A STUDY OF ENVIRONMENTAL VARIANCE GENETIC CONTROL FOR UTERINE CAPACITY IN RABBITS

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ABSTRACT

Data from ten generations divergent selection experiment for uterine capacity in rabbits were analysed to estimate the genetic parameters using a model which postulates that environmental variance is partly under genetic control. The posterior mean of additive variance at variance level was 0.12 and the highest posterior interval at 95% did not include zero. The estimated correlation between the additive genetic effects on the mean and those on the variance was -0.74 with a posterior interval far away from zero. A study of model fit/model comparison was also carried out using three different approaches: 1) a version of model checking, based on the regression of the average sampling variance of records within individuals on mean phenotypic values; 2) the deviance information criterion, an index that encapsulates the fit of a model and its complexity; 3) cross validation based on CPOs. The three approaches provided statistical support for the genetically structured heterogeneous variance model.

Keys words: Environmental variance, Uterine capacity, Bayesian methods, Model checking.

INTRODUCTION

In animal breeding, selection has focused on improving the mean of traits, such as litter size in prolific species (pigs and rabbits). However, the variance of the trait also has important economic consequences. Thus, it is desirable that, e.g., a rabbit produces not only large litters but also litters of similar size across parities. In recent years evidence has been reported indicating that environmental variation may be partly under genetic control in rabbit weight at birth (Garreau *et al.*, 2004; Bolet *et al.*, 2007), in pig litter size (Sorensen and Waagepetersen, 2003), in snails growth (Ros *et al.*, 2004) and poultry (Rowe *et al.*, 2005). Also, Mackay and Lyman (2005) showed substantial (genetic) variation in the environmental coefficient of variation in abdominal bristle number among chromosome substitution lines in Drosophila melanogaster.

In this work inferences are presented based on a Gaussian mixed model with heterogeneous residual variance (San Cristobal-Gaudy *et al.*, 1998) adjusted to uterine capacity data (the maximal number of fetuses that the dam is able to support at birth when ovulation rate is not a limiting factor) from an experiment of divergent selection in rabbit. The objective of this work is mainly to investigate whether the data provide support for the model postulating that environmental variation for uterine capacity is partly under genetic control.

MATERIALS AND METHODS

Animals

The data originate from a ten generation divergent selection experiment for uterine capacity in rabbits. Animals were derived from a synthetic population of the experimental farm at the Universidad

Politécnica de Valencia. Uterine capacity was estimated as litter size in unilateral ovariectomized does, which doubles the number of ova shed by the remaining ovary. The left ovary was removed in all does before puberty via midventral incision between 14 and 16 weeks of age. The females were first mated at 18 weeks of age and thereafter 10 days after parturition, producing in total up to four parities. Details of the technique are given by Santacreu *et al.* (1990). Selection was performed on estimated breeding values for litter size up to four parities, by using a BLUP procedure and a repeatability animal model with year-season and parity fixed effects, but males were selected within 59 sire families in order to reduce inbreeding. Reproduction was organized in discrete generations. Data from ten generations of selection were used. In each divergent selection line, there were approximately 40 females and 12 male parents each generation. Number of records was approximately the same for high and low line. The total number of records for uterine capacity was 2,996. The number of animals in the pedigree was 1,161 from which 85 belong to the base population.

Model Fitted

The selection experiment was analysed with two models of different levels of complexity.

Model 1

Model 1 is the classical repeatability additive genetic model that was used to carry out selection decisions during the course of the experiment. It assumes that the sampling model of the data, given location parameters b, a, and p and given the residual variance σ^2_e, is the normal process

$y \mid b,a,p, \sigma^2_e \sim N(Xb + Za + Wp, I\sigma^2_e)$,

where now b contains year-season and parity effects with thirty and four levels, respectively. Vectors a and p contain additive genetic values (1161 levels) and permanent effects (929 levels) respectively, and σ^2_e is the residual variance. The known incidence matrices are X, Z and W and I is the identity matrix.Vectors p and a were assumed to be a priori independently and normally distributed; that is

$p \mid \sigma^2_p \sim N(0, \sigma^2_p I)$

$a \mid \sigma^2_a \sim N(0, A\sigma^2_a)$

where A is the known additive genetic relationship matrix. The vector b was assigned an unbounded uniform prior distribution and the variance components σ^2_p, σ^2_a, σ^2_e, scaled inverted chi square distributions. This model assumes homogeneity of environmental variation. It was fitted using a Gibbs sampling algorithm, as described, for example, in Sorensen and Gianola (2002).

