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A Lack-Of-Fit Test with Screening in Sufficient Dimension Reduction

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Abstract: It is of fundamental importance to infer how the conditional mean of the response varies with the predictors. Sufficient dimension reduction techniques reduce the dimension by identifying a minimal set of linear combinations of the original predictors without loss of information. This paper is concerned with testing whether a given small number of linear combinations of the original ultrahigh dimensional covariates is sufficient to characterize the conditional mean of the response. We first introduce a novel consistent lack-of-fit test statistic when the dimensionality of covariates is moderate. The proposed test is shown to be \( n \)-consistent under the null hypothesis and root-\( n \)-consistent under the alternative hypothesis. A bootstrap procedure is also developed to approximate p-values and its consistency has been theoretically studied. To deal with ultrahigh dimensionality, we introduce a two-stage lack-of-fit test with screening (LOFTS) procedure based on data splitting strategy. The data are randomly partitioned into two equal halves. In the first stage, we apply the martingale difference correlation based screening to one half of the data and select a moderate set of covariates.
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In the second stage, we perform the proposed test based on the selected covariates using the second half of the data. The data splitting strategy is crucial to eliminate the effect of spurious correlations and avoid the inflation of Type-I error rates. We also demonstrate the effectiveness of our two-stage test procedure through comprehensive simulations and two real-data applications.

Key words and phrases: Bootstrap; Central mean subspace, Data splitting, Lack-of-fit test, Sufficient dimension reduction, Variable Selection.

1. Introduction

Let $\mathbf{x} = (X_1, \ldots, X_p)^T \in \mathbb{R}^p$ be a covariate vector and $\mathbf{y} = (Y_1, \ldots, Y_q)^T \in \mathbb{R}^q$ be a response vector. It is of fundamental importance to infer how the conditional mean of $\mathbf{y}$ varies with the predictors. Sufficient dimension reduction techniques have become important and useful in high dimensional data analysis. It is aimed to identify a few linear combinations of the original high dimensional covariates while retaining all the information about $E(\mathbf{y} | \mathbf{x})$. Cook and Li (2002) assumed that there exists a $p \times d_0$ matrix $\beta$ such that

$$E(\mathbf{y} | \mathbf{x}) = E(\mathbf{y} | \beta^T \mathbf{x}),$$

which implies that the conditional mean function $E(\mathbf{y} | \mathbf{x})$ depends on $\mathbf{x}$ only through $d_0$ linear combinations $\beta^T \mathbf{x}$. This model not only retains the
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flexibility of nonparametric modeling but also enjoys the interpretability of parametric modeling. Since $\beta$ is not identifiable, Cook and Li (2002) defined the Central Mean Subspace (CMS), denoted by $S_{E(\gamma|x)}$, as the smallest column space of $\beta$, where the corresponding smallest column numbers, denoted by $d_0$, is defined as the structural dimension. To recover $S_{E(\gamma|x)}$, Li and Duan (1989) suggested to use the ordinary least squares estimator when $x$ follows an elliptical distribution particularly when $d_0 = 1$. Cook and Li (2002) proved that the column space of $\{\text{var}(x)\}^{-1}\text{cov}(x, y)$ belongs to the CMS $S_{E(\gamma|x)}$ when $x$ satisfies the linearity condition. Xia, et. al. (2002) proposed a minimum average variance estimation (MAVE) when the covariates are continuous. Ma and Zhu (2012) developed a semiparametric approach to dimension reduction. Ma and Zhu (2014) further investigated the inference and estimation efficiency of the central mean subspace for sufficient dimension reduction. Zhu and Zhong (2015) considered estimation of the CMS for multivariate response data. One can refer to Ma and Zhu (2013a) for a comprehensive review on dimension reduction.

Most work in the dimension reduction literature focused on estimation of the central mean subspace. However, model diagnostic studies have not received much attention within the context of dimension reduction. It is fundamental to study whether a given small number of linear combinations
of the original high dimensional covariates is sufficient to characterize the conditional mean of $y$. That is, we test the following null hypothesis, for a given $d_0 \geq 1$,

$$H_0 : E(y \mid x) = E(y \mid \beta^T x), \text{ for some } p \times d_0 \text{ matrix } \beta. \quad (1.2)$$

of the reduction model. However, the challenges associated with designing a general test for (1.2) especially for ultrahigh dimensional covariates are not to be addressed.

For ultrahigh dimensional data where the number of covariates is much higher than the sample size, the aforementioned dimension reduction methods do not work because their asymptotic normality results may require the dimensionality divergence rate satisfy $p = o(n^{1/3})$ (Zhu, Zhu and Feng, 2010). In addition, as pointed by Zhang, Yao and Shao (2018), the testing problem such as $H_0 : E(\varepsilon \mid x) = 0$ almost surely without assuming a parametric model is very challenging since we are targeting a general class of alternative, and the power may decrease quickly owing to the growing dimension and nonlinear dependence. It is natural and crucial to assume the sparsity principle that only a small set of covariates, denoted by $\mathcal{A}$, truly contributes to the response. Let $x_{\mathcal{A}} = \{X_k, k \in \mathcal{A}\}$ stand for the covariates indexed by $\mathcal{A}$. Under the sparsity assumption, the null hypothesis (1.2) can be written as

$$H_0 : ~ E(y \mid x) = E(y \mid \beta_{\mathcal{A}}^T x_{\mathcal{A}}), \text{ for some } |\mathcal{A}| \times d_0 \text{ matrix } \beta_{\mathcal{A}}, \quad (1.3)$$

where $|\mathcal{A}|$ represents the cardinality of $\mathcal{A}$. Without loss of generality, we assume $\beta = (\beta_{\mathcal{A}}^T, 0_{d_0 \times (p-|\mathcal{A}|)})^T$ where $0_{d_0 \times (p-|\mathcal{A}|)}$ denotes a $d_0 \times (p - |\mathcal{A}|)$ matrix of zeros. However, $\mathcal{A}$ is generally unknown. Sure independence
screening approaches (Fan and Lv 2008; Zhu, et. al. 2011; Li, Zhong and Zhu 2012) have been developed to screen out irrelevant covariates and estimate \( \mathcal{A} \) for ultrahigh dimensional data. Refer to Liu, Zhong and Li (2015) for a review on variable screening. In particular, Shao and Zhang (2014) proposed a martingale difference correlation (MDC) which imposes few parametric assumptions on the mean regression form \( E(y \mid x) \) and retains the model-free flavor of sufficient dimension reduction.

In this paper, we first assume that there exists a surrogate index set \( \mathcal{S} \) with a moderate size such that \( \mathcal{A} \subseteq \mathcal{S} \) and develop a novel consistent lack-of-fit test statistic for (1.3) based on the moderate covariates set \( \mathcal{S} \). We demonstrate that the hypothesis based on \( \mathcal{S} \) is equivalent to (1.3) as long as \( \mathcal{A} \subseteq \mathcal{S} \) in Theorem 1. The proposed test is shown to be \( n \)-consistent under the null hypothesis and root-\( n \)-consistent under the alternative hypothesis.

