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MM ALGORITHMS FOR VARIANCE COMPONENT ESTIMATION AND SELECTION IN LOGISTIC LINEAR MIXED MODEL

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Abstract: Logistic linear mixed model is widely used in experimental designs and genetic analysis with binary traits. Motivated by modern applications, we consider the case with many groups of random effects and each group corresponds to a variance component. When the number of variance components is large, fitting the logistic linear mixed model is challenging. We develop two efficient and stable minorization-maximization (MM) algorithms for the estimation of variance components based on the Laplace approximation of the logistic model. One of them leads to a simple iterative soft-thresholding algorithm for variance component selection using maximum penalized approximated likelihood. We demonstrate the variance component estimation and selection performance of our algorithms by simulation studies and a real data analysis.

Key words and phrases: Generalized linear mixed model (GLMM), Laplace approximation, MM algorithm, variance components selection

1. Introduction

Generalized linear mixed model (GLMM) is an extension of generalized

linear model to incorporate random effects accounting for heterogeneity among responses (McCulloch and Neuhaus, 2001; Stroup, 2012). It is widely used in clustered, longitudinal, and panel data analysis (Zeger and Karim, 1991; Breslow and Clayton, 1993). Logistic linear mixed model is one of the GLMMs for binary responses and assumes

$$\begin{aligned} y_j | \eta_j &\sim \text{Bernoulli}(\mu_j) \\ \mu_j &= 1 / \{1 + \exp(-\eta_j)\} \end{aligned} \tag{1.1}$$

for $j = 1, \dots, n$ and $\eta = (\eta_1, \dots, \eta_n)^T$ takes the form

$$\eta = X\beta + Z_1u_1 + \dots + Z_mu_m,$$

where X and $Z = (Z_1, \dots, Z_m)$ are known predictor matrices, β is the coefficient vector for fixed effects, and $u_i \sim N(0_{q_i}, \sigma_i^2 I_{q_i})$ are independent random effects. Because

$$\eta \sim N(X\beta, \sigma_1^2 Z_1 Z_1^T + \dots + \sigma_m^2 Z_m Z_m^T),$$

we call $\sigma_1^2, \dots, \sigma_m^2$ variance components.

Logistic linear mixed model finds applications in agriculture, econometrics, biology and genetics. Two motivating examples are the analysis of variance (ANOVA) for dichotomous responses (Anderson and Aitkin, 1985; Quené and Van den Bergh, 2008) and the quantitative trait loci (QTL) mapping for binary traits (Yi and Xu, 1999; Che and Xu, 2012). In ANOVA, Z_i

corresponds to each factor or their interactions. In modern applications, the number of factors can be large and the number of interaction terms increases quadratically with the number of factors. In QTL mapping, Z_i corresponds to a gene region. The number of genes m is at order of $10^2 \sim 10^3$ in a typical genetic study. In Section 4 and 5, we will discuss further about these two applications as well as associated analysis using our proposed algorithms.

In general direct maximization of the GLMM likelihood function is computationally intractable because it involves potentially high-dimensional integrals. The existing methods involve various forms of approximations. The first class of methods use numerical integration such as Gaussian quadrature (Davidian and Gallant, 1992) and adaptive Gaussian quadrature (Pinheiro and Bates, 1995). These methods are applicable only to low dimensional integrals and thus limited to problems where data form very small independent clusters. The second type of methods invoke the Laplace approximation (Wolfinger, 1993; Shun and McCullagh, 1995) or its variants such as the penalized quasi-likelihood (Breslow and Clayton, 1993) and the integrated nested Laplace approximation (Rue et al., 2009). The third class of methods resort to Monte Carlo methods to approximate either the original integral (Sung and Geyer, 2007) or the E step of EM algorithm (Booth and Hobert, 1999). Pinheiro and Bates (1995) compare and discuss penal-

ized quasi-likelihood (PQL), Laplace approximation, importance sampling, Gaussian quadrature, and adaptive Gaussian quadrature (AGQ). They conclude that Laplace approximation and adaptive Gaussian quadrature give the “best mix of efficiency and accuracy”. In this paper, we propose algorithms based on the Laplace approximation of the log-likelihood function because AGQ is numerically infeasible for the ANOVA and genetic applications we are considering.

Our primary interest is in the estimation and selection of variance components. Researchers have worked on selecting fixed effects in GLMMs (Groll and Tutz, 2014; Schelldorfer et al., 2014). For random effects selection, however, most procedures are developed in the framework of linear mixed models (Bondell et al., 2010; Ahn et al., 2012) for quantitative responses. In contrast only few references discuss random effects selection in GLMM. Ibrahim et al. (2011) develop a simultaneous fixed and random effects selection procedure based on the SCAD and adaptive LASSO penalties using a Monte Carlo EM for general mixed models. Cai and Dunson (2006) propose a method for random effect selection in GLMMs within the Bayesian framework using a stochastic search MCMC algorithm. Pan and Huang (2014) propose a backfitting algorithm to select effective random effects based on penalized quasi-likelihood (PQL) function. However

all the above mentioned papers study the clustered data with repeated measurements on the subjects. They assume n independent subjects with observations $(y_1, X_1, Z_1), \dots, (y_n, X_n, Z_n)$ and

$$E(y_i | X_i, Z_i, b_i) = g(\eta_i) = g(X_i\beta + Z_ib_i), \quad (1.2)$$

where $g(\cdot)$ is some known link function, X_i and Z_i are known matrices and $b_i \sim N_q(0, D)$ is the random effect. Here, D is the unknown covariance matrix shared by the subjects that is to be estimated by maximizing some penalized likelihood. For example, Ibrahim et al. (2011) perform the penalization on the Cholesky decomposition of D , denoted as Γ , such that each row of Γ either are all not zero or all zero and Pan and Huang (2014) penalize on positive elements proportional to the standard deviation of the random effects b_i . In this paper, we propose an algorithm for selection of random effects by shrinking the variances of ineffective random effects towards zero based on penalized likelihood defined in Section 3.3. There are two key differences between our variance components selection and previous work. First, model (1.2) is not the same as model (1.1) we want to address in this paper even though they both can deal with clustered data as well as non-clustered data. Model (1.1) assumes that the random effects $u_i \sim N(0_{q_i}, \sigma_i^2 I_{q_i})$ are independent. If we write model (1.1) in the framework of model (1.2), then the covariance in model (1.1) is diagonal with some

equality constraints on the random effect variances while the covariance in model (1.2) can be any covariance matrix. Second, the random effects selection on model (1.2) is selecting individual random effect while for model (1.1) we are selecting groups of random effects, i.e. the random effects in each u_i are either all selected or not. To the best of our knowledge, there exist no literature about variance components selection for model (1.1).

