Robust approach for variable selection with high dimensional longitudinal data analysis

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Summary. This paper proposes a new robust smooth-threshold estimating equation to select important variables and automatically estimate parameters for high dimensional longitudinal data. A novel working correlation matrix is proposed to capture correlations within the same subject. The proposed procedure works well when the number of covariates \( p \) increases as the number of subjects \( n \) increases. The proposed estimates are competitive with the estimates obtained with the true correlation structure, especially when the data are contaminated. Moreover, the proposed method is robust against outliers in the response variables and/or covariates. Furthermore, the oracle properties for robust smooth-threshold estimating equations under “large \( n \), diverging \( p \)” are established under some regularity conditions. Extensive simulation studies and a yeast cell cycle data are used to evaluate the performance of the proposed method, and results show that our proposed method is competitive with existing robust variable selection procedures.

Keywords: Automatic variable selection; High dimensional covariates; Outliers; robustness; Tukey’s biweight method; Working correlation structure.
1 Introduction

Longitudinal data is usually collected by repeatedly observing the results for each subject at several points in time. It has been widely used in medical and economic research over the past decade. High-dimensional longitudinal data consisting of repeated measurements with a large number of covariates has become increasingly common in practical application. The number of covariates can be quite large, especially when the interactions of various factors are considered. Nevertheless, there is only a subset of covariates related to the response variables, and the redundant variables can affect the accuracy and efficiency of estimation. Therefore, it is important to develop a new methodology to select the important variables in high-dimensional longitudinal data.

To select the important variables in longitudinal data analysis, Pan (2001) proposed a quasi-likelihood information criterion (QIC) based on an independence assumption, which can be used to select variables and working correlation matrices. Wang and Qu (2009) combined the Bayesian information criterion with quadratic inference function, which does not require the full likelihood or quasi-likelihood. However, these two methods can be computationally intensive when the dimension of covariates $p$ is large. Tian et al. (2014) extended the SCAD-penalized quadratic inference function to analyze semiparametric varying coefficient partially linear models. Their proposed procedure simultaneously selects significant variables in the parametric components and the nonparametric components. Li et al. (2013) proposed an automatic variable selection procedure using smooth-threshold generalized estimating equations, which are based on the generalized estimating equations (GEE). Most of the above-mentioned methods only focused on the fixed dimension $p$. Thus, Wang et al. (2012) proposed a penalized GEE using a SCAD penalty and proved the asymptotic properties under the framework of large sample size $n$ and diverging $p$. The important feature of their method is that the consistency of model selection holds even if the working correlation structure is mis-
specified. However, the methods mentioned above are all based on the GEE. When the longitudinal data are contaminated or follow a heavy-tailed distribution, these methods are sensitive to response and/or covariates outliers. For example, in a large-scale yeast cell gene expression study reported by Spellman et al. (1998), genome-wide mRNA levels for 6178 yeast open reading frames that can determine which amino acids will be encoded by a gene were recorded. The yeast cell cycle gene expression data cover approximately two cell-cycle periods and were collected at 7-minute intervals for 119 minutes, for a total of 18-time points measured at M/G1-G1-S-G2-M stages. Figure 1 reveals that there exist strong correlations and the correlation matrix is never a commonly used exchangeable or autoregressive matrix. Furthermore, apart from the strong correlations, we find that there are some outliers in the gene expression data (see Figure 2). Figure 3 indicates that abundant influence points occur in the observations of some important transcription factors, such as ASH1, MBP1, SWI4, and SWI6, which may lead to biased estimation and prediction. Some researchers have proposed various methods to identify important transcription factors (TFs) from a large set of transcription factors that are associated with gene expression levels and capture a complex relationship among those factors (Luan et al., 2003; Wang et al., 2007, 2012). Nevertheless, few researches focus on the robustness against outliers on observations and most of them fail to capture the underlying correlation structure within gene expression level on multiple observations.

Robust methods are desirable for contaminated data. Therefore, Fan et al. (2012) proposed robust penalized estimating equations based on Huber’s function for linear regression with longitudinal data, which is robust against outliers in response, but is sensitive to outliers in covariates. The regulated parameter in Huber’s function is directly specified. Lv et al. (2015) explored a weighted variable selection method based on an exponential squared loss (Wang et al., 2013) and a commonly used working correlation matrix for high dimensional longitudinal data, and they also provided a data-driven method to select the parameter in the exponential squared loss. These two methods are
robust, but their work only looked at a specific case in which the variable dimension was no larger than the sample size, that is $p < n$.

In this article, we construct robust weighted estimating functions based on Tukey’s biweight score equations, which are robust for outliers in response and/or covariates. Different from [Li et al. (2013)] using robust residuals to estimate the correlation parameter, we propose a novel robust working correlation matrix to capture the correlations, which is more close to the true correlation matrix than the exchangeable and AR(1) correlation matrices, and performs competitively with the true correlation structure in variable selection. Following [Li et al. (2013)] and [Chang et al. (2018)], we establish robust smooth-threshold estimating equations for parameter estimation and variable selection. Furthermore, we prove the asymptotic properties of the proposed method under “large $n$ and diverging $p$” setting. Robust estimating equations using bounded scores and leverage-based weights are robust against outliers and can reduce the bias when errors follow a heavy-tailed distribution. The proposed method can be applied to sparse marginal models under the large $n$ small $p$, large $n$ diverging $p$, and small $n$ large $p$.

The rest of the article is organized as follows: In Section 2.1, we construct a robust estimating equation (RTGEE) for parameter estimation and variable selection. In Section 2.2, we apply an iterative algorithm to solve the smooth-threshold generalized estimating equations. In Section 2.3, we establish an effective criterion for tuning parameter selection. In Section 3, we establish the oracle properties of the proposed method. In Section 4, we carry out extensive simulation studies to evaluate the performance of the proposed method. In Section 5, we analyze a yeast cell cycle dataset to illustrate the proposed method. Finally, in Section 6, we draw some conclusions.


2 Robust smooth-threshold GEE

Suppose that \( Y_i = (y_{i1}, \ldots, y_{im_i})^T \) are measurements collected at times \((t_{i1}, \ldots, t_{im_i})\) for the \(i\)th subject, where \(i = 1, \ldots, n\). Let \( X_i = (x_{i1}, \ldots, x_{im_i}) \) be the corresponding covariate vector, in which \(x_{ij} = (x_{ij1}, \ldots, x_{ijp})^T\) is a \(p \times 1\) vector. Assume that observations from the same subject are correlated, and observations from different subjects are independent. Denote the marginal mean of \(y_{ij}\) by \(\mu_{ij} = E(y_{ij}|x_{ij}) = g(x_{ij}^T\beta)\), where \(g(\cdot)\) is the inverse of the known link function, \(\beta = (\beta_1, \ldots, \beta_p)^T\) is an unknown parameter vector, and variance of \(y_{ij}\) is \(\text{Var}(y_{ij}|x_{ij}) = \phi v(\mu_{ij})\) with a variance function \(v(\cdot)\) and a scale parameter \(\phi\). Let \(\mu_i = (\mu_{i1}, \ldots, \mu_{im_i})^T\) and \(A_i = \phi \text{diag}(v(\mu_{i1}), \ldots, v(\mu_{im_i}))\) be a diagonal matrix. The covariance matrix of \(Y_i\) is \(\text{Cov}(Y_i) = A_i^{-1/2}R_T A_i^{-1/2}\), where \(R_T\) is the true correlation matrix of \(Y_i\).

2.1 Methodology

We consider a new efficient and robust Tukey’s biweight generalized estimating equation (RTGEE) for marginal longitudinal data:

\[
U_n(\beta, \alpha) = \sum_{i=1}^{n} U_i(\beta) = \sum_{i=1}^{n} D_i^T V_i^{-1} h_i^b (\mu_i(\beta)) = 0, \tag{1}
\]

where \(D_i = \partial\mu_i/\partial\beta, V_i = R_i(\alpha)A_i^{1/2}, h_i^b (\mu_i) = W_i \left[ \tilde{\psi}_b (\mu_i(\beta)) - C_i (\mu_i(\beta)) \right]\) with \(C_i (\mu_i) = E \left[ \tilde{\psi}_b (\mu_i(\beta)) \right]\), and \(W_i\) is a diagonal weight matrix used to downweight the effect of leverage points. One such leverage point, the \(j\)th element, is

\[
w_{ij} = w(x_{ij}) = \min \left\{ 1, \left( \frac{b_0}{(x_{ij} - m_x)^T S_x^{-1} (x_{ij} - m_x)} \right)^\frac{2}{3} \right\},
\]

where \(r \geq 1, b_0\) is the 0.95 quantile of the \(\chi^2\) distribution with \(p\) degrees of freedom, and \(m_x\) and \(S_x\) are some robust estimators of the location and scale of \(x_{ij}\). The robust
function $\tilde{\psi}_b(\mu_i) = \psi_b \left( A_i^{-1/2} (Y_i - \mu_i) \right)$ is given as follows:

$$\psi_b(u) = \begin{cases} u \left[ 1 - \left( \frac{u}{b} \right)^2 \right]^2 & \text{if } |u| \leq b \\ 0 & \text{if } |u| > b \end{cases},$$

which is the derivative of Tukey’s biweight loss function.