We suggest a bootstrap procedure to approximate the p-values and theoretically show that the bootstrap procedure is consistent. The second goal is to introduce a new two-stage approach based on data random splitting strategy for testing (1.2) when the dimensionality of covariates is ultrahigh. To be specific, we first randomly partition data into two equal halves. In the first stage, we apply the MDC-screening to one half of the data and select a moderate set of covariates to estimate the index set \( \mathcal{S} \). In the second
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stage, we perform the proposed test for (1.2) based on the selected set in
the second half of the data. Note that the data split strategy is crucial to
eliminate the effect of spurious correlations and avoid the inflation of Type-
I error rates of the test. Furthermore, to avoid potential type-I error rate
inflation when some important covariates are missed with a nonignorable
probability, we also provide a multi-split strategy in the extension.

The rest of this paper is organized as follows. Section 2 introduces
the details of the two-stage test procedure. In Section 3, we study the
theoretical justification for the test procedure. Section 4 demonstrates the
finite-sample performance through comprehensive simulations and two real
data applications. We add an extension on multi-splitting strategy in Sec-
tion 5. All technical proofs are relegated to the supplemental material.

A word on notation. Let \( x_S \) be the covariate vector indexed by \( S \), \(|c| \) be
the absolute value of a generic constant \( c \). For a complex-valued function
\( \psi \), \( \|\psi\|^2 = \psi^\dagger \overline{\psi} \) and \( \overline{\psi} \) is the conjugate of \( \psi \), and for a matrix \( \beta \in \mathbb{R}^{p \times d_0} \),
\( \|\beta\|^2 = \{\text{tr}(\beta^\dagger \beta)\}^{1/2} \). In addition, \( \text{span}(\beta) \) denotes the column space of \( \beta \),
\( S_{E(y|x)} \) and \( S_{E(y|x_S)} \) denote the central mean subspace of \( y \) given \( x \) and the
central mean subspace of \( y \) given \( x_S \), respectively. The sign \( \xrightarrow{D} \) denotes
convergence in distribution.
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2. A New Testing Procedure

In this section, we first propose a lack-of-fit test statistic in the population level based on a surrogate index set $S$ with a moderate size such that $A \subseteq S$. Then, we estimate the test statistic and further develop a two-stage lack-of-fit test with screening procedure.

2.1 A Lack-of-Fit Test Statistic

Under the sparsity assumption, this hypothesis can be formulated as (1.3) where $A$ represents the index set of covariates which truly contributes to the response. However, $A$ is generally unknown which makes it practically infeasible to directly propose a test for (1.3). To deal with this issue, we first suppose that these exists a surrogate index set $S$ with a moderate size which satisfies that $A \subseteq S$. Then, we consider the following null hypothesis

$$H_0: E(y | x) = E(y | \beta^S_S x_S), \text{ for some } |S| \times d_0 \text{ matrix } \beta_S.$$

(2.1)

The natural question then arises: whether testing (2.1) is equivalent to testing (1.3)? The following theorem answers this question.

**Theorem 1.** In addition to the sparsity assumption, we assume that both $S_{E(y|x)}$ and $S_{E(y|x_S)}$ exist and are uniquely defined, then testing (2.1) is equivalent to testing (1.3) for an arbitrary index set $S$ as long as $A \subseteq S$. 
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We emphasize the importance of Theorem 1 because it guarantees that testing (2.1) is equivalent to testing (1.3) as long as \( A \subseteq S \). This allows the two-stage procedure feasible for ultrahigh dimensional testing problems which will be discussed in the next subsection.

Next, we propose a new consistent lack-of-fit test for testing (2.1) in the population level based on the index set \( S \). In the sufficient dimension reduction context without any further regression model assumption, we define the error term \( \varepsilon \overset{\text{def}}{=} y - E(y \mid \beta_S^T x_S) \). The null hypothesis \( H_0 \) in (2.1) is equivalent to \( E(\varepsilon \mid x_S) = 0 \). It is further equivalent to \( \left\| E(\varepsilon \exp(is^T x_S)) \right\|^2 = 0 \) for all \( s \in \mathbb{R}^{|S|\times 1} \) using Fourier transformation, where \( i \) stands for an imaginary unit, i.e., \( i^2 = -1 \). We further note that

\[
\left\| E(\varepsilon \exp(is^T x_S)) \right\|^2 = E\left[ \varepsilon_1^T \varepsilon_2 \exp\{is^T(x_{1,S} - x_{2,S})\} \right],
\]

where \( (x_{1,S}, y_1) \) and \( (x_{2,S}, y_2) \) are two independent copies of \( (x_S, y) \). Then, for an arbitrary weight function \( \omega(s) > 0 \), testing \( H_0 \) in (2.1) equals to checking whether

\[
E \left\{ \int_{\mathbb{R}^{|S|}} \varepsilon_1^T \varepsilon_2 \exp\{is^T(x_{1,S} - x_{2,S})\} \omega(s) ds \right\} = 0, \quad (2.2)
\]

where the expectation \( E \) is taken with respect to \( (x_{1,S}, y_1) \) and \( (x_{2,S}, y_2) \). Then, the left-hand side of (2.2) can be considered as a test statistic. Borrowing the ideas of \[\text{Szekely, Rizzo and Bakirov} \quad (2007)\] and \[\text{Shao and} \]
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Zhang (2014), we specifically choose \( \omega(s) = (c_0\|s\|^{1+|S|})^{-1} \) where \( c_0 = \frac{\pi^{(1+|S|)/2}}{\Gamma\{(1+|S|)/2\}} \). Then, by \( E(\varepsilon_1) = E(\varepsilon_2) = 0 \) and Lemma 1 of Székely, Rizzo and Bakirov (2007), this test statistic has a closed form,

\[
T \overset{\text{def}}{=} E \left[ \int_{\mathbb{R}^{|S|}} (c_0\|s\|^{1+|S|})^{-1} \varepsilon_1^T \varepsilon_2 \exp\{i s^T(x_{1,S} - x_{2,S})\} ds \right] \\
= E \left\{ \int_{\mathbb{R}^{|S|}} (c_0\|s\|^{1+|S|})^{-1} \varepsilon_1^T \varepsilon_2 ds \right\} \\
- E \left[ \int_{\mathbb{R}^{|S|}} (c_0\|s\|^{1+|S|})^{-1} \varepsilon_1^T \varepsilon_2 [1 - \cos\{s^T(x_{1,S} - x_{2,S})\}] ds \right] \\
= -E(\varepsilon_1^T \varepsilon_2 \|x_{1,S} - x_{2,S}\|). \quad (2.3)
\]

In general, \( T \geq 0 \). And \( T = 0 \) if and only if \( H_0 \) in (2.1) is true. This motivates us to utilize a consistent estimator of \( T \) as our test statistic for testing (2.1). The large values of \( T \) provide stronger evidence against the null hypothesis (2.1).