In this paper, based on the minorization-maximization (MM) principle (Lange et al., 2000), we propose two novel algorithms for variance component estimation under two different parameterizations of logistic linear mixed model and then extend to variance component selection by incorporating penalization. The first parameterization is efficient for estimating parameters without penalty, while the second easily generalizes to penalized estimation. Both algorithms are simple to implement and numerically stable. Our simulation studies and real data analysis demonstrate that the proposed algorithms outperform the commonly used tools and are scalable to high-dimensional problems.

2. Preliminaries

Throughout we reserve Greek letters for parameters and indicate the current iteration number by a superscript t .

2.1. The MM principle

The MM principle (Lange et al., 2000; Hunter and Lange, 2004) for maximizing an objective function $f(\theta)$ involves two M-steps. The first M-step minorizes the objective function $f(\theta)$ by a surrogate function $g(\theta | \theta^{(t)})$ at the current iterate $\theta^{(t)}$. Minorization is a combination of a tangent condition $f(\theta^{(t)}) = g(\theta^{(t)} | \theta^{(t)})$ and a domination condition $f(\theta) \geq g(\theta | \theta^{(t)})$ for $\theta \neq \theta^{(t)}$. The second M-step is defined by the iterates:

$$\theta^{(t+1)} = \arg \max_{\theta} g(\theta | \theta^{(t)}). \quad (2.1)$$

Because

$$f(\theta^{(t+1)}) \geq g(\theta^{(t+1)} | \theta^{(t)}) \geq g(\theta^{(t)} | \theta^{(t)}) = f(\theta^{(t)}), \quad (2.2)$$

the MM iterates satisfy the ascent property, which drives the objective function uphill and makes the MM algorithm remarkably stable.

Our derivation of the MM algorithms for variance components estimation and selection hinges on two minorizations.

2.2. Supporting hyperplane minorization

If $f(\theta)$ is convex and differentiable, then the supporting hyperplane

$$g(\theta) = f(\theta^{(t)}) + \nabla f(\theta^{(t)})^T (\theta - \theta^{(t)}) \quad (2.3)$$

is a minorization function of $f(\theta)$ at $\theta^{(t)}$ (Hunter and Lange, 2004).

For symmetric matrices we write $A \preceq B$ when $B - A$ is positive semidef-

inite. A matrix-valued function f is said to be (matrix) convex if

$$f\{\lambda A + (1 - \lambda)B\} \preceq \lambda f(A) + (1 - \lambda)f(B)$$

for all A, B , and $\lambda \in [0, 1]$. Since the negative log determinant function $f(B) = -\log \det B$ is convex on the set of positive definite matrices (Boyd and Vandenberghe, 2004) and the supporting hyperplane of $f(B)$ is

$$\begin{aligned} g(B) &= f(B^{(t)}) + \nabla f(B^{(t)})^T (B - B^{(t)}) \\ &= -\log \det B^{(t)} - \text{tr} \left\{ (B^{(t)})^{-1} (B - B^{(t)}) \right\}, \end{aligned}$$

the supporting hyperplane minorization described above yields the following inequality

$$-\log \det B \geq -\log \det B^{(t)} - \text{tr} \left\{ (B^{(t)})^{-1} (B - B^{(t)}) \right\}. \quad (2.4)$$

2.3. Quadratic minorization

If a convex function $f(\theta)$ is twice differentiable and there exists a matrix M such that $M \preceq \nabla^2 f(\theta)$ for all θ , then

$$g(\theta) = f(\theta^{(t)}) + \nabla f(\theta^{(t)})^T (\theta - \theta^{(t)}) + \frac{1}{2} (\theta - \theta^{(t)})^T M (\theta - \theta^{(t)}) \quad (2.5)$$

is a minorization function of $f(\theta)$ at $\theta^{(t)}$ (Hunter and Lange, 2004).

3. Algorithms for estimation

3.1. Model formulation 1

The likelihood for model (1.1) is

$$L(\beta, \sigma) = \int \exp\{h(u | \beta, \sigma^2)\} du, \quad (3.1)$$

where $\sigma = (\sigma_1, \dots, \sigma_m)^T$ with $\sigma_i \geq 0$ for $i = 1, \dots, m$, $\sigma^2 = (\sigma_1^2, \dots, \sigma_m^2)^T$

and the complete log-likelihood is

$$\begin{aligned} h(u | \beta, \sigma^2) &= \sum_j \{y_j \eta_j - \ln(1 + e^{\eta_j})\} - \frac{1}{2} \sum_{i=1}^m \left(q_i \ln \sigma_i^2 + \frac{\|u_i\|_2^2}{\sigma_i^2} \right) \\ &= \sum_j \{y_j \eta_j - \ln(1 + e^{\eta_j})\} - \frac{1}{2} \sum_{i=1}^m \frac{\|u_i\|_2^2}{\sigma_i^2} + \text{terms without } u_i. \end{aligned}$$

Direct optimization of the likelihood defined in (3.1) is computationally challenging because of the integral. The Laplace approximation (LA) to the likelihood $L(\beta, \sigma)$ is obtained by replacing $h(u | \beta, \sigma^2)$ by its second-order Taylor expansion at the conditional maximum. Given current iterate (β, σ) , let u^* be the maximizer of h and $\eta^* = X\beta + Zu^*$ where $Z = (Z_1, Z_2, \dots, Z_m)$.

