Published in final edited form as:
J R Stat Soc Series B Stat Methodol. 2011 June ; 73(3): 325–349. doi:10.1111/j.1467-9868.2010.00764.x.

Penalized Composite Quasi-Likelihood for Ultrahigh-Dimensional Variable Selection

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Summary

In high-dimensional model selection problems, penalized least-square approaches have been extensively used. This paper addresses the question of both robustness and efficiency of penalized model selection methods, and proposes a data-driven weighted linear combination of convex loss functions, together with weighted L_1-penalty. It is completely data-adaptive and does not require prior knowledge of the error distribution. The weighted L_1-penalty is used both to ensure the convexity of the penalty term and to ameliorate the bias caused by the L_1-penalty. In the setting with dimensionality much larger than the sample size, we establish a strong oracle property of the proposed method that possesses both the model selection consistency and estimation efficiency for the true non-zero coefficients. As specific examples, we introduce a robust method of composite L1-L2, and optimal composite quantile method and evaluate their performance in both simulated and real data examples.

Keywords

Composite QMLE; LASSO; Model Selection; NP Dimensionality; Oracle Property; Robust statistics; SCAD

1. Introduction

Feature extraction and model selection are important for sparse high dimensional data analysis in many research areas such as genomics, genetics and machine learning. Motivated by the need of robust and efficient high dimensional model selection method, we introduce a new penalized quasi-likelihood estimation for linear model with high dimensionality of parameter space.

Consider the estimation of the unknown parameter $\boldsymbol{\beta}$ in the linear regression model

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$$Y = \mathbf{X}\beta + \varepsilon, \tag{1}$$

where $\mathbf{Y} = (Y_1, \cdots, Y_n)^T$ is an n-vector of response, $\mathbf{X} = (\mathbf{X}_1, \cdots, \mathbf{X}_n)^T$ is an $n \times p$ matrix of independent variables with $\mathbf{X}_i^T$ being its i-th row, $\boldsymbol{\beta} = (\beta_1, \ldots, \beta_p)^T$ is a p-vector of unknown parameters and $\boldsymbol{\varepsilon} = (\varepsilon_1, \ldots, \varepsilon_n)^T$ is an n-vector of i.i.d. random errors with mean zero, independent of $\mathbf{X}$. When the dimension p is high it is commonly assumed that only a small number of predictors actually contribute to the response vector $\mathbf{Y}$, which leads to the sparsity pattern in the unknown parameters and thus makes variable selection crucial. In many applications such as genetic association studies and disease classifications using high-throughput data such as microarrays with gene-gene interactions, the number of variables p can be much larger than the sample size n. We will refer to such problem as ultrahigh-dimensional problem and model it by assuming $\log p = O(n^{\delta})$ for some $\delta \in (0, 1)$. Following Fan and Lv (2010), we will refer to p as a non-polynomial order or NP-dimensionality for short.

Popular approaches such as LASSO (Tibshirani, 1996), SCAD (Fan and Li, 2001), adaptive LASSO (Zou, 2006) and elastic-net (Zou and Zhang, 2009) use penalized least-square regression:

$$\widehat{\beta} = \arg\min_{\beta} \sum_{i=1}^{n} \left(Y_i - \mathbf{X}_i^T \beta\right)^2 + n \sum_{j=1}^{p} p_{\lambda}(|\beta_j|). \tag{2}$$

where $p_{\lambda}(\cdot)$ is a specific penalty function. The quadratic loss is popular for its mathematical beauty but is not robust to non-normal errors and presence of outliers. Robust regressions such as the least absolute deviation and quantile regressions have recently been used in variable selection techniques when p is finite (Wu and Liu, 2009; Zou and Yuan, 2008; Li and Zhu, 2008). Other possible choices of robust loss functions include Huber's loss (Huber, 1964), Tukey's bisquare, Hampel's psi, among others. Each of these loss functions performs well under a certain class of error distributions: quadratic loss is suitable for normal distributions, least absolute deviation is suitable for heavy-tail distributions and is the most efficient for double exponential distributions, Huber's loss performs well for contaminated normal distributions. However, none of them is universally better than all others. How to construct an adaptive loss function that is applicable to a large collection of error distributions?

We propose a simple and yet effective quasi-likelihood function, which replaces the quadratic loss by a weighted linear combination of convex loss functions:

$$\rho_{\mathbf{w}} = \sum_{k=1}^{K} w_k \rho_k, \tag{3}$$

where $\rho_1, \ldots, \rho_K$ are convex loss functions and $w_1, \ldots, w_K$ are positive constants chosen to minimize the asymptotic variance of the resulting estimator (see Section 3.3). From the point of view of nonparametric statistics, the functions $\{\rho_1, \cdots, \rho_K\}$ can be viewed as a set of basis functions, not necessarily orthogonal, used to approximate the unknown log-likelihood function of the error distribution. When the set of loss functions is large, the quasi-likelihood function can well approximate the log-likelihood function and therefore yield a nearly efficient method. This kind of ideas appeared already in traditional statistical inference with finite dimensionality (Koenker, 1984; Bai et al., 1992). We will extend it to the sparse statistical inference with NP-dimensionality.

The quasi-likelihood function (3) can be directly used together with any penalty function such as L_p-penalty with $0 < p < 1$ (Frank and Friedman, 1993), LASSO i.e. L_1-penalty (Tibshirani, 1996), SCAD (Fan and Li, 2001), hierarchical penalty (Bickel et al., 2008), resulting in the penalized composite quasi-likelihood problem:

$$\min_{\beta} \sum_{i=1}^{n} \rho_{\mathbf{w}}(Y_i - \mathbf{X}_i^T \beta) + n \sum_{j=1}^{p} p_{\lambda}(|\beta_j|). \tag{4}$$

Instead of using folded-concave penalty functions, we use the weighted L_1-penalty of the form

$$n \sum_{j=1}^{p} \gamma_{\lambda}(|\beta_j^{(0)}|)|\beta_j|$$

for some function γ_λ and initial estimator $\boldsymbol{\beta}^{(0)}$, to ameliorate the bias in L_1-penalization (Fan and Li, 2001; Zou, 2006; Fan and Lv, 2010) and to maintain the convexity of the problem. This leads to the following convex optimization problem:

$$\widehat{\beta}_{\mathbf{w}} = \operatorname*{argmin}_{\beta} \sum_{i=1}^{n} \rho_{\mathbf{w}} \left(Y_i - \mathbf{X}_i^T \beta \right) + n \sum_{j=1}^{p} \gamma_{\lambda}(|\beta_j^{(0)}|)|\beta_j| \tag{5}$$

When $\gamma_\lambda(\cdot) = p_\lambda'(\cdot)$, the derivative of the penalty function, (5) can be regarded as the local linear approximation to problem (4) (Zou and Li, 2008). In particular, LASSO (Tibshirani, 1996) corresponds to $\gamma_\lambda(x) = \lambda$, SCAD reduces to (Fan and Li, 2001)

$$\gamma_{\lambda}(x) = \lambda\{I(x \le \lambda) + \frac{(a\lambda - x)_+}{(a-1)\lambda} I(x > \lambda)\}, \tag{6}$$

and adaptive LASSO (Zou, 2006) takes $\gamma_\lambda(x) = \lambda|x|^{-a}$ where $a > 0$.

There is a rich literature in establishing the oracle property for penalized regression methods, mostly for large but fixed p (Fan and Li, 2001; Zou, 2006; Yuan and Lin, 2007; Zou and Yuan, 2008). One of the early papers on diverging p is the work by Fan and Peng (2004) under conditions of $p = O(n^{1/5})$. More recent works of the similar kind include Huang et al. (2008), Zou and Zhang (2009), Xie and Huang (2009), which assume that the number of non-sparse elements s is finite. When the dimensionality p is of polynomial order, Kim et al. (2008) recently gave the conditions under which the SCAD estimator is an oracle estimator. We would like to further address this problem when $\log p = O(n^{\delta})$ with $\delta \in (0, 1)$ and $s = O(n^{\alpha_0})$ for $\alpha_0 \in (0, 1)$, that is when the dimensionality is of exponential order.

The paper is organized as follows. Section 2 introduces an easy to implement two-step computation procedure. Section 3 proves the strong oracle property of the weighted L_1-penalized quasi-likelihood approach with discussion on the choice of weights and corrections for convexity. Section 4 defines two specific instances of the proposed approach and compares their asymptotic efficiencies. Section 5 provides a comprehensive simulation study as well as a real data example of the SNP selection for the Down syndrome. Section 6 is devoted to the discussion. To facilitate the readability, all the proofs are relegated to the Appendices A, B & C.

2. Penalized adaptive composite quasi-likelihood

We would like to describe the proposed two-step adaptive computation procedure and defer the justification of the appropriate choice of the weight vector $\mathbf{w}$ to Section 3.

In the first step, one will get the initial estimate $\hat{\boldsymbol{\beta}}^{(0)}$ using the LASSO procedure, i.e:

$$\widehat{\beta}^{(0)} = \arg\min_{\beta} \sum_{i=1}^{n} \left(Y_i - \mathbf{X}_i^T \beta\right)^2 + n\lambda \sum_{j=1}^{p} |\beta_j|.$$

and estimate the residual vector $\boldsymbol{\varepsilon}^0 = \mathbf{Y} - \mathbf{X}\hat{\boldsymbol{\beta}}^{(0)}$ (for justification see discussion following Condition 2). The matrix $\mathbf{M}$ and vector $\mathbf{a}$ are calculated as follows:

$$\mathbf{M}_{kl} = \frac{1}{n} \sum_{i=1}^{n} \psi_k(\varepsilon_i^0)\psi_l(\varepsilon_i^0), \text{ and } \quad a_k = \frac{1}{n} \sum_{i=1}^{n} \partial\psi_k(\varepsilon_i^0), \quad (k, l = 1, \ldots, K),$$

where $\psi_k(t)$ is a choice of the subgradient of $\rho_k(t)$, ε_i^0 is the i-th component of $\boldsymbol{\varepsilon}^0$, and a_k should be considered as a consistent estimator of $E\partial\psi_k(\varepsilon)$, which is the derivative of $E\psi_k(\varepsilon + c)$ at $c = 0$. For example, when $\psi_k(x) = \text{sgn}(x)$, then $E\psi_k(\varepsilon + c) = 1 - 2F_\varepsilon(-c)$ and $E\partial\psi_k(\varepsilon) = 2f_\varepsilon(0)$. The optimal weight is then determined as

$$\mathbf{w}_{opt} = \text{argmin}_{\mathbf{w} \geq 0, \mathbf{a}^T \mathbf{w} = 1} \mathbf{w}^T \mathbf{M} \mathbf{w}. \tag{7}$$

In the second step, one calculates the quasi maximum likelihood estimator (QMLE) using weights $\mathbf{w}_{opt}$ as

$$\widehat{\beta}^{a} = \arg\min_{\beta} \sum_{i=1}^{n} \rho_{\mathbf{w}_{opt}}\left(Y_i - \mathbf{X}_i^T \beta\right) + n \sum_{j=1}^{p} \gamma_\lambda(|\widehat{\beta}_j^{(0)}|)|\beta_j|. \tag{8}$$

Note that, depending on the choice of γ_λ, zero is not an absorbing state in the minimization problem (8). For example, using local linear approximation to SCAD as γ_λ, will allow those elements that are estimated as zero in the initial estimate $\boldsymbol{\beta}^{(0)}$, to escape from zero, whereas those nonvanishing elements can be estimated as zero in (8). This property is not demostrated in the adaptive LASSO of Zou (2006).

The number of loss functions K is typically small or moderate in practice. Problem (7) can be easily solved using a quadratic programming algorithm. The resulting vector $\mathbf{w}_{opt}$ can have vanishing components, automatically eliminating inefficient loss functions in the second step (8) and hence learning the best approximation of the unknown log-likelihood function. This can lead to considerable computational gains. See Section 4 for additional details.

Problem (8) is a convex optimization problem when ρ_k's are all convex and $\gamma_\lambda(|\widehat{\beta}_j^{(0)}|)$ are all nonnegative. This class of problems can be solved with fast and efficient computational algorithms such as pathwise coordinate optimization (Friedman et al., 2008) and least angle regression (Efron et al., 2004).

One particular example of the proposed methodology, is the combination of L_1 and L_2 regressions, in which $K = 2$, $\rho_1(t) = |t - b_0|$ and $\rho_2(t) = t^2$. Here b_0 denotes the median of error distribution ε. If the error distribution is symmetric, then $b_0 = 0$. If the error distribution is completely unknown, b_0 is unknown and can be estimated from the residual vector $\{\varepsilon_i^0\}$ or being regarded as an additional parameter and optimized together with $\boldsymbol{\beta}$ in (8). Another example is the combination of multiple quantile check functions, that is,

$$\rho_k(t)=\tau_k(t-b_k)_+ + (1-\tau_k)(t-b_k)_-,$$

where $\tau_k \in (0, 1)$ is a preselected quantile and b_k is the τ_k-quantile of the error distribution. Again, when b_k's are unknown, they can be estimated using the sample quantiles τ_k of the estimated residuals $\boldsymbol{\varepsilon}^0$ or along with $\boldsymbol{\beta}$ in (8). See Section 4 for additional discussion.