Guided by the idea of Ueki (2009), we select important variables via an efficient and robust smooth-threshold GEE:

$$(I_p - \Delta) U_n(\beta, \alpha) + \Delta \beta = 0, \quad (2)$$

where $I_p$ is the $p$-dimensional identity matrix, and $\Delta = \text{diag} \{ \hat{\delta}_1, \hat{\delta}_2, \ldots, \hat{\delta}_p \}$ is a diagonal matrix, in which $\hat{\delta}_j = \min \left\{ 1, \eta / |\hat{\beta}_j(0)|^{(1+\tau)} \right\}$ with a consistent estimator $\hat{\beta}_j(0)$ of $\beta_j$. When $\hat{\delta}_j = 1$, we shrink $\hat{\beta}_j$ to zero and thus obtain a sparse estimator. The parameter $\tau$ can be selected among $(0.5, 1, 2)$ according to a suggestion from numerical studies in Zou (2006). In simulation studies, we found that $\tau = 1$ is highly effective for the numerical simulations.

Let $\hat{\beta}$ be a consistent estimator of $\beta$, and let $\hat{e}_i = (\phi A_i)^{-1/2} \left( Y_i - \mu_i(\hat{\beta}) \right)$ be the standardized Pearson residuals. For a chosen score function $\psi_b(\cdot)$, corresponding robust residuals are denoted as $\psi_b(e_i) = \{ \psi_b(e_{i1}), \ldots, \psi_b(e_{im_i}) \}^T$. To solve equation (2), we need to specify the working correlation matrix $R_i(\alpha)$. Instead of estimating a constant correlation parameter for a specific correlation structure such as exchangeable and the first-order autoregressive correlation structures, here we estimate the correlation coefficient vector $\alpha$ via constructing a new unstructured correlation matrix which is more close to the true correlation matrix:

$$R_u = \frac{1}{n} \sum_{i=1}^{n} \psi_b(\hat{e}_i) \psi_b^T(\hat{e}_i). \quad (3)$$

To guarantee the diagonal elements of $R_u$ are equal to 1, and the off diagonal elements of $R_u$ belong to $(-1, 1)$, we reconstruct the working correlation matrix $R_u$ and propose
the following matrix:

\[ R_{un} = B_\alpha^{-1/2} R_u B_\alpha^{-1/2}, \]  

(4)

where \( B_\alpha = \text{diag}(\sum_{i=1}^{n} \psi^2_{\beta}(\hat{\epsilon}_{i1}) / n, \sum_{i=1}^{n} \psi^2_{\beta}(\hat{\epsilon}_{i2}) / n, \ldots, \sum_{i=1}^{n} \psi^2_{\beta}(\hat{\epsilon}_{im}) / n). \) Accordingly, we assign \( R_{un} \) as an estimate of the working correlation matrix \( R_i(\alpha) \), in which \( \alpha \) is a correlation parameter vector. Hence, the diagonal elements of \( R_{un} \) are equal to 1, and the off diagonal elements of \( R_{un} \) which are estimates of the vector \( \alpha \) always lie in \((-1, 1)\) according to Cauchy–Schwarz inequality.

To obtain the standardized Pearson residuals \( \hat{\epsilon}_z \), we need to specify the scale parameter \( \phi \). Here, we use the robust median absolute deviation to estimate \( \phi \) (Wang et al., 2005):

\[ \hat{\phi} = 1.483 \text{ median } \{ |\hat{\eta}_{ij} - \text{median}(\hat{\eta}_{ij})| \}^2, \]  

(5)

where \( \hat{\eta}_{ij} = A_{ij}^{-1/2} (y_{ij} - \mu_{ij}(\hat{\beta})) \).

### 2.2 Algorithm

To select the important variables and estimate the regression parameters in the marginal models, we follow a Fisher scoring iterative algorithm to implement the procedures as follows:

Step 1. Give an initial estimator \( \hat{\beta}^{(0)} \), for example, one can use the MM-estimator as an initial value to ensure stability. Let \( k = 0 \).

Step 2. Estimate the scale parameter \( \hat{\phi} \) using (5) with the current estimator \( \hat{\beta}^{(k)} \).

Compute the working correlation matrix \( \hat{R}_i \) using (4), and we get

\[ V_i \left\{ \mu_i(\hat{\beta}^{(k)}), \hat{\phi}^{(k)} \right\} = \hat{R}_i A_i^{1/2} \left( \hat{\beta}^{(k)}, \hat{\phi}^{(k)} \right) . \]

Step 3. For a given \( \lambda \), we update the estimator of \( \beta \) via the following iterative formula:

\[ \hat{\beta}^{(k+1)} = \hat{\beta}^{(k)} - \left\{ \left( \sum_{i=1}^{n} D_i^T \Omega_i \left( \mu_i(\beta) \right) D_i + \hat{G} \right)^{-1} \left( U_n(\beta) + \hat{G} \beta \right) \right\}_{\beta=\hat{\beta}^{(k)}}, \]  

(6)
where $\hat{G} = \left(I_p - \Delta\right)^{-1} \Delta$, and $\Omega_i(\mu_i(\beta)) = V_i^{-1}(\mu_i(\beta)) \Gamma_i(\mu_i(\beta))$, in which

$$\Gamma_i(\mu_i(\beta)) = \mathbb{E}\left[\dot{h}_i^b(\mu_i(\beta))\right] = \mathbb{E}\left[\partial h_i^b(\mu_i(\beta))/\partial \mu_i\right]_{\mu_i=\hat{\mu}_i(\beta)},$$

Step 4. Repeat Steps 2–3 until the algorithm converges. Here we set stop condition $||\beta^{(k+1)} - \hat{\beta}^{(k)}||^2 < \epsilon$, where $\epsilon$ is a small number and takes a fixed value of $\epsilon = 10^{-8}$.

With the given $\lambda$ and $b$, the corresponding parameter estimator of $\beta$ is denoted as $\hat{\beta}_b^\lambda$. According to the iterative algorithm mentioned above, we obtain a sandwich formula to estimate the asymptotic covariance matrix of $\hat{\beta}_b^\lambda$:

$$\text{Cov}(\hat{\beta}_b^\lambda) \approx \left[\hat{\Sigma}_n\left(\mu_i(\hat{\beta}_b^\lambda)\right)\right]^{-1} \hat{H}_n\left(\mu_i(\hat{\beta}_b^\lambda)\right) \left[\hat{\Sigma}_n\left(\mu_i(\hat{\beta}_b^\lambda)\right)\right]^{-1},$$

where

$$\hat{H}_n\left(\mu_i(\hat{\beta}_b^\lambda)\right) = \sum_{i=1}^n D_i^T V_i^{-1}\left(\mu_i(\hat{\beta}_b^\lambda)\right) \left[h_i^b(\hat{\mu}_i(\hat{\beta}_b^\lambda)) \Gamma_i\left(\mu_i(\hat{\beta}_b^\lambda)\right) D_i\right] V_i^{-1}(\hat{\mu}_i(\hat{\beta}_b^\lambda)) D_i^T,$$

and

$$\hat{\Sigma}_n\left(\mu_i(\hat{\beta}_b^\lambda)\right) = \sum_{i=1}^n D_i^T V_i^{-1}\left(\mu_i(\hat{\beta}_b^\lambda)\right) \Gamma_i\left(\mu_i(\hat{\beta}_b^\lambda)\right) D_i.$$

### 2.3 Selection of tuning parameters

To effectively select important variables using the proposed method, we need to choose proper tuning parameters $b$ and $\lambda$ as mentioned in Section 2.2, which determines the robustness of the estimator and consistency of variable selection respectively. For a given $\lambda$, we select the optimal parameter $b$ in $\psi_b(u)$ from a series of candidates by minimizing the determinant value of the covariance matrix of $\hat{\beta}_b^\lambda$:

$$b_{\lambda}^{opt} = \min_b \det(\text{Cov}(\hat{\beta}_b^\lambda))$$

The covariance matrix Cov($\hat{\beta}_b^\lambda$) can be obtained from (7). In our simulations, we take a series of candidates satisfying asymptotic efficiency higher than 0.7 compared to the
Gaussian distribution, which have been listed in Table 2 in Riani et al. (2014). For the regularization parameter \( \lambda \) selection, we adopt the PWD-type criterion proposed by Li et al. (2013) to choose regularization parameter \( \lambda \) for (2):

\[
\text{RPWD}_{\lambda} = \sum_{i=1}^{n} \left\{ h_{i}^{b_{\text{opt}}}(\mu_{i}(\hat{\beta}_{\lambda})) \right\}^{T} R_{i}^{-1}(\mu_{i}(\hat{\beta}_{\lambda})) \left\{ h_{i}^{b_{\text{opt}}}(\mu_{i}(\hat{\beta}_{\lambda})) \right\} + df_{\lambda} \log(n), \tag{9}
\]

where \( \hat{\beta}_{\lambda} \) is the estimator of \( \beta \) for a given \( \lambda \) and the corresponding optimal \( b \) as in (8).

Denote \( df_{\lambda} = \sum_{j=1}^{p} 1(\hat{\delta}_{j} \neq 1) \) as the number of nonzero elements of the estimators. We choose \( \lambda \), which corresponds to the minimizer of \( \text{RPWD}_{\lambda} \), as an optimal value among a series of candidate values with a convergent solution \( \hat{\beta}_{\lambda}^{b} \) under each \( \lambda \) and \( b \) values.

### 3 Asymptotic properties

In this section, we will establish large sample properties of the proposed estimator under a “large \( n \), diverging \( p \)” framework, which allows \( p_{n} \) to diverge to \( \infty \) as \( n \) increases. The detailed proof of following Propositions are presented in the Appendix 1 in the Supplementary Information.