Then the approximated log-likelihood is

$$\begin{aligned} L_{\text{LA}}(\beta, \sigma) &= h(u^* | \beta, \sigma^2) - \frac{1}{2} \ln \det \nabla^2 \{-h(u^* | \beta, \sigma^2)\} \\ &= \sum_j \{y_j \eta_j^* - \ln(1 + e^{\eta_j^*})\} - \frac{1}{2} \sum_{i=1}^m q_i \ln \sigma_i^2 - \frac{1}{2} \sum_{i=1}^m \frac{\|u_i^*\|_2^2}{\sigma_i^2} \\ &\quad - \frac{1}{2} \ln \det \{Z^T W^* Z + \text{blkdiag}(\sigma_1^{-2} I_{q_1}, \dots, \sigma_m^{-2} I_{q_m})\} \\ &= \sum_j \{y_j \eta_j^* - \ln(1 + e^{\eta_j^*})\} - \frac{1}{2} \sum_{i=1}^m \frac{\|u_i^*\|_2^2}{\sigma_i^2} \\ &\quad - \frac{1}{2} \ln \det \left(W^{*-1} + \sum_i \sigma_i^2 Z_i Z_i^T \right) - \frac{1}{2} \ln \det W^* \\ &\quad + \text{terms without } \beta, \sigma^2, \end{aligned} \quad (3.2)$$

where $W^* = \text{diag}(w^*)$ is a diagonal matrix with entries

$$w_j^* = p_j^*(1 - p_j^*) = \frac{e^{\eta_j^*}}{(1 + e^{\eta_j^*})^2} \quad \text{and} \quad p_j^* = \frac{e^{\eta_j^*}}{(1 + e^{\eta_j^*})}.$$

Detailed derivations of the approximated log-likelihood (3.2) are in the Supplementary Materials S1. The MM algorithm cycles through following updates of u , β and σ^2 .

1. To maximize $h(u \mid \beta, \sigma^2)$, the gradient and Hessian are

$$\begin{aligned} \nabla_u h &= Z^T(y - p) - \begin{pmatrix} \sigma_1^{-2}u_1 \\ \vdots \\ \sigma_m^{-2}u_m \end{pmatrix} \\ \nabla_u^2 h &= -\{Z^T W Z + \text{blkdiag}(\sigma_1^{-2}I_{q_1}, \dots, \sigma_m^{-2}I_{q_m})\}, \end{aligned}$$

where $p = (p_1, \dots, p_n)^T$ with $p_j = e^{\eta_j} / (1 + e^{\eta_j})$ and $W = \text{diag}(w_1, \dots, w_n)$ with $w_j = p_j(1 - p_j)$. Since each w_j is upper bounded by 0.25, it follows that

$$\nabla_u^2 h \succeq -\{0.25Z^T Z + \text{blkdiag}(\sigma_1^{-2}I_{q_1}, \dots, \sigma_m^{-2}I_{q_m})\}.$$

Thus we can construct a quadratic minorization function at $u^{(l)}$ using (2.5) and maximizing the quadratic surrogate gives the MM update

$$u^{(l+1)} = u^{(l)} + \{0.25Z^T Z + \text{blkdiag}(\sigma_1^{-2}I_{q_1}, \dots, \sigma_m^{-2}I_{q_m})\}^{-1} \nabla_u h(u^{(l)}) \quad (3.3)$$

To find the maximizer u^* given β, σ^2 , we iterate the MM update (3.3) until convergence. Note that the indicated matrix inverse in (3.3) only needs to be done once and remains constant through the iterations.

2. Updating β given σ^2 and u^* is a regular logistic regression with offset Zu^* . We invoke a similar MM update as above

$$\beta^{(t+1)} = \beta^{(t)} + (0.25X^T X)^{-1} X^T (y - p^*). \quad (3.4)$$

Again the matrix inverse $(0.25X^T X)^{-1}$ only needs to be done once.

3. To update σ^2 given β and u^* , the minorization (2.4) leads to the surrogate function

$$g(\sigma^2 | \sigma^{2(t)}) = -\frac{1}{2} \sum_{i=1}^m \frac{\|u_i^*\|_2^2}{\sigma_i^2} - \frac{1}{2} \sum_{i=1}^m \sigma_i^2 \text{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + c^{(t)} \quad (3.5)$$

where $c^{(t)}$ is a constant irrelevant to optimization. Maximization of $g(\sigma^2 | \sigma^{2(t)})$ with respect to σ^2 yields the explicit MM update

$$\sigma_i^{2(t+1)} = \left[\frac{\|u_i^*\|_2^2}{\text{tr} \left\{ Z_i^T (\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1})^{-1} Z_i \right\}} \right]^{\frac{1}{2}}.$$

When $q \ll n$, the Woodbury formula facilitates the inversion

$$\begin{aligned} & \left(\sum_i \sigma_i^{(t)2} Z_i Z_i^T + W^{*-1} \right)^{-1} \\ &= W^* - W^* Z(\sigma) \{ I_q + Z(\sigma)^T W^* Z(\sigma) \}^{-1} Z(\sigma)^T W^*, \end{aligned}$$

where $Z(\sigma) = (\sigma_1 Z_1, \dots, \sigma_m Z_m)$. Since the iterate is derived based on MM principle, it possesses the ascent property

$$L_{LA}(\sigma^{(t+1)} \mid \beta, u^*) \geq L_{LA}(\sigma^{(t)} \mid \beta, u^*). \quad (3.6)$$

Detailed proof is presented in the Supplementary Materials S3.

Like the penalized iteratively reweighted least squares (PIRLS) algorithm described in Bates et al. (2015), parameter estimates are determined for a fixed weights matrix W^* and then the weights are updated to the current estimates and the process is repeated. The resulting algorithm is extremely simple to implement. Algorithm 1 summarizes the MM algorithm for parameter estimation of the logistic linear mixed model (1.1). Each iteration involves one-step update of β and σ^2 . Several more steps of updating β and σ^2 give similar results in practice.

3.2. Model formulation 2

In Laplace approximated log-likelihood (3.2), we have σ_i in the denominator, thus it cannot be combined with penalized estimation which will shrink some of σ_i s to zero. Therefore we consider another reparameterization of model (1.1) by assuming that η takes the form

$$\eta = X\beta + \sigma_1 Z_1 u_1 + \dots + \sigma_m Z_m u_m, \quad (3.7)$$

where $u_i \sim N(0_{q_i}, I_{q_i})$ are independent. Let $u = (u_1^T, \dots, u_m^T)^T \in \mathcal{R}^q$ be the

Input : y, X, Z_1, \dots, Z_m

Output: MLE $\hat{\beta}, \hat{\sigma}_1^2, \dots, \hat{\sigma}_m^2$

Initialize $\beta^{(0)}, \sigma_i^{(0)} > 0, i = 1, \dots, m$;

repeat

$u^* \leftarrow \arg \max_u h(u \mid \sigma^{2(t)}, \beta^{(t)})$;