2.2 Two-Stage Lack-of-Fit Test with Screening

In order to estimate the test statistic \( T \), we first study how to find an index set \( S \) to contain the true covariates set \( A \) and estimate the error term \( \varepsilon = y - E(y | \beta_S^T x_S) \). To this end, we propose a two-stage testing procedure based on data splitting strategy. We randomly partition the random sample \( D \overset{\text{def}}{=} \{(x_i, y_i), i = 1, \ldots, n\} \) into two halves. In the first stage, we screen out as many irrelevant covariates as possible based on the
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First half $D_1 \overset{\text{def}}{=} \{(x_i, y_i), i = 1, \ldots, n_1\}$ to obtain an index set $S$ with a moderate size, where $n_1$ is the integer part of $n/2$. In the second stage, we develop a novel consistent lack-of-fit test for testing (1.3) using the second half of the data $D_2 \overset{\text{def}}{=} \{(x_i, y_i), i = n_1 + 1, \ldots, n_1 + n_2\}$.

Stage 1: Feature Screening

Feature screening approaches are developed to screen out irrelevant covariates and retain the truly relevant ones in a moderate set for ultrahigh dimensional data. In the first stage, we apply the martingale difference correlation (MDC) based screening proposed by Shao and Zhang (2014) to the first half of the data and select a moderate set of covariates.

The martingale difference divergence (MDD) of $y$ given each covariate $X_j$ is defined by

$$
\text{MDD}(y \mid X_j)^2 = \frac{1}{c_q} \int_{\mathbb{R}^q} \frac{\|g_{y,X_j}(s) - E(y)g_{X_j}(s)\|^2}{\|s\|^{1+q}} ds,
$$

(2.4)

where $g_{y,X_j}(s) = E(y e^{is^T X_j})$, $g_{X_j}(s) = E(e^{is^T X_j})$, $c_q = \pi^{(1+q)/2}/\Gamma(1+q)/2$ and $\Gamma(\cdot)$ is the gamma function. The martingale difference correlation $\text{MDC}(y \mid X_j)$ is the normalized version of $\text{MDD}(y \mid X_j)$. $\text{MDC}(y \mid X_j) = 0$ if and only if $E(y \mid X_j) = E(y)$ almost surely when $E(\|y\|^2 + X_j^2) < \infty$.

That is, when $\text{MDC}(y \mid X_j) = 0$, the conditional mean of $y$ given $X_j$ is independent of $X_j$. Shao and Zhang (2014) proposed to utilize the estimated MDC of the response given a covariate as the marginal utility to rank the
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importance of all covariates and select a moderate set of covariates with top ranks. One may refer to Shao and Zhang (2014) for the calculation of the sample martingale difference correlation.

As mentioned by Cook and Li (2002), regression analysis is mostly concerned with inferring about the conditional mean of the response given the covariates. The MDC-based screening shares this spirit and inherits the model-free flavor of sufficient dimension reduction. We apply the MDC-based screening to $D_1$, the first half of the data, and select the set of covariates defined by

$$S = \{ j : \widehat{MDC}(y \mid X_j) \text{ is among the top } s \text{ largest of all } p \text{ sample } \hat{MDC} \text{ values} \}.$$  

By slight abuse of notation, we still use $S$ to represent the selected set by screening. Under some regularity assumptions, the sure screening property holds for the MDC-based screening. That is, $P(A \subseteq S) \to 1$ as the sample size approaches the infinity. Then, Theorem $1$ and the sure screening property together justifies that testing (2.1) is asymptotically equivalent to testing (1.3).

Stage 2: A Lack-of-Fit Test

Next, we elaborate how to estimate the test statistic $T$. First, we suggest to use the profile least squares approach to recover $S_{E(y \mid X_S)}$. It amounts
to minimize the profile least squares and obtain the following estimator

\[
\hat{\beta}_{S,-d_0} \overset{\text{def}}{=} \arg \min_{b \in \mathbb{R}^{(|S| - d_0) \times d_0}} \sum_{i=n_1+1}^{n} \|y_i - \hat{m}(x_{S,d_0,i} + b^T x_{S,-d_0,i})\|^2,
\]

where \( x_{S,d_0} \) is the vector of the first \( d_0 \) elements of \( x_S \) and \( x_{S,-d_0} \) is the vector of the rest. Here we restrict the upper \( d_0 \times d_0 \) submatrix of \( \beta_S \) to be an identity matrix to ensure that \( \beta_S \) itself is identifiable (Ma and Zhu 2013b) for a given \( d_0 \). \( \hat{\beta}_{S,-d_0} \) is a \(|S| - d_0 \times d_0\) matrix composed of the lower \(|S| - d_0\) rows of \( \beta_S \). For an arbitrary \( b \in \mathbb{R}^{(|S| - d_0) \times d_0} \), we estimate 

\[
\hat{m}(x_{S,d_0,i} + b^T x_{S,-d_0,i}) \]

with the leave-one-out kernel estimator, defined as

\[
\hat{m}(x_{S,d_0,i} + b^T x_{S,-d_0,i}) \overset{\text{def}}{=} \sum_{j=n_1+1, j \neq i}^{n} \frac{K_h(x_{S,d_0,j} + b^T x_{S,-d_0,j} - x_{S,d_0,i} - b^T x_{S,-d_0,i})y_j}{K_h(x_{S,d_0,j} + b^T x_{S,-d_0,j} - x_{S,d_0,i} - b^T x_{S,-d_0,i})},
\]

where \( K_h(\cdot) = K(\cdot/h)/h^{d_0} \), \( K(\cdot) \) is a product of \( d_0 \) univariate kernel functions and \( h \) is the bandwidth. Then we estimate \( T \) by

\[
T_{n_2} \overset{\text{def}}{=} \text{tr} \left( -\frac{1}{n_2^2} \sum_{i=n_1+1}^{n_1+n_2} \sum_{j=n_1+1}^{n_1+n_2} \hat{\varepsilon}_i \hat{\varepsilon}_j^T \|x_{i,S} - x_{j,S}\| \right), \tag{2.5}
\]

where \( \hat{\varepsilon} = y - \hat{m}(\hat{\beta}_S^T x_S) \). In practice, larger values of \( T_{n_2} \) provide stronger evidence against \( H_0 \) in (2.1).

Since the null hypothesis (2.1) is concerned with studying whether a given small number of linear combinations of covariates is sufficient to characterize the conditional mean of \( y \), the test based on \( T_{n_2} \) is essentially a lack-of-fit test. Thus, we name this two-stage test procedure as a Lack-
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Of-Fit Test with Screening (LOFTS) procedure and summarizes it in the following algorithm.

**Algorithm 1** The LOFTS Procedure

**Step 1.** Randomly split the random sample into two even halves, $D_1$ and $D_2$.

**Step 2.** Apply the MDC-based screening to $D_1$ and select the moderate set $S$.

**Step 3.** Test (2.1) based on the test statistic $T_{n_2}$ using $D_2$. The associated p-value can be obtained using the bootstrap procedure (Algorithm 2 in Section 3).

