Methods and Techniques for Variance Component Estimation in Animal Breeding[a] - Review -

C. Lee*
Lab of Statistical Genetics, Institute of Environment & Life Science, Hallym University, Chuncheon 200-702, Korea

ABSTRACT : In the class of models which include random effects, the variance component estimates are important to obtain accurate predictors and estimators. Variance component estimation is straightforward for balanced data but not for unbalanced data. Since orthogonality among factors is absent in unbalanced data, various methods for variance component estimation are available. REML estimation is the most widely used method in animal breeding because of its attractive statistical properties. Recently, Bayesian approach became feasible through Markov Chain Monte Carlo methods with increasingly powerful computers. Furthermore, advances in variance component estimation with complicated models such as generalized linear mixed models enabled animal breeders to analyze non-normal data. (*Asian-Aus. J. Anim. Sci. 2000. Vol. 13, No. 3 : 413-422*)

Key Words : Generalized Linear Mixed Model, Gibbs Sampling, Likelihood, Markov Chain Monte Carlo, Posterior, REML

INTRODUCTION

Mixed models have been extensively used in Animal Breeding applications. In the class of models, the prediction of random effects that include breeding values assumes known variances. However, we do not know the variances in field data and should estimate variance components. Therefore, accurate prediction of breeding values depends on accurate variance component estimation. Many animal breeders have made efforts to develop a variety of statistical approaches and computing algorithms for variance component estimation.

This paper reviewed essential landmark research on variance component estimation in animal breeding. Many references on sophisticated mathematical statistics were given for the purpose of understanding basic ideas, but some of them are complicated to deal with. This paper gives a brief description about solving fixed and random effects under the assumption of known variances. Also, the current review deals with the development of various methods to estimate variance components. A variety of methods: analysis of variance (ANOVA)-based methods, minimum variance quadratic unbiased estimation (MIVQUE), likelihood-based methods, Gibbs sampling, method R, and the methods with nonlinear models, are discussed.

FUNDAMENTALS

This section gives a description of fundamental ideas on mixed models. A general form of the mixed models and Hendersons mixed model equations (MME) are presented. For more details, see the text by Henderson (1984) and its supplement by Searle (1998).

Mixed linear models

A general formulation of mixed linear models is:

$$y=X\beta+Zu+e \qquad (1)$$

where y is the vector of n observations, β is the vector of unknown fixed effects, u is the vector of unknown random effects, and e is the vector of residuals. The X and Z are the known design matrices for the fixed and random effects, respectively. The first and second moments of the random variables are defined as:

$$E\begin{bmatrix} y \\ u \\ e \end{bmatrix}=\begin{bmatrix} X\beta \\ 0 \\ 0 \end{bmatrix},\quad Var\begin{bmatrix} y \\ u \\ e \end{bmatrix}=\begin{bmatrix} V & ZG & R \\ ZG' & G & 0 \\ R & 0 & R \end{bmatrix} \qquad (2)$$

where $V=ZGZ'+R$. In animal breeding applications with a single trait model where the random vector u includes only additive genetic effects, the variances of random variables are simply expressed as $G=A\sigma_a^2$ and $R=I\sigma_e^2$ where A is the numerator relationship matrix, σ_a^2 is the additive genetic variance, σ_e^2 is the residual variance.

Estimation of fixed and random effects

In order to estimate the fixed and random effects, the following Henderson's MME are utilized (Henderson, 1973).

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z+G^{-1} \end{bmatrix}\begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix}=\begin{bmatrix} X' & R^{-1} & y \\ Z' & R^{-1} & y \end{bmatrix} \qquad (3)$$

Under the assumption of known (co)variances, the

* Address reprint request to C. Lee. Tel: +82-261-240-1974, Fax: +82-361-241-3422, E-mail: clee@sun.hallym.ac.kr.