Let \( \beta_{0} = (\beta_{01}, \ldots, \beta_{0p_{n}})^{T} \) be the true value of \( \beta \), where \( \beta \in \Theta, \Theta \subseteq \mathbb{R}^{p_{n}} \) is a bounded \( p_{n} \)-dimensional vector. Without loss of generality, we denote \( \beta_{0} = (\beta_{01}^{T}, \beta_{02}^{T})^{T} \), where \( \beta_{02} = 0 \), and the elements of \( \beta_{01} \) are assumed to be nonzero in the dimension of \( s_{n} \), which can also diverge with \( n \). We partition \( \beta_{0} \) into active (nonzero) coefficient sets \( \mathcal{A}_{0} = \{ j : \beta_{0j} \neq 0 \} \) with \( |\mathcal{A}_{0}| = s_{n} \) and inactive (zero) coefficient sets \( \mathcal{A}_{0}^{c} = \{ j : \beta_{0j} = 0 \} \). We define the active set \( \mathcal{A} = \left\{ j : \hat{\delta}_{j} \neq 1 \right\} \) as the set of indices of nonzero estimated coefficients. Under the following conditions, we present the consistency of the proposed estimator.

C1. Assume \( x_{ij} \) for \( 1 \leq i \leq n \) and \( 1 \leq j \leq m_{i} \) satisfy \( \sup_{i,j} \| x_{ij} \| = O \left( \sqrt{p_{n}} \right) \).

C2. The unknown parameter \( \beta \) belongs to a compact subset \( \Theta \subseteq \mathbb{R}^{p_{n}} \), and the true
parameter value $\beta_0$ lies in the interior of $\Theta$. Furthermore, we assume that the estimator of the correlation parameter vector $\hat{\alpha}$ is $\sqrt{p_n/n}$-consistent given $\beta$ and $\phi$ for some $\alpha$, that is, $\|\hat{\alpha} - \alpha\| = O_p\left(\sqrt{p_n/n}\right)$, and $|\partial \hat{\alpha}(\beta, \phi)/\partial \phi| \leq H(Y, \beta)$, where $H(\cdot, \cdot)$ is a bounded function for samples $Y$ and $\beta$.

C3. Denote $X_{i}^{h,b} = X_{i}^{T} h_{0,i}^{b}(e_{i})$. There exists finite positive constants $c_1 \leq c_2$ such that $\forall 1 \leq j \leq m_i$:

$$c_1 \leq \lambda_{\min} \left( n^{-1} \sum_{i=1}^{n} X_{i}^{h,b} \left\{ X_{i}^{h,b} \right\}^{T} \right) \leq \lambda_{\max} \left( n^{-1} \sum_{i=1}^{n} X_{i}^{h,b} \left\{ X_{i}^{h,b} \right\}^{T} \right) \leq c_2,$$

where $h_{0,i}^{b}(e_{i})$ centers $Y_{i}$ by its true mean $\mu_{0,i}$ with $\mu_{0,i} = \mu_{i}(\beta_0)$.

C4. $\sup_{i \geq 1} E \|h_{0,i}^{b}(e_{i})\|^{2+\delta} < \infty$ for some $\delta > 0$, and $0 < \sup_{i} Eh_{0,i}^{b}(e_{i}) (h_{0,i}^{b}(e_{i}))^{T} < \infty$, where $h_{i}^{b}(e_{i})$ centers by $\mu_{i} = \mu_{i}(\beta)$.

C5. There exists a positive constant $c$ such that $0 < c \leq \inf_{i,j} v(\mu_{ij}) \leq \sup_{i,j} v(\mu_{ij}) < \infty$. The functions $C_{ij}(\mu_{ij}) = E \left[ \psi_{b} \left( A_{ij}^{-1/2} (y_{ij} - \mu_{ij}) \right) \right]$, $v(\cdot)$ and $g(\cdot)$ have bounded second derivatives. The function $\psi_{b}(\cdot)$ is piecewise twice differentiable, and the second derivatives are bounded.

C6. Assume that $E \|U_n(\beta_0)\|^2 < \infty$ and there exists $\delta > 0$ such that

$$\lim_{n \to \infty} \frac{\sum_{i=1}^{n} E \|U_{i}(\beta_0)\|^{2+\delta}}{(E \|U_n(\beta_0)\|^2)^{1+\delta/2}} = 0.$$

C7. Matrix

$$\Sigma = \lim_{n \to \infty} n^{-1} \sum_{i=1}^{n} \left[ D_{0,i}^{T} V_{0,i}^{-1} \Gamma_{0,i} (\mu_{i}(\beta_0)) D_{0,i} \right]$$

is positive definite. Matrix

$$B = \lim_{n \to \infty} n^{-1} \sum_{i=1}^{n} D_{0,i}^{T} V_{0,i}^{-1} \text{cov} \left( h_{i}^{b}(\mu_{i}(\beta_0)) \right) \left( V_{0,i}^{-1} \right)^{T} D_{0,i}$$

is also positive definite.
C8. For any positive \( \lambda, \tau, p_n, \) and \( s_n, (p_n/n)^{(1+\tau)/2} \lambda^{-1} \to 0, \) \( n^{-1/2} \lambda^2 = o(1), \) and \( s_n n^{-1/2} = o(1), \) such as \( s_n = O(n^{1/3}). \)

**Remark** Condition C1 is a common assumption in the M-estimator with diverging dimension [Portnoy, 1985], and it holds almost surely under some weak moment conditions for \( x_{ij} \) from spherically symmetric distributions. Condition C2 is established to ensure the \( \sqrt{p_n/n} \)-consistency of \( \hat{R}_i(\alpha) \) in Section 2.1, which can be verified using similar analysis in [He et al. (2005)]. Taking the spirit of Lemma 3.7 in [Wang (2011)], we set condition C3, which is especially useful when establishing the asymptotic normality in Proposition 2. Similar to [Lv et al. (2015)], conditions C4–C5 can be easily checked under bounded score function \( \psi_b(\cdot) \), and they are usually combined with assumptions C6–C7, which are also necessary for the central limit theory and hold in most cases. Condition C8 is established for exploring convergence rate and asymptotic properties, which controls the order of diverging number \( p_n \) and \( s_n \) precisely, and we point out a series theoretical values for regularization parameter \( \lambda \). Note that a preliminary \( \sqrt{p_n/n} \)-consistent estimator \( \beta_0 \) is needed in both Proposition 1 and Proposition 2, which can be obtained by solving the generalized estimating equations under independent working correlation structure as in Example 1 in [Wang (2011)] when \( p_n \to \infty. \)

**Proposition 1** Suppose the regularity conditions C1–C8 hold, then we have

\[
\left\| \hat{\beta}_{\lambda,\tau} - \beta_0 \right\| = O_p \left( \sqrt{p_n/n} \right).
\]

**Proposition 2** Under conditions C1–C8, and if \( n^{-1} p_n^3 = o(1) \), as \( n \to \infty \), we have

1. variable selection consistency, \( P (A = A_0) \to 1; \)
2. asymptotic normality: \( \forall \alpha_n \in R^{s_n} \) such that \( \| \alpha_n \| = 1, \)

\[
\sqrt{n} \alpha_n^T B_{A_0}^{-1/2} \Sigma_{A_0} \left( \hat{\beta}_{\lambda,\tau,A} - \beta_{A_0} \right) \overset{d}{\to} N \left( 0, 1 \right),
\]

where \( \Sigma_{A_0} \) and \( B_{A_0} \) are the first \( s_n \times s_n \) submatrices of \( \Sigma \) and \( B. \)
Proposition 1 implies that our proposed estimator can achieve \( \sqrt{\frac{p_n}{n}} \)-consistency. Proposition 2 shows that such consistent estimators possess the sparsity property and oracle property (Fan and Li 2001) when we choose proper \( \lambda \) and \( \tau \). With a probability approaching 1, our proposed method can correctly select the nonzero coefficients and estimate them as efficiently as if we know the correct submodel in advance.

4 Simulation studies

We conduct simulation studies to assess the performance of the proposed RTGEE method, the smooth-threshold generalized estimating equation (SGEE) proposed by Li et al. (2013), the robust smooth-threshold generalized estimating equation (RSGEE) corresponding to Huber’s score function, and the efficient and robust generalized estimating equation (ERSGEE) proposed by Lv et al. (2015) for continuous normal data and heavy-tailed data under setups \( p < n \), large \( n \) and diverging \( p \), and \( p > n \).

For each procedure, the true correlation structure of the response is exchangeable (EXC) with the correlation coefficient \( \alpha = 0.7 \). For each setup in the simulations, we generate 100 datasets and apply the iterative algorithm mentioned in Section 2.2 to estimate \( \beta \) and select important variables at the same time. Furthermore, we also consider the situation in which the true correlation structure is AR(1) with correlation parameter \( \alpha = 0.7 \) for the continuous data. The simulation results show similar patterns and are presented in Tables 1–6 in the supplementary materials. Finally, we also consider the count data, and the results are listed in Tables 7–8 in the supplementary materials.

We compare these four methods under three working correlation matrices (EXC, AR(1), \( R_{un} \)) according to the following terms: the average number of correctly identified insignificant variables (C), the average number of incorrectly identified significant variables (IC), the correctly fitted odds (CF, the odd of identifying both significant vari-
ables and insignificant variables correctly over 100 simulations), the biases of estimators, the standard deviance (SD) of estimators, the proportion of estimators fall into the 95% confidence interval (CI), the average of mean squared prediction error (AMSEPE), the median of mean squared prediction error (MMSPE), where MSPE = \( n^{-1} \sum_{i=1}^{n} (\hat{y}_i - y_i)^2 \), and the average mean square error (AMSE), which is the average of \( \|\hat{\beta} - \beta_0\|^2 \) over 100 simulations. To demonstrate the efficiency of estimators, we compare the relative efficiency among three robust methods in Figures 4–6, which is defined as the ratio of the AMSE for SGEE to the AMSE for each robust method, from which a higher value represents higher efficiency. We present partial results in Tables 1–6 and more details can be found in Tables 9–14 in Appendix 2 in the supplementary information.