**Step 4.** Reject (2.1) and (1.3) if p-value $< \alpha$, the significance level.

**Remark 1:** It is worth noting that the data splitting technique is crucial in the proposed two-stage LOFTS procedure for ultrahigh dimensional data. If we do not split the data, a naive two-stage procedure is as follows. In the first stage, the MDC-screening is applied to the full sample data. In the second stage, the proposed test is conducted based on the selected covariates using the same data. In theory, this method works well and is even more efficient if $S$ happens to be $A$ exactly in the first stage. However, it is usually difficult to achieve in ultrahigh dimensional problems. Some inactive covariates which may contribute to the response in the finite sample level are often recruited in the first screening stage of the naive two-stage procedure, so the type-I error rates will be inflated for testing (2.1). One can refer to the simulations results in Section 4. This phenomenon owns
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to spurious correlations that are inherent in ultrahigh dimension problems \cite{Fan, Guo and Hao, 2012}. The data splitting technique can eliminate spurious correlations and further avoid the size inflation. Because the two halves of the data set are independent, a covariate which has a large spurious sample correlation with the response over the first half has a small chance to be highly correlated with the response in the second half. Hence, its influence on the size of the test in the second stage is negligible.

**Remark 2:** Feature screening can efficiently reduce the dimensionality of covariates in the first stage and retain the truly important covariates in the asymptotical sense. However, some important covariates may be missed in the finite sample level. In this sense, the choice of the reduced model size may be crucial for the screening procedure to work. \cite{Fan and Lv, 2008} suggested a hard thresholding where the reduced model size is proportional to $[n/\log n]$. \cite{Wu, Boos and Stefanski, 2007}, \cite{Zhu, et. al, 2011} and \cite{Li, Zhong, Li and Wu, 2014} proposed a soft-thresholding rule by introducing auxiliary variables. To reduce this risk in practice, one may choose a relatively large set $S$ if he believes that the size of important covariates is relatively large; or apply the iterative version of the MDC-based screening to avoid missing some important covariates which are marginally uncorrelated with the response. Another strategy to enhance the performance of
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Data splitting technique is multiple data splitting which will discussed in Section 5.

Remark 3: The number of linear combinations of covariates, $d_0$, in (2.1) is prespecified before the lack-of-fit test procedure. The null hypothesis $H_0$ holds trivially if we specify $d_0 = |S|$ by letting $\beta_A$ is an $|S| \times |S|$ identity matrix. It is of great interest to determine the smallest number of linear combinations of covariates to sufficiently capture regression information of $E(y \mid x_S)$. For instance, the optimal value of $d_0$ is 1 for a general single-index model. For a given dimension $d_0$, if $H_0$ is rejected at some level of significance, then we can conclude that $\beta_A^T x_S$ is not sufficient to characterize the conditional mean $E(y \mid x_S)$ and some additional linear combinations of $x_S$ are further needed. In practice, we can sequentially perform the two-stage LOFTS procedure for $d_0$ starting from 1 to $|S|$ until we fail to reject $H_0$ to determine the optimal value of $d_0$.

3. Theoretical Properties

In this section, we study theoretical properties of the proposed test, including the asymptotic distribution under the null hypothesis and the asymptotic distributions under both global and local alternative hypotheses. We also propose a bootstrap procedure to calculate the associated p-value. The
regularity conditions are provided in the Appendix.

Theorem 2 in the following states the asymptotic null distribution of the test statistic under the null hypothesis \((2.1)\).

**Theorem 2.** Assume Conditions (C1)-(C5) hold, under \(H_0\) in \((2.1)\),

\[
n_2 T_{n_2} \xrightarrow{D} \|\zeta(s)\|_\omega^2 \overset{\text{df}}{=} \int_{s \in \mathbb{R}^{|S|}} \|\zeta(s)\|^2 (c_0 ||s||^{1+|S|})^{-1} ds, \quad \text{as } n_2 \to \infty,
\]

where \(\zeta(s)\) denotes a complex-valued Gaussian random process with mean zero and covariance function \(\text{cov}\{\zeta(s), \zeta^T(s_0)\}\) defined in \((??)\) of the Supplement.

However, the asymptotic distribution of \(T_{n_2}\) under \(H_0\) is unfortunately not tractable because \(\|\zeta(s)\|_\omega^2\) hinges upon the unknown joint distribution of \((x_S, y)\). In practice, we propose the bootstrap procedure in Algorithm 2 to calculate the associated p-value.

Theorem 3 states the consistency of the bootstrap procedure.

**Theorem 3.** Assume Conditions (C1)-(C5) hold, we have that \(n_2 \tilde{T}_{n_2} \xrightarrow{D} \|\zeta(s)\|_\omega^2\), as \(n_2 \to \infty\).

We remark that although it is not tractable in Theorem 2, the asymptotic distribution of \(T_{n_2}\) under \(H_0\) is necessary to derive. Because Theorem 3 shows that the asymptotic null distribution of the bootstrapped test statistic is same as that of the original test statistic. It implies that the bootstrap
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Algorithm 2 The Bootstrap Procedure

**Step 1.** Obtain \( \hat{\beta}_S \) and \( \hat{m}(\hat{\beta}_S^T x_S) \) using the second half \( D_2 \), and calculate the residuals \( \tilde{\varepsilon}_i = y_i - \hat{m}(\hat{\beta}_S^T x_{S,i}) \), for \( i = n_1 + 1, n_1 + 2, \ldots, n \). Then, compute the test statistic \( T_{n_2} \) in (2.5).

**Step 2.** Draw the weights \( \delta_i \) independently from \( \{1, -1\} \) at random with probability 0.5. Let \( \tilde{\varepsilon}_i = \varepsilon_i \delta_i \) and generate \( \tilde{y}_i = \hat{m}(\hat{\beta}_S^T x_{S,i}) + \tilde{\varepsilon}_i \), for \( i = n_1 + 1, n_1 + 2, \ldots, n \).

**Step 3.** Repeat Step 1 and calculate the test statistic \( \tilde{T}_{n_2} \) based on (2.5) using the new bootstrapped data set \((x_i, \tilde{y}_i)\), \( i = n_1 + 1, n_1 + 2, \ldots, n \).

**Step 4.** Repeat Step 2 and 3 1,000 times to obtain \( \tilde{T}_{n_2}^{(1)}, \tilde{T}_{n_2}^{(2)}, \ldots, \tilde{T}_{n_2}^{(1,000)} \). The associated p-value is obtained by \( 1000^{-1} \sum_{b=1}^{1000} I(\tilde{T}_{n_2}^{(b)} \geq T_{n_2}) \), where \( I(\cdot) \) is an indicator function. Reject \( H_0 \) if the p-value < \( \alpha \), a given significance level.

The procedure is able to provide asymptotically valid inference for the proposed lack-of-fit test.

Next, we consider two kinds of alternative hypotheses. The global alternative hypothesis can be specified in the following

\[
H_{1g} : E(y \mid x) = E(y \mid B_S^T x_S), \text{ for some } |S| \times d_1 \text{ matrix } B_S, d_0 < d_1 \leq |S|(3.1)
\]

Under \( H_{1g} \), \( d_0 \) linear combinations of covariates are not sufficient to recover the CMS \( S_{E(y|x_S)} \). We also consider a sequence of local alternatives:

\[
H_{1l} : y = m(\beta_S^T x_S) + C_{n_2} g(B_S^T x_S) + \varepsilon, \quad (3.2)
\]

for some \(|S| \times d_1 \text{ matrix } B_S, d_0 < d_1 \leq |S|\),

where \( \beta_S \) is a subspace of \( B_S \) and \( C_{n_2} \rightarrow 0 \) makes \( H_{1l} \) become local alterna-
4. NUMERICAL STUDIES

tives. Under $H_{1l}$, we have that $E(\varepsilon \mid x_S) = 0$ and $\beta_S^T x_S$ is not sufficient to characterize the conditional mean function $E(y \mid x_S)$. However, as $n_2 \to \infty$, $H_{1l}$ approaches $H_0$. Then the asymptotic distributions under both global and local alternative hypotheses are presented in Theorem 4.