3. Sampling properties and their applications

In this section, we plan to establish the sampling properties of estimator (5) under the assumption that the number of parameters (true dimensionality) p and the number of non-vanishing components (effective dimensionality) $s = \|\boldsymbol{\beta}^*\|_0$ satisfy $\log p = O(n^\delta)$ and $s = O(n^{\alpha_0})$ for some $\delta \in (0, 1)$ and $\alpha_0 \in (0, 1)$. Particular focus will be given to the oracle property of Fan and Li (2001), but we will strengthen it and prove that estimator (5) is equal to an oracle estimator with overwhelming probability. Fan and Lv (2010) were among the first to discuss the oracle properties with NP dimensionality using the full likelihood function in generalized linear models with a class of folded concave penalties. We work on a quasi-likelihood function and a class of weighted convex penalties.

3.1. Asymptotic properties

To facilitate presentation, we relegate technical conditions and the details of proofs to the Appendix. We consider more generally the weighted L_1-penalized estimator with nonnegative weights $d_1, \cdots, d_p$. Let

$$L_n(\beta)=\sum_{i=1}^{n}\rho_{\mathbf{w}}\left(Y_i-\mathbf{X}_i^T\beta\right)+n\lambda_n\sum_{j=1}^{p}d_j|\beta_j| \tag{9}$$

denote the penalized quasi-likelihood function. The estimator in (5) is a particular case of (9) and corresponds to the case with $d_j=\gamma_\lambda(|\beta_j^{(0)}|)/\lambda_n$.

Without loss of generality, assume that parameter $\boldsymbol{\beta}^*$ can be arranged in the form of $\beta^*=(\beta_1^{*T},\mathbf{0}^T)^T$, with $\beta_1^* \in R^s$ a vector of non-vanishing elements of $\boldsymbol{\beta}^*$. Let us call $\widehat{\beta}^{\mathbf{o}}=(\widehat{\beta}_1^{\mathbf{o}T},\mathbf{0}^T)^T \in R^p$ the biased oracle estimator, where $\widehat{\beta}_1^{\mathbf{o}}$ is the minimizer of $L_n(\boldsymbol{\beta}_1, \mathbf{0})$ in R^s

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and $\mathbf{0}$ is the vector of all zeros in R^{p-s}. Here, we suppress the dependence of $\hat{\boldsymbol{\beta}}^{\mathbf{o}}$ on $\mathbf{w}$ and $\mathbf{d} = (d_1, \cdots, d_p)^T$. The estimator $\hat{\boldsymbol{\beta}}^{o}$ is called the biased oracle estimator, since the oracle knows the true submodel $\mathcal{M}_*=\{j:\beta_j^* \neq 0\}$, but nevertheless applies a penalized method to estimate the non-vanishing regression coefficients. The bias becomes negligible when the weights in the first part are zero or uniformly small (see Theorem 3.2). When the design matrix $\mathbf{S}$ is non-degenerate, the function $L_n(\beta_1, \mathbf{0})$ is strictly convex and the biased oracle estimator is unique, where $\mathbf{S}$ is a submatrix of $\mathbf{X}$ such that $\mathbf{X} = [\mathbf{S}, \mathbf{Q}]$ with $\mathbf{S}$ and $\mathbf{Q}$ being $n \times s$ and $n \times (p - s)$ sub-matrices of $\mathbf{X}$, respectively.

The following theorem shows that $\hat{\boldsymbol{\beta}}^{\mathbf{o}}$ is the unique minimizer of $L_n(\boldsymbol{\beta})$ on the whole space $\mathbf{R}^p$ with an overwhelming probability. As a consequence, $\hat{\boldsymbol{\beta}}_{\mathbf{w}}$ becomes the biased oracle. We establish the following theorem under conditions on the non-stochastic vector $\mathbf{d}$ (see Condition 2). It is also applicable to stochastic penalty weights as in (8); see the remark following Condition 2.

Theorem 3.1—Under Conditions 1–4, the estimators $\hat{\boldsymbol{\beta}}^{\mathrm{o}}$ and $\hat{\boldsymbol{\beta}}_{\mathbf{w}}$ exist and are unique on a set with probability tending to one. Furthermore,

$$P(\widehat{\beta}_{\mathbf{w}}=\widehat{\beta}^{\mathbf{o}}) \geq 1-(p-s)\exp\{-cn^{(\alpha_0-2\alpha_1)_+ +2\alpha_2}\}$$

for a positive constant c.

For the previous theorem to be nontrivial, we need to impose the dimensionality restriction $\delta < (\alpha_0 - 2\alpha_1)_+ + 2\alpha_2$, where α_1 controls the rate of growth of the correlation coefficients between the matrices $\mathbf{S}$ and $\mathbf{Q}$, the important predictors and unimportant predictors (see Condition 5) and $\alpha_2 \in [0, 1/2)$ is a non-negative constant, related to the maximum absolute value of the design matrix [see Condition 4]. It can be taken as zero and is introduced to deal with the situation where $(\alpha_0 - 2\alpha_1)_+$ is small or zero so that the result is non-trivial. The larger α_2 is, the more stringent restriction is imposed on the choice of λ_n. When the above conditions hold, the penalized composite quasi-likelihood estimator $\hat{\boldsymbol{\beta}}_{\mathbf{w}}$ is equal to the biased oracle estimator $\hat{\boldsymbol{\beta}}^{\mathbf{o}}$, with probability tending to one exponentially fast.

Remark 1: The result of Theorem 3.1 is stronger than the oracle property defined in Fan and Li (2001) once the properties of $\hat{\boldsymbol{\beta}}^{o}$ are established (see Theorem 3.2). It was formulated by Kim et al. (2008) for the SCAD estimator with polynomial dimensionality p. It implies not only the model selection consistency and but also sign consistency (Zhao and Yu, 2006; Bickel et al., 2008, 2009):

$$P(\mathrm{sgn}(\widehat{\beta}_{\mathbf{w}})=\mathrm{sgn}(\beta^*))=P(\mathrm{sgn}(\widehat{\beta}^{o})=\mathrm{sgn}(\beta^*)) \to 1.$$

In this way, the result of Theorem 3.1 nicely unifies the two approaches in discussing the oracle property in high dimensional spaces.

Let $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ and $\hat{\boldsymbol{\beta}}_{\mathbf{w}2}$ be the first s components and the remaining $p - s$ components of $\hat{\boldsymbol{\beta}}_{\mathbf{w}}$, respectively. According to Theorem 3.1, we have $\hat{\boldsymbol{\beta}}_{\mathbf{w}2} = \mathbf{0}$ with probability tending to one. Hence, we only need to establish the properties of $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$.

Theorem 3.2—Under Conditions 1–5, the asymptotic estimation loss of non-vanishing component $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ is controlled by $D_n = \max\{d_j: j \in \mathcal{M}_*\}$ with

$$\left\|\widehat{\beta}_{\mathbf{w}1}-\beta_1^*\right\|_2=O_P\left\{\sqrt{s}(\lambda_n D_n+n^{-1/2})\right\}.$$

Furthermore, when $0 \le \alpha_0 < 2/3$, $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ possesses asymptotic normality:

$$\mathbf{b}^T(\mathbf{S}^T\mathbf{S})^{1/2}\left(\widehat{\beta}_{\mathbf{w}1}-\beta_1^*\right)\xrightarrow{\mathcal{D}}\mathcal{N}(0,\sigma_{\mathbf{w}}^2) \tag{10}$$

where $\mathbf{b}$ is a unit vector in $\mathbb{R}^s$ and

$$\sigma_{\mathbf{w}}^2=\frac{\sum_{k,l=1}^K w_k w_l E[\psi_k(\varepsilon)\psi_l(\varepsilon)]}{\left(\sum_{k=1}^K w_k E[\partial\psi_k(\varepsilon)]\right)^2}. \tag{11}$$

Since the dimensionality s depends on n, the asymptotic normality of $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ is not well defined in the conventional probability sense. The arbitrary linear combination $\mathbf{b}^T\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ is used to overcome the technical difficulty. In particular, any finite component of $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ is asymptotically normal. The result in Theorem 3.2 is also equivalent to the asymptotic normality of the linear combination $\mathbf{B}^T\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ stated in Fan and Peng (2004), where $\mathbf{B}$ is a $q \times s$ matrix, for any given finite number q.

This theorem relates to the results of Portnoy (1985) in classical setting (corresponding to $p = s$) where he established asymptotic normality of M-estimators when the dimensionality is not higher than $o(n^{2/3})$.

3.2. Covariance Estimation

The asymptotic normality (10) allows us to do statistical inference for non-vanishing components. This requires an estimate of the asymptotic covariance matrix of $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$. Let $\hat{\boldsymbol{\varepsilon}} = \mathbf{Y} - \mathbf{S}^T\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ be the residual and $\hat{\varepsilon}_i$ be its i-th component. A simple substitution estimator of $\sigma_{\mathbf{w}}^2$ is

$$\widehat{\sigma}_{\mathbf{w}}^2=\frac{n\sum_{k,l=1}^K w_k w_l \sum_{i=1}^n \psi_k(\widehat{\varepsilon}_i)\psi_l(\widehat{\varepsilon}_i)}{\left(\sum_{k=1}^K w_k \sum_{i=1}^n \partial\psi_k(\widehat{\varepsilon}_i)\right)^2}.$$

See also the remark proceeding (7). Consequently, by (10), the asymptotic variance-covariance matrix of $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ is given by

$$\widehat{\sigma}_{\mathbf{w}}^2(\mathbf{S}^T\mathbf{S})^{-1}. \tag{12}$$

Another possible estimator of the variance and covariance matrix is to apply the standard sandwich formula. In Section 5, through simulation studies, we show that this formula has good properties for both p smaller and larger than n (see Tables 3 and 4 and comments at the end of Section 5.1).

3.3. Choice of weights

Note that only the factor $\sigma^2_{\mathbf{w}}$ in equation (11) depends on the choice of **w** and it is invariant to the scaling of **w**. Thus, the optimal choice of weights for maximizing efficiency of the estimator $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ is

$$\mathbf{w}_{opt}=\arg\min_{\mathbf{w}}\mathbf{w}^T\mathbf{M}\mathbf{w} \quad \text{s.t.} \quad \mathbf{a}^T\mathbf{w}=1, \quad \mathbf{w}\geq 0 \tag{13}$$

where **M** and **a** are defined in Section 2 using an initial estimator, independent of the weighting scheme **w**. Note that, the quadratic optimization problem (13) does not have a closed form solution, but can easily be solved numerically for a moderate *K*.

Remark 2—The above efficiency gain, over the least-squares, could be better understood from the likelihood point of view. Let $f(t)$ denote the unknown error density. The most efficient loss function is the unknown log-likelihood function, $-\log f(t)$. But since we have no knowledge of it, the set $\mathcal{F}_K$, consisting of convex combinations of $\{\rho_k(\cdot)\}_{k=1}^K$ given in (3), could be viewed as a collection of basis functions used to approximate it. The broader the set $\mathcal{F}_K$ is, the better it can approximate the log-likelihood function and the more efficient the estimator $\hat{\boldsymbol{\beta}}^a$ in (8) becomes. Therefore, we refer to $\rho_{\mathbf{w}}$ as the quasi-likelihood function.

3.4. One-step penalized estimator

The restriction of $\mathbf{w}\geq 0$ guarantees the convexity of $\rho_{\mathbf{w}}$ so that the problem (5) becomes a convex optimization problem. However, this restriction may cause substantial loss of efficiency in estimating $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ (see Table 1). We propose a one-step penalized estimator to overcome this drawback while avoiding non-convex optimization. Let $\hat{\boldsymbol{\beta}}$ be the estimator based on the convex combination of loss functions (5) and $\hat{\boldsymbol{\beta}}_1$ be its nonvanishing components. The one-step estimator is defined as

$$\widehat{\beta}^{\mathrm{OS}}_{\mathbf{w}1}=\widehat{\beta}_1-\left[\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)\right]^{-1}\Phi_{n,\mathbf{w}}(\widehat{\beta}_1), \quad \widehat{\beta}^{\mathrm{OS}}_{\mathbf{w}2}=\mathbf{0}, \tag{14}$$

where

$$\Phi_{n,\mathbf{w}}(\widehat{\beta}_1)=\sum_{i=1}^n\psi_{\mathbf{w}}(Y_i-\mathbf{S}_i^T\widehat{\beta}_1)\mathbf{S}_i, \text{ and } \Omega_{n,\mathbf{w}}(\widehat{\beta}_1)=\sum_{i=1}^n\partial\psi_{\mathbf{w}}(Y_i-\mathbf{S}_i^T\widehat{\beta}_1)\mathbf{S}_i\mathbf{S}_i^T.$$

Theorem 3.3—Under Conditions 1–5, if $\left\|\widehat{\beta}_1-\beta_1^*\right\|=O_P(\sqrt{s/n})$, then the one-step estimator $\widehat{\beta}^{os}_{\mathbf{w}}$ (14) enjoys the asymptotic normality:

$$\mathbf{b}^T(\mathbf{S}^T\mathbf{S})^{1/2}\left(\widehat{\beta}^{os}_{\mathbf{w}1}-\beta_1^*\right)\xrightarrow{\mathcal{D}}\mathcal{N}(0,\sigma^2_{\mathbf{w}}), \tag{15}$$

provided that $s = o(n^{1/3})$, $\partial\psi(\cdot)$ is Lipchitz continous, and $\lambda_{\max}(\sum_{i=1}^n\left\|\mathbf{S}\right\|_i\mathbf{S}_i\mathbf{S}_i^T)=O(n\sqrt{s})$, where $\lambda_{\max}(\cdot)$ denote the maximum eigenvalue of a matrix and $\sigma^2_{\mathbf{w}}$ is defined as in Theorem 3.2.