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solutions obtained from the MME are best linear unbiased predictor (BLUP) respectively for $\hat{\beta}$ and $\hat{u}$ (Henderson et al., 1959; Henderson, 1963). If $G=A\sigma_u^2$ and $R=I\sigma_e^2$, their inverses can be easily calculated since Henderson (1976) and Quaas (1976) developed efficient algorithms to directly calculate the inverted numerator relationship matrix, A^{-1}. Since the size of the coefficient matrix is often huge in animal breeding, the solutions cannot be obtained by direct inversion of the coefficient matrix. Then the MME are solved by Jacobi and Gauss-Seidel iteration (Golub and Van Loan, 1983; Misztal and Gianola, 1987).

A BRIEF DESCRIPTION OF TRADITIONALLY IMPORTANT METHODS

As previously addressed, the variances in practice are not known, and variance components should be estimated from field data. This section presents a brief review of important methods of variance component estimation prior to likelihood-based estimation. For more details, see Searle et al. (1992).

Analysis of variance-based methods

Estimation of variance has been developed from Fisher's (1925) ANOVA table which summarizes a partitioning of observed variability. The principle of ANOVA method is to equate ANOVA sums of squares to their expected values which are linear functions of the variance components. Those expected values must be such as to not include functions of fixed effects. Variance components are estimated by solving a system of equations. For balanced data, ANOVA estimators are best quadratic unbiased estimators and they are reduced to best unbiased estimators under normality. For unbalanced data, uniformly best variance component estimators do not exist. Henderson (1953) developed three different sets of quadratic forms by adapting the ANOVA method for unbalanced data (Later, Henderson developed method IV which was more closely related to the quadratics used in MIVQUE, so often called Diagonal MIVQUE). Henderson's Method I uses quadratics that are analogous to the sums of squares from balanced data and is applicable to random models in which X $\beta=1\mu$. Henderson's Method II is a translation invariant procedure which adjusts the data for fixed effects and then uses a variant of Method I. Henderson's Method III is the fitting constants method which uses the reductions in sums of squares due to fitting one model and its submodels. This method is not unique in specifying reductions in sums of squares. The method III is applicable to mixed models. For sampling variances of the estimators from the three methods, closed form expressions are possible, but they would be very complicated; no one has derived them.

Variance components estimated by ANOVA-based methods are not necessarily nonnegative, which is a fatal property for researchers to avoid. A great merit of the ANOVA-based methods is unbiasedness of their estimates. However, covariance structure created from genetic relationships in a population under selection led variance component estimates to be biased (Sorenson and Kennedy, 1984).

Minimum variance (or norm) quadratic unbiased estimation

Another method to estimate variance components was developed with desirable properties of unbiasedness and minimum variance. It is called the minimum variance quadratic unbiased estimation (MIVQUE). The MIVQUE assumes normality. On the other hand, in minimum norm quadratic unbiased estimation (MINQUE) a known Euclidean norm is minimized instead of the unknown variance. The MINQUE does not require the normality assumption and reduces to MIVQUE under normality. For details of the both methods, see the series of articles by LaMotte (1970, 1973) and Rao (1970, 1971a, b, 1972). The articles may be elegant from theoretical point of view, but lacking in applying the methods to real data. Solving MIVQUE/MINQUE equations requires no iteration. However, solutions to the equations depend on the choice of the pre-assigned estimates of the variance components, and furthermore needing the estimates makes MINQUE useless. The MIVQUE/MINQUE equations are similar to those for restricted maximum likelihood (REML). Hocking and Kutner (1975) observed that MINQUE equals to a first iterate of REML. In practice, it is often suggested to solve the MINQUE/MIVQUE equations repeatedly up to convergence. Harville (1977) found that the estimates at the convergence equal to REML solutions. Therefore, if the solutions are within the parameter spaces, they are equivalent to REML estimates.

