Global and Simultaneous Hypothesis Testing for High-Dimensional Logistic Regression Models

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Abstract

High-dimensional logistic regression is widely used in analyzing data with binary outcomes. In this paper, global testing and large-scale multiple testing for the regression coefficients are considered in both single- and two-regression settings. A test statistic for testing the global null hypothesis is constructed using a generalized low-dimensional projection for bias correction and its asymptotic null distribution is derived. A minimax lower bound for the global testing is established, which shows that the proposed test is asymptotically minimax optimal. For testing the individual coefficients simultaneously, multiple testing procedures are proposed and shown to control the false discovery rate (FDR) and falsely discovered variables (FDV) asymptotically. Simulation studies are carried out to examine the numerical performance of the proposed tests and their superiority over existing methods. The testing procedures are also illustrated by analyzing a metabolomics study that investigates the association between fecal metabolites and pediatric Crohn’s disease and the effects of treatment on such associations.

KEY WORDS: False discovery rate; Global testing; Large-scale multiple testing; Minimax lower bound.

1 INTRODUCTION

Logistic regression models have been applied widely in genetics, finance, and business analytics. In many modern applications, the number of covariates of interest usually grows with, and sometimes far exceeds, the number of observed samples. In such high-dimensional settings, statistical problems such as estimation, hypothesis testing, and construction of confidence intervals become much more challenging than those in the classical low-dimensional settings. The increasing technical difficulties
usually emerge from the non-asymptotic analysis of both statistical models and the corresponding computational algorithms.

In this paper, we consider testing for high-dimensional logistic regression model:

\[
\log \left( \frac{\pi_i}{1 - \pi_i} \right) = X_i^\top \beta, \quad \text{for } i = 1, ..., n. \tag{1.1}
\]

where \( \beta \in \mathbb{R}^p \) is the vector of regression coefficients. The observations are i.i.d. samples \( Z_i = (y_i, X_i) \) for \( i = 1, ..., n \), and we assume

\[
y_i | X_i \sim \text{Bernoulli}(\pi_i), \tag{1.2}
\]

independently for each \( i = 1, ..., n \).

1.1 Global and Simultaneous Hypothesis Testing

It is important in high-dimensional logistic regression to determine 1) whether there are any associations between the covariates and the outcome and, if yes, 2) which covariates are associated with the outcome. The first question can be formulated as testing the global null hypothesis \( H_0 : \beta = 0 \); and the second question can be considered as simultaneously testing the null hypotheses \( H_{0,i} : \beta_i = 0 \) for \( i = 1, ..., p \). Besides such single logistic regression problems, hypothesis testing involving two logistic regression models with regression coefficients \( \beta^{(1)} \) and \( \beta^{(2)} \) in \( \mathbb{R}^p \) is also important. Specifically, one is interested in testing the global null hypothesis \( H_0 : \beta^{(1)} = \beta^{(2)} \), or identifying the differentially associated covariates through simultaneously testing the null hypotheses \( H_{0,i} : \beta_i^{(1)} = \beta_i^{(2)} \) for each \( i = 1, ..., p \).

Estimation for high-dimensional logistic regression has been studied extensively. van de Geer (2008) considered high-dimensional generalized linear models (GLMs) with Lipschitz loss functions, and proved a non-asymptotic oracle inequality for the empirical risk minimizer with the Lasso penalty. Meier et al. (2008) studied the group Lasso for logistic regression and proposed an efficient algorithm that leads to statistically consistent estimates. Negahban et al. (2009) obtained the rate of convergence for the \( \ell_1 \)-regularized maximum likelihood estimator under GLMs using restricted strong convexity property. Plan and Vershynin (2013) connected sparse logistic regression to one-bit compressed sensing and developed a unified theory for signal estimation with noisy observations.

In contrast, statistical inference for high-dimensional logistic regression has only been recently addressed. van de Geer et al. (2014) considered constructing confidence intervals and statistical tests for single or low-dimensional components of the regression coefficients in high-dimensional GLMs. Belloni et al. (2016) considered estimating and constructing the confidence regions for a regression coefficient of primary interest in GLMs. Recently, Sur et al. (2017) considered the likelihood ratio test for high-dimensional logistic regression under the setting that \( p/n \to \kappa \) for some constant \( \kappa < 1/2 \), and showed that the asymptotic null distribution of the log-likelihood ratio
statistic is a rescaled $\chi^2$ distribution. Cai et al. (2017) proposed a global test and a procedure for testing simultaneous hypotheses for differential networks against sparse alternatives under Markov random field model. Nevertheless, the problems of global testing and large-scale simultaneous testing for high-dimensional logistic regression models with $p \gtrsim n$ remain unsolved.

In this paper, we first consider global and multiple testing for a single high-dimensional logistic regression model. The global test statistic is constructed as the maximum of squared standardized statistics for individual coefficients, which are based on a two-step standardization procedure. The first step is to correct the bias of the logistic Lasso estimator using a generalized low-dimensional projection (LDP) method, and the second step is to normalize the resulting nearly unbiased estimators by their estimated standard errors. We show that the asymptotic null distribution of the test statistic is a Gumbel distribution and that the resulting test is minimax optimal under the Gaussian design by establishing the minimax separation distance between the null space and alternative space. For large-scale multiple testing, data-driven testing procedures are proposed and shown to control the false discovery rate (FDR) and falsely discovered variables (FDV) asymptotically. The framework for testing for single logistic regression is then extended to the setting of testing two logistic regression models.

The main contributions of the present paper are threefold.

1. We propose novel procedures for both the global testing and large-scale simultaneous testing for high dimensional logistic regressions. The dimension $p$ is allowed to be as large as some exponential order of the sample size $n$. Specifically, we require $\log p = O(n^r)$ for some $0 < r < 1/5$. With global alternatives characterized by the $\ell_{\infty}$ norm, the global test is shown to be minimax rate optimal with the optimal separation distance of order $\sqrt{\log p/n}$.

2. Following similar ideas in Ren et al. (2016) and Cai et al. (2017), our construction of the test statistics depends on a generalized version of the LDP method for bias correction (Zhang and Zhang, 2014). The original LDP method relies on the linearity between the covariates and outcome variable. For logistic regression, the generalized approach first finds a linearization of the regression function, and the weighted LDP is then applied. Besides its usefulness in logistic regression, the generalized LDP method is flexible and can be applied to other nonlinear regression problems (see Section 7 for a detailed discussion).

3. The minimax lower bound is obtained for the global hypothesis testing under the Gaussian design. The lower bound depends on the calculation of the $\chi^2$-divergence between two logistic regression models. To the best of our knowledge, this is the first lower bound result for high-dimensional logistic regression under the Gaussian design.
1.2 Other Related Work

We should note that a different but related problem, namely inference for high-dimensional linear regression, has been well studied in the literature. Zhang and Zhang (2014), van de Geer et al. (2014), and Javanmard and Montanari (2014) considered confidence intervals and testing for low-dimensional parameters of the high-dimensional linear regression model and developed methods based on a two-stage de-biased estimator that corrects the bias introduced at the first stage due to regularization. Cai and Guo (2017) studied minimaxity and adaptivity of confidence intervals for general linear functionals of the regression vector.

The problems of global testing and large-scale simultaneous testing for high-dimensional linear regression have been studied by Liu and Luo (2014) and more recently by Xia et al. (2018). An inverse regression approach is used and testing procedures are constructed based on coordinate-wise standardized test statistics. However, unlike linear regression, the outcome variable in logistic regression is binary and does not follow a joint multivariate normal distribution along with the covariates. Thus the inverse regression approach therein cannot be directly applied to logistic regression problems. In the Markov random field setting, Ren et al. (2016) and Cai et al. (2017) constructed pivotal/test statistics based on the de-biased LDP estimators for node-wise logistic regressions with binary covariates. Nevertheless, the results for sparse high-dimensional logistic regression models with general continuous covariates remain unknown.

Other related problems include joint testing and false discovery rate control for high-dimensional multivariate regression (Xia et al., 2018) and testing for high-dimensional precision matrices and Gaussian graphical models (Liu, 2013; Xia et al., 2015), where the inverse regression approach and de-biasing are also used in the construction of the test statistics. Such statistics are then used for testing the global null with extreme value type asymptotic null distributions or to perform multiple testing that controls the false discovery rate.

1.3 Organization of the Paper and Notations

The rest of the paper is organized as follows. In Section 2, we propose the global test and establish its optimality. In Section 3, we present the multiple testing procedures and show that they control the FDR/FDP or FDV asymptotically. The framework is extended to the two-sample setting in Section 4. In Section 5, the numerical performance of the proposed tests are evaluated through extensive simulations. In Section 6, the methods are illustrated by an analysis of a metabolomics study. Further extensions and related problems are discussed in Section 7. In Section 8, some of the main theorems are proved. The proofs of other theorems as well as technical lemmas, and some further discussions are collected in the online Supplementary Materials.

Throughout our paper, for a vector $\mathbf{a} = (a_1, \ldots, a_n)^\top \in \mathbb{R}^n$, we define the $\ell_p$ norm $\|\mathbf{a}\|_p = \left( \sum_{i=1}^n a_i^p \right)^{1/p}$, and the $\ell_\infty$ norm $\|\mathbf{a}\|_\infty = \max_{1 \leq j \leq n} |a_i|$. $\mathbf{a}_{-j} \in \mathbb{R}^{n-1}$ stands for the subvector of $\mathbf{a}$ without the $j$ the component. We denote $\text{diag}(a_1, \ldots, a_n)$ as the $n \times n$ diagonal matrix whose
diagonal entries are \( a_1, ..., a_n \). For a matrix \( A \in \mathbb{R}^{p \times q} \), \( \lambda_i(A) \) stands for the \( i \)-th largest singular value of \( A \) and \( \lambda_{\text{max}}(A) = \lambda_1(A), \lambda_{\text{min}}(A) = \lambda_{p \times q}(A) \). For a smooth function \( f(x) \) defined on \( \mathbb{R} \), we denote \( \dot{f}(x) = df(x)/dx \) and \( \ddot{f}(x) = d^2f(x)/dx^2 \). Furthermore, for sequences \( \{a_n\} \) and \( \{b_n\} \), we write \( a_n = o(b_n) \) if \( \lim_n a_n/b_n = 0 \), and write \( a_n = O(b_n) \), \( a_n \lesssim b_n \) or \( b_n \gtrsim a_n \) if there exists a constant \( C \) such that \( a_n \leq Cb_n \) for all \( n \). We write \( a_n \asymp b_n \) if \( a_n \lesssim b_n \) and \( a_n \gtrsim b_n \). For a set \( A \), we denote \( |A| \) as its cardinality. Lastly, \( C, C_0, C_1, ... \) are constants that may vary from place to place.

2 GLOBAL HYPOTHESIS TESTING

In this section, we consider testing the global null hypotheses

\[
H_0 : \beta = 0 \quad \text{vs.} \quad H_1 : \beta \neq 0,
\]

under the logistic regression model with random designs. The global testing problem corresponds to the detection of any associations between the covariates and the outcome.

Our construction of the global testing procedure begins with a bias-corrected estimator built upon a regularized estimator such as the \( \ell_1 \)-regularized M-estimator. For high-dimensional logistic regression, the \( \ell_1 \)-regularized M-estimator is defined as

\[
\hat{\beta} = \arg\min_{\beta} \left\{ \frac{1}{n} \sum_{i=1}^{n} \left[ -y_i \beta^\top X_i + \log(1 + e^{\beta^\top X_i}) \right] + \lambda \|\beta\|_1 \right\}, \quad (2.1)
\]

which is the minimizer of a penalized log-likelihood function. Negahban et al. (2009) showed that, under the condition that \( X_i \) are i.i.d. sub-gaussian with \( (\beta, \Sigma) \in \Theta(k) \) (see (A3) in Section 2.2), standard high-dimensional estimation error bounds for \( \hat{\beta} \) under the \( \ell_1 \) or \( \ell_2 \) norm can be obtained by choosing \( \lambda \asymp \sqrt{\log p/n} \). Once we obtain the initial estimator \( \hat{\beta} \), our next step is to correct the bias of \( \hat{\beta} \).

For technical reasons, we split the samples so that the initial estimation step and the bias correction step are conducted on separate and independent datasets. Without loss of generality, we assume there are \( 2n \) samples, divided into two subsets \( \mathcal{D}_1 \) and \( \mathcal{D}_2 \), each with \( n \) independent samples. The initial estimator \( \hat{\beta} \) is obtained from \( \mathcal{D}_1 \). In the following, we construct a nearly unbiased estimator \( \hat{\beta} \) based on \( \hat{\beta} \) and the samples from \( \mathcal{D}_2 \), using the generalized LDP approach. Throughout the paper, the samples \( Z_i = (X_i, Y_i), i = 1, ..., n \), are from \( \mathcal{D}_2 \), which are independent of \( \hat{\beta} \).
2.1 Construction of the Test Statistic via Generalized Low-Dimensional Projection

Let $X$ be the design matrix whose $i$-th row is $X_i$. We rewrite the logistic regression model defined by (1.1) and (1.2) as

$$y_i = f(\beta^\top X_i) + \epsilon_i$$  \hspace{1cm} (2.2)

where $f(u) = e^u/(1 + e^u)$ and $\epsilon_i$ is error term. To correct the bias of the initial estimator $\hat{\beta}$, we consider the Taylor expansion of $f(u_i)$ at $\hat{u}_i$ for $u_i = \beta^\top X_i$ and $\hat{u}_i = \hat{\beta}^\top X_i$

$$f(u_i) = f(\hat{u}_i) + \dot{f}(\hat{u}_i)(u_i - \hat{u}_i) + Re_i$$

where $Re_i$ is the reminder term. Plug this into the regression model (2.2), we have

$$y_i = f(\hat{u}_i) + \dot{f}(\hat{u}_i)X_i^\top \hat{\beta} = \dot{f}(\hat{u}_i)X_i^\top \beta + (Re_i + \epsilon_i).$$  \hspace{1cm} (2.3)

By rewriting the logistic regression model as (2.3), we can treat $y_i - f(\hat{u}_i) + \dot{f}(\hat{u}_i)X_i^\top \hat{\beta}$ on the left hand side as the new response variable, whereas $\dot{f}(\hat{u}_i)X_i$ as the new covariates and $Re_i + \epsilon_i$ as the noise. Consequently, $\beta$ can be considered as the regression coefficient of this approximate linear model.

The bias-corrected estimator, or, the generalized LDP estimator $\hat{\beta}$ is defined as

$$\hat{\beta}_j = \hat{\beta}_j + \frac{\sum_{i=1}^n v_{ij}(y_i - f(\hat{\beta}^\top X_i))}{\sum_{i=1}^n v_{ij}\dot{f}(\hat{\beta}^\top X_i)X_{ij}}, \quad j = 1, \ldots, p,$$  \hspace{1cm} (2.4)

where $X_{ij}$ is the $j$-th component of $X_i$ and $v_j = (v_{1j}, v_{2j}, \ldots, v_{nj})^\top$ is the score vector that will be determined carefully [Ren et al., 2016; Cai et al., 2017]. More specifically, we define the weighted inner product $\langle \cdot, \cdot \rangle_n$ for any $a, b \in \mathbb{R}^n$ as $\langle a, b \rangle_n = \sum_{i=1}^n \hat{f}(\hat{u}_i)a_i b_i$, and denote $\langle \cdot, \cdot \rangle$ as the ordinary inner product defined in Euclidean space. Combining (2.3) and (2.4), we can write

$$\hat{\beta}_j - \beta_j = \frac{\langle v_j, \epsilon \rangle}{\langle v_j, x_j \rangle_n} + \frac{\langle v_j, Re \rangle}{\langle v_j, x_j \rangle_n} - \frac{\langle v_j, h_{-j} \rangle_n}{\langle v_j, x_j \rangle_n},$$  \hspace{1cm} (2.5)

where $x_j \in \mathbb{R}^n$ denote the $j$-th column of $X$, $h_{-j} = X_{-j}(\hat{\beta}_{-j} - \beta_{-j})$ where $X_{-j} \in \mathbb{R}^n \times \mathbb{R}^{p-1}$ is the submatrix of $X$ without the $j$-th column, and $Re = (Re_1, \ldots, Re_n)^\top$ with $Re = f(u_i) - f(\hat{u}_i) - \dot{f}(\hat{u}_i)(u_i - \hat{u}_i)$. We will construct score vector $v_j$ so that the first term on the right hand side of (2.5) is asymptotically normal, while the second and third terms, which together contribute to the bias of the generalized LDP estimator $\hat{\beta}_j$, are negligible.

To determine the score vector $v_j$ efficiently, let us consider the following node-wise regression among the covariates

$$x_j = X_{-j} \gamma_j + \eta_j, \quad j = 1, \ldots, p,$$
where $\eta_j$ is independent of $x_k, k \neq j$. Intuitively, if we set $v_j = \hat{W}^{-1}\eta_j$ for $\hat{W} = \text{diag}(\hat{f}(\hat{u}_1), \ldots, \hat{f}(\hat{u}_n))$, then it should follow that

$$\langle v_j, h_{-j} \rangle_n \leq \max_{k \neq j} |\langle v_j, x_k \rangle_n| \cdot \|\hat{\beta} - \beta\|_1 = \max_{k \neq j} |\langle \eta_j, x_k \rangle| \cdot \|\hat{\beta} - \beta\|_1 \approx 0.$$ 

In practice, we use the node-wise Lasso to obtain an estimate of $\eta_j$. For $X$ from $D_2$ and $\hat{\beta}$ obtained from $D_1$, the score $v_j$ is obtained by calibrating the Lasso-generated residue $\hat{\eta}_j$, i.e.

$$v_j(\lambda) = \hat{W}^{-1}\hat{\eta}_j(\lambda), \quad \hat{\eta}_j(\lambda) = x_j - X_{-j}\hat{\gamma}_j(\lambda),$$

$$\hat{\gamma}_j(\lambda) = \arg\min_b \left\{ \frac{\|x_j - X_{-j}b\|^2}{2n} + \lambda \|b\|_1 \right\}. \quad (2.6)$$

Clearly, $v_j(\lambda)$ depends on the tuning parameter $\lambda$. Define the following quantities

$$\zeta_j(\lambda) = \max_{k \neq j} \frac{|\langle v_j(\lambda), x_k \rangle_n|}{\|v_j(\lambda)\|_n}, \quad \tau_j(\lambda) = \frac{\|v_j(\lambda)\|_n}{|\langle v_j(\lambda), x_j \rangle_n|}. \quad (2.7)$$

The tuning parameter $\lambda$ can be determined through $\zeta_j(\lambda)$ and $\tau_j(\lambda)$ by the algorithm in Table 1, which is adapted from the algorithm in Zhang and Zhang (2014).

Table 1: Computation of $v_j$ from the Lasso (2.6)

| Input: An upper bound $\zeta_j^*$ for $\zeta_j$, with default value $\zeta^* = \sqrt{2\log p}$, tuning parameters $\kappa_0 \in [0, 1]$ and $\kappa_1 \in (0, 1)$; Step 1: If $\zeta_j(\lambda) > \zeta_j^*$ for all $\lambda > 0$, set $\zeta_j^* = (1 + \kappa_1) \inf_{\lambda > 0} \zeta_j(\lambda); \lambda \leftarrow \max\{\lambda : \zeta_j(\lambda) \leq \zeta_j^*\}, \zeta_j^* \leftarrow \zeta_j(\lambda), \tau_j^* \leftarrow \tau_j(\lambda); \text{ Step 2: } \lambda_j \leftarrow \min\{\lambda : \tau_j(\lambda) \leq (1 + \kappa_0)\tau_j^*\}; v_j \leftarrow v_j(\lambda_j), \tau_j \leftarrow \tau_j(\lambda_j), \zeta_j \leftarrow \zeta_j(\lambda_j) \right.$ | Output: $\lambda_j, v_j, \tau_j, \zeta_j$ |

Once $\hat{\beta}_j$ and $\tau_j$ are obtained, we define the standardized statistics

$$M_j = \frac{\hat{\beta}_j}{\tau_j},$$

for $j = 1, \ldots, p$. The global test statistic is then defined as

$$M_n = \max_{1 \leq j \leq p} M_j^2. \quad (2.8)$$

### 2.2 Asymptotic Null Distribution

We now turn to the analysis of the properties of the global test statistic $M_n$ defined in (2.8). For the random covariates, we consider both the Gaussian design and the bounded design. Under the
Gaussian design, the covariates are generated from a multivariate Gaussian distribution with an unknown covariance matrix $\Sigma \in \mathbb{R}^{p \times p}$. In this case, we assume

(A1). $X_i \sim N(0, \Sigma)$ independently for each $i = 1, \ldots, n$.

