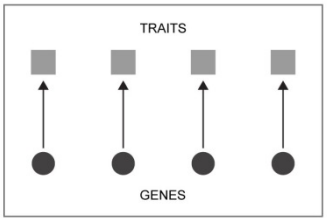
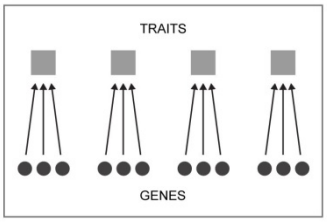
Chapter 6: Inheritance of Multiple Traits

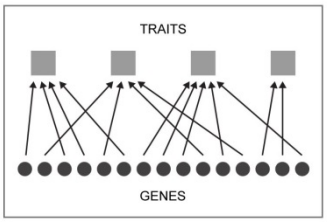
Overview.- The *G*-matrix provides a useful way to model inheritance when multiple traits are affected by many genes and genetically coupled. The *G*-matrix is a *m* trait x *m* trait table with genetic variances on its main diagonal and genetic covariances elsewhere. The genetic covariance between two traits summarizes genetic connections arising from linkage disequilibrium and pleiotropy. The entire G-matrix, as well as its constituent genetic variances and covariances, can be visualized as a stable balance between opposing forces. This stable equilibrium represents a compromise between alternative structures imposed by the processes of selection, mutation, recombination and migration. Studies of the effects of mutation on pairs of traits often reveal pleiotropy. Studies of multiple trait inheritance often reveal appreciable genetic correlations between traits, especially when those traits are parts of a functional complex.

6.00 The genotype-phenotype map for multiple characters

The relationship between genes and traits in quantitative genetics, the genotype-phenotype map, is a compromise between reality and tractability. In reality the causal path from a gene to a trait involves complex interactions with other genes and the environment. The implicit map that we will use is based on the ideas that traits are affected by many genes (polygeny) of small effect, that individual genes affect more than one trait (pleiotropy), and that environment exerts a residual, nonheritable influence on trait expression (Fig. 5.0). These simple ideas can be used to construct a useful and tractable model of inheritance that can also be used as a foundation for modeling more complicated paths from gene to trait. In the rest of this book, we will employ the model shown in Fig. 5.0c, which incorporates multiple traits, polygeny, and pleiotropy but no additional complications. {Ask Ivan to redraw the bottom panel so it illustrates pleiotropy; or add a panel with pleiotropy!}

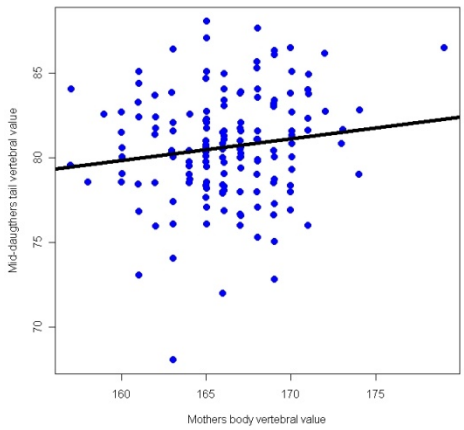






6.01 Multivariate resemblance between parents and offspring, the *G*-matrix

The multivariate generalization of genetic variance is the *G*-matrix, the key player in models for the inheritance of multiple traits. The G-matrix summarizes multivariate information about parent-offspring resemblance, just as a single scatterplot captures heritability in the univariate case. Returning to our example of vertebral numbers in garter snakes (Fig. 5.5) that we used to estimate heritabilities, Fig. 6.1 shows cross trait plots, one trait in mothers is plotted against another trait in daughters. These two plots can be used to estimate another kind of genetic parameter, the genetic covariance between body and tail vertebral numbers.



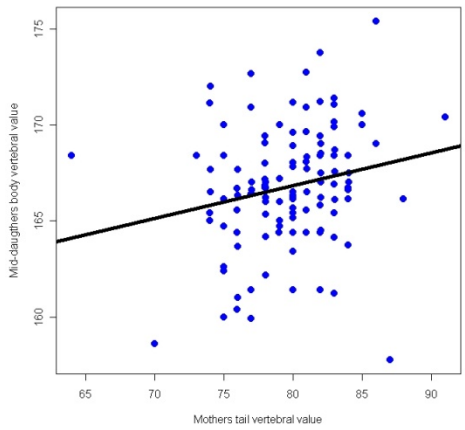


Figure 6.1 Examples of genetic covariance estimated from offspring-parent plots in the garter snake *T. elegans* (inland population). (a) The average tail vertebral count of daughters as a function of mother's body vertebral count, n = 154. (b) The average body vertebral count of daughters as a function of mother's tail vertebral count, n = 117. The estimate of genetic covariance based on both sets of data is 3.78 ± 1.67 s.e. (Phillips & Arnold 1999)

Converting the information in Figs. 5.5 and 6.1 into three parameter estimates, we can display the information in the following table, a G-matrix,

$$G = \begin{bmatrix} G_{11} & G_{12} \\ G_{12} & G_{22} \end{bmatrix} = \begin{bmatrix} 8.17 & 3.78 \\ 3.78 & 8.16 \end{bmatrix},$$

in which G_{11}=8.17 is the additive genetic variance for body vertebral number, G_{22}=8.16 is the additive genetic variance for tail vertebral number, and G_{12} =3.78 is the additive genetic covariance between body and tail vertebral numbers (Arnold & Phillips 1999, Phillips & Arnold 1999). The new element in this estimation exercise is genetic covariance, which describes how two traits run together in families. In the current example with only two traits, the G-matrix houses a single genetic covariance, but with m traits the G-matrix would be populated with $(m^2-m)/2$ covariances. The G-matrix is a convenient repository for all this information. More importantly, in matrix form all of that inheritance information can be used to make predictions about multivariate responses to selection and drift. To appreciate the important role that the G-matrix plays, we need to consider its conceptual underpinnings and its relationship to four other matrices, ***P***, ***E***, ***M*** and ***U***. None of these matrices are novel. We have seen each of them in univariate guise, as scalar variables in Chapter 5.