4.1 Heavy-tailed continuous data

We generate the continuous data from the following model:

\[
y_{ij} = x_{ij1}\beta_1 + x_{ij2}\beta_2 + \cdots + x_{ijp}\beta_p + \epsilon_{ij}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, m_i.
\]  

Without loss of generality, we consider the balanced data with \( m_i = 10 \) for \( i = 1, \ldots, n \). Covariates \( x_{ij} = (x_{ij1}, \ldots, x_{ijp})^T \) follow a multivariate normal distribution with a mean of zero and the correlation between the \( k \)th and \( l \)th component of \( x_{ij} \) being \( 0.5^{|l-k|} \). The random error vectors \( \epsilon_i = (\epsilon_{i1}, \ldots, \epsilon_{i10})^T \) are generated from a multivariate Student’s \( t \)-distribution with three degrees of freedom \( T_3(0, R(\alpha)) \). The true coefficients are assumed to be \( \beta = (0.7, 0.7, -0.4, 0, \ldots, 0)^T \) with nonzero coefficients \( d = 3 \) and \( p - d \) coefficients being zero.

I. We first test performance when \( p = 20 \) and \( n = 100 \) under the following scenarios:

Case 1: There is no contamination on the dataset.

Case 2: We randomly add 20% \( y \)-outliers following \( N(10, 1) \) on \( y_{ij} \).
Case 3: We randomly add 10% $x$-outliers on $x_{ij1}$, following a Student’s $t$-distribution with three degrees of freedom. Meanwhile, we change response variables in the same way as Case 2.

II. Next we consider “large $n$ and diverging $p$”.

The true coefficients are set as $\beta = (0.7, 0.7, -0.4, 0.7, 0.7, -0.4, \ldots, 0_{p_n-s_n})$ with $p_n = \lfloor 4n^{2/5} \rfloor - 5$ and the scale of nonzero coefficients $s_n = \lfloor p_n/5 \rfloor$ for $n = 200$, where $\lfloor s \rfloor$ denotes the largest positive integer value not greater than $s$. In addition, the observation times $m_i$ are randomly generated from 2 to 5. The other settings are same as those in $p < n$.

III. We set $p = 300$ and $n = 100$, and the true coefficients vector $\beta = (0.7, 0.7, -0.4, 0, \ldots, 0)^T$ is a $p$-dimensional vector with only three nonzero components. Other conditions are the same as $p < n$. To ensure the stability of simulations, we decrease the proportions of outliers as follows:

Case $2'$: We randomly add 10% $y$-outliers following $N(10,1)$ on $y_{ij}$.

Case $3'$: We randomly add 10% $x$-outliers on $x_{ij1}$ following a Student’s $t$ distribution with three degrees of freedom, and we randomly add 10% $y$-outliers, similar to Case $2'$.

The simulation results for I, II, and III are presented in Tables 1–3, respectively. From Table 1, it is evident that non-robust SGEE has manifest shortcomings in variable selection compared with the other three robust methods according to the value of CF even in the no contamination case. When there are outliers in data sets, the defect of SGEE shows more clearly no matter the variable selection or coefficient estimation. In contrast, the three robust methods (RSGEE, ERSGEE, and RTGEE) perform well, even in a misspecified correlation structure. However, when adding outliers to the response variables, ERSGEE and our proposed method, RTGEE, perform better in terms of IC and CF than SGEE and RSGEE. RTGEE is more competitive with ERSGEE in
both coefficients estimation and variable selection when adding $x$-outliers and $y$-outliers simultaneously. RTGEE has a smaller estimation error (MMSPE) and higher CF than the other three methods. Furthermore, we find that, as a type of misspecified correlation structure, the results under $R_{un}$ are superior over AR(1) and competitive with true correlation structure EXC, especially when there are outliers in the dataset. The $R_{un}$ boosts the performance of non-robust SGEE in variable selection and significantly decreases prediction and estimation error compared to AR(1). Figure 4 depicts the relative efficiency for RSGEE, ERSGEE, and RTGEE under I settings. The left plot A shows that our proposed estimator has higher relatively efficiency than the other two robust methods for contaminated heavy-tailed data, and it is more obvious when there are both $x$-outliers and $y$-outliers.

When $p$ is diverging, the results in Table 2 indicate that the proposed method is comparable with RSGEE and ERSGEE in Case 1 and Case 2 and performs better than RSGEE and ERSGEE when the covariates have outliers. In Case 3, our proposed method performs superiorly over the other methods regardless of the estimation or variable selection, which confirms that our proposed method has superiority under diverging $p$. We notice that the CI of our proposed estimator always fly floats around 95%, even with contamination, which implies the asymptotic normality of our proposed estimator and gives a numerical validation of Proposition 2 established in Section 3. It is appealing to us that almost all the methods perform better under our proposed working correlation structure $R_{un}$, even better than estimated true correlation structure regardless of whether there are outliers. The proposed method outperforms when the data are contaminated (see Figure 5).

From Table 3 and plot E in Figure 6, we can see that ERSGEE and RTGEE show superiority in variable selection compared to SGEE and RSGEE when there are no outliers. When outliers are added, our proposed method is superior to ERSGEE with
a lower MMSPE and higher relatively efficiency, implying RTGEE can keep robustness against outliers even under $p > n$ and misspecified working correlation structure.

### 4.2 Continuous normal data

We generate response variable according to model (10), and the covariates are generated in the same way as in Section 4.1. The random error vectors $\epsilon_i = (\epsilon_{i1}, \ldots, \epsilon_{i10})$ are generated from a $N_{10}(0, R(\alpha))$ with the correlation coefficient $\alpha = 0.7$. Other settings are the same as those in Section 4.1, except that when testing the performance of the foregoing methods in a sparse model under $p > n$, we decrease the proportions of outliers as follows:

- **Case 2″**: We randomly convert 10% of $y_{ij}$ into $y_{ij} + 5$.

- **Case 3″**: We artificially add 5% $x$-outliers on $x_{ij1}$ following a $t(3)$ distribution as well as $y$-outliers which are same with Case 2″.

The corresponding results are listed in Tables 4–6. From Table 4, when there are no outliers added on response and/or covariates, SGEE can perform well as expected, whereas, it is inferior to robust methods no matter in parameter estimation or variable selection in contaminated datasets. It is noticeable that our proposed unstructured working correlation matrix $R_{un}$ performs competitively with the true correlation matrix, and it is superior to wrongly assigned working correlation matrix (e.g. AR(1)), especially when there are outliers on response and/or covariates.

In Table 5, when $p$ is diverging, SGEE can not perform as well as robust methods even if there are no outliers added. Among robust methods, ERSGEE and RTGEE perform similarly well and they are superior to RSGEE when there are outliers in datasets. Furthermore, RTGEE has significant advantages with higher relative efficiency than ERSGEE, especially under the wrongly assigned working correlation structure, according
to plot D in Figure 5. The reasonable performance of our proposed estimators in CI verifies the oracle properties again.

When $p > n$, the results in Table 6 show that SGEE is affected by outliers more obviously in variable selection compared with robust methods. Although RTGEE and ERSGEE perform relatively similar well, where they are superior to RSGEE greatly when outliers are added on covariates, RTGEE performs better in terms of estimation accuracy with lower MMSPE.

5 Real data analysis

The cell cycle is one of the most important processes for cell growth, DNA replication, chromosome segregation, and daughter cells’ division. Investigating the functions of gene expression during the cell cycle process can give an insight into how the cell cycle affects biological processes and cell cycle regulation. Transcription factors (TFs) are a critical part of the cell cycle process, where they have been shown to influence gene expression by regulating the flow of genetic information from DNA to mRNA during the cell cycle process. We are interested in selecting important TFs from a large set of candidates that are associated with yeast gene expression levels.

We apply the proposed RTGEE method to analyze the yeast cell cycle gene expression dataset, which was mentioned in Section 1. Our investigation indicates that log-transformed gene expression levels and observations of TFs contain many underlying outliers, thus it is worthwhile to reanalyze the yeast cell cycle via robust procedures. In this section, we apply SGEE, RSGEE, ERSGEE, and RTGEE to the dataset of the G1 stage in a yeast cell cycle with 1132 observations (283 cell-cycled-regularized genes observed over 4-time points). The dataset is available in R package PGEE.

The scatter plot in Figure 7 depicts the complicated functional relationship among
gene expression level and TFs, which is highly dependent on varying time, hence we consider following model, which is the same as Wang et al. (2012),

\[ y_{ij} = \beta_0 + \beta_1 t_{ij} + \sum_{k=1}^{96} \beta_k x_{ik} + \epsilon_{ij}, \quad i = 1, \ldots, 283, \quad j = 1, \ldots, 4, \]

where the response variable \( y_{ij} \) is the log-transformed gene expression level of gene \( i \) measured at time point \( j \), the covariates \( x_{ik} \) are the matching score of the binding probability of the \( k \)th transcription factor on the promoter region of the \( i \)th gene for \( k = 1, \ldots, 96 \), and \( t_{ij} \) represents the time points. We consider three correlation structures: EXC, AR(1), and \( R_{un} \) for \( \epsilon_{ij} \). Table 7 summarizes the selected numbers of TFs and the mean squared error for cross validation procedures (MSE_CV) to assess the goodness of fit:

\[ \text{MSE}_{CV} = \frac{1}{n} \sum_{i=1}^{n} \left\| \hat{Y}_i - \hat{X}_i \hat{\beta}_{(-i)} \right\|^2, \]

where \( \hat{\beta}_{(-i)} \) is the estimator obtained based on the data excluding the \( i \)th subject. The parameter estimates of the selected TFs are also given in Table 7.