In animal breeding applications with a single trait model where u includes only additive genetic effects, Sorenson and Kennedy (1984) and Van Tassell et al. (1995) obtained MIVQUE of the genetic and residual variances by deriving the following equation:

$$\begin{bmatrix} \hat{\sigma}_u^2 \\ \hat{\sigma}_e^2 \end{bmatrix} = \begin{bmatrix} tr(C_{11}A^{-1}C_{11}WZAZ'W) & tr(C_{12}A^{-1}C_{12}'WW) \\ tr(ZAZ') - tr(CWZAZ'W) & n - tr(CWW) \end{bmatrix} \begin{bmatrix} Q_1 \\ Q_2 \end{bmatrix} \quad (4)$$

where C is the inverse of the coefficient matrix in MME, $C=[C_{11}\ C_{12}]$, $W=[X\ \ Z]$, $Q_1=\hat{u}'A^{-1}u$, and $Q_2=y'y-y'WCW'y$. Sorenson and Kennedy (1984) and Van Tassell et al. (1995) reported that the MIVQUE of

variance components were biased and their mean squared errors were large.

LIKELIHOOD-BASED METHODS

This section gives procedures for using likelihood functions. For details, see Quaas (1991) and Searle et al. (1992). Nowadays REML estimation is considered as a standard method to estimate variance components with mixed models.

Maximum likelihood

Hartley and Rao (1967) developed maximum likelihood (ML) procedure to the estimation of variance components. Assuming that $y \sim N(X\beta, V)$, the log likelihood function of y is:

$$l_{\beta,\sigma^2|y} \propto -.5\log|V| - .5(y-X\beta)'V^{-1}(y-X\beta). \quad (5)$$

Equating the derivatives of this function with respect to variance components to zero gives ML estimates of the variance components if the solutions from the equations are in the parameter space. This is because the likelihood function must be maximized within the parameter space. So, if the ML estimate is the boundary value of the parameter space, then the likelihood is likely to differ from zero at the maximum. For details, see Henderson (1973), Laird (1982), and Searle et al. (1992). Especially, Laird (1982) and Searle et al. (1992) presented expectation-maximization (EM) algorithms. The ML estimator has attractive features of large sample properties (Hartley and Rao, 1967). First, the estimators are asymptotically unbiased. Second, the asymptotic dispersion matrix of the estimators is available. It is expressed as the inverse of Fishers information matrix. The dispersion matrix is a function of the unknown variance components. It can be calculated if those components are replaced by their corresponding estimates. Then it is an estimated dispersion matrix. Third, the dispersion matrix of the estimators asymptotically achieves the Cramer-Rao lower bound for the dispersion matrix of unbiased estimators. That is, the estimators have the property of asymptotic efficiency (Mood et al., 1974; Casella and Berger, 1990).

In animal breeding applications, the empirical variance component estimates did not differ from their corresponding input values in the simulation study of Rothschild et al. (1979). The ML estimators have almost the same statistical properties as REML regardless of merit or demerit. However, ML does not take account of the degrees of freedom which are involved in estimating fixed effects, while REML overcomes the problem. Only this difference has led researchers to prefer REML to ML, especially in animal breeding analyses where the number of levels for fixed effects are usually large.

Restricted maximum likelihood

Patterson and Thompson (1971) derived restricted maximum likelihood to estimate variance components. In order to account for the loss in degrees of freedom on estimating fixed effects, the method uses restricted likelihood where estimates of the fixed effects are adjusted, i.e. linearly independent error contrasts $\boldsymbol{K'y}$, where $\boldsymbol{K'X = 0}$ and $\boldsymbol{K'}$ has full row rank, are used instead of $\boldsymbol{y}$. This method led the variance component estimators to be invariant to constraints to get estimates of the fixed effects. The likelihood of $\boldsymbol{K'y}$ with $\boldsymbol{K'y \sim N(0,K'VK)}$ is as follows:

$$l_{\sigma^2|K'y}(=l_R) \propto -.5\log|K'VK| - .5y'K(K'VK)^{-1}K'y \quad (6)$$

In fact, maximizing the restricted likelihood does not require knowing reference to the matrix of the error contrasts (K), and the likelihood function is expressed as follows (Harville, 1977):

$$l_R \propto -.5\{\log|V| + \log|X'V^{-1}X| + (y-X\hat{\beta})'V^{-1}(y-X\hat{\beta})\}. \quad (7)$$

