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Prediction of additive and dominance effects in selected or unselected populations with inbreeding

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Summary. A genetic model with either 64 or 1,600 unlinked biallelic loci and complete dominance was used to study prediction of additive and dominance effects in selected or unselected populations with inbreeding. For each locus the initial frequency of the favourable allele was 0.2, 0.5, or 0.8 in different alternatives, while the initial narrow-sense heritability was fixed at 0.30. A population of size 40 (20 males and 20 females) was simulated 1,000 times for five generations. In each generation 5 males and 10 or 20 females were mated, with each mating producing four or two offspring, respectively. Breeding individuals were selected randomly, on own phenotypic performance or such yielding increased inbreeding levels in subsequent generations. A statistical model containing individual additive and dominance effects but ignoring changes in mean and genetic covariances associated with dominance due to inbreeding resulted in significantly biased predictions of both effects in generations with inbreeding. Bias, assessed as the average difference between predicted and simulated genetic effects in each generation, increased almost linearly with the inbreeding coefficient. In a second statistical model the average effect of inbreeding on the mean was accounted for by a regression of phenotypic value on the inbreeding coefficient. The total dominance effect of an individual in that case was the sum of the average effect of inbreeding and an individual effect of dominance. Despite a high mean inbreeding coefficient (up to 0.35), predictions of additive and dominance effects obtained with this model were empirically unbiased for each initial frequency in the absence of selection and 64 unlinked loci. With phenotypic selection of 5 males and only 10 females in each generation and 64 loci, however, predictions of additive and dominance effects were significantly biased. Observed biases disappeared with 1,600 loci for allelic frequencies at 0.2 and 0.5. Bias was due to a considerable change in allelic frequency with phenotypic selection. Ignoring both the covariance between additive and dominance effects with inbreeding and the change in dominance variance due to inbreeding did not significantly bias prediction of additive and dominance effects in selected or unselected populations with inbreeding.

Key words: Finite-locus model – Dominance – Inbreeding – Selection

Introduction

Mixed model methodology is used widely in animal breeding. In most applications, however, only additive genetic effects are considered. The accurate prediction of non-additive effects may be important in for example, the accurate prediction of additive genetic merit, selection of clones in plant or animal breeding, or selection of mates based on their specific combining ability (Allaire and Henderson 1965; DeStefano and Hoeschele 1992). Non-additive genetic effects result from interactions between genes at the same locus (dominance) or at different loci (epistasis). In this study only dominance is considered.

In noninbred populations, the prediction of dominance effects is straightforward but computationally demanding (Henderson 1985). The dominance relationship matrix can be computed from the additive genetic relationship matrix, inverted, and then applied in mixed model equations. Hoeschele and VanRaden (1991) presented a method to compute directly the inverse of the

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dominance relationship matrix in noninbred populations. The prediction of additive and dominance effects in noninbred populations requires knowledge of the additive and dominance variance in the base population. Intense selection in finite animal breeding populations will increase average inbreeding levels. Inbreeding complicates the genetic covariance structure of the population. Computation of the genetic covariance between two relatives with arbitrary levels of inbreeding requires knowledge of three extra genetic parameters: (1) the sum over loci of the squared complete inbreeding depressions, (2) the dominance variance in the completely inbred population, and (3) the covariance between additive and dominance effects in the completely inbred population (e.g. Harris 1964; Jacquard 1974). In addition, inbreeding may reduce the mean phenotypic value of the population, referred to as inbreeding depression (Falconer 1989).

Two methods for predicting additive and dominance effects in populations with inbreeding have been suggested. One method accounts for the average effect of inbreeding on the mean by including the inbreeding coefficient as a covariate in the model while ignoring the reduction of base dominance variance due to inbreeding, increase of dominance variance of completely inbred individuals, and the covariance between additive and dominance effects with inbreeding (Kennedy et al. 1988). An individual's total dominance effect is estimated as the sum of the average effect of inbreeding on the mean and an individual effect of dominance. This method was examined for populations with an average inbreeding coefficient of at most 0.08, selection of the 25% phenotypically best males and all females, and for initial allelic frequencies at 0.5 and 0.8 (Uimari and Kennedy 1990). In these situations, predictions of additive and dominance effects were empirically unbiased.

The other method for predicting additive and dominance effects in populations with inbreeding accounts for all of the changes in mean and genetic covariance with inbreeding (Smith and Mäki-Tanila 1990). The exact genetic covariance matrix between additive effects of gametes and dominance effects of gamete pairs existing in animals and other non-existing gamete pairs, the so-called extended genomic matrix (**E** matrix), is formed using tabular rules. To predict additive effects of gametes and dominance effects of (non)-existing gamete pairs, the inverse of **E** is required. Matrix **E** is singular, however, for only two alleles per locus. The prediction of additive and dominance effects via direct inversion of **E** is not suitable for genetic models with biallelic loci (Smith and Mäki-Tanila 1990), which was the model of interest in the present study. Properties of the **E** matrix and the possibility of predicting individual additive and dominance effects by extracting only those elements that involve animals deserves further study.