The results indicate that the robust methods (RSGEE, ERSGEE, and RTGEE) select 25 TFs, while non-robust method (SGEE) select more TFs, from which, we find that significant TFs such as MBP1, SWI4, and SWI6 are selected by both robust and non-robust methods, which have been reported to function during the G1 stage in Simon et al. (2001). In addition, TFs such as FKH2, GAT3, GCR2, NDD1, SRD1, STB1 are commonly selected by all of the methods, and they are also confirmed in Wang et al. (2012). ABF1 is selected by SGEE in Wang et al. (2012), but not by the robust methods. Nevertheless, the transcription factor YAP5 noted as an important factor in Banerjee and Zhang (2003) is consistently selected by all of the methods considered in our research, but not selected by Wang et al. (2012). Similarly, TFs such as MET31 and GCR1 selected by our robust methods have been verified in Tsai et al. (2005) and Song et al. (2014) respectively, while not been found in Wang et al. (2012).
In particular, Table 7 presents the mean squared error (MSECV) and also gives the running time of procedures. For this dataset analysis, our proposed method, RTGEE, performs better than other robust methods with the lower mean squared error under EXC and AR(1), and ERSGEE performs better than RSGEE. All of the methods using R un can be more competitive than other working correlation structures, though it can be more time-consuming. The longer running time of ERSGEE and our procedure RTGEE than other methods is associated with the fact that a wide range of tuning parameters is considered as in Section 2.3. To the best of our experience over abundant simulations, we recommend \( b = 7.0414 \) for RTGEE in this yeast data analysis, which can also lead to a sufficient variable selection while saving a lot of time.

6 Conclusions

This article develops a robust automatic variable selection procedure, RTGEE, in the longitudinal marginal models by utilizing the robustness of Tukey’s Biweight criterion. A new robust working correlation structure is proposed for taking account of the correlations, which is competitive with other misspecified working correlation structures. According to our simulation results, achieving high effectiveness and consistency in robust variable selection, the proposed working correlation can be a substitute for the true correlation structure. The correlation parameters in the proposed correlation matrix depend on the number of the repeated measurements \( m_i \). When \( m_i \) is large compare with the sample size, the accuracy of the correlation matrix estimation will decrease, and the computation will increase. Hence, the number of the repeated measurements cannot be too large. If \( m = \max_i \{ m_i \} \) is diverging or large than the sample size, the computation and the theorems need to be restructured, which will be studied in future work. We apply smooth-threshold estimating equations to select the important variables. This approach is conceptually simple, easy to implement, and does not need penalty functions.
Furthermore, this approach eliminates the irrelevant parameters by shrinking them to zero and simultaneously estimates the nonzero coefficients. Previous researchers have proposed similar robust smooth-threshold estimating equations (Fan et al., 2012; Lv et al., 2015). Nevertheless, the robustness of our method is still competitive regardless of whether the conditions are regular or there are more severe setting conditions. From our numerical studies, we can conclude that our proposed method is robust for both response variables and covariates in longitudinal marginal models. It is especially competitive under a heavy tail distribution, and it has broad prospects when the dimension of covariates is larger than the sample size.

Robust variable selection for ultrahigh-dimensional data is gaining more traction in the biomedical area, and in future research, our proposed method can be extended to cases where the dimension of covariates is in the exponential order of the sample size. However, some guiding theoretical research for parameter selection criterion needs to be conducted when applying our procedure to ultrahigh-dimensional data.

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Table 1: Correlated continuous data for \( n > p \) (\( p = 20 \) and \( n = 100 \)) with \( \epsilon_{ij} \) following a \( t(3) \) distribution: Comparison of SGEE, RSGEE, ERSGEE, and the proposed method RTGEE with three different working correlation matrices (exchangeable, AR(1) and unstructured).

| Scenario | R | Method | \( \beta_1 \) | \( \beta_2 \) | \( \beta_3 \) | MMSPE | No.of Zeros | CI | IC | CF |
|----------|---|--------|---------|---------|---------|-------|------------|----|----|----|
| Case 1   | EXC | SGEE | 0.96    | 0.94    | 0.95    | 0.0029 | 16.65 | 0.05 | 0.74 |
|          |     | RSGEE| 0.95    | 0.94    | 0.95    | 0.0016 | 16.91 | 0.00 | 0.92 |
|          |     | ERSGEE | 0.93   | 0.96    | 0.93    | 0.0020 | 16.96 | 0.00 | 0.96 |
|          |     | RTGEE | 0.96    | 0.95    | 0.95    | 0.0022 | 17.00 | 0.00 | 1.00 |
|          | AR(1) | SGEE | 0.95    | 0.94    | 0.96    | 0.0042 | 16.42 | 0.02 | 0.60 |
|          |     | RSGEE | 0.96    | 0.95    | 0.98    | 0.0023 | 16.88 | 0.02 | 0.90 |
|          |     | ERSGEE | 0.95   | 0.94    | 0.91    | 0.0023 | 16.95 | 0.00 | 0.95 |
|          |     | RTGEE | 0.94    | 0.96    | 0.95    | 0.0028 | 17.00 | 0.00 | 1.00 |
|          | Ran | SGEE | 0.96    | 0.95    | 0.95    | 0.0025 | 16.55 | 0.05 | 0.70 |
|          |     | RSGEE | 0.95    | 0.95    | 0.96    | 0.0021 | 16.92 | 0.00 | 0.93 |
|          |     | ERSGEE | 0.95   | 0.94    | 0.94    | 0.0017 | 16.96 | 0.00 | 0.96 |
|          |     | RTGEE | 0.95    | 0.93    | 0.97    | 0.0029 | 17.00 | 0.00 | 1.00 |
| Case 2   | EXC | SGEE | 0.95    | 0.93    | 0.92    | 0.0740 | 15.37 | 0.06 | 0.33 |
|          |     | RSGEE | 0.97    | 0.95    | 0.97    | 0.0078 | 16.89 | 0.01 | 0.90 |
|          |     | ERSGEE | 0.93   | 0.95    | 0.95    | 0.0028 | 16.96 | 0.00 | 0.96 |
|          |     | RTGEE | 0.92    | 0.98    | 0.96    | 0.0021 | 17.00 | 0.00 | 1.00 |
|          | AR(1) | SGEE | 0.95    | 0.94    | 0.97    | 0.0807 | 15.06 | 0.00 | 0.27 |
|          |     | RSGEE | 0.96    | 0.95    | 0.98    | 0.0095 | 16.90 | 0.01 | 0.91 |
|          |     | ERSGEE | 0.96   | 0.96    | 0.95    | 0.0036 | 16.96 | 0.00 | 0.96 |
|          |     | RTGEE | 0.92    | 0.97    | 0.95    | 0.0030 | 17.00 | 0.00 | 1.00 |
|          | Ran | SGEE | 0.92    | 0.91    | 0.93    | 0.0768 | 15.63 | 0.03 | 0.38 |
|          |     | RSGEE | 0.96    | 0.95    | 0.98    | 0.0079 | 16.90 | 0.02 | 0.90 |
|          |     | ERSGEE | 0.94   | 0.96    | 0.96    | 0.0026 | 16.93 | 0.00 | 0.94 |
|          |     | RTGEE | 0.94    | 0.97    | 0.99    | 0.0023 | 17.00 | 0.01 | 0.99 |
| Case 3   | EXC | SGEE | 0.95    | 0.95    | 0.92    | 8.3204 | 15.94 | 0.05 | 0.42 |
|          |     | RSGEE | 0.90    | 0.96    | 0.96    | 0.0084 | 16.90 | 0.04 | 0.88 |
|          |     | ERSGEE | 0.94   | 0.95    | 0.96    | 0.0048 | 16.90 | 0.00 | 0.90 |
|          |     | RTGEE | 0.96    | 0.93    | 0.94    | 0.0027 | 17.00 | 0.06 | 0.94 |
|          | AR(1) | SGEE | 0.94    | 0.92    | 0.93    | 0.0728 | 15.86 | 0.03 | 0.45 |
|          |     | RSGEE | 0.93    | 0.96    | 0.95    | 0.0089 | 16.90 | 0.05 | 0.88 |
|          |     | ERSGEE | 0.94   | 0.95    | 0.97    | 0.0067 | 16.90 | 0.00 | 0.90 |
|          |     | RTGEE | 0.93    | 0.93    | 0.94    | 0.0030 | 17.00 | 0.06 | 0.94 |
|          | Ran | SGEE | 0.96    | 0.92    | 0.94    | 0.0770 | 15.87 | 0.04 | 0.42 |
|          |     | RSGEE | 0.93    | 0.95    | 0.96    | 0.0088 | 16.94 | 0.04 | 0.92 |
|          |     | ERSGEE | 0.97   | 0.94    | 0.94    | 0.0046 | 16.91 | 0.00 | 0.91 |
|          |     | RTGEE | 0.96    | 0.91    | 0.93    | 0.0032 | 17.00 | 0.07 | 0.93 |
Table 2: Correlated continuous data for large $n$ and diverging $p$ ($n = 200$ and $p_n = [4n^{2/5}] - 5$) with $\epsilon_{ij}$ following a $t(3)$ distribution: Comparison of SGEE, RSGEE, ERSGEE, and the proposed method RTGEE with three different working correlation matrices (exchangeable, AR(1) and unstructured).