Model 2

The Model 2 was proposed by SanCristobal-Gaudy *et al*. (1998) in which it postulates that environmental variance is heterogeneous and partly under genetic control. The sampling model for the data is Gaussian:

$y \mid b,a,p,b^*,a^*,p^* \sim N(\mu, diag((\sigma^2_i)^n_{i=1}))$,

Where y is the vector of data for litter size and $diag((\sigma^2_i)^n_{i=1})$ is the diagonal matrix with diagonal entries σ^2_i,

$(\log \sigma^2_i)^n_{i=1} = X^*b + Za^* + Wp^*$ and $\mu = (\mu)^n_{i=1} = Xb + Za + Wp$

The vectors b and b^* contain effects associated with year-season and lactation status, with the same levels as Model 1, and X, Z and W are known incidence matrices. Vectors p and p^* contain permanent environmental effect for litter size and are assumed to be independently normally distributed

$p \mid \sigma^2_p \sim N(0, \sigma^2_p I)$

$p^* \mid \sigma^2_{p^*} \sim N(0, \sigma^2_{p^*} I)$

Vector (a^T, a^{*T}) contain normally distributed additive genetic effects

$$\begin{pmatrix} \mathbf{a} \\ \mathbf{a}* \end{pmatrix} \mid \mathbf{G} \quad N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \mathbf{G} \otimes \mathbf{A}\right), \text{Where } \mathbf{G} = \begin{pmatrix} \begin{bmatrix} \sigma^2_a & \rho\sigma_a\sigma_{a^*} \\ \rho\sigma_a\sigma_{a^*} & \sigma^2_{a^*} \end{bmatrix} \end{pmatrix}$$

A is the additive relationship matrix, ρ is the coefficient of genetic correlation, and (σ^2_a, $\sigma^2_{a^*}$) are additive genetic variances associated with the distribution of (a, a^*). Briefly, a priori, b, b* were assigned normal distributions with zero mean vector and diagonal matrix with very large diagonal elements. The variance parameters σ^2_a, $\sigma^2_{a^*}$, σ^2_p, $\sigma^2_{p^*}$ were assigned scaled inverted chi-squared distributions (ν=4 and S=0.45) and ρ was assigned a uniform prior bounded between -1 and 1. The

implementation was based on the MCMC (Markov chain Monte Carlo) algorithm proposed by Sorensen and Waagepetersen (2003). The results reported from each model are based on MCMC runs consisting of 1000000 iterations. Convergence was tested using the Z criterion of Geweke (Sorensen and Gianola, 2002) and Monte Carlo sampling errors were computed using time-series procedures described in Geyer (1992).

Model Checking and Model Comparison

Three approaches were used to question the validity of the models. First, a version of model checking is presented, based on the regression of the average sampling variance of records within individuals, on mean phenotypic values. Second, the deviance information criterion (DIC) provides a comparison of the global quality of two or more models, accounting for model complexity (Spiegelhalter *et al*., 2002). Finally, cross validation based on CPOs (Gelfand *et al*., 1996) provides a more detailed inspection disclosing which specific data points are better fitted by the models. In addition, the set of CPOs contain the same information about model performance as the Bayes factor (Besag, 1974) (when the latter exists), and in this way, it provides also a measure of the models' overall quality.

RESULTS AND DISCUSSION

Variance components

Table 1 shows Monte Carlo estimates of posterior means and of 95% posterior intervals for variance components derived from Model 1 and Model 2. The additive variance σ^2_a is a little higher and the permanent environmental variance σ^2_p a little lower in the case of Model 2. The posterior mean of the correlation coefficient is -0.74. In perfect agreement with the results of Ibanez-Escriche *et al.* (2008) in non ovariectomized does. The Monte Carlo estimate of the 95% posterior interval indicates that the support of the posterior distribution is shifted a long way from zero. Moreover, the posterior means for σ^2_{a*} and σ^2_{p*} were similar and their 95% posterior intervals did not include the zero.