In this paper, the impact of level of inbreeding and intensity of selection on prediction of additive and dominance effects will be studied for different allelic frequencies using the approximate method proposed by Kennedy et al. (1988). Simulation at the individual locus level was used to compare predicted additive and dominance effects with corresponding simulated values. Strictly additive genetic models were studied to compare the finite-locus model with the infinitesimal model.

Methods

Simulation

This study followed the simulation strategy of Uimari and Kennedy (1990). The simulated trait was affected by a finite number (64 or 1,600) of unlinked, biallelic loci, each with an equal effect, and was measured on males and females. At each locus the genotypic value of the heterozygote was either intermediate or equal to that of the favourable homozygote. An individual's genetic value was the sum of its genetic values for all loci affecting the trait. A normally distributed environmental deviation was added to each genotypic value such that the narrow-sense heritability was 0.30 in the base generation.

Each simulated population included five generations. The initial generation contained 20 males and 20 females whose genes were randomly chosen from a base population in Hardy-Weinberg proportions and gametic phase equilibrium. For each locus the frequency of the favourable allele (p) in the base population was 0.2, 0.5, or 0.8 in different simulated populations. Corresponding additive and dominance variances in the noninbred base population at the animal level equalled: 52.43 and 6.55 for $p=0.2$, 32 and 16 for $p=0.5$, and 3.28 and 6.55 for $p=0.8$. To produce progeny, 5 males and 10 or 20 females were mated, with each mating resulting in two or one offspring of each sex, respectively. Breeding individuals were selected randomly, on own phenotypic performance or such yielding increased inbreeding levels in subsequent generations. For those selected at random or on their own performance, males and females were also mated randomly. Increased inbreeding levels in subsequent generations were obtained by maximizing the number of matings between closely related individuals (e.g. full sibs), denoted by full-sib mating. Full-sib mating was studied to examine the effect of inbreeding on prediction of additive and dominance effects in the absence of selection. Different intensities of female selection (proportion selected of 100% versus 50%) were used to analyze its effect on prediction of additive and dominance effects.

For each alternative 1,000 replicates were examined.

Evaluation

At the end of the last generation phenotypic information on individuals in all five generations was used to estimate additive and dominance effects using the known additive and dominance variance of the base population. Statistical models with and without a regression on inbreeding were used to examine the average effect of inbreeding on the mean:

$$y_i = \mu + a_i + d_i + e_i \qquad \text{(a)}$$

$$y_i = \mu + a_i + d_i + bF_i + e_i \qquad \text{(b)}$$

where y_i is the phenotypic value of animal i, μ is the base population mean, a_i is the additive effect of animal i, d_i is the dominance effect of animal i, b is the regression of the phenotypic value (y_i) on the inbreeding coefficient (F_i), and e_i is the random error term of animal i. For the model with regression, a dominance effect corrected for the average effect of inbreeding ($\hat{d}_i^*$) was predicted as:

$$\hat{d}_i^* = \hat{d}_i + \hat{b}F_i \tag{1}$$

The regression of phenotypic value on the inbreeding coefficient will account for the average effect of inbreeding on the mean. For a one-locus model with two alleles, the mean of an unselected population with an average inbreeding coefficient F (μ_F), ignoring genetic drift, can be written as (Kempthorne 1957):

$$\mu_F = (p^2 + pqF) \cdot a + (2pq(1-F)) \cdot d + (q^2 + pqF) \cdot -a \tag{2}$$
$$= \mu_R - 2pqdF = \mu_R + bF$$

Where μ_R is the mean in the noninbred random mating population ($a(p-q) + 2pqd$); p, q is the frequency of the favourable and unfavourable allele, respectively; a, d, $-a$ is the genotypic value of the favourable homozygote, the heterozygote and the unfavourable homozygote, respectively; F is the average inbreeding coefficient in the population; b is the regression coefficient, which equals the complete inbreeding depression or $\mu_I - \mu_R = -2pqd$, where μ_I is the mean in the completely inbred population ($a(p-q)$).

