

Genetic Components of Variation in *Nemophila menziesii* Undergoing Inbreeding: Morphology and Flowering Time

Ruth G. Shaw, Diane L. Byers and Frank H. Shaw

Department of Ecology, Evolution, and Behavior, University of Minnesota, Saint Paul, Minnesota 55108

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ABSTRACT

The standard approaches to estimation of quantitative genetic parameters and prediction of response to selection on quantitative traits are based on theory derived for populations undergoing random mating. Many studies demonstrate, however, that mating systems in natural populations often involve inbreeding in various degrees (*i.e.*, self matings and matings between relatives). Here we apply theory developed for estimating quantitative genetic parameters for partially inbreeding populations to a population of *Nemophila menziesii* recently obtained from nature and experimentally inbred. Two measures of overall plant size and two of floral size expressed highly significant inbreeding depression. Of three dominance components of phenotypic variance that are defined under partial inbreeding, one was found to contribute significantly to phenotypic variance in flower size and flowering time, while the remaining two components contributed only negligibly to variation in each of the five traits considered. Computer simulations investigating selection response under the more complete genetic model for populations undergoing mixed mating indicate that, for parameter values estimated in this study, selection response can be substantially slowed relative to predictions for a random mating population. Moreover, inbreeding depression alone does not generally account for the reduction in selection response.

WIDESPREAD interest in assessing the potential for response to either artificial or natural selection has motivated numerous studies of quantitative genetic variation within populations of plants and animals. These studies have generally employed experimental designs in which traits are measured on progeny obtained from controlled crosses, where parents are chosen and assigned mates at random (Comstock and Robinson 1948). Components of phenotypic variance obtained from such approaches are therefore understood to refer to a random mating population, as are the resulting predictions of selection response. Extensions of these approaches accommodate assortative mating, *i.e.*, mate pairing according to phenotypic similarity with respect to a particular trait (Crow and Kimura 1970; Falconer and Mackay 1996), a mating scheme that corresponds in some cases to the mating pattern in particular populations of interest (*e.g.*, human; Fisher 1918) and that tends to increase statistical power and precision of estimates of genetic components.

Investigations of mating systems of numerous wild populations have, however, indicated that deviations from random mating are the rule and that inbreeding is common (reviewed in Schemske and Lande 1985; Thornhill 1993; Waller 1986). Mating systems can,

in principle, encompass a wide range of relationships between mating individuals (see Waser 1993, pp. 1–4) and thus lead to broad variation in the degree of inbreeding of the resulting offspring. Exhaustive inference of the relationships between all mating pairs has not been possible, but variable inbreeding (*i.e.*, “mixed mating systems”), resulting in intermediate average rates of inbreeding, has now been documented for a wide variety of species, especially plants, and interpopulation variation in rates of inbreeding is also well established (see Table 1 for recent estimates).

These findings of substantial rates of inbreeding in many taxa have motivated studies to assess consequences of inbreeding. Many of these focus on detecting and quantifying inbreeding depression, the rate of reduction in the mean value of a trait in a population relative to the increase in the degree of inbreeding. Inbreeding depression has long been recognized (*e.g.*, Falconer and Mackay 1996, Table 14.1) and has now been documented for many taxonomic groups (*e.g.*, reviews in Thornhill 1993). Theory predicting effects of mating systems on degree of inbreeding depression and the reverse (*e.g.*, Lande and Schemske 1985; Charlesworth and Charlesworth 1987; Uyenoyama *et al.* 1992; Waller 1993; Schultz and Willis 1995) has prompted further empirical investigation of the relationship between the degree of inbreeding and inbreeding depression (*e.g.*, Latter *et al.* 1995; Doums *et al.* 1996; Husband and Schemske 1996; Johnston and Schoen 1996; Mayer *et al.* 1996; Ballou 1997). Likewise, predictions of effects of mating system on genetic

Corresponding author: Ruth G. Shaw, Department of Ecology, Evolution and Behavior, University of Minnesota, 1987 Upper Buford Circle, 100 Ecology, Saint Paul, MN 55108.
E-mail: rshaw@superb.ecology.umn.edu

TABLE 1
Ranges of estimates of self-fertilization rates in natural populations of plants

Species	Selfing rate ^a	Reference
<i>Amsincka spectabilis</i>	0.33–0.998	Johnston and Schoen (1996)
<i>Ardisia escallonioides</i>	0.00–0.61	Pascarella (1997)
<i>Carapa procera</i>	0.15–0.37	Doligez and Joly (1997)
<i>Cavanillesia platanifolia</i>	0.33–0.76	Murawski and Hamrick (1991)
<i>Clarkia tembloriensis</i>	0.13–0.97	Holtsford and Ellstrand (1989)
<i>Collinsia heterophylla</i>	0.36–0.68	Charlesworth and Mayer (1995)
<i>Decodon verticillatus</i>	0.13–0.4	Eckert and Barrett (1994)
<i>Eichhornia paniculata</i>	0.04–0.998	Barrett and Husband (1990)
<i>Lupinus nanus</i>	0.19–0.29	Karoly (1994)
<i>Nemophila menziesii</i>	0.01–0.28	C. T. Schick (personal communication)
<i>Posidonia australis</i>	0.73–0.90	Waycott and Sampson (1997)
<i>Schiedea lydtei</i>	0.13–0.31	Norman <i>et al.</i> (1997)

^a In all cases, the estimates are inferred under assumptions of the mixed mating model using the method of Ritland and Jain (1981).

variability have stimulated empirical study of relationships between them (reviewed in Charlesworth and Charlesworth 1995).

The common finding of partial inbreeding in natural populations suggests that quantitative genetic predictions of R , the per-generation response to selection, may often be misleading when, as is typical, they use the breeder's equation,

$$R = h^2 S, \quad (1)$$

where h^2 is the narrow-sense heritability and S is the selection differential, which assumes random mating, as a basis for prediction. Extension of quantitative genetic theory to account for arbitrary levels of inbreeding and degrees of relationship was initiated by Harris (1964), who proposed formulations of genetic components of variation in quantitative traits for populations undergoing inbreeding. He showed that, in principle, inbreeding introduces components of variance specifically associated with dominance effects of alleles when autozygous [meaning, here and throughout, identical by descent (IBD)]. Cockerham (1971) developed expressions for the covariances of inbred relatives and provided recursive algorithms for calculating them. Weir and Cockerham (1977) provided a thorough treatment of the components of variance arising in inbred populations in general for two loci and, barring epistasis, for an arbitrary number of loci. Cockerham and Weir (1984) considered covariances of relatives further and suggested experimental designs for estimation of genetic components of variance with inbreeding. Smith and Mäki-Tanila (1990) extended Henderson's (1988) mixed model approach to obtain a more general method to estimate the components of variance in partially inbred populations.