The one-step estimator (14) overcomes the convexity restriction and is always well defined, whereas (5) is not uniquely defined when convexity of $\rho_{\mathbf{w}}$ is ruined. Note that if we remove the constraint of $w_k \geq 0$ ($k = 1, \ldots, K$), the optimal weight vector in (13) is equal to

$$\mathbf{w}_{opt}=\mathbf{M}^{-1}\mathbf{a} \text{ and } \sigma^2_{\mathbf{w}_{opt}}=(\mathbf{a}^T\mathbf{M}^{-1}\mathbf{a})^{-1}.$$

This can be significantly smaller than the optimal variance obtained with convexity constraint, especially for multi-modal distributions (see Table 1).

The above discussion prompts a further improvement of the penalized adaptive composite quasi-likelihood in Section 2. Use (8) to compute the new residuals and new matrix **M** and vector **a**. Compute the optimal unconstrained weight $\mathbf{w}_{opt} = \mathbf{M}^{-1}\mathbf{a}$ and the one-step estimator (14).

4. Examples

In this section, we discuss two specific examples of penalized quasi-likelihood regression. The proposed methods are complementary, in the sense that the first one is computationally easy but loses some general flexibility while the second one is computationally intensive but efficient in a broader class of error distributions.

4.1. Penalized Composite L_1-L_2 regression

First, we consider the combination of L_1 and L_2 loss functions, that is, $\rho_1(t) = |t - b_0|$ and $\rho_2(t) = t^2$. The nuisance parameter b_0 is the median of the error distribution. Let $\widehat{\beta}_{\mathbf{w}}^{L_1-L_2}$ denote the corresponding penalized estimator as the solution to the minimization problem:

$$\arg\min_{\beta,b_0} w_1\sum_{i=1}^{n}\left|Y_i - b_0 - \mathbf{X}_i^T\beta\right| + w_2\sum_{i=1}^{n}\left(Y_i - \mathbf{X}_i^T\beta\right)^2 + n\sum_{j=1}^{p}\gamma_\lambda(|\beta_j^{(0)}|)|\beta_j|. \quad (16)$$

If the error distribution is symmetric, then $b_0 = 0$ and the minimization problem (16) can be recast as a penalized weighted least square regression

$$\arg\min_{\beta}\sum_{i=1}^{n}\left(\frac{w_1}{\left|Y_i - \mathbf{X}_i^T\widehat{\beta}^{(0)}\right|} + w_2\right)\left(Y_i - \mathbf{X}_i^T\beta\right)^2 + n\sum_{j=1}^{p}\gamma_\lambda(|\beta_j^{(0)}|)|\beta_j|$$

which can be efficiently solved by pathwise coordinate optimization (Friedman et al., 2008) or least angle regression (Efron et al., 2004).

If $b_0 \neq 0$, the penalized least-squares problem (16) is somewhat different from (5) since we have an additional parameter b_0. Using the same arguments, and treating b_0 as an additional parameter for which we solve in (16), we can show that the conclusions of Theorems 3.2 and 3.3 hold with the asymptotic variance equal to

$$\sigma^2_{L_1-L_2}(\mathbf{w})=\frac{w_1^2/4+w_2^2\sigma^2+w_2w_1B}{(w_1f(b_0)+w_2)^2}, \quad (17)$$

where $B = E[\varepsilon\,(I(\varepsilon > b_0) - I(\varepsilon < b_0))]$ and $f(\cdot)$ is the density of ε. This will hold when b_0 is either known or unknown. Explicit optimization of (17) is not trivial and we go through it as follows.

Since $\sigma^2_{L_1-L_2}(\mathbf{w})$ is invariant to the scale of $\mathbf{w}$, by setting $w_1/w_2 = c\sigma$, we have

$$\sigma^2_{L_1-L_2}(c)=\sigma^2\frac{c^2/4+1+a_\varepsilon c}{(b_\varepsilon c+1)^2}. \quad (18)$$

where $a_\varepsilon = B/\sigma$ and $b_\varepsilon = \sigma f(b_0)$. Note that

$$|B| \le E|\varepsilon|[I(\varepsilon>b_0)+I(\varepsilon<b_0)] \le \sigma.$$

Hence, $|a_\varepsilon| \le 1$ and $c^2/4+1+a_\varepsilon c=(c/2+a_\varepsilon)^2+1-a_\varepsilon^2 \ge 0$.

The optimal value of c over $[0, \infty)$ can be easily computed. If $a_\varepsilon b_\varepsilon < 0.5$, then the optimal value is obtained at

$$c_\varepsilon=2(2b_\varepsilon - a_\varepsilon)_+/(1-2a_\varepsilon b_\varepsilon). \quad (19)$$

In particular, when $2b_\varepsilon \le a_\varepsilon$, $c_\varepsilon = 0$, and the optimal choice is the least-squares estimator. When $a_\varepsilon b_\varepsilon = 0.5$, if $2b_\varepsilon \le a_\varepsilon$, then the minimizer is $c_\varepsilon = 0$. In all other cases, the minimizer is $c_\varepsilon = \infty$ i.e. we are left to use L_1 regression alone.

The above result shows the limitation of the convex combination, i.e. $c \ge 0$. In many cases, we are left alone with the least-squares or least absolute deviation regression without improving efficiency. The efficiency can be gained and achieved by allowing negative weights via the one-step technique as in Section 3.4. Let $g(c) = (c^2/4 + 1 + a_\varepsilon c)/(b_\varepsilon c + 1)^2$. The function $g(c)$ has a pole at $c = -1/b_\varepsilon$ and a unique critical point

$$c_{opt}=2(2b_\varepsilon - a_\varepsilon)/(1-2a_\varepsilon b_\varepsilon), \quad (20)$$

provided that $a_\varepsilon b_\varepsilon \ne 1/2$. Consequently, the function $g(c)$ can not have any local maximizer (otherwise, from the local maximizer to the point $c = -1/b_\varepsilon$, there must exist a local minimizer, which is also a critical point). Hence, the minimum value is attained at c_{opt}. In other words,

$$\min_w \sigma^2_{L_1-L_2}(\mathbf{w})=\sigma^2\min_c g(c)=d_\varepsilon\sigma^2, \quad (21)$$

where

$$d_\varepsilon = g(c_{opt}) = (1 - a_\varepsilon^2)/(4b_\varepsilon^2 - 4a_\varepsilon b_\varepsilon + 1). \tag{22}$$

Since the denominator can be written as $(a_\varepsilon - 2b_\varepsilon)^2 + (1 - a_\varepsilon^2)$, we have $d_\varepsilon \le 1$, namely, it outperforms the least-squares estimator, unless $a_\varepsilon = 2b_\varepsilon$. Similarly, it can be shown that

$$d_\varepsilon = \frac{1 - a_\varepsilon^2}{4b_\varepsilon^2[1 - a_\varepsilon^2 + (2a_\varepsilon - 1/b_\varepsilon)^2/4]} \le \frac{1}{4b_\varepsilon^2},$$

namely, it outperforms the least absolute deviation estimation, unless $a_\varepsilon b_\varepsilon = 1/2$.

Remark 3—When error distribution is symmetric unimodal, $b_\varepsilon \ge 1/\sqrt{12}$, according to Chapter 5 of Lehmann (1983). The worst scenario for the L_1-regression in comparison with the L_2-regression is the uniform distribution (see Chapter 5, Lehmann (1983)), which has the relatively efficiency of merely 1/3. For such uniform distribution, $a_\varepsilon = \sqrt{3}/2$ and $b_\varepsilon = 1/\sqrt{12}$, $d_\varepsilon = 3/4$, and $c_{opt} = -2/\sqrt{3}$. Hence, the best L_1-L_2 is 4 times better than L_1 regression alone. More comparisons about the weighted L_1-L_2 combination with L_1 and least-squares are given in Table 1(Section 4.3).

4.2. Penalized Composite Quantile Regression

The weighted composite quantile regression (CQR) was first studied by Koenker (1984) in classical statistical inference setting. Zou and Yuan (2008) used equally weighted CQR (ECQR) for penalized model selection with p large but fixed. We show that the efficiency of ECQR can be substantially improved by properly weighting and extend the work to the case of $p \gg n$. Consider K different quantiles, $0 < \tau_1 < \tau_2 < \ldots < \tau_K < 1$. Let $\rho_k(t) = \tau_k(t - b_k)_+ + (1 - \tau_k)(t - b_k)_-$. The penalized composite quantile regression estimator $\hat{\boldsymbol{\beta}}^{\mathrm{cqr}}$ is defined as the solution to the minimization problem

$$\arg\min_{b_1,\ldots,b_k,\beta} \sum_{k=1}^{K} w_k \sum_{i=1}^{n} \rho_k\left(Y_i - \mathbf{X}_i^T\beta\right) + n\sum_{j=1}^{p} \gamma_\lambda(|\beta_j^{(0)}|)|\beta_j|, \tag{23}$$

where b_k is the estimator of the nuisance parameter $b_k^* = F^{-1}(\tau_k)$, the τ_k-th quantile of the error distribution. Note that $b_1, \cdots, b_K$ are nuisance parameters and the minimization at (23) is done with respect to them too. After some algebra we can confirm that the conclusions of Theorems 3.2 and 3.3 continue to hold with the asymptotic variance as

$$\sigma_{\mathrm{cqr}}^2(\mathbf{w}) = \frac{\sum_{k,k'=1}^{K} w_k w_{k'}(\min(\tau_k, \tau_{k'}) - \tau_k\tau_{k'})}{\left(\sum_{k=1}^{K} w_k f(F^{-1}(\tau_k))\right)^2}. \tag{24}$$

As shown in Koenker (1984) and Bickel (1973), when $K \to \infty$, the optimally weighted CQR (WCQR) is as efficient as the maximum likelihood estimator, always more efficient than

ECQR. Computationally, the minimization problem in equation (23) can be casted as a large scale linear programming problem by expanding the covariate space with new ancillary variables. Thus, it is computationally intensive to use too many quantiles. In Section 4.3, we can see that usually no more than ten quantiles are adequate for WCQR to approach the efficiency of MLE, whereas determining the optimal value of K in ECQR seems difficult since the efficiency is not necessarily an increasing function of K (Table 2). Also, some of the weights in $\mathbf{w}_{opt}$ are zero, hence making WCQR method computationally less intensive than ECQR. From our experience in large p and small n situations, this reduction tends to be significant.

The optimal convex combination of quantile regression uses the weight

$$\mathbf{w}_{opt}^{+}=\operatorname{argmin}_{\mathbf{w}\geq 0,\mathbf{a}^{T}\mathbf{w}=1}\mathbf{w}^{T}\mathbf{M}\mathbf{w}, \tag{25}$$

where $\mathbf{a} = (f(F^{-1}(\tau_1)), \cdots, f(F^{-1}(\tau_K)))^T$ and $\mathbf{M}$ is a $K \times K$ matrix whose (i, j)-element is $\min(\tau_i, \tau_j) - \tau_i\tau_j$. The optimal combination of quantile regression, which is obtained by using the one-step procedure, uses the weight

$$\mathbf{w}_{opt}=\mathbf{M}^{-1}\mathbf{a}. \tag{26}$$

Clearly, both combinations improve the efficiency of ECQR and the optimal combination is most efficient among the three (see Table 1). When the error distributions are skewed or multimodal, the improvement can be substantial.

4.3. Asymptotic Efficiency Comparison

In this section, we studied the asymptotic efficiency of proposed estimators under several error distributions. For comparison, we also included L_1 regression, L_2 regression and ECQR. The error distribution ranges from the symmetric to asymmetric distributions: double exponential (DE), t distribution with degree of freedoms 4 (t_4), normal $\mathcal{N}(0, 1)$, Gamma $\Gamma(3, 1)$, Beta $\mathcal{B}(3, 5)$, a scale mixture of normals (MN_s) $0.1N(0, 25) + 0.9N(0, 1)$ and a location mixture of normals (MN_l) $0.7N(-1, 1) + 0.3N(7/3, 1)$. To keep the comparison fair and to satisfy the first assumption of mean zero error terms, we first centered the error distribution to have mean zero.