In the case of bounded design, we assume instead

(A2). $X_i$ for $i = 1, \ldots, n$ are i.i.d. random vectors satisfying $\mathbb{E} X_i = 0$ and $\max_{1 \leq i \leq n} \|X_i\|_{\infty} \leq T$ for some constant $T > 0$.

Define the $\ell_1$ ball

$$B_1(k) = \left\{ \Omega = (\omega_{ij}) \in \mathbb{R}^{p \times p} : \max_{1 \leq i \leq p} \sum_{j=1}^{p} \min \left| \omega_{ij} \right| \sqrt{\frac{n}{\log p}}, 1 \leq k \right\}.$$  

In general, $B_1(k)$ includes any matrix $\Omega$ whose rows $\omega_i$ are $\ell_0$ sparse with $\|\omega_i\|_0 \leq k$ or $\ell_1$ sparse with $\|\omega_i\|_1 \leq k \sqrt{\log p / n}$ for all $i = 1, \ldots, p$. The parameter space of the covariance matrix $\Sigma$ and the regression vector $\beta$ are defined as following.

(A3). The parameter space $\Theta(k)$ of $\theta = (\beta, \Sigma) \in \mathbb{R}^p \times \mathbb{R}^{p \times p}$ satisfies

$$\Theta(k) = \left\{ (\beta, \Sigma) : \|\beta\|_0 \leq k, M^{-1} \leq \lambda_{\min}(\Sigma) \leq \lambda_{\max}(\Sigma) \leq M, \Sigma^{-1} \in B_1(k) \right\},$$

for some constant $M \geq 1$.

The following theorem states that the asymptotic null distribution of $M_n$ under either the Gaussian or bounded design is a Gumbel distribution.

**Theorem 2.1.** Let $M_n$ be the test statistic defined in (2.8), $D$ be the diagonal of $\Sigma^{-1}$ and $(\xi_{ij}) = D^{-1/2} \Sigma^{-1} D^{-1/2}$. Suppose $\max_{1 \leq i < j \leq p} |\xi_{ij}| \leq c_0$ for some constant $0 < c_0 < 1$, $\log p = O(n^r)$ for some $0 < r < 1/5$, and

1. under the Gaussian design, we assume (A1) (A3) and $k = o(\sqrt{n} / \log^3 p)$; or
2. under the bounded design, we assume (A2) (A3) and $k = o(\sqrt{n} / \log^{5/2} p)$.

Then under $H_0$, for any given $x \in \mathbb{R}$,

$$P(M_n - 2 \log p + \log \log p \leq x) \to \exp \left( - \frac{1}{\sqrt{\pi}} \exp(-x/2) \right), \quad \text{as} \ (n, p) \to \infty.$$ 

The condition that $\log p = o(n^r)$ for some $0 < r < 1/5$ is consistent with those required for testing the global hypothesis in high-dimensional linear regression (Xia et al., 2018) and for testing two-sample covariance matrices (Cai et al., 2013). It allows the dimension $p$ to be exponentially large comparing to the sample size $n$, which is much flexible than the likelihood ratio test considered in Sur et al. (2017) where the dimension can only scale as $p < n$. Under the Gaussian design, it is required that the sparsity $k$ is $o(\sqrt{n} / \log^3 p)$ whereas for the bounded design, it suffices that the sparsity $k$ to be $o(\sqrt{n} / \log^{5/2} p)$.
Remark 1. The analysis can be extended to test $H_0 : \beta_G = 0$ versus $H_1 : \beta_G \neq 0$ for a given index set $G$. Specifically, we can construct the test statistic as $M_{G,n} = \max_{i \in G} M_i^2$ and obtain a similar Gumbel limiting distribution by replacing $p$ by $|G|$, as $(n, |G|) \to \infty$. The sparsity condition thus should be forwarded to the set $G$.

Based on the limiting null distribution, the asymptotically $\alpha$ level test can be defined as

$$\Phi_\alpha(M_n) = I\{M_n \geq 2 \log p - \log \log p + q_\alpha\},$$

where $q_\alpha$ is the $1 - \alpha$ quantile of the Gumbel distribution with the cumulative distribution function $\exp\left(-\frac{1}{\sqrt{\pi}} \exp(-x/2)\right)$, i.e.

$$q_\alpha = -\log(\pi) - 2 \log \log(1 - \alpha)^{-1}.$$  

The null hypothesis $H_0$ is rejected if and only if $\Phi_\alpha(M_n) = 1$.

2.3 Minimax Separation Distance and Optimality

In this subsection, we answer the question: “What is the essential difficulty for testing the global hypothesis in logistic regression.” To fix ideas, we begin with defining the minimax separation distance that measures such essential difficulty for testing the global null hypothesis at a given level and type II error. In particular, we consider the alternative

$$H_1 : \|\beta\|_\infty \geq \rho$$

for some $\rho > 0$.

By fixing a level $\alpha > 0$ and a type II error probability $\delta > 0$, we can define the $\delta$-separation distance of a level $\alpha$ test procedure $\Phi_\alpha$ for given design covariance $\Sigma \in \Theta(k)$ as

$$\rho(\Phi_\alpha, \delta, \Sigma) = \inf \left\{ \rho > 0 : \inf_{\beta \in \Theta(k) : \|\beta\|_\infty \geq \rho} P_\theta(\Phi_\alpha = 1) \geq 1 - \delta \right\}$$

$$= \inf \left\{ \rho > 0 : \sup_{\beta \in \Theta(k) : \|\beta\|_\infty \geq \rho} P_\theta(\Phi_\alpha = 0) \leq \delta \right\}.$$

The $\delta$-separation distance $\rho(\Phi_\alpha, \delta, \Theta(k))$ over $\Theta(k)$ can thus be defined by taking the supremum over all the covariance matrices $\Sigma \in \Theta(k)$, so that

$$\rho(\Phi_\alpha, \delta, \Theta(k)) = \sup_{\Sigma \in \Theta(k)} \rho(\Phi_\alpha, \delta, \Sigma),$$

which corresponds to the minimal $\ell_\infty$ distance such that the null hypothesis $H_0$ is well separated from the alternative $H_1$ by the test $\Phi_\alpha$. In general, $\delta$-separation distance is an analogue of the
statistical risk in estimation problems. It characterizes the performance of a specific α-level test with a guaranteed type II error δ. Consequently, we can define the (α, δ)-minimax separation distance over Θ(k) and all the α-level tests as
\[
ρ^*(α, δ, Θ(k)) = \inf_{Φ_α} ρ(Φ_α, δ, Θ(k)).
\]
The definition of (α, δ)-minimax separation distance generalizes the ideas of Ingster (1993), Baraud (2002) and Verzelen (2012). The following theorem establishes the minimax lower bound of the (α, δ)-separation distance for testing the global null hypothesis over the parameter space Θ(k) under the Gaussian design.

**Theorem 2.2.** Assume that α + δ ≤ 1. Under the Gaussian design, if (A1) and (A3) hold and
\[
k ≲ \min\{p^γ, n/\log p\}
\]
for some 0 < γ < 1/2, then the (α, δ)-minimax separation distance has the lower bound
\[
ρ^*(α, δ, Θ(k)) \geq c \sqrt{\frac{\log p}{n}}
\]
for some constant c > 0.

In order to show the above lower bound is asymptotically sharp, we prove that it is actually attainable under certain circumstances, by our proposed global test Φ_α. In particular, for the bounded design, we make the following additional assumption.

(A4). It holds that \(P(\max_{1 \leq i \leq n} |β^T X_i| \geq C) = O(p^{-c})\) for some constant C, c > 0.

**Theorem 2.3.** Suppose that \(\log p = O(n^r)\) for some 0 < r < 1. Under the alternative \(H_1: \|β\|_∞ \geq \rho\) with \(\rho = c_2 \sqrt{\log p/n}\), and

1. under the Gaussian design, assume (A1) (A3) hold, \(\|β\|_2 \leq C(\log \log p)/\sqrt{\log n}\) for \(C \leq \min\{√2/\lambda_{\max}(Σ), (2r √2/λ_{\max}(Σ))^{-1}\}\) and \(k = o(√n/\log^3 p)\); or

2. under the bounded design, assume (A2) (A3) (A4), and \(k = o(√n/\log^{5/2} p)\).

Then as \((n, p) → ∞\),
\[
P_{H_1}(Φ_α(M_n) = 1) → 1.
\]

In order to show the power optimality of our proposed test, in Theorem 3, (A4) is assumed for the bounded case and \(\|β\|_2 = O(\log \log p/√{\log n})\) is required for the Gaussian case. In particular, since \(\log p = O(n^r)\) for some 0 < r < 1, we have \(\log \log p \lesssim r \log n\), and as a consequence \(\log \log p/√{\log n}\) can be as large as \(√{\log n}\). In general, Theorem 2 and Theorem 3 imply that our proposed global test is minimax optimal over the alternative space \(Θ(k) \cap \{\|β\|_∞ \geq √{\log p/n}\} \cap \{\|β\|_2 \lesssim \log \log p/√{\log n}\}\) with growing size. However, under the bounded design, it is unclear whether the same lower bound \(√{\log p/n}\) can be established.
3 LARGE-SCALE MULTIPLE TESTING

Denote by $\beta$ the true coefficient vector in the model and denote $H_0 = \{ j : \beta_j = 0, j = 1, \cdots, p \}$, $H_1 = \{ j : \beta_j \neq 0, j = 1, \cdots, p \}$. In order to identify the indices in $H_1$, we consider simultaneous testing of the following null hypotheses

$$H_{0,j} : \beta_j = 0 \quad \text{vs.} \quad H_{1,j} : \beta_j \neq 0, \quad 1 \leq j \leq p.$$ 

Apart from identifying as many nonzero $\beta_j$ as possible, to obtain results of practical interest, we would like to control the false discovery rate (FDR) as well as the false discovery proportion (FDP), or the number of falsely discovered variables (FDV).

3.1 Construction of Multiple Testing Procedures

Recall that in Section 2, we define the standardized statistics

$$M_j = \hat{\beta}_j / \tau_j,$$

for $j = 1, \ldots, p$. For a given threshold level $t > 0$, each individual hypothesis $H_{0,j} : \beta_j = 0$ is rejected if $|M_j| \geq t$. Therefore for each $t$, we can define

$$\text{FDP}(t) = \frac{\sum_{j \in H_0} I\{|M_j| \geq t\}}{\max \left\{ \sum_{j=1}^p I\{|M_j| \geq t\}, 1 \right\}}, \quad \text{FDR}(t) = E[\text{FDP}(t)],$$

and the expected number of falsely discovered variables

$$\text{FDV}(t) = E \left[ \sum_{j \in H_0} I\{|M_j| \geq t\} \right].$$

Procedure Controlling FDR/FDP. In order to control the FDR/FDP at a pre-specified level $0 < \alpha < 1$, we can set the threshold level as

$$\tilde{t}_1 = \inf \left\{ 0 \leq t \leq \sqrt{2 \log p} : \frac{\sum_{j \in H_0} I\{|M_j| \geq t\}}{\max \left\{ \sum_{j=1}^p I\{|M_j| \geq t\}, 1 \right\}} \leq \alpha \right\},$$

(3.1)

where the upper bound $\sqrt{2 \log p}$ is due to the fact that each $M_j$ is marginally approximate standard normal, so that

$$P\left( \max_{j \in H_0} |M_j| \geq \sqrt{2 \log p} \right) \to 0 \quad \text{as} \ (n, p) \to \infty.$$ 

(3.2)

In general, the ideal choice $\tilde{t}_1$ is unknown and needs to be estimated because it depends on the knowledge of the true null $H_0$. Let $G_0(t)$ be an estimate of the proportion of the nulls falsely
rejected by the procedure among all the true nulls at the threshold level $t$. Specifically,

$$G_0(t) = \frac{1}{p_0} \sum_{j \in H_0} I\{|M_j| \geq t\}, \quad (3.3)$$

where $p_0 = |H_0|$. In practice, it is reasonable to assume that the true alternatives are sparse. If the sample size is large, we can use the tails of normal distribution $G(t) = 2 - 2\Phi(t)$ to approximate $G_0(t)$. In fact, it will be shown that

$$\sup_{0 \leq t \leq b_p} \left| \frac{G_0(t)}{G(t)} - 1 \right| \to 0 \quad (3.4)$$

in probability as $(n, p) \to \infty$, where $b_p \leq \sqrt{2 \log p}$, which will be determined later. To summarize, we have the following logistic multiple testing (LMT) procedure controlling the FDR and the FDP.

**Procedure 1 (LMT).** Let $0 < \alpha < 1$ and define

$$\hat{t} = \inf \left\{ 0 \leq t \leq \sqrt{2 \log p} : \frac{pG(t)}{\max \{ \sum_{j=1}^{p} I\{|M_j| \geq t\}, 1 \}} \leq \alpha \right\}. \quad (3.5)$$

If $\hat{t}$ in (3.5) does not exist, then let $\hat{t} = \sqrt{2 \log p}$. We reject $H_{0,j}$ whenever $|M_j| \geq \hat{t}$.

**Procedure Controlling FDV.** For large-scale inference, it is sometimes more desirable to control the FDV instead of the usual FDR/FDP, especially when the sample size is small (Liu and Luo, 2014). FDV control also provides an intuitive description of type I error in variable selection. In this case, FDV control can be achieved by a suitable modification of the FDP controlling procedure introduced above. Specifically, we propose the following FDV controlling logistic multiple testing (LMT_V) procedure.

**Procedure 2 (LMT_V).** For a given tolerable number of falsely discovered variables $r < p$, let

$$\hat{t}_{FDV} = G^{-1}(r/p). \quad (3.6)$$

$H_{0,j}$ is rejected whenever $|M_j| \geq \hat{t}_{FDV}$.

### 3.2 Theoretical Properties for Multiple Testing Procedures

In this section we show that our proposed multiple testing procedures control the theoretical FDR/FDP or FDV asymptotically. For simplicity, our theoretical results are obtained under the bounded design scenario. For FDR/FDP control, we need the an additional assumption on the interplay between the dimension $p$ and the parameter space $\Theta(k)$. 

Define $F_{jk} = E[\eta_j \eta_k / \hat{f}(u_i)]$ for $1 \leq j, k \leq p$, and $\rho_{jk} = F_{jk} / \sqrt{F_{jj} F_{kk}}$. Denote

$$B(\delta) = \{(j, k) : \lvert \rho_{jk} \rvert \geq \delta, i \neq j\}, \quad A(\epsilon) = B((\log p)^{-2-\epsilon}).$$

**(A5).** Suppose that for some $\epsilon > 0$ and $q > 0$,

$$\sum_{(j,k) \in A(\epsilon) \cap H_0} \frac{2|\rho_{jk}|}{p^{1+|\rho_{jk}|}} = O(p^2/(\log p)^2).$$

The following proposition shows that $M_j$ is asymptotically normal distributed and $G_0(t)$ is well approximated by $G(t)$.

**Proposition 1.** Under (A2) (A3) and (A4), suppose $p \leq n^r$ for some constant $r > 0$, $k = o(\sqrt{n}/\log^{5/2} p)$, then for any $r > 0$ and $b > 0$, as $(n, p) \to \infty$,

$$\sup_{j \in H_0} \sup_{0 \leq t \leq b \sqrt{\log p}} \left| \frac{P(|M_j| \geq t)}{2 - 2\Phi(t)} - 1 \right| \to 0. \tag{3.7}$$

If in addition we assume (A5), then

$$\sup_{0 \leq t \leq b_p} \left| \frac{G_0(t)}{G(t)} - 1 \right| \to 0 \tag{3.8}$$

in probability, where $\Phi$ is the cumulative distribution function of the standard normal distribution, $b_p = G^{-1}(c_p/p)$ and $c_p \to \infty$ for some sequence $c_p = o(p)$.

The following theorem provides the asymptotic FDR and FDP control of our procedure.

**Theorem 3.1.** Under the conditions of Proposition 1, suppose as $(n, p) \to \infty$, for some constant $c_1$,

$$\sum_{j \in H_1} I\{|\beta_j| \geq c_1 \sqrt{\log p/n}\} \to \infty, \tag{3.9}$$

we have for $\hat{t}$ defined in our LMT procedure,

$$\lim_{(n,p) \to \infty} \frac{\text{FDR}(\hat{t})}{\alpha p_0/p} \leq 1, \quad \lim_{(n,p) \to \infty} P\left( \frac{\text{FDP}(\hat{t})}{\alpha p_0/p} \leq 1 + \epsilon \right) = 1 \tag{3.10}$$

for any $\epsilon > 0$.

For the FDV control procedure, we have the following theorem.

**Theorem 3.2.** Under (A2) (A3) and (A4), assume $p \leq n^c$ for some $c > 0$ and $k = o(\sqrt{n}/\log^{5/2} p)$. 


Then we have for \( \hat{t}_{FDV} \) defined in our LMT\(_V\) procedure

\[
\lim_{(n,p) \to \infty} \frac{\text{FDV}(\hat{t}_{FDV})}{rp_0/p} = 1.
\]  

(3.11)

4 TESTING FOR TWO LOGISTIC REGRESSION MODELS

In some applications, it is also interesting to consider hypothesis testing that involves two separate logistic regression models of the same dimension. Specifically, for \( \ell = 1, 2 \) and \( i = 1, \ldots, n_\ell \), where \( n_1 \not\asymp n_2 \),

\[
y^{(\ell)}_i = f(\beta^{(\ell)\top} X^{(\ell)}_i) + \epsilon^{(\ell)}_i
\]

(4.1)

where \( f(u) = e^u/(1 + e^u) \), and \( \epsilon^{(\ell)}_i \) is a binary random variable such that \( y^{(\ell)}_i | X^{(\ell)}_i \sim \text{Bernoulli}(f(\beta^{(\ell)\top} X^{(\ell)}_i)) \). The global null hypothesis \( H_0 : \beta^{(1)} = \beta^{(2)} \) implies that there is overall no difference in association between covariates and the response. If this null hypothesis is rejected, we are interested in simultaneously testing the hypotheses \( H_{0,j} : \beta^{(1)}_j = \beta^{(2)}_j \) for each \( j = 1, \ldots, p \).

To test the global null

\[ H_0 : \beta^{(1)} = \beta^{(2)} \quad \text{vs.} \quad H_1 : \beta^{(1)} \neq \beta^{(2)}, \]

we can first obtain \( \hat{\beta}^{(\ell)}_j \) and \( \tau^{(\ell)}_j \) for each model, and then calculate the coordinate-wise standardized statistics

\[
T_j = \frac{\hat{\beta}^{(1)}_j}{\sqrt{2\tau^{(1)}_j}} - \frac{\hat{\beta}^{(2)}_j}{\sqrt{2\tau^{(2)}_j}}, \quad \text{for } j = 1, \ldots, p.
\]

Define the global test statistic as \( T_n = \max_{1 \leq j \leq p} T_j^2 \), it can be shown that the limiting null distribution is also a Gumbel distribution. The \( \alpha \) level global test is thus defined as \( \Phi_\alpha(T_n) = I\{T_n \geq 2 \log p - \log \log p + q_\alpha\} \), where \( q_\alpha = -\log(\pi) - 2\log(1 - \alpha)^{-1} \).

For multiple hypotheses testing of two regression vectors

\[ H_{0,j} : \beta^{(1)}_j = \beta^{(2)}_j \quad \text{vs.} \quad H_{1,j} : \beta^{(1)}_j \neq \beta^{(2)}_j, \quad j = 1, \ldots, p, \]

we define the test statistics \( T_j = (\hat{\beta}^{(1)}/\tau^{(1)}_j - \hat{\beta}^{(2)}/\tau^{(2)}_j)/\sqrt{2} \), for \( j = 1, \ldots, p \). The two-sample multiple testing procedure is given as follows.

**Procedure 3.** Let \( 0 < \alpha < 1 \) and define

\[
\hat{t} = \inf \left\{ 0 \leq t \leq \sqrt{2\log p} : \frac{pG(t)}{\max \left\{ \sum_{j=1}^p I\{|T_j| \geq t\}, 1 \right\} \leq \alpha \right\}. \tag{4.2}
\]

If \( \hat{t} \) in \([4,2]\) does not exist, then let \( \hat{t} = \sqrt{2\log p} \). We reject \( H_{0,j} \) whenever \( |M_j| \geq \hat{t} \).
Similar theoretical FDR/FDP controlling results can be derived. For reasons of space, we delay all the technical discussions to our online Supplementary Materials.