These methods for partitioning genetic variation of quantitative traits in inbreeding populations paved the

way for prediction of selection response with inbreeding, and interest in the interplay between selection and inbreeding has been growing over the past decade. Wright and Cockerham (1985) and Meuwissen and Woolliams (1994) developed expressions for predicting short-term responses to selection. Recently, this work has been considerably extended by Kelly (1998), who has developed recursions for additive and inbred dominance variance components in mixed mating populations undergoing selection. On the basis of extensive simulation studies, de Boer and colleagues concluded that the variance components and their random effects associated with homozygous dominance can, given the relatively slight inbreeding in many livestock populations, be safely ignored in the prediction of genetic merit in livestock (de Boer and van Arendonk 1992; de Boer and Hoeschele 1993).

Considering the converse effects of selection on rates of inbreeding, Wray and Thompson (1990) developed theory for predicting inbreeding in finite populations undergoing selection (see also Woolliams *et al.* 1993). Methods for maximizing response to artificial selection while restricting increase in inbreeding have also been compared (Toro and Perez-Enciso 1990; Brisbane and Gibson 1995). To predict selection response over many generations, it is necessary to take into account genetic processes in addition to inbreeding, including drift, linkage disequilibrium, and the input of variation by spontaneous mutation, as accomplished by Wei *et al.* (1996).

Despite these developments, little empirical work has taken advantage of theory addressing the effects of inbreeding on the structure of quantitative genetic variation and on response to selection. Two such studies concern domesticated populations (maize, Cornelius 1988; and sheep, Shaw and Woolliams, 1999). Here, we present a study of an annual plant, *Nemophila menziesii*.

sii, experimentally inbred from a random sample of a wild population. We measured pedigreed plants that differ in degree of inbreeding for morphological traits, as well as time of flowering. We partitioned phenotypic variation of these traits according to models that account for inbreeding as summarized below. We demonstrate that genetic components of variance specific to inbreeding populations make substantial contributions to phenotypic variance in our inbred population of *N. menziesii*. Simulations based on our estimates indicate that evolution in partially inbreeding populations, even over few generations, can differ strongly from predictions employing narrow-sense heritability alone, as well as predictions corrected to allow for inbreeding depression.

THEORY, MATERIALS AND METHODS

Theory: Considering effects on a trait, y , measured in an individual bearing alleles i and j at a single segregating locus, we can use a general model to separate genetic effects from effects due to environmental conditions:

$$y = X\beta + a_i + a_j + d_{ij} + e.$$

Here, β is a column vector of fixed effects (most simply, having a single element, the overall mean, but more generally, including as additional elements effects of specified levels of factors potentially influencing the trait, for example, blocks or nutrient treatments), and X is a row vector, with elements of 1 to represent exposure of this individual to a given effect and 0 otherwise. Thus, $X\beta$ is a sum of fixed effects pertaining to the individual's observed phenotype y , including the overall mean and effects of specified environments. Genetic effects a_i and d_{ij} are defined with reference to a random mating population; a_i are additive effects of allele i , $a_i + a_j$ is the breeding value, and d_{ij} is the dominance deviation for the interaction between the alleles i and j (*i.e.*, the difference between the genotypic value and the breeding value for the genotype bearing the i and j alleles; Falconer and Mackay 1996). e is a residual random effect of the microenvironment unique to the individual (Falconer and Mackay 1996). The variance of a population is simply the variance of the sum of the random effects, $a_i + a_j + d_{ij} + e$. When individuals are randomized over the available microenvironments, the residual effects, e , are uncorrelated with the genetic effects, and this variance can be written in terms of the quantities $\text{Var}(a)$, $\text{Cov}(a_i, a_j)$, $\text{Var}(d)$, $\text{Cov}(a_i + a_j, d_{ij})$, and $\text{Var}(e)$. In the absence of epistasis (as we assume throughout), the model extends to account for effects of multiple loci. Then, for each multilocus genotype, the breeding value is the sum over loci of $a_i + a_j$ and the dominance deviation is the sum over loci of d_{ij} , both generally considered to be normally distributed within a population. Likewise, the four genetic components of

variation are each sums over loci of the contribution of (co)variance from each locus.

In a random mating population, Hardy-Weinberg frequencies ensure that

$$\begin{aligned} E(a) &= E(d) = 0 \\ \text{Cov}(a_i, a_j) &= 0 \\ \text{Cov}(a_i + a_j, d_{ij}) &= 0, \end{aligned} \quad (2)$$

so $E(y) = X\beta$, with E denoting expectation taken over all alleles segregating in the population at all loci. Then the phenotypic variance of the population, V_p , can be written as the sum

$$V_p = V_A + V_D + V_E$$

of the additive and dominance genetic variances and the environmental or residual variance.

Compared to a random mating population, inbreeding increases the frequencies of homozygous genotypes, or more specifically, of autozygous genotypes, in which pairs of homologous alleles are IBD. In this case, the expectation of the dominance deviations does not remain zero. The expected trait value $E(y)$ of an individual inbred to degree F then includes inbreeding depression μ_F , *i.e.*, the (nonzero) expectation of the autozygous dominance effects, expressed in inbreds,

$$E(y) = X\beta + \mu_F = X\beta + F \sum p_i d_{ii}, \quad (3)$$

where p_i is the frequency of the i th allele segregating in the population, d_{ii} is the dominance deviation of the genotype with the i th allele autozygous, and the summation is over alleles at the locus under consideration. Thus, the second term represents inbreeding depression, defined as the linear change in the trait mean in response to change in inbreeding (Falconer and Mackay 1996, Equation 14.2; Lynch and Walsh 1998, Equation 10.3). This expression applies regardless of the nature of dominance.

Apart from its widely recognized effect on the population mean, inbreeding alters the population variance, in part because inbreeding destroys the simplifications given in Equations 2 and also because the variance of autozygous dominance deviations may differ from the variance of dominance deviations under random mating (V_D , above). In the framework developed by Harris (1964) and Weir and Cockerham (1977), the variance associated with autozygous dominance comprises three distinct components:

1. $V_{D1} = E(d_{ii}^2) - (E(d_{ii}))^2$, the total variance due to autozygous dominance effects. This is the dominance variance of a completely inbred population.
2. $H^* = (E(d_{ii}))^2$, the squared per-locus inbreeding depression, summed over loci.
3. $\text{Cov}(a, d) = E(a_i d_{ii})$, the covariance between the additive effect of alleles and their autozygous dominance deviations.