| Scenario | $R$  | Method | $\beta_1$ | $\beta_2$ | $\beta_3$ | MMSPE | No. of Zeros |
|----------|------|--------|-----------|-----------|-----------|-------|--------------|
|          |      |        | CI        | CI        | CI        |       | C | IC | CF |
| Case 1   | EXC  | SGEE   | 0.93      | 0.95      | 0.93      | 0.0301| 21.58 | 0.06 | 0.46 |
|          |      | RSGEE  | 0.96      | 0.95      | 0.94      | 0.0143| 22.75 | 0.05 | 0.84 |
|          |      | ERSGEE | 0.94      | 0.93      | 0.91      | 0.0158| 22.81 | 0.07 | 0.88 |
|          |      | RTGEE  | 0.97      | 0.95      | 0.89      | 0.0119| 22.98 | 0.12 | 0.87 |
|          | AR(1)| SGEE   | 0.93      | 0.93      | 0.95      | 0.0274| 21.48 | 0.05 | 0.45 |
|          |      | RSGEE  | 0.93      | 0.95      | 0.94      | 0.0143| 22.82 | 0.06 | 0.85 |
|          |      | ERSGEE | 0.96      | 0.95      | 0.95      | 0.0164| 22.51 | 0.00 | 0.83 |
|          |      | RTGEE  | 0.93      | 0.92      | 0.96      | 0.0129| 22.71 | 0.02 | 0.86 |
|          | Run  | SGEE   | 0.94      | 0.92      | 1.00      | 0.0214| 22.67 | 0.39 | 0.48 |
|          |      | RSGEE  | 0.95      | 0.95      | 0.94      | 0.0069| 22.98 | 0.06 | 0.92 |
|          |      | ERSGEE | 0.93      | 0.92      | 0.94      | 0.0118| 22.93 | 0.06 | 0.89 |
|          |      | RTGEE  | 0.95      | 0.94      | 0.97      | 0.0071| 23.00 | 0.02 | 0.98 |
| Case 2   | EXC  | SGEE   | 0.97      | 0.99      | 0.98      | 0.3731| 19.05 | 0.01 | 0.15 |
|          |      | RSGEE  | 0.96      | 0.97      | 0.98      | 0.0501| 22.35 | 0.06 | 0.72 |
|          |      | ERSGEE | 0.95      | 0.94      | 0.87      | 0.0218| 22.94 | 0.12 | 0.84 |
|          |      | RTGEE  | 0.93      | 0.95      | 0.92      | 0.0193| 22.93 | 0.08 | 0.87 |
|          | AR(1)| SGEE   | 0.97      | 0.93      | 0.95      | 0.3781| 18.84 | 0.01 | 0.10 |
|          |      | RSGEE  | 0.92      | 0.96      | 0.94      | 0.0479| 22.28 | 0.05 | 0.72 |
|          |      | ERSGEE | 0.95      | 0.94      | 0.87      | 0.0213| 22.91 | 0.12 | 0.84 |
|          |      | RTGEE  | 0.96      | 0.95      | 0.93      | 0.0201| 22.77 | 0.05 | 0.84 |
|          | Run  | SGEE   | 0.97      | 0.94      | 0.98      | 0.3429| 18.82 | 0.03 | 0.13 |
|          |      | RSGEE  | 0.96      | 0.95      | 0.87      | 0.0352| 22.93 | 0.12 | 0.81 |
|          |      | ERSGEE | 0.96      | 0.92      | 0.88      | 0.0174| 22.97 | 0.12 | 0.85 |
|          |      | RTGEE  | 0.97      | 0.95      | 0.92      | 0.0146| 22.93 | 0.07 | 0.86 |
| Case 3   | EXC  | SGEE   | 0.99      | 0.99      | 0.93      | 0.3062| 18.86 | 0.02 | 0.10 |
|          |      | RSGEE  | 0.96      | 0.95      | 0.98      | 0.0341| 22.69 | 0.08 | 0.79 |
|          |      | ERSGEE | 0.97      | 0.95      | 0.85      | 0.0213| 23.00 | 0.14 | 0.86 |
|          |      | RTGEE  | 0.97      | 0.97      | 0.92      | 0.0192| 22.91 | 0.10 | 0.87 |
|          | AR(1)| SGEE   | 0.94      | 0.94      | 0.92      | 0.2950| 18.82 | 0.01 | 0.08 |
|          |      | RSGEE  | 0.96      | 0.95      | 0.91      | 0.0337| 22.72 | 0.08 | 0.81 |
|          |      | ERSGEE | 0.98      | 0.92      | 0.86      | 0.0183| 22.93 | 0.14 | 0.83 |
|          |      | RTGEE  | 0.97      | 0.96      | 0.94      | 0.0168| 22.77 | 0.05 | 0.84 |
|          | Run  | SGEE   | 0.94      | 0.96      | 0.93      | 0.3040| 18.73 | 0.01 | 0.13 |
|          |      | RSGEE  | 0.95      | 0.94      | 0.87      | 0.0247| 22.98 | 0.13 | 0.85 |
|          |      | ERSGEE | 0.94      | 0.93      | 0.85      | 0.0141| 23.00 | 0.14 | 0.86 |
|          |      | RTGEE  | 0.95      | 0.92      | 0.92      | 0.0114| 22.97 | 0.08 | 0.89 |
Table 3: Correlated continuous data for $p > n$ ($n = 100$ and $p = 300$) with $\epsilon_{ij}$ following a $t(3)$ distribution: Comparison of SGEE, RSGEE, ERSGEE, and the proposed method RTGEE with three different working correlation matrices (exchangeable, AR(1) and unstructured).

| Scenario | R   | Method | $\beta_1$ | $\beta_2$ | $\beta_3$ | MMSPE  | No.of Zeros |
|----------|-----|--------|-----------|-----------|-----------|--------|-------------|
| Case 1   | EXC | SGEE   | 0.93      | 0.95      | 0.96      | 0.0057 | 293.16      |
|          |     | RSGEE  | 0.94      | 0.96      | 0.97      | 0.0015 | 296.83      |
|          |     | ERSGEE | 0.95      | 0.94      | 0.95      | 0.0021 | 297.00      |
|          |     | RTGEE  | 0.95      | 0.94      | 0.96      | 0.0020 | 296.99      |
|          |     | AR(1)  | 0.96      | 0.83      | 1.00      | 0.1159 | 295.53      |
|          |     | SGEE   | 0.97      | 0.97      | 0.97      | 0.0023 | 296.80      |
|          |     | RSGEE  | 0.95      | 0.94      | 0.97      | 0.0029 | 296.98      |
|          |     | ERSGEE | 0.95      | 0.94      | 0.97      | 0.0025 | 296.98      |
|          |     | RTGEE  | 0.95      | 0.94      | 0.97      | 0.0023 | 296.98      |
|          |     | $R_{un}$| 0.94     | 0.96     | 0.95      | 0.0045 | 294.26      |
|          |     | SGEE   | 0.97      | 0.97      | 0.97      | 0.0029 | 296.98      |
|          |     | RSGEE  | 0.95      | 0.94      | 0.97      | 0.0021 | 296.98      |
|          |     | ERSGEE | 0.95      | 0.94      | 0.97      | 0.0020 | 296.99      |
|          |     | RTGEE  | 0.95      | 0.94      | 0.97      | 0.0023 | 296.98      |
| Case 2'  | EXC | SGEE   | 0.95      | 0.96      | 0.89      | 0.3216 | 271.30      |
|          |     | RSGEE  | 0.96      | 0.95      | 0.97      | 0.0034 | 296.67      |
|          |     | ERSGEE | 0.95      | 0.96      | 0.96      | 0.0027 | 296.90      |
|          |     | RTGEE  | 0.94      | 0.94      | 0.94      | 0.0027 | 296.95      |
|          |     | AR(1)  | 0.96      | 0.92      | 1.00      | 0.1445 | 289.53      |
|          |     | SGEE   | 0.97      | 0.93      | 0.90      | 0.0050 | 296.85      |
|          |     | RSGEE  | 0.97      | 0.90      | 0.87      | 0.0035 | 296.98      |
|          |     | ERSGEE | 0.97      | 0.91      | 0.88      | 0.0034 | 296.98      |
|          |     | RTGEE  | 0.97      | 0.91      | 0.88      | 0.0034 | 296.98      |
|          |     | $R_{un}$| 0.97   | 0.95     | 0.90      | 0.3642 | 271.55      |
|          |     | SGEE   | 0.96      | 0.95      | 0.96      | 0.0039 | 296.66      |
|          |     | RSGEE  | 0.96      | 0.95      | 0.96      | 0.0039 | 296.66      |
|          |     | ERSGEE | 0.97      | 0.95      | 0.95      | 0.0031 | 296.90      |
|          |     | RTGEE  | 0.94      | 0.95      | 0.95      | 0.0028 | 296.89      |
| Case 3'  | EXC | SGEE   | 0.96      | 0.96      | 0.94      | 0.6168 | 242.35      |
|          |     | RSGEE  | 0.94      | 0.95      | 0.94      | 0.0042 | 296.75      |
|          |     | ERSGEE | 0.93      | 0.92      | 0.93      | 0.0026 | 296.87      |
|          |     | RTGEE  | 0.94      | 0.93      | 0.95      | 0.0026 | 296.87      |
|          |     | AR(1)  | 0.94      | 0.95      | 0.93      | 0.7165 | 242.15      |
|          |     | SGEE   | 0.94      | 0.95      | 0.93      | 0.0052 | 296.78      |
|          |     | RSGEE  | 0.95      | 0.93      | 0.93      | 0.0028 | 296.87      |
|          |     | ERSGEE | 0.96      | 0.93      | 0.93      | 0.0030 | 296.87      |
|          |     | RTGEE  | 0.94      | 0.94      | 0.93      | 0.0030 | 296.87      |
|          |     | $R_{un}$| 0.93   | 0.95     | 0.96      | 0.6998 | 242.27      |
|          |     | SGEE   | 0.94      | 0.94      | 0.93      | 0.0039 | 296.79      |
|          |     | RSGEE  | 0.94      | 0.93      | 0.93      | 0.0029 | 296.88      |
|          |     | ERSGEE | 0.94      | 0.94      | 0.93      | 0.0027 | 296.87      |
|          |     | RTGEE  | 0.94      | 0.94      | 0.93      | 0.0027 | 296.87      |
Table 4: Correlated continuous data with $\epsilon_{ij}$ following a normal distribution for $n > p$ ($p = 20$ and $n = 100$): Comparison of SGEE, RSGEE, ERSGEE, and the proposed method RTGEE with three different working correlation matrices (exchangeable, AR(1) and unstructured).

