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Estimates of Additive and Non-Additive Genetic Variances with Varying Levels of Inbreeding

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Abstract: In this study, two populations with varying percentages of animals in full-sib families were simulated. For each population, two combinations of additive and dominance genetic variances of different relative magnitudes were considered thereby creating 4 sub-populations. For each sub-population, a further 3 populations (I1, I2, I3) were created with varying degree of inbreeding level (0, 0.02 and 0.05) resulting in a total of 12 populations. Constant residual variance was used in all populations. Variance components were estimated using the tilde-hat approximation to REML based on sire-dam model. Both additive and dominance genetic variances were estimated with high degree of accuracy and the level of inbreeding did not seem to result in changes in the magnitudes of the genetic variances. At low levels of inbreeding, accounting for inbreeding in genetic evaluations may not be necessary.

Key words: Populations, variance components, estimates, full-sibs, simulation

INTRODUCTION

The partitioning of the total variance into its components allows the determination of the relative importance of the various determinants of the phenotype, in particular the role of heredity versus environment (Falconer, 1996). The role of heredity takes two forms: determination of individuals' phenotype by their genotypes or determination of individuals' phenotypes by the genes transmitted from the parents. The assessment of both forms is increasingly becoming important. However, livestock genetic evaluations in most livestock species currently use the additive genetic model. This is the case even though considerable research has shown the need for genetic evaluation accounting for dominance effects for particular traits and populations (Norris *et al.*, 2006; Wei and Van der Werf, 1993; Misztal *et al.*, 1995, 1998; Varona *et al.*, 1997; Rye and Mao, 1998). The reason for not considering dominance and epistatic genetic effects has largely been because of difficulties associated with their estimation (Bridges and Knapp, 1987; Fenster *et al.*, 1997). A limiting factor in the analysis of non-additive genetic models has been the ability to compute the inverses of non-additive genetic covariance matrices for large populations. Additionally, accounting for inbreeding in dominance

analysis for medium to large populations also poses a computational problem. However, new computing programs have been developed to address this challenge. The wide use of artificial insemination and embryo transfer coupled with the large-scale application of new reproductive technologies such as embryo splitting, cloning etc is increasing the frequency of genetically identical, full-sib and three-quarter sib groups in livestock populations and thus necessitating the use of non-additive genetic models in livestock genetic evaluations (Chalh and El Gazzah, 2004).

Genetic covariance between individuals in random mating, non-inbred population for quantitative traits is a well defined linear function of the genetic variance components assuming small contributions from many unlinked loci (Cockerham, 1954). In inbred populations, inbreeding may complicate the genetic covariance structure of populations (De Boer and Hoeschele, 1993; Kelly and Arathi, 2003). In the presence of inbreeding, genetic variance is redistributed (Falconer, 1996). The changes in gene frequency due to inbreeding cause some variance that was dominance or epistatic in the ancestral population to become additive within the pure breeds. Consequently, it is possible for additive and even total variance within breeds to increase at low levels of

inbreeding (Miller and Goddard, 1998) and inability to account for inbreeding in genetic evaluations may bias estimates of the genetic variances. Therefore, the objective of this study was to investigate the changes in estimates of genetic variances under varying levels of inbreeding.

MATERIALS AND METHODS

The study by Norris *et al.* (2002) showed that in populations with a large number of animals having dominance genetic relationship (20% or greater), estimates of dominance genetic variances can be obtained with improved accuracy even when the dominance genetic effect in the population is of small magnitude. The present study is an extension of the Norris *et al.* (2002) study. This simulation study was carried out at the University of Limpopo, South Africa in 2008.

Two populations with 50% (P1) and 100% (P2) of animals in full-sib families were simulated. The number of animals in each population was 10000 and each full-sib family had 25 animals. For each population, combinations of additive variance, V_A and dominance variance, V_D were considered: V1 ($V_A=800, V_D=200$), V2 ($V_A=500, V_D=500$), thereby creating 4 populations, each with 10000 animals. The residual variance was constant at 2000 in all populations. From each population, a further 3 populations (I1, I2, I3) were created with varying degree of inbreeding level (0, 0.02 and 0.05) resulting in a total of 12 sub-populations. The populations are denoted as follows in Table 1. Population P1-V1-I1 for instance had 50% of animals in full-sib families with additive and dominance genetic variances of 800 and 200, respectively. The inbreeding level was zero. The descriptions of the other populations are given in the Table 1 under the properties column.

Each population was simulated for 20 replicates.