Thus, the variance of autozygous dominance deviations can differ from that of "random" dominance deviations (*i.e.*, dominance deviations attributable to allelic combinations that are not IBD). To emphasize this, we relabel V_D , the dominance variance in a randomly mating population, to V_{DR} . Using these definitions, the variance of individual phenotypes can be written as

$$(1 + F)V_A + (1 - F)V_{DR} + 4FCov(a, d) + FV_{DI} + F(1 - F)H^* + V_E \quad (4)$$

(Harris 1964; Weir and Cockerham 1977), which reduces to the familiar three-component expression for V_p if $F = 0$. A sixth genetic component of variance defined by Cockerham and Weir (1984) is necessary if the inbreeding coefficients vary among individuals and are unknown. Because, in this study, the base generation of plants has $F = 0$ and the subsequent pedigree is known, we are able to include individual inbreeding coefficients explicitly in our model and, thus, eliminate the need for this component (de Boer and Hoeschele 1993, p. 250). Covariances between relatives expected under this model are complicated (Weir and Cockerham 1977) but can be calculated using recursive algorithms given by Cockerham (1971).

Study species: *N. menziesii* is a self-compatible annual plant of the family Hydrophyllaceae. It is native to California and Oregon. Munz (1959) described the species as a "very variable complex." Within Riverside and San Bernardino Counties, differences in plant stature, leaf morphology, and flower color and size distinguish mountain populations from those below 800 m, and these differences are maintained under common conditions (R. G. Shaw, G. A. J. Platenkamp and R. H. Podolsky, unpublished data). The flowers bear nectar and tend to attract diverse pollinating insects (Cruden 1972; Andersson 1994). They are also protandrous, a trait that allows removal of pollen from a given flower before its stigma is receptive. Thus, the potential for avoidance of autogamy is great. However, in the population we studied, unvisited flowers readily self-pollinate, and these flowers produce viable seeds (R. G. Shaw and D. L. Byers, personal observations). Moreover, seeds have no specialized dispersal mechanism or apparent means of long-distance dispersal. These aspects of the plant's biology indicate that inbred matings, whether by selfing or by mating between close relatives, may commonly contribute offspring to succeeding generations in the population under consideration. In a field study of several mountain populations of *N. menziesii*, C. T. Schick (personal communication) estimated selfing rates as high as 28%, even in populations that failed to set fruit in the absence of pollinators. To assess the potential genetic and evolutionary impact of partial inbreeding in this population, we experimentally inbred plants and assayed the following traits: two measures of overall plant size, height, and number of nodes at first

flower, two measures of floral size, petal length and width, and days to first flower.

Genetic design and trait assays: Estimation of the components of genetic variance that arise with inbreeding requires observations on groups of individuals in which pairs can be predicted (from the pedigree) to share alleles in autozygous form (thus contributing information for V_{DI} and H^*) or with one individual autozygous and the other heterozygous [contributing information for $Cov(a, d)$; Cockerham and Weir 1984]. On the basis of a simulation study (F. H. Shaw, unpublished results; see also Cockerham and Weir 1984), the crossing scheme (Figure 1) was judged suitable for estimating the variance components that contribute to phenotypic variance under inbreeding, in addition to the "random" genetic components.

To obtain parents for the initial crosses, seedlings were collected in January 1990 from an uncultivated area of the University of California at Riverside (UCR) Botanic Gardens. Seedlings were sampled at 2-m intervals along parallel transects 2 m apart to reduce the chance of sampling close relatives. These plants were grown to maturity in a greenhouse at UCR. A total of 52 plants chosen at random served as paternal parents (sires) and 156 as maternal parents (dams) in a nested crossing design (a distinct set of 3 dams crossed with each sire). The progeny of these crosses, termed generation 1, are considered the reference generation, with inbreeding coefficients (F) of zero [Shaw *et al.* (1995) report genetic variation in response to biotic conditions in a field experiment using progeny of these crosses]. Plants of generation 1 used in this study and all later generations were grown, crossed, and measured in a greenhouse at the University of Minnesota.

In January 1994, 40 of these 52 progeny groups (half-sibships, each comprising three full-sibships) were chosen at random as sources of parents in the next series of crosses; a distinct set of eight progeny groups was chosen at random for each of five crossing blocks (Figure 1). Within each block, five progeny groups were designated at random as sources of sires in further matings, while the remaining three progeny groups provided individuals to be used as dams. Individuals randomly chosen from these progeny groups were grown, and measures of petal length and width were obtained for each. Within each crossing block, plants were mated factorially, yielding progeny in generation 2 with $F = 0$ [a study based on these crosses is reported in Byers *et al.* (1997)]. In addition, all maternal plants were self-pollinated, the resulting progeny (also generation 2) having $F = 0.5$.

Assays of generation 2 and a further series of crosses were initiated in December 1994. Generation 2 was subsampled to establish 10 crossing blocks, 2 from each of the crossing blocks of the previous generation. In generation 2, each crossing block consisted of nine individuals descended from one pair of grandsires in the