For a model with nl unlinked, biallelic loci in gametic phase equilibrium, the theoretical value of b equals:

$$b = -2 \sum_{k=1}^{nl} p_k q_k d_k \tag{3}$$

Mixed model equations used to obtain estimates of additive and dominance effects require the inverse of the additive genetic ($\mathbf{A}^{-1}$) and the dominance genetic ($\mathbf{D}^{-1}$) relationship matrix. The effect of inbreeding was accounted for in the construction of $\mathbf{A}^{-1}$ (Henderson 1975). Matrix $\mathbf{D}$ was computed from elements of $\mathbf{A}$ ignoring inbreeding, and inverted (Henderson 1985). Matrix $\mathbf{D}^{-1}$ was also obtained directly (Hoeschele and VanRaden 1991). Results from each strategy were almost identical, but in the present simulations obtaining $\mathbf{D}^{-1}$ directly required more CPU time. As the number of animals increases, however, obtaining $\mathbf{D}^{-1}$ directly will be more efficient than inverting $\mathbf{D}$. To obtain estimates of additive and dominance effects the mixed model equations were solved using iteration on the data (Schaeffer and Kennedy 1986). Solutions were considered stable when the convergence criterion which equals the sum of squares of differences in solutions between iterations divided by the sum of squares of the most recent solutions, was less than 10^{-10}.

Estimated additive and dominance effects were compared to corresponding simulated effects. Bias was assessed as the average difference between predicted individual additive and dominance effects and corresponding simulated effects in each generation. Biases observed in subsequent generations varying in average inbreeding level or in simulated populations differing in female selection intensity were compared to examine the average effect of selection and/or inbreeding on prediction of genetic effects. An individual's simulated additive (or dominance) effect was the sum of the simulated additive (or dominance) effects for all loci affecting the trait, which were computed relative to the random mating noninbred base population (Falconer 1989). This is consistent with the infinitesimal model, which assumes negligible changes in allelic frequency due to selection. Simulated additive or dominance variances in each generation were calculated directly as:

$$\sigma^2_{g_t} = \frac{1}{n-1} (\mathbf{g}_t' \mathbf{g}_t - \bar{g}_t^2) \tag{4}$$

where $\mathbf{g}_t$ is a vector of simulated additive or dominance effects for n animals in generation t, respectively.

Infinitesimal model versus the finite-locus model

Estimated additive and dominance effects were computed assuming an infinitesimal model. This model supposes an almost infinite number of unlinked loci, each with a small effect, which results in a negligible change in allelic frequency due to selection (Bulmer 1980). The number of loci in the finite-locus model must be large enough to assess the properties of the infinitesimal model, especially stability of allelic frequencies under selection. For a given genetic variance, the expected change in frequency of an allele at one locus, after one generation of selection, is inversely proportional to the square root of the number of loci of equal effect (Crow and Kimura 1970). As in Uimari and Kennedy (1990), a genetic model with 64 unlinked loci was examined. The expected initial increase in frequency of the favourable allele for an initial frequency of 0.5 equals 5%, with phenotypic selection of 5 males and 10 females in each generation. Reducing this expected increase in allelic frequency to about 1% requires 1,600 loci. An additional genetic model with 1,600 loci was considered, therefore, in which the total genetic variance was unchanged. Consequently, additive and dominance variances at the animal level and the covariance between additive and dominance effects arising with inbreeding were unaffected.

A strictly additive genetic model was used to examine whether the infinitesimal model could be approximated by a finite number of unlinked loci for five generations, with and without selection. In the absence of selection, the expected additive variance assuming an infinitesimal model was computed according to Van der Werf and De Boer (1990):

$$E(\sigma^2_{a_t}) = \frac{1}{n-1} \operatorname{tr}(\mathbf{Q}\mathbf{A}_t) \sigma^2_a \tag{5}$$

where $\mathbf{A}_t$ is the matrix of additive genetic relationships between n animals in generation t and $\mathbf{Q} = (\mathbf{I} - \frac{1}{n}\mathbf{J})$, where $\mathbf{I}$ is an $n \times n$ identity matrix and $\mathbf{J}$ is an $n \times n$ matrix in which all elements equal 1. With selection, the simulated additive variance obtained with the finite-locus model was compared with the simulated variance obtained with an infinitesimal model.

Results and discussion

Additivity at 64 or 1,600 loci

Strictly additive genetic models with 64 or 1,600 loci were used to compare the finite-locus model with the infinitesimal model. For each locus the initial frequency of the favourable allele was 0.2, 0.5, or 0.8 in different simulated populations, while the genetic difference among homozygotes equalled 2 or 0.4 with 64 or 1,600 loci, respectively. Consequently, the additive genetic variance was dependent on the initial allelic frequency.