$p^* \leftarrow 1 / \{1 + \exp(-X\beta^{(t)} - Zu^*)\}$;

$\beta^{(t+1)} \leftarrow \beta^{(t)} + (0.25X^T X)^{-1} X^T (y - p^*)$;

$p^* \leftarrow 1 / \{1 + \exp(-X\beta^{(t+1)} - Zu^*)\}$;

$W^* \leftarrow \text{diag}\{p^*(1 - p^*)\}$;

$\sigma_i^{2(t+1)} \leftarrow \left[\frac{\|u_i^*\|_2^2}{\text{tr}\{Z_i^T (\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1})^{-1} Z_i\}} \right]^{\frac{1}{2}}, \quad i = 1, \dots, m$;

until *objective value converges*;

Algorithm 1: MMLA1 - a MM algorithm to maximize the Laplace approximation of likelihood for model (1.1).

concatenated random effects and $Z = (Z_1, \dots, Z_m) \in \mathcal{R}^{n \times q}$, $q = \sum_{i=1}^m q_i$.

Then $\eta = X\beta + ZDu$, where $D = \text{blkdiag}(\sigma_1 I_{q_1}, \dots, \sigma_m I_{q_m})$ and the complete log-likelihood is

$$h(u \mid \beta, \sigma) = \sum_j \{y_j \eta_j - \ln(1 + e^{\eta_j})\} - \frac{1}{2} \|u\|_2^2 + \text{terms without } u.$$

Given current iterate (β, σ) , let u^* be the maximizer of h and $\eta^* = X\beta +$

ZDu^* . Then the approximated log-likelihood is

$$\begin{aligned}
 & L_{\text{LA}}(\beta, \sigma) \\
 &= h(u^* \mid \beta, \sigma) - \frac{1}{2} \ln \det \nabla^2 \{-h(u^* \mid \beta, \sigma)\} \\
 &= \sum_j \{y_j \eta_j^* - \ln(1 + e^{\eta_j^*})\} - \frac{1}{2} \|u^*\|_2^2 - \frac{1}{2} \ln \det (D^T Z^T W^* Z D + I_q) \\
 &= \sum_j \{y_j \eta_j^* - \ln(1 + e^{\eta_j^*})\} - \frac{1}{2} \|u^*\|_2^2 - \frac{1}{2} \ln \det \left(W^{*-1} + \sum_i \sigma_i^2 Z_i Z_i^T \right) \\
 &\quad - \frac{1}{2} \ln \det W^* + \text{terms without } \beta, \sigma^2. \tag{3.8}
 \end{aligned}$$

Detailed derivations of the above approximated log-likelihood can be found in the Supplementary Materials S2. Maximizing $h(u \mid \beta, \sigma)$ follows similar MM updates as in (3.3). Given σ^2 and β , u^* can be found through MM iterates

$$u^{(l+1)} = u^{(l)} + \{0.25(ZD)^T ZD + I_q\}^{-1} \nabla_u h(u^{(l)} \mid \beta, \sigma^2)$$

until convergence, where $\nabla_u h(u^{(l)} \mid \beta, \sigma^2) = D^T Z^T (y - p) - u^{(l)}$. Updating β given u^* and σ^2 is the same as update in (3.4).

Updating σ^2 given β and u^* depends on three minorizations, which differ from the first reparameterization. Quadratic minorization implies that

$$\begin{aligned}
 -1^T \ln(1 + e^{\eta^*}) &\geq -p^{(t)T} (\eta^* - \eta^{*(t)}) - \frac{1}{8} \|\eta^* - \eta^{*(t)}\|_2^2 + c^{(t)} \\
 &= -p^{(t)T} Z D u^* - \frac{1}{8} \|Z(D - D^{(t)})u^*\|_2^2 + c^{(t)}, \tag{3.9}
 \end{aligned}$$

where $c^{(t)}$ is an irrelevant constant, $p^{(t)}$ is a vector with the j th element equal to $e^{\eta_j^{*(t)}} / (1 + e^{\eta_j^{*(t)}})$ and $\eta_j^{*(t)}$ is the j th element of $\eta^{*(t)} = X\beta + ZD^{(t)}u^*$.

The Cauchy inequality implies that

$$\begin{aligned} -\|Z(D - D^{(t)})u^*\|_2^2 &= -\left\| \sum_{i=1}^m Z_i u_i^* (\sigma_i - \sigma_i^{(t)}) \right\|_2^2 \\ &\geq -\left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\} \sum_{i=1}^m (\sigma_i - \sigma_i^{(t)})^2, \end{aligned} \quad (3.10)$$

where $(Z_i u_i^*)_j$ is the j th element of vector $Z_i u_i^*$. Combining (3.9), (3.10)

and (2.4) gives the overall minorization function

$$\begin{aligned} g(\sigma | \sigma^{(t)}) &= \sum_{i=1}^m \sigma_i (y - p^{(t)})^T Z_i u_i^* - \frac{1}{8} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\} \sum_{i=1}^m (\sigma_i - \sigma_i^{(t)})^2 \\ &\quad - \frac{1}{2} \sum_{i=1}^m \sigma_i^2 \operatorname{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + c^{(t)}, \end{aligned} \quad (3.11)$$

where σ_i are nicely separated and only involve quadratic terms. Maximization of $g(\sigma | \sigma^{(t)})$ results the following update

$$\sigma_i^{(t+1)} = \frac{(y - p^{(t)})^T Z_i u_i^* + \frac{1}{4} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\} \sigma_i^{(t)}}{\operatorname{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + \frac{1}{4} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\}}. \quad (3.12)$$

To account for the non-negative constraint of σ , at each iteration we set $\sigma_i^{(t+1)} = \max(0, \sigma_i^{(t+1)})$. Algorithm 2 summarizes the MM algorithm for model formulation 2 defined in (3.7).