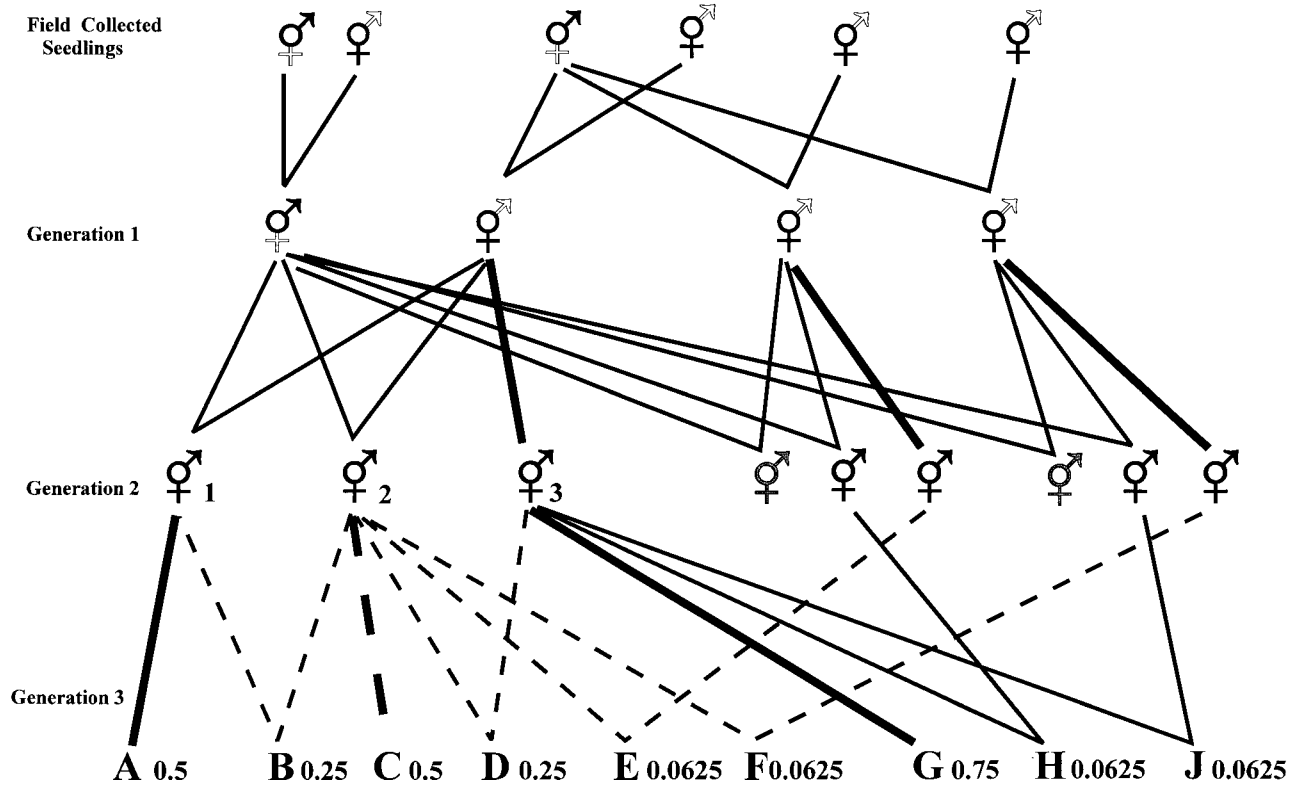


Figure 1.—A portion of the crossing design illustrating an example of all of the distinct types of crosses. Field-collected seedlings were crossed in a nested design to produce generation 1, followed by a factorial design with selfs to produce generation 2. Crosses of plants in generation 2 are illustrated by all the crosses of a trio comprising two full-sibs and their maternal self-sib. The functional gender of each plant is indicated by solid black symbols. Heavy lines indicate selfing. Dashes emphasize crosses made to individual 2 in generation 2. Inbreeding coefficients are given for representative individuals in generation 3.

founding generation (Figure 1). This group was composed of three trios, each comprising a pair of full-sibs and a self-sib (maternal half-sib produced by selfing the maternal parent). These trios were chosen such that they had in common the maternal grandsire and also, in the case of the noninbred individuals, the sire. In addition, two plants within each trio (in Figure 1, plants 2 and 3, with $F = 0$ and $F = 0.5$, respectively) were each crossed to a randomly chosen plant that shared no ancestors in the known pedigree. Individuals chosen for the next series of crosses according to the above scheme, together with an additional five full-sibs of each, were grown and measured (see below). The crosses produced seeds with the following array of inbreeding coefficients: 0, 0.06, 0.25, 0.5, and 0.75. All crosses were carried out reciprocally. We refer to the offspring from this set of crosses as generation 3.

Assays of generation 3 and a further series of crosses were initiated in August 1995. Five plants from each set of progeny (e.g., A–J in Figure 1) were grown and measured. One individual from each full-sib group was selfed to produce progeny not considered further here.

Summarizing the available observations, petal length and width were measured on the 114 individuals representing generation 1, and five traits, date of first flower, size (height and number of nodes) at first flower, and

petal length and width for the first opened flowers, were measured on 450 and 1226 individuals in generations 2 and 3, respectively. Single petals of each of 3–5 flowers were measured in millimeters with digital calipers. Height was measured with a meter rule in centimeters. Progeny from every level of inbreeding planned were measured, but not every lineage was represented fully according to the design given above, as a result of germination failure, mortality, or sterility (Table 2). To the extent that deviations from the intended design are due to selection, they are likely to bias estimates of inbreeding depression (*i.e.*, indicating weaker inbred-

TABLE 2

Number of individuals measured by design and sample

	Inbreeding coefficient				
	0	0.0625	0.25	0.5	0.75
Generation 2					
Design	360			174	
Sample	308			142	
Generation 3					
Design	295	590	585	295	145
Sample	219	383	364	180	80

ing depression than the actual), but to have negligible influence on maximum likelihood estimates of the variance components, according to a simulation study of Shaw and Woolliams (1999).

Analysis: Restricted maximum likelihood (REML) was used to estimate the parameters of the full model (Equations 3 and 4) of trait determination and to test hypotheses (Shaw 1987; Shaw and Woolliams 1999). Quantile plots of residuals confirmed the validity of the normality assumption of the REML analysis. Because all crosses were done reciprocally, variance due to maternal effect could readily be distinguished from the genetic components defined in Equation 4. Thus, all models also included a random maternal effect with variance V_M . For simplicity, maternal effects were treated as perfectly correlated between individuals having the same maternal parent. They were thus modeled as arising either from environmental effects unique to maternal individuals or from cytoplasmic genetic effects. To estimate inbreeding depression as the linear change in the trait mean in response to degree of inbreeding, F of each individual was included as a linear covariate in all analyses. Estimation of inbreeding depression in this way appropriately accounts for the lack of independence between individuals linked through the pedigree structure (see Lynch and Walsh 1998, pp. 262–265, for discussion of this issue). A fixed effect for the block (spatial and temporal) in which each plant was grown was also included in each analysis. In preliminary analyses, tests of the effect of maternal inbreeding were also conducted by including maternal F as a covariate. However, effects of maternal inbreeding were consistently found to be weak and not significant (in contrast to Hauser and Loeschke 1996), and these are not considered further.

Likelihood ratios (Kendall and Stuart 1973) were used for hypothesis testing. The null hypothesis that $\text{Cov}(a, d_i) = 0$ was tested first, by eliminating that parameter and comparing the likelihood of that reduced model to the likelihood of the full model. V_A and V_{D1} were tested by a similar procedure, except that $V_A = 0$ or $V_{D1} = 0$ requires that $\text{Cov}(a, d_i) = 0$. Thus, the covariance was omitted from the model for tests of these two variance components. Other components were tested against the full model, using 2.7 as the critical value for $\alpha = 0.05$. This is appropriate when the null hypothesis coincides with the feasible limit for the parameter (*i.e.*, variance components less than zero are not allowed; Self and Liang 1987). We also compared the variance of autozygous dominance deviations with that of random dominance deviations by testing the null hypothesis that V_{D1} equals V_{DR} . Standard errors of components of variance were obtained from diagonal elements of the asymptotic variance-covariance matrix of the maximum likelihood estimates (Searle *et al.* 1993; see appendix). These can be used for an approximate test of the param-

eters, but do not completely coincide with the more rigorous likelihood ratio test.