Results from five generations of random mating between 5 randomly chosen males and all 20 females are given in Table 1 for the 64-loci model. The mean simulated additive effect in each generation was close to zero. The variance of simulated additive effects, however, declined as a result of the establishment of covariances between animals and the increase in average inbreeding coefficient. Simulated additive variances agreed well with expected additive variances assuming an infinitesimal model. Predictions of additive effects were empirically

Table 1. Mean (μ_a) and variance of simulated additive effects (σ_a^2), expected additive variance, mean predicted minus simulated additive effects (â-a), and mean frequency of the favourable allele (p) in generations 1, 3, and 5 with random selection and mating, averaged over 1,000 replicates for 64 loci, additive gene action, and initial p (p_i) at 0.2, 0.5, and 0.8 (empirical standard error between brackets)[a]

p_i	Generation[b]	μ_a	σ_a^2	E(σ_a^2)[c]	â-a	p
0.2	1	−0.01 (0.02)	20.60 (0.15)	20.48	0.01 (0.02)	0.20
	3	−0.05 (0.05)	19.15 (0.18)	19.07	0.03 (0.04)	0.20
	5	−0.05 (0.07)	18.09 (0.17)	18.12	0.04 (0.04)	0.20
0.5	1	0.02 (0.03)	32.11 (0.22)	32.00	−0.02 (0.03)	0.50
	3	0.01 (0.06)	29.98 (0.28)	29.80	0.01 (0.05)	0.50
	5	0.12 (0.08)	28.53 (0.26)	28.32	−0.01 (0.05)	0.50
0.8	1	0.02 (0.02)	20.64 (0.15)	20.48	−0.02 (0.02)	0.80
	3	0.01 (0.05)	19.34 (0.19)	19.07	−0.01 (0.04)	0.80
	5	0.08 (0.07)	18.31 (0.18)	18.12	−0.02 (0.04)	0.80

[a] Proportion selected is 25% for males and 100% for females

[b] Mean F in generations 1, 3 and 5, is 0.00, 0.03 and 0.08 respectively, independent of initial allelic frequency

[c] Expected variance according to equation [5] in text

Table 2. Mean (μ_a) and variance of simulated additive effects (σ_a^2), mean expected additive variance, mean predicted minus simulated additive effects (â-a), and mean frequency of the favourable allele (p) in generations 1, 3, and 5 of phenotypic selection averaged over 1,000 replicates for 64 loci, additive gene action, and initial p (p_i) at 0.2, 0.5, and 0.8 (empirical standard error between brackets)[a]

p_i	Generation[b]	μ_a	σ_a^2	E(σ_a^2)[c]	â-a	p
0.2	1	−0.02 (0.02)	20.84 (0.15)	20.40 (0.14)	0.02 (0.02)	0.20
	3	4.85 (0.06)	18.70 (0.18)	16.54 (0.15)	−0.04 (0.04)	0.24
	5	9.35 (0.08)	18.35 (0.18)	15.00 (0.14)	−0.19 (0.05)	0.27
0.5	1	0.01 (0.03)	32.23 (0.23)	31.87 (0.23)	−0.01 (0.03)	0.50
	3	5.74 (0.06)	25.56 (0.24)	25.85 (0.24)	−0.01 (0.05)	0.54
	5	10.67 (0.08)	22.85 (0.22)	23.44 (0.22)	0.02 (0.05)	0.58
0.8	1	0.02 (0.02)	20.55 (0.15)	20.40 (0.14)	−0.02 (0.02)	0.80
	3	4.46 (0.05)	14.31 (0.14)	16.54 (0.15)	−0.03 (0.04)	0.83
	5	7.85 (0.06)	11.78 (0.11)	15.00 (0.14)	0.21 (0.04)	0.86

[a] Proportion selected is 25% for males and 50% for females

[b] Mean F in generations 1, 3 and 5, is 0.00, 0.04 and 0.11 respectively, independent of initial allelic frequency

[c] Expected variance based on simulation with infinitesimal model

unbiased. As expected, the average frequency of the favourable allele was unchanged in the absence of selection.

Phenotypic selection of 5 males and 10 females in each generation changed the mean simulated additive genetic merit, variance of simulated additive genetic merit, and allelic frequency for both models with 64 and 1,600 loci (Tables 2 and 3). Selection increased mean additive genetic merit, while additive variance declined due to the establishment of covariances between animals, the increase of inbreeding, and gametic-phase disequilibrium. In addition, additive variance changed as a result of changes in allelic frequency.

Changes in allelic frequency due to selection were consistent with the expectations (Crow and Kimura 1970, p. 229), e.g. both the expected and the realized initial change in average allelic frequency for 64 loci and $p = 0.5$ equalled 5%. As expected, the increase in average frequency of the favourable allele was greater with 64 than with 1,600 loci. Consequently, the additive variance with 1,600 loci was closer to the additive variance with an infinitesimal model than the additive variance with 64 loci in later generations.