5 SIMULATION STUDIES

In this section we examine the numerical performance of the proposed tests. For the global testing, we evaluate the type I errors and powers in various settings. For the multiple testing, we compare the proposed multiple testing procedure with the Benjamini-Hochberg (BH) procedure (Benjamini and Hochberg, 1995) based on our proposed test statistics, and show that the BH procedure is much more conservative in FDR control and has lower power in all cases.

5.1 Global Hypothesis Testing

In the following simulations, we consider a variety of dimensions, sample sizes, and sparsity of the models. For alternative hypotheses, the dimension of the covariates $p$ ranges from 400, 600, 800 to 1000, and the sparsity $k$ ranges from 2, 4 to 8. The sample sizes $n$ are determined by the ratio $p/n$ that takes values of 2, 3 or 4.

To generate the design matrix $X$, we consider the Gaussian design with two types of covariance structure:

- Independent Covariates: $\Sigma = I$;
- Blockwise-Correlated Covariates: $\Sigma = \Sigma_B$, where $\Sigma_B$ is a $p \times p$ blockwise diagonal matrix including 10 equal-sized blocks, whose diagonal elements are 1’s and off-diagonal elements are set as 0.

For the alternative hypothesis in single regression case, suppose $S$ is the support of the regression coefficients $\beta$ and $|S| = k$. Set $\beta_j = \rho 1\{j \in S\}$ for $j = 1, ..., p$. For the two-sample testing, we set the null hypothesis $H_0 : \beta^{(1)} = \beta^{(2)} = 0$, the alternative hypothesis $H_1 : \beta^{(1)} = 0, \beta^{(2)}_j = \rho 1\{j \in S\}$ for $j = 1, ..., p$ and $|S| = k$. For better illustrations, we let $\rho = 0.5$ and 0.75 for the single regression cases whereas $\rho = 0.7$ and 1 for the two-regression cases. The design covariance matrices $\Sigma^{(1)} = \Sigma^{(2)} = \Sigma$. For the tuning parameters, we set $\kappa_0 = 0$ and $\kappa_1 = 0.9$, and use 5-folds cross-validation to select $\lambda$ in every Lasso algorithm.

Table 2 shows the empirical type I errors of our proposed global test at level $\alpha = 0.05$ for both single regression and two regressions based on 1000 simulations, indicating the correct type I errors of the proposed global tests. Figure 1 and 2 shows the empirical powers under various settings for testing single regression and two regressions, respectively. As we expect, the power increases as $p, n$ or $\rho$ grows.
Table 2: Type I errors of the proposed global test with $\alpha = 0.05$ for single regression ($H_0 : \beta = 0$) and two regressions ($H_0 : \beta^{(1)} = \beta^{(2)}$).

<table>
<thead>
<tr>
<th>$p/n$</th>
<th>$\Sigma = I$</th>
<th>$\Sigma = \Sigma_B$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$p = 400$</td>
<td>$600$</td>
</tr>
<tr>
<td>Single regression</td>
<td>2</td>
<td>0.035</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.033</td>
</tr>
<tr>
<td>Two regressions</td>
<td>2</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.046</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.029</td>
</tr>
</tbody>
</table>

5.2 Multiple Hypotheses Testing

For the multiple hypotheses testing, we denoted our proposed FDR controlling test as LMT. In single regression setting, given the support $S$ such that $|S| = k$, we set $\beta_j = \rho 1\{j \in S\}$ for $j = 1, \ldots, p$. In the setting with two logistic regressions, we set $\beta^{(1)}_j = 0$ and $\beta^{(2)}_j = \rho 1\{j \in S\}$ for $j = 1, \ldots, p$. The entries of the design matrices are generated from a uniform distribution on $[-2, 2]$.

The choice of $\kappa_0$, $\kappa_1$ and $\lambda$ are the same as the global testing.

We consider settings where $\alpha = 0.05$ and $\rho = 0.5$. For our proposed multiple testing procedure (3.5) and (4.2), our initial simulations indicate that the theoretical upper bound $\sqrt{2 \log p}$ for the threshold $\hat{t}$ often leads to conservative tests. To address this issue, we recommend using $\hat{t} = \sqrt{0.5 \log p}$ instead in practice if $\hat{t}$ in (3.5) or (4.2) doesn’t exist. The simulation results presented in this section show that the recommended upper bound $\sqrt{0.5 \log p}$ leads to tests reaching the nominal FDR with good power. Figure 3 shows the empirical FDRs and Figure 4 shows the powers of our LMT and the BH procedure based on 1000 replications for single and two logistic regressions settings, where the power if defined as the proportion of the number of correctly discovered variables divided by the number of truly associated variables. The BH procedure is clearly too conservative, and our proposed LMT test is much more powerful than the BH procedure in all the settings.

For our proposed test that controls FDV (denoted as LMT$_V$), by setting desired FDV level $r = 10$, we apply our method to the same set of settings and the resulting empirical FDV and powers are summarized in Table 3. Our proposed LMT$_V$ has the correct control of FDV in all the settings and the power increases as $p$ or $n$ grows.

6 REAL DATA ANALYSIS

We illustrate our proposed methods by analyzing a dataset from the Pediatric Longitudinal Study of Elemental Diet and Stool Microbiome Composition (PLEASE) study, a prospective cohort study
to investigate the effects of inflammation, antibiotics, and diet as environmental stressors on the gut microbiome in pediatric Crohn’s disease (Lewis et al., 2015; Lee et al., 2015; Ni et al., 2017). The study considered the association between pediatric Crohn’s disease and fecal metabolomics by collecting fecal samples of 90 pediatric patients with Crohn’s disease at baseline, 1 week, and 8 weeks after initiation of either anti-tumor necrosis factor (TNF) or enteral diet therapy, as well as those from 25 healthy control children (Lewis et al., 2015). In details, an untargeted fecal metabolomic analysis was performed on these samples using liquid chromatography-mass spectrometry (LC-MS). Metabolites with more than 80% missing values across all samples were removed from the analysis. For each metabolite, samples with the missing values were imputed with its minimum abundance across samples. To avoid potential large outliers, for each sample, the metabolite abundances were further normalized by dividing 90% cumulative sum of the abundances of all metabolites. The
Figure 2: Empirical powers for the two-sample global hypothesis for various combinations of the dimension $p$, sample size $n$, sparsity $s$ and covariance structure. Top panel: $\Sigma = I$; bottom panel: $\Sigma = \Sigma_B$.

normalized abundances were then log transformed and used in all analyses. The metabololomics annotation was obtained from Human Metabolome Database (Lee et al., 2015). In total, for each sample, abundances of 335 known metabolites were obtained and used in our analysis.

6.1 Association Between Metabolites and Crohn’s Disease Before and After Treatment

We first test the overall association between 335 characterized metabolites and Crohn’s disease by fitting a logistic regression using the data of 25 healthy controls and 90 Crohn’s disease patients at the baseline. We obtain a global test statistic of 433.88 with a $p$-value $< 0.001$, indicating a strong association between Crohn’s disease and fecal metabolites. At the FDR $< 5\%$, our multiple
Figure 3: Boxplots of the empirical FDRs of LMT and BH procedures for single logistic regression (left) and two logistic regressions (right).

Figure 4: Empirical powers of LMT and BH procedures with $\alpha = 0.05$ for single logistic regression (top panel) and two logistic regressions (bottom panel).
Table 3: Empirical performance of LMT$_V$ with FDV level $r = 10$ for single logistic regression and two logistic regressions.

<table>
<thead>
<tr>
<th>$\rho$</th>
<th>$s$</th>
<th>$p/n$</th>
<th>Empirical FDV</th>
<th>Empirical Power</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>$p = 400$</td>
<td>$600$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single logistic regressions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5.83</td>
<td>7.43</td>
<td>7.30</td>
<td>7.63</td>
</tr>
<tr>
<td>2</td>
<td>5.16</td>
<td>6.36</td>
<td>7.00</td>
<td>6.83</td>
</tr>
<tr>
<td>4</td>
<td>5.56</td>
<td>6.10</td>
<td>5.67</td>
<td>6.73</td>
</tr>
<tr>
<td>2</td>
<td>5.93</td>
<td>6.07</td>
<td>5.70</td>
<td>6.00</td>
</tr>
<tr>
<td>0.5</td>
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<td>5.60</td>
<td>6.20</td>
<td>5.67</td>
</tr>
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<td>4</td>
<td>5.13</td>
<td>4.80</td>
<td>6.13</td>
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<td>2</td>
<td>3.93</td>
<td>4.20</td>
<td>4.13</td>
<td>4.20</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>4.43</td>
<td>5.00</td>
<td>4.07</td>
</tr>
<tr>
<td>4</td>
<td>4.20</td>
<td>3.83</td>
<td>3.80</td>
<td>4.47</td>
</tr>
<tr>
<td>Two logistic regressions</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2</td>
<td>4.74</td>
<td>6.67</td>
<td>5.43</td>
<td>5.33</td>
</tr>
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<td>4.33</td>
<td>5.26</td>
<td>5.20</td>
<td>5.84</td>
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<td>3.86</td>
<td>4.16</td>
<td>3.90</td>
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<td>2</td>
<td>5.40</td>
<td>4.27</td>
<td>5.10</td>
<td>4.90</td>
</tr>
<tr>
<td>0.5</td>
<td>4</td>
<td>5.30</td>
<td>3.70</td>
<td>5.67</td>
</tr>
<tr>
<td>4</td>
<td>4.83</td>
<td>4.50</td>
<td>4.76</td>
<td>4.46</td>
</tr>
<tr>
<td>2</td>
<td>4.60</td>
<td>3.23</td>
<td>4.30</td>
<td>4.94</td>
</tr>
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<td>8</td>
<td>3</td>
<td>3.63</td>
<td>3.73</td>
<td>4.17</td>
</tr>
<tr>
<td>4</td>
<td>2.90</td>
<td>3.54</td>
<td>2.95</td>
<td>3.98</td>
</tr>
</tbody>
</table>

testing procedure selects four metabolites, including C14:0.sphingomyelin, C24:1.Ceramide.(d18:1) and 3-methyladipate/pimelate (see Table 4). Recent studies have demonstrated that sphingolipid metabolites, particularly ceramide and sphingosine-1-phosphate, are signaling molecules that regulate a diverse range of cellular processes that are important in immunity, inflammation and inflammatory disorders \cite{Maceyka2014}. In fact, ceramide acts to reduce tumor necrosis factor (TNF) release \cite{Rozenova2010} and has important roles in the control of autophagy, a process strongly implicated in the pathogenesis of Crohn’s disease \cite{Barrett2008, Sewell2012}.

We next investigate whether treatment of Crohn’s disease alters the association between metabolites and Crohn’s disease by fitting two separate logistic regressions using the metabolites measured one week or 8 weeks after the treatment. At each time point, a significant association is detected based on our global test (p-value < 0.001). One week after the treatment, we observe six metabolites associated with Crohn’s disease, including all four identified at the baseline and two additional metabolites, beta-alanine and adipate (see Table 4). The beta-alanine and adipate associations are likely due to that beta-alanine and adipate are important ingredients of the enteral nutrition treat-
ment of Crohn’s disease. However, it is interesting that at 8 weeks after the treatment, valine, C16.carnitine and C18.carnitine are identified to be associated with Crohn’s disease together with 3-methyladipate/pimelate and beta-alanine. It is known that carnitine plays an important role in Crohn’s disease, which might be a consequence of the underlying functional association between Crohn’s disease and mutations in the carnitine transporter genes (Peltekova et al. 2004; Fortin 2011). Deficiency of carnitine can lead to severe gut atrophy, ulceration and inflammation in animal models of carnitine deficiency (Shekhawat et al. 2013). Our results may suggest that the treatment increases carnitine, leading to reduction of inflammation.

Table 4: Significant metabolites associated with Crohn’s disease (coded as 1 in logistic regression) at the baseline, one week and 8 weeks after treatment with FDR < 5%. The refitted regression coefficients show the direction of the association.

<table>
<thead>
<tr>
<th>Disease Stage</th>
<th>HMDB ID</th>
<th>Synonyms</th>
<th>Refitted Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>00885</td>
<td>C16:0.cholesteryl ester</td>
<td>4.45</td>
</tr>
<tr>
<td></td>
<td>12097</td>
<td>C14:0.sphingomyelin</td>
<td>1.74</td>
</tr>
<tr>
<td></td>
<td>04953</td>
<td>C24:1.Ceramide.(d18:1)</td>
<td>4.25</td>
</tr>
<tr>
<td></td>
<td>00555</td>
<td>3-methyladipate/pimelate</td>
<td>-12.82</td>
</tr>
<tr>
<td>Week 1</td>
<td>06726</td>
<td>C20:4.cholesteryl ester</td>
<td>2.17</td>
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<tr>
<td></td>
<td>12097</td>
<td>C14:0.sphingomyelin</td>
<td>2.06</td>
</tr>
<tr>
<td></td>
<td>04949</td>
<td>C16:0.Ceramide.(d18:1)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>00555</td>
<td>3-methyladipate/pimelate</td>
<td>-6.10</td>
</tr>
<tr>
<td></td>
<td>00056</td>
<td>beta-alanine</td>
<td>2.95</td>
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<tr>
<td></td>
<td>00448</td>
<td>adipate</td>
<td>-4.50</td>
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<tr>
<td>Week 8</td>
<td>00883</td>
<td>valine</td>
<td>1.40</td>
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<td></td>
<td>00222</td>
<td>C16.carnitine</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>00848</td>
<td>C18.carnitine</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>00555</td>
<td>3-methyladipate/pimelate</td>
<td>-5.95</td>
</tr>
<tr>
<td></td>
<td>00056</td>
<td>beta-alanine</td>
<td>0.63</td>
</tr>
</tbody>
</table>

6.2 Comparison of Metabolite Associations Between Responders and Non-Responders

To compare the metabolic association with Crohn’s disease for responders \((n = 47)\) and non-responders \((n = 34)\) eight weeks after treatment, we fit two logistic regression models, responder versus normal control and non-responder versus normal control. Our global test shows that there is an overall difference in regression coefficients for responders and for non-responders when compared to the normal controls \((p-value < 0.001)\). We next apply our proposed multiple testing procedure to identify the metabolites that have different regression coefficients in these two different logistic regression models. At the FDR < 0.05, our procedure identifies 9 metabolites with different regression coefficients (see Table 5). It is interesting that all these 9 metabolites have the same signs of the refitted coefficients, while the actual magnitudes of the associations between responders...
and non-responders when compared to the normal controls are different. Besides C24:4.cholesteryl
ester, beta-alanine, valine, C18.carnitine and 3-methyladipate/pimelate that we observe in pre-
vious analyses, metabolites 5-hydroxytryptophan, nicotinate, and succinate also have differential
associations between responders and non-responders when compared to the controls.

Table 5: Significant metabolites identified via logistic regression of responder vs normal control
and non-responder vs normal control for FDR \( \leq 5\% \).

<table>
<thead>
<tr>
<th>HMDB ID</th>
<th>Synonyms</th>
<th>Refitted Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Responder vs. Normal</td>
</tr>
<tr>
<td>06726</td>
<td>C20:4.cholesteryl ester</td>
<td>0.139</td>
</tr>
<tr>
<td>01043</td>
<td>Linoleic.acid</td>
<td>-0.686</td>
</tr>
<tr>
<td>00472</td>
<td>5-hydroxytryptophan</td>
<td>1.000</td>
</tr>
<tr>
<td>00556</td>
<td>beta-alanine</td>
<td>0.503</td>
</tr>
<tr>
<td>00883</td>
<td>valine</td>
<td>0.628</td>
</tr>
<tr>
<td>00848</td>
<td>C18.carnitine</td>
<td>1.100</td>
</tr>
<tr>
<td>01488</td>
<td>nicotinate</td>
<td>-1.936</td>
</tr>
<tr>
<td>00254</td>
<td>succinate</td>
<td>0.750</td>
</tr>
<tr>
<td>00555</td>
<td>3-methyladipate/pimelate</td>
<td>-1.989</td>
</tr>
</tbody>
</table>

7 DISCUSSION

In this paper, for both global and multiple testing, the precision matrix \( \Omega = \Sigma^{-1} \) of the covariates
is assumed to be sparse and unknown. Nodewise regression among the covariates is used to learn
such structure for construction of the debiased estimator. However, if the prior knowledge of
\( \Omega = I \) is available, the algorithm can be much simplified. Specifically, instead of incorporating
the Lasso estimators as in (2.6), we let \( v_j = \tilde{W}^{-1}x_j \) and \( \tau_j = \|v_j\|_n/(v_j,x_j) \) for each \( j = 1, ..., p \).
The theoretical properties of the resulting global testing and multiple testing procedures still hold,
while the computational efficiency is improved dramatically. Unfortunately, however, from our
theoretical analysis, even with the knowledge of \( \Omega = I \), the theoretical requirement for the model
sparsity \( (k = o(\sqrt{n}/\log^3 p) \) in the Gaussian case and \( k = o(\sqrt{n}/\log^{5/2} p) \) in the bounded case) cannot be relaxed due to the nonlinearity of the problem.

As mentioned in the introduction, the logistic regression model can be viewed as a special case
of the single index model \( y = f(\beta^\top x) + \epsilon \) where \( f \) is a known transformation function [Yang et al. 2015]. Based on our analysis, it is clear that the theoretical results are not limited to the sigmoid
transfer function. In fact, the proposed methods can be applied to a wide range of transformation
functions satisfying the following conditions: (C1) \( f \) is continuous and for any \( u \in \mathbb{R}, 0 < f(u) < 1 \; \); (C2) for any \( u_1, u_2 \in \mathbb{R}, \) there exists a constant \( L > 0 \) such that \( |f(u_1) - f(u_2)| \leq L|u_1 - u_2| \); and (C3) for any constant \( C > 0, \) there exists \( \delta > 0 \) such that for any \( |u| \leq C, \ f(u) \geq \delta \). Examples
include but are not limited to the following function classes

- **Cumulative density functions:** \( f(x) = P(X \leq x) \) for some continuous random variable \( X \) supported on \( \mathbb{R} \). In particular, when \( X \sim N(0,1) \), the resulting model becomes the probit regression.

- **Affine hyperbolic tangent functions:** \( f(x) = \frac{1}{2}\tanh(ax + b) + 1 \) for some parameter \( a, b \in \mathbb{R} \). In particular, \((a, b) = (1, 0)\) corresponds to \( f(x) = e^x/(1 + e^x) \).

- **Generalized logistic functions:** \( f(x) = (1 + e^{-x})^{-\alpha} \) for some \( \alpha > 0 \).

Besides the problems we considered in this paper, it is also of interest to construct confidence intervals for functionals of the regression coefficients, such as \( \|\beta\|_1 \), \( \|\beta\|_2 \), or \( \theta^T \beta \) for some given loading vector \( \theta \). In modern statistical machine learning, logistic regression is considered as an efficient classification method (Abramovich and Grinshtein, 2017). In practice, a predicted label with an uncertainty assessment is usually preferred. Therefore, another important problem is the construction of predictive intervals of the conditional probability \( \pi^* \) associated with a given predictor \( X^* \). These problems are related to the current work and are left for future investigations.

## 8 PROOFS OF THE MAIN THEOREMS

In this section, we prove Theorems 2.1, Theorem 2.2 and Proposition 1 in the paper. The proofs of other results, including Theorems 3-5, and the technical lemmas, are given in the online Supplementary Materials.

**Proof of Theorem 2.1**

Define \( F_{jj} = \mathbb{E}[\eta_{ij}^2 / \dot{f}(u_i)] \). Under \( H_0 \), \( F_{jj} = 4\mathbb{E}[\eta_{ij}^2] = 4/\omega_{jj} \), and by (A3), \( c < F_{jj} < C \) for \( j = 1, ..., p \) and some constant \( C \geq c > 0 \). Define statistics

\[
\tilde{M}_j = \frac{\langle v_j, \epsilon \rangle}{\|v_j\|_n}, \quad \text{and} \quad M_j = \sum_{i=1}^n \frac{\eta_{ij} \epsilon_i / \dot{f}(u_i)}{\sqrt{nF_{jj}}}, \quad j = 1, ..., p.
\]

and \( \hat{M}_n = \max_j \tilde{M}_j^2, \tilde{M}_n = \max_j M_j^2 \). The following lemma shows that \( \hat{M}_n \) and therefore \( \hat{M}_n \) are good approximations of \( M_n \).

**Lemma 1.** Under the condition of Theorem 1, the following events

\[
B_1 = \left\{ |\hat{M}_n - M_n| = o(1) \right\}, \quad B_2 = \left\{ |\hat{M}_n - M_n| = o\left( \frac{1}{\log p} \right) \right\},
\]

hold with probability at least \( 1 - O(p^{-c}) \) for some constant \( c > 0 \).