6.02 multivariate model for phenotypic value

Here we assume the same polygenic model for inheritance as in section 5.x, but consider the case of multiple traits, each affected by multiple loci, possibly with effects on multiple traits. Assuming no dominance and no epistasis, the model takes a simple form. Under these assumptions, each of the m additive genetic values is a sum of allelic effects within and across loci. Phenotypic (***z***), genetic (***x***), and environmental values (***e***) are each m x 1 column vectors, so that in the two-trait case

$$z = x + e = \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} e_1 \\ e_2 \end{bmatrix}. \qquad (6.00)$$

As before, we will assume no correlation or interaction between genetic and environmental values, so that ***z***, ***x*** and ***e*** are multivariate normal in distribution with means,

$$\bar{z} = \bar{x} + \bar{e} \quad (6.01)$$

and variance/covariance matrices

$$P = G + E\,, \quad (6.02)$$

where ***G***, ***P*** and ***E*** denote, respectively, additive genetic, phenotypic, and environmental variance-covariance matrices. The diagonal, variance elements of ***P***, ***G***, and ***E*** familiar from Chap 4. The off-diagonal elements in ***P*** are phenotypic covariances that in turn arise from covariance in genetic and environmental values (Fig. 6.2 = Bivariate distributions of *x*, *z*, and *e* with increasing numbers of loci and different values of genetic and environmental correlation). We will consider genetic covariance in detail because of its importance in affecting evolutionary responses to selection and finite population size.

Is it reasonable to assume that the distributions of *x* and *e* are multivariate normal? … Central Limit theorem … finding a transformation of scale so that the assumption applies …

In principle, we can determine the genetic value of an individual by assessing the phenotypic value of offspring produced by breeding that individual to a large, random sample of mating partners. In the multivariate case, that individual will have multiple genetic values, one for each of *m* traits. If we plot the genetic values for two traits for many individuals, we will obtain the kind of statistical clouds shown in Fig. 6.3a. Such scatterplots can reveal patterns in the covariance between pairs of traits. To quantify those patterns, it is often useful to calculate the genetic correlation between two traits,

$$r_g = G_{ij} / \sqrt{G_{ii} G_{jj}}\,, \quad (6.03)$$

where G_{ij} is the genetic covariance for the two traits, and G_{ii} and G_{jj} are their genetic variances. For example, from the garter snake example above, we can determine that the genetic correlation between body and tail vertebral numbers is $r_g = 3.78/\sqrt{8.17 * 8.16} = 0.46$. As usual for correlations, $-1 \le r_g \le 1$. If genetic values for the two traits are independent, $r_g = 0$ and the cloud will be elliptical, or circular if the two traits have the same genetic variance, with no inclination (Fig. 6.3a). If genetic values are positively correlated, $r_g > 0$ and the cloud has a positive inclination, as in Fig. 6.3b. A negative correlation, $r_g < 0$, means that the cloud has a negative inclination (Fig. 6.3c).

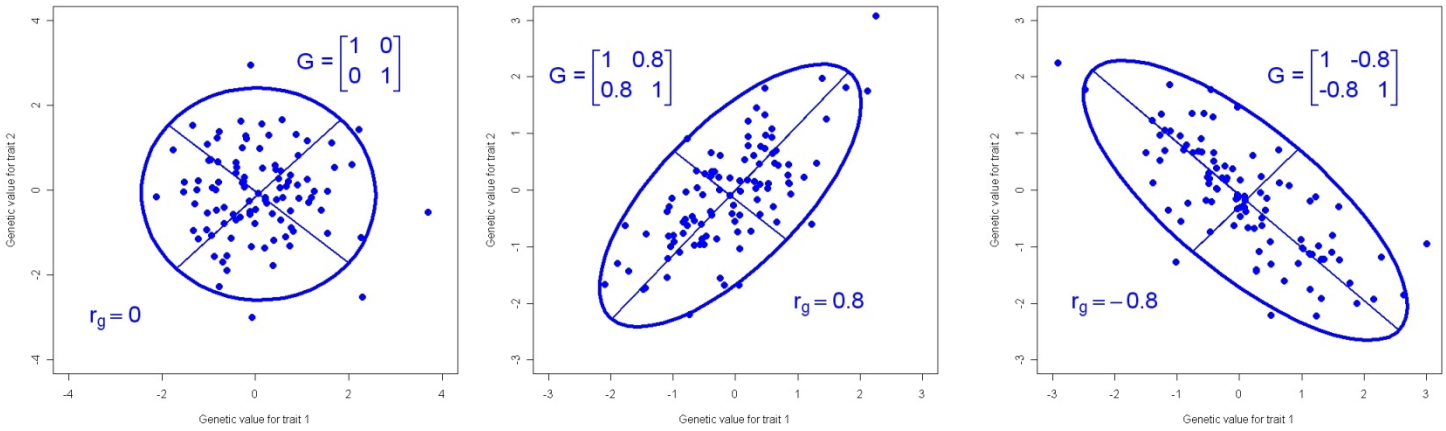


Fig. 6.3 Hypothetical bivariate samples of genetic values (n = 100) from bivariate normal distributions with genetic correlations, r_g , of (a) 0, (b) 0.8, and (c) -0.8.