Harville (1977) and Searle (1979) developed another equivalent form:

$$l_R \propto -.5\{\log|R| + \log|G| + |C| + y'Py\} \quad (8)$$

where $P=V^{-1}-V^{-1}X(X'V^{-1}X)^{-1}X'V^{-1}$. As in ML, REML estimates must be in the parameter space. In addition to the attractive large sample properties shown in ML, the REML estimators are likely to have the property of unbiasedness if the values which maximize the likelihood are in the parameter space when considering that, for balanced data, the solutions to REML equations are equivalent to those from ANOVA (Patterson and Thompson, 1974; Corbeil and Searle, 1976; Searle et al., 1992). In animal breeding, a number of simulation studies showed that input values of the variance components were obtained by REML regardless of selection (e.g., Jensen and Mao, 1991; Lee and Pollak, 1997a; Schenkel and Schaeffer, 1998). However, note that parent misidentification or splitting data cannot explain the selection. Random deletion or misidentification of parent identifications in selected populations results in significant differences between variance component estimates and their corresponding input values. Thus correct and complete pedigree information is important (Lee and Pollak, 1997b; Kennedy and Sorenson 1988; Schaeffer et al. 1998). Partitioning data by gender and analyzing only male (or female) data did not account for selection on

females (males), and variance component estimates differed from their input values (Lee and Pollak, 1997a).

Since the likelihood functions (6), (7), and (8) are highly nonlinear, there are no closed form solutions for variance components. Development of computing algorithms for REML estimation of variance components has been a nontrivial task and a great concern (Harville, 1977; Harville and Callanan, 1990; Searle et al., 1992). Various maximization methods are available, and these methods are typically divided into the three types: 1) methods using first and second derivatives of the likelihood, 2) methods using only first derivative, and 3) derivative free methods.

The standard method to maximize the likelihood is to use its first and second derivatives with respect to variance components (Patterson and Thompson, 1971; Thompson, 1973; Meyer, 1983; Searle et al., 1992). The representative gradient methods may be Newton-Raphson method and Fisher scoring (Press et al., 1992; Searle et al., 1992). Searle et al. (1992) described a general form of the various gradient methods to determine the search direction for the next step of iteration. The parameters are iteratively calculated as following:

$$\sigma^{2(r-1)} = \sigma^{2(r)} + s^{(r)} M^{(r)} \frac{\partial l_R}{\partial \sigma^2}\Big|_{\sigma^{2(r)}}. \qquad (9)$$

where M is the multiplier matrix which modifies the step direction, and s is the scalar which modifies the step size. For the Newton-Raphson method, s=1 and M=the negative inversed Hessian matrix. For the Fisher Scoring method, s=1 and M=the negative inversed expected information matrix. Replacing the Hessian matrix in the Newton-Raphson algorithm by an approximation leads to a quasi-Newton method which does not require second derivatives. For details on quasi-Newton methods, see Kennedy and Gentle (1980). Johnson and Thompson (1995) proposed average information method with s=1 and M=AI,

$$AI(\sigma_i^2, \sigma_j^2) = .5\left\{ -\frac{\partial^2 l_R}{\partial \sigma_i^2 \partial \sigma_j^2} + E\left(-\frac{\partial^{2\partial^2} l_R}{\partial \sigma_i^2 \partial \sigma_j^2}\right)\right\}$$

$$= y' P \frac{\partial V}{\partial \sigma_i^2} P \frac{\partial V}{\partial \sigma_j^2} Py \,, \qquad (10)$$

by adding the following second derivative of the log likelihood and its expected value:

$$\frac{\partial^2 l_R}{\partial \sigma_i^2 \partial \sigma_j^2} = .5tr\left\{ P\frac{\partial V}{\partial \sigma_i^2} P\frac{\partial V}{\partial \sigma_j^2}\right\} - y' P\frac{\partial V}{\partial \sigma_i^2} P\frac{\partial V}{\partial \sigma_j^2} Py \qquad (11)$$