It follows that under the event \( B_1 \cap B_2 \), let \( y_p = 2 \log p - \log \log p + x \) and \( \epsilon_n = o(1) \), we have

\[
P_{H_0}(\hat{M}_n \leq y_p - \epsilon_n) \leq P_{H_0}(M_n \leq y_p) \leq P_{H_0}(\hat{M}_n \leq y_p + \epsilon_n).
\]

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Therefore it suffices to prove that for any $t \in \mathbb{R}$, as $(n,p) \to \infty$,

$$
P_{H_0}(\hat{M}_n \leq y_p) \to \exp \left(-\frac{1}{\sqrt{\pi}} \exp(-x/2)\right).$$

(8.1)

Now define

$$
\hat{M}_j = \frac{1}{\sqrt{nF_{jj}}} \sum_{i=1}^{n} \hat{Z}_{ij}, \quad j = 1, \ldots, p.
$$

where $\hat{Z}_{ij} = v_{ij}^0 \epsilon_i 1\{|v_{ij}^0 \epsilon_i| \leq \tau_n\} - \mathbb{E}[v_{ij}^0 \epsilon_i 1\{|v_{ij}^0 \epsilon_i| \leq \tau_n\}]$ for $\tau_n = \log(p + n)$, $v_{ij}^0 = \eta_{ij} / \hat{f}(u_i)$ and $\hat{M}_n = \max_j \hat{M}_j^2$. The following lemma states that $\hat{M}_n$ is close to $\hat{M}_n$.

**Lemma 2.** Under the condition of Theorem 1, $|\hat{M}_n - \hat{M}_n| = o(1)$ with probability at least $1 - O(p^{-c})$ for some constant $c > 0$.

By Lemma ??, it suffices to prove that for any $t \in \mathbb{R}$, as $(n,p) \to \infty$,

$$
P_{H_0}(\hat{M}_n \leq y_p) \to \exp \left(-\frac{1}{\sqrt{\pi}} \exp(-x/2)\right).$$

(8.2)

To prove this, we need the classical Bonferroni inequality.

**Lemma 3. (Bonferroni inequality)** Let $B = \bigcup_{k=1}^{p} B_k$. For any integer $k < p/2$, we have

$$
\sum_{t=1}^{2k} (-1)^{t-1} F_t \leq P(B) \leq \sum_{t=1}^{2k-1} (-1)^{t-1} F_t,
$$

(8.3)

where $F_t = \sum_{1 \leq i_1 < \ldots < i_t \leq p} P(B_{i_1} \cap \ldots \cap B_{i_t})$.

By Lemma ??, for any integer $0 < q < p/2$,

$$
\sum_{d=1}^{2q} (-1)^{d-1} \sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left(\bigcap_{k=1}^{d} F_{j_k}\right) \leq P\left(\max_{1 \leq j \leq p} \hat{M}_j^2 \geq y_p\right) \\
\leq \sum_{d=1}^{2p-1} (-1)^{d-1} \sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left(\bigcap_{k=1}^{d} F_{j_k}\right),
$$

(8.4)

where $F_{j_k} = (\hat{M}_{j_k}^2 \geq y_p)$. Now let $w_{ij} = \hat{Z}_{ij} / \sqrt{F_{jj}}$ for $j = 1, \ldots, p$, and $W_i = (w_{i,j_1}, \ldots, w_{i,j_d})^\top$ for $1 \leq i \leq n$. Define $\|a\|_{\min} = \min_{1 \leq i \leq d} |a_i|$ for any vector $a \in \mathbb{R}^d$. Then we have

$$
P\left(\bigcap_{k=1}^{d} F_{j_k}\right) = P\left(\left\|n^{-1/2} \sum_{i=1}^{n} W_i\right\|_{\min} \geq y_p^{1/2}\right).
$$
Then it follows from Theorem 1.1 in Zaitsev [1987] that

$$P\left( \left\| n^{-1/2} \sum_{i=1}^{n} W_i \right\|_{\text{min}} \geq y_p^{1/2} \right) \leq P\left( \left\| N_d \right\|_{\min} \geq y_p^{1/2} - \epsilon_n (\log p)^{-1/2} \right) + c_1 d^{5/2} \exp \left\{ - \frac{n^{1/2} \epsilon_n}{c_2 d^{5/2} \tau_n (\log p)^{1/2}} \right\}, \quad (8.5)$$

where $c_1 > 0$ and $c_2 > 0$ are constants, $\epsilon_n \to 0$ which will be specified later, and $N_d = (N_{m_1}, \ldots, N_{m_d})$ is a normal random vector with $E(N_d) = 0$ and $\text{cov}(N_d) = \text{cov}(W_1)$. Here $d$ is a fixed integer that does not depend on $n,p$. Because $\log p = o(n^{1/5})$, we can let $\epsilon_n \to 0$ sufficiently slow, say, $\epsilon_n = \sqrt{\log^5 p/n}$, so that for any large $c > 0$,

$$c_1 d^{5/2} \exp \left\{ - \frac{n^{1/2} \epsilon_n}{c_2 d^{5/2} \tau_n (\log p)^{1/2}} \right\} = O(p^{-c}). \quad (8.6)$$

Combining (8.5), (8.6) and (8.8), we have

$$P\left( \max_{1 \leq j \leq p} M^2_j \geq y_p \right) \leq \sum_{d=1}^{2p-1} (-1)^{d-1} \sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left( \left\| N_d \right\|_{\min} \geq y_p^{1/2} - \epsilon_n (\log p)^{-1/2} \right) + o(1). \quad (8.7)$$

Similarly, one can derive

$$P\left( \max_{1 \leq j \leq p} M^2_j \geq y_p \right) \geq \sum_{d=1}^{2p} (-1)^{d-1} \sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left( \left\| N_d \right\|_{\min} \geq y_p^{1/2} + \epsilon_n (\log p)^{-1/2} \right) + o(1). \quad (8.8)$$

Now we use the following lemma from Xia et al. [2018].

**Lemma 4.** For any fixed integer $d \geq 1$ and real number $t \in \mathbb{R}$,

$$\sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left( \left\| N_d \right\|_{\min} \geq y_p^{1/2} \pm \epsilon_n (\log p)^{-1/2} \right) = \frac{1}{d!} \left( \frac{1}{\sqrt{\pi}} \exp(-t/2) \right)^d (1 + o(1)).$$

It then follows from the above lemma, (8.7) and (8.8) that

$$\lim_{n,p \to \infty} P\left( \max_{1 \leq j \leq p} M^2_j \geq y_p \right) \leq \sum_{d=1}^{2p} (-1)^{d-1} \frac{1}{d!} \left( \frac{1}{\sqrt{\pi}} \exp(-t/2) \right)^d,$$

$$\lim_{n,p \to \infty} P\left( \max_{1 \leq j \leq p} M^2_j \geq y_p \right) \geq \sum_{d=1}^{2p-1} (-1)^{d-1} \frac{1}{d!} \left( \frac{1}{\sqrt{\pi}} \exp(-t/2) \right)^d,$$

for any positive integer $p$. By letting $p \to \infty$, we obtain (8.5) and the proof is complete. \qed
Proof of Theorem 2.2. The proof essentially follows from the general Le Cam’s method described in Section 7.1 of Baraud (2002). The key elements can be summarized as the following lemma that reduces the lower bound problem to calculation of the total variation distance between two posterior distributions.

Lemma 5. Let \( \mathcal{H}_1 \) be some subset in an \( \ell_2 \) bounded Hilbert space and \( \rho \) some positive number. Let \( \mu_\rho \) be some probability measure on \( \mathcal{H}_1 = \{ \theta \in \Theta, \| \theta \| = \rho \} \). Set \( P_{\mu_\rho} = \int P_\theta \mu_\rho(\theta) \), \( P_0 \) as the (posterior) distribution at the null, and denote by \( \Phi_\alpha \) the level-\( \alpha \) tests, we have

\[
\inf_{\Phi_\alpha} \sup_{\theta \in \mathcal{H}_1} P_\theta(\Phi_\alpha = 0) \geq \inf_{\Phi_\alpha} P_{\mu_\rho}(\Phi_\alpha = 0) \geq 1 - \alpha - \frac{1}{2} TV(P_{\mu_\rho}, P_0),
\]

where \( TV(P_{\mu_\rho}, P_0) \) denotes the total variation distance between \( P_{\mu_\rho} \) and \( P_0 \).

Now since by definition \( \rho^*(\Phi_\alpha, \delta, \Theta(k)) \geq \rho^*(\Phi_\alpha, \delta, \Sigma) \) for any \( \Sigma \in \Theta(k) \), by Lemma ??, it suffices to construct \( \mathcal{H}_1 \) for \( \beta \in \Theta(k) \) and find a lower bound \( \rho_1 = \rho(\eta) \) such that

\[
\forall \rho \leq \rho_1 \quad \inf_{\Phi_\alpha} P_{\mu_\rho}(\Phi_\alpha = 0) \geq 1 - \alpha - \eta = \delta.
\]

(8.9)

for fixed covariance \( \Sigma = I \). In this case, an upper bound for the \( \chi^2 \)-divergence between \( P_{\mu_\rho} \) and \( P_0 \), defined as

\[
\chi^2(P_{\mu_\rho}, P_0) = \int \left( \frac{dP_{\mu_\rho}}{dP_0} \right)^2 - 1,
\]

can be obtained by carefully constructing the alternative space \( \mathcal{H}_1 \). Since \( TV(f, g) \leq \sqrt{\chi^2(f, g)} \) (see p.90 of Tsybakov (2009)), it follows that

\[
\inf_{\Phi_\alpha} P_{\mu_\rho}(\Phi_\alpha = 0) \geq 1 - \alpha - \frac{1}{2} \sqrt{\chi^2(P_{\mu_\rho}, P_0)}.
\]

By choosing \( \rho_1 = \rho(\eta) \) such that for any \( \rho \leq \rho_1 \), \( \chi^2(P_{\mu_\rho}, P_0) \leq 4\eta^2 = 4(1 - \alpha - \delta)^2 \), we have (??) holds. In the following, we will construct the alternative space \( \mathcal{H}_1 \) and derive an upper bound of \( \chi^2(P_{\mu_\rho}, P_0) \) where \( P_0 \) corresponds to the null space \( \mathcal{H}_0 \) defined at a single point \( \beta = 0 \). We divide the proofs into two parts. Throughout, the design covariance matrix is chosen as \( \Sigma = I \).

Step 1: Construction of \( \mathcal{H}_1 \). Firstly, for a set \( M \), we define \( \ell(M, n) \) as the set of all the \( n \)-element subsets of \( M \). Let \( [1 : p] = \{1, ..., p\} \), so \( \ell([1 : p], k) \) contains all the \( k \)-element subsets of \([1 : p] \). We define the alternative parameter space

\[
\mathcal{H}_1 = \left\{ (\beta, I) \in \mathbb{R}^p \times \mathbb{R}^{p \times p} : \beta_j = \rho 1\{j \in I\} \text{ for } I \in \ell([1 : p], k) \right\}.
\]
In other words, $H_1$ contains all the $k$-sparse vectors $\beta(I)$ whose nonzero components $\rho$ are indexed by $I$. Apparently, for any $\beta \in H_1$, it follows $\|\beta\|_\infty = \rho$ and $H_1 \subseteq \Theta(k)$.

**Step 2: Control of $\chi^2(P_{\pi H_1}, P_0)$**. Let $\pi$ denote the uniform prior of the random index set $I$ over $\ell([1 : p], k)$. This prior induces a prior distribution $\pi_{H_1}$ over the parameter space $H_1$. For $\{(0, I)\} = H_0$, the corresponding joint distribution of the data $\{(X_i, y_i)\}_{i=1}^n$ is

$$f = \prod_{i=1}^n p(X_i, y_i) = \frac{1}{(2\pi)^{np/2}} \prod_{i=1}^n \frac{1}{2} e^{-\|x_i\|_2^2/2}.$$ 

Similarly, the posterior distribution of the samples over the prior $\pi_{H_1}$ is denoted as

$$g = \prod_{i=1}^n \int_{H_1} p(X_i, y_i; \beta) \pi_{H_1} = \frac{1}{(\pi)^n} \prod_{i=1}^n \sum_{\beta \in H_1} p(X_i, y_i; \beta).$$

As a result, we have the following lemma controlling $\chi^2(P_{\pi H_1}, P_0) = \chi^2(g, f)$.

**Lemma 6.** Let $\rho^2 = \frac{1}{n} \log (1 + \frac{p}{h(\eta)k^2})$ where $h(\eta) = [\log(4\eta^2 + 1)]^{-1}$ and $\eta = 1 - \alpha - \delta$, then we have $\chi^2(g, f) \leq 4(1 - \alpha - \delta)^2$.

Combining Lemma ?? and Lemma ??, we know that for $\alpha, \delta > 0$ and $\alpha + \delta < 1$, if $\rho_1 = \sqrt{\frac{1}{n} \log (1 + \frac{p}{h(\eta)k^2})}$, then

$$\forall \rho \leq \rho_1, \quad \inf_{\Phi} \sup_{\beta \in \Theta(k) : \|\beta\|_\infty \geq \rho} P_0(\Phi = 0) \geq \delta.$$ 

Therefore, it follows that

$$\rho^*(\alpha, \delta, \Theta(k)) \geq \rho^*(\alpha, \delta, I) \geq \sqrt{\frac{1}{n} \log \left(1 + \frac{p}{k^2}\right)}.$$ 

(8.10)

This completes the proof.

**Proof of Proposition 1.** By similar argument as in Lemma 1, we can prove the following lemma.

**Lemma 7.** Assume (A2) (A3) and (A4), $k = o(\sqrt{n}/\log^{5/2} p)$, then

$$\max_{j \in H_0} |\tilde{M}_j - M_j| = o\left(\frac{1}{\sqrt{\log p}}\right), \quad \max_{j \in H_0} |\tilde{M}_j - M_j| = o\left(\frac{1}{\sqrt{\log p}}\right),$$

hold with probability at least $1 - O(p^{-c})$ for some constant $c > 0$. 

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For (3.7), by Lemma 6.1 in [Liu 2013], we have

$$\max_{1 \leq j \leq p} \sup_{0 \leq t \leq 4 \sqrt{\log p}} \left| \frac{P(|\tilde{M}_j| \geq t)}{G(t)} - 1 \right| \leq C(\log p)^{-2-\gamma_1} \quad (8.11)$$

for some constant $0 < \gamma_1 < 1/2$. So (3.7) follows from Lemma ??, and the fact that $G(t + o(1/\sqrt{\log p}))/G(t) = 1 + o(1)$ uniformly in $0 \leq t \leq \sqrt{2\log p}$.

For (3.8), it suffices to show that

$$\sup_{0 \leq t \leq d_p} \left| \frac{\sum_{j \in \mathcal{H}_0} I\{M_j \geq t\}}{p_0 G(t)} - 1 \right| \to 0 \quad \text{in probability.} \quad (8.12)$$

Let $z_0 < z_1 < \ldots < z_{d_p} \leq 1$ and $t_i = G^{-1}(z_i)$, where $z_0 = c_p/p$, $z_i = c_p/p + 2^{i/3}e^{i\delta}/p, d_p = [\log((p - c_p)/c_p^{2/3})]^{1/\delta} < \delta < 1$, which will be specified later. We have $G(t_i)/G(t_{i+1}) = 1 + o(1)$ uniformly in $i$, and $t_0/\sqrt{2\log(p/c_p)} = 1 + o(1)$. Note that uniformly for $1 \leq j \leq m$, $G(t_i)/G(t_{i-1}) \to 1$ as $p \to \infty$. The proof of (??) reduces to show that

$$\max_{0 \leq i \leq d_p} \left| \frac{\sum_{j \in \mathcal{H}_0} I\{M_j \geq t_i\}}{p_0 G(t_i)} - 1 \right| \to 0 \quad (8.13)$$

in probability. In fact, for each $\epsilon > 0$, we have

$$P\left( \max_{0 \leq t \leq d_p} \left| \frac{\sum_{j \in \mathcal{H}_0} I\{M_j \geq t\}}{p_0 G(t)} \right| \geq t_i \right) \leq \sum_{j=0}^{d_p} P\left( \left| \frac{\sum_{j \in \mathcal{H}_0} I\{M_j \geq t\}}{p_0 G(t)} \right| \geq \epsilon/2 \right).$$

Set $I(t) = \sum_{j \in \mathcal{H}_0} I\{M_j \geq t\}$. By Markov’s inequality $P(|I(t_i)| \geq \epsilon/2) \leq \frac{E[I(t_i)]^2}{\epsilon^2/4}$, and it suffices to show $\sum_{j=0}^{d_p} E[I(t_i)]^2 = o(1)$. To do this, by (??),

$$E[I^2(t)] = \frac{\sum_{j \in \mathcal{H}_0} [P(|\tilde{M}_j| \geq t) - 2P(|\tilde{M}_j| \geq t) - P^2(|\tilde{M}_j| \geq t)]}{p_0^2 G^2(t)} + \frac{\sum_{j,k \in \mathcal{H}_0, j \neq k} [P(|\tilde{M}_j| \geq t, |\tilde{M}_k| \geq t) - P(|\tilde{M}_j| \geq t)P(|\tilde{M}_k| \geq t)]}{p_0^2 G^2(t)} \leq \frac{C}{p_0 G(t)} + \frac{1}{p_0^2} \sum_{(j,k) \in A(\epsilon) \cap \mathcal{H}_0} \frac{P(|\tilde{M}_j| \geq t, |\tilde{M}_k| \geq t)}{G^2(t)} + \frac{1}{p_0^2} \sum_{(j,k) \in A(\epsilon) \cap \mathcal{H}_0} \left[ \frac{P(|\tilde{M}_j| \geq t, |\tilde{M}_k| \geq t)}{G^2(t)} - 1 \right] = \frac{C}{p_0 G(t)} + I_{11}(t) + I_{12}(t).$$
For \((j,k) \in \mathcal{A}(\epsilon) \cap \mathcal{H}_0\), applying Lemma 6.1 in [Liu (2013)], we have \(I_{12}(t) \leq C(\log p)^{-1-\xi}\) for some \(\xi > 0\) uniformly in \(0 < t < \sqrt{2\log p}\). By Lemma 6.2 in [Liu (2013)], for \((j,k) \in \mathcal{A}(\epsilon) \cap \mathcal{H}_0\), we have

\[
P(|\tilde{M}_j| \geq t, |\tilde{M}_k| \geq t) \leq C(t + 1)^{-2} \exp \left( - \frac{t^2}{1 + |\rho_{jk}|} \right).
\]

So that

\[
I_{11}(t) \leq C \frac{1}{p_0} \sum_{(j,k) \in \mathcal{A}(\epsilon) \cap \mathcal{H}_0} (t + 1)^{-2} \exp \left( - \frac{t^2}{1 + |\rho_{jk}|} \right) G^{-2}(t) \leq C \frac{1}{p_0} \sum_{(j,k) \in \mathcal{A}(\epsilon) \cap \mathcal{H}_0} [G(t)]^{-\frac{2|\rho_{jk}|}{1+|\rho_{jk}|}}.
\]

Note that for \(0 \leq t \leq b_p\), we have \(G(t) \geq G(b_p) = c_p/p\), so that by assumption (A5) it follows that for some \(\epsilon, q > 0\),

\[
I_{11}(t) \leq C \sum_{(j,k) \in \mathcal{A}(\epsilon) \cap \mathcal{H}_0} p^{\frac{2|\rho_{jk}|}{1+|\rho_{jk}|} + q-2} = O(1/(\log p)^2).
\]

By the above inequalities, we can prove (??) by choosing \(0 < \delta < 1\) so that

\[
\sum_{i=0}^{d_p} \mathbb{E}[I(t_i)]^2 \leq C \sum_{i=0}^{d_p} (pG(t_i))^{-1} + Cd_p[(\log p)^{-1-\delta} + (\log p)^{-2}] \\
\leq C \sum_{i=0}^{d_p} \frac{1}{c_p + c_p^{2/3} e^{i\delta}} + o(1) \\
= o(1).
\]

**References**


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Supplement to “Global and Simultaneous Hypothesis Testing for High-Dimensional Logistic Regression Models”

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Abstract

In this supplementary material we prove Theorem 3-5 in the main paper and the technical lemmas. The technical results of the two-sample testing discussed in Section 4 of the main paper are included in the appendix.