6.03 The causes of genetic covariance

Genetic covariance has two distinct proximate causes, pleiotropy and linkage disequilibrium. *Pleiotropy* means that the alleles at a particular locus have effects on each of the traits in question. Pleiotropy is an almost universal feature of mutation (Caspari 1952) and will be considered in detail in the next section. Aggregating such pleiotropic effects within and across loci can produce positive or negative genetic covariance or even cancellation so that the aggregate gives little or no indication of pleiotropy. *Linkage disequilibrium*, the second cause of genetic correlations, refers to a statistical relationship between two loci (section 5.7), but in the present case we are concerned with loci that affect two different traits . For example, linkage disequilibrium is positive if a positive effect on a trait by an allele at one locus is positively correlated with a positive effect on another trait by an allele at a second locus. Linkage disequilibrium can contribute to a negative genetic covariance if the alleles at the two loci have opposite effects on the two traits. {use a version of the figure from Arnold 198x = evol physiol}

Linkage disequilibrium can arise from and be maintained by correlational selection … erosion of linkage disequilibrium by recombination ... {need a figure here; the grasshoppers}

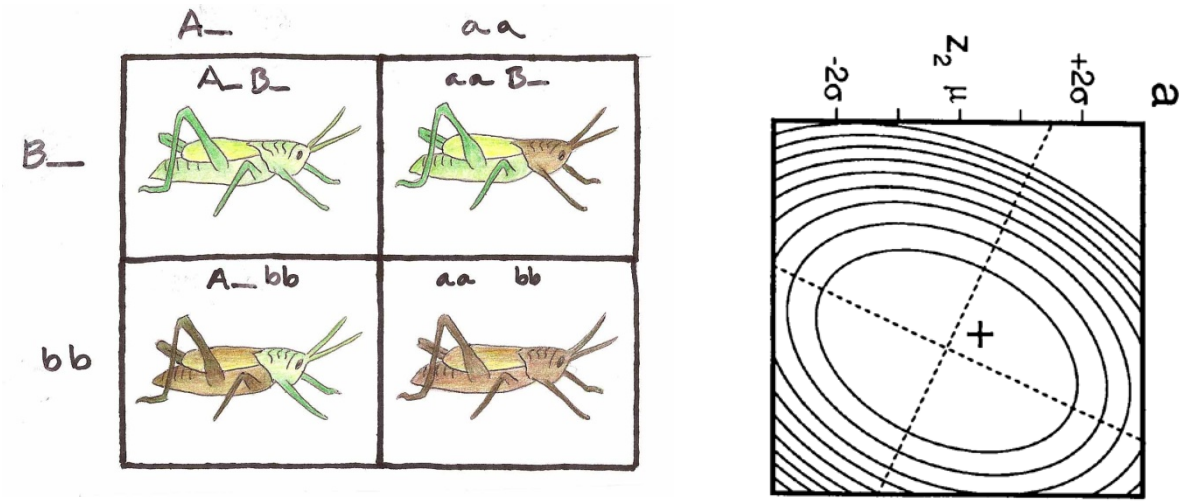


Figure 6.4 Correlational selection can create and maintain linkage disequilibrium. In a hypothetical example, suppose that the *A* locus affects the color of the head of a grasshopper, so that *A*_ (*AA* and *Aa*) grasshoppers have green heads and *aa* grasshoppers have brown heads. Suppose that the *B* locus affects the color of the body, so that *B*_ (*BB* and *Bb*) grasshoppers have green bodies and *bb* grasshoppers have brown bodies. Correlational selection acting on this inheritance scheme can produce linkage disequilibrium. Suppose, for example, that color matched grasshoppers are favored in the population because they are harder for predators to detect. In contrast, color miss-matched grasshoppers stand out against both green and brown backgrounds and fall prey to predators on both backgrounds. This selection scheme is shown in Fig. 6.4b. … {this caption needs editing as well as a companion figure showing correlational selection that favors A_B_ and aabb, see place-holder}

Diagnosing the cause of genetic correlation is usually a matter of guesswork, because the requisite discriminating experiments are difficult to conduct. Pleiotropy is the likely (but unproven) cause of genetic covariance between body and tail vertebrae in the garter snake example; we can easily imagine that some genes affect vertebral counts in both regions. Likewise, the positive genetic correlations that are frequently observed in the sizes of homologous structures probably reflect pleiotropic gene action (Lande 1979). On the other hand, a genetic correlation between traits that are unlikely to share developmental pathways may reflect linkage disequilibrium. The case of escape behavior and coloration in garter snakes is a case in point (Brodie 1992, 1993). Pleiotropy seems an unlikely explanation for the genetic correlation observed between these different kinds of traits (Fig. 6.5). Furthermore, linkage disequilibrium seems probable because the genetic correlation ( ) has the same sign as the correlational selection that has been documented in the same population (see Figure x.y). We expect exactly this kind of correspondence if multivariate stabilizing selection shaped the pattern of genetic covariance arising from linkage disequilibrium, as in the hypothetical grasshopper example.