Table 1 shows the asymptotic relative efficiency of each estimator compared to MLE. $L_1 - L_2^{+}$ and L_1-L_2 indicate the optimal convex L_1-L_2 combination and optimal L_1-L_2 combination, respectively. While L_1 regression can have higher or lower efficiency than L_2 regression in different error distributions, $L_1 - L_2^{+}$ and L_1-L_2 regressions are consistently more efficient than both of them. WCQR$^+$ denote the optimal convex combination of multiple quantile regressions and WCQR represent the optimal combination. In all quantile regressions, quantiles $(\frac{1}{K+1}, \ldots, \frac{K}{K+1})$ were used. As shown in Table 1, WCQR$^+$ and WCQR always outperform ECQR and the differences are more significant in double exponential distribution and asymmetric distributions such as Gamma and Beta. In DE, t_4 and $\mathcal{N}(0, 1)$, nine quantiles are usually adequate for WCQR$^+$ and WCQR to achieve full efficiency. In $\Gamma(3, 1)$ and $\mathcal{B}(3, 5)$, they need 29 quantiles to achieve efficiency close to MLE while the other estimators are significantly inefficient. This difference is most expressed in multimodal distributions, MN_s and MN_l, with WCQR outperforming all. One of the possible problems with ECQR is that the efficiency does not necessarily increase with K, making the choice of K harder. For example, for the double exponential distribution, the relative efficiency decreases with K. This is understandable, as $K = 1$ is optimal: Putting more and odd number of quantiles dilutes the weights.

In Table 2 we illustrate both the adaptivity of the proposed composite QMLE methodology and computational efficiency of WCQR$^+$ over ECQR by showing the positions of zero of the optimal nonnegative weight vector $\mathbf{w}_{opt}^{+}$. For $K = 9$, only 1 quantile is needed in the DE case, 5 and 6 quantiles are needed for MN_l and MN_s and 7 quantiles for t_4, Gamma and Beta. Only in the normal distribution, all 9 quantiles are used. Therefore, WCQR$^+$ can dramatically reduce the computational complexity of ECQR in large scale optimization problems where $p \gg n$.

5. Finite Sample Study

5.1. Simulated example

In the simulation study, we consider the classical linear model for testing variable selection methods used by Fan and Li (2001)

$$y=\mathbf{x}^T\beta^*+\varepsilon,\ \ \mathbf{x}\sim N(0,\textstyle\sum_{\mathbf{x}}),\ \ (\textstyle\sum_{\mathbf{x}})_{i,j}=(0.5)^{|i-j|}.$$

The error vector varies from uni- to multi-modal and heavy to light tails distributions in the same way as in Tables 1 and 2, and is centered to have mean zero. The data has $n = 100$ observations. We considered two settings where $p = 12$ and $p = 500$, respectively. In both settings, $(\beta_1, \beta_2, \beta_5) = (3, 1.5, 2)$ and the other coefficients are equal to zero. We implemented penalized L_1, L_2, composite $L_1 - L_2^+$, L_1-L_2, ECQR, WCQR$^+$ and WCQR using quantiles (10%, 20%, ···, 90%). The local linear approximation of SCAD penalty (6) was used and the tuning parameter in the penalty was selected using five fold cross validation. We compared different methods by: (1) model error, which is defined as $\mathrm{ME}(\hat{\boldsymbol{\beta}}) = (\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}^*)^T E(\boldsymbol{X}^T\boldsymbol{X})(\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}^*)$; (2) the number of correctly classified non-zero coefficients, i.e. the true positive (TP); (3) the number of incorrectly classified zero coefficients, i.e. the false positive (FP); (4) the multiplier $\hat{\sigma}_{\mathbf{w}}$ of the standard error (SE)(12). A total of 100 replications were performed and the median of model error (MME), the average of TP and FP are reported in Table 3. The median model errors of oracle estimators were calculated as the benchmark for comparison.

From the results presented in Table 3 and Table 4, we can see that penalized composite $L_1 - L_2^+$ regression takes the smaller of the two model errors of L_1 and L_2 in all distributions except in $\mathcal{B}(3, 5)$ where it outperforms both. As expected, optimal L_1-L_2 outperforms $L_1 - L_2^+$ and brings a smaller number of FP, especially in multimodal and unsymmetric distributions. Also, both $L_1 - L_2^+$ and L_1-L_2 perform reasonably well when compared to ECQR, but with much less computational burden. WCQR$^+$ and WCQR in both Tables 3 and 4 have smaller model errors and smaller number of false positives than ECQR. Similar conclusions can be made from Figure 1, which compares the boxplots of the model errors of the five methods (WCQR$^+$ and $L_1 - L_2^+$ are not shown) under different distributions in the case of $n = 100$, $p = 500$. For $p \ll n$ in Table 3 we didn't include LASSO estimator since it behaves reasonably well in that setting. For $p \gg n$ in Table 4, we included LASSO estimator as a reference. Table 4 shows that LASSO has bigger model errors, more false positives and higher standard errors (usually by a factor of 10) than any other five SCAD based methods discussed.

In addition to the ME in Tables 3 and 4, we reported the multiplier $\hat{\sigma}_{\mathbf{w}}$ of the asymptotic variance (see equation (12)). Being the only part of SE that depends on the choice of weights $\mathbf{w}$ and loss functions ρ_k, we explored it's behavior when the dimensionality grows from $p \ll n$ to $p \gg n$. Both Tables 3 and 4 confirm the stability of the formula throughout the two settings and all five CQMLE methods. Only Lasso estimator being unable to specify the correct sparsity set when $p \gg n$, inflates $\hat{\sigma}_{\mathbf{w}}$ for one order of magnitude compared to other CQMLEs. Note that WCQR$^+$ keeps the smallest value of $\hat{\sigma}_{\mathbf{w}}$ and all L_1-L_2, $L_1 - L_2^+$, WCQR and WCQR$^+$ have smaller SEs than the classical L_1, L_2 or ECQR methods.

5.2. Real Data Example

In this section, we applied proposed methods to expression quantitative trait locus (eQTL) mapping. Variations in gene expression levels may be related to phenotypic variations such as susceptibility to diseases and response to drugs. Therefore, to understand the genetic basis of gene expression, variation is an important topic in genetics. The availability of genome-wide single nucleotide polymorphism (SNP) measurement has made it possible and reasonable to perform the high resolution eQTL mapping on the scale of nucleotides. In our analysis, we conducted the *cis*-eQTL mapping for the gene CCT8. This gene is located within the Down Syndrome Critical Region on human chromosome 21, on the minus strand. The over expression of CCT8 may be associated with Down syndrome phenotypes.

We used the SNP genotype data and gene expression data for the 210 unrelated individuals of the International HapMap project (International HapMap Consortium, 2003), which include 45 Japanese in Tokyo, Japan, 45 Han Chinese in Beijing, China, 60 Utah parents with ancestry from northern and western Europe (CEPH) and 60 Yoruba parents in Ibadan, Nigeria and they are available in PLINK format (Purcell, et al 2007) [http://pngu.mgh.harvard.edu/purcell/plink/]. We included in the analysis more than 2 million SNPs with minor allele frequency greater than 1% and missing data rate less than 5%. The gene expression data were generated by Illumina Sentrix Human-6 Expression BeadChip and have been normalized (ith quantile normalization across replicates and median normalization across individuals) independently for each population (Stranger, et al 2007) [ftp://ftp.sanger.ac.uk/pub/genevar/].

Specifically, we considered the *cis*-candidate region to start 1 Mb upstream of the transcription start site (TSS) of CCT8 and to end 1 Mb downstream of the transcription end site (TES), which includes 1955 SNPs in Japanese and Chinese, 1978 SNPs in CEPH and 2146 SNPs in Yoruba. In the following analysis, we grouped Japanese and Chinese together into the Asian population and analyzed the three populations Asian, CEPH and Yoruba separately. The additive coding of SNPs (e.g. 0,1,2) was adopted and was treated as categorical variables instead of continuous ones to allow non-additive effects, i.e., two dummy variables will be created for categories 1 and 2 respectively. The category 0 represents the major, normal population. The missing SNP measurements were imputed as 0's. The response variable is the gene expression level of gene CCT8, measured by microarray.

In the first step, the ANOVA F-statistic was computed for each SNP independently and a version of independent screening method of Fan and Lv (2008) was implemented. This method is particularly computationally efficient in ultra-high dimensional problems and here we retained the top 100 SNPs with the largest F-statistics. In the second step, we applied to the screened data the penalized L_2, L_1, $L_1 - L_2^+$, L_1-L_2, ECQR, WCQR$^+$ and WCQR with local linear approximation of SCAD penaly. All the four composite quantile regressions used quantiles at (10%, …, 90%). LASSO was used as the initial estimator and the tuning parameter in both LASSO and SCAD penalty was chosen by five fold cross validation. In all the three populations, the L_1-L_2 and $L_1 - L_2^+$ regressions reduced to L_2 regression. This is not unexpected due to the gene expression normalization procedure. In addition, WCQR reduced to WCQR$^+$. The selected SNPs, their coefficients and distances from transcription starting site (TSS) are summarized in Tables 5, 6 and 7.

In Asian population (Table 5), the five methods are reasonably consistent in not only variables selection but also coefficients estimation (in terms of signs and order of magnitude). WCQR uses the weights (0.19, 0.11, 0.02, 0, 0.12, 0.09, 0.18, 0.19, 0.10). There are four SNPs chosen by all five methods. Two of them, rs2832159 and rs2245431, up-regulate gene expression, while rs9981984 and rs16981663 down-regulate gene expression. The ECQR selects the largest set of SNPs, while L_1 regression selects the smallest set.

In CEPH population (Table 6), all five methods consistently selected the same seven SNPs with only ECQR choosing two additional SNPs. WCQR uses the weight (0.19, 0.21, 0, 0.04, 0.03, 0.07, 0.1, 0.21, 0.15). The coefficient estimations were also highly consistent. Deutsch et al (2007) performed a similar *cis*-eQTL mapping for the gene CCT8 using the same CEPH data as here. They considered a 100kb region surrounding the gene, which contains 41 SNPs. Using ANOVA with correction for multiple tests, they identified four eQTLs, rs965951, rs2832159, rs8133819 and rs2832160, among which rs965951 possessing the smallest p-value. Our analysis verified rs965951 to be an eQTL but did not find the other SNPs to be associated with the gene expression of CCT8. In other words, conditioning on the presence of SNP rs965951 the other three make little additional contributions.

The analysis of Yoruba population yields a large number of eQTLs (Table 7). The ECQR again selects the largest set of 44 eQTLs. The L_1 regression selects 38 eQTLs. The L_2 regression and WCQR both select 27 SNPs, 26 of which are the same. WCQR uses the weight (0.1, 0, 0.17, 0.16, 0.11, 0.3, 0, 0, 0.16). The coefficients estimated by different methods are mostly consistent (in terms of signs and order of magnitude), except that the coefficients estimates for rs8134601, rs7281691, rs6516887 and rs2832159 by ECQR and L_1 have different signs from those of L_2 and WCQR.

The eQTLs are almost all located within 500kb upstream TSS or 500kb downstream TES (Figure 2) and from 100kb upstream TSS to 350 kb downstream TES.

6. Discussion

In this paper, a robust and efficient penalized quasi-likelihood approach is introduced for model selection with NP-dimensionality. It is shown that such an adaptive learning technique has a strong oracle property. As specific examples, two complementary methods of penalized composite L_1-L_2 regression and weighted composite quantile regression are introduced and they are shown to possess good efficiency and model selection consistency in ultrahigh dimensional space. Numerical studies show that our method is adaptive to unknown error distributions and outperforms LASSO (Tibshirani, 1996) and equally weighted composite quantile regression (Zou and Yuan, 2008).

The penalized composite quasi-likelihood method can also be used in sure independence screening (Fan and Lv, 2008; Fan and Song, 2010) or iterated version (Fan, et al, 2009), resulting in a robust variable screening and selection. In this case, the marginal regression coefficients or contributions will be ranked and thresholded. It can also be applied to the aggregation problems of classification (Bickel et al., 2009) where the usual L_2 risk function could be replaced with composite quasi-likelihood function. The idea can also be used to choose the loss functions in machine learning. For example, one can adaptively combine the hinge-loss function in the support vector machine, the exponential loss in the AdaBoost, and the logistic loss function in logistic regression to yield a more efficient classifier.

Acknowledgments

We are grateful to the referees, the Associate Editor and the Joint Editor for their many helpful comments. This research was partially supported by NSF Grants DMS-0704337 and DMS- 0714554 and NIH Grant R01-GM072611. The bulk of the work was conducted while Weiwei Wang was a postdoctoral fellow at Princeton University.

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Appendix A: Regularity Conditions

Let D_k be the set of discontinuity points of $\psi_k(t)$, which is a subgradient of ρ_k. Assume that the distribution of error terms F_ε is smooth enough so that $F_\varepsilon(\cup_{k=1}^K D_k)=0$. Additional regularity conditions on ψ_k are needed, as in Bai et al. (1992).