1 Proofs of Theorem 3-5

Proof of Theorem 3. Define $M'_{j} = \tau_{j}^{-1}(\hat{\beta}_{j} - \beta_{j})$, and $M'_n = \max_j (M'_j)^2$, we have $-\beta_j/\tau_j = M'_j - M_j$. Thus

$$\frac{\beta_j^2}{\tau_j^2} \leq 2(M'_j)^2 + 2M_j^2,$$

for all $j$, (1.1)

and

$$\max_j \frac{\beta_j^2}{\tau_j^2} \leq 2M'_n + 2M_n.$$ 

(1.2)

The main idea for proving Theorem 3 is that, in order to show that $M_n$ is “large”, we show that $M'_n$ is “small” while $\max_j \beta_j^2/\tau_j^2$ is “large” under the condition of Theorem 3. In the following, we consider the Gaussian design and the bounded design separately. For the Gaussian design, we divide the proof into two parts.

Gaussian Design, Case 1. $\|\beta\|_2 \lesssim (\log p)^{-1/2}$. In this case, $\beta^T X_i$ are i.i.d. $N(0, \beta^T \Sigma \beta)$. By Lemma 6 in Cai et al. (2014), we have

$$P\left( \max_{1 \leq i \leq n} |\beta^T X_i| \geq \|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log p} \right) = O(p^{-c}),$$

(1.3)
then (A4), or $P(\max_{1 \leq i \leq n} |\beta^T X_i| \leq c) \to 1$ for some constant $c > 0$, holds. Consequently, the following lemma can be established by similar arguments as the proof of Lemma 1.

**Lemma 8.** Under the condition of Theorem 3, suppose (A4) hold, then

$$P(|M_j'| \geq \sqrt{C_0 \log p}) = O(p^{-c})$$

for some constants $C_0, c > 0$.

By Lemma ??, we have

$$P(M_n' \geq C_0 \log p) = O(p^{-c})$$

for some $C_0, c > 0$. On the other hand, to bound $\tau_j$, we start with the inequality

$$\|\hat{\eta}_j\|_2 / \langle \hat{\eta}_j, X_j \rangle \leq \frac{C_2}{\sqrt{n}}$$

obtained as (??) in the proof of Lemma 1. By (A4), there exists some constant $0 < \kappa < 1$ such that $\kappa < |f(u_i)| < 1 - \kappa$ with high probability. Then it follows that

$$1 - \hat{f}(\hat{u}_i) \leq \xi \hat{f}(\hat{u}_i), \quad \text{where } \xi = \frac{1 - \kappa + \kappa^2}{\kappa(1 - \kappa)}.$$  

Thus, since

$$\|v_j\|_n - \|\hat{\eta}_j\|_2 \leq \sqrt{\sum_{i=1}^n (\hat{f}(\hat{u}_i) - \hat{f}^2(\hat{u}_i))v_{ij}^2} \leq \sqrt{\sum_{i=1}^n \hat{f}^2(\hat{u}_i)v_{ij}^2} = \xi^{1/2}\|\hat{\eta}_j\|_2,$$

we have, with probability at least $1 - O(p^{-c})$,

$$\tau_j = \frac{\|v_j\|_n}{\langle v_j, X_j \rangle_n} \leq (1 + \xi^{1/2}) \frac{\|\hat{\eta}_j\|_2}{\langle \hat{\eta}_j, X_j \rangle} \leq C_2 \frac{1 + \xi^{1/2}}{\sqrt{n}} = C_3 \frac{\xi^{1/2}}{\sqrt{n}},$$

for some constant $C_3 > 0$. Therefore, since $\|\beta\|_\infty \geq c_2 \sqrt{\log p}/n$,

$$\max_j \beta_j^2 / \tau_j \geq c_2^2 \frac{\log p}{n} \cdot C_3^{-2} n = C_4 \log p$$

with probability converging to 1. In particular, when $c_2$ is chosen such that the constant $C_4 - 2C_0 \geq 4$, then under $H_1$, combining (??) (??) and (??), we have $P_{H_1}(\Phi_\alpha(M_n) = 1) \to 1$ as $(n, p) \to \infty$.

**Gaussian Design, Case 2.** $(\log p)^{-1/2} \lesssim \|\beta\|_2$. In this case, we have

$$\|\beta\|_\infty \geq \sqrt{\|\beta\|_2^2 / k} \gtrsim (k \log p)^{-1/2}.$$  

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By (1.2), with probability at least $1 - O(n^{-c})$,

$$
\min_{1 \leq i \leq n} \hat{f}(u_i) \geq \frac{\exp(\|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log n})}{(1 + \exp(\|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log n}))^2} \geq \frac{1}{4e^{\|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log n}}} \tag{1.9}
$$

Let

$$
L(n) = e^{-\|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log n}} / 4,
$$

it follows that with probability at least $1 - O(n^{-c})$,

$$
1 - \hat{f}(\hat{u}_i) \leq \xi \hat{f}(\hat{u}_i), \quad \text{where } \xi = \frac{1 - L(n)}{L(n)}.
$$

Thus, with probability at least $1 - O(n^{-c})$

$$
\tau_j = \frac{\|v_j\|_n}{\langle v_j, x_j \rangle_n} \leq (1 + \xi_2^{1/2}) \frac{\|\hat{u}_j\|_2}{\langle \hat{u}_j, x_j \rangle} \leq C_2 \frac{1 + \xi_2^{1/2}}{\sqrt{n}} \leq \frac{C_3 e^{\|\beta\|_2 \sqrt{0.5\lambda_{\max}(\Sigma) \log n}}}{\sqrt{n}}, \tag{1.10}
$$

for some constant $C_3 > 0$. Therefore, for $j = \arg \max |\beta_j|$, plug in (1.2) and $k = o(\sqrt{n}/\log^3 p)$, we have

$$
\beta_j^2 / \tau_j^2 \geq \frac{n}{k \log p} e^{-\|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log n}} \geq C_4 \sqrt{n} \log^2 p e^{-\|\beta\|_2 \sqrt{2\lambda_{\max}(\Sigma) \log n}} \tag{1.11}
$$

with probability at least $1 - O(n^{-c})$. Observe that as long as $\|\beta\|_2 \leq C \sqrt{\log n}$ for $C = 2 \sqrt{2\lambda_{\max}(\Sigma)}^{-1}$ (which is true since by assumption $\log \log p \lesssim r \log n$ and $\|\beta\|_2 \leq C \log \log p / \sqrt{\log n}$ for some $C \leq (2r \sqrt{2\lambda_{\max}(\Sigma)})^{-1}$), we have

$$
\beta_j^2 / \tau_j^2 \geq C_4 \log^2 p \tag{1.12}
$$

with probability at least $1 - O(n^{-c})$.

Now we show that for the same $j = \arg \max |\beta_j|$, 

$$
P((M_j')^2 \geq C_0 \log p) = O(n^{-c}) \tag{1.13}
$$

for some $C_0, c > 0$. This can be established by the following lemma.

**Lemma 9.** Under the condition of Theorem 3, if $\|\beta\|_2 \gtrsim (\log p)^{-1/2}$, then for any $j = 1, ..., p$,

$$
P(M_j' \geq C_1 \sqrt{ \log p }) = O(n^{-c}) \tag{1.14}
$$

for some constants $C_1, c > 0$.

Therefore, by (1.2) (1.3) and (1.4), we have

$$
M_n \geq M_j' \geq \frac{1}{2} C_4 \log^2 p - C_0 \log p
$$
with probability at least $1 - O(n^{-c})$. Thus $P_{H_1}(\Phi_\alpha(M_n) = 1) \to 1$ as $n \to \infty$.

**Bounded Design.** The proof under the bounded design follows the same argument as the Case 1 of the Gaussian design, thus is omitted.

**Proof of Theorem 4.** By Proposition 1 and the definition (16) of $\hat{t}$, it suffices to show that

$$P(0 \leq \hat{t} \leq b_p) \to 1$$

(1.15)

where $b_p = G^{-1}(c_p/p)$ and $c_p \to \infty$ for some sequence $c_p = o(p)$. Here since

$$G(\sqrt{2\log p}) = 2\Phi(-\sqrt{2\log p}) \leq \frac{2}{p\sqrt{2\log p}},$$

it follows that $b_p \leq \sqrt{2\log p}$.

Note that for $j \in B = \{j : |\beta_j| \geq c_1\sqrt{\log p/n}\}$, we have uniformly for $j \in B$,

$$P(|M_j| \geq \sqrt{2\log p}) \to 1$$

(1.16)

in probability. To see this, consider

$$M'_j = \tau_j^{-1}(\tilde{\beta}_j - \beta_j),$$

we have for all $j \in B$,

$$|\beta_j/\tau_j| \leq |M_j| + |M'_j|,$$

By Lemma 8, we have

$$\max_{j \in B} |M'_j| \leq C_2\sqrt{\log p},$$

with probability at least $1 - O(p^{-c})$. Combining with (??), we have

$$|M_j| \geq |\beta_j/\tau_j| - |M'_j| \geq (c_1^2C_3^{-2} - C_2^2)\log p,$$

with probability at least $1 - O(p^{-c})$. So by properly choosing $c_1$ depending on $C_2$ and $C_3$, we can obtain (??). Thus

$$\frac{\sum_{j \in B} P(|M_j| \geq \sqrt{2\log p})}{|B|} \to 1$$

in probability. By Markov’s inequality, we have

$$\frac{\sum_{j \in B} I\{|M_j| \geq \sqrt{2\log p}\}}{|B|} \to 1$$
By definition of \( \hat{t} \) in (16), \((30)\) is implied by
\[
G(b_p)p \max \left\{ \sum_{j=1}^p I\{ |M_j| \geq b_p \}, 1 \right\} = \max \left\{ \sum_{j=1}^p I\{ |M_j| \geq b_p \}, 1 \right\} \leq \alpha.
\]

Now note that
\[
\max \left\{ \sum_{j=1}^p I\{ |M_j| \geq b_p \}, 1 \right\} \geq \max \left\{ \sum_{j \in B} I\{ |M_j| \geq b_p \}, 1 \right\} \geq \max \left\{ \sum_{j \in B} I\{ |M_j| \geq \sqrt{2 \log p} \}, 1 \right\}
\]
It follows that
\[
G(b_p)p \max \left\{ \sum_{j=1}^p I\{ |M_j| \geq b_p \}, 1 \right\} \lesssim \frac{c_p |B|}{|B|} \leq \alpha
\]
for sufficiently large \((n,p)\), as long as we can find \(c_p\) only depending \(|B|\) and \(\alpha\), such that the last inequality holds. Therefore we have proven \((30)\).

**Proof of Theorem 5.** By (18) in Proposition 1, let \(t = \hat{t}_{FDV} \), it follows that as \((n,p) \to \infty\),
\[
\sup_{j \in \mathcal{H}_0} \left| \frac{P(|M_j| \geq \hat{t}_{FDV})}{G(\hat{t}_{FDV})} - 1 \right| \to 0,
\]

So that by noting that \(G(\hat{t}_{FDV}) = r/p\), we have as \((n,p) \to \infty\),
\[
\left| \frac{\sum_{j \in \mathcal{H}_0} P(|M_j| \geq \hat{t}_{FDV})}{r/p} - p_0 \right| \to 0,
\]
which completes the proof of (22).

2 Proofs of Technical Lemmas

**Proof of Lemma 1.** We start with the following lemma. In general, we will prove Lemma 1 under more general conditions posed in this lemma.

**Lemma 10.** If one of the following two conditions holds,

(C1) under Gaussian design, assume \((A1) (A3)\) hold, \(k = o(\sqrt{n}/\log^3 p)\), and \(\|X\beta\|_{\infty} \leq c_2\) for some constant \(c_2 > 0\);

(C2) under the bounded design, assume \((A2) (A3) (A4)\) hold, and \(k = o(\sqrt{n}/\log^{5/2} p)\),

then
\[
\max_{1 \leq j \leq p} \left| \frac{\|v_j\|}{\sqrt{n}} - F_{jj}^{1/2} \right| = o\left( \frac{1}{\log p} \right)
\]
in probability.
Lemma 11. Under the Gaussian design, assume (A1) and (A3) hold, the following events

\[
A_0 = \left\{ \| \hat{\beta} - \beta \|_1 = O \left( k \sqrt{\frac{\log p}{n}} \right) \right\},
\]
\[
A_1 = \left\{ \max_{1 \leq j \leq p} \frac{1}{n} \| X_{-j} (\hat{\gamma}_j - \gamma_j) \|_2^2 = O \left( k \left( \frac{\log p}{n} \right) \right) \right\},
\]
\[
A_2 = \left\{ \max_{1 \leq j \leq p} \| \hat{\gamma}_j - \gamma_j \|_1 = O \left( k \sqrt{\frac{\log p}{n}} \right) \right\},
\]
\[
A_3 = \left\{ \max_{i,j} | \hat{\eta}_{ij} - \eta_{ij} | = O \left( \frac{k \log p}{\sqrt{n}} \right) \right\},
\]

hold with probability at least \( 1 - O(p^{-c}) \) for some constant \( c > 0 \). In addition, if \( \| X\beta \|_\infty \leq c_1 \) for some constant \( c_1 > 0 \) and \( k = o(n) \), the following events

\[
A_4 = \left\{ \max_i \left| \frac{1}{f(\hat{u}_i)} - \frac{1}{f(u_i)} \right| = O \left( \frac{k \log p}{\sqrt{n}} \right) \right\},
\]
\[
A_5 = \left\{ \max_{1 \leq j \leq p} \frac{\| v_j \|_n}{\sqrt{n}} - F_{jj}^{1/2} = O \left( \frac{\sqrt{k \log p}}{n^{1/4}} \right) \right\},
\]

hold with probability at least \( 1 - O(p^{-c}) \) for some constant \( c > 0 \).

In particular, in (C1) of Lemma 11, we assume that \( k = o(\sqrt{n} / \log^3 p) \), so \( A_5 \) in Lemma 11 implies Lemma ?? under (C1). On the other hand, under the bounded design, we have the following lemma.

Lemma 12. Under the bounded design, assume (A2) (A3) and (A4) hold, \( k = o(n/\log p) \), then events \( A_0, A_1, A_2 \) (in Lemma 11) and

\[
A_3' = \left\{ \max_{i,j} | \hat{\eta}_{ij} - \eta_{ij} | = O \left( k \sqrt{\frac{\log p}{n}} \right) \right\},
\]
\[
A_4' = \left\{ \max_i \left| \frac{1}{f(\hat{u}_i)} - \frac{1}{f(u_i)} \right| = O \left( k \sqrt{\frac{\log p}{n}} \right) \right\},
\]
\[
A_5' = \left\{ \max_{1 \leq j \leq p} \frac{\| v_j \|_n}{\sqrt{n}} - F_{jj}^{1/2} = O \left( \frac{\sqrt{k \log^{1/4} p}}{n^{1/4}} \right) \right\},
\]

hold with probability at least \( 1 - O(p^{-c}) \) for some constant \( c > 0 \).

In (C2) of Lemma ??, we assume that \( k = o(\sqrt{n} / \log^{5/2} p) \), so event \( A_5' \) in Lemma 12 implies Lemma ?? under (C2). Now we proceed to prove Lemma 1.
For event $B_1$, we first show that

$$\max_j |\tilde{M}_j - \tilde{M}_j| = o\left(\frac{1}{\sqrt{\log p}}\right),$$

(2.2)

holds in probability. To see this, note that for any $j$,

$$|\tilde{M}_j - \tilde{M}_j| \leq \frac{\langle v_j, \epsilon \rangle}{\|v_j\|_n} - \frac{\langle v_j, \epsilon \rangle}{\sqrt{nF_{jj}}} + \left|\frac{\sum_{i=1}^{n} \eta_{ij} \epsilon_i / \hat{f}(u_i)}{\sqrt{nF_{jj}}}\right|$$

$$= T_1 + T_2.$$

It follows that

$$T_1 \leq \left|\frac{1}{\sqrt{n}} \sum_{i=1}^{n} v_{ij} \epsilon_i \right| \cdot \left|\frac{\sqrt{n}}{\|v_j\|_n} - \frac{1}{\sqrt{F_{jj}}}\right|.$$  

(2.3)

To bound $T_1$, by Lemma ??, we only need to obtain an upper bound of $\left|\frac{1}{\sqrt{n}} \sum_{i=1}^{n} v_{ij} \epsilon_i \right|$. Note that conditional on $X$ and $\hat{\beta}$, $v_{ij}$ is fixed and $v_{ij} \epsilon_i$ are conditional independent sub-gaussian random variables. In particular, we have $E[v_{ij} \epsilon_i | X, \hat{\beta}] = 0$ and $E[v_{ij}^2 \epsilon_i^2 | X, \hat{\beta}] \leq v_{ij}^2$. Thus, by concentration of independent sub-gaussian random variables, for any $t \geq 0$

$$P\left(\frac{1}{n} \sum_{i=1}^{n} v_{ij} \epsilon_i \geq t \big| X, \hat{\beta}\right) \leq \exp\left(-\frac{t^2n^2}{2 \sum_{i=1}^{n} v_{ij}^2}\right).$$

It then follows that

$$P\left(\frac{1}{n} \sum_{i=1}^{n} v_{ij} \epsilon_i \geq t\right) = \int P\left(\frac{1}{n} \sum_{i=1}^{n} v_{ij} \epsilon_i \geq t \big| X, \hat{\beta}\right) dP_{X, \hat{\beta}} \leq \mathbb{E} \exp\left(-\frac{t^2n^2}{2 \sum_{i=1}^{n} v_{ij}^2}\right).$$

Let $t = C\sqrt{\log p / n}$, we have

$$P\left(\frac{1}{n} \sum_{i=1}^{n} v_{ij} \epsilon_i \geq C\sqrt{\frac{\log p}{n}}\right) \leq \mathbb{E} \exp\left(-\frac{c \log p}{2 \sum_{i=1}^{n} v_{ij}^2 / n}\right).$$

(2.4)

Now under either (C1) or (C2), we have

$$\left|\frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 - \frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 / \hat{f}^2(u_i)\right| \leq \max_i |\eta_{ij}^2 / \hat{f}(\hat{u}_i)^2 - \eta_{ij}^2 / \hat{f}^2(u_i)| = o_P(1).$$
To see this, by Lemma ?? and Lemma ??, we have

\[
\max_i |\hat{\eta}_{ij}^2 / \hat{f}^2(\hat{u}_i) - \eta_{ij}^2 / f^2(u_i)| \leq \max_i \frac{|\hat{\eta}_{ij}^2 \hat{f}^2(\hat{u}_i) - \eta_{ij}^2 \hat{f}^2(u_i)|}{r^2(r^2 - o(1))}
\leq \max_i \frac{|\hat{\eta}_{ij}^2 \hat{f}^2(\hat{u}_i) - \hat{\eta}_{ij}^2 \hat{f}^2(\hat{u}_i)|}{r^2(r^2 - o(1))}
= \begin{cases} 
O(k \log p/\sqrt{n}) & \text{under (C1)} \\
O(k \log^{1/2} p/\sqrt{n}) & \text{under (C2)}
\end{cases}
\]

with probability at least \(1 - O(p^{-c})\). By concentration inequality for sub-exponential random variables \(\eta_{ij}^2 / f^2(u_i)\) (see the arguments following (??) in the proof of Lemma 10 for more details), we have

\[
P\left(\frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 / f^2(u_i) > C + \sqrt{\frac{\log p}{n}}\right) = O(p^{-c})
\]

for some \(C, c > 0\). Thus it follows that

\[
P\left(\frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 > C\right) = O(p^{-c}).
\]

for some \(C, c > 0\). Now notice that

\[
\mathbb{E} \exp \left( - \frac{c \log p}{2} \frac{1}{\sum_{i=1}^{n} v_{ij}^2 / n} \right) \leq \mathbb{E} \left[ \exp \left( - \frac{c \log p}{2} \frac{1}{\sum_{i=1}^{n} v_{ij}^2 / n} \right) 1\left\{ \frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 \leq C \right\} \right] + \mathbb{E} \left[ \exp \left( - \frac{c \log p}{2} \frac{1}{\sum_{i=1}^{n} v_{ij}^2 / n} \right) 1\left\{ \frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 > C \right\} \right]
\leq p^{-1/2C} + O(p^{-c})
= O(p^{-c}),
\]

by (??), we have

\[
P\left(\frac{1}{\sqrt{n}} \sum_{i=1}^{n} v_{ij} \epsilon_i \geq C \sqrt{\log p}\right) = O(p^{-c}). \quad (2.5)
\]