6.04 Estimating the G-matrix from covariances among relatives

The theory and procedures for estimating the G-matrix are straight-forward extensions of the univariate covariance approach (Mode & Robinson 1963). In particular, our general expression for resemblance between relatives 5.6 still applies. In the cross-trait approach, one trait is expressed in one kind of relative (e.g., offspring) and another trait is expressed in the other kind of relative (e.g., parents). Alternatively, a

single kind of relative (e.g., paternal half-sibs) is used to estimate genetic covariance. In either case, all of the variance terms on the right side of 5.6 become covariance terms. For example, consider the cross-trait resemblance between mothers and daugthers displayed in Fig. 6.1. Ignoring epistatic contributions, that cross trait covariance equals one half the additive genetic covariance between body and tail vertebral numbers, since $r = ½$ and $u = 0$. This mapping between phenotypic resemblance and genetic parameters, provided by 5.6, was used to estimate the elements of the G-matrix in 6.0.

We can now appreciate that certain kinds of relatives are more useful that others in estimating the *G*-matrix. Parent-offspring data are often useful, especially if one or both of the parents do not exert parental effects, because dominance effects do not contribute to resemblance and because epistatic contributions are limited to additive interactions and are in any case likely to be small. These same virtues apply to paternal half sibs, but maternal half sibs are may yield problematic estimates because of shared maternal environments and the possibility of maternal effects. As a general rule, large family sizes lead to better estimates of additive genetic values and better estimates of G (i.e., smaller standard errors). The rule is not absolute, however. A cap on the total number of phenotypes that can be scored will mean that the investigator must choose whether to increase the number of families or the number of individuals sampled in each family (Robertson 196x). Formulas and guidelines are available to design an optimal allocation of effort.

The biological characteristics of each study system also play a large role in estimating and interpreting G-matrices. In garter snakes, for example, litter sizes average about 10, so optimizing an estimation design means scoring all the littermates that are available and maximizing the number of litters. Although mothers thermoregulate during pregnancy and pass nutrients to developing embryos, maternal effects are not inevitable. Experimental manipulations show that scale count means (e.g., body and tail vertebral counts) are remarkably immune to temperature effects (Arnold & Peterson 2002) and neonatal feeding preferences are unaffected by the mother's diet during pregnancy (Burghardt ref). These results mean that some of the best *a priori* candidates for maternal effects do not actually complicate the interpretation of estimates based on mother-offspring resemblance. The best estimation design and the interpretation of estimates needs to be decided on a case-by-case basis that takes into account biological circumstances and experimental evidence.

The multivariate analog of our univariate expression for heritability (5.3) is

$$Cov(x,z)P^{-1} = GP^{-1}, \text{ (6.04)}$$

which is a matrix of partial regressions of breeding values on particular parental phenotypic values, holding other phenotypic values constant. We will return to this realization in Chapter 8? , when we consider how the effects of selection in one generation are transmitted into the next generation.

6.045 Estimating the G-matrix with the animal model

The advantages that the animal model offers over the covariance approach carries over to the multivariate case. In particular the animal model offers great flexibility in accounting for fixed effects (e.g., spatial and temporal differences in rearing condition, sex, age, etc.), as well as for multiple kinds of relationship. The model looks much the same as it did in the univariate case (see Chapter 5),

$$z = Xb + Zu + e,$$

$$VAR(z) = ZFZ^T + R,$$

$$F = VAR(u)$$

$$R = VAR(e),$$

but now vectors representing each trait are stacked one on top of the other in the column vectors z, *b*, *u*, and *e*, and the design matrices *X* and *Z* are partitioned into submatrices, according to relations within and between traits. So, for example in the simple case of 5 related individuals, each with observations on two traits, let the additive genetic and environmental variance-covariance matrices be

$$G = \begin{bmatrix} G_{11} & G_{12} \\ G_{12} & G_{22} \end{bmatrix} \text{ and}$$

$$E = \begin{bmatrix} E_{11} & E_{12} \\ E_{12} & E_{22} \end{bmatrix}.$$

$$\text{Then } X^T = \begin{bmatrix} 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 \end{bmatrix},$$

$$b^T = [\mu_1 \quad \mu_2].$$

In *u* the 5 breeding values for trait 1 (individuals 1 through 5) are stacked on top of the 5 breeding values for trait 2 (individuals 1 through 5), with analogous stacking in *z* and *e*. The design matrix for *u* is

$$Z = I,$$

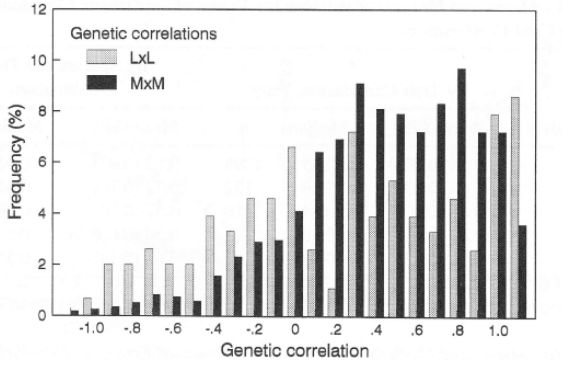
$$F = \begin{bmatrix} AG_{11} & AG_{12} \\ AG_{12} & AG_{22} \end{bmatrix}, \text{ and}$$

$$R = \begin{bmatrix} IE_{11} & IE_{12} \\ IE_{12} & IE_{22} \end{bmatrix},$$

where *I* is an identity matrix of order 5, and A is the symmetric 5 x 5 relationship matrix for the 5 individuals (Henderson 1984). With more traits, the same book-keeping conventions are retained, the vectors are stacked higher, and the matrices have more partitions. Details for implementing the multivariate animal model, with estimation of the G-matrix, are described by Meyer (2007) and Hadfield (2010). Assumptions of the approach are briefly discussed in Chapter 5.