Estimates for the component H^* were all negative, but their substantial sampling variances and very small likelihood ratio test statistics suggest that these are attributable to sampling error. If inbreeding depression is due to the composite effects of many loci, H^* , which is the sum of the squares of these single locus effects, should be near zero. The component H^* is not reported in our analyses because it was invariably constrained to zero to satisfy feasibility.

Simulations: To assess the impact of the complete dominance model (Equations 3 and 4) and partial inbreeding on projected short-term response to selection on a quantitative trait, we simulated finite populations undergoing five generations of selection on a single trait with genetic determination corresponding to that estimated for height and for petal width. Populations of size 100 were simulated as noninbred progeny of 20 unrelated founders. Each founder was assigned 2 unique alleles at each of 30 loci (1200 alleles in all). This contrasts with previous simulations of this model that use only two alleles per locus in different frequencies (de Boer and Hoeschele 1993; Kelly 1998). The biallelic approach has advantages (variance components can be easily calculated from allele frequencies; Cockerham and Weir 1984) and disadvantages (autozygosity occurs without inbreeding, and artificial dependencies varying with allelic frequencies exist between the variance components). Under the full genetic model, correlated values for the additive effect (a_i) and autozygous dominance deviation (d_{ij}) for each allele were sampled from

$$\begin{pmatrix} a_i \\ d_{ij} \end{pmatrix} \sim N \begin{pmatrix} 0 & \frac{V_A}{2 \text{nloc}} & \frac{\text{Cov}(a, d_i)}{\text{nloc}} \\ \frac{\text{id}}{\text{nloc}} & \frac{\text{Cov}(a, d_i)}{\text{nloc}} & \frac{V_{D1}}{\text{nloc}} \end{pmatrix},$$

where nloc is the number of loci, and id is the inbreeding depression. Each non-IBD combination of alleles within a locus was given a random dominance deviation (d_{ij} for alleles i and j) drawn from a normal distribution with mean zero and variance V_{DR} . From these elements, genotypic values were obtained for each combination of alleles at each locus. For comparison, two simpler models were also simulated: Model 1 with V_p composed of only the components of variance defined for random mating populations and Model 2, as Model 1, but including inbreeding depression. In both these simpler models, V_{D1} is set equal to V_{DR} ; *i.e.*, the variance of dominance deviations for autozygous genotypes is assumed the same as for heterozygous genotypes. Transmission of alleles at each locus from one generation to the next was simulated by Mendelian segregation and free recombination into gametes. Phenotypic values were then obtained as the sum of the genotypic values over loci and an independent environmental effect simulated from a normal distribution with mean zero and variance V_E .

Distinct mating systems were simulated: random mating, 20% selfing, and 50% selfing (with the remaining matings at random in the latter two cases). In each case, 100 offspring were produced from the individuals in the mating pool for each generation. For five initial generations, transmission proceeded by the specified mating system, in the absence of selection. Thereafter, we imposed linear directional selection on the phenotype for five generations, according to the following scheme: individuals in generation k joined the mating pool with probability

$$p = w + \frac{s \times w \times (y - \mu)}{V_p},$$

where y is the potential parent's phenotype, μ and V_p are mean and variance of the phenotypic values in generation k (respectively), w is the mean probability of mating (fixed at 0.5 for all simulations), and s is the selection differential, *i.e.*, the covariance between fitness (here determined by mating probability p) and the character under selection (y). We specified s as 0.44. Altogether 1000 simulations were conducted for each combination of the three genetic models and three mating schemes.

RESULTS

Morphological traits: For each of the morphological traits, additive genetic variance (V_A) made highly significant contributions to the phenotypic variance. Narrow-sense heritabilities of the traits (computed with V_p as for a random mating population, as the sum of V_A , V_E , V_{DR} , and V_M ; Table 3) ranged from 16% for petal length to 26% for height, while additive genetic coefficients of variation, CV_A , ranged from 5% for petal length to 15% for node number. Highly significant inbreeding depression was also consistently found (Table 3), indicating that, with inbreeding, plants tended to decline in size with respect to each of these characters.

The estimates of variance components associated with dominance differed among traits far more strikingly. In the case of whole-plant size traits (plant height and node number), although inbreeding depression was detected as significant for both traits and the random component of dominance variance, V_{DR} , was significant for node number, V_{DI} appeared to be negligible. In the case of node number, the likelihood was maximized at a very small negative value for this variance component, indicating that the best estimate for both V_{DI} and $Cov(a, d)$ is zero; under this constraint, the estimates of the remaining components and their standard errors differed little from the values given. Thus, for both overall size traits, the phenotypic variance was largely accounted for by the components, V_A , V_E , V_{DR} , and V_M .

For the petal size traits, V_{DR} of petal width was significant, but that for petal length, similar in magnitude

TABLE 3
Results from the analyses of the different traits

Traits	Variance components						Fixed effects	
	V_A	V_E	V_{DR}	$Cov(a, d)$	V_{DI}	V_M	Trait mean	Inbreeding depression
Height (mm)	16.29 (4.96)^a	42.32 (2.98)	1.83 (3.69)	-2.45 (5.01)	1.65 (12.47)	1.27 (0.93)	33.6 (1.0)	-6.6 (1.2)
No. of nodes	1.86 (0.75)	3.75 (0.40)	1.89 (0.64)	0.05 (0.75)	-0.07 (1.79)	0.68 (0.20)	9.2 (0.3)	-1.13 (0.34)
Petal length (mm)	0.33 (0.14)	1.45 (0.11)	0.17 (0.14)	0.02 (0.16)	0.51 (0.48)	0.07 (0.04)	10.6 (0.14)	-0.72 (0.20)
Petal width (mm)	0.25 (0.09)	0.75 (0.06)	0.14 (0.08)	-0.11 (0.11)	0.52 (0.33)	0.03 (0.02)	7.23 (0.10)	-0.63 (0.17)
No. of days to flowering	17.25 (6.10)	29.37 (3.33)	8.80 (4.37)	-8.23 (7.58)	43.10 (23.30)	4.01 (1.36)	34.3 (0.9)	0.36 (1.33)

Boldface indicates variance components and inbreeding depression slopes that are significant.