Thus, combining with Lemma ??, we have

\[
T_1 \leq C \sqrt{\log p} \cdot o\left(\frac{1}{\log p}\right) = o\left(\frac{1}{\sqrt{\log p}}\right),
\]
with probability at least $1 - O(p^{-c}).$ On the other hand,

$$T_2 \leq F^{-1/2}_{jj} \left| \frac{1}{\sqrt{n}} \sum_{i=1}^{n} v_{ij} \epsilon_i - \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \eta_{ij} \epsilon_i / \hat{f}(u_i) \right|$$

$$= F^{-1/2}_{jj} \left| \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \epsilon_i \left[ \frac{\hat{\eta}_{ij}}{\hat{f}(u_i)} - \frac{\eta_{ij}}{f(u_i)} \right] \right|.$$ 

Following the same conditional argument as (??), we have

$$P \left( \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \epsilon_i \left[ \frac{\hat{\eta}_{ij}}{\hat{f}(u_i)} - \frac{\eta_{ij}}{f(u_i)} \right] \geq t \right) \leq \mathbb{E} \exp \left( - \frac{t^2}{2 \sum_{i=1}^{n} \alpha_{ij}^2 / n} \right)$$

where $\alpha_{ij} = \frac{\eta_{ij}}{f(u_i)} - \frac{\eta_{ij}}{f(u_i)}.$ Under (C2), we have $\alpha_{ij}^2 = O \left( \frac{k^2 \log p}{n} \right).$ Then

$$P \left( \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \epsilon_i \left[ \frac{\hat{\eta}_{ij}}{\hat{f}(u_i)} - \frac{\eta_{ij}}{f(u_i)} \right] \geq t \right) \leq \exp \left( - \frac{nt^2}{2k^2 \log p} \right) + O(p^{-c}).$$

Let $t = k \log p / \sqrt{n},$ we have

$$P \left( \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \epsilon_i \left[ \frac{\hat{\eta}_{ij}}{\hat{f}(u_i)} - \frac{\eta_{ij}}{f(u_i)} \right] \geq \frac{k \log p}{\sqrt{n}} \right) = O(p^{-c}).$$

Therefore $T_2 = O \left( \frac{k \log p}{\sqrt{n}} \right) = o(1 / \sqrt{\log p})$ with probability at least $1 - O(p^{-c})$ as long as $k = o(\sqrt{n} / \log^{3/2} p).$ Under (C1), similar argument yields $T_2 = o(1 / \sqrt{\log p})$ with probability at least $1 - O(p^{-c})$ as long as $k = o(\sqrt{n} / \log^2 p).$ Using a union bound argument across $j = 1, \ldots, p,$ we prove that (??) holds in probability. Using the same argument, we can prove

$$P \left( \max_j |\hat{M}_j| > C \sqrt{\log p} \right) = O(p^{-c}).$$ 

(2.6)

Therefore, we have

$$|\hat{M}_n - \bar{M}_n| \leq \max_j |\hat{M}_j^2 - \bar{M}_j^2| \leq C(\max_j |\hat{M}_j|) \cdot \max_j |\hat{M}_j - \bar{M}_j| = o(1)$$

with probability at least $1 - O(p^{-c}).$ This completes the proof of event $B_1.$

For event $B_2,$ note that

$$|\hat{M}_n - M_n| \leq \max_j |\hat{M}_j^2 - M_j^2| \leq C(\max_j |M_j|) \cdot \max_j \left( \frac{|\langle v_j, R e_j \rangle|}{\|v_j\|_n} + \frac{|\langle v_j, h_{-j} \rangle|}{\|v_j\|_n} \right).$$ 

(2.7)
To bound $\max_j |\langle v_j, Re \rangle|/\|v_j\|_n$, by Lemma ?? and mean value theorem,

$$\frac{|\langle v_j, Re \rangle|}{\|v_j\|_n} \leq \frac{\sum_{i=1}^n v_{ij} (f(\hat{u}_i) - f(u^*_i))(\hat{u}_i - u_i)}{\sqrt{n}(F_{jj}^{1/2} - o_P(1))}$$

Under (C1), $\max_{i,j} |v_{ij}| = O_P(\sqrt{\log p})$ and thereby

$$\left| \sum_{i=1}^n v_{ij} (f(\hat{u}_i) - f(u^*_i))(\hat{u}_i - u_i) \right| \leq \sum_{i=1}^n (\hat{u}_i - u_i)^2 \cdot \max_{i,j} |v_{ij}| = \|X(\hat{\beta} - \beta)\|_2^2 \cdot O(\sqrt{\log p})$$

$$= O(k \log^{3/2} p)$$

with probability at least $1 - O(p^{-c})$. Thus

$$\max_j \frac{|\langle v_j, Re \rangle|}{\|v_j\|_n} = O\left(\frac{k \log^{3/2} p}{\sqrt{n}}\right)$$

in probability. Under (C2), $\max_{i,j} |v_{ij}| = O_P(1)$ and thereby

$$\left| \sum_{i=1}^n v_{ij} (f(\hat{u}_i) - f(u^*_i))(\hat{u}_i - u_i) \right| \leq \sum_{i=1}^n (\hat{u}_i - u_i)^2 \cdot \max_{i,j} |v_{ij}| = \|X(\hat{\beta} - \beta)\|_2^2 \cdot O(1)$$

$$= O(k \log p)$$

with probability at least $1 - O(p^{-c})$. Thus

$$\max_j \frac{|\langle v_j, Re \rangle|}{\|v_j\|_n} = O\left(\frac{k \log p}{\sqrt{n}}\right) \quad (2.8)$$

In general, either (C1) or (C2) implies that

$$\max_j |\langle v_j, Re \rangle|/\|v_j\|_n = o(\log^{-3/2} p) \quad (2.9)$$

with probability at least $1 - O(p^{-c})$. On the other hand, to bound $\max_j |\langle v_j, h_{-j} \rangle|/\|v_j\|_n$, by Proposition 1 (ii) in [Zhang and Zhang (2014)](Zhang2014), we know that if we choose $\lambda = C \sqrt{\log p/n}$, then under (C1) or (C2)

$$\max_{k \neq j} \frac{\langle \hat{\eta}_j, x_k \rangle}{\|\hat{\eta}_j\|_2} \leq C_1 \sqrt{2 \log p}, \quad \frac{\|\hat{\eta}_j\|_2}{\langle \hat{\eta}_j, x_j \rangle} \leq C_2 \sqrt{n} \quad (2.10)$$

with probability at least $1 - O(p^{-c})$. Note that

$$\|\hat{\eta}_j\|_2 = \sqrt{\sum_{i=1}^n \hat{\eta}_{ij}^2} = \sqrt{\sum_{i=1}^n \hat{f}^2(\hat{u}_i)v_{ij}^2} \leq \sqrt{\sum_{i=1}^n \hat{f}(\hat{u}_i)v_{ij}^2} = \|v_j\|_n,$$
we have
\[ \eta_j = \max_{k \neq j} \frac{(v_j, x_k)_n}{\|v_j\|_n} \leq C_1 \sqrt{2 \log p} \] (2.11)
in probability. Therefore under either (C1) or (C2)
\[ \frac{|\langle v_j, h_{-j} \rangle|}{\|v_j\|_n} \leq \|v_j\|_n^{-1} \sum_{i=1}^n v_{ij} \hat{f}(\hat{u}_i) X_{i,-j} (\hat{\beta}_{-j} - \beta_{-j}) \leq \max_{k \neq j} \frac{|\langle v_j, x_k \rangle_n|}{\|v_j\|_n} \cdot \|\hat{\beta} - \beta\|_1 \]

with \( \eta_j \|\hat{\beta} - \beta\|_1 = O\left(\frac{k \log p}{\sqrt{n}}\right) \)
with probability at least \( 1 - O(p^{-c}) \). Back to (??), note that \( \max_j |\hat{M}_n| \leq \max_j |\hat{M}_n| + o_P(1) = O_P(\sqrt{\log p}) \), we have
\[ |\hat{M}_n - M_n| = o\left(\frac{1}{\log p}\right) \]
with probability at least \( 1 - O(p^{-c}) \).

**Proof of Lemma 2.** The lemma is proved under the Gaussian design. For the bounded design, by definition \( \hat{M}_j \) is essentially the same as \( \hat{M}_j \). Note that

\[ \max_{i \leq j \leq p} \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbb{E}[|v_{ij}^0 \epsilon_i| 1\{|v_{ij}^0 \epsilon_i| \geq \tau_n\}] \leq C n^{1/2} \max_{i,j} \mathbb{E}[|v_{ij}^0 \epsilon_i| 1\{|v_{ij}^0 \epsilon_i| \geq \tau_n\}] \]
\[ \leq C n^{1/2} (p + n)^{-1} \max_{i,j} \mathbb{E}[|v_{ij}^0 \epsilon_i| e^{v_{ij}^0 \epsilon_i}|] \]
\[ \leq C n^{1/2} (p + n)^{-1}, \]

where the last inequality follows from
\[ \mathbb{E}[|v_{ij}^0 \epsilon_i| e^{v_{ij}^0 \epsilon_i}|] \leq C_1 \sqrt{\mathbb{E}(v_{ij}^0)^2} \sqrt{\mathbb{E} \exp(2|v_{ij}^0 \epsilon_i|)} \leq C_2 \]
by sub-gaussianity of \( v_{ij}^0 \). Hence, if \( \max_{i,j} |v_{ij}^0 \epsilon_i| \leq \tau_n \), then
\[ \hat{Z}_{ij} = v_{ij}^0 \epsilon_i - \mathbb{E}[v_{ij}^0 \epsilon_i 1\{|v_{ij}^0 \epsilon_i| \leq \tau_n\}] \]

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and thereby

\[
\max_j |\hat{M}_j - \tilde{M}_j| \leq \max_{1 \leq j \leq p} \left| \frac{1}{\sqrt{nF_{jj}}} \sum_{i=1}^{n} \mathbb{E}[v_{ij}^0 \epsilon_i 1\{v_{ij}^0 \epsilon_i \leq \tau_n\}] \right|
\]

\[
= \max_{1 \leq j \leq p} \left| \frac{1}{\sqrt{nF_{jj}}} \sum_{i=1}^{n} \mathbb{E}[v_{ij}^0 \epsilon_i 1\{v_{ij}^0 \epsilon_i \geq \tau_n\}] \right|
\]

\[
\leq \max_{1 \leq j \leq p} \frac{1}{\sqrt{nF_{jj}}} \sum_{i=1}^{n} \mathbb{E}[|v_{ij}^0 \epsilon_i| 1\{|v_{ij}^0 \epsilon_i| \geq \tau_n\}]
\]

\[
\leq C n^{1/2}(p + n)^{-1}
\]

\[
= O(1/\log p).
\]

Then we have

\[
P\left( \max_j |\hat{M}_j - \tilde{M}_j| \geq C(\log p)^{-1} \right) \leq P\left( \max_{i,j} |v_{ij} \epsilon_i| \geq \tau_n \right) = O(p^{-c}). \quad (2.12)
\]

Now by the fact that

\[
|\hat{M}_n - \tilde{M}_n| \leq 2 \max_j |\hat{M}_j| \max_j |\tilde{M}_j - \tilde{M}_j| + \max_j |\tilde{M}_j - \tilde{M}_j|^2,
\]

it suffices to apply (??) and (??) in the proof of Lemma 1.

**Proof of Lemma 6.** By definition, we have

\[
\chi^2(g, f) = \int \frac{g^2}{f} - 1
\]

\[
= \frac{1}{(p)^{2n}} \prod_{i=1}^{n} \int (\sum_{\beta \in \mathcal{H}_1} p(X_i, y_i; \beta))^2 - 1
\]

\[
= \frac{1}{(p)^{2n}} \prod_{i=1}^{n} \sum_{\beta \in \mathcal{H}_1} \sum_{\beta' \in \mathcal{H}_1} \int \frac{p(X_i, y_i; \beta)p(X_i, y_i; \beta')}{p(X_i, y_i)} - 1. \quad (2.13)
\]
Note that

\[
\int \frac{p(X_i, y_i; \beta)p(X_i, y_i; \beta')}{p(X_i, y_i)} \, \mathrm{d}X_i \, \mathrm{d}y_i = \frac{1}{(2\pi)^{p/2}} \int \frac{2 \exp(-\frac{1}{2} X_i^\top X_i + y_i X_i^\top (\beta + \beta'))}{[1 + \exp(X_i^\top \beta)][1 + \exp(X_i^\top \beta')] \, \mathrm{d}X_i \, \mathrm{d}y_i
\]

\[
= \frac{1}{(2\pi)^{p/2}} \int \frac{2 \exp(-\frac{1}{2} X_i^\top X_i + X_i^\top (\beta + \beta'))}{[1 + \exp(X_i^\top \beta)][1 + \exp(X_i^\top \beta')] \, \mathrm{d}X_i
\]

\[
+ \frac{1}{(2\pi)^{p/2}} \int \frac{2 \exp(-\frac{1}{2} X_i^\top X_i)}{[1 + \exp(X_i^\top \beta)][1 + \exp(X_i^\top \beta')] \, \mathrm{d}X_i
\]

\[
= \mathbb{E} h(X; \beta, \beta')
\]

where in the last equality, the expectation is with respect to a standard multivariate normal random vector \( X \sim N(0, I_p) \) and

\[
h(X; \beta, \beta') = \frac{2(1 + e^{X^\top (\beta + \beta')})}{(1 + e^{X^\top \beta})(1 + e^{X^\top \beta'})} = 1 + \frac{e^{X^\top \beta} - 1}{e^{X^\top \beta} + 1} \frac{e^{X^\top \beta'} - 1}{e^{X^\top \beta'} + 1}
\]

\[
= 1 + \tanh \left( \frac{X^\top \beta}{2} \right) \tanh \left( \frac{X^\top \beta'}{2} \right)
\]

**Lemma 13.** If \((X, Y) \sim N(0, \Sigma)\) with \( \Sigma = \sigma^2 \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix} \) for some \( \sigma^2 \leq 1 \), then it follows

\[
\mathbb{E} \tanh \left( \frac{X}{2} \right) \tanh \left( \frac{Y}{2} \right) \leq \sigma^2 \rho.
\]

Now since \( X_i^\top \beta \sim N(0, k \rho^2) \), where we can choose \( \rho \) such that \( k \rho^2 \leq 1 \). By Lemma ??, let \( j = |\text{supp}(\beta) \cap \text{supp}(\beta')| = |I \cap I'| \) be the number of intersected components between \( \beta \) and \( \beta' \), we have

\[
\chi^2(g, f) \leq \left( 1 + \frac{1}{(p)}^2 \sum_{\beta \in \mathcal{H}_1} \sum_{\beta' \in \mathcal{H}_1} \beta^\top \beta' \right)^n - 1
\]

\[
= \left( 1 + \frac{1}{(p)}^2 \sum_{\beta \in \mathcal{H}_1} \sum_{\beta' \in \mathcal{H}_1} j \rho^2 \right)^n - 1
\]

Note that for \( \beta, \beta' \) uniformly picked from \( \mathcal{H}_1 \), \( j \) follows a hypergeometric distribution

\[
P(J = j) = \binom{k}{j} \binom{p-k}{j}^2 \frac{k}{p}, \quad j = 0, 1, \ldots, k.
\]
Then
\[
\chi^2(g, f) \leq (1 + \rho^2 \mathbb{E} J)^n - 1 \\
= \exp(n \log(1 + \mathbb{E} J \rho^2)) - 1 \\
\leq \exp(n \rho^2 \mathbb{E} J) - 1.
\]

As shown on page 173 of [Aldous, 1985], $J$ has the same distribution as the random variable $\mathbb{E}(Z|B_n)$ where $Z$ is a binomial random variable of parameters $(k, k/p)$ and $B_n$ some suitable $\sigma$-algebra. Thus by Jensen’s inequality we have
\[
\mathbb{E}e^{nJ\rho^2} \leq \left(1 - \frac{k}{p} + \frac{k}{p} e^{n\rho^2}\right)^k.
\]

Let
\[
\rho^2 = \frac{1}{n} \log \left(1 + \frac{p}{h(\eta)k^2}\right),
\]
where $h(\eta) = [\log(4\eta^2 + 1)]^{-1}$ and $\eta = 1 - \alpha - \delta$, we have
\[
\mathbb{E}e^{n\rho^2J} \leq e^{1/h(\eta)},
\]
so that
\[
\chi^2(g, f) \leq 4\eta^2 = 4(1 - \alpha - \delta)^2.
\]

Proof of Lemma ??.
Note that
\[
|M'_j| = \left|\frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij} \epsilon_i - \mathbb{E} \hat{\eta}_{ij} \epsilon_i\right| \leq \frac{|\langle v_j, \epsilon \rangle|}{\|v_j\|_n} + \frac{|\langle v_j, Re \rangle|}{\|v_j\|_n} + \frac{|\langle v_j, h - j \rangle|}{\|v_j\|_n}.
\]

We bound the above three terms one by one. Firstly, by concentration of sub-exponential random variables $\hat{\eta}_{ij}^2$ (see (??) in the proof of Lemma 10 for details) and (2.18), we have
\[
P\left(\frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 - \mathbb{E} \hat{\eta}_{ij}^2 \geq (\log p)^{-1}\right) = O(p^{-c}) \tag{2.16}
\]

Then we have
\[
\frac{|\langle v_j, \epsilon \rangle|}{\|v_j\|_n} \leq \frac{n^{-1/2} \sum_{i=1}^{n} \hat{\eta}_{ij} \epsilon_i}{\sqrt{\sum_{i=1}^{n} \hat{\eta}_{ij}^2/n}} \leq \frac{C}{\sqrt{n}} \sum_{i=1}^{n} \hat{\eta}_{ij} \epsilon_i \leq \frac{C}{\sqrt{n}} \sum_{i=1}^{n} \xi_i.
\]

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Conditional on $X$ and $\hat{\beta}$, we have $E[\xi_i|X,\hat{\beta}] = 0$ and $E[\xi_i^2|X,\hat{\beta}] \leq \tilde{\eta}_{ij}^2/\hat{f}^2(\hat{u}_i) = \alpha_{ij}(n)$. By concentration inequality for independent sub-gaussian random variables $\xi_i|X,\hat{\beta}$, we have for any $t \geq 0$

$$P\left(\frac{1}{n} \sum_{i=1}^{n} \xi_i \geq t \mid X,\hat{\beta}\right) \leq \exp\left(-\frac{t^2n^2}{2 \sum_{i=1}^{n} \alpha_{ij}(n)}\right).$$

It then follows that

$$P\left(\frac{1}{n} \sum_{i=1}^{n} \xi_i \geq t\right) = \int P\left(\frac{1}{n} \sum_{i=1}^{n} \xi_i \geq t \mid X,\hat{\beta}\right) dP_{X,\hat{\beta}} \leq E\exp\left(-\frac{t^2n^2}{2 \sum_{i=1}^{n} \alpha_{ij}(n)}\right).$$

Let $t = C\sqrt{\log p/n}$, we have

$$P\left(\frac{1}{n} \sum_{i=1}^{n} \xi_i \geq C\sqrt{\log p/n}\right) \leq \exp\left(-\frac{c \log p}{2 \sum_{i=1}^{n} \alpha_{ij}(n)/n}\right). \quad (2.17)$$

Now since with probability at least $1 - O(n^{-c})$, $\alpha_{ij}(n) \leq \tilde{\eta}_{ij}^2 L(n)^{-2}$, or

$$P\left(\frac{1}{n} \sum_{i=1}^{n} \alpha_{ij}(n) \geq L(n)^{-2} \frac{1}{n} \sum_{i=1}^{n} \tilde{\eta}_{ij}^2\right) = O(n^{-c}),$$

by (2.17), we have

$$P\left(\frac{1}{n} \sum_{i=1}^{n} \alpha_{ij}(n) \geq CL(n)^{-2}\right) = O(n^{-c})$$

for some $C, c > 0$. Now notice that

$$E\exp\left(-\frac{c \log p}{2 \sum_{i=1}^{n} \tilde{\eta}_{ij}^2/n}\right) \leq E\left[\exp\left(-\frac{c \log p}{2 \sum_{i=1}^{n} \alpha_{ij}/n}\right) 1\left\{\frac{1}{n} \sum_{i=1}^{n} \alpha_{ij} \leq CL(n)^{-2}\right\}\right] + E\left[\exp\left(-\frac{c \log p}{2 \sum_{i=1}^{n} \alpha_{ij}/n}\right) 1\left\{\frac{1}{n} \sum_{i=1}^{n} \alpha_{ij} > CL(n)^{-2}\right\}\right] \leq p^{-1/(2CL^{-2}(n))} + O(n^{-c'}) = O(n^{-c}),$$

where we used the fact that

$$p^{-1/(2CL^{-2}(n))} \asymp p^{-1/\exp(c\|\beta\|_2 \sqrt{\log n})} \lesssim n^{-c}$$
as long as \( \|\beta\|_2 = O\left(\frac{\log \log p}{\sqrt{\log n}}\right) \). As a result, by (?), we have

\[
P\left(\frac{1}{\sqrt{n}} \sum_{i=1}^{n} \xi_i \geq C \sqrt{\log p}\right) = O(n^{-c}). \tag{2.18}
\]

To bound \( |\langle v_j, Re \rangle|/\|v_j\|_n \), by mean value theorem,

\[
|\langle v_j, Re \rangle| \leq n^{-1/2} \left| \sum_{i=1}^{n} v_{ij} (\hat{f}(\hat{u}_i) - \hat{f}(u_i^*)) (\hat{u}_i - u_i) \right| \leq \sqrt{\sum_{i=1}^{n} \hat{v}_{ij}^2 / n}
\]

Note that \( \max_i |v_{ij}| = O(\sqrt{\log pL^{-1}(n)}) \) with probability at least \( 1 - O(n^{-c}) \), thereby

\[
\left| \sum_{i=1}^{n} v_{ij} (\hat{f}(\hat{u}_i) - \hat{f}(u_i^*)) (\hat{u}_i - u_i) \right| \leq \sum_{i=1}^{n} (\hat{u}_i - u_i)^2 \cdot \max_{i,j} |v_{ij}|
\]

\[
= |X(\hat{\beta} - \beta)| \leq O(L^{-1}(n) \sqrt{\log p}) = O(k \log^{3/2} p L^{-1}(n))
\]

with probability at least \( 1 - O(n^{-c}) \). Since \( \|\beta\|_2 \leq C \left(\frac{\log \log p}{\sqrt{\log n}}\right) \), for some \( C \leq \sqrt{2/\lambda_{\max}(\Sigma)} \), we have

\[
\frac{|\langle v_j, Re \rangle|}{\|v_j\|_n} = O\left(\frac{k \log^{3/2} p}{L(n) \sqrt{n}}\right) = o\left(\sqrt{p}\right) \tag{2.19}
\]

with probability at least \( 1 - O(n^{-c}) \). Finally, to bound \( \max_j |\langle v_j, h_{-j} \rangle|/\|v_j\|_n \), by (?), we have

\[
\frac{|\langle v_j, h_{-j} \rangle|}{\|v_j\|_n} = O\left(\frac{k \log p}{\sqrt{n}}\right) = o(1) \tag{2.20}
\]

with probability at least \( 1 - O(n^{-c}) \). Combining (?), (?), and (?), we have proven Lemma ??.