6.05 The prevalence of phenotypic and genetic correlations

…reviews of ***G***, ***P*** and ***E*** estimates **aside from Roff's review of gen corrs, what else is out there? (Fig. 6.6 = distributions of rg or – if available – G, P and E)



Roff's 1997 book Fig 3.4 histogram of gen corrs for morphological traits = MxM; mean=0.25, median=0.17; n=493; note – this distribution doesn't seem to be truncated above +1.0, the last bin is apparently 1.1 and not anything over 1.0.

Analyses of dimensionality of G-matrices by Houle or others? Who is working on this? Theory/simulations by Wagner postdoc = M. Panalev(sp) …**

6.06 Approximating the G-matrix with the P-matrix

Because the estimation of ***G*** demands the assembly of replicated sets of relatives (or a pedigree), it is natural to seek shortcuts in cases in which these operations are difficult or impossible. … *P* as an approximation of *G* (Cheverud 1988; Waitt & Levin 1998, Willis et al 1991) … a built-in correlation between *P* and *G* … see also Lande (1979, p. 405) with refs for similarity between *G* and *E*

6.07 Maternal effects

Consideration of maternal effects requires a more complicated model than (6.00) …

$$z_{oi} = x_{oi} + e_{oi} + \sum_{j=1}^{n} m_{ij} z^{*}_{mj} ,$$

where the subscript *oi* denotes the *ith* trait in offspring, m_{ij} is the maternal effect of the *jth* maternal trait on the *ith* offspring trait, and z^{*}_{ij} is the *jth* maternal trait after selection (Kirkpatrick & Lande 1989). The covariance between the traits of mothers and the traits of offspring is no longer simply ***G*** but is instead a function of three matrices, ***G***, ***m***, and ***P*** {for more detail see K&L 89, their appendix equation A8}.

{in conclusion allude to paternal effects with refs}

6.08 Input from mutation, the *M*-matrix

Mutation is the well-spring for inheritance, the ultimate source for genetic variation described by the G-matrix. Our formulation for input to genetic variation from mutation will consist of two fundamental ingredients, just as it did in the univariate case: a total, genome-wide mutation rate and a multivariate distribution of allelic effects. As in the univariate case, we will adopt Kimura's (1965) infinite-alleles model for mutations at a locus. In the multivariate case, however, we need to incorporate *pleiotropy* into our mutation model. In other words, a new mutation at a particular locus may affect a number of phenotypic traits, and each of those effects must be specified (Fig. 6.7, based on figure in Arnold et al. 2008). We will assume that the per locus distribution of effects is multivariate normal with a mean of zero and a variance/covariance matrix, ***M***. The diagonal elements in this *m* x *m* symmetric M-matrix are the variances in mutational effects for each of the *m* traits. The off-diagonal elements are covariances in mutational effects for pairs of traits. In the bivariate case, the M-matrix takes the following form

$$M = \begin{bmatrix} M_{11} & M_{12} \\ M_{12} & M_{22} \end{bmatrix}, \quad (6.05)$$

where, for example, M_{11} is the mutational variance for trait 1 and M_{12} is the mutational covariance for traits 1 and 2, a reflection of pleiotropy. It will prove useful to express this covariance as a *mutational correlation*

$$r_{\mu} = M_{12} / \sqrt{M_{11} M_{22}} \, . \quad (6.06)$$

Summing up, we can think of mutation as producing effects on two or more traits, so that the resulting statistical cloud of effects forms a bivariate normal distribution which in turn is summarized by the M-matrix (Figure 6.7). In the 2-trait case, with equal mutational variances, the shape of this bivariate cloud is determined by the mutational correlation, r_{μ}.

So far we have considered the mutational effects of a single, typical locus. A simple way to extend this model across the entire genome is to assume that although the mutations at each locus are independent, their effects are drawn from an identical multivariate distributions. We can make a companion assumption about mutation rate, so that the total mutation rate across entire diploid genome for our traits is ζ. The total input from mutation each generation to our entire set of traits is given by a U-matrix that represents the product of the total mutation rate across the genome and the M-matrix,

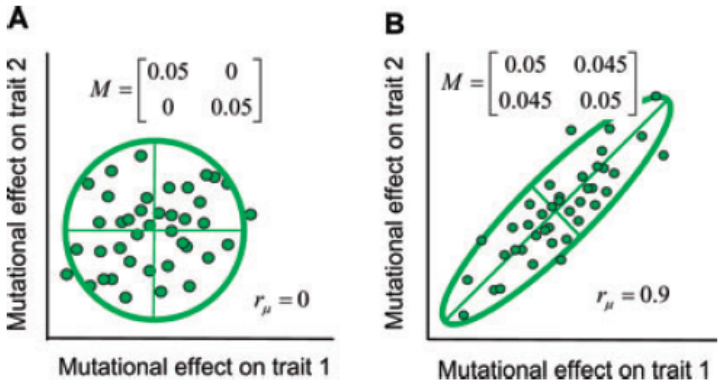


Figure 3. The distribution of new mutational effects on two traits from a particular locus can be represented as a cloud of values or a matrix, M. The 95% confidence ellipses for each data cloud are shown. The axes inside each ellipse are eigenvectors (principal components). (A) A cloud of mutations with no correlation (r_μ = 0). (B) A cloud of mutations with a strong positive correlation in mutational effects ($r_\mu = 0.9$).

$$U = \zeta M \quad (6.07)$$

(Lande 1980a). The assumptions that lead to (6.07) are not as hazardous as they may seem. Even if mutational effects were produced by a set of distributions that varied from place to place in the genome with a spatially-variable mutation rate, we could still aggregate their those rates and effects into a single U-matrix. The assumptions of spatial homogeneity en route to 6.07 are problematic only when we are forced to decompose the U-matrix in particular applications.