Condition 1

The function ψ_k satisfies $E[\psi_k(\varepsilon_1+c)] = a_k c+o(|c|)$ as $|c| \to 0$, for some $a_k > 0$. For sufficiently small $|c|$, $g_{kl}(c) = E[(\psi_k(\varepsilon_1 + c) - \psi_k(\varepsilon_1))(\psi_l(\varepsilon_1 + c) - \psi_l(\varepsilon_1))]$ exists and is continuous at $c = 0$, where $k, l = 1, \ldots, K$. The error distribution satisfies the following Cramér condition: $E|\psi_{\mathbf{w}}(\varepsilon_i)|^m \le m!RK^{m-2}$, for some constants R and K.

This condition implies that $E\psi_k(\varepsilon_i) = 0$, which is an unbiased score function of parameter $\boldsymbol{\beta}$. It also implies that $E\partial\psi_k(\varepsilon_i) = a_k$ exists. The following two conditions are important for establishing sparsity properties of parameter $\hat{\boldsymbol{\beta}}_{\mathbf{w}}$ by controlling the penalty weighting scheme $\mathbf{d}$ and the regularization parameter λ_n.

Condition 2

Assume that $D_n = \max\{d_j: j \in \mathcal{M}_*\} = o(n^{\alpha_1-\alpha_0/2})$ and $\lambda_n D_n = O(n^{-(1+\alpha_0)/2})$. In addition, $\liminf \min\{d_j: j \in \mathcal{M}_*^c\}>0$.

The first statement is to ensure that the bias term in Theorem 3.2 is negligible. It is needed to control the bias due to the convex penalty. The second requirement is to make sure that the weights $\mathbf{d}$ in the second part are uniformly large so that the vanishing coefficients are estimated as zero. It can also be regarded as a normalization condition, since the actual weights in the penalty are $\{\lambda_n d_j\}$.

Remark 3

The LASSO estimator will not satisfy the first requirement of Condition 2 unless λ_n is small and $\alpha_1 > \alpha_0/2$. However, note that the result of Theorem 3.1 applies to LASSO estimator as well ($d_j = 1$). Moreover, under the sparse representation condition (Zhao and Yu, 2006), Fan and Lv (2010) show that with probability tending to one, the LASSO estimator is model selection consistent with $\|\widehat{\beta}_1 - \beta_1^*\|_\infty = O(n^{-\gamma}\log n)$, when the minimum signal

$\beta_n^* = \min\{|\beta_j^*|, j \in \mathcal{M}_*\} \geq n^{-\gamma}\log n$. They also show that the same result holds for the SCAD-type estimators under weaker conditions. Using one of them as the initial estimator, the weight $d_j = \gamma_\lambda(\widehat{\beta_j^0})/\lambda$ in (8) would satisfy Condition 2, on a set with probability tending to one, for γ_λ being LLA SCAD. This is due to the fact that with γ_λ (·) given by (6), for $j \in \mathcal{M}_*^c$, $d_j = \gamma_\lambda(0)/\lambda = 1$, whereas for $j \in \mathcal{M}_*$, $d_j \leq \gamma_\lambda(\beta_n^*/2)/\lambda = 0$, as long as $\beta_n^* \gg n^{-\gamma}\log n = O(\lambda_n)$. In other words, the results of Theorems 3.1 and 3.2 are applicable to the penalized estimator (8) with data driven random weights. In that sense, Condition 2 can be regarded as a condition on the choice of the weighting function γ_λ.

Condition 3

The regularization parameter $\lambda_n \gg n^{-1/2+(\alpha_0-2\alpha_1)_+/2+\alpha_2}$, where parameter α_1 is defined in Condition 5 and $\alpha_2 \in [0, 1/2)$ is a constant, bounded by the restriction in Condition 4.

We use the following notation throughout the proof. Let **B** be a matrix. Denote by $\lambda_{\min}(\mathbf{B})$ and $\lambda_{\max}(\mathbf{B})$ the minimum and maximum eigenvalue of the matrix **B** when it is a square symmetric matrix. Let $\|\mathbf{B}\| = \lambda_{\max}^{1/2}(\mathbf{B}^T\mathbf{B})$ be the operator norm and $\|\mathbf{B}\|_\infty$ the largest absolute value of the elements in **B**. As a result, $\|\cdot\|$ is the Euclidean norm when applied to a vector. Define $\|\mathbf{B}\|_{2,\infty} = \max_{\|\mathbf{v}\|_2=1} \|\mathbf{B}\mathbf{v}\|_\infty$.

Condition 4

The matrix $\mathbf{S}^T\mathbf{S}$ satisfies $C_1 n \leq \lambda_{\min}(\mathbf{S}^T\mathbf{S}) \leq \lambda_{\max}(\mathbf{S}^T\mathbf{S}) \leq C_2 n$ for some positive constants C_1, C_2. There exists $\xi > 0$ such that

$$\sum_{i=1}^{n} (\|\mathbf{S}_i\| / n^{1/2})^{(2+\xi)} \to 0,$$

where $\mathbf{S}_i^T$ is the i-th row of **S**. Furthermore, assume that the design matrix satisfies $\|\mathbf{X}\|_\infty = O(n^{1/2-(\alpha_0-2\alpha_1)_+/2-\alpha_2})$ and $\max_{j \notin \mathcal{M}_*} \|\mathbf{X}_j^*\|^2 = O(n)$, where $\mathbf{X}_j^*$ is the j-th column of **X**.

Condition 5

Assume that

$$\sup_{\beta \in \mathcal{B}(\beta_1^*, \beta_n^*)} \|\mathbf{Q}\, diag\{\partial \boldsymbol{\psi}_{\mathbf{w}}(\beta)\}\mathbf{S}\|_{2,\infty} = O(n^{1-\alpha_1}).$$
$$\max_{\beta \in \mathcal{B}(\beta_1^*, \beta_n^*)} \lambda_{\min}^{-1}\left(\mathbf{S}^T diag\{\partial \boldsymbol{\psi}_{\mathbf{w}}(\beta)\}\mathbf{S}\right) = O_p(n^{-1}),$$

where $\mathcal{B}(\beta_1^*, \beta_n^*)$ is an s-dimensional ball centered at β_1^* with radius β_n^* and $diag(\partial \boldsymbol{\psi}\mathbf{w}(\boldsymbol{\beta}))$ is the diagonal matrix with i-th element equal to $\partial\psi_{\mathbf{w}}(Y_i - \mathbf{S}_i^T\beta)$.

Appendix B: Lemmas

Recall that $\mathbf{X} = (\mathbf{S}, \mathbf{Q})$ and $\mathcal{M}_* = \{1, \cdots, s\}$ is the true model.

Lemma 6.1

Under Conditions 2 and 4, the penalized quasi-likelihood $L_n(\boldsymbol{\beta})$ defined by (9) has a unique global minimizer $\widehat{\beta}=(\widehat{\beta}_1^T, \mathbf{0}^T)^T$, if

$$\sum_{i=1}^{n} \psi_{\mathbf{w}}\left(Y_i - \mathbf{X}_i^T \widehat{\beta}\right) \mathbf{S}_i + n\lambda_n \mathbf{d}_{\mathcal{M}_*} \circ sgn(\widehat{\beta}_1)=\mathbf{0}, \tag{B.1}$$

$$\left\|\mathbf{z}(\widehat{\beta})\right\|_\infty < n\lambda_n, \tag{B.2}$$

where $\mathbf{z}(\widehat{\beta})=\mathbf{d}_{\mathcal{M}_*^c}^{-1} \circ \sum_{i=1}^{n} \psi_{\mathbf{w}}\left(Y_i - \mathbf{X}_i^T \widehat{\beta}\right) \mathbf{Q}_i$, $\mathrm{d}_{\mathcal{M}_*}$ and $\mathbf{d}_{\mathcal{M}_*^c}$ stand for the subvectors of $\mathbf{d}$, consisting of its first s elements and the last p − s elements respectively, and sgn and ∘ (the Hadamard product) in (B.1) are taken coordinatewise. Conversely, if $\hat{\boldsymbol{\beta}}$ is a global minimizer of $L_n(\boldsymbol{\beta})$, then (B.1) holds and (B.2) holds with strict inequality replaced with non-strict one.

Proof of Lemma 6.1

Under conditions 2 and 4, $L_n(\boldsymbol{\beta})$ is strictly convex. Necessary conditions (B.1) and (B.2) are direct consequences of the Karush-Kuhn-Tucker conditions of optimality. The sufficient condition follows from similar arguments as those in the proof of Theorem 1 in Fan and Lv (2010) and the strict convexity of the function $L(\boldsymbol{\beta})$.

Lemma 6.2

Under Conditions 1–5 we have that biased oracle estimator $\hat{\boldsymbol{\beta}}^{\mathbf{o}}$ exists, is unique and satisfies

$$\left\|\widehat{\beta}^{\mathbf{o}} - \beta^*\right\|_2 = O_P\left(\sqrt{s/n} + \lambda_n \left\|\mathbf{d}_0\right\|\right),$$

where $\mathbf{d}_0$ is the subvector of $\mathbf{d}$, consisting of its first s elements.

Proof of Lemma 6.2

Since $\widehat{\beta}_2^{\mathbf{o}}=\beta_2^*=0$, we only need to consider the subvector of the first s components. Let us first show the existence of the biased oracle estimator. We can restrict our attention to the s-dimensional subspace $\{\boldsymbol{\beta} \in \mathbb{R}^p: \beta_{\mathcal{M}_0^c}=\mathbf{0}\}$. Our aim is to show that

$$P\left(\inf_{\left\|\mathbf{u}\right\|=1} L_n(\beta_1^* + \gamma_n \mathbf{u}, \mathbf{0}) > L_n(\beta^*)\right) \to 1, \tag{B.3}$$

for sufficiently large γ_n. Here, there is a minimizer inside the ball $\left\|\beta_1 - \beta_1^*\right\| < \gamma_n$, with probability tending to one. Using the strict convexity of $L_n(\boldsymbol{\beta})$, this minimizer is the unique global minimizer.

By the Taylor expansion at $\gamma_n = 0$, we have

$$L_n(\beta_1^*+\gamma_n\mathbf{u},\mathbf{0}) - L_n(\beta_1^*,\mathbf{0})=T_1+T_2,$$

where

$$\begin{aligned}T_1=&-\gamma_n\sum_{i=1}^n\psi_{\mathbf{w}}(\varepsilon_i)\mathbf{S}_i^T\mathbf{u}+\frac{1}{2}\gamma_n^2\sum_{i=1}^n\partial\psi_{\mathbf{w}}(\varepsilon_i-\overline{\gamma}_n\mathbf{S}_i^T\mathbf{u})(\mathbf{S}_i^T\mathbf{u})^2\\ =&-I_1+I_2\\ T_2=&n\lambda_n\sum_{j=1}^s d_j(|\beta_j^*+\gamma_n u_j|-|\beta_j^*|).\end{aligned}$$

where $\bar{\gamma}_n \in [0, \gamma_n]$. By the Cauchy-Schwarz inequality,

$$|T_2| \le n\gamma_n\lambda_n\left\|\mathbf{d}_0\right\|\left\|\mathbf{u}\right\|=n\gamma_n\lambda_n\left\|\mathbf{d}_0\right\|.$$

Note that for all $\|\mathbf{u}\| = 1$, we have

$$|I_1| \le \gamma_n\left|\left|\sum_{i=1}^n\psi_{\mathbf{w}}(\varepsilon_i)\mathbf{S}_i\right|\right|$$

and

$$E\left|\left|\sum_{i=1}^n\psi_{\mathbf{w}}(\varepsilon_i)\mathbf{S}_i\right|\right| \le \left(E\psi_{\mathbf{w}}^2(\varepsilon)\sum_{i=1}^n\left\|\mathbf{S}_i\right\|^2\right)^{1/2}=\left(E\psi_{\mathbf{w}}^2(\varepsilon)\mathrm{tr}(\mathbf{S}^T\mathbf{S})\right)^{1/2},$$

which is of order $O(\sqrt{ns})$ by Condition 4. Hence, $I_1=O_p(\gamma_n\sqrt{ns})$ uniformly in $\mathbf{u}$.

Finally, we deal with I_2. Let $H_i(c) = \inf_{|v|\le c}\{\partial\psi_{\mathbf{w}}(\varepsilon_i - v)\}$. By Lemma 3.1 of Portnoy (1984), we have

$$\begin{aligned}I_2 \ge& \gamma_n^2\sum_{i=1}^n H_i(\gamma_n|\mathbf{S}_i^T\mathbf{u}|)(\mathbf{S}_i^T\mathbf{u})^2\\ \ge& c\gamma_n^2 n,\end{aligned}$$

for a positive constant c. Combining all of the above results, we have with probability tending to one that

$$L_n(\beta_1^*+\gamma_n\mathbf{u},\mathbf{0}) - L_n(\beta_1^*,\mathbf{0}) \ge n\gamma_n\{c\gamma_n - O_P(\sqrt{s/n}) - \lambda_n\left\|\mathbf{d}_0\right\|\},$$

where the right hand side is larger than 0 when $\gamma_n = B(\sqrt{s/n} + \lambda_n \|\mathbf{d}_0\|)$ for a sufficiently large $B > 0$. Since the objective function is strictly convex, there exists a unique minimizer $\widehat{\beta}_1^o$ such that

$$\left\|\widehat{\beta}_1^o - \beta_1^*\right\| = O_P(\sqrt{s/n} + \lambda_n \|\mathbf{d}_0\|).$$

Lemma 6.3

Under the conditions of Theorem 3.2, for any s-dimensional unit vector **b** the following holds

$$[\mathbf{b}^T \mathbf{A}_n \mathbf{b}]^{-1/2} \sum_{i=1}^{n} \psi_{\mathbf{w}}(\varepsilon_i) \mathbf{b}^T \mathbf{S}_i \xrightarrow{\mathcal{D}} \mathcal{N}(0,1) \tag{B.4}$$

with $\mathbf{A}_n = E\psi_{\mathbf{w}}^2(\varepsilon)\mathbf{S}^T\mathbf{S}$ and $\mathcal{D}$ denoting convergence in distribution.