However, for the 64-loci model predictions of additive effects remained empirically unbiased when the initial frequency was 0.5, whereas with initial frequencies of 0.2 or 0.8 selection produced biased ($\alpha = 0.05$) predictions of additive effects in later generations. This results from the fact that the change of the additive variance due to the change in allelic frequency with selection, which is ignored in mixed model methodology, is relatively larger with extreme than with intermediate initial frequencies (Falconer 1989).

Biases observed with extreme initial frequencies and 64 loci were reduced when 1,600 loci were considered. Increasing the number of loci decreased the average

Table 3. Mean (μ_a) and variance of simulated additive effects (σ^2_a), mean expected additive variance, mean predicted minus simulated additive effects (â-a), and mean frequency of the favourable allele (p) in generations 1, 3, and 5 of phenotypic selection averaged over 1,000 replicates for 1,600 loci, additive gene action, and initial p (p_i) at 0.2, 0.5, and 0.8 (empirical standard error between brackets)[a]

p_i	Generation[b]	μ_a	σ^2_a	$E(\sigma^2_a)$[c]	â-a	p
0.2	1	0.01 (0.02)	20.60 (0.15)	20.40 (0.15)	−0.01 (0.02)	0.20
	3	4.70 (0.05)	16.65 (0.16)	16.54 (0.15)	0.02 (0.04)	0.21
	5	8.84 (0.07)	15.59 (0.14)	15.00 (0.14)	−0.04 (0.04)	0.21
0.5	1	−0.01 (0.03)	31.87 (0.23)	31.87 (0.23)	0.01 (0.03)	0.50
	3	5.78 (0.07)	25.83 (0.25)	25.85 (0.24)	0.07 (0.05)	0.51
	5	10.86 (0.09)	23.32 (0.22)	23.44 (0.22)	0.03 (0.05)	0.52
0.8	1	0.05 (0.02)	20.27 (0.15)	20.40 (0.15)	−0.05 (0.02)	0.80
	3	4.58 (0.05)	15.94 (0.15)	16.54 (0.15)	0.02 (0.04)	0.81
	5	8.45 (0.07)	14.40 (0.14)	15.00 (0.14)	0.06 (0.04)	0.81

[a] Proportion selected is 25% for males and 50% for females

[b] Mean F in generations 1, 3 and 5, is 0.00, 0.04 and 0.11 respectively, independent of initial allelic frequency

[c] Expected variance based on simulation with infinitesimal model

Table 4. Mean predicted minus simulated additive and dominance effects (empirical standard error between brackets) and average inbreeding level (F) in generations 1, 3, and 5 of random or full-sib mating without selection averaged over 1,000 replicates with complete dominance and an initial frequency of favourable allele of 0.5[a]

		Additive effects		Dominance effects		
		Analysis model[b]		Analysis model		
Mating type	Generation	[a]	[b]	[a]	[b]	F
Random	1	−0.02 (0.03)	−0.02 (0.03)	0.07 (0.02)	0.01 (0.02)	0.00
	3	−0.65 (0.05)	0.02 (0.05)	0.93 (0.03)	−0.01 (0.02)	0.03
	5	−1.52 (0.05)	−0.02 (0.06)	2.28 (0.03)	0.03 (0.04)	0.08
Full-sib	1	0.00 (0.03)	0.00 (0.03)	0.16 (0.02)	0.01 (0.02)	0.00
	3	−3.01 (0.05)	−0.04 (0.06)	3.90 (0.03)	0.05 (0.04)	0.14
	5	−7.07 (0.07)	0.00 (0.09)	8.84 (0.05)	0.00 (0.09)	0.35

[a] Proportion selected is 25% for males and 100% for females

[b] Model [a] without and model [b] with regression on inbreeding

change in allelic frequency due to selection and, as a result, the corresponding change of the additive variance. The genetic model with 64 loci will be used to study the prediction of additive and dominance effects in unselected populations, while both 64- and 1,600-loci models will be considered in selected populations.

Complete dominance at 64 loci with random selection

After five generations of random or full-sib mating between 5 males and all 20 females in the absence of directional selection, additive and dominance effects were predicted with statistical models (a) and (b) for varying initial allelic frequencies (Tables 4 and 5). For each mating strategy and an initial allelic frequency of 0.5, model (a) resulted in empirically biased ($\alpha = 0.05$) predictions of additive and dominance effects in generations with inbreeding (Table 4). The average underestimation of additive effects, however, was slightly smaller than the average overestimation of dominance effects. Hence, total genetic effects were biased upwards. Observed biases for additive and dominance effects increased almost linearly with the average inbreeding coefficient (F). Inclusion of F as covariate in the model resulted in empirically unbiased predictions of additive and dominance effects for random and full-sib mating strategies.