6.09 Estimating the M-matrix.

Our empirical knowledge of the *M*-matrix is limited because the requisite experiments have focused on a few kinds of traits in a small sample of organisms … design of MA experiments (Fig. 6.8)estimates of μ and $\boldsymbol{M}$ from mutation accumulation experiments …

6.10 Mutation-selection balance

It is natural to assume that the entire G-matrix might equilibrate to the opposing forces of mutation and stabilizing selection, just as we assumed equilibration of genetic variance in the univariate case. As before, our results pertain only to the case of inifinite population size. Using the multitrait generalization of Kimura's (1965) inifinite-alleles mutation model that we have just described (section 6.2), we can consider a population experiencing multivariate stabilizing selection and ask about the state of G-matrix at equilibrium (Lande's 1980a). Not surprisingly, the expression for the equilibrium G-matrix is a function of the total mutational input and the curvature of the adaptive landscape, but the expression is considerably more complicated than in the univariate case (5.x), even if we assume that the trait distribution and the AL are multivariate Gaussian,

$$\hat{G} \cong \tilde{\omega}^{1/2}[\tilde{\omega}^{-1/2} U \tilde{\omega}^{-1/2}]^{1/2} \tilde{\omega}^{1/2}, \quad (6.08)$$

where $\tilde{\omega} \equiv \omega + E \cong \omega + P$ (Lande 1980a). Despite the intimidating complexity of this expression, its message meshes with our intution. The size of the equilibrium *G* is enhanced by large mutation input and

trimmed by strong stabilizing selection (small ω). The shape of the equilibrium G-matrix will be compromise between the shapes of the M-matrix (via U) and the AL. {Fig. 6.9 use 6.08 and associated program to produce a figure showing Ghat as a function of the shapes of U and omega-tilda, a kind of precursor to output from Jones et al simulations; the trick however is to get U sized realistically compared with omega-tilda – could use the simulations as a guide}

We can derive expressions for G as it approaches its equilibrium, but those expressions depend on the details of per locus distributions of mutational effects and do not lend themselves to broad generalization (Lande 1980a, Barton …). The change in G induced by selection within a generation, however, is approximately

$$\Delta_s G = G(\gamma - \beta\beta^T)G = -G(\omega + P)^{-1}G \text{ , (6.09)}$$

where the last expression for the change in G assumes a Gaussian ISS (Lande 1980a, Phillips & Arnold 1989). At equilibrium, the losses due to selection are balanced by the input from mutation and recombination, so that

$$U = -\Delta_s G \text{ , (6.10)}$$

(Lande 1980a) … {show the bivariate distribution of x with $\boldsymbol{G}$ ellipse wobbling under mutation-selection balance with some fixed values for effective population size (N_e) and $\boldsymbol{\omega}$; could produce this picture by running a simulation to produce multiple samples of $\boldsymbol{G}$ before and after selection, converting the two sets to ellipses and then superimposing the replicates of the two kinds}

{a sentence or short paragraph here pointing out that infinite pop size assumed and that the loss of genetic var/covar due to finite pop size in the context of mut-seln-drift balance will be considered in a later chapter}

An implication of (6.07), which we will explore in later chapters, is that multivariate selection will tend to shape the G-matrix in its own image. …genetic and phenotypic integration (Olson & Miller 1958; Arnold 1992, 1994)

Chapter 10: Response of Multiple Traits to Selection

Overview.- In the short term, multivariate response of the trait mean to directional selection is a function of the *G*-matrix and the vector of selection gradients, $\boldsymbol{\beta}$. Directional selection on a particular trait is expected to change the mean of that trait, but selection may also induce responses in genetically correlated traits. This phenomenon is familiar to plant and animal breeders, who often observe undesirable correlated responses to selection. In the common case in which natural selection acts on the multivariate phenotype, the initial response may be biased towards traits with abundant genetic variation. On long time scales, evolution may be constrained for certain kinds of traits, especially those that represent trait combinations with low mutation rates and little standing genetic variation.

10.1 Multivariate response to directional selection

The response of multiple traits to selection is a function of the G-matrix and the vector of selection gradients, β

$$\Delta\bar{z} = GP^{-1}s = G\beta \quad (10.00)$$

Focusing on the the two-trait case, we see that the response to selection of each trait is composed of two terms,

$$\begin{bmatrix}\Delta\bar{z}_1\\ \Delta\bar{z}_2\end{bmatrix} = \begin{bmatrix}G_{11} & G_{12}\\ G_{12} & G_{22}\end{bmatrix}\begin{bmatrix}\beta 1\\ \beta 2\end{bmatrix} = \begin{bmatrix}G_{11}\beta_1 + G_{12}\beta_2\\ G_{12}\beta_1 + G_{22}\beta_2\end{bmatrix}, \quad (10.01)$$