$$-E\left\{\frac{\partial^2 l_R}{\partial \sigma_i^2 \partial \sigma_j^2}\right\} = .5tr\left\{ P\frac{\partial V}{\partial \sigma_i^2} P\frac{\partial V}{\partial \sigma_j^2}\right\} \qquad (12)$$

where computation of the trace terms are much more complex than in first derivative of (13) below. For derivation of (11) and (12), see Searle et al. (1992). In order to solve the problems on convergence or on parameter boundary condition, the s and M can be replaced by other values (Meyer and Smith, 1996). For convergence problems, see Searle et al. (1992), Johnson and Thompson (1995), Gilmour et al. (1995), and Meyer and Smith (1996).

In order to reduce computational burdens, methods without second derivative were developed. First partial derivative of the restricted likelihood with respect to a variance component is shown below (Searle et al. 1992):

$$\frac{\partial l_R}{\partial \sigma_i^2} = -.5tr(P\frac{\partial V}{\partial \sigma_i^2}) + .5y' P\frac{\partial V}{\partial \sigma_i^2} Py \qquad (13)$$

Equating the sets of derivative (9) to zeros leads to a simple REML algorithm (Harville, 1977; Searle, 1979). The estimates of genetic and environmental variances can be obtained using various methods such as the EM algorithm (Dempster et al., 1977; Searle et al., 1992), the successive approximations (Henderson, 1984), or the Broyden, Fletcher, Goldfarb, Shannos (BFGS) algorithm (for example, see Robinson (1988)). The most commonly used method is the EM algorithm, but there is no unique EM algorithm. The following equations can be used for the iteration in the algorithm:

$$\hat{\sigma}_a^{2\,(r+1)} = [\,\hat{u}'^{(r)} A^{-1} \hat{u}^{(r)} + tr(A^{-1} C^{22(r)})]/n_a \qquad (14)$$
$$\hat{\sigma}_e^{2\,(r+1)} = y'(y - X\,\hat{\beta}^{(r)} - Z\,\hat{u}^{(r)})/(n - r_X)$$

where generalized inverse of the coefficient matrix in MME is equal to:

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ ZR^{-1}X & ZR^{-1}Z + G^{-1} \end{bmatrix}^{-} = C^{-} = \begin{bmatrix} C^{11} & C^{12} \\ C^{21} & C^{22} \end{bmatrix}, \qquad (15)$$

and $\mathbf{n}_a$ is the number of levels of random effect. The inverse is approximated by many methods. Yet, recently various Monte Carlo methods received most attention (Garcia-Cortes et al., 1992, 1995; Guo and Thompson, 1994; Groeneveld and Garcia-Cortes, 1998). The EM algorithm accommodates the boundary conditions on the REML parameter estimates while many other methods may lead to nonpositive definite covariance matrices. For details on the methods for getting constrained estimates, see Harville (1977). In the EM algorithm, convergence rate is slow. In order to overcome the problem, acceleration methods (Laird et al., 1987; Mantysaari and Van Vleck, 1989; Misztal et al., 1992) or reparameterizations (Thompson and Meyer, 1986) are incorporated. For more details on

EM algorithm, see Quaas (1991) and Searle et al. (1992).

The final category to maximize the restricted likelihood does not require any derivatives, so called derivative free REML (Smith and Graser, 1986; Graser et al., 1987). It requires much longer times to compute the likelihood than the other methods to search for its maximum directly. In the log restricted likelihood (8), the computationally demanding terms are $\log|C|$ and $y'Py$ which can be obtained by Gaussian elimination (Smith and Graser, 1986). Meyer (1988, 1989 and 1991) incorporated the method and simplex method (Nelder and Mead, 1965) into her masterpiece program, DFREML, in which variance components can be estimated with various animal models. Boldman and Van Vleck (1991) computed $\log|C|$ and $y'Py$ using Choleski factorization with sparse matrix routines in SPARSPAK of George et al. (1980). Boldman et al. (1995) incorporated the method and simplex method into a package program, MTDFREML. For details on the simplex method or other methods for direct research of the maximum of the restricted likelihood, see Press et al. (1992) and Boldman et al. (1995). The derivative free approach costs less computing time than the EM approach for the small number of parameters, but more for the large number (Misztal, 1994; Johnson and Thompson, 1995).