^a Standard error.

but substantially smaller in relation to the remaining components, was not. The estimates of V_{DR} were substantially exceeded by the estimates for V_{DI} . These were up to four times as large as V_{DR} and contributed significantly to V_p (petal length, $P < 0.025$; petal width, $P < 0.05$), despite their large standard errors in the full model (Table 3). The differences between V_{DI} and V_{DR} were not detected as significant. The covariance between additive effects and autozygous dominance deviations [$Cov(a, d_i)$] was estimated as positive for petal length and negative for petal width; in neither case was it significantly different from zero ($P > 0.5$ and 0.15 , respectively). Thus, the additive effects of alleles associated with these traits appear to be weakly correlated with their autozygous dominance deviations.

Although the design had sufficient power to detect V_{DI} for floral size traits as significant, it tended to yield lower precision for estimates of V_{DI} and $Cov(a, d_i)$ than for the other components of variation (Table 3). Moreover, the sampling covariance between these two parameters was substantial and negative (see appendix; *e.g.*, sampling correlation was -0.76 and -0.83 for petal length and width, respectively), as was that between $Cov(a, d_i)$ and V_A (sampling correlation was -0.61 and -0.73 for petal length and width). Thus, the inclusion in the model of $Cov(a, d_i)$ can substantially affect the estimates of V_A and V_{DI} . Under a model omitting $Cov(a, d_i)$, the estimates of V_A for petal length and width were 0.35 ± 0.11 and 0.17 ± 0.06 , respectively, and the estimates of V_{DI} were 0.56 ± 0.33 and 0.25 ± 0.18 , respectively.

Other contributions to variation in these morphological traits were also substantial. Differences between generations were detected (not shown), with plants in later generations tending to be larger in whole plant measures, but smaller in size of petals. These generation effects are distinct from effects of inbreeding. Maternal variance (V_M) was detected as highly significant for two traits, number of nodes and petal length, and accounted for 8 and 3% of the variance in those traits, respectively.

Flowering date: The effect of inbreeding on mean time to flowering was positive, indicating that more inbred plants tend to flower later, but this effect was not statistically significant. Considering estimates of genetic components of variance, both V_A and V_{DR} were substantial, with h^2 computed as for a random mating population of $\sim 30\%$ and CV_A of 12.3%. V_{DI} was extremely large, greatly surpassing V_E , and highly significant. In comparison, $Cov(a, d_i)$ was relatively small ($r_{a,d_i} = -0.3$) and did not differ significantly from zero. The weakness of both this covariance and the inbreeding depression for this trait suggests that dominance at the loci influencing this trait is not strongly directional. V_M accounted for $\sim 7\%$ of the random mating phenotypic variance and was highly significant.

Simulations of selection response: Before the onset of selection, the simulated populations accumulate in-

breeding approximately according to predictions accounting for the numbers of individuals (Falconer and Mackay 1996, p. 67; here, 20 founders and 100 individuals every generation thereafter). For example, in all random mating simulations, the average inbreeding before selection in generation 6 is 0.047 (not shown, prediction of 0.044). Selection increases the rate of accumulation of inbreeding (generation 10: $F = 0.09$ vs. prediction in the absence of selection of 0.07), as expected (*e.g.*, Robertson 1961; Wray and Thompson 1990; Santiago and Caballero 1995). Predictions are likewise confirmed for the case of a random mating population with dominance contributions to the trait restricted to the random dominance (V_{DR} ; *i.e.*, Model 1). Here, the average response observed over 5 generations in our simulations closely approximates that given by Equation 1 (predictions: height, 0.6 cm; petal width, 0.48 mm); however, even under this simple model of genetic determination, partial selfing modifies the response to selection substantially, enhancing it in the case of 50% selfing by $\sim 5\%$ per generation over the prediction based on the narrow-sense heritability. This effect is expected, because inbreeding induces a correlation between the effects of the two alleles that individuals carry at a locus and, thus, increases the contribution of V_A to the phenotypic variance (see Equation 4). The increases in selection response that we observe under Model 1 with partial inbreeding are quantitatively consistent with this effect. In these and all other simulations, the realized selection differential (not shown) very closely matched the specified selection differential, deviating by $< 1\%$ per generation for petal width and $< 2.3\%$ for plant height. These slight differences between specified and realized selection differential do not account for deviations in selection response from predictions or for differences in response among the genetic models or mating schemes.

Inbreeding depression affecting the mean of the trait in opposition to the direction of selection (Model 2), as found for plant height and petal width, can dramatically slow response to selection in all three mating schemes. In the case of the random mating population, this reduction results from inbreeding caused by finite population size alone. With partial selfing, the population mean can quickly decline below its initial value and not regain it, despite gradual increases due to selection (*e.g.*, Figure 2, b and c). The observed reductions in trait mean relative to means observed in the absence of inbreeding depression (Model 1) closely match the predictions from standard theory [Falconer and Mackay (1996, Chap. 14), *i.e.*, the product of the mean coefficient of inbreeding and the inbreeding depression slope, -6.6 for height and -0.63 for petal width; Table 3]. Considering the case of 50% selfing, the mean F at generation 10 is 0.4, such that the expected reduction in mean for height is 2.7 and for petal width is 0.25.

Under the full model (Model 3), when the estimate

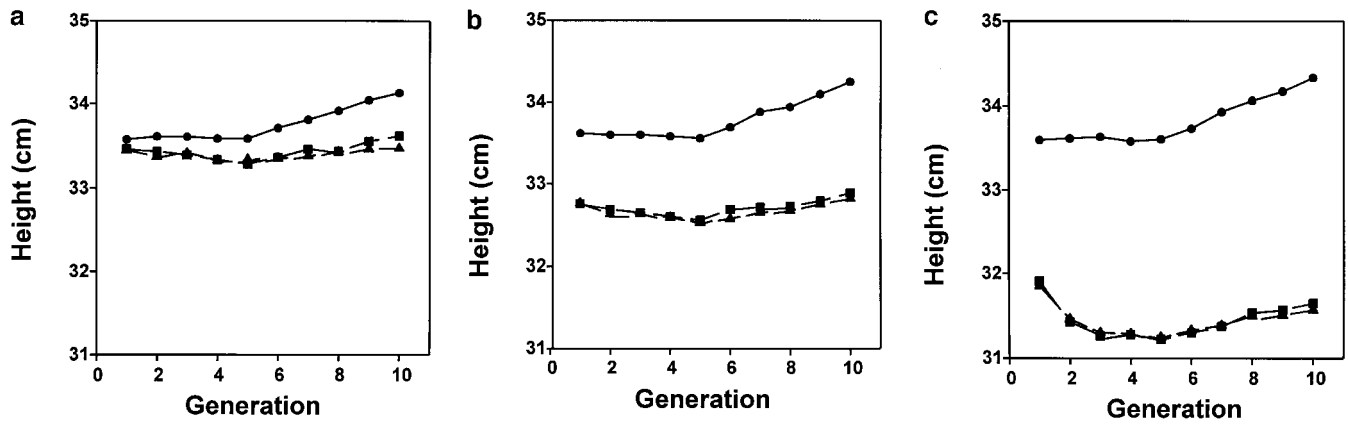


Figure 2.—Changes in mean plant height over 10 generations observed in the simulation study of directional selection under three mating schemes: (a) random mating, (b) 20% selfing, and (c) 50% selfing. Responses are shown for three genetic models with parameter values estimated for *N. menziesii* (Table 3): Model 1 (solid line, circles) involves only those genetic components of variation defined for a random mating population, V_A , V_{DR} , and V_E ; model 2 (long dashes, squares) includes these and inbreeding depression; model 3 (short dashes, triangles) corresponds to the full model (Equations 3 and 4). Each point represents the mean of 1000 simulations; see text for further details. Symbols exceed the size of the standard errors of the means.