Proof of Lemma 6.3

By Condition 1, since $\mathbf{S}_i$ is independent of $\psi_{\mathbf{w}}(\varepsilon_i)$, we have $E\psi_{\mathbf{w}}(\varepsilon_i)\mathbf{S}_i = 0$, and

$$\mathrm{Var}\left[[\mathbf{b}^T \mathbf{A}_n \mathbf{b}]^{-1/2} \sum_{i=1}^{n} \psi_{\mathbf{w}}(\varepsilon_i) \mathbf{b}^T \mathbf{S}_i\right] = 1. \tag{B.5}$$

To complete proof of the lemma, we only need to check the Lyapounov condition. By Condition 1, $E|\psi_{\mathbf{w}}(\varepsilon)|^{2+\xi} < \infty$. Furthermore, Condition 4 implies

$$\mathbf{b}^T \mathbf{A}_n \mathbf{b} = E\psi_{\mathbf{w}}^2(\varepsilon)\mathbf{b}^T \mathbf{S}\mathbf{S}^T \mathbf{b} \geq c_1 n,$$

for a positive constant c_1. Using these together with the Cauchy-Schwartz inequality, we have

$$\begin{aligned}\sum_{i=1}^{n} E\left|[\mathbf{b}^T \mathbf{A}_n \mathbf{b}]^{-1/2} \psi_{\mathbf{w}}(\varepsilon_i) \mathbf{b}^T \mathbf{S}_i\right|^{2+\xi} &= O(1) \sum_{i=1}^{n} \left|n^{-1/2} \mathbf{b}^T \mathbf{S}_i\right|^{2+\xi} \\ &= O(1) \sum_{i=1}^{n} \left|n^{-1/2} \|\mathbf{S}_i\|\right|^{2+\xi}\end{aligned}$$

which tends to zero by Condition 4. This completes the proof.

The following Bernstein's inequality can be found in Lemma 2.2.11 of der Vaart and Wellner (1996).

Lemma 6.4

Let $Y_1, \cdots, Y_n$ be independent random variables with zero mean such that $E|Y_i|^m \le m! M^{m-2} v_i/2$, for every $m \ge 2$ (and all i) and some constants M and v_i. Then

$$P(|Y_1+\cdots+Y_n|>t) \le 2\exp\{-\frac{t^2}{2(v+Mt)}\},$$

for $v \ge v_1 + \cdots v_n$.

Then the following inequality (B.6) is a consequence of previous Bernstein's inequality. Let $\{Y_i\}$ satisfy the condition of Lemma 6.4 with $v_i \equiv 1$. For a given sequence $\{a_i\}$, $E|a_i Y_i|^m \le m!|a_i M|^{m-2} a_i^2/2$. A direct application of Lemma 6.4 yields

$$P(|a_1 Y_1+\cdots+a_n Y_n|>t) \le 2\exp\{-\frac{t^2}{2(\sum_{i=1}^n a_i^2+M\max_i|a_i|t)}\}. \tag{B.6}$$

Appendix C: Proofs of Theorems

Proof of Theorem 3.1

We only need to show that $\hat{\boldsymbol{\beta}}^o$ is the unique minimizer of $L(\boldsymbol{\beta})$ in $\mathbb{R}^p$ on a set Ω_n which has a probability tending to one. Since $\widehat{\beta}_1^o$ already satisfies (B.1), we only need to check (B.2).

We now define the set Ω_n. Let

$$\boldsymbol{\xi}=(\xi_1,\cdots,\xi_p)^T=\sum_{i=1}^n \psi_{\mathbf{w}}\left(Y_i-\mathbf{X}_i^T\beta^*\right)\mathbf{X}_i$$

and consider the event $\Omega_n=\left\{\|\boldsymbol{\xi}_{\mathcal{M}_*^c}\|_\infty \le u_n\sqrt{n}\right\}$ with u_n being chosen later. Then, by Condition 1 and Bernstein's inequality, it follows directly from (B.6) that

$$P\{|\xi_j|>t\} \le 2\exp\left\{-\frac{t^2}{2(\left\|\mathbf{X}_j^*\right\|^2 R+tK\left\|\mathbf{X}_j^*\right\|_\infty)}\right\},$$

where $\mathbf{X}_j^*$ is the j-th column of $\mathbf{X}$. Taking $t=u_n\sqrt{n}$, we have

$$P\{|\xi_j|>u_n\sqrt{n}\} \le 2\exp\left\{-\frac{u_n^2}{2(R\left\|\mathbf{X}_j^*\right\|^2/n+Ku_n\left\|\mathbf{X}_j^*\right\|_\infty/\sqrt{n})}\right\} \le e^{-cu_n^2}, \tag{C.1}$$

for some positive constant $c > 0$, by Condition 4. Thus, by using the union bound, we conclude that

$$P(\Omega_n) \geq 1 - \sum_{j \in \mathcal{M}_*^c} P\{|\xi_j| > u_n \sqrt{n}\} \geq 1 - 2(p - s)e^{-cu_n^2}.$$

We now check whether (B.1) holds on the set Ω_n. Let $\boldsymbol{\Psi}_{\mathbf{w}}(\boldsymbol{\beta})$ be the n-dimensional vector with the i-th element $\psi_{\mathbf{w}}(Y_i - \mathbf{X}_i^T\beta)$. Then, by Condition 2

$$\begin{aligned}\left\|\mathbf{z}(\widehat{\beta}^o)\right\|_\infty &\leq \|\mathbf{d}_{\mathcal{M}_*^c}^{-1} \circ \boldsymbol{\xi}_{\mathcal{M}_*^c}\|_\infty + \|\mathbf{d}_{\mathcal{M}_*^c}^{-1} \circ \mathbf{Q}^T[\boldsymbol{\psi}_{\mathbf{w}}(\widehat{\beta}^o) - \boldsymbol{\psi}_{\mathbf{w}}(\beta^*)]\|_\infty \\ &= O\left(n^{1/2}u_n + \|\mathbf{Q}^T \mathrm{diag}(\partial\boldsymbol{\psi}_{\mathbf{w}}(\mathbf{v}))\mathbf{S}(\widehat{\beta}_1^o - \beta_1^*)\|_\infty\right)\end{aligned} \tag{C.2}$$

where $\mathbf{v}$ lies between $\hat{\boldsymbol{\beta}}^o$ and β_1^*. By Condition 5, the second term in (C.2) is bounded by

$$O(n^{1-\alpha_1})\left\|\widehat{\beta}_1^o - \beta_1^*\right\| = O_P\{n^{1-\alpha_1}(\sqrt{s/n} + \lambda_n\left\|\mathbf{d}_0\right\|)\},$$

where the equality follows from Lemma 6.2. By the choice of parameters,

$$(n\lambda_n)^{-1}\left\|\mathbf{z}(\widehat{\beta}^o)\right\|_\infty = O\{n^{-1/2}\lambda_n^{-1}(u_n + n^{(\alpha_0 - 2\alpha_1)/2}) + D_n n^{\alpha_0/2 - \alpha_1}\} = o(1),$$

by taking $u_n = n^{(\alpha_0 - 2\alpha_1)_+/2 + \alpha_2}$. Hence, by Lemma 6.1, $\hat{\boldsymbol{\beta}}^o$ is the unique global minimizer.

Proof of Theorem 3.2

By Theorem 3.1, $\widehat{\beta}_{\mathbf{w}1} = \widehat{\beta}_1^o$ almost surely. It follows from Lemma 6.2 that

$$\left\|\widehat{\beta}_{\mathbf{w}1} - \beta_1^*\right\| = O_P\{\sqrt{s}(\lambda_n D_n + 1/\sqrt{n})\}.$$

This establishes the first part of the Theorem.

Let $Q_n(\beta_1) = \sum_{i=1}^n \psi_{\mathbf{w}}(Y_i - \mathbf{S}_i^T\beta_1)\mathbf{S}_i$. By Taylor's expansion at the point β_1^*, we have

$$Q_n(\widehat{\beta}_{\mathbf{w}1}) = Q_n(\beta_1^*) + \partial Q_n(\mathbf{v})(\widehat{\beta}_{\mathbf{w}1} - \beta_1^*),$$

where $\mathbf{v}$ lies between the points $\hat{\boldsymbol{\beta}}_{\mathbf{w}1}$ and β_1^* and

$$\partial Q_n(\mathbf{v}) = -\sum_{i=1}^{n} \partial\psi_{\mathbf{w}}(Y_i - \mathbf{S}_i^T\mathbf{v})\mathbf{S}_i\mathbf{S}_i^T. \tag{C.3}$$

By Lemma 6.2, $\left\|\mathbf{v} - \beta_1^*\right\| \le \left\|\widehat{\beta}_{\mathbf{w}1} - \beta_1^*\right\| = o_P(1)$.

By using (B.2), we have

$$Q_n(\widehat{\beta}_{\mathbf{w}1}) + n\lambda_n\mathbf{d}_0 \circ \mathrm{sgn}(\widehat{\beta}_{\mathbf{w}1}) = 0,$$

or equivalently,

$$\widehat{\beta}_{\mathbf{w}1} - \widehat{\beta}_1^* = -\partial Q_n(\mathbf{v})^{-1}Q_n(\beta_1^*) - \partial Q_n(\mathbf{v})^{-1}n\lambda_n\mathbf{d}_0 \circ \mathrm{sgn}(\widehat{\beta}_{\mathbf{w}1}). \tag{C.4}$$

Note that $\|\mathbf{d}_0 \circ \mathrm{sgn}(\hat{\boldsymbol{\beta}}_{\mathbf{w}1})\| = \|\mathbf{d}_0\|$. We have for any vector $\mathbf{u}$,

$$\left|\mathbf{u}^T\partial Q_n(\mathbf{v})^{-1}\mathbf{d}_0 \circ \mathrm{sgn}(\widehat{\beta}_{\mathbf{w}1})\right| \le \left\|\partial Q_n(\mathbf{v})^{-1}\right\| \cdot \left\|\mathbf{u}\right\| \cdot \left\|\mathbf{d}_0\right\|.$$

Consequently, for any unit vector $\mathbf{b}$,

$$\begin{aligned}\|\mathbf{b}^T(\mathbf{S}^T\mathbf{S})^{1/2}\partial Q_n(\mathbf{v})^{-1}\mathbf{d}_0 \circ \mathrm{sgn}(\widehat{\beta}_{\mathbf{w}1})\| &\le \lambda_{\max}^{1/2}(\mathbf{S}^T\mathbf{S})\lambda_{\min}^{-1}(\partial Q_n(\mathbf{v}))\sqrt{s}D_n \\ &= O_P(\sqrt{s/n}D_n),\end{aligned}$$

by using Conditions 4 and 5. This shows that the second term in (C.4), when multiplied by the vector $\mathbf{b}^T(\mathbf{S}^T\mathbf{S})^{1/2}$ is of order

$$O_P(\sqrt{sn}\lambda_n D_n) = o_P(1),$$

by Condition 2. Therefore, we need to establish the asymptotic normality of the first term in (C.4). This term is identical to the situation dealt by Portnoy (1985). Using his result, the second conclusion of Theorem 3.2 follows. This completes the proof.