a *direct response* to selection on the trait in question and an a *correlated response* due to selection on the other trait. The direct response is what we might expect from the univariate case, $G_{ii}\beta_i$. The correlated response, on the other hand, is mediated through the genetic covariance between the to traits, G_{12}. As a consequence multivariate selection can produce surprises in the response to selection. Consider the case in which β_1 is positive. The direct response is then necessarily positive if $G_{11}>0$, but it can't be negative. The correlated response could be positive, reinforcing the direct response. Or the correlated response could be negative, if either G_{11} or β_2 are negative (but not both), contradicting the direct response (Fig. 10.0). In extreme cases, the correlated response could overwhelm the direct response, so that the trait evolves in the opposite direction to its selection gradient. The possibility of non-obvious response is especially obvious when we consider the response of one trait, z_1, to selection on an entire set of q traits,

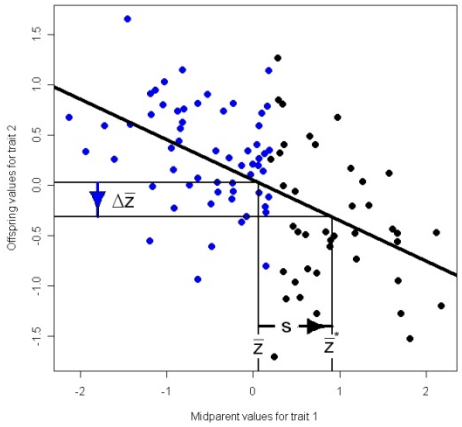
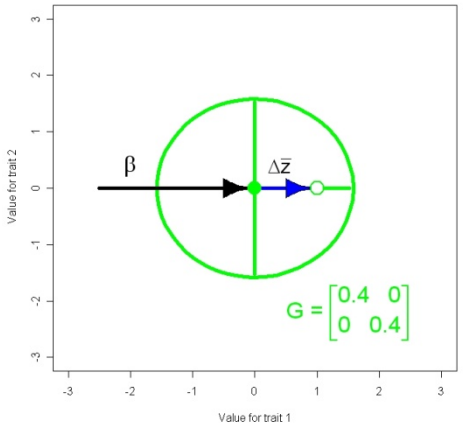


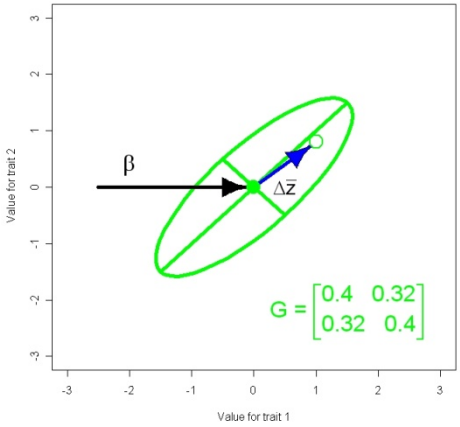
Figure 10.0. A correlated response to selection when the genetic correlation is negative. In these hypothetical data, truncation selection acts only on trait 1. The sample of actual parents, after selection, is shown in black. Other conventions as in Fig. 9.0. Even though selection favors higher values of trait 1, trait 2 evolves in the opposite direction because of a negative genetic correlation ($r_g = 0.47$).

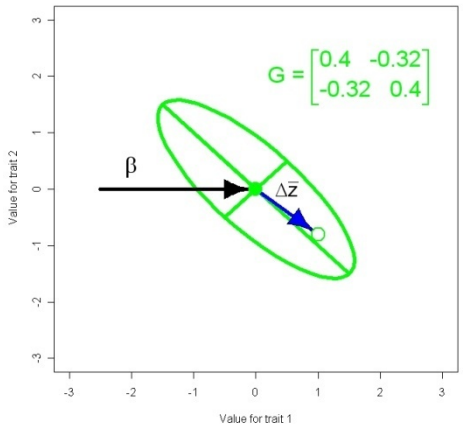
$$\Delta\bar{z}_1 = G_{11}\beta_1 + G_{12}\beta_2 + \ldots + G_{1q}\beta_q = G_{11}\beta_1 + \sum_{i=2}^{q} G_{1i}\beta_i \,.$$

Because the summation term represents the entire set of correlated responses of z_1 to selection on the other *q-1* traits, it might easily amplify or overwhelm the direct response, depending on the signs and magnitudes of the elements in both the first row of the *G*-matrix and in $\boldsymbol{\beta}$.

The game of pool is a useful analogy for developing intuition about how two correlated traits respond to selection. The response of the ball to the cue stick represents $\Delta\bar{z}$ (Fig. 10.1). The angle of the cue and and its force in hitting the ball represent, respectively, the angle and length of the vector $\boldsymbol{\beta}$. If the two traits are not genetically correlated and have the same genetic variances, the reponse of the ball to the cue is exactly what we would expect from a conventional pool table. If we hit the ball at a 25 deg angle, it moves away at a 25 deg angle, a hit at 75 deg yields a 75 deg response, etc. (Fig. 10.1a). Genetic correlation changes the behavior of the ball, but in predictable ways (Fig. 10.1b and c). Even with genetic correlation, the ball responds in the normal way if our cue is aligned with the major or the minor eigenvectors of the G-matrix. We get an especially strong response when the cue is aligned with the major eigenvector, but a much reduced response when it is aligned with the minor eigenvector. If we hit the ball at any other angle, the ball moves at an angle biased towards the direction of the major eigenvector. In other words, at any other angle, correlated responses to selection come into play so that $\Delta\bar{z}$ is not proportional to $\boldsymbol{\beta}$.