When all loci have two alleles with allelic frequencies of 0.5, however, the covariance between additive and dominance effects, which is ignored in model (b), is zero. This covariance is nonzero if allelic frequencies are different from 0.5 (Harris 1964). Therefore, initial frequencies of 0.2 and 0.8 were considered (Table 5). Average inbreeding coefficients in these cases were equal to those given in Table 4. Ignoring the covariance between additive and dominance effects with inbreeding and the change in dominance variance due to inbreeding did not

Table 5. Mean predicted[a] minus simulated additive and dominance effects (empirical standard error between brackets) and mean inbreeding level (F) in generations 1, 3, and 5 of random or full-sib mating without selection averaged over 1,000 replicates, for complete dominance and initial allelic frequency of 0.2 or 0.8[b]

		Additive effects		Dominance effects	
		Frequency		Frequency	
Mating type	Generation[c]	0.2	0.8	0.2	0.8
Random	1	0.02 (0.04)	−0.01 (0.01)	0.00 (0.01)	−0.01 (0.01)
	3	0.04 (0.06)	−0.01 (0.02)	0.01 (0.02)	−0.01 (0.01)
	5	0.06 (0.07)	0.00 (0.02)	0.03 (0.04)	−0.01 (0.02)
Full-sib	1	0.00 (0.04)	0.00 (0.01)	0.00 (0.01)	−0.01 (0.01)
	3	0.02 (0.07)	0.00 (0.02)	−0.03 (0.04)	−0.02 (0.02)
	5	0.09 (0.12)	0.04 (0.03)	−0.12 (0.12)	−0.06 (0.03)

[a] Statistical model [b] with regression on inbreeding

[b] Proportion selected is 25% for males and 100% for females

Table 6. Mean predicted minus simulated average additive and dominance effects (empirical standard error between brackets), mean inbreeding level (F), and frequency of favourable allele (p) in generations 1, 3, and 5 of phenotypic selection averaged over 1,000 replicates, with complete dominance, 64 loci, and an initial p of 0.5[a]

	Additive effects		Dominance effects			
	Analysis model[b]		Analysis model			
Generation	[a]	[b]	[a]	[b]	F	p
1	−0.01 (0.03)	−0.01 (0.03)	0.05 (0.02)	−0.01 (0.02)	0.00	0.50
3	−0.68 (0.05)	0.00 (0.05)	0.92 (0.02)	0.01 (0.03)	0.03	0.53
5	−1.52 (0.06)	−0.08 (0.06)	2.34 (0.03)	0.10 (0.04)	0.08	0.55

[a] Proportion selected is 25% for males and 100% for females

[b] Statistical model [a] with and model [b] without regression on inbreeding

significantly bias predictions of additive and dominance effects in unselected populations with inbreeding (Table 5).

Complete dominance at 64 or 1,600 loci with phenotypic selection

After five generations of random mating between the phenotypically 5 best males and all 20 females, additive and dominance effects were predicted with statistical models (a) and (b). Mean predicted minus simulated additive and dominance effects in generations one, three, and five are given in Table 6 for 64 loci and an initial allelic frequency of 0.5. For model (a) the predicted additive and dominance effects in generations with inbreeding were biased ($\alpha = 0.05$) by about the same amount as with random selection of males and females. For model (b) and phenotypic selection, predicted dominance effects in generation five were slightly biased ($\alpha = 0.05$).

With a selection of 10 instead of 20 females in each generation and 64 unlinked biallelic loci, model (b) resulted in significantly biased ($\alpha = 0.05$) prediction of both additive and dominance effects in generations with inbreeding (Table 7). Observed biases might be due to ignoring the covariance between additive and dominance effects and the change in dominance variance due to inbreeding and/or to ignoring changes in allelic frequency in simulated and estimated additive and dominance effects.

With 1,600 unlinked, biallelic loci and an initial allelic frequency of 0.5, predictions of additive and dominance effects were empirically unbiased. When the initial allelic frequency is 0.5, however, and changes in average allelic frequency due to selection are small, the covariance between additive and dominance effects is negligible. The absolute covariance is largest with an initial allelic frequency around 0.2 (Harris 1964). Increasing the number of loci with an initial frequency of 0.2 also decreased observed biases considerably, although predicted dominance effects remained slightly higher than corresponding simulated effects in generation five. Increasing the number of loci decreased the average change in allelic

Table 7. Mean predicted[a] minus simulated additive and dominance effects (empirical standard error between brackets) and mean frequency of favourable allele (p) in generations 1, 3, and 5 of phenotypic selection averaged over 1,000 replicates, with complete dominance and 64 or 1,600 loci[b]