GIBBS SAMPLING

Harville (1977) gave a review on Bayesian inference for variance components, and Gianola and Fernando (1986) brought Bayesian methods to animal breeding. In the Bayesian approach, many methods are used for marginalization of the joint posterior density of variance components. In general, marginal posterior densities were approximated (e.g. Laplaces method (Tierney and Kadane (1986)) except for analytical integration with simple univariate models (Gianola et al., 1990). Dramatic development became feasible with a numerical method called Markov chain Monte Carlo (MCMC) procedures such as the Metropolis-Hastings algorithm (Metropolis et al., 1953; Hastings, 1970) and Gibbs sampling (Geman and Geman, 1984; Gelfand and Smith, 1990; Gelfand et al., 1990; Casella and George, 1990; Tanner, 1996). The MCMC is not restricted in only Bayesian inference, and might be applied to likelihood inference if analytic procedures are not available. For example, see Geyer and Thompson (1992) and Guo and Thompson (1994).

Full conditional posterior densities have been derived for the application of Gibbs sampling to animal breeding by many researchers: Wang et al. (1993) for sire models, Lee and Pollak (1995) for sire-maternal grandsire models, Wang et al. (1994) and Van Tassell et al. (1995) for animal models, Jensen et al. (1994) for maternal effect models, Van Tassell and Van Vleck (1996) for multivariate models, Sorenson et al. (1995) for threshold models, and Thaller and Hoeschele (1996a, 1996b) for linkage analyses. In this section, Bayesian inferences for variance components and a Gibbs sampling procedure are briefly described in a simple animal breeding context. For details on Bayesian and MCMC, see Bernardo and Smith (1994), Tanner (1996), Gilks et al. (1996), and Lehmann and Casella (1996).

Bayesian inference using Gibbs sampler

The joint posterior density of unknowns in mixed models are formulated as:

$$p(\beta, u, \sigma^2 \mid y) \propto p(y \mid \beta, u, \sigma^2) \times p(\beta, u, \sigma^2) \qquad (16)$$

which consists of the likelihood and the joint prior density. For the latter, β, u and σ^2 are assumed to have Uniform, Normal, and inverted Gamma distributions respectively. Personal beliefs are included in the prior information, but improper prior leads improper posterior (Hobert and Casella, 1996). Inference about variance component is based on the marginal posterior density:

$$p(\sigma^2|y) = \int_{\beta, u} p(\beta, u, \sigma^2|y) d\beta\, du. \qquad (17)$$

Bayesian inference overcomes the problem on non-BLUP of breeding values when using REML variance component estimates. Bayesian approach always gives exact posterior densities of variance components while REML estimates have unknown distributions for small data sets (Gianola and Fernando, 1986). The optimum Bayes decision rule under quadratic loss is the posterior mean rather than the posterior mode. REML estimates are joint modes of all variance components rather than marginal modes which give a better approximation of the posterior mean (Gianola and Foulley, 1990).

The Gibbs sampler is a method of numerical integration that iteratively generates samples from the full conditional densities of all the unknowns as shown below:

1) set initial values for β, u, σ_a^2 and σ_e^2;
2) generate β and update β;
3) generate u and update u;
4) generate σ_a^2 and update σ_a^2;
5) generate σ_e^2 and update σ_e^2;
6) repeat from 2) to 5) many times.