{Here a short paragraph on random and other kinds of skewers … need illustrations as well … pull together refs for Cheverud, Revell and others}

10.2 Multivariate response to selection in a set of replicate populations of finite size

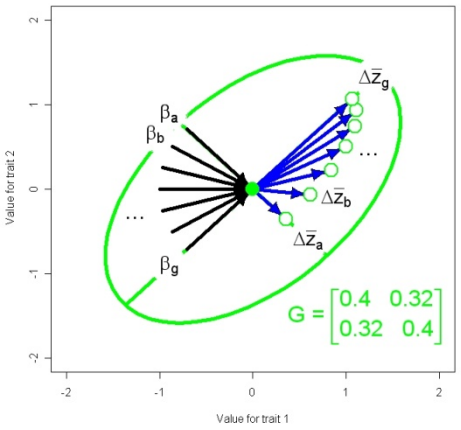
Random error in the sampling of parents each generation will add a stochastic component to the deterministic response to selection (10.00) each generation. In the single trait case we saw that drift yielded a distribution of replicate means about the deterministic response to selection (Fig. 9.01), In the two trait case, drift yields a bivariate distribution of means about the deterministic response (Fig. 10.2 = Bivariate responses to selection as a function of population size, separate panels contrasting selection on one trait with selection acting on both traits).

10.3 Multivariate response to deliberate selection

… the focus here is on empirical literature in which **multivar** dir seln has been imposed and response has been measured over one to several dozen generations ... begin with expression for a seln index … Fig. 10.3 = Correlated responses to deliberate selection in …{figure panels from various empirical studies}.

10.4 Multivariate response to selection in natural populations

… the focus is on studies in which the G-matrix has been estimated and response has been assessed for one or a few generations … Darwin's finches may supply a key example in which both short term beta and G have been estimated and used to make and test predictions … Fig. 10.4 = Plots of bivariate responses as a function of time in finch beaks.



10.5 The net selection gradient

{Add intro to stress examination of longer time scale } … If we know how much the trait mean has changed in an evolving lineage, we can reconstruct a selection vector that could account for that change. To do the reconstruction we need to know the *G*-matrix for the traits in question and we will need to make some assumptions about the stability of that matrix. We can apply (10.00) generation by generation to predict the total change in $\bar{z}$ after *t* generations, denoting the *G*-matrices and β-vectors that might be peculiar to each generation with subscripts,

$$\sum_{i=0}^{t-1} G_i\beta_i = \sum_{i=0}^{t-1} \Delta\bar{z}_i = [\bar{z}_t - \bar{z}_0].$$

If the *G*-matrix is constant the algebra is simplified so that

$$G\sum_{i=0}^{t-1} \beta_i = [\bar{z}_t - \bar{z}_0].$$

We can rearrange this expression and define the *net selection gradient* as

$$net\beta \equiv \sum_{i=0}^{t-1} \beta_i = G^{-1}[\bar{z}_t - \bar{z}_0]$$

(Lande 1979). This net selection gradients represents the minimum force of directional selection needed to account for the total net change in the multivariate mean … pool cue analogy = Fig. 10.5 …

If the trajectory of $\bar{z}$ is complicated, rather than linear, responses to selection in opposite directions will tend to cancel and will not be represented in the reconstructed gradient. Just as $[\bar{z}_t - \bar{z}_0]$ represents the net change in the mean, $G^{-1}[\bar{z}_t - \bar{z}_0]$ estimates the net selection needed to produce that change … Turelli's objection … Jones et al.'s (2004, 2010) rejoinders … the Turelli effect and its size under various scenarios … the issue of skew in the distribution of breeding values and its effect on net-beta …}

{for a list of empirical estimates of net-beta see Jones et al. 2010; choose one of these to illustrate results in the bivariate case; perhaps use the unpublished Phillips & Arnold calc for the g-snake vert and scale count case; discuss the distinction between net-beta and distance on the AL, i.e., net-beta may incorporate dir seln that corrects for corr responses to seln …}

10.6 Minimum selective mortality

$$\beta = G^{-1}\Delta\bar{z}$$

$$I = \beta^T z = \beta_1 z_1 + \beta_2 z_2 + \ldots + \beta_q z_q = \Delta\bar{z}^T G^{-1} z$$

(Lande 1979). … selection on the index *I* converts the problem of selection on the vector ***z*** into a univariate problem. The formulas in section 9.5 can be used to calculate the mininum selection mortality needed to produce a particular magnitude of change in *I* by truncation selection…{not clear whether there are any useful inplementations of this approach or if it is even practical – consider and if not, delete this section}

10.7 Multivariate issues in QTL analysis

Differentiation in the floral structures of monkey flowers (*Mimulus*) provides a particularly illuminating example of multivariate response in which both ecological circumstances and genomic consequences are well understood. … *M. lewisii* and *M. cardinalis* … adaptation to bee versus hummingbird pollination … multiple traits evolve during the shift in pollinators (Bradshaw et al. 1998, Bradshaw and Schemske 1999) … the differentiated traits affect the color and morphology of flowers as well as rewards to pollinators … many of these traits are polygenic with loci at scattered locations across the genome … a major locus, however, affects petal color … field studies of experimental plots of second generation hybrids reveal strong selection by pollinators on this locus. *** insert figures here showing parental flower types; genomic locations of QTLs***