	64 loci			1,600 loci		
Generation[c]	Additive	Dominance	p	Additive	Dominance	p
			Initial p is 0.2			
1	0.04 (0.04)	0.01 (0.01)	0.20	−0.01 (0.04)	−0.01 (0.01)	0.20
3	−0.18 (0.07)	0.16 (0.03)	0.24	0.01 (0.06)	−0.02 (0.03)	0.21
5	−0.70 (0.08)	0.78 (0.06)	0.27	−0.04 (0.08)	0.13 (0.05)	0.21
			Initial p is 0.5			
1	−0.01 (0.03)	0.00 (0.02)	0.50	0.01 (0.03)	−0.03 (0.02)	0.50
3	−0.13 (0.05)	0.14 (0.03)	0.54	0.01 (0.05)	0.02 (0.03)	0.51
5	−0.21 (0.06)	0.34 (0.05)	0.58	0.01 (0.06)	0.02 (0.04)	0.51

[a] Statistical model [b] with regression on inbreeding

[b] Proportion selected is 25% for males and 50% for females

[c] Mean F in generations 1, 3, and 5 is 0.00, 0.04, and 0.11, respectively, independent of the allelic frequency

frequency due to selection, while additive and dominance covariances were unaffected. Moreover, it reduced possible skewness of the genetic distribution (Mäki-Tanila and Kennedy 1986). Consequently, ignoring both the covariance between additive and dominance effects, and the change in dominance variance due to inbreeding did not significantly bias predictions of additive and dominance effects in selected populations with inbreeding. Observed biases with selection were mostly due to ignoring allelic frequency changes in simulated and estimated additive and dominance effects.

Uimari and Kennedy (1990) also concluded that including inbreeding as a covariate in the model of analysis resulted in empirically unbiased predictions of additive and dominance effects in selected and unselected populations with inbreeding. The maximum average inbreeding coefficient in their simulation, however, equalled 0.08, which is much lower than the maximum of 0.35 in the present study. They did not observe significant bias in selected populations due to instability of allelic frequencies because only males were selected in each generation and the number of replicates was smaller.

Neglecting the effect of inbreeding on genetic covariances associated with dominance, however, might result in considerable over- or underestimation of individual additive and dominance effects in each generation, although predictions are on average unbiased. A comparison of the accuracies of the prediction of additive and dominance effects obtained with the approximate method (Kennedy et al. 1988) and the exact method (Smith and Mäki-Tanila 1990) will give information on the prediction error variance of additive and dominance effects.

Table 8. Theoretical and mean predicted regression coefficients (empirical standard error between brackets) obtained with statistical model with regression on inbreeding in selected and unselected populations for varying initial allelic frequency p_i and 64 loci

	No selection			
p_i	Theoretical b[a]	Random mating	Full-sib mating	Selection
0.2	−20.48	−20.09 (0.49)	−20.67 (0.28)	−23.80 (0.51)
0.5	−32.00	−31.43 (0.39)	−31.98 (0.24)	−31.18 (0.40)
0.8	−20.48	−20.10 (0.17)	−20.65 (0.12)	−15.31 (0.15)

[a] Theoretical value of regression coefficient b according to equation [3]

Estimation of and theoretical value of the average effect of inbreeding

Mean predicted regression coefficients obtained with statistical model (b) are given in Table 8 for populations with and without selection, varying initial allelic frequency, and 64 loci. In addition, the theoretical value of the regression coefficient in the absence of selection is given, which is computed according to equation (3). Estimated regression coefficients obtained with model (b) corresponded well with theoretical coefficients in the absence of selection. With selection, however, equation (3) can not be used to determine the theoretical value of the regression coefficient because the population is neither in Hardy-Weinberg (Falconer 1989) nor in gametic-phase equilibrium (Bulmer 1980). As a result of selection against the unfavourable homozygote, the frequency of this genotype will decrease. Therefore, the estimated regression coefficient will decrease when the initial frequency of the favourable allele is smaller than 0.5 and increase when it is larger than 0.5, as can be seen in Table 8.

Simulation of dominance with the infinitesimal model

Present and previous simulations (Uimari and Kennedy 1990) of populations with additive and dominance gene action and inbreeding have used finite-locus (64 or 1,600 loci) models. In the absence of inbreeding, recurrence equations relating offspring genetic merits to parental values exist, and these allow the simulation of additive and dominance effects with the infinitesimal model. An individual's additive genetic effect is simulated as the average of it's parental values plus Mendelian sampling, while an individual's dominance effect is a function of it's sire-dam combination effect plus Mendelian sampling (Hoeschele and VanRaden 1991). Unlike a finite-locus model, the infinitesimal model does not require assumptions on the number of loci, the number of alleles per locus and corresponding allelic frequencies, and the genetic values of all possible genotypes at a locus. However, required recurrence equations to simulate additive and dominance effects in populations with inbreeding are currently not available.