The samples obtained during the burn-in period where Gibbs sampling chain has not yet reached the

equilibrium distribution are discarded. The samples during post burn-in period are kept only every k iterations to reduce the correlation between consecutive samples. Parameters with slow mixing (high lag correlation) may lead to convergence problems (Wang et al., 1993; Sorenson et al, 1995; Thaller and Hoeschele, 1996a, 1996b; Wang et al., 1997). Therefore, cautions are needed for determining burn-in period and for calculating lag correlation (Raftery and Lewis, 1992; Gelman and Rubin, 1992; Cowles and Carlin, 1996). The tool for determining burn-in period is often called convergence diagnostics. One of the convergence diagnostics is to monitor an arbitrary function of the Monte Carlo output. However, the method can mislead since the convergence of monitored function does not guarantee convergence of other unmonitored functions. Another convergence diagnostics is to run multiple chains. Each chain may be converged, but comparing the multiple chains may show clear differences in the apparent stationary distributions. However, computing costs too much.

As a point estimate, the posterior mean estimate of variance component can be calculated based on the expected value of inverted Gamma variables:

$$E(\sigma_a^2|SSA)=\frac{\frac{SSA}{2}+\frac{1}{\gamma_a}}{\frac{n_a}{2}+\nu_a-1} \quad \text{and}$$

$$E(\sigma_e^2|SSE)=\frac{\frac{SSE}{2}+\frac{1}{\gamma_e}}{\frac{n}{2}+\nu_e-1} \qquad (18)$$

where $\nu_a(\nu_e)$ is the scale parameter of inverted Gamma distribution for $\sigma_a^2(\sigma_e^2)$, $\gamma_a(\gamma_e)$ is the shape parameter of inverted Gamma distribution for $\sigma_a^2(\sigma_e^2)$, $SAA = u'A^{-1}u$, and $SEE=(y-X\beta-Zu)'(y-X\beta-Zu)$. Computing packages are available for Gibbs sampling algorithm: MTGSAM by Van Tassell and Van Vleck (1996) and VCE by Groeneveld and Garcia-Cortes (1998). Gibbs sampling is an increasingly useful tool for variance component estimation not only with mixed models but also with beyond mixed models such as threshold models of Gianola and Foulley (1983) and Harville and Mee (1984), survival models of Smith and Quaas (1984) and Ducrocq et al. (1988), major gene models of Hoeschele (1988), and Bernoulli and Poisson models of Foulley et al. (1987).

METHOD R

Reverter et al. (1994) developed Method R as an algorithm to estimate variance components without inversion of the coefficient matrix or its approximation. In the method R, the regression coefficient is defined as:

$$R_c=\frac{\hat{u}'_j A^{-1}\hat{u}_j}{\hat{u}'_{j'}A^{-1}\hat{u}_j} \qquad (19)$$

where $\hat{u}_j$ and $\hat{u}_{j'}$ are the predictors in the analysis j and j' (j<j'). If the regression coefficient is not equal to 1, variance components are over- or underestimated. Iteration strategies allow the estimates to be converged (Reverter et al., 1994). Although robust statistical theory to assess the properties of Method R estimates is not yet available, they are empirically unbiased (Reverter et al., 1994) and the confidence intervals for heritability are reliable (Mallinckrodt et al., 1997).

VARIANCE COMPONENT ESTIMATION WITH NONLINEAR MODELS

Mixed models were combined with Nelder and Wedderburns (1972) generalized linear models (GLM) where observations have the distributions of exponential families, and systematic effects are monotonically linked to the mean. The combined models are called generalized linear mixed models (GLMM) and have the combined properties of both. This class of models includes various models developed in animal breeding. For example, threshold mixed models (Gianola and Foulley, 1983; Harville and Mee, 1984), survival mixed models (Smith and Quaas, 1984; Ducrocq et al., 1988), and Bernoulli and Poisson mixed models (Foulley et al., 1987) can be categorized as GLMM. This section briefly gives a frequentist approach for variance component estimation with GLMM. For details on GLM and GLMM, see McCullagh and Nelder (1989) and Breslow and Clayton (1993) respectively.