**Theorem 4.** Assume conditions (C1)-(C5) in the Appendix hold.

(i) Under global alternative in (3.1), as $n_2 \to \infty$,

$$n_2^{1/2}(T_{n_2} - T) \overset{D}{\to} \mathcal{N}(0, \sigma_0^2),$$

where the variance $\sigma_0^2 \overset{\text{def}}{=} 4\text{var}(Z_1 + Z_2 + Z_3)$, and $Z_1$, $Z_2$ and $Z_3$ are defined in (??)-(??) of the Supplement, respectively.

(ii) Under the local alternative in (3.2) with $C_{n_2} = n_2^{-1/2}$, as $n_2 \to \infty$,

$$n_2T_{n_2} \overset{D}{\to} \|\zeta_0(s)\|^2 \overset{\text{def}}{=} \int_{s \in \mathbb{R}^{|S|}} \|\zeta_0(s)\|^2(c_0\|s\|^{1+|S|}-1)ds,$$

where $\zeta_0(s)$ denotes a complex-valued Gaussian random process with the mean function defined in (??) and the covariance function $\text{cov}\{\zeta_0(s), \zeta_0(s_0)\}$ defined in (??) of the Supplement.

4. Numerical Studies

**Example 1.** We examine the finite-sample performance of the proposed two-stage test procedure by simulations. Consider the following two regres-
sion models

Model (I): \[ Y = (3 + \beta_1 x)^2 + c(\beta_2^T x)^2 + \varepsilon, \]

Model (II): \[ Y = \beta_1^T x + (3 + \beta_4^T x)^2 + c(\beta_5^T x)^2 + \varepsilon, \]

where \( x = (X_1, \ldots, X_p)^T \) is generated from a multivariate normal distribution with mean zero and covariance matrix \( \Sigma = (\sigma_{kl})_{p \times p} \) with \( \sigma_{kl} = 0.5^{|k-l|} \) for \( k, l = 1, \ldots, p \), and \( \varepsilon \sim N(0,1) \). Here, we set \( \beta_1 = (0.25, 0.25, 0.25, 0.25, 0, \ldots, 0)^T, \beta_2 = (0, 1, 0, 0, 0, \ldots, 0)^T, \beta_3 = (3, 0, 3, 0, 0, \ldots, 0)^T, \beta_4 = (0, 0.5, 0, 0, 0, \ldots, 0)^T \) and \( \beta_5 = (0, 0, 2, 0, 0, \ldots, 0)^T \). In both models, the value \( c = 0 \) corresponds to the null hypotheses while \( c \neq 0 \) represents the alternatives. Thus, the CMS \( S_{E(Y|x)} \) only depends on \( \beta_1^T x \) under \( H_0 \) but two linear combinations \( (\beta_1^T x, \beta_2^T x) \) under \( H_1 \) in Model (I). For Model (II), \( S_{E(Y|x)} \) is two-dimensional under the null but three-dimensional under the alternative.

We consider the sample size \( n = 200 \) and the covariate dimension \( p = 2000 \). Each sample is randomly divided into two equal halves. We perform the LOFTS procedure in Algorithm 1: Utilize MDC-based screening based on the first half \( D_1 = \{(x_i, Y_i), i = 1, \ldots, 100\} \) to obtain a selected model \( S \) and test the hypothesis \( (2.1) \) based on the second half \( D_2 = \{(x_i, S, Y_i), i = 101, \ldots, 200\} \). To compare its empirical performance, we further consider the following two procedures: (1) A naive two-stage test procedure, denoted
by “NAIVE”. We perform both the MDC-based screening and the lack-of-fit test on the same full sample. (2) An oracle test procedure, denoted by “Oracle”. In the second stage, we directly conduct the test based on \{ (x_{iA}, Y_i), i = 101, \ldots, 200 \} as the true model \( A \) is known. We repeat simulations 1,000 times and summarize their finite-sample performances.

**Remark:** For simplicity, we test the null hypothesis \([2.1]\) with \( d_0 = 1 \) for Model (I) and \( d_0 = 2 \) for Model (II) to compare the performances of the test procedures in simulations. As a practical byproduct of the two-stage LOFTS procedure, one can sequentially perform the procedure for \( d_0 \) starting from 1 to \(|S|\) and the optimal value of \( d_0 \) is determined when the corresponding null hypothesis fails to be rejected at some significance level.

**Screening Performances:** In the two-stage LOFTS procedure, the first-stage screening performance is crucial for the follow-up test according to Theorem[1]. The MDC-based screening method is effective to include almost all truly important covariates into the selected models in this example. Since it is not our main contribution in this paper, we only report the screening performance in the supplementary material. One may refer to Shao and Zhang (2014) for more numerical justifications of the MDC-based screening.

**Size Performances:** Next we evaluate the size performances of four test
procedures for Models (I) and (II) when \( c = 0 \), including our proposed LOFTS, the naive two-stage method, the oracle procedure and the DRMA procedure proposed by Guo, Wang and Zhu (2016). Since the DRMA procedure is proposed for parametric single index model, we only report their results for Model (I). The critical values of the lack-of-fit test procedure are decided through the proposed bootstrap procedure in Algorithm 2. We take four significance levels into consideration: \( \alpha = 0.01, 0.02, 0.05 \) and \( 0.10 \), and two different sizes of the selected models: \(|S| = 8\) and \(16\). The empirical Type-I error rates based on 1,000 repetitions for Models (I) and (II) are charted in Table 1. In addition, the QQ plots of the empirical p-values and the uniform distribution are charted in Panels (A) and (B) of Figure 1. It can be clearly seen that the empirical Type-I error rates of the LOFTS procedure, the DRMA procedure and the oracle method are pretty close to the user-specified significance levels. However, the empirical Type-I error rates of the naive two-stage method are obviously larger than the significance levels, especially when the selected model size becomes large. The inflation of Type-I errors in the naive two-stage procedure is due to spurious correlations between the response and some unimportant covariates in the ultrahigh dimensional data. The results further support the importance of the data splitting strategy which can efficiently eliminate
4. NUMERICAL STUDIES

the effect of spurious correlations.