3.3. MM algorithm for maximizing the penalized approximated likelihood

<p>Input : y, X, Z_1, \dots, Z_m</p> <p>Output: MLE $\hat{\beta}, \hat{\sigma}_1^2, \dots, \hat{\sigma}_m^2$</p> <p>Initialize $\beta^{(0)}, \sigma_i^{(0)} > 0, i = 1, \dots, m$;</p> <p>repeat</p> <div style="border-left: 1px solid black; border-right: 1px solid black; padding: 0 10px;"> <p>$D^{(t)} = \text{diag} \left(\sigma_1^{(t)} \mathbf{1}_{q_1}, \dots, \sigma_m^{(t)} \mathbf{1}_{q_m} \right)$;</p> <p>$u^* \leftarrow \arg \max_u h(u \mid \sigma^{2(t)}, \beta^{(t)})$;</p> <p>$p^{(t)} \leftarrow 1 / \{1 + \exp(-X\beta^{(t)} - ZD^{(t)}u^*)\}$;</p> <p>$\beta^{(t+1)} \leftarrow \beta^{(t)} + (0.25X^T X)^{-1} X^T (y - p^{(t)})$;</p> <p>$p^{(t)} \leftarrow 1 / \{1 + \exp(-X\beta^{(t+1)} - ZD^{(t)}u^*)\}$;</p> <p>$W^* \leftarrow \text{diag} \{p^{(t)}(1 - p^{(t)})\}$;</p> <p>$\sigma_i^{2(t+1)} \leftarrow$</p> <p>$\max \left[0, \frac{(y-p^{(t)})^T Z_i u_i^* + \frac{1}{4} \{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \} \sigma_i^{(t)}}{\text{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + \frac{1}{4} \{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \}} \right], \quad i =$</p> <p>$1, \dots, m$;</p> </div> <p>until <i>objective value converges</i>;</p>
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Algorithm 2: MMLA2 - a MM algorithm to maximize the Laplace approximation of likelihood for model (3.7).

For variance component selection, we consider the penalization approach using lasso penalty. Since the minorization function of σ derived in second model formulation is a quadratic function of σ , it meshes well

with penalized estimation. Other penalties such as the adaptive lasso (Zou, 2006) and smoothly clipped absolute deviation (SCAD) (Fan and Li, 2001) lead to similar algorithms.

The lasso penalized approximated log-likelihood is

$$-L_{\text{LA}}(\beta, \sigma) + \lambda \sum_{i=1}^m |\sigma_i|. \quad (3.13)$$

Finding u^* to maximize $h(u \mid \beta, \sigma)$ and updating β are the same as described in algorithm 2. The only difference lies in the update of σ given u^* and β in (3.12), which now becomes

$$\begin{aligned} \sigma_i^{(t+1)} &= \arg \min_{\sigma_i} \sigma_i^2 \left[\frac{1}{2} \text{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + \frac{1}{8} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\} \right] \\ &\quad - \sigma_i \left[(y - p^{(t)})^T Z_i u_i^* + \frac{1}{4} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\} \sigma_i^{(t)} \right] + \lambda |\sigma_i| \quad (3.14) \\ &= ST(z_i, \gamma_i), \end{aligned}$$

where

$$ST(z, \gamma) = \arg \min_x \frac{1}{2}(x - z)^2 + \gamma|x| = \text{sng}(z) (|z| - \gamma)_+ \quad (3.15)$$

is the soft-thresholding operator and

$$\begin{aligned} z_i &= \frac{(y - p^{(t)})^T Z_i u_i^* + \frac{1}{4} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\} \sigma_i^{(t)}}{\text{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + \frac{1}{4} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\}}, \\ \gamma_i &= \frac{\lambda}{\text{tr} \left\{ \left(\sum_i \sigma_i^{2(t)} Z_i Z_i^T + W^{*-1} \right)^{-1} Z_i Z_i^T \right\} + \frac{1}{4} \left\{ \sum_{j=1}^n \sum_{i=1}^m (Z_i u_i^*)_j^2 \right\}}. \end{aligned}$$

3.4. Choice of regularization parameter

The best λ can be selected over a grid using Akaike information criterion (AIC), Bayesian information criterion (BIC), or cross-validation. Here we consider AIC and BIC. Since it is hard to evaluate the log likelihood function, we replace it by its Laplace approximation. Specifically, we use

$$\text{BIC}(\lambda) = -2L_{\text{LA}}(\hat{\beta}, \hat{\sigma}^2) + \log(n) \times \text{df}(\lambda)$$

$$\text{AIC}(\lambda) = -2L_{\text{LA}}(\hat{\beta}, \hat{\sigma}^2) + 2 \times \text{df}(\lambda),$$

where $\text{df}(\lambda)$ is the number of non-zeros in $\hat{\sigma}^2(\lambda)$. In the following simulation studies, we compare AIC and BIC on variance component selection.

4. Simulation studies

4.1. Random effects ANOVA

In this section we compare the estimation error and runtime of the MM algorithms (MMLA1 and MMLA2) to three different implementations: (1) the `glmer()` function in the popular `lme4` package in R (Bates et al., 2015) (2) `glmm()` function in the `glmm` package in R (Knudson, 2016) and (3) `stan_glmer()` function in the `rstanarm` package in R (Stan Development Team, 2016). `glmer()` fits a generalized linear mixed-effects model and the default (`nAGQ=1`) uses Laplace approximation to approximate the original log-likelihood. `glmm()` calculates and maximizes the Monte Carlo likelihood approximation (MCLA) (Geyer, 1990) to find Monte Carlo maximum likeli-

hood estimates (MCMLEs) (Sung and Geyer, 2007) for the fixed effects and variance components. `rstanarm` package is an R interface to the Stan C++ library for Bayesian estimation. `stan_glmr()` adds independent prior distributions on the regression coefficients as well as priors on the covariance matrices of the group-specific parameters and perform Bayesian inference via MCMC.

We simulated data from the following two-way ANOVA model with crossed random effects

$$\begin{aligned} P(y_{ijk} = 1) &= 1/(\exp(-\eta_{ijk})) \\ \eta_{ijk} &= x_1\beta_1 + x_2\beta_2 + x_3\beta_3 + \alpha_i + \gamma_j + (\alpha\gamma)_{ij}, \\ i &= 1, \dots, 5, j = 1, \dots, 5, k = 1, \dots, c, \end{aligned}$$

where $\alpha_i \sim N(0, \sigma_\alpha^2)$, $\gamma_j \sim N(0, \sigma_\gamma^2)$ and $(\alpha\gamma)_{ij} \sim N(0, \sigma_{\alpha\gamma}^2)$ are jointly independent. Here i indexes levels in factor 1, j indexes levels in factor 2, and k indexes observations in the (i, j) -combination. This corresponds to $m = 3$ variance components. Table 1 displays the results when there are $a = b = 5$ levels of each factor, the number of observations c in each combination of factor levels varies from 2 to 200, and the true parameter values are $(\beta_1, \beta_2, \beta_3, \sigma_\alpha^2, \sigma_\gamma^2, \sigma_{\alpha\gamma}^2) = (0.6, 1.0, -1.0, 0.5, 0.9, 0.3)$. For each scenario, we simulated 50 replicates. The sample size was $n = abc$ for each

replicate. Therefore the largest model in Table 1 involves covariance matrix of size 5000×5000 . For $c = 100$ and 200 , we omit the results of `glm` and `rstanarm` since they take too much time when sample size gets larger and the whole simulation takes more than a week to complete.