| Scenario | R   | Method | $\beta_1$ CI | $\beta_2$ CI | $\beta_3$ CI | MMSPE | No.of Zeros | C  | IC | CF |
|----------|-----|--------|--------------|--------------|--------------|-------|-------------|----|----|----|
| Case 1   | EXC | SGEE   | 0.94 0.98    | 0.98         | 0.0008       | 16.99 | 0.02 0.97  |
|          |     | RSGEE  | 0.96 0.98    | 0.98         | 0.0008       | 16.97 | 0.02 0.95  |
|          |     | ERSGEE | 0.95 0.97    | 0.96         | 0.0008       | 16.99 | 0.00 0.99  |
|          |     | RTGEE  | 0.96 0.98    | 0.98         | 0.0009       | 17.00 | 0.02 0.98  |
|          |     | AR(1)  | 0.96 0.97    | 0.99         | 0.0009       | 16.90 | 0.01 0.91  |
|          |     | RSGEE  | 0.95 0.96    | 0.96         | 0.0011       | 16.97 | 0.04 0.93  |
|          |     | ERSGEE | 0.95 0.93    | 0.95         | 0.0013       | 17.00 | 0.00 1.00  |
|          |     | RTGEE  | 0.94 0.98    | 0.98         | 0.0011       | 17.00 | 0.01 0.99  |
| R_un     |     | SGEE   | 0.93 0.99    | 0.99         | 0.0009       | 16.97 | 0.01 0.96  |
|          |     | RSGEE  | 0.96 0.98    | 0.98         | 0.0010       | 16.96 | 0.02 0.94  |
|          |     | ERSGEE | 0.95 0.98    | 0.95         | 0.0010       | 17.00 | 0.00 1.00  |
|          |     | RTGEE  | 0.95 0.98    | 0.98         | 0.0009       | 17.00 | 0.02 0.98  |
| Case 2   | EXC | SGEE   | 0.95 0.94    | 0.91         | 0.0528       | 16.75 | 0.05 0.75  |
|          |     | RSGEE  | 0.96 0.94    | 0.98         | 0.0046       | 16.94 | 0.01 0.93  |
|          |     | ERSGEE | 0.96 0.94    | 0.96         | 0.0017       | 16.99 | 0.00 0.99  |
|          |     | RTGEE  | 0.96 0.95    | 0.98         | 0.0014       | 17.00 | 0.02 0.98  |
|          |     | AR(1)  | 0.97 0.94    | 1.00         | 0.0779       | 16.94 | 0.27 0.67  |
|          |     | RSGEE  | 0.96 0.95    | 0.97         | 0.0057       | 16.95 | 0.02 0.93  |
|          |     | ERSGEE | 0.92 0.96    | 0.93         | 0.0022       | 16.99 | 0.00 0.99  |
|          |     | RTGEE  | 0.94 0.96    | 0.96         | 0.0021       | 17.00 | 0.02 0.98  |
| R_un     |     | SGEE   | 0.96 0.96    | 0.92         | 0.0633       | 16.81 | 0.04 0.79  |
|          |     | RSGEE  | 0.97 0.97    | 0.96         | 0.0051       | 16.96 | 0.01 0.95  |
|          |     | ERSGEE | 0.93 0.95    | 0.96         | 0.0018       | 16.99 | 0.00 0.99  |
|          |     | RTGEE  | 0.94 0.97    | 0.98         | 0.0016       | 16.99 | 0.02 0.97  |
| Case 3   | EXC | SGEE   | 0.95 0.97    | 0.94         | 0.0537       | 16.66 | 0.04 0.75  |
|          |     | RSGEE  | 0.95 0.97    | 0.96         | 0.0047       | 16.93 | 0.00 0.94  |
|          |     | ERSGEE | 0.94 0.97    | 0.95         | 0.0024       | 16.91 | 0.00 0.93  |
|          |     | RTGEE  | 0.96 0.95    | 0.95         | 0.0017       | 16.99 | 0.05 0.94  |
|          |     | AR(1)  | 0.92 0.98    | 0.94         | 0.0583       | 16.59 | 0.04 0.69  |
|          |     | RSGEE  | 0.95 0.95    | 0.94         | 0.0048       | 16.86 | 0.00 0.88  |
|          |     | ERSGEE | 0.94 0.93    | 0.95         | 0.0024       | 16.90 | 0.00 0.90  |
|          |     | RTGEE  | 0.94 0.95    | 0.95         | 0.0022       | 16.96 | 0.05 0.92  |
| R_un     |     | SGEE   | 0.95 0.96    | 0.93         | 0.0577       | 16.56 | 0.04 0.68  |
|          |     | RSGEE  | 0.96 0.95    | 0.96         | 0.0055       | 16.88 | 0.00 0.89  |
|          |     | ERSGEE | 0.95 0.94    | 0.95         | 0.0026       | 16.90 | 0.00 0.90  |
|          |     | RTGEE  | 0.95 0.96    | 0.96         | 0.0022       | 16.94 | 0.04 0.90  |
Table 5: Correlated continuous data for large $n$ and diverging $p$ ($n = 200$ and $p_n = [4n^{2/5}] - 5$) with $\epsilon_{ij}$ following a normal distribution: Comparison of SGEE, RSGEE, ERSGEE, and the proposed method RTGEE with three different working correlation matrices (exchangeable, AR(1) and unstructured).

| Scenario | $R$   | Method   | $\hat{\beta}_1$ | $\hat{\beta}_2$ | $\hat{\beta}_3$ | MMSPE | No.of Zeros |
|----------|-------|----------|------------------|------------------|------------------|-------|-------------|
| Case 1   | EXC   | SGEE     | 0.98             | 0.99             | 0.95             | 0.0068| 22.48       |
|          |       | RSGEE    | 0.93             | 0.95             | 0.99             | 0.0060| 22.83       |
|          |       | ERSGEE   | 0.96             | 0.96             | 0.95             | 0.0111| 22.93       |
|          |       | RTGEE    | 0.93             | 0.98             | 0.94             | 0.0061| 22.97       |
|          | AR(1) | SGEE     | 0.93             | 0.92             | 0.98             | 0.0069| 22.47       |
|          |       | RSGEE    | 0.92             | 0.93             | 0.98             | 0.0065| 22.83       |
|          |       | ERSGEE   | 0.95             | 0.96             | 0.93             | 0.0117| 22.94       |
|          |       | RTGEE    | 0.92             | 0.94             | 0.98             | 0.0059| 22.94       |
|          | $R_{un}$ | SGEE   | 0.93             | 0.96             | 0.99             | 0.0039| 22.64       |
|          |       | RSGEE    | 0.94             | 0.94             | 0.99             | 0.0039| 22.98       |
|          |       | ERSGEE   | 0.96             | 0.96             | 0.95             | 0.0079| 22.91       |
|          |       | RTGEE    | 0.94             | 0.96             | 0.98             | 0.0038| 22.98       |
| Case 2   | EXC   | SGEE     | 0.95             | 0.99             | 0.99             | 0.2582| 21.37       |
|          |       | RSGEE    | 0.95             | 0.97             | 0.97             | 0.0232| 22.69       |
|          |       | ERSGEE   | 0.93             | 0.99             | 0.94             | 0.0101| 22.92       |
|          |       | RTGEE    | 0.93             | 0.93             | 0.94             | 0.0088| 22.93       |
|          | AR(1) | SGEE     | 0.96             | 0.94             | 0.95             | 0.2511| 21.17       |
|          |       | RSGEE    | 0.93             | 0.96             | 0.96             | 0.0248| 22.62       |
|          |       | ERSGEE   | 0.95             | 0.95             | 0.95             | 0.0096| 22.95       |
|          |       | RTGEE    | 0.94             | 0.96             | 0.96             | 0.0122| 22.91       |
|          | $R_{un}$ | SGEE   | 0.95             | 0.93             | 0.97             | 0.1980| 21.32       |
|          |       | RSGEE    | 0.94             | 0.95             | 0.96             | 0.0154| 22.99       |
|          |       | ERSGEE   | 0.98             | 0.95             | 0.94             | 0.0088| 23.00       |
|          |       | RTGEE    | 0.96             | 0.93             | 0.94             | 0.0061| 23.00       |
| Case 3   | EXC   | SGEE     | 0.99             | 0.99             | 0.99             | 0.2307| 21.09       |
|          |       | RSGEE    | 0.96             | 0.99             | 0.93             | 0.0205| 22.63       |
|          |       | ERSGEE   | 0.97             | 0.94             | 0.92             | 0.0094| 23.00       |
|          |       | RTGEE    | 0.95             | 0.96             | 0.94             | 0.0084| 22.99       |
|          | AR(1) | SGEE     | 0.95             | 0.96             | 0.94             | 0.2386| 21.09       |
|          |       | RSGEE    | 0.94             | 0.95             | 0.93             | 0.0200| 22.71       |
|          |       | ERSGEE   | 0.94             | 0.92             | 0.94             | 0.0087| 23.00       |
|          |       | RTGEE    | 0.95             | 0.92             | 0.94             | 0.0083| 23.00       |
|          | $R_{un}$ | SGEE   | 0.95             | 0.96             | 0.95             | 0.2146| 21.07       |
|          |       | RSGEE    | 0.94             | 0.97             | 0.95             | 0.0146| 22.97       |
|          |       | ERSGEE   | 0.95             | 0.93             | 0.93             | 0.0067| 23.00       |
|          |       | RTGEE    | 0.95             | 0.96             | 0.96             | 0.0061| 23.00       |
Table 6: Correlated continuous data for $p > n$ ($n = 100$ and $p = 300$) with $\epsilon_{ij}$ following a normal distribution: Comparison of SGEE, RSGEE, ERSGEE, and the proposed method RTGEE with three different working correlation matrices (exchangeable, AR(1) and unstructured).