Table 1: The empirical Type-I error rates when $c = 0$.

| Model | $\alpha$ | LOFTS $|S| = 8$ | LOFTS $|S| = 16$ | NAIVE $|S| = 8$ | NAIVE $|S| = 16$ | Oracle $|S| = 8$ | Oracle $|S| = 16$ | DRMA $|S| = 8$ | DRMA $|S| = 16$ |
|-------|----------|----------------|----------------|-------------|----------------|----------------|----------------|----------------|----------------|----------------|
| (I)   | 0.01     | 0.010          | 0.011          | 0.021       | 0.041          | 0.015          | 0.011          | 0.013          | 0.015          | 0.013          |
|       | 0.02     | 0.017          | 0.020          | 0.044       | 0.064          | 0.020          | 0.020          | 0.025          | 0.020          | 0.025          |
|       | 0.05     | 0.046          | 0.054          | 0.096       | 0.117          | 0.052          | 0.051          | 0.049          | 0.051          | 0.049          |
|       | 0.10     | 0.114          | 0.105          | 0.152       | 0.209          | 0.095          | 0.098          | 0.088          | 0.098          | 0.088          |
| (II)  | 0.01     | 0.013          | 0.017          | 0.021       | 0.026          | 0.009          | -              | -              | -              | -              |
|       | 0.02     | 0.026          | 0.027          | 0.031       | 0.039          | 0.016          | -              | -              | -              | -              |
|       | 0.05     | 0.045          | 0.049          | 0.076       | 0.087          | 0.054          | -              | -              | -              | -              |
|       | 0.10     | 0.105          | 0.106          | 0.118       | 0.151          | 0.112          | -              | -              | -              | -              |

**Power Performances:** When $c \neq 0$, the previous null hypotheses are no longer true. For instance, the response depends on three different linear combinations in Model (II) when $c \neq 0$. We consider a sequence of values of $c = 0.2, 0.4, 0.6, 0.8$ and $1$ to compare the empirical powers of the LOFTS and oracle procedures. Note that the “oracle” means the set of truly important covariates is assumed known in the second test stage. We choose the two significance levels: $\alpha = 0.05$ and $0.10$, and two reduced model sizes, $|S| = 8$ and 16. Table 2 summarizes the simulation results which show that the proposed two-stage LOFTS procedure is powerful to detect the significance of the tests. As the signal intensity parameter $c$ increases, the empirical powers also increases. Once the true set $A$ can be contained, the smaller the selected model size is, the larger the empirical
Figure 1: QQ plots of the empirical p-values and the uniform distribution for Model (I) in Panel (A) and Model (II) in Panel (B) in Example 1.

powers are. This phenomenon further confirms the importance of screening out irrelevant covariates in the ultrahigh dimensional test problems. Note that the outstanding size and power performances of the oracle procedure also demonstrate the advantage of the proposed lack-of-fit test.

**Sequential Test Performances:** By performing our proposed LOFTS sequentially, we can determine the smallest number of linear combinations of covariates to sufficiently capture regression information of \( E(y \mid x_S) \). The procedure is conducted as follows. Start with \( d_0 = 1 \), test the null hypothesis \( \text{(1.2)} \) using the LOFTS. If the hypothesis is rejected, increase \( d_0 \) by one and perform the test again. Stop when the first null hypothesis is not rejected in the test series. The corresponding value of \( d_0 \), denoted
### 4. NUMERICAL STUDIES

#### Table 2: The empirical powers when $c \neq 0$ at $\alpha = 0.05$ or 0.10.

| Model | $c$  | LOFTS $|S| = 8$ | LOFTS $|S| = 16$ | Oracle $|S| = 8$ | Oracle $|S| = 16$ | DRMA $|S| = 8$ | DRMA $|S| = 16$ |
|-------|-----|--------------|-----------------|----------------|-----------------|----------------|----------------|
| (I)   | 0.2 | 0.243 0.369  | 0.162 0.247     | 0.572 0.692    | 0.099 0.160    | 0.068 0.127    |
|       | 0.4 | 0.652 0.756  | 0.469 0.580     | 0.965 0.988    | 0.253 0.343    | 0.173 0.284    |
|       | 0.6 | 0.853 0.908  | 0.702 0.779     | 0.995 0.997    | 0.496 0.620    | 0.382 0.495    |
|       | 0.8 | 0.944 0.976  | 0.831 0.896     | 1.000 1.000    | 0.722 0.806    | 0.561 0.674    |
|       | 1.0 | 0.963 0.980  | 0.893 0.937     | 1.000 1.000    | 0.836 0.906    | 0.702 0.796    |
| (II)  | 0.2 | 0.965 0.977  | 0.646 0.768     | 1.000 1.000    | -               | -               |
|       | 0.4 | 0.999 0.999  | 0.921 0.971     | 1.000 1.000    | -               | -               |
|       | 0.6 | 0.998 0.999  | 0.963 0.982     | 1.000 1.000    | -               | -               |
|       | 0.8 | 1.000 1.000  | 0.943 0.976     | 1.000 1.000    | -               | -               |
|       | 1.0 | 0.997 0.997  | 0.923 0.965     | 1.000 1.000    | -               | -               |

The symbol $\hat{d}$, is the estimate of $d^*$ that represents the smallest number of linear combinations of covariates to sufficiently recover the CMS. We report the empirical distributions of $\hat{d}$ at the significance level $\alpha = 0.05$ based on 1000 simulations for Model (I) and (II) in Table 3. It can be seen that the LOFTS sequential tests are able to estimate the true structural dimension correctly with large probabilities, especially when $|S| = 8$ and $c = 0$ or $c$ is large.

We also compare our results with the method of iterative Hessian transformation (IHT) proposed by [Cook and Li (2004)] and the validated information criterion based method (VIC) by [Ma and Zhang (2015)], we only report the corresponding results when the reduced model size is 8, for simplicity. For the VIC method, since we are targeting on the structural dimen-
4. NUMERICAL STUDIES

Table 3: The empirical distributions of $\hat{d}$ at the significance level $\alpha = 0.05$.

| Model | $c$ | $d^*$ | $|S| = 8$ | $|S| = 16$ |
|-------|-----|-------|-----------|-----------|
|       |     |       | 1  2  3  4 | 1  2  3  4 |
| (I)   | 0   | 1     | 0.954 0.032 0.002 0.012 | 0.946 0.038 0.004 0.012 |
|       | 0.2 | 2     | 0.757 0.218 0.009 0.016 | 0.838 0.128 0.015 0.019 |
|       | 0.4 | 2     | 0.348 0.607 0.017 0.028 | 0.531 0.432 0.017 0.020 |
|       | 0.6 | 2     | 0.147 0.803 0.022 0.028 | 0.298 0.652 0.018 0.032 |
|       | 0.8 | 2     | 0.056 0.897 0.018 0.029 | 0.169 0.786 0.019 0.026 |
|       | 1.0 | 2     | 0.037 0.907 0.023 0.033 | 0.107 0.844 0.010 0.039 |
| (II)  | 0   | 2     | 0.000 0.955 0.019 0.026 | 0.003 0.948 0.030 0.019 |
|       | 0.2 | 3     | 0.001 0.035 0.923 0.041 | 0.012 0.346 0.607 0.035 |
|       | 0.4 | 3     | 0.011 0.001 0.940 0.048 | 0.078 0.073 0.807 0.042 |
|       | 0.6 | 3     | 0.050 0.002 0.907 0.041 | 0.234 0.024 0.705 0.037 |
|       | 0.8 | 3     | 0.000 0.000 0.969 0.031 | 0.006 0.052 0.901 0.041 |
|       | 1.0 | 3     | 0.001 0.003 0.965 0.031 | 0.034 0.059 0.870 0.037 |

sion of the central mean space, we only examine the validated information criterion in semiparametric principal Hessian direction estimators. From Table 4, we can see that our LOFTS procedure outperforms both methods in our limited experiments. The IHT method often underestimates the structural dimension, this is mainly because the largest estimated eigenvalues often dominates the others. Although the estimated dimension using the validated information criterion converges to the true structural dimension in probability, there is no guarantee for the finite sample performance, especially when the sample size is small and the reduced model size is large. Our LOFTS procedure, however, avoids this problem through the proposed bootstrap procedure.
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Table 4: The empirical distributions of $\hat{d}$ of IHT and VIC when $|S| = 8$.  