Table 1: Monte Carlo estimates of posterior means (first row for each model) and of 95% highest posterior density intervals (second row for each model) of variance components. σ^2_a (σ^2_{a*}): additive variance at the level of the mean (variance); σ^2_p (σ^2_{p*}): permanent environmental variance at the level of the mean (variance); ρ: genetic correlation

Model	σ^2_a	σ^2_p	ρ	σ^2_{a*}	σ^2_{p*}
1	0.59	0.51	-	-	-
	0.32;0.86	0.28;0.8	-	-	-
2	0.82	0.44	-0.74	0.16	0.12
	0.48;1.28	0.20;0.72	-0.90;0.52	0.10;0.25	0.07;0.18

Model checking and model comparison

The 929 females with records were sorted according to their mean uterine capacity (across parities) and divided into 11 groups of approximately 85 individuals. Mean uterine capacity and average variance of records (parities) within individuals was computed for each group. In order to visually explorer a possible association between mean and variance, the average group variances were plotted against the group averages (Figure 1). Also, a linear regression was fitted and the estimate is - 0:23 (standard error 0.07), indicating that as uterine capacity increases, the variation among records within an individual decreases.

Figure 2 (left) shows the difference in CPO's between Model 2 and Model, where the CPO's are sorted from the smallest to the largest for the 2996 records. For approximately 2/3 of the data there is very little difference in the CPO's for both models. However, for the remaining 1/3 of the data, Model 2 shows a better fit. Figure 2 (right) shows which points are best fitted by Model 2. The data are ordered from the smallest to the largest value of uterine capacity. There is wide overlap for both models, with the exception of observations in the center of the distribution, where Model 2 results in a better fit than Model 1.

The Monte Carlo estimates of the DICs for Model 1, and 2 are 7810, and 7719 respectively. Based on 10 replicates, the respective Monte Carlo standard deviations are 10.50, and 0.27, respectively. This analysis favours Model 2, followed by Model 1

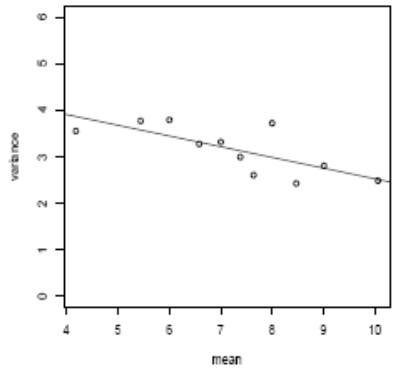

Figure 1: Association between group average sampling variances between uterine capacity records across parities within individuals, versus group mean uterine capacity (averaged over parities)

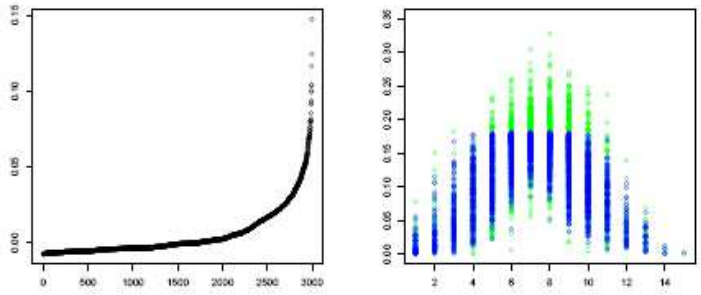

Figure 2: Left: Difference in conditional posterior ordinates (CPO's) between Model 2 and Model 1, sorted, from smallest to largest difference. Right: CPO's from Model 1 (dark points) and Model 2 (light points) plotted against uterine capacity

CONCLUSIONS

In the present work two models were compared using various criteria and the results of this exercise favour Model 2. The association between the variance between records within individuals and uterine capacity in Figure 1 suggest an association between environmental variation and additive genetic values affecting mean uterine capacity. This was further supported by fitting Model 2 from which the posterior distribution of the correlation coefficient ρ was obtained. The mean of this posterior distribution was -0.74 and the support was shifted a long way from the value of zero (see Table 1). Further, the Monte Carlo estimate of the 95% posterior interval of the additive genetic variance associated with the environmental variance was (0.10, 0.25) and the support is comfortably away from extremely small values in the vicinity of zero.

The deviance information criterion favours Model 2 relative to the other model. This agrees well with the analysis based on the conditional predictive ordinates. For two thirds of the data, the CPO's are hardly distinguishable, but for the remaining third, the CPO's favour Model 2.

The results of the analyses reported would indicate that the environmental variance of uterine capacity is partly controlled by additive genes. Besides, there is a high negative association between the additive genes affecting the mean and those affecting environmental variance for uterine capacity. From a breeding

perspective, it is interesting due to this open the possibility of reducing the environmental variance of uterine capacity and increasing his mean by means of selection.

ACKNOWLEDGEMENTS

The help provided by Rasmus Waagepetersen, Maria Jose Argente y Maria Antonia Santacreu in preparing this paper and comments made are gratefully acknowledged.

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