We made the following observations. Two MM algorithms (MMLA1 and MMLA2) have very close results, but MMLA2 takes longer time to converge than MMLA1, especially when the number of groups c is large. This is what we expected since the surrogate function derived in MMLA2 involves two more layers of minorizations, which result in slower convergence. The `glmer()` function failed to converge in many replicates when $c = 2$ and produced much worse estimates than MM algorithms. For other values of c , `glmer()` delivered estimates comparable to MM algorithm but was $3 \sim 4$ fold slower than MMLA1. `glm` and `stan_glmer()` are much slower since they involve sampling and their estimation performance are not good. The core algorithm in `glmer()` is coded in C and extensively utilizes sparse linear algebra. Our MM algorithms are implemented in the high-level Julia language and ignore sparsity structure. Although it is hard to draw conclusions based on implementations in different languages, this example clearly demonstrates the efficiency and scalability of the MM algorithms for GLMM estimation.

4.2. Genetic example

In this section, we use a genetic example to demonstrate the performance of variable selection using our algorithm derived in Section 3.3. Consider the QTL mapping example introduced in Section 1

$$g(\mu) = X\beta + G\gamma,$$

where G is an $n \times k$ genotype matrix for k variants of interest, $g(\mu) = \text{logit}(\mu)$, β are fixed effects, and γ are random genetic effects with $\gamma \sim \text{Normal}(0, \sigma^2 I_k)$. The response y is an $n \times 1$ vector of binary trait measurements with mean μ . One way to identify important genes is to test the null hypothesis $\sigma^2 = 0$ for each region separately and then adjust for multiple testing (Lee et al., 2014). Here we consider the joint model for all regions instead of marginal tests

$$g(\mu) = X\beta + s_1^{-1/2}G_1\gamma_1 + \cdots + s_m^{-1/2}G_m\gamma_m, \quad (4.1)$$

where $\gamma_i \sim N(0, \sigma_i^2 I)$ and select the variance components σ_i^2 via the penalization (3.13). Here s_i is the number of variants in region i , and the weights $s_i^{-1/2}$ put all variance components on the same scale.

In this simulation study, we use the genetic data from COPDGene exome sequencing study (Regan et al., 2011), which has 399 subjects and genotype information of 16,610 genes. The covariate matrix X contains

intercept, age, sex, and the top 3 principal components in the mean effects. We consider four experimental settings for sparse random effects.

In all the examples, we set $\beta = (0.1, -1.0, 0.8, -0.3, -1.2, 1.5)$ and randomly select m genes $G_i, i = 1, \dots, m$, from the COPD data.

- Setting 1: $\sigma^2 = (5.0, 7.5, 10.0, 0_{m-3}^T)^T$ with m varying from 5, 10, 20, 100
- Setting 2: $\sigma^2 = (10, 15, 20, 0_{m-3}^T)^T$ with m varying from 5, 10, 20, 100
- Setting 3: $\sigma^2 = (5, 6, 7, 8, 9, 10, 0_{m-6}^T)^T$ with m varying from 10, 20, 40, 100
- Setting 4: $\sigma^2 = (10, 12, 14, 16, 18, 20, 0_{m-6}^T)^T$ with m varying from 10, 20, 40, 100

We use mean squared error (MSE) = $\|\hat{\beta} - \beta\|^2$ to evaluate the performance of fixed effect estimation. Four measures are used to assess the variable selection performance: the number of truly non-zero variance components that are selected as non-zero variance components (denoted as “True Positive”), the number of truly zero variance components that are selected as non-zero variance components (denoted as “False Positive”), the frequency of exactly selecting the correct variance components (denoted by “Exact”), and the frequency of over-selecting variance components (denoted

by “Over”). In each experimental setting, 100 data sets are simulated from the model, and we report the average performance over the 100 runs for both AIC and BIC. Table 2, 3, 4 and 5 summarize the results for the above four settings. We can see that our proposed method for variable selection does a good job in identifying the significant random effects. For example, under Setting 1 and Setting 2 for different m , our method based on both AIC and BIC can identify the truly significant random effects 97% ~ 99% of the time with AIC more prone to over-selection than BIC. Setting 3 and Setting 4 are more challenging since they involve a larger number of random effects. But our method can still identify the non-zero random effect 96% of the time under $m = 10$ when using AIC.

5. Real data analysis

In this real data analysis, we still use the data from COPDGene exome sequencing study described in the above simulated genetic example. The binary trait is smoke or not (denoted as **smoke**). There are 399 individuals with 646,125 genetic variants in 16,610 genes. The covariates include **age**, **sex**, and the top 3 principal components. Because the number of genes is too large, we first screen the 16,610 genes down to 200 genes according to their marginal p-values from the Sequence Kernel Association Test (SKAT) and then carry out penalized estimation of the 200 variance components in

the joint model (4.1). This is similar to the sure independence screening strategy for selecting mean effects (Fan and Lv, 2008). AIC selects 16 genes, while BIC criteria selects only one gene “AFAP1L2”. Table 6 lists the top 5 genes selected using AIC criteria (PLVC-AIC) and SKAT. We can see that the top 3 genes selected using both methods are the same but with different order. To compare the selection performance between SKAT and PLVC-AIC, we evaluate the log-likelihood of model (4.1) with the top 5 genes listed in Table 6 entering the model one by one. To evaluate the log-likelihood, we use the R package `bernor` which implements the Monte Carlo approximation method described in Sung and Geyer (2007). From Figure 1, we can see that the log-likelihood with genes selected by PLVC-AIC is above that of SKAT, which in some sense indicates that genes selected by PLVC-AIC explain more variability in the model.