<table>
<thead>
<tr>
<th>Model</th>
<th>$c$</th>
<th>$d^*$</th>
<th>IHT 1 2 3 4</th>
<th>VIC 1 2 3 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>(I)</td>
<td>0</td>
<td>1</td>
<td>0.960 0.039 0.001 0.000</td>
<td>0.836 0.164 0.000 0.000</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>1</td>
<td>0.926 0.073 0.001 0.000</td>
<td>0.830 0.170 0.000 0.000</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>1</td>
<td>0.821 0.168 0.011 0.000</td>
<td>0.787 0.213 0.000 0.000</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
<td>1</td>
<td>0.730 0.258 0.012 0.000</td>
<td>0.714 0.284 0.002 0.000</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>1</td>
<td>0.583 0.398 0.019 0.000</td>
<td>0.601 0.397 0.002 0.000</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td>0.466 0.514 0.020 0.000</td>
<td>0.437 0.563 0.000 0.000</td>
</tr>
</tbody>
</table>

|       | 0   | 2     | 0.395 0.558 0.047 0.000 | 0.105 0.538 0.357 0.000 |
|       | 0.2 | 3     | 0.026 0.941 0.033 0.000 | 0.004 0.858 0.138 0.000 |
|       | 0.4 | 3     | 0.002 0.928 0.070 0.000 | 0.000 0.787 0.213 0.000 |
|       | 0.6 | 3     | 0.000 0.897 0.103 0.000 | 0.000 0.701 0.299 0.000 |
|       | 0.8 | 3     | 0.000 0.857 0.142 0.001 | 0.000 0.613 0.381 0.006 |
|       | 1   | 3     | 0.000 0.808 0.190 0.002 | 0.000 0.554 0.430 0.016 |

**Example 2.** We apply our proposed two-stage LOFTS procedure to a rat eye microarray expression data set which is available from Gene Expression Omnibus with accession number GSE5680. In this study, 120 twelve-week-old male rats were selected for tissue harvesting from the eyes and 31,042 different probe sets were measured for microarray analysis. In Scheetz, et. al (2006) and Huang, Ma and Zhang (2008), 18,976 probes that were considered adequately expressed and exhibited at least two-fold variation were retained in order to take deep insight into genetic variation involved in human’s eye disease. The response variable TRIM32 at probe 1389163_at, one of the selected 18,976 probes, was recently found to cause

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Bardet-Biedl syndrome (Chiang, et. al 2006). In our study, we aim to check if there exists a single linear combination of the gene expression levels that is sufficient to predict the expression level of the gene TRIM32.

We randomly partition this random sample into two halves, each with 60 observations, and marginally standardize all variables. We perform the MDC-based screening method to reduce the covariate dimension from 18,975 to 8 and 16, respectively. Denote $x_{S_1} = (X_1, \ldots, X_8)^T$ and $x_{S_2} = (X_1, \ldots, X_{16})^T$ the covariates retained in the screening stage. We apply the profile least squares approach to estimate $\beta_{S_1}$ based on $\{(x_{j,S_1}, Y_j), j = 61, \ldots, 120\}$ and $\beta_{S_2}$ based on $\{(x_{j,S_2}, Y_j), j = 61, \ldots, 120\}$. To ensure identifiability of $\beta_{S_1}$ and $\beta_{S_2}$, we fix the coefficient of $X_1$ to be 1. Table 5 exhibits the estimate coefficients (denoted by “coef”), along with their respective standard deviations (denoted by “std”) and p-values. With two different model sizes, both estimates agree very well: $X_4$, $X_6$, $X_7$ and $X_8$, in addition to $X_1$, are important at the significance level $\alpha = 0.05$, $X_3$ and $X_5$ are important if only eight covariates are retained, $X_9$ becomes important if sixteen covariates are selected.

Next, we check whether a single linear combination of the retained covariates suffices to predict the expression level of TRIM32, based on $\{(x_{j,S_1}, Y_j), j = 61, \ldots, 120\}$ and $\{(x_{j,S_2}, Y_j), j = 61, \ldots, 120\}$, respectively.
Table 5: The estimated coefficients, the standard errors and the p-values when $|S| = 8$ and $|S| = 16$, respectively, in Example 2.

| $|S|$ | \(\hat{\beta}_2\) | \(\hat{\beta}_3\) | \(\hat{\beta}_4\) | \(\hat{\beta}_5\) | \(\hat{\beta}_6\) | \(\hat{\beta}_7\) | \(\hat{\beta}_8\) |
|------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 8    | 0.043           | 1.772           | -6.750          | -5.762          | -6.783          | 4.364           | -3.251          |
|      | 0.824           | 0.828           | 2.794           | 2.596           | 2.643           | 1.848           | 1.346           |
|      | 0.959           | 0.037           | 0.019           | 0.030           | 0.013           | 0.022           | 0.019           |
|      | \(\hat{\beta}_2\) | \(\hat{\beta}_3\) | \(\hat{\beta}_4\) | \(\hat{\beta}_5\) | \(\hat{\beta}_6\) | \(\hat{\beta}_7\) | \(\hat{\beta}_8\) |
| 16   | 0.711           | 0.270           | -2.087          | -1.191          | -1.778          | 1.990           | -1.355          |
|      | 0.741           | 0.460           | 0.914           | 0.730           | 0.714           | 0.893           | 0.630           |
|      | 0.341           | 0.559           | 0.026           | 0.108           | 0.016           | 0.030           | 0.036           |
|      | \(\hat{\beta}_9\) | \(\hat{\beta}_{10}\) | \(\hat{\beta}_{11}\) | \(\hat{\beta}_{12}\) | \(\hat{\beta}_{13}\) | \(\hat{\beta}_{14}\) | \(\hat{\beta}_{15}\) | \(\hat{\beta}_{16}\) |
|      | -1.766          | -0.941          | -0.679          | 0.964           | -0.393          | 0.764           | -0.607          | 0.115           |
|      | 0.757           | 0.606           | 0.919           | 0.732           | 0.866           | 0.635           | 0.656           | 0.708           |
|      | 0.023           | 0.126           | 0.463           | 0.193           | 0.652           | 0.234           | 0.358           | 0.872           |

The p-values obtained by our test procedures are 0.765 and 0.479 respectively, indicating that we have no evidence to reject the null hypothesis and a single linear combination indeed suffices to describe how the expression level of the gene TRIM32 varies with other genes. To further justify this test result, we chart the scatterplots of the response versus the standardized \((x_j^T S_1^T \hat{\beta}_{S_1})\) and \((x_j^T S_1^T \hat{\beta}_{S_2})\) in Panels (A) and (B) of Figure 2 respectively. The solid lines are fitted by local linear approximation where the bandwidths are decided through leave-one-out cross validation and the dashed lines are the 95% pointwise confidence intervals. It is clearly observed that the response can be described very well using only one single linear combination of the selected covariates.
5. AN EXTENSION: MULTIPLE SPLITTING

Figure 2: The scatterplots of the response versus standardized $(x_j^tS_1\hat{\beta}_{S_1})$ in panel (A) and versus standardized $(x_j^tS_2\hat{\beta}_{S_2})$ in panel (B) in Example 2.