Records were simulated and analyzed according to the following sire and dam model:

$$y_{ijk} = \mu + s_i + m_j + sm_{ij} + e_{ijk} \tag{1}$$

where, μ is the population mean, s_i is the additive effect of sire $\sim N(0, 1/4\sigma_a^2)$, m_j is the additive effect of dam $\sim N(0, 1/4\sigma_a^2)$, sm_{ij} is the dominance effect due to interaction of sire and dam $\sim N(0, 1/4\sigma_d^2)$. e_{ijk} is the residual effect $\sim N(0, \sigma_e^2 + 1/2\sigma_a^2 + 3/4\sigma_d^2)$.

Derivation of additive (a) and dominance (d) genetic values (Hoeschele and VanRaden, 1991):

$$a = 0.5a_s + 0.5a_d + m_a$$

$$d = fd_{s,d} + m_d$$

where, a_s and a_d are the additive genetic effects of sire and dam, respectively. $fd_{s,d}$ is combination of sire with dam due to interaction of genes from the sire with genes from the dam. m_a and m_d are the respective additive and dominance genetic effects due to mendelian sampling.

$$\text{Var}(m_a) = 0.5 \sigma_a^2; \text{Var}(m_d) = 0.75 \sigma_d^2$$

The above sire-dam model can be written in matrix notation on an individual animal basis as:

$$y = Za + Zd + e \tag{2}$$

where, y is the data vector, a is the vector of random additive effects for sire and dam, d is the vector of random dominance effects, e is the vector of residuals and Z are known matrices corresponding to a and d , respectively.

Variance components were estimated using the tilde-hat approximation to REML (Van Raden and Jung, 1988). The inverse relationship matrices, A^{-1} and D^{-1} were computed directly by algorithms described by Henderson (1976) and Hoeschele and VanRaden (1991). Computations were done using FORTRAN programs INVERS and NONAD2 written by Hoeschele (1991).

Table 1: Populations description

| Populations | Properties |
|-------------|---|
| P1-V1-I1 | 50% full-sib families, $V_A=800$ and $V_D=200$, Inbreeding level = 0 |
| P1-V1-I2 | 50% full-sib families, $V_A=800$ and $V_D=200$, Inbreeding level = 0.02 |
| P1-V1-I3 | 50% full-sib families, $V_A=800$ and $V_D=200$, Inbreeding level = 0.05 |
| P1-V2-I1 | 50% full-sib families, $V_A=500$ and $V_D=500$, Inbreeding level = 0 |
| P1-V2-I2 | 50% full-sib families, $V_A=500$ and $V_D=500$, Inbreeding level = 0.02 |
| P1-V2-I3 | 50% full-sib families, $V_A=500$ and $V_D=500$, Inbreeding level = 0.05 |
| P2-V1-I1 | 100% full-sib families, $V_A=800$ and $V_D=200$, Inbreeding level = 0 |
| P2-V1-I2 | 100% full-sib families, $V_A=800$ and $V_D=200$, Inbreeding level = 0.02 |
| P2-V1-I3 | 100% full-sib families, $V_A=800$ and $V_D=200$, Inbreeding level = 0.05 |
| P2-V2-I1 | 100% full-sib families, $V_A=500$ and $V_D=500$, Inbreeding level = 0 |
| P2-V2-I2 | 100% full-sib families, $V_A=500$ and $V_D=500$, Inbreeding level = 0.02 |
| P2-V2-I3 | 100% full-sib families, $V_A=500$ and $V_D=500$, Inbreeding level = 0.05 |

RESULTS AND DISCUSSION

The estimates of genetic variances under varying levels of inbreeding in sub-populations with 50% of animals in full-sib families are shown in Table 2. The estimated genetic variances are shown in Table 2 and 3 while on the table footnotes the simulated genetic variances are indicated. The estimated genetic variances (additive and dominance) are similar ($p > 0.05$) to the true simulated variances in all populations. Additionally, these variances are similar to the simulated variances irrespective of the level of inbreeding. The results on the ability to accurately estimate non-additive genetic variances in populations with a high number of animals with non-additive relationships support an earlier study by Norris *et al.* (2002) which indicated that in populations with at least 20% of animals with non-additive relationships, accurate estimations of dominance variance is achievable. There is conflicting information on the effect of inbreeding or inbreeding depression on the estimation of genetic variances. De Boer and Arendonk (1992) used a genetic model with either 64 or 1,600 unlinked biallelic loci and complete dominance to study prediction of additive and dominance effects in selected or unselected populations with inbreeding. When changes in mean and genetic covariances associated with dominance due to inbreeding were ignored, significantly biased predictions of additive and dominance effects in generations with inbreeding resulted. Bias, assessed as the average difference between predicted and simulated genetic effects in each generation, increased almost linearly with the inbreeding coefficient. When the genetic variation underlying a quantitative trait is controlled by genes that act additively within and between loci, the additive genetic variance within a population following a