of V_{DI} is substantial and that of $Cov(a, d_i)$ is small and negative, as for petal width, selection response can be reduced substantially further, with somewhat greater reduction the higher the selfing rate (Figure 3). For plant height, where V_{DI} makes a far smaller contribution to variation, the reduction of selection response under Model 3, relative to Model 2, is relatively slight. The discrepancy between the responses under Models 2 and 3 is essentially eliminated when $Cov(a, d_i)$ is absent (not shown; means for each generation coincide with those for Model 2 within 1.5%).

DISCUSSION

In keeping with many previous studies of inbreeding in diverse organisms (see Introduction), this work has demonstrated strong inbreeding depression in a population of *N. menziesii* recently collected from nature.

Matings between more closely related individuals produced progeny that were smaller overall and bore smaller flowers. Beyond this, we have quantified the novel components of genetic variance expected to arise with inbreeding, V_{DI} , H^* , and $Cov(a, d_i)$. Although the study gave no evidence that these components contribute to variation in two measures of plant size (height and number of nodes), it demonstrated that V_{DI} contributes substantially to genetic variation in three reproductive traits (petal length and width and flowering date).

In the petal size traits, significant inbreeding depression is accompanied by significant V_{DI} , although not by significant $Cov(a, d_i)$. Thus, inbreeding increases the genetic variance for the trait, but this increase in variance is accompanied by a reduction in the mean, opposing selection favoring larger flower size. For both petal size traits, estimates of V_{DI} appreciably exceeded those for V_{DR} , although the difference was not detected as

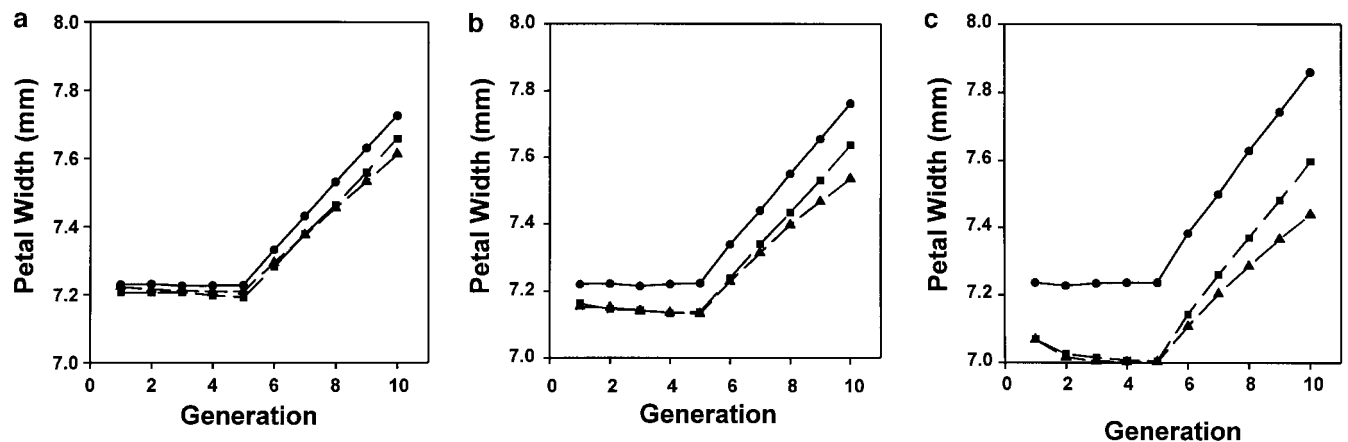


Figure 3.—Changes in mean petal width over 10 generations observed in the simulation study of directional selection under three mating schemes. Panels and symbols are as in Figure 2.

significant; in the case of petal length, V_{DR} was not significant. These findings may illuminate earlier ones in which V_D was not detected in progeny resulting from random mating, despite apparent inbreeding depression (e.g., of seed mass; Montalvo and Shaw 1994). Evidently, the component of dominance variance attributable to effects that contribute to inbreeding depression, V_{DI} , may, as in this case, be large even though V_{DR} is negligible.

A surprising pattern of genetic determination was found for the two size traits, height and node number at flowering. These traits showed clear inbreeding depression, yet no detectable homozygous dominance variance (V_{DI}). Similarly, Shaw and Williams (1999), in their study of sheep subjected to rapid inbreeding, could not detect significant V_{DI} or $Cov(a, d_i)$ for live weight in a large pooled dataset of crossbred lambs although strong evidence of V_{DR} and inbreeding depression were found. In that case, the estimate of V_{DI} was similar in magnitude to that of V_{DR} . One possible explanation for these results is that the contribution of each of very many loci to inbreeding depression, although consistent in reducing the trait value, is individually extremely small, and thus the variance of the homozygous dominance deviations cannot be detected.

In only one of the traits studied, flowering time, was the estimate of inbreeding depression not significant. This trait exhibited substantial V_{DR} and V_{DI} , however. Taken together, these results indicate that, for this trait, the homozygous dominance deviations are not strongly directional. Inbreeding thus enhances the variance for flowering time without significantly affecting the mean.

Under partial inbreeding, prediction of selection response is problematic, in part because individuals are expected to vary in their degree of inbreeding, because the covariance between parent and offspring, on which selection response depends, involves all the dominance components in addition to V_A and because allele frequencies and linkage disequilibrium, and hence the components of variance, change more rapidly with inbreeding and selection than with selection alone. Although special cases of selection with inbreeding have been considered (Wright and Cockerham 1985; Kelly 1998), no general analytical treatment accounting for all of these complications is available. Simulations of short-term selection response, based on our estimates of the variance components for three traits, show that response can be appreciably less than predicted from the breeder's equation (Equation 1) when traits are subject to the complete dominance model in populations undergoing partial inbreeding. Moreover, even if mating is at random, IBD that accrues because of drift in small populations and that can be increased by selection can significantly affect selection response when autozygous dominance deviations differ from random dominance deviations in their effects on the phenotype.