Generalized linear mixed models

A general formulation of GLMM can be expressed as a two-stage hierarchical model. In the first stage, the conditional density for given u has a distribution of the exponential family:

$$f_{y|u}(y|u,\beta,\phi)=\exp\left\{\frac{y\eta'_i-b(\eta'_i)}{a(\phi)}+c(y,\phi)\right\} \qquad (20)$$

where a, b, c are known functions and ϕ is a vector of dispersion parameters. The canonical parameter (η) is

$$\eta'_i=x'_i\beta+z'_i u \qquad (21)$$

where x'_i is the i^{th} row of X, and z'_i is the i^{th} row of Z. In the second stage, the density function for u is assumed as $u \sim N(0,G)$. In this class of models, the

likelihood,

$$L(\phi, G|y) = \int \int \prod_{i=1}^{n} f_{y_i|u}(y|u, \beta, \phi) f_u(u|G) d\beta du \quad (22)$$

is hardly obtained in closed form due to high dimensional integrals. Various methods were suggested to avoid the problem. As an example, maximum adjusted profile hierarchical likelihood estimation (MAPHLE), which does not require approximations, is presented. For details on other methods, see Breslow and Clayton (1993) for penalized quasi-likelihood, McCulloch (1994) for simulation-based method, Tempelman and Gianola (1993) for Laplace approximation, and Sorenson et al. (1995) for Gibbs sampling.

Maximum adjusted profile hierarchical likelihood estimation

The hierarchical likelihood is defined as addition of logarithms of the density functions,

$f_{y|u}(y|u, \beta, \phi)$ and $f_u(u|G)$, in the two stages above:

$$l_h = l(\eta', \phi|y|u) + l(G|u).$$

Adjusted profile hierarchical likelihood is defined as (Cox and Reid, 1987; Lee and Nelder, 1996):

$$l_{ap|h} = l_h + .5 \log\{det(2\pi\phi H^{-1})\}|_{\beta=\hat{\beta}, u=u}$$

where H is the expected Hessian matrix,

$$H = \begin{pmatrix} X'WX & X'WZ \\ Z'WX & Z'WZ + U \end{pmatrix},$$

W is the GLM weight function (McCullagh and Nelder, 1989), and $U = -\phi\{\partial^2 l(G|u)/\partial ui\, \partial uj\}$. Lee (1998) developed MAPHLE for Poisson GLMM in animal breeding. The Newton-Raphson method was applied to maximizing the likelihood. The MAPHLE is an expansion of REML to nonlinear models. The MAPHLE is justified by method of moments.

CLOSING REMARKS

Intensive computing (e.g., for Gibbs sampling) became feasible through availability of powerful computers, and advances in the efficiency of computing algorithms made possible the increasingly complex models, e.g., GLMM presented in the previous section, log-linear structural models of San Cristobal et al. (1993), models with non-normal random effects (Lee and Lee, 1998), and multistage hierarchical models. Computing time can be reduced not only by determining an efficient variance component estimation method but also by using various techniques such as sparse matrix routines (SPARSPAK of George et al. (1980) and FSPAK of Misztal (1990)), reduced animal models (Quaas and Pollak, 1980), transformation especially in multiple trait analysis (Jensen and Mao, 1988; Misztal et al., 1995; Ducrocq and Chapuis, 1997), and reparameterization (Thompson and Meyer, 1986; Harville and Callanan, 1990; Groeneveld, 1994). Further impressive progress on efficient computing algorithms is important for estimation of variance components with computationally demanding methods.

However, cautions with the methods should be stressed. For the Bayesian approach, many animal breeders used flat priors for variance components because the mode of the marginal posterior density with the priors corresponds to REML estimator (Harville, 1977). However, theoretically improper posterior is obtained (Hobert and Casella, 1996). As discussed earlier, care on the convergence of Gibbs sampling chain is also needed. For the class of GLMM, the joint maximization of the likelihood led to lack of the two desirable statistical properties: consistency and invariance (McCulloch and Feng, 1996).

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