Proof of Theorem 3.3

First of all, by Taylor expansion,

$$\Phi_{n,\mathbf{w}}(\widehat{\beta}_1) = \Phi_{n,\mathbf{w}}(\beta_1^*) + \Omega_{n,\mathbf{w}}(\overline{\beta}_1)(\widehat{\beta}_1 - \beta_1^*), \tag{C.5}$$

where $\bar{\boldsymbol{\beta}}_1$ lies between β_1^* and $\hat{\boldsymbol{\beta}}_1$. Consequently,

$$\left\|\bar{\beta}_1-\widehat{\beta}_1\right\|\leq\left\|\beta_1^*-\widehat{\beta}_1\right\|=o_P(1).$$

By the definition of the one step estimator (14) and (C.5), we have

$$\widehat{\beta}_{\mathbf{w}1}^{\mathrm{OS}}-\beta_1^*=\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)^{-1}\Phi_{n,\mathbf{w}}(\beta_1^*)+\mathbf{R}_n, \tag{C.6}$$

where

$$\mathbf{R}_n=\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)^{-1}\left\{\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)-\Omega_{n,\mathbf{w}}(\bar{\beta}_1)\right\}(\widehat{\beta}_1-\beta_1^*).$$

We first deal with the remainder term. Note that

$$\left\|\mathbf{R}_n\right\|\leq\|\{\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)\}^{-1}\|\cdot\|\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)-\Omega_{n,\mathbf{w}}(\bar{\beta}_1)\|\cdot\left\|\widehat{\beta}_1-\beta_1^*\right\| \tag{C.7}$$

and

$$\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)-\Omega_{n,\mathbf{w}}(\bar{\beta}_1)=\sum_{i=1}^n f_i(\widehat{\beta}_1,\bar{\beta}_1)\mathbf{S}_i\mathbf{S}_i^T, \tag{C.8}$$

where $f_i(\widehat{\beta}_1,\bar{\beta}_1)=\partial\psi(Y_i-\mathbf{S}_i^T\widehat{\beta}_1)-\partial\psi(Y_i-\mathbf{S}_i^T\bar{\beta}_1)$. By the Liptchiz continuity, we have

$$|f_i(\widehat{\beta}_1,\bar{\beta}_1)|\leq C\left\|\mathbf{S}_i\right\|\cdot\left\|\widehat{\beta}_1-\bar{\beta}_1\right\|,$$

where C is the Liptchiz coefficient of $\partial\psi_{\mathbf{w}}(\cdot)$. Let $\mathbf{I}_s$ be the identity matrix of order s and $b_n=\lambda_{\max}\{\sum_{i=1}^n\left\|\mathbf{S}_i\right\|\mathbf{S}_i\mathbf{S}_i^T\}$. By (C.8), we have

$$\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)-\Omega_{n,\mathbf{w}}(\bar{\beta}_1)\leq C\left\|\widehat{\beta}_1-\bar{\beta}_1\right\|\sum_{i=1}^n\left\|\mathbf{S}_i\right\|\mathbf{S}_i\mathbf{S}_i^T\leq C\left\|\widehat{\beta}_1-\bar{\beta}_1\right\|b_n\mathbf{I}_s.$$

Hence, all of the eigenvalues of the matrix is no larger than $C\|\widehat{\boldsymbol{\beta}}_1-\bar{\boldsymbol{\beta}}_1\|b_n$. Similarly, by (C.8),

$$\Omega_{n,\mathbf{w}}(\widehat{\beta}_1)-\Omega_{n,\mathbf{w}}(\bar{\beta}_1)\geq -C\left\|\widehat{\beta}_1-\bar{\beta}_1\right\|\sum_{i=1}^n\left\|\mathbf{S}_i\right\|\mathbf{S}_i\mathbf{S}_i^T\geq -C\left\|\widehat{\beta}_1-\bar{\beta}_1\right\|b_n\mathbf{I}_s,$$

and all of its eigenvalue should be at least $-C\|\hat{\boldsymbol{\beta}}_1 - \bar{\boldsymbol{\beta}}_1\| b_n$. Consequently,

$$\|\Omega_{n,\mathbf{w}}(\widehat{\beta}_1) - \Omega_{n,\mathbf{w}}(\overline{\beta}_1)\| \le C \left\|\widehat{\beta}_1 - \overline{\beta}_1\right\| b_n.$$

By Condition 5 and the assumption of $\hat{\boldsymbol{\beta}}_1$, it follows from (C.7) that

$$\left\|\mathbf{R}_n\right\| = O_P(s/n \cdot b_n/n) = O_P(s^{3/2}/n).$$

Thus, for any unit vector $\mathbf{b}$,

$$\mathbf{b}^T(\mathbf{S}^T\mathbf{S})^{1/2}\mathbf{R}_n \le \lambda_{\max}^{1/2}(\mathbf{S}^T\mathbf{S}) \left\|\mathbf{R}_n\right\| = O_P(s^{3/2}/n^{1/2}) = o_P(1).$$

The main term in (C.6) can be handled by using Lemma 6.3 and the same method as Portnoy (1985). This completes the proof.

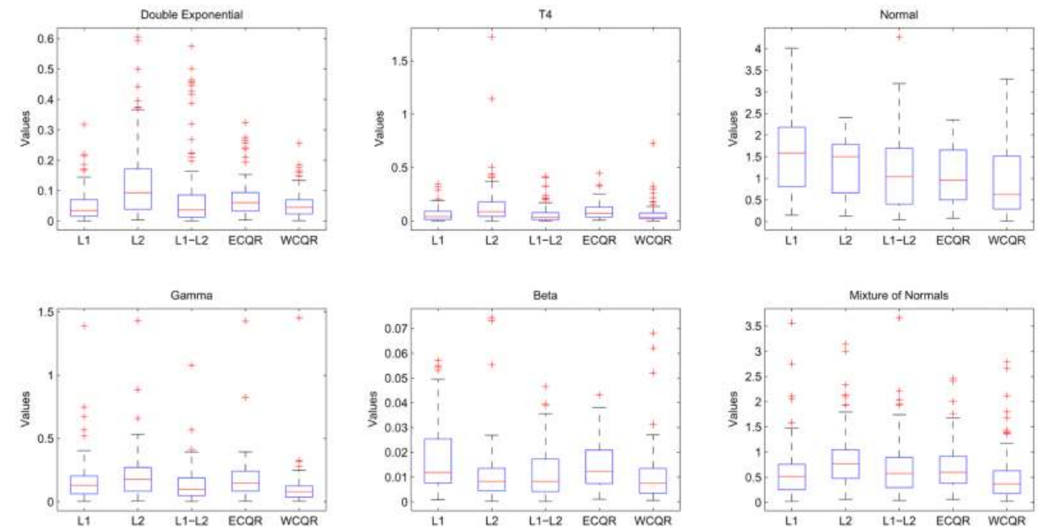

Fig. 1.

Boxplots of Median model error (MME) of L_1, L_2, L_1-L_2, ECQR and WCQR methods under different distributional settings with n = 100, p = 500

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Fig. 2.
Chromosome locations of identified eQTLs of the gene CCT8 with grey region as the CCT8's coding region. The eQTLs selected by any of the five methods are shown.

Table 1

Asymptotic relative efficiency compared to MLE

$f(\varepsilon)$		**DE**	t_4	$\mathcal{N}$ **(0, 1)**	**Γ (3, 1)**	$\mathcal{B}$ **(3, 5)**	**MN$_s$**	**MN$_l$**
	L_1	1.00	0.80	0.63	0.29	0.41	0.61	0.35
	L_2	0.50	0.35	1.00	0.13	0.68	0.05	0.14
	$L_1 - L_2^{\dagger}$	$1.00^{\#}$	0.85	1.00	0.34	0.68	0.61	0.63
	L_1-L_2	$1.00^{\#}$	0.85	1.00	0.44	0.80	0.61	0.63
ECQR	$K = 3$	0.84	0.94	0.86	0.43	0.59	0.76	0.44
	5	0.83	0.97	0.89	0.47	0.65	0.78	0.50
	9	0.82	0.97	0.92	0.49	0.68	0.77	0.52
	19	0.82	0.97	0.94	0.50	0.69	0.75	0.54
	29	0.83	0.97	0.95	0.51	0.71	0.76	0.54
WCQR$^+$	$K = 3$	$0.95^{\dagger}$	0.94	0.87	0.51	0.61	0.76	0.60
	5	0.96	0.97	0.91	0.59	0.70	0.78	0.69
	9	0.97	0.98	0.95	0.69	0.78	0.79	0.77
	19	0.98	0.99	0.98	0.80	0.86	0.80	0.83
	29	0.99	0.99	0.99	0.85	0.90	0.80	0.84
WCQR	$K = 3$	$0.95^{\ddagger}$	0.94	0.87	0.51	0.61	0.76	0.61
	5	0.96	0.97	0.91	0.60	0.72	0.78	0.76
	9	0.98	0.98	0.95	0.70	0.80	0.79	0.88
	19	0.99	0.99	0.98	0.81	0.88	0.92	0.95
	29	0.99	0.99	0.99	0.86	0.92	0.93	0.97

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Table 2

Optimal weights of convex composite quantile regression with $K = 9$ quantiles

$f(\varepsilon)$	DE	t_4	$\mathcal{N}(0, 1)$	$\Gamma(3,1)$	$\mathcal{B}(3,5)$	MN$_s$	MN$_l$
Quantile							
1/10	0	0	0.20	0.56	0.39	0.06	0.36
2/10	0	0.12	0.11	0.15	0.10	0.23	0.11
3/10	0	0.14	0.09	0.08	0.11	0.17	0.10
4/10	0	0.14	0.08	0.06	0.05	0.10	0.01
5/10	1	0.16	0.06	0.05	0	0.14	0
6/10	0	0.14	0.08	0.04	0	0	0
7/10	0	0.14	0.09	0	0.05	0	0
8/10	0	0.12	0.11	0	0.09	0	0
9/10	0	0	0.20	0.05	0.20	0.30	0.29

Table 3

Simulation results (n = 100, p = 12) where †, ‡ represent Median model error (MME) of the oracle and penalized estimator respectively

$f(\varepsilon)$		DE	t_4	$\mathcal{N}$(0, 3)	Γ (3,1)	$\mathcal{B}$(3,5)	MN$_s$
L_1	Oracle	0.029†	0.050	0.122	0.082	0.0010	0.043
	Penalized	0.035‡	0.053	0.128	0.097	0.0011	0.051
	(TP, FP)	(3,1.83)	(3,0.8)	(3,0.84)	(3,1)	(3,0.54)	(3,0.93)
	SD×10^2	0.646	0.767	0.570	0.950	0.112	0.244
L_2	Oracle	0.047	0.043	0.073	0.064	0.00056	0.083
	Penalized	0.059	0.054	0.106	0.100	0.0011	0.091
	(TP, FP)	(3,0.82)	(3,1.61)	(3,1.89)	(3,1.35)	(3,3.76)	(3,1.47)
	SD×10^2	0.779	0.762	0.485	0.869	0.129	0.179
$L_1 - L_2^+$	Oracle	0.036	0.043	0.070	0.070	0.00061	0.051
	Penalized	0.037	0.049	0.102	0.099	0.00077	0.058
	(TP, FP)	(3,2.49)	(3,2.39)	(3,1.97)	(3,2.09)	(3,2.42)	(3,2.69)
	SD×10^1	0.717	0.702	0.518	0.876	0.095	0.169
L_1-L_2	Oracle	0.036	0.043	0.070	0.063	0.00060	0.051
	Penalized	0.037	0.049	0.102	0.078	0.00063	0.058
	(TP, FP)	(3,2.49)	(3,2.39)	(3,1.97)	(3,2.05)	(3,2.42)	(3,2.69)
	SD×10^2	0.717	0.702	0.518	0.846	0.075	0.169
ECQR	Oracle	0.031	0.046	0.069	0.063	0.00065	0.033
	Penalized	0.042	0.046	0.107	0.074	0.00091	0.040
	(TP, FP)	(3,1.88)	(3,1.57)	(3,2.04)	(3,1.83)	(3,1.88)	(3,1.38)
	SD×10^2	0.654	0.562	0.488	0.813	0.087	0.177
WCQR$^+$	Oracle	0.033	0.047	0.068	0.052	0.00065	0.036
	Penalized	0.039	0.041	0.100	0.054	0.00070	0.037
	(TP, FP)	(3,0.55)	(3,1.47)	(3, 0.74)	(3,0.61)	(3,0.98)	(3,0.62)
	SD×10^1	0.440	0.612	0.498	0.715	0.071	0.174
WCQR	Oracle	0.033	0.047	0.068	0.048	0.00058	0.028

$f(\varepsilon)$		**DE**	t_4	$\mathcal{N}$ **(0, 3)**	**Γ (3,1)**	$\mathcal{B}$ **(3,5)**	**MN**$_s$
	Penalized	0.039	0.041	0.100	0.050	0.00062	0.030
	(TP, FP)	(3,0.55)	(3,1.47)	(3, 0.74)	(3,0.61)	(3,0.98)	(3,0.62)
	SD×10^1	0.440	0.612	0.498	0.650	0.061	0.132

Table 4

Simulation results (n = 100, p = 500) were †, ‡ are Median model error (MME) of oracle and penalized estimator respectively