Results indicate that including the average effect of inbreeding on the mean and ignoring the effect of inbreeding on genetic covariances associated with dominance gave empirically unbiased predictions of additive and dominance effects in selected and unselected populations with inbreeding. This concept might be used to approximate the simulation of additive and dominance effects with an infinitesimal model. An individual's dominance effect ignoring inbreeding (d_i) was simulated as it's sire-dam combination effect plus Mendelian sampling, where a sire-dam combination effect is a function of combination effects of the sire with the parents of the dam, the dam with the parent of the sire, and among parents combination effects (Hoeschele and VanRaden 1991). To simulate the total dominance effect (d_i^*) of an individual (equation (1)) the average effect of inbreeding on the mean is required. Given the underlying genetic model, the value of the regression of phenotype on inbreeding can be computed when changes in allelic frequency due to selection are ignored.

To compare both approaches of simulating dominance effects in populations with inbreeding, we simulated five generations of full-sib mating between 5 males and all 20 females with a finite (64 loci) and an infinitesimal model. Mean and variances of simulated additive and dominance genetic effects for an initial allelic frequency of 0.5 are given in Table 9. Mean additive and dominance genetic merit and additive variance agreed well in both simulations. As expected, mean additive genetic merit was close to zero in the absence of selection, while mean dominance effect declined linearly with the inbreeding coefficient. Reduction of the additive variance was due to the establishment of covariances between individuals and the increase in average inbreeding coefficient. In the finite-locus model, inbreeding decreased dominance variance while variation in inbreeding coefficient resulted in an increase in dominance variance. The infinitesimal model ignores changes of

Table 9. Mean additive (μ_a) and dominance effects (μ_d), variances (σ^2_a, σ^2_d), and the covariance (σ_{ad}) simulated with the finite-locus model or the infinitesimal model for full-sib mating averaged over 1,000 replicates (empirical standard error between brackets)[a]

Generation[b]	μ_a	μ_d	σ^2_a	σ^2_d	σ_{ad}
	Simulation with finite-locus (64) model				
1	0.00 (0.03)	−0.01 (0.02)	32.16 (0.23)	16.00 (0.12)	−0.06 (0.12)
2	0.05 (0.06)	0.00 (0.02)	30.35 (0.29)	15.94 (0.12)	−0.07 (0.12)
3	0.06 (0.09)	−4.45 (0.03)	29.31 (0.32)	21.58 (0.15)	0.20 (0.15)
4	−0.04 (0.13)	−7.86 (0.04)	25.19 (0.29)	18.88 (0.14)	0.10 (0.13)
5	−0.07 (0.15)	−11.25 (0.05)	22.55 (0.25)	16.91 (0.14)	0.18 (0.13)
	Simulation with infinitesimal model				
1	−0.05 (0.03)	0.01 (0.02)	31.85 (0.23)	16.13 (0.12)	0.01 (0.11)
2	−0.10 (0.06)	0.02 (0.02)	29.95 (0.29)	16.00 (0.12)	−0.06 (0.12)
3	−0.03 (0.09)	−4.38 (0.03)	28.82 (0.30)	22.18 (0.16)	0.01 (0.14)
4	−0.04 (0.13)	−7.84 (0.03)	25.47 (0.29)	20.68 (0.15)	−0.09 (0.14)
5	0.04 (0.15)	−11.22 (0.03)	22.17 (0.24)	20.51 (0.16)	−0.04 (0.13)

[a] Proportion selected is 25% for males and 100% for females

[b] Mean F in generations 1, 2, 3, 4, and 5 was 0.00, 0.00, 0.14, 0.25, and 0.35, respectively, in both the finite-locus model and the infinitesimal model

dominance variance due to inbreeding. Consequently, with an initial allelic frequency of 0.5 simulated dominance variance was too high in later generations, while the average dominance effect was correctly simulated. In addition, the infinitesimal model ignores the covariance between additive and dominance effects with inbreeding. This covariance is, however, zero when the initial allelic frequency is 0.5 (Table 9).

Thus, simulation of additive and dominance effects with the approximate infinitesimal model accounts for the average effect of inbreeding on the mean, while ignoring its effect on genetic covariances associated with dominance. Assumptions on the actual number of loci and alleles, corresponding allelic frequencies, and genetic values of genotypes possible at each locus, however, are not required.

Conclusions

A statistical model containing individual additive and dominance effects, but ignoring changes in mean and genetic covariances associated with dominance due to inbreeding, resulted in significantly biased predictions of both effects. Bias increased almost linearly with the inbreeding coefficient.

A statistical model accounting for the average effect of inbreeding on the mean, while ignoring its effects on genetic covariances associated with dominance, resulted in empirically unbiased predictions of additive and dominance effects in selected and unselected populations with inbreeding for varying initial allelic frequencies at 64 or 1,600 unlinked, biallelic loci.

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