Results for Model 2, involving inbreeding depression alone (with $V_{DI} = V_{DR}$), showed reductions in selection response of up to 70% per generation, depending on the mating scheme. Our simulations further showed that when this genetic model applies, short-term selection in partially inbreeding populations can be well predicted by summing the response expected from the breeder's equation (Equation 1) and the effect on the mean due to inbreeding depression. We found, moreover, that this approach to predicting selection response closely approximated the average response in our simulations, even with the much larger values of V_{DI} that we found for petal width, as long as $Cov(a, d_i)$ was specified as zero. However, when additive effects of alleles are not independent of autozygous dominance deviations (Model 3), striking differences from these predictions arise. Even with the small, negative estimates of $Cov(a, d_i)$ we obtained for petal width, response to selection toward larger petals is reduced substantially more than can be simply accounted for by inbreeding depression. Negative $Cov(a, d_i)$ implies that the higher the effect of an individual allele, the more extreme tends to be its contribution, in autozygous state, to inbreeding depression, and thus, selection exacerbates inbreeding depression. The simulations show that even the moderate values of $Cov(a, d_i)$ we estimated can strongly affect selection response. Given the precision of our estimates, however, we cannot reject the null hypothesis that the true value of this parameter is zero for any trait. If future work consistently fails to demonstrate definitively that $Cov(a, d_i)$ contributes to genetic variance in inbreeding populations, then it appears that valid short-term predictions can be obtained by the composite method above, requiring only estimates of V_A and inbreeding depression, both of which can be estimated from genetic designs far simpler than the cumbersome pedigrees required to estimate all the parameters of Model 3.

These dominance effects on selection can be viewed as distinct causes of selection decline in addition to those modeled by Robertson and Hill (1983) for finite populations undergoing selection, drift, and accumulation of negative linkage disequilibrium, leading to reduction in additive genetic variance. Neither of these processes is directly modeled in our simulations, but must be taken into account in longer range predictions of selection response (Wei *et al.* 1996). Our simulations complement Kelly's (1998) analytical and simulation results showing reduction in genetic variance and selection response with partial inbreeding. Kelly's "structured linear model" accounts for the inbreeding coefficient of each individual by partitioning the population into cohorts having different numbers of sequential selfing events in their immediate ancestry. His simulations, therefore, provide insight into selection response in a large population when all inbreeding is due to selfing. When population size is small, or when pollen and seed distribution is spatially limited, consanguine-

ous matings occur in a less predictable manner and result in a broad range of individual inbreeding coefficients. An approach suggested by Cockerham and Weir (1984) to account for variation in inbreeding is inclusion of a further component of variance attributable to variation in individual inbreeding coefficient in a population with a known mean (equilibrium) inbreeding coefficient.

We know of few empirical studies in which effects of nonrandom mating on the structure of genetic variation have been assessed. Cornelius (1988) attempted to estimate the genetic components that may arise under inbreeding in a population of maize, but detected none of them as statistically significant. Similarly, in a study of sheep experimentally inbred in six populations (three representing distinct breeds and three crosses between breeds), Shaw and Woolliams (1999) found little evidence of contributions of genetic components theoretically defined for inbred populations. For live weight of purebred lambs, they did find significant V_{DI} and $Cov(a, d)$, but the analysis of that particular dataset suffered from bias due to the pooling of several breeds. For the larger dataset of crossbred lambs, where this bias was minimal, substantial inbreeding depression and significant V_A and V_{DR} were detected, but estimates of V_{DI} were distinguishable neither from those of V_{DR} nor from zero, even though they were comparable to the estimates of V_A . Because the size of this experiment was smaller than the one presented here (e.g., the pooled number of crossbred lambs is 1480), and the design involved a large number of fixed effects accounting for variation in environmental conditions over a span of 20 years, the statistical power of this study may have been insufficient for detection of these novel components.

Taking a distinct approach in a study of *Plantago lanceolata*, Tonsor and Goodnight (1997) compared estimates of heritability from plants produced by random mating with estimates from progenies arising from matings according to the natural distribution of pollen dispersal. Among nine traits studied, for only reproductive dry weight was the heritability found to be marginally significantly greater under the localized mating scheme. Thus, the limited evidence available differs from our study in suggesting that novel components of genetic variation defined for inbred populations tend to make minor contributions to their phenotypic variance.

Our findings of substantial V_{DI} contributing to variation in three traits expressed under inbreeding suggest that further studies of the components of genetic variance in partially inbreeding populations would be of value. An accumulation of evidence that, apart from V_{DI} , inbred dominance components are negligible could justify appreciable simplification in experimental designs used to study genetic variation under inbreeding. However, it is premature to rule out the importance of the remaining components even in the population of *N. menziesii* we studied. It remains to be seen whether

expression of variation in other characters or under field conditions is subject to gene action involving the remaining components not detected in the present study.

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The matrices of sampling variances and covariances
for each trait

V_A	V_E	V_{DR}	Cov (a, d)	V_{DI}	V_M
Trait = height					
24.63	-3.61	-8.26	-17.25	27.06	-0.65
	8.90	-5.30	0.90	-7.84	0.07
		13.60	8.64	-16.77	-0.94
			25.12	-49.54	0.10
				155.52	-0.08
					0.86
Trait = nodes ($\times 100$)					
56.12	-5.08	-25.19	-39.24	60.73	-1.36
	16.30	-14.52	-0.13	-14.92	0.23
		40.79	24.08	-36.35	-0.10
			56.10	-109.79	0.18
				321.2	-0.34
					3.89
Trait = petal length ($\times 100$)					
1.85	-0.19	-0.83	-1.35	2.2	-0.06
	1.19	-0.86	0.07	-1.58	4.0×10^{-3}
		1.83	0.80	-1.10	-0.02
			2.70	-5.97	-3.0×10^{-3}
				24.17	7.0×10^{-3}
					0.13
Trait = petal width ($\times 100$)					
0.80	-0.10	-0.34	-0.73	1.41	-0.02
	0.39	-0.29	0.13	-0.78	1.0×10^{-3}
		0.66	0.31	-0.42	-0.01
			1.29	-3.11	-1.0×10^{-3}
				10.91	1.0×10^{-3}
					0.03
Trait = days to flowering					
38.27	-5.23	-14.78	-34.46	65.51	-0.75
	11.16	-8.34	4.76	-24.74	0.15
		22.50	15.08	-23.22	-0.12
			57.45	-132.48	0.10
				412.99	-0.33
					1.86