$f(\varepsilon)$		DE	t_4	$\mathcal{N}$ (0,3)	Γ (3,1)	$\mathcal{B}$ (3,5)	MN_s
Lasso	Oracle	0.039†	0.039	0.035	0.0719	0.062	0.176
	Penalized	1.775‡	1.759	8.687	2.662	1.808	6.497
	(TP,FP)	(3,94.46)	(3,94.26)	(3,96.80)	(3,95.59)	(3,86.88)	(3,96.55)
	SD×10^2	3.336	3.257	0.578	3.167	0.989	0.539
L_1	Oracle	0.025	0.031	0.382	0.096	0.0094	0.281
	Penalized	0.035	0.039	1.342	0.131	0.0120	0.514
	(TP,FP)	(3,4.53)	(3,4.47)	(3,5.32)	(3,4.56)	(3,8.10)	(3,4.58)
	SD×10^2	0.268	0.274	0.144	0.461	0.215	0.101
L_2	Oracle	0.035	0.043	0.207	0.078	0.0057	0.187
	Penalized	0.093	0.086	1.187	0.175	0.0073	0.764
	(TP,FP)	(3,12.31)	(3,10.64)	(3,11.00)	(3,8.02)	(3,18.75)	(3,16.93)
	SD×10^1	0.865	0.828	0.281	0.168	0.396	0.238
$L_1 - L_2^{+}$	Oracle	0.193	0.035	0.224	0.080	0.0061	0.195
	Penalized	0.036	0.036	1.160	0.097	0.0077	0.576
	(TP,FP)	(3,17.92)	(3,12.58)	(3,15.87)	(3,15.43)	(3,14.05)	(3,17.92)
	SD×10^2	0.226	0.235	0.396	0.144	0.235	0.207
L_1-L_2	Oracle	0.035	0.035	0.224	0.079	0.0050	0.195
	Penalized	0.036	0.036	1.160	0.095	0.0069	0.576
	(TP,FP)	(3,17.92)	(3,12.58)	(3,15.87)	(3,15.43)	(3,14.05)	(3,17.92)
	SD×10^2	0.226	0.235	0.905	0.150	0.190	0.207
ECQR	Oracle	0.029	0.024	0.252	0.057	0.0064	0.207
	Penalized	0.060	0.070	0.764	0.148	0.0118	0.599
	(TP,FP)	(3,8.71)	(3,8.43)	(3,7.78)	(3,9.59)	(3,9.69)	(3,8.91)
	SD×10^1	0.469	0.475	0.153	0.716	0.213	0.139
WCQR+	Oracle	0.028	0.027	0.223	0.050	0.0066	0.204

$f(\varepsilon)$		DE	t_4	$\mathcal{N}$ (0,3)	Γ (3,1)	$\mathcal{B}$ (3,5)	MN_s
	Penalized	0.045	0.037	0.595	0.079	0.0076	0.368
	(TP,FP)	(3,3.97)	(3,3.76)	(3, 3.93)	(3,3.66)	(3,4.85)	(3,4.05)
	SD×10^1	0.244	0.266	0.112	0.273	0.120	0.084
WCQR	Oracle	0.028	0.027	0.223	0.048	0.0048	0.160
	Penalized	0.045	0.037	0.595	0.062	0.0060	0.280
	(TP,FP)	(3,3.97)	(3,3.76)	(3,3.93)	(3,3.66)	(3,4.85)	(3,4.05)
	SD×10^1	0.224	0.219	0.112	0.180	0.110	0.060

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Table 5

eQTLs for gene CCT8 in Japanese and Chinese (n = 90).

SNP	L_2	$L_1 - L_2^{+}$ L_1-L_2	L_1	ECQR	WCQR+ WCQR	Distance from TSS (kb)
rs16981663	$-0.11_{(0.03)}$	$-0.11_{(0.03)}$	$-0.09_{(0.04)}$	$-0.10_{(0.03)}$	$-0.09_{(0.03)}$	−998
rs16981663**	$0.08_{(0.06)}$	$0.08_{(0.06)}$		$0.04_{(0.06)}$		−998
rs9981984	$-0.12_{(0.03)}$	$-0.12_{(0.03)}$	$-0.10_{(0.04)}$	$-0.09_{(0.03)}$	$-0.12_{(0.03)}$	−950
rs7282280				$0.05_{(0.03)}$		−231
rs7282280**				$-0.07_{(0.05)}$		−231
rs2245431**	$0.33_{(0.10)}$	$0.33_{(0.10)}$	$0.36_{(0.11)}$	$0.37_{(0.09)}$	$0.38_{(0.10)}$	−89
rs2832159	$0.21_{(0.04)}$	$0.21_{(0.04)}$	$0.30_{(0.04)}$	$0.20_{(0.04)}$	$0.23_{(0.04)}$	13
rs1999321**	$0.11_{(0.07)}$	$0.11_{(0.07)}$		$0.14_{(0.07)}$		84
rs2832224	$0.07_{(0.03)}$	$0.07_{(0.03)}$		$0.06_{(0.03)}$	$0.04_{(0.03)}$	86

** is the indicator for SNP equal to 2 and otherwise is the indicator for 1. SE of the estimates is reported in the parenthesis.

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Table 6

eQTLs for gene CCT8 in CEPH ($n = 60$).

SNP	L_2	$L_1 - L_2^{+}L_1$-L_2	L_1	ECQR	WCQR+ WCQR	Distance from TSS (kb)
rs2831459	0.20 (0.07)	0.20 (0.07)	0.19 (0.08)	0.17 (0.07)	0.18 (0.07)	−999
rs7277536	0.18 (0.09)	0.18 (0.09)	0.09 (0.11)	0.14 (0.09)	0.23 (0.09)	−672
rs7278456**	0.36 (0.11)	0.36 (0.11)	0.21 (0.13)	0.40 (0.11)	0.35 (0.11)	−663
rs2248610	0.08 (0.04)	0.08 (0.04)	0.09 (0.05)	0.10 (0.05)	0.06 (0.05)	−169
rs965951	0.11 (0.05)	0.11 (0.05)	0.13 (0.06)	0.03 (0.06)	0.12 (0.05)	−13
rs3787662	0.12 (0.06)	0.12 (0.06)	0.08 (0.07)	0.13 (0.06)	0.12 (0.06)	78
rs2832253				0.10 (0.07)		117
rs2832332				0.08 (0.05)		382
rs13046799	−0.16 (0.05)	−0.16 (0.05)	−0.14 (0.06)	−0.14 (0.05)	−0.16 (0.05)	993

** is the indicator for SNP equal to 2 and otherwise is the indicator for 1. SE of the estimates is reported in the parenthesis.

Table 7

eQTLs of gene CCT8 in Yoruba (n = 60).

SNP	L_2	$L_1 - L_2^+ L_1\text{-}L_2$	L_1	ECQR	WCQR$^+$ WCQR	Distance from TSS (kb)
rs9982023**			$0.12_{(0.05)}$	$0.14_{(0.04)}$		−531
rs1236427				$0.15_{(0.04)}$		−444
rs2831972	$-0.22_{(0.06)}$	$-0.22_{(0.06)}$	$-0.16_{(0.07)}$	$-0.30_{(0.05)}$	$-0.30_{(0.06)}$	−360
rs2091966**	$-0.21_{(0.11)}$	$-0.21_{(0.11)}$	$-0.57_{(0.16)}$	$-0.39_{(0.13)}$	$-0.20_{(0.11)}$	−358
rs2832010	$-0.04_{(0.03)}$	$-0.04_{(0.03)}$	$-0.18_{(0.08)}$	$-0.32_{(0.05)}$	$-0.07_{(0.03)}$	−336
rs2832024			$0.14_{(0.09)}$	$0.26_{(0.06)}$		−332
rs2205413	$-0.08_{(0.04)}$	$-0.08_{(0.04)}$	$-0.15_{(0.05)}$	$-0.16_{(0.04)}$	$-0.04_{(0.03)}$	−330
rs2205413**				$-0.29_{(0.05)}$		−330
rs2832042**	$0.14_{(0.04)}$	$0.14_{(0.04)}$	$0.23_{(0.05)}$	$0.23_{(0.04)}$	$0.13_{(0.04)}$	−330
rs2832053**				$-0.12_{(0.13)}$		−315
rs2832053			$0.09_{(0.04)}$	$0.06_{(0.02)}$		−315
rs8130766	$-0.01_{(0.03)}$	$-0.01_{(0.03)}$	$-0.14_{(0.05)}$	$-0.10_{(0.03)}$	$-0.04_{(0.03)}$	−296
rs16983288**	$-0.13_{(0.07)}$	$-0.13_{(0.07)}$	$-0.28_{(0.08)}$	$-0.28_{(0.05)}$	$-0.15_{(0.06)}$	−288
rs16983303	$-0.06_{(0.03)}$	$-0.06_{(0.03)}$	$-0.10_{(0.02)}$	$-0.15_{(0.03)}$	$-0.09_{(0.03)}$	−283
rs8134601**	$0.18_{(0.11)}$	$0.18_{(0.11)}$	$0.15_{(0.12)}$	$0.16_{(0.07)}$	$0.19_{(0.10)}$	−266
rs8134601	$-0.16_{(0.12)}$	$-0.16_{(0.12)}$	$0.08_{(0.15)}$	$0.25_{(0.11)}$	$-0.17_{(0.11)}$	−266
rs7276141**			$-0.06_{(0.12)}$	$0.15_{(0.11)}$		−264
rs7281691	$0.23_{(0.10)}$	$0.23_{(0.10)}$	$-0.03_{(0.13)}$	$-0.18_{(0.10)}$	$0.26_{(0.09)}$	−263
rs7281691**	$-0.14_{(0.09)}$	$-0.14_{(0.09)}$	$-0.05_{(0.13)}$	$-0.23_{(0.09)}$	$-0.12_{(0.09)}$	−263
rs1006903**	$-0.01_{(0.05)}$	$-0.01_{(0.05)}$	$0.13_{(0.06)}$	$0.07_{(0.04)}$	$0.01_{(0.05)}$	−246
rs7277685			$0.07_{(0.05)}$	$0.06_{(0.03)}$		−240
rs9982426	$0.02_{(0.03)}$	$0.02_{(0.03)}$	$0.12_{(0.04)}$	$0.18_{(0.05)}$		−238
rs2832115				$-0.08_{(0.05)}$		−225
rs11910981	$-0.09_{(0.03)}$	$-0.09_{(0.03)}$	$-0.15_{(0.03)}$	$-0.19_{(0.03)}$	$-0.08_{(0.03)}$	−160
rs2243503				$0.07_{(0.06)}$		−133

SNP	L_2	$L_1 - L^+_2$ L_1-L_2	L_1	ECQR	WCQR+ WCQR	Distance from TSS (kb)
rs2243552			$0.10_{(0.03)}$	$0.03_{(0.05)}$		−128
rs2247809	$0.01_{(0.06)}$	$0.01_{(0.06)}$	$0.18_{(0.07)}$	$0.26_{(0.06)}$	$0.01_{(0.05)}$	−116
rs878797**	$0.11_{(0.06)}$	$0.11_{(0.06)}$	$0.26_{(0.07)}$	$0.23_{(0.05)}$	$0.05_{(0.06)}$	−55
rs6516887	$0.07_{(0.04)}$	$0.07_{(0.04)}$	$-0.05_{(0.07)}$	$-0.09_{(0.04)}$	$0.07_{(0.04)}$	−44
rs8128844			$-0.10_{(0.06)}$	$-0.17_{(0.05)}$	$0.02_{(0.04)}$	−24
rs965951**	$0.10_{(0.10)}$	$0.10_{(0.10)}$	$0.28_{(0.11)}$	$0.26_{(0.08)}$	$0.13_{(0.09)}$	−13
rs2070610			$0.18_{(0.05)}$	$0.17_{(0.04)}$		−0
rs2832159	$0.06_{(0.06)}$	$0.06_{(0.06)}$	$-0.04_{(0.07)}$	$-0.20_{(0.06)}$	$0.11_{(0.05)}$	13
rs2832178**	$-0.16_{(0.06)}$	$-0.16_{(0.06)}$	$-0.16_{(0.08)}$	$-0.20_{(0.06)}$	$-0.24_{(0.06)}$	34
rs2832186			$-0.06_{(0.07)}$	$0.12_{(0.05)}$		38
rs2832190**	$-0.41_{(0.06)}$	$-0.41_{(0.06)}$	$-0.25_{(0.11)}$	$-0.20_{(0.08)}$	$-0.49\ _{(0.06)}$	42
rs2832190	$-0.22_{(0.05)}$	$-0.22_{(0.05)}$	$-0.16_{(0.05)}$	$-0.26_{(0.06)}$	$-0.28\ _{(0.05)}$	42
rs7275293			$0.13_{(0.12)}$	$0.32_{(0.09)}$		54
rs16983792	$-0.11_{(0.04)}$	$-0.11_{(0.04)}$	$-0.10_{(0.05)}$	$-0.18_{(0.04)}$	$-0.14_{(0.04)}$	82
rs2251381**			$-0.11_{(0.08)}$	$-0.15_{(0.05)}$		85
rs2251517**	$-0.25_{(0.05)}$	$-0.25_{(0.05)}$	$-0.26_{(0.07)}$	$-0.27_{(0.05)}$	$-0.28_{(0.05)}$	86
rs2251517	$-0.11_{(0.04)}$	$-0.11_{(0.04)}$	$-0.19_{(0.05)}$	$-0.23_{(0.03)}$	$-0.15_{(0.04)}$	86
rs2832225				$-0.07_{(0.03)}$		87
rs7283854			$0.10_{(0.04)}$	$0.13_{(0.02)}$		443

** is the indicator for SNP equal to 2 and otherwise is the indicator for 1. SE of the estimates is reported in the parenthesis.