Besides, we also compare the prediction performance between the top 5 genes selected by PLVC-AIC and SKAT. We evaluate the prediction performance using model (4.1) by including the genotype matrix G_i of the corresponding selected genes similar to what is done in Wu et al. (2011). For example, if the genotype matrix of the top k genes selected are $G_{h_1}, G_{h_2}, \dots, G_{h_k}$, then the predictive model becomes

$$g(\mu) = X\beta + s_{h_1}^{-1/2}G_{h_1}\gamma_1 + \dots + s_{h_k}^{-1/2}G_{h_k}\gamma_k = X^*\beta^*,$$

where $X^* = (X, s_{h_1}^{-1/2}G_{h_1}, \dots, s_{h_k}^{-1/2}G_{h_k})$ and $\beta^* = (\beta^T, \gamma_1^T, \dots, \gamma_k^T)$. This is the ordinary logistic regression model that can be used for prediction. Table 7 summarizes the prediction performance using 5-fold cross validation as the top 5 genes selected by both methods entering the model (4.1) one by one. We can see that on average the model with genes selected by PLVC-AIC performs slightly better than SKAT in terms of prediction. The penalization approach for selecting variance components warrants further theoretical study. This real data analysis demonstrates that the proposed simple MM algorithm scales to high-dimensional problems.

6. Discussion

This paper discusses two MM algorithms for variance component estimation and selection in the logistic linear mixed model. The algorithms are simple to implement and scale to models with a large number of variance components. Other extensions are possible. This paper only considers the binary response. The extension of the algorithm MMLA1 to the Poisson count data is straightforward with almost identical derivation. There is work on selecting fixed effects in GLMMs in literature. Here we only focus on random effects selection. Our algorithms can be easily extend to selecting fixed and random effects simultaneously. We leave a thorough study of these topics to future research.

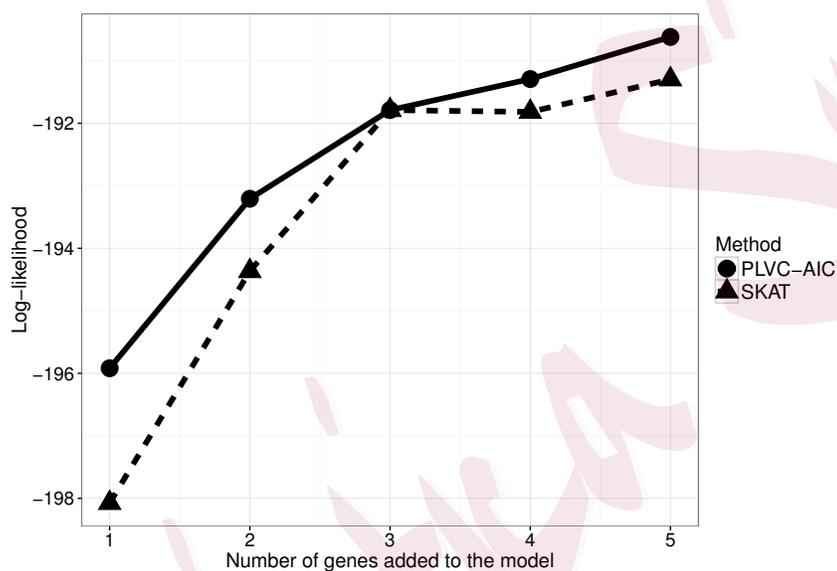


Figure 1: Log-likelihood evaluation with top 5 genes selected by PLVC-AIC and SKAT added to the model respectively in an association study of 200 genes and the complex trait `smoke`.

Supplementary Materials

Supplementary materials include the detailed derivation of (3.2), (3.8) and technical proof of the ascent property in (3.6).

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Table 1: Comparison of the MM algorithms with two different parameterizations (MMLA1 and MMLA2) and the `glmer()` function (with `nAGQ=1`) in the `lme4` package, `rstanarm` package, and `glmm` package. Standard errors are given in parentheses. Results for `rstanarm` and `glmm` with $c = 100, 200$ are not reported because the simulation takes more than 1 week.

c	Method	runtime	$\beta_1(0.6)$	$\beta_2(1.0)$	$\beta_3(-1.0)$	$\sigma_\alpha^2(0.5)$	$\sigma_\gamma^2(0.9)$	$\sigma_{\alpha\gamma}^2(0.3)$
2	MMLA1	0.19(0.55)	0.68(0.51)	1.08(0.43)	-0.92(0.51)	0.52(0.91)	1.03(1.55)	0.22(0.37)
	MMLA2	0.14(0.12)	0.68(0.51)	1.08(0.43)	-0.92(0.51)	0.52(0.91)	1.04(1.56)	0.22(0.37)
	<code>lme4</code>	0.46(0.37)	2.83(7.22)	3.52(7.39)	-2.42(4.04)	187(753)	108(580)	558(2049)
	<code>rstanarm</code>	8.15(0.49)	0.91(0.69)	1.42(0.45)	-1.20(0.58)	1.38(1.32)	2.14(2.23)	2.60(1.86)
	<code>glmm</code>	23.95(45.66)	0.64(0.53)	0.91(0.55)	-0.76(0.59)	1.54(3.13)	0.03(0.07)	0.06(0.14)
8	MMLA1	0.10(0.03)	0.55(0.21)	0.96(0.24)	-0.98(0.20)	0.36(0.33)	0.96(0.94)	0.34(0.34)
	MMLA2	0.17(0.08)	0.55(0.21)	0.96(0.24)	-0.98(0.20)	0.36(0.33)	0.96(0.94)	0.34(0.34)
	<code>lme4</code>	0.37(0.10)	0.60(0.23)	1.04(0.27)	-1.07(0.22)	0.42(0.38)	1.15(1.13)	0.47(0.48)
	<code>rstanarm</code>	21.85(1.15)	0.61(0.24)	1.05(0.27)	-1.09(0.22)	0.68(0.44)	1.48(1.20)	0.72(0.53)
	<code>glmm</code>	224.53(492.52)	0.46(0.17)	0.82(0.24)	-0.85(0.17)	0.78(1.50)	0.02(0.03)	0.04(0.08)
50	MMLA1	0.19(0.10)	0.58(0.07)	1.01(0.08)	-1.00(0.08)	0.52(0.43)	0.96(0.81)	0.31(0.16)
	MMLA2	1.65(0.52)	0.58(0.07)	1.01(0.08)	-1.00(0.08)	0.52(0.43)	0.94(0.72)	0.31(0.16)
	<code>lme4</code>	0.92(0.12)	0.59(0.07)	1.03(0.08)	-1.02(0.09)	0.54(0.45)	1.01(0.86)	0.32(0.17)
	<code>rstanarm</code>	198.38(26.88)	0.59(0.07)	1.04(0.08)	-1.02(0.09)	0.82(0.58)	1.37(0.92)	0.42(0.21)
	<code>glmm</code>	3613.26(2272.85)	0.48(0.09)	0.86(0.12)	-0.84(0.12)	0.88(1.39)	0.04(0.06)	0.04(0.07)
100	MMLA1	0.58(0.18)	0.61(0.06)	1.01(0.06)	-1.00(0.06)	0.65(0.46)	0.94(0.61)	0.30(0.11)
	MMLA2	4.28(0.78)	0.61(0.06)	1.01(0.06)	-1.00(0.06)	0.67(0.44)	0.91(0.54)	0.30(0.11)
	<code>lme4</code>	1.49(0.18)	0.62(0.06)	1.02(0.06)	-1.01(0.06)	0.67(0.47)	0.97(0.63)	0.31(0.12)
	<code>rstanarm</code>	—	—	—	—	—	—	—
	<code>glmm</code>	—	—	—	—	—	—	—
200	MMLA1	0.98(0.16)	0.60(0.04)	0.99(0.04)	-0.99(0.04)	0.45(0.33)	0.92(0.62)	0.29(0.12)
	MMLA2	13.49(3.42)	0.60(0.04)	0.99(0.04)	-0.99(0.04)	0.50(0.33)	0.91(0.51)	0.29(0.12)
	<code>lme4</code>	2.76(0.33)	0.60(0.04)	1.00(0.04)	-1.00(0.04)	0.46(0.33)	0.94(0.63)	0.30(0.13)
	<code>rstanarm</code>	—	—	—	—	—	—	—
	<code>glmm</code>	—	—	—	—	—	—	—

