. We examine this index, and the component responses, in Volume 3.

Direct Selection on σ^2_E Using Repeated-Records

While σ^2_E can change as a consequence of simple selection on trait value, a breeder may wish to target σ^2_E directly. The most conceptually straight-forward approach to do so would be selecting those individuals with the smallest residual variances under a repeated-measures design. We considered this design in Chapter 13 to reduce environmental noise when select-

ing on the *mean* trait value of an individual, but here the target is the actual *variation* among the records themselves. Individuals are chosen based on the index

$$I_i = \frac{1}{n-1}\sum_{=1}^{n}(z_{ij} - \overline{z}_i)^2, \tag{17.11}$$

where z_{ij} denotes the jth record (observation) from individual i, with selection for uniformity favoring individuals with smaller I_i values. Natural selection can also act in a repeated-records setting, such as on the within-individual variation in flowering time. Depending on the ecological setting, selection can favor individuals with either larger or smaller values within-individual variances (Devaus and Lande 2009). Assuming the exponential model for σ^2_E, San Cristobal-Gaudy et al. (1998) and Ibáñez-Escriche et al. (2008b) approximated the expected response in the mean breeding value of A_v given selection intensity $\overline{\imath}$ over the index I as

$$R_{A_a} \simeq \overline{\imath}\,\frac{\sigma^2(A_v)}{\sqrt{\exp\left[\sigma^2(A_v)\right]\left[(n+1)/(n-1)\right]-1}}, \tag{17.12}$$

where n is the number of repeated records per individual. More exact expressions are given in Ibáñez-Escriche et al. (2008b), who also examine the power and required sample sizes when using repeated-measures selection experiments to detect heritable environmental variation.

Under a strict repeated-records design, all observations in I_i have the same genotype. A related design is to select based on variation in trait value among the *offspring* of an individual. For example, Garreau et al. (2008) selected rabbit dams based upon Equation 17.11, but now the observations were the weights of her offspring (suitably corrected for fixed effects such as litter size and parity). As mentioned previously, offspring mortality is lower within litters with more similar weights, and such selection conceivably occurs in natural populations as well. Here the multiple records are based on individuals with potentially different genotypes, and hence a large litter variance could arise from a high breeding value for σ^2_E, segregation of a major gene, nonadditive variance, or (most likely) some combination of these. Garreau et al. observed a significant responses in the first generation in both up- and down-selected lines. In subsequent generations, the selection pressure was weaker in their experiment, but response was largely flat. While these data are consistent with a response in σ^2_E, the majority of the initial response may simply arise from selection for, or against, females heterozygous for major genes influencing weight.

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