**Proof of Lemma ??**. Events \( A_0 \) \( A_1 \) and \( A_2 \) are the standard estimation and prediction bounds for the Lasso estimators (e.g. see Negahban et al. (2009) and Bickel et al. (2009)), and thereby we omit the proofs. For event \( A_3 \), note that under \( A_2 \) we have

\[
\max_{i,j} |\hat{\eta}_{ij} - \eta_{ij}| = \max_{i,j} |X_{i,-j} (\hat{\gamma}_j - \gamma_j)| \leq \max_{i,j} \|X_{i,-j}\|_{\infty} \max_j \|\hat{\gamma}_j - \gamma_j\|_1 \leq C k \log p \sqrt{n}
\]

where the last inequality follows from that fact that

\[
P\left(\max_{1 \leq i \leq p} \|X_i\| \geq \sqrt{C \log p}\right) \leq \frac{1}{p^c} \tag{2.21}
\]

for some sufficiently large constant \( C, c > 0 \), which is a consequence of the Gaussian tail probability bound \( 1 - \Phi(x) \leq \frac{1}{2} \phi(x) \) by taking \( x = \sqrt{C \log p} \) for some sufficiently large \( C > 0 \).

For event \( A_4 \), since \( \|X\beta\|_{\infty} \leq c_2 \) for some constant \( c_2 > 0 \), there exists some constant \( 0 < \kappa < 1 \)
such that $\kappa < |f(u_i)| < 1 - \kappa$ and thereby $\dot{f}(u_i) \geq \kappa(1 - \kappa)$ for all $i$. $A_4$ then follows from the following lemma, event $A_0$ and (??).

**Lemma 14.** Let $f(x) = \frac{x^c}{1+x^c}$, then uniformly over $a, b \in \mathbb{R}$, it holds that

$$\left| \frac{1}{\dot{f}(a)} - \frac{1}{\dot{f}(b)} \right| \leq \max\{\dot{f}(a), \dot{f}(b)\} \left| a - b \right| \leq \frac{1}{\dot{f}(a)\dot{f}(b)} \left| a - b \right|. \quad (2.22)$$

For event $A_5$, by the fact that $v_{ij} = \hat{\eta}_{ij} / \dot{f}(\hat{u}_i)$, it follows that

$$\left| \frac{1}{\sqrt{n}} \|v_{ij}\|_n - F_{jj}^{1/2} \right| = \left| \left[ \frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 \dot{f}(\hat{u}_i) \right]^{1/2} - F_{jj}^{1/2} \right| \leq \left| \frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 \dot{f}(\hat{u}_i) - F_{jj} \right|^{1/2}$$

$$\leq \left| \frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 / \dot{f}(\hat{u}_i) - \frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 / \dot{f}(\hat{u}_i) \right|^{1/2} + \left| \frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 / \dot{f}(\hat{u}_i) - F_{jj} \right|^{1/2}$$

$$\leq \left| \frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 \left[ \frac{1}{\dot{f}(\hat{u}_i)} - \frac{1}{\dot{f}(\hat{u}_i)} \right] \right|^{1/2} + \left| \frac{1}{n} \sum_{i=1}^{n} (\hat{\eta}_{ij} - \hat{\eta}_{ij}) / \dot{f}(\hat{u}_i) \right|^{1/2}$$

$$= I_1 + I_2 + I_3.$$

To bound $I_2$, note that $\|X\beta\|_\infty \leq c$ implies $\max_i \dot{f}(u_i) \geq r$ for some constant $r > 0$, and that $\hat{\eta}_j - \eta_j = X_j(\hat{\gamma}_j - \gamma_j)$, we have

$$I_2^2 \leq \frac{1}{rn} \sum_{i=1}^{n} |\hat{\eta}_{ij}^2 - \eta_{ij}^2| \leq \frac{1}{rn} \sum_{i=1}^{n} [|\hat{\eta}_{ij} - \eta_{ij}|^2 + 2|\hat{\eta}_{ij} - \eta_{ij}| \cdot |\eta_{ij}|]$$

$$\leq \frac{1}{rn} \|X_j(\hat{\gamma}_j - \gamma_j)\|_2^2 + \frac{2C\sqrt{\log p}}{rn} \|X_j(\hat{\gamma}_j - \gamma_j)\|_1$$

$$\leq \frac{1}{rn} \|X_j(\hat{\gamma}_j - \gamma_j)\|_2^2 + \frac{2C\sqrt{\log p}}{r\sqrt{n}} \|X_j(\hat{\gamma}_j - \gamma_j)\|_2. \quad (2.23)$$

Therefore, by event $A_1$, as long as $k < n$,

$$I_2^2 \leq C_1 k \frac{\log p}{n} + C_2 \frac{\log p}{\sqrt{n}} = O\left(\sqrt{k \log p} \sqrt{\frac{n}{\sqrt{n}}} \right) \quad (2.24)$$

with probability at least $1 - O(p^{-c})$ for some $c > 0$. By $A_4$ and (??), we have, with probability at least $1 - O(p^{-c})$ for some $c > 0$,

$$I_1^2 \leq \frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 \cdot Ck \frac{\log p}{\sqrt{n}} \leq \left[ \frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 + o(1) \right] \cdot Ck \frac{\log p}{\sqrt{n}} \leq C'k \frac{\log p}{\sqrt{n}},$$

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where the last inequality follows from the concentration inequality

\[ P\left(\frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 - \mathbb{E}\eta_{ij}^2 \geq \sqrt{\frac{\log p}{n}}\right) = O(p^{-c}). \quad (2.25) \]

To show this, we need to introduce the following norms for random variables. The sub-gaussian norm of a random variable \(U\) is defined as \(\|U\|_{\psi_2} = \sup_{q \geq 1} \frac{1}{\sqrt{q}}(\mathbb{E}|U|^q)^{1/q}\), and the sub-exponential norm of a random variable is defined as \(\|U\|_{\psi_1} = \sup_{q \geq 1} q^{-1}(\mathbb{E}|U|^q)^{1/q}\). By definition \(\eta_{ij}\) are sub-gaussian with \(\|\eta_{ij}\|_{\psi_2} < C < \infty\) and therefore

\[ \|\eta_{ij}\|_{\psi_1} = \sup_{q \geq 1} q^{-1}(\mathbb{E}|\eta_{ij}|^2)^{1/q} = \sup_{q \geq 1} q^{-1/2}(\mathbb{E}|\eta_{ij}|^{2q})^{1/2} = \|\eta_{ij}\|_{\psi_2} < C^2 < \infty. \]

So \(\eta_{ij}^2\) with \(i = 1, \ldots, n\) are i.i.d. sub-exponential random variables. Then (2.25) follows from standard concentration inequality for sub-exponential random variables (see, for example, Proposition 5.16 in Vershynin (2010)). Similarly, we can show \(\eta_{ij}^2/\hat{f}(u_i)\) are sub-exponential and therefore

\[ I_3^2 = \left| \frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 / \hat{f}(u_i) - F_{jj} \right| = O\left(\sqrt{\frac{\log p}{n}}\right) \]

with probability at least \(1 - O(p^{-c})\) for some \(c > 0\). Thus, \(I_1 + I_2 + I_3 = O\left(\frac{\sqrt{k \log p}}{n^{1/4}}\right)\).

**Proof of Lemma 5.3.** Events \(A_0\), \(A_1\), and \(A_2\) follow the same argument as in Lemma 5.3. For event \(A_3',\) by \(A_1, A_2\) and boundedness of \(X\), we have

\[ \max_{i,j} |\hat{\eta}_{ij} - \eta_{ij}| = \max_{i,j} |X_{i,-j}(\hat{\gamma}_j - \gamma_j)| \leq \max_{i,j} \|X_{i,-j}\|_\infty \max_j \|\hat{\gamma}_j - \gamma_j\|_1 \leq Ck \sqrt{\frac{\log p}{n}} \]

For event \(A_4',\) by (A4), there exists some constant \(r > 0\) such that \(\hat{f}(u_i) \geq r\) for all \(i\) with probability at least \(1 - O(p^{-c})\). \(A_4'\) then follows from Lemma 5.3. For event \(A_5',\) as the proof of \(A_5\) in Lemma 5.3, we have

\[
\left| \sqrt{\frac{1}{n} \sum_{i=1}^{n} v_{ij}^2 \hat{f}(u_i) - F_{jj}^2} \right| \leq \left| \frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 \left[ \frac{1}{\hat{f}(u_i)} - \frac{1}{\hat{f}(u_i)} \right] \right|^{1/2} + \left| \frac{1}{n} \sum_{i=1}^{n} (\eta_{ij}^2 - \eta_{ij}^2) / \hat{f}(u_i) \right|^{1/2} \\
+ \left| \frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 / \hat{f}(u_i) - F_{jj} \right|^{1/2} = I_1 + I_2 + I_3.
\]

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To bound $I_2$, note that $P(\max_i \hat{f}(u_i) \leq r) = O(p^{-c})$, and that $\hat{\eta}_j - \eta_j = X_{-j}(\hat{\gamma}_j - \gamma_j)$, by $A_1$,

$$I_2^2 \leq \frac{1}{rn} \sum_{i=1}^{n} |\hat{\eta}_{ij}^2 - \eta_{ij}^2| \leq \frac{1}{rn} \sum_{i=1}^{n} [|\hat{\eta}_{ij} - \eta_{ij}|^2 + 2|\hat{\eta}_{ij} - \eta_{ij}| \cdot |\eta_{ij}|]$$

$$\leq \frac{1}{rn} \|X_{-j}(\hat{\gamma}_j - \gamma_j)\|^2 + \frac{2C}{rn} \|X_{-j}(\hat{\gamma}_j - \gamma_j)\|_1$$

$$\leq \frac{1}{rn} \|X_{-j}(\hat{\gamma}_j - \gamma_j)\|^2 + \frac{2C}{r\sqrt{n}} \|X_{-j}(\hat{\gamma}_j - \gamma_j)\|_2$$

$$\leq C_1 k \frac{\log p}{n} + C_2 \sqrt{k \frac{\log p}{n}} = O\left(\sqrt{k \frac{\log p}{n}}\right)$$

(2.26)

with probability at least $1 - O(p^{-c})$ for some $c > 0$. For $I_1$, by $A_4'$ and boundedness of $X$, we have, with probability at least $1 - O(p^{-c})$ for some $c > 0$,

$$I_1^2 \leq \frac{1}{n} \sum_{i=1}^{n} \hat{\eta}_{ij}^2 \cdot C \sqrt{k \frac{\log p}{n}} = O\left(k \sqrt{\frac{\log p}{n}}\right).$$

Finally, by concentration inequality for sub-exponential random variables $\eta_{ij}^2 / \hat{f}(u_i)$ for $i = 1, ..., n$, we have

$$I_3^2 = \left| \frac{1}{n} \sum_{i=1}^{n} \eta_{ij}^2 / \hat{f}(u_i) - F_{jj} \right| = O\left(\sqrt{\frac{\log p}{n}}\right)$$

with probability at least $1 - O(p^{-c})$ for some $c > 0$. Thus, $I_1 + I_2 + I_3 = O\left(\sqrt{\frac{k \log p}{n^2}}\right)$. $\Box$

**Proof of Lemma 2.7.** By normalization, we only need to consider $(X, Y)$ with $\text{Var}(X) = \text{Var}(Y) = 1$ and $\mathbb{E}XY = \rho$ and prove

$$\mathbb{E} \tanh\left(\frac{\sigma X}{2}\right) \tanh\left(\frac{\sigma Y}{2}\right) \leq \sigma^2 \rho.$$  

(2.27)

Note that the inner product

$$\langle X, Y \rangle = \mathbb{E}XY$$

defines a Hilbert space on $L^2(\Omega, \mathcal{F}, \mu)$. Then the above inequality is equivalent to

$$\left\langle \tanh\left(\frac{\sigma X}{2}\right), \tanh\left(\frac{\sigma Y}{2}\right) \right\rangle \leq \sigma^2 \langle X, Y \rangle.$$

Consider the Hermite polynomials $H_n(x), x \in \mathbb{R}, n = 0, 1, ...$ which are defined as

$$H_n = \frac{(-1)^n}{n!} e^{x^2/2} \frac{d^n}{dx^n} (e^{-x^2/2}),$$

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so that in particular \( H_0(x) = 1, H_1(x) = x, H_2(x) = (x^2 - 1)/2 \), and in general \( H_n(x) \) is a polynomial of order \( n \). The Hermite polynomials satisfy the following basic identities

\[
\begin{align*}
H_n'(x) &= H_{n-1}(x) \\
(n + 1)H_{n+1}(x) &= xH_n(x) - H_{n-1}(x), \\
H_n(-x) &= (-1)^n H_n(x),
\end{align*}
\]

for all \( n \geq 1 \). For \( X, Y \) that are \( N(0, 1) \) random variables that are jointly Gaussian, it can be shown (see, for example, Section 2.10 of [Kolokoltsov (2011)](#)) that

\[
\langle H_n(X), H_m(Y) \rangle = \mathbb{E}(H_n(X)H_m(Y)) = \begin{cases} 
0 & \text{if } m \neq n, \\
\frac{1}{\pi} (\mathbb{E}XY)^n & \text{if } m = n.
\end{cases}
\]

Now we would like to expand the function \( \tanh(\sigma x/2) \) in terms of orthogonal Hermite polynomials as

\[
\tanh(\sigma x/2) = \sum_{n=0}^{\infty} C_n H_n(x).
\]

To calculate the coefficients \( C_n \), simply note that

\[
C_n = \frac{\langle \tanh(\sigma X/2), H_n(X) \rangle}{\langle H_n(X), H_n(X) \rangle} = \frac{(-1)^n}{(2\pi)^{1/2}} \int \tanh \left( \frac{\sigma x}{2} \right) d^n \frac{\phi^{(n)}(x)}{d \phi^{(n)}(x)} dx.
\]

Denote \( \phi(x) = e^{-x^2/2} \), we have

\[
C_n = \frac{(-1)^n}{(2\pi)^{1/2}} \int \tanh \left( \frac{\sigma x}{2} \right) \phi^{(n)}(x) dx.
\]

Note that \( \phi(x) \) is an even function and \( \tanh(x) \) is an odd function, so the integrand \( \phi^{(n)}(x) \tanh(\sigma x/2) \) is an odd function for all odd \( n > 0 \). Therefore \( C_{2k} = 0 \) for any \( k \geq 0 \). Now we calculate for \( k \geq 0 \),

\[
C_{2k+1} = \frac{1}{\sqrt{2\pi}} \int \tanh \left( \frac{\sigma x}{2} \right) H_{2k+1}(x) \phi(x) dx
\]

\[
= \frac{2}{\sqrt{2\pi}} \int_0^\infty \tanh \left( \frac{\sigma x}{2} \right) H_{2k+1}(x) \phi(x) dx
\]

\[
\leq \frac{2}{\sqrt{2\pi}} \int_0^\infty \sinh \left( \frac{\sigma x}{2} \right) H_{2k+1}(x) \phi(x) dx
\]

\[
= (\sigma/2)^{2k+1} e^{\sigma^2/16} / \sqrt{2}
\]
where the last equality follows from equation 7.387 on p.806 of Gradshteyn and Ryzhik (2014).

Now we calculate

\[
\langle \tanh \left( \frac{\sigma X}{2} \right), \tanh \left( \frac{\sigma Y}{2} \right) \rangle = \left\langle \sum_{n=0}^{\infty} C_n H_n(X), \sum_{n=0}^{\infty} C_n H_n(Y) \right\rangle = \sum_{n=0}^{\infty} C_n^2 (H_n(X), H_n(Y)) = \frac{e^{\sigma^2/8}}{2} \sinh \left( \frac{\sigma^2 \rho}{4} \right)
\]

Now it follows

\[
\sinh \left( \frac{\sigma^2 \rho}{4} \right) \leq \sigma^2 \rho,
\]

since \( \sinh(x/4) \leq x \) for \( 0 \leq x \leq 1 \). To prove this, note that

\[
\frac{d}{dx} (\sinh(x/4) - x) = \frac{1}{4} \cosh(x/4) - 1 < 0
\]

when \( 0 \leq x \leq 1 \). So \( \sinh(x/4) - x \) takes its maximum at \( x = 0 \), which is 0. Thus (2.30) follows given the fact that \( \sigma^2 \leq 1 \). Therefore, we have

\[
\mathbb{E} \tanh \left( \frac{\sigma X}{2} \right) \tanh \left( \frac{\sigma Y}{2} \right) \leq \frac{e^{\sigma^2/8}}{2} \sigma^2 \rho \leq \sigma^2 \rho.
\]

\[ \square \]

**Proof of Lemma 2.2**. Since \( \hat{f}(x) = \frac{e^x}{(1+e^x)^2} \), by mean value theorem, for any \( a, b \in \mathbb{R} \), we have for some \( c \) between \( a \) and \( b \),

\[
|\hat{f}(a) - \hat{f}(b)| = |a - b| \hat{f}(c) \leq |a - b| \max \{ \hat{f}(a), \hat{f}(b) \}
\]

by monotonicity of \( \hat{f}(x) \). The rest of the proof follows from

\[
\left| \frac{1}{\hat{f}(a)} - \frac{1}{\hat{f}(b)} \right| = \frac{|\hat{f}(a) - \hat{f}(b)|}{\hat{f}(a)\hat{f}(b)}.
\]

\[ \square \]

**A Technical Results for Two-Sample Testing**

In this section, we discuss the implications of our results on single logistic regression problems to the two-sample settings.
A.1 Two-Sample Global Hypothesis Testing

For testing two-sample global null hypothesis

\[ H_0 : \beta^{(1)} = \beta^{(2)} \quad \text{vs.} \quad H_1 : \beta^{(1)} \neq \beta^{(2)}. \]

Informed by the previous results, we construct the global two-sample testing procedure as follows. First we obtain \( \hat{\beta}_j^{(1)} \) and \( \hat{\beta}_j^{(2)} \) for each group, and calculate the coordinate-wise standardized statistics

\[ T_j = \frac{\hat{\beta}_j^{(1)}}{\sqrt{2r_j^{(1)}}} - \frac{\hat{\beta}_j^{(2)}}{\sqrt{2r_j^{(2)}}}, \]

for \( j = 1, ..., p \). Then we calculate the difference the global test statistics is defined as

\[ T_n = \max_{1 \leq j \leq p} T_j^2. \]  

The following corollary states the asymptotic null distribution for the global test statistics \( M_n \) under bounded design. In particular, we assume the parameters \( (\beta^{(\ell)}, \Sigma^{(\ell)}) \) for \( \ell = 1, 2 \) come from the same parameter space \( \Theta(k) \).