| Scenario | R     | Method | $\beta_1$ | $\beta_2$ | $\beta_3$ | MMSPE | No.of Zeros |
|----------|-------|--------|-----------|-----------|-----------|-------|-------------|
|          |       |        | CI | CI | CI |       | C | IC | CF |
| Case 1   | EXC   | SGEE   | 0.96 | 0.95 | 0.95 | 0.0012 | 296.51 | 0.05 | 0.75 |
|          |       | RSGEE  | 0.94 | 0.97 | 0.97 | 0.0012 | 296.90 | 0.03 | 0.89 |
|          |       | ERSGEE | 0.96 | 0.98 | 0.98 | 0.0023 | 297.00 | 0.02 | 0.98 |
|          |       | RTGEE  | 0.95 | 0.98 | 0.97 | 0.0011 | 297.00 | 0.02 | 0.98 |
|          | AR(1) | SGEE   | 0.96 | 0.98 | 0.98 | 0.0017 | 296.36 | 0.02 | 0.72 |
|          |       | RSGEE  | 0.97 | 0.95 | 0.95 | 0.0017 | 296.86 | 0.05 | 0.87 |
|          |       | ERSGEE | 0.93 | 0.97 | 0.98 | 0.0032 | 297.00 | 0.02 | 0.98 |
|          |       | RTGEE  | 0.95 | 0.99 | 0.98 | 0.0016 | 297.00 | 0.01 | 0.99 |
|          | Run   | SGEE   | 0.96 | 0.97 | 0.97 | 0.0011 | 296.55 | 0.03 | 0.76 |
|          |       | RSGEE  | 0.95 | 0.96 | 0.96 | 0.0011 | 296.89 | 0.04 | 0.87 |
|          |       | ERSGEE | 0.96 | 0.93 | 0.93 | 0.0023 | 297.00 | 0.07 | 0.93 |
|          |       | RTGEE  | 0.96 | 0.94 | 0.94 | 0.0010 | 297.00 | 0.06 | 0.94 |
| Case 2"  | EXC   | SGEE   | 0.95 | 0.94 | 0.98 | 0.0566 | 283.38 | 0.02 | 0.26 |
|          |       | RSGEE  | 0.94 | 0.96 | 0.99 | 0.0020 | 296.81 | 0.01 | 0.87 |
|          |       | ERSGEE | 0.94 | 0.96 | 0.97 | 0.0018 | 296.99 | 0.03 | 0.96 |
|          |       | RTGEE  | 0.95 | 0.96 | 0.98 | 0.0014 | 296.97 | 0.02 | 0.96 |
|          | AR(1) | SGEE   | 0.96 | 0.95 | 0.98 | 0.0374 | 277.70 | 0.02 | 0.25 |
|          |       | RSGEE  | 0.96 | 0.95 | 0.97 | 0.0023 | 296.77 | 0.03 | 0.82 |
|          |       | ERSGEE | 0.96 | 0.95 | 0.97 | 0.0024 | 296.99 | 0.03 | 0.96 |
|          |       | RTGEE  | 0.98 | 0.97 | 0.98 | 0.0019 | 296.97 | 0.02 | 0.95 |
|          | Run   | SGEE   | 0.94 | 0.95 | 0.97 | 0.0546 | 276.36 | 0.03 | 0.24 |
|          |       | RSGEE  | 0.93 | 0.96 | 0.98 | 0.0019 | 296.84 | 0.02 | 0.87 |
|          |       | ERSGEE | 0.94 | 0.96 | 0.97 | 0.0022 | 296.99 | 0.03 | 0.96 |
|          |       | RTGEE  | 0.94 | 0.97 | 0.97 | 0.0018 | 296.98 | 0.03 | 0.95 |
| Case 3"  | EXC   | SGEE   | 0.96 | 0.92 | 0.91 | 0.0549 | 282.37 | 0.09 | 0.18 |
|          |       | RSGEE  | 0.97 | 0.94 | 0.96 | 0.0024 | 296.75 | 0.04 | 0.78 |
|          |       | ERSGEE | 0.93 | 0.95 | 0.96 | 0.0020 | 296.97 | 0.04 | 0.94 |
|          |       | RTGEE  | 0.96 | 0.96 | 0.96 | 0.0016 | 296.97 | 0.04 | 0.94 |
|          | AR(1) | SGEE   | 0.95 | 0.91 | 0.90 | 0.0407 | 286.46 | 0.09 | 0.23 |
|          |       | RSGEE  | 0.96 | 0.93 | 0.96 | 0.0033 | 296.82 | 0.04 | 0.84 |
|          |       | ERSGEE | 0.97 | 0.95 | 0.96 | 0.0027 | 296.97 | 0.04 | 0.94 |
|          |       | RTGEE  | 0.97 | 0.95 | 0.96 | 0.0022 | 296.97 | 0.04 | 0.94 |
|          | Run   | SGEE   | 0.95 | 0.93 | 0.90 | 0.0653 | 281.18 | 0.10 | 0.19 |
|          |       | RSGEE  | 0.95 | 0.94 | 0.96 | 0.0028 | 296.86 | 0.04 | 0.84 |
|          |       | ERSGEE | 0.93 | 0.95 | 0.96 | 0.0025 | 296.97 | 0.04 | 0.94 |
|          |       | RTGEE  | 0.94 | 0.96 | 0.96 | 0.0020 | 296.97 | 0.04 | 0.94 |
Table 7: The parameter estimates of selected TFs, the mean squared error for cross validation procedures under three correlation structures, and the running time (s means seconds) for four procedures in the yeast cell-cycle process.

| Covariates | SGEE | MSE CV | RSGEE | MSE CV | ERSGEE | MSE CV | RTGEE | MSE CV |
|------------|------|--------|-------|--------|--------|--------|-------|--------|
| EXC AR(1)  | 0.098| 1.780  | 0.105 | 1.802  | 0.068  | 1.847  | 0.121 | 1.822  |
| intercept  | 0.010| 2.232  | 0.008 | 2.202  | 0.113  | 2.186  | 0.121 | 2.070  |
| MSE CV     | 2.417| 2.042  | 0.004 | 1.969  | 1.260  | 1.862  | 1.377 | 40.735 |
| Time (s)   | 73.160| 40.044 | 0.004 | 1.858  | 0.004 | 1.858  | 0.004 | 1.858  |
Figure 1: The correlation plots of the log-transformed gene expression level. Here “y1” represents the first observation, and so forth. The correlation coefficients among factors, the density maps of them, and the scatter plots of two factors lie on the upper right triangle, the diagonal, and the lower left triangle, respectively.

Figure 2: The boxplots of log-transformed gene expression level over four time points.
Figure 3: The boxplots of four important TFs: ASH1, MBP1, SWI4, and SWI6 over four time points.

Figure 4: Comparison of RSGEE, ERSGEE, and RTGEE on relative efficiency (compared to SGEE) with three different working correlation matrices under three contamination scenarios. The left figure A represents simulation I for heavy-tailed data, and the right figure B represents simulation I for the normal data.
Figure 5: Comparison of RSGEE, ERSGEE, and RTGEE on relative efficiency (compared to SGEE) with three different working correlation matrices under three contamination scenarios. The left figure C represents simulation II for heavy-tailed data, and the right figure D represents simulation II for the normal data.

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Figure 6: Comparison of RSGEE, ERSGEE, and RTGEE on relative efficiency (compared to SGEE) with three different working correlation matrices under three contamination scenarios. The left figure E represents simulation III for the heavy-tailed data, and the right figure F represents simulation III for the normal data.

Figure 7: The scatter plots of gene expression level versus four important TFs: FKH2, MBP1, SWI4, and SWI6. Here “Y” represents the log-transformed gene expression level.
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