To further examine the prediction performance of single-index models based on the selected covariates, we calculate the mean squared prediction errors based on leave-one-out cross validation. The mean squared prediction error are 0.3801 based on $\{(x_j^tS_1\hat{\beta}_{S_1}, Y_j), j = 1, \ldots, 120\}$, 0.4297 based on $\{(x_j^tS_2\hat{\beta}_{S_2}, Y_j), j = 1, \ldots, 120\}$. This indicates that the selected covariates are probably truly predictive for the expression level of the gene TRIM32 and a single linear combination of these covariates is probably sufficient to characterize the conditional mean of the response.

5. An Extension: Multiple Splitting

In the proposed two-stage testing procedure, the sure screening property that $\mathcal{A} \subseteq \mathcal{S}$ with probability tending to one is crucial to guarantee that
testing \((2.1)\) is asymptotically equivalent to testing \((1.3)\). However, in the sample level, some important variables may be unfortunately missed in the first screening stage due to limitation of the sample size, violation of some assumption or data randomness. In this case, the empirical Type-I error rates may be inflated. To deal with this issue, one may consider to utilize the iterated MDC-based screening to reduce the risk of missing important variables. Another efficient solution is the multi-splitting strategy in the light of Meinshausen, Meier and Bühlmann (2009). That is, one can divide the sample repeatedly \((B\) times), and obtain one p-value from each sample splitting using the LOFTS procedure. For all p-values, denoted by \(p_1, \ldots, p_B\), we define

\[Q(\gamma) = \min \left[1, q_\gamma \left(\{p_i/\gamma\}\right)\right],\]

for \(\gamma \in (\gamma_{\text{min}}, 1)\), where \(q_\gamma \left(\{p_i/\gamma\}\right)\) is the \(\gamma\)th quantile of \(\{p_i/\gamma\}\) for \(i = 1, \ldots, B\). Here, \(\gamma_{\text{min}} \in (0, 1)\) is a lower bound for \(\gamma\), typically 0.05 or 1/B in practice. The adjusted p-value is then given by \(Q(\gamma)\) for any fixed \(\gamma\). However, a proper selection of \(\gamma\) may be difficult in practice. An adaptive version is defined as follows: Let \(\gamma_{\text{min}} \in (0, 1)\) be a lower bound for \(\gamma\), typically 0.05, and

\[Q^*(\gamma) = \min \left\{1, (1 - \log\gamma_{\text{min}}) \inf_{\gamma \in (\gamma_{\text{min}}, 1)} Q(\gamma)\right\}.\]
5. AN EXTENSION: MULTIPLE SPLITTING

With the adjusted p-value and the adaptive version of the p-value, the type-I error remains controlled at level $\alpha$ asymptotically. This result is presented in the following theorem.

**Theorem 5.** Assume $\lim_{n \to \infty} P(A \subset S_i) = 1$ where $S_i$ is the selected model in the screening stage based on the $i$th sample splitting, then

$$\lim_{n \to \infty} \sup P\{Q(\gamma) \leq \alpha\} \leq \alpha, \quad \lim_{n \to \infty} \sup P\{Q^*(\gamma) \leq \alpha\} \leq \alpha.$$ 

We also perform a toy example to illustrate how the type-I error remains controlled at level $\alpha$ when some important covariates are missed with a nonignorable probability. We generate $Y$ from the following regression model

$$Y = X_1 + X_2 + X_3 + 0.5X_4 + \varepsilon,$$

where $x = (X_1, \ldots, X_p)^T$ except $X_4$ are drawn from multivariate normal distribution with mean zero and covariance matrix $\Sigma = (\rho_{kl})_{p \times p}$ with $\rho_{kl} = 0.5^{\lfloor k-l \rfloor}$, $k, l = 1, \ldots, p$. $X_4$ is generated from another regression model $X_4 = (0.5 - X_1 - X_3)^2 + \varepsilon_1$ and $\varepsilon$ follows the standard normal distribution and is independent of $x$, $\varepsilon_1$ is an independent copy of $\varepsilon$. The sample size is also set to be 200 while the dimensionality of the covariates is 1000, the reduced model size $|\mathcal{S}| = 5$ and the bootstrapped times in the LOFTS procedure is 300 for simplicity. In addition, the multi-splitting procedure is repeated 50
Table 6: The empirical type-I errors for difference splitting techniques.

<table>
<thead>
<tr>
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<th>single-splitting</th>
<th>multi-splitting</th>
</tr>
</thead>
<tbody>
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<td>0.01 0.02 0.05 0.10</td>
<td>0.01 0.02 0.05 0.10</td>
</tr>
<tr>
<td>empirical</td>
<td>0.054 0.077 0.135 0.220</td>
<td>0.001 0.002 0.037 0.095</td>
</tr>
</tbody>
</table>

*times. In our simulations, $X_4$ are missed 204 times out of 1000 replicates, which makes the corresponding type-I error inflated. From Table 6, we can see that the multi-splitting strategy could improve the single-splitting technique and can well maintain the empirical type-I errors at the nominal levels $\alpha = 0.05$ and $\alpha = 0.10$.

**Supplementary Materials**

All technical proofs and the screening performance in the simulation are included in a separate online supplemental file.

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Appendix: Regularity Conditions

(C1) (The Kernel Function) The univariate kernel function $K(\cdot)$ is a density function with compact support. It is symmetric about zero and Lipschitz continuous. In addition, it satisfies

$$
\int K(v) dv = 1, \quad \int v^i K(v) dv = 0, 1 \leq i \leq t - 1, \quad 0 \neq \int v^t K(v) dv < \infty.
$$

(C2) (The Density) The probability density function of $\beta_0^T x_S$, denoted by $f(\beta_0^T x_S)$ is bounded away from 0 to infinity.

(C3) (The Derivatives) The $(t - 1)$th derivatives of the mean function $m(\beta_0^T x_S)$, the density function $f(\beta_0^T x_S)$ and $m(\beta_0^r x_S)f(\beta_0^T x_S)$ are locally Lipschitz-continuous with respect to $\beta_0^T x_S$. 
(C4) *(The Bandwidth)* The bandwidth $h$ satisfies $h = O(n^{-\kappa})$, for some $\kappa$ which satisfies $(2t)^{-1} < \kappa < (2d)^{-1}$.

(C5) *(The Moment)* The covariates used in the test stage statisfy that

$$E(\|x_S\|^2) / |S| < \infty.$$ 

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