Table 2: Estimation and selection results for Setting 1.

m	Criteria	MSE (β)	Variance components selection			
			True Positive (3)	False Positive (0)	Exact	Over
5	AIC	0.31(0.20)	2.98	0.33	66%	32%
	BIC	0.31(0.20)	2.98	0.15	84%	14%
10	AIC	0.27(0.17)	2.96	1.14	26%	70%
	BIC	0.29(0.18)	2.93	0.61	50%	44%
20	AIC	0.26(0.16)	2.96	2.01	11%	86%
	BIC	0.29(0.17)	2.87	1.25	17%	72%
100	AIC	0.30(0.18)	2.74	2.95	4%	71%
	BIC	0.38(0.21)	2.50	0.57	27%	24%

Table 3: Estimation and selection results for Setting 2.

m	Criteria	MSE (β)	Variance components selection			
			True Positive (3)	False Positive (0)	Exact	Over
5	AIC	0.37(0.22)	2.99	0.40	63%	36%
	BIC	0.38(0.22)	2.99	0.22	79%	20%
10	AIC	0.33(0.20)	2.98	1.17	28%	70%
	BIC	0.36(0.21)	2.98	0.68	44%	54%
20	AIC	0.34(0.22)	2.98	1.60	25%	74%
	BIC	0.38(0.24)	2.95	0.85	39%	58%
100	AIC	0.37(0.19)	2.83	3.31	3%	80%
	BIC	0.48(0.22)	2.68	0.61	38%	30%

Table 4: Estimation and selection results for Setting 3.

m	Criteria	MSE (β)	Variance components selection			
			True Positive (6)	False Positive (0)	Exact	Over
10	AIC	0.78(0.30)	5.96	0.84	34%	62%
	BIC	0.83(0.32)	5.66	0.33	54%	25%
20	AIC	0.73(0.27)	5.88	1.49	15%	73%
	BIC	0.82(0.32)	5.56	0.48	41%	32%
40	AIC	1.04(0.33)	5.68	1.96	15%	57%
	BIC	1.17(0.37)	4.96	0.74	29%	27%
100	AIC	0.85(0.34)	5.40	2.54	2%	48%
	BIC	0.98(0.38)	4.82	0.63	12%	14%

Table 5: Estimation and selection results for Setting 4.

m	Criteria	MSE (β)	Variance components selection			
			True Positive (6)	False Positive (0)	Exact	Over
10	AIC	1.06(0.32)	5.97	0.85	32%	65%
	BIC	1.09(0.32)	5.91	0.56	45%	47%
20	AIC	1.02(0.34)	5.96	1.36	15%	81%
	BIC	1.07(0.34)	5.92	0.70	38%	54%
40	AIC	1.44(0.39)	5.74	1.82	13%	62%
	BIC	1.51(0.40)	5.54	0.85	29%	39%
100	AIC	1.18(0.42)	5.72	2.10	6%	68%
	BIC	1.29(0.43)	5.29	0.71	21%	22%

Table 6: Top 5 genes selected by (1) the lasso penalized variance component model (3.13) with AIC criterion (PLVC-AIC) and (2) SKAT in an association study of 200 genes and the binary trait **smoke**.

No.	PLVC-AIC			SKAT		
	Gene	Marginal p-value	# Variants	Gene	Marginal p-value	# Variants
1	AFAP1L2	6.0×10^{-4}	18	KIAA1377	5.7×10^{-4}	14
2	RREB1	6.0×10^{-4}	18	RREB1	6.0×10^{-4}	18
3	KIAA1377	5.7×10^{-4}	14	AFAP1L2	6.0×10^{-4}	18
4	PSG5	3.7×10^{-3}	11	KARS	6.1×10^{-4}	15
5	TDRD1	1.2×10^{-3}	14	PZP	1.0×10^{-3}	21

Table 7: 5-fold cross validation performance on prediction accuracy with top 5 genes selected by PLVC-AIC and SKAT added to the model respectively in an association study of 200 genes and the complex trait **smoke**.

No. of genes entered into model	Prediction accuracy	
	PLVC-AIC	SKAT
1	79.4%(6.2%)	78.2%(4.6%)
2	79.9%(6.0%)	77.9%(2.9%)
3	80.7%(4.1%)	80.7%(4.1%)
4	81.7%(2.3%)	80.7%(5.4%)
5	81.4%(3.4%)	78.7%(5.8%)