**Theorem A.1.** Let \( T_n \) be the test statistics defined in (2.8), \( D^{(\ell)} \) be the diagonal of \( [\Sigma^{(\ell)}]^{-1} \) and \( (\xi^{(\ell)}_{ij}) = [D^{(\ell)}]^{-1/2}[\Sigma^{(\ell)}]^{-1}[D^{(\ell)}]^{-1/2} \). Suppose \( \max_{1 \leq i < j \leq p} |\xi^{(\ell)}_{ij}| \leq c_0 < 1 \) for some constant \( 0 < c_0 < 1, \log p = O(n^r) \) for some \( 0 < r < 1/5 \), and

1. under the Gaussian design, we assume (A1) (A3) and \( k = o(\sqrt{n}/\log^3 p) \); or
2. under the bounded design, we assume (A2) (A3) and \( k = o(\sqrt{n}/\log^{5/2} p) \).

Then under \( H_0 \), for any \( x \in \mathbb{R} \), then under \( H_0 \), for any \( x \in \mathbb{R} \),

\[ P(T_n - 2 \log p + \log \log p \leq x) \rightarrow \exp \left(-\frac{1}{\sqrt{\pi}} \exp(-x/2)\right), \quad \text{as} \ (n,p) \rightarrow \infty. \]

Based on the limiting null distribution, the asymptotically \( \alpha \) level tests can be defined as follows:

\[ \Phi_\alpha(T_n) = I\{T_n \geq 2 \log p - \log \log p + q_\alpha\}, \]

where \( q_\alpha = -\log(\pi) - 2 \log \log(1-\alpha)^{-1} \). The null hypothesis \( H_0 \) is rejected if and only if \( \Phi_\alpha(T_n) = 1 \).

A.2 Two-Sample Multiple Hypotheses Testing

Consider simultaneously testing the two-sample hypothesis

\[ H_{0,j} : \beta_{j}^{(1)} = \beta_{j}^{(2)} \quad \text{vs.} \quad H_{1,j} : \beta_{j}^{(1)} \neq \beta_{j}^{(2)}, \quad j = 1, ..., p. \]
As a consequence of the previous analysis, we propose the following two-sample multiple testing procedure controlling FDR/FDP or FDV.

**Two-Sample FDR/FDP Control Procedure.** Define test statistics

\[ T_j = \left( \frac{\hat{\beta}_j^{(1)}}{\tau_j^{(1)}} - \frac{\hat{\beta}_j^{(2)}}{\tau_j^{(2)}} \right) / \sqrt{2}, \]

for \( j = 1, \ldots, p \). Let \( 0 < \alpha < 1 \) and define

\[ \hat{t} = \inf \left\{ 0 \leq t \leq \sqrt{2 \log p} : \frac{pG(t)}{\max \{ \sum_{j=1}^p I\{ |T_j| \geq t \}, 1 \}} \leq \alpha \right\}. \quad (A.2) \]

We reject \( H_{0,j} \) whenever \( |M_j| \geq \hat{t} \).

**Two-Sample FDV Control Procedure.** For a given tolerable number of falsely discovered variables \( r \), let

\[ \hat{t}_{FDV} = G^{-1}(r/p). \quad (A.3) \]

We reject \( H_{0,j} \) whenever \( |T_j| \geq \hat{t}_{FDV} \).

Recall that we define quantity

\[ \tau_j^{(\ell)} = \frac{\|v_j^{(\ell)}\|_n}{\langle v_j^{(\ell)}, x_j^{(\ell)} \rangle_n} \]

for \( \ell = 1, 2 \). The following theorems provide the asymptotic behavior of our proposed testing procedures. For simplicity, we only consider the bounded design scenario.

**Theorem A.2.** Assume the conditions of Proposition 1 are satisfied for each group of the samples, suppose as \( (n,p) \to \infty \), for some constant \( c_1 > 0 \) and \( d_n \to 0 \),

\[ \sum_{j \in H_1} I\left\{ P\left( \left| \frac{\beta_j^{(1)}}{\tau_j^{(1)}} - \frac{\beta_j^{(2)}}{\tau_j^{(2)}} \right| \leq c_1 \sqrt{\log p} \right) = O(d_n) \right\} \to \infty, \quad (A.4) \]

we have

\[ \lim_{(n,p) \to \infty} \frac{\text{FDR}}{\alpha p_0/p} \leq 1, \quad \lim_{(n,p) \to \infty} P\left( \frac{\text{FDP}}{\alpha p_0/p} \leq 1 + \epsilon \right) = 1. \quad (A.5) \]

for any \( \epsilon > 0 \).

**Theorem A.3.** Under (A2) (A3) and (A4), assume \( p \leq n^r \) for some \( r > 0 \) and \( k = o(\sqrt{n} / \log^{5/2} p) \). Then

\[ \lim_{(n,p) \to \infty} \frac{\text{FDV}}{\tau p_0/p} = 1. \quad (A.6) \]
A.3 Proofs of the Results in Appendix A

In this section, we prove Theorem ?? and Theorem ?? in Appendix A. The proof of Theorem ?? is the same as the proof of Theorem 5, thus is omitted.

Proof of Theorem ?? Define $F_{jj}^{(l)} = \mathbb{E}[(\eta_{ij}^{(l)})^2/\hat{f}(u_i^{(l)})]$ and $n \times n_1 \times n_2$. Define statistics

$$\tilde{M}_j = \frac{\langle v_j^{(1)}, \epsilon_j^{(1)} \rangle}{\|v_j^{(1)}\|_n} - \frac{\langle v_j^{(2)}, \epsilon_j^{(2)} \rangle}{\|v_j^{(2)}\|_n}, \quad \hat{M}_j = \frac{\sum_{i=1}^{n_1} \eta_{ij}^{(1)} \epsilon_i^{(1)}/\hat{f}(u_i^{(1)})}{\sqrt{n_1 F_{jj}^{(1)}}} - \frac{\sum_{i=1}^{n_2} \eta_{ij}^{(2)} \epsilon_i^{(2)}/\hat{f}(u_i^{(2)})}{\sqrt{n_2 F_{jj}^{(2)}}},$$

for $j = 1, \ldots, p$, and thereby $\hat{M}_n = \max_j \hat{M}_j^2, \tilde{M}_n = \max_j \tilde{M}_j^2$.

Lemma 15. Under the condition of Theorem ??, the following events

$$B_1 = \left\{ |\tilde{M}_n - \hat{M}_n| = o(1) \right\}, \quad B_2 = \left\{ |\tilde{M}_n - M_n| = o\left(\frac{1}{\log p}\right) \right\},$$

hold with probability at least $1 - O(p^{-c})$ for some constant $C, c > 0$.

The proof of the above lemma follows directly from the proof of Lemma 1.

It follows that under the event $B_1 \cap B_2$, let $y_p = 2 \log p - \log \log p + x$ and $\epsilon_n = o(1)$, we have

$$P_{H_0}(M_n \leq y_p - \epsilon_n) \leq P_{H_0}(M_n \leq y_p) \leq P_{H_0}(\tilde{M}_n \leq y_p + \epsilon_n).$$

Therefore it suffices to prove that for any $t \in \mathbb{R}$, as $(n, p) \to \infty$,

$$P_{H_0}(M_n \leq y_p) \to \exp\left(-\frac{1}{\sqrt{\pi}} \exp(-x/2)\right). \quad (A.7)$$

Now define

$$\hat{M}_j = \frac{\sum_{i=1}^{n_1} \hat{Z}_{ij}^{(1)}}{\sqrt{n_1 F_{jj}^{(1)}}} - \frac{\sum_{i=1}^{n_2} \hat{Z}_{ij}^{(2)}}{\sqrt{n_2 F_{jj}^{(2)}}}, \quad j = 1, \ldots, p,$$

where $\hat{Z}_{ij}^{(l)} = v_{ij}^{0, \ell} \epsilon_i^{(l)} 1\{|v_{ij}^{0, \ell} \epsilon_i^{(l)}| \leq \tau_n\} - \mathbb{E}[v_{ij}^{0, \ell} \epsilon_i^{(l)} 1\{|v_{ij}^{0, \ell} \epsilon_i^{(l)}| \leq \tau_n\}]$ for $\tau_n = \log p$, $v_{ij}^{0, \ell} = \eta_{ij}^{(l)}/\hat{f}(u_i^{(l)})$ and $\hat{M}_n = \max_j \hat{M}_j^2$. Equivalently, we can write

$$\hat{M}_j = \frac{1}{n_1} \sum_{i=1}^{n_1+n_2} w_{ij}, \quad j = 1, \ldots, p,$$

where

$$w_{ij} = \frac{\hat{Z}_{ij}^{(1)}}{\sqrt{F_{jj}^{(1)}}}, \quad \text{for } i = 1, \ldots, n_1,$$
and
\[ w_{ij} = \sqrt{\frac{n_1}{n_2}} \frac{\hat{Z}_{ij}^{(2)}}{\sqrt{F_{jj}^{(2)}}}, \quad \text{for } i = n_1 + 1, ..., n_1 + n_2. \]

By similar statement in Lemma 2, it suffices to prove that for any \( t \in \mathbb{R} \), as \((n, p) \to \infty\),
\[ P_{H_0}(\hat{M}_n \leq y_p) \to \exp \left( -\frac{1}{\sqrt{\pi}} \exp(-x/2) \right). \quad (A.8) \]

By Lemma 3 in the main paper, for any integer \( 0 < q < p/2 \),
\[
\sum_{d=1}^{2q} (-1)^{d-1} \sum_{1 \leq j_1 < ... < j_d \leq p} P \left( \bigcap_{k=1}^{d} F_{j_k} \right) \leq P \left( \max_{1 \leq j \leq p} \hat{M}_j^2 \geq y_p \right) \leq \sum_{d=1}^{2p-1} (-1)^{d-1} \sum_{1 \leq j_1 < ... < j_d \leq p} P \left( \bigcap_{k=1}^{d} F_{j_k} \right), \quad (A.9)
\]

where \( F_{j_k} = (\hat{M}_{j_k}^2 \geq y_p) \). Now let \( W_i = (w_{i,j_1}, ..., w_{i,j_d})^T \) for \( 1 \leq i \leq n_1 + n_2 \). Define \( \|a\|_{\text{min}} = \min_{1 \leq i \leq d} |a_i| \) for any vector \( a \in \mathbb{R}^d \). Then we have
\[ P \left( \bigcap_{k=1}^{d} F_{j_k} \right) = P \left( \left\| n_1^{-1/2} \sum_{i=1}^{n_1+n_2} W_i \right\|_{\text{min}} \geq y_p^{1/2} \right). \]

Then it follows from Theorem 1.1 in Zaitsev (1987) that
\[ P \left( \left\| n_1^{-1/2} \sum_{i=1}^{n_1+n_2} W_i \right\|_{\text{min}} \geq y_p^{1/2} \right) \leq P \left( \|N_d\|_{\text{min}} \geq y_p^{1/2} - \epsilon_n (\log p)^{-1/2} \right) + c_1 d^{5/2} \exp \left\{ - \frac{n_1^{1/2} \epsilon_n}{c_2 d^{3/2} \tau_n (\log p)^{1/2}} \right\}, \quad (A.10) \]

where \( c_1 > 0 \) and \( c_2 > 0 \) are constants, \( \epsilon_n \to 0 \) which will be specified later, and \( N_d = (N_{m_1}, ..., N_{m_d}) \) is a normal random vector with \( \mathbb{E}(N_d) = 0 \) and \( \text{cov}(N_d) = \text{cov}(W_1) + n_2/n_1 \text{cov}(W_{n_1+1}) \). Here \( d \) is a fixed integer that does not depend on \( n, p \). Because \( \log p = o(n^{1/5}) \), we can let \( \epsilon_n \to 0 \) sufficiently slowly, say, \( \epsilon_n = \sqrt{\frac{\log^3 p}{n}} \), so that for any large \( c > 0 \),
\[ c_1 d^{5/2} \exp \left\{ - \frac{n_1^{1/2} \epsilon_n}{c_2 d^{3/2} \tau_n (\log p)^{1/2}} \right\} = O(p^{-c}). \quad (A.11) \]
Combining (??), (??) and (??), we have
\[
P\left( \max_{1 \leq j \leq p} \hat{M}_j^2 \geq y_p \right) \leq \sum_{d=1}^{2p-1} (-1)^{d-1} \sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left( \|N_d\|_{\min} \geq y_p^{1/2} - \epsilon_n (\log p)^{-1/2} \right) + o(1) .
\] (A.12)

Similarly, one can derive
\[
P\left( \max_{1 \leq j \leq p} \hat{M}_j^2 \geq y_p \right) \geq \sum_{d=1}^{2p} (-1)^{d-1} \sum_{1 \leq j_1 < \ldots < j_d \leq p} P\left( \|N_d\|_{\min} \geq y_p^{1/2} + \epsilon_n (\log p)^{-1/2} \right) + o(1) .
\] (A.13)

Using Lemma 4 in the main paper, it then follows from (??) and (??) that
\[
\lim_{n,p \to \infty} P\left( \max_{1 \leq j \leq p} \hat{M}_j^2 \geq y_p \right) \leq \sum_{d=1}^{2p} (-1)^{d-1} \frac{1}{d!} \left( \frac{1}{\sqrt{\pi}} \exp(-t/2) \right)^d ,
\]
\[
\lim_{n,p \to \infty} P\left( \max_{1 \leq j \leq p} \hat{M}_j^2 \geq y_p \right) \geq \sum_{d=1}^{2p-1} (-1)^{d-1} \frac{1}{d!} \left( \frac{1}{\sqrt{\pi}} \exp(-t/2) \right)^d ,
\]
for any positive integer \( p \). By letting \( p \to \infty \), we obtain (??) and the proof is complete. \( \square \)

**Proof of Theorem ??**. Define statistics
\[
\hat{M}_j = \frac{\langle v_j^{(1)}, \epsilon^{(1)} \rangle}{\|v_j^{(1)}\|_n} - \frac{\langle v_j^{(2)}, \epsilon^{(2)} \rangle}{\|v_j^{(2)}\|_n} , \quad \text{and} \quad \hat{M}_j = \frac{\sum_{i=1}^{n_1} \eta_{ij}^{(1)} \epsilon_i^{(1)} / \hat{f}(u_i^{(1)})}{\sqrt{n_1 F_{jj}^{(1)}}} - \frac{\sum_{i=1}^{n_2} \eta_{ij}^{(2)} \epsilon_i^{(2)} / \hat{f}(u_i^{(2)})}{\sqrt{n_2 F_{jj}^{(2)}}} ,
\]
for \( j = 1, \ldots, p \). We need the following lemma. The proof is the same as the proof of Lemma 7 and is omitted here.

**Lemma 16.** Assume (A2) (A3) and (A4), \( k = o(\sqrt{n}/\log^{5/2} p) \), the following events
\[
D_1 = \left\{ \max_{j \in \mathcal{H}_0} |\hat{M}_j - \hat{M}_j| = o\left( \frac{1}{\sqrt{\log p}} \right) \right\} ,
\]
\[
D_2 = \left\{ \max_{j \in \mathcal{H}_0} |\hat{M}_j - M_j| = o\left( \frac{1}{\sqrt{\log p}} \right) \right\} ,
\]
hold with probability at least \( 1 - O(p^{-c}) \) for some constant \( c > 0 \).

We first show
\[
\sup_{j \in \mathcal{H}_0} \sup_{0 \leq t \leq b / \sqrt{\log p}} \left| \frac{P(|M_j| \geq t)}{2 - 2\Phi(t)} - 1 \right| \to 0 .
\] (A.14)
By Lemma 6.1 in [Liu (2013)], we have
\[
\max_{1 \leq j \leq p} \sup_{0 \leq t \leq 4 \sqrt{\log p}} \frac{|P(\hat{M}_j \geq t) - 1|}{G(t)} \leq C(\log p)^{-2-\gamma_1}
\] (A.15)
for some constant \(0 < \gamma_1 < 1/2\). So (??) follows from Lemma ?? and the fact that \(G(t + o(1/\sqrt{\log p}))/G(t) = 1 + o(1)\) uniformly in \(0 \leq t \leq \sqrt{2 \log p}\).

Next we claim
\[
\sup_{0 \leq t \leq b_p} \left| \frac{G(t)}{G_0(t)} - 1 \right| \to 0.
\] (A.16)
In fact, it suffices to show that
\[
\sup_{0 \leq t \leq b_p} \left| \frac{\sum_{j \in \mathcal{H}_0} I\{|\hat{M}_j| \geq t\}}{p_0 G(t)} - 1 \right| \to 0
\] (A.17)
in probability. And this can be proven by following the same argument for the proof of (19).

Now by (??) and (??), it suffices to show
\[
P(0 \leq \hat{t} \leq b_p) \to 1
\] (A.18)
where \(b_p = G^{-1}(c_p/p)\) and \(c_p \to \infty\) for some sequence \(c_p = o(p)\). Hence \(b_p \leq \sqrt{2 \log p}\). Note that for \(j \in \mathcal{B} = \{ j : P(|\beta_j^{(1)}/\tau_j^{(1)} - \beta_j^{(2)}/\tau_j^{(2)}| \leq c_1 \sqrt{\log p}) = o_P(1) \}\), we have uniformly for \(j \in \mathcal{B}\),
\[
P(|M_j| \geq \sqrt{2 \log p}) \to 1
\] (A.19)
in probability. To see this, consider
\[
M'_j = (\hat{\beta}_j^{(1)} - \beta_j^{(1)})/\tau_j^{(1)} - (\hat{\beta}_j^{(2)} - \beta_j^{(2)})/\tau_j^{(2)} = M_j - (\beta_j^{(1)}/\tau_j^{(1)} - \beta_j^{(2)}/\tau_j^{(2)}),
\]
we have for all \(j \in \mathcal{B}\),
\[
|\beta_j^{(1)}/\tau_j^{(1)} - \beta_j^{(2)}/\tau_j^{(2)}| \leq |M_j| + |M'_j|.
\]
Now since for \(j \in \mathcal{B}\),
\[
P\left( |\beta_j^{(1)}/\tau_j^{(1)} - \beta_j^{(2)}/\tau_j^{(2)}| \geq c_1 \sqrt{\log p} \right) \to 1,
\]
and that
\[
P\left( \max_{j \in \mathcal{B}} |M'_j| \leq C_2 \sqrt{\log p} \right) \to 1.
\]
So it follows that, by properly choosing \(c_1\) depending on \(C_1\) and \(C_2\), (??) holds. Thus
\[
\frac{\sum_{j \in \mathcal{B}} P(|M_j| \geq \sqrt{2 \log p})}{|\mathcal{B}|} \to 1
\]
in probability. By Markov’s inequality, we have

$$\sum_{j \in B} I\{|M_j| \geq \sqrt{2 \log p}\} \rightarrow 1$$

By definition of $\hat{t}$ in (4.2), (4.2) is implied by

$$G(b_p)p \max \{ \sum_{j=1}^{p} I\{|M_j| \geq b_p\}, 1 \} \leq \max \{ \sum_{j=1}^{p} I\{|M_j| \geq b_p\}, 1 \} \leq \alpha.$$ 

Now note that

$$\max \{ \sum_{j=1}^{p} I\{|M_j| \geq b_p\}, 1 \} \geq \max \{ \sum_{j \in B} I\{|M_j| \geq b_p\}, 1 \} \geq \max \{ \sum_{j \in B} I\{|M_j| \geq \sqrt{2 \log p}\}, 1 \}$$

It follows that

$$\frac{G(b_p)p}{\max \{ \sum_{j=1}^{p} I\{|M_j| \geq b_p\}, 1 \}} \leq \frac{c_p}{|B|} < \alpha$$

for sufficiently large $(n, p)$, as long as we can find $c_p$ such that the last inequality holds. Therefore we have proven (4.2).