bottleneck event or inbreeding is expected to decrease by a proportion F , the inbreeding coefficient of the population (Wang *et al.*, 1998). However, there indication that additive genetic variance and heritability of some quantitative traits within populations can actually increase following population bottlenecks (Wang *et al.*, 1998; Whitlock and Fowler, 1999). The study by Russell *et al.* (1984) investigated changes in variances with increased inbreeding in beef cattle showed that the changes do not generally follow the theoretical expectations for the redistribution of genetic variances. Whitlock and Fowler (1999) performed a large-scale experiment on the effects of inbreeding and population bottlenecks on the additive genetic and environmental variance for morphological traits in *Drosophila melanogaster* lines and found that the mean change in additive genetic variance was in very good agreement with classical additive theory, decreasing proportionally to the inbreeding coefficient of the lines.

In a study by Takayoshi *et al.* (2007) on the relationships among estimates of additive genetic variance, dominance genetic variance and inbreeding depression for type traits in Holstein population of Japan, the estimates of inbreeding depressions had significantly negative relationship with the estimates of dominance genetic standard deviations. De Boer and Hoeschele (1993) showed that for a biallelic locus with complete dominance and for favorable gene frequencies that are about 0.20 or about 0.80, large effects of inbreeding depression were linked to high dominance variance.

The estimates of genetic variances under varying levels of inbreeding in sub-populations with 100% of animals in full-sib families are shown in Table 3. Similar results are observed in these subpopulations as those with 50% of animals in full-sib families. The

Table 2: Genetic variances in populations with 50% full-sibs under different levels of inbreeding

| Population | Additive variance | SE | Dominance variance | SE | Residual variance | SE |
|------------|-------------------|----|--------------------|----|-------------------|----|
| P1V1I1 | 790 | 25 | 208 | 27 | 2040 | 6 |
| P1V1I2 | 788 | 26 | 210 | 28 | 2048 | 6 |
| P1V1I3 | 794 | 30 | 211 | 29 | 2049 | 6 |
| P1V2I1 | 480 | 24 | 520 | 26 | 2123 | 6 |
| P1V2I1 | 484 | 25 | 516 | 26 | 2099 | 6 |
| P1V2I1 | 482 | 30 | 517 | 25 | 2114 | 6 |

P1-50% full-sib families, V1-($V_A = 800$ and $V_D = 200$): Simulated (true) genetic variances, V2-($V_A = 500$ and $V_D = 500$): Simulated (true) genetic variances, I1: No. inbreeding, I2: 0.02 inbreeding, I3: 0.05 inbreeding, SE: Standard error

Table 3: Genetic variances in populations with 100% full-sibs under different levels of inbreeding

| Population | Additive variance | SE | Dominance variance | SE | Residual variance | SE |
|------------|-------------------|----|--------------------|----|-------------------|----|
| P2V1I1 | 810 | 26 | 208 | 28 | 2051 | 6 |
| P2V1I2 | 805 | 27 | 799 | 31 | 2048 | 6 |
| P2V1I3 | 798 | 29 | 214 | 29 | 2037 | 6 |
| P2V2I1 | 490 | 25 | 505 | 28 | 2124 | 6 |
| P2V2I1 | 494 | 25 | 507 | 27 | 2114 | 6 |
| P2V2I1 | 489 | 27 | 515 | 29 | 2117 | 6 |

P2-100% full-sib families, V1-($V_A = 800$ and $V_D = 200$): Simulated (true) genetic variances, V2-($V_A = 500$ and $V_D = 500$): Simulated (true) genetic variances, I1: No. inbreeding, I2: 0.02 inbreeding, I3: 0.05 inbreeding, SE: Standard error

estimated genetic variances (additive and dominance) are similar ($p > 0.05$) to the true simulated variances and these variances are similar to the simulated variances irrespective of the level of inbreeding. It is worth noting that the inbreeding levels in this study were very low compared to other studies and therefore the stability in the estimation of genetic variances may be due to these low levels of inbreeding. However, a study by Miller and Goddard (1998) in which they modeled additive and non-additive genetic effects within and between breeds in multi breed evaluation, showed that at low levels of inbreeding within a breed, most non-additive genetic variation exists within-breed, indicating that models which do not account for within-breed non-additive genetic variation could be missing the largest source of variation.

CONCLUSION

In the presence of inbreeding, the common practice is account for it by including inbreeding depression as a covariate. This study seems to indicate that at low levels of inbreeding, genetic variances can still be estimated with accuracy. Therefore, it may not necessary to account for inbreeding in such cases thus removing some of the computational challenges associated with incorporating dominance relationships and inbreeding coefficients in genetic analysis.

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