

Joint Estimation and Inference for Multiple Multi-layered Gaussian Graphical Models

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Abstract: The rapid development of high-throughput technologies has enabled generation of data from biological processes that span multiple layers, like genomic, proteomic or metabolomic data; and pertain to multiple sources, like disease subtypes or experimental conditions. In this work we propose a general statistical framework based on graphical models for horizontal (i.e. across conditions or subtypes) and vertical (i.e. across different layers containing data on molecular compartments) integration of information in such datasets. We start with decomposing the multi-layer problem into a series of two-layer problems. For each two-layer problem, we model the outcomes at a node in the lower layer as dependent on those of other nodes in that layer, as well as all nodes in the upper layer. Following the biconvexity of our objective function, this estimation problem decomposes into two parts, where we use neighborhood selection and subsequent refitting of the precision matrix to quantify the dependency of two nodes in a single layer, and use group-penalized least square estimation to quantify the directional dependency of two nodes in different layers. Finally, to test for differences in these directional dependencies across multiple sources, we devise a hypothesis testing procedure that utilizes already computed neighborhood selection coefficients for nodes in the upper layer. We establish theoretical results for the validity of this testing procedure and the consistency of our estimates, and also evaluate their performance through simulations and a real data application.

Keywords: Data integration; Gaussian Graphical Models; Neighborhood selection; Group lasso

1 Introduction

1.1 Notations and terminology

We shall denote scalars by small letters, vectors by bold small letters and matrices by bold capital letters. For any matrix \mathbf{A} , $(\mathbf{A})_{ij}$ denote its element in the $(i, j)^{\text{th}}$ position. For $a, b \in \mathbb{N}$, we denote the set of all $a \times b$ real matrices by $\mathbb{M}(a, b)$. For any positive integer c , define $\mathcal{I}_c = \{1, \dots, c\}$.

2 Model

Consider the two-layered setup:

$$\mathbb{X}^k = (X_1^k, \dots, X_p^k)^T \sim \mathcal{N}(0, \Sigma_x^k) \quad (2.1)$$

$$\mathbb{Y}^k = \mathbb{X}^k \mathbf{B}^k + \mathbb{E}^k; \quad \mathbb{E}^k = (E_1^k, \dots, E_p^k)^T \sim \mathcal{N}(0, \Sigma_y^k) \quad (2.2)$$

$$\mathbf{B}^k \in \mathbb{M}(p, q); \quad \Omega_x^k = (\Sigma_x^k)^{-1}; \quad \Omega_y^k = (\Sigma_y^k)^{-1} \quad (2.3)$$

Want to estimate $\{(\Omega_x^k, \Omega_y^k, \mathbf{B}^k); k \in \mathcal{I}_K\}$ from data $\mathcal{Z}^k = \{(\mathbf{Y}^k, \mathbf{X}^k); \mathbf{Y}^k \in \mathbb{M}(n, q), \mathbf{X}^k \in \mathbb{M}(n, p), k \in \mathcal{I}_K\}$. in presence of known grouping structures $\mathcal{G}_x, \mathcal{G}_y, \mathcal{H}$ respectively.

Estimation of $\{\Omega_x^k\}$ done using JSEM. For the other part, we use the following two-step procedure:

1. Run neighborhood selection on y -network incorporating effects of x -data and an additional blockwise group penalty:

$$\min_{\mathcal{B}, \Theta} \left\{ \sum_{j=1}^q \frac{1}{n_k} \left[\sum_{k=1}^K \|\mathbf{Y}_j^k - (\mathbf{Y}_{-j}^k - \mathbf{X}^k \mathbf{B}_{-j}^k) \boldsymbol{\theta}_j^k - \mathbf{X}^k \mathbf{B}_j^k\|^2 + \sum_{j \neq i} \sum_{g \in \mathcal{G}_y^{ij}} \lambda_{ij}^g \|\boldsymbol{\theta}_{ij}^{[g]}\| \right] + \sum_{b \in \mathcal{G}_x \times \mathcal{G}_y \times \mathcal{H}} \eta^b \|\mathbf{B}^{[b]}\| \right\} \quad (2.4)$$

$$= \min \{f(\mathcal{Y}, \mathcal{X}, \mathcal{B}, \Theta) + P(\Theta) + Q(\mathcal{B})\} \quad (2.5)$$

where $\Theta = \{\Theta_i\}, \mathcal{B} = \{\mathbf{B}^k\}, \mathcal{Y} = \{\mathbf{Y}^k\}, \mathcal{X} = \{\mathbf{X}^k\}, \mathcal{E} = \{\mathbf{E}^k\}$.

This estimates \mathcal{B} **(possibly refit and/or within-group threshold)**.

2. Step I part 2 and step II of JSEM (see 15-656 pg 6) follows to estimate $\{\Omega_y^k\}$.

The objective function is bi-convex, so we are going to do the following in step 1-

- Start with initial estimates of \mathcal{B} and Θ , say $\mathcal{B}^{(0)}, \Theta^{(0)}$.
- Iterate:

$$\Theta^{(t+1)} = \arg \min \{f(\mathcal{Y}, \mathcal{X}, \mathcal{B}^{(t)}, \Theta^{(t)}) + P(\Theta^{(t)})\} \quad (2.6)$$

$$\mathcal{B}^{(t+1)} = \arg \min \{f(\mathcal{Y}, \mathcal{X}, \mathcal{B}^{(t)}, \Theta^{(t+1)}) + Q(\mathcal{B}^{(t)})\} \quad (2.7)$$

- Continue till convergence.

3 Conditions

Conditions A1 from JSEM paper holds for \mathcal{X} and \mathcal{E} . Also A2, A3 from JSEM paper.

4 Results

To prove the results in this section, we shall use a reparametrization of the neighborhood coefficients at the lower level. Specifically, notice that for $j \in \mathcal{I}_q, k \in \mathcal{I}_K$, the corresponding summand in $f(\mathcal{Y}, \mathcal{X}, \mathcal{B}, \Theta)$ can be rearranged as

$$\begin{aligned} \|\mathbf{Y}_j^k - \mathbf{X}^k \mathbf{B}_j^k - (\mathbf{Y}_{-j}^k - \mathbf{X}^k \mathbf{B}_{-j}^k) \boldsymbol{\theta}_j^k\|^2 &= \|\mathbf{Y}_j^k - \mathbf{Y}_{-j}^k \boldsymbol{\theta}_j^k - (\mathbf{X}^k \mathbf{B}_j^k - \mathbf{X}^k \mathbf{B}_{-j}^k \boldsymbol{\theta}_j^k)\|^2 \\ &= \|(\mathbf{Y} - \mathbf{X} \mathbf{B}) \mathbf{T}_j^k\|^2 \end{aligned}$$

where

$$T_{jj'}^k = \begin{cases} 1 & \text{if } j = j' \\ -\theta_{jj'}^k & \text{if } j \neq j' \end{cases}$$

Thus, with $\mathbf{T}^k := (\mathbf{T}_j^k)_{j \in \mathcal{I}_q}$, we have

$$f(\mathcal{Y}, \mathcal{X}, \mathcal{B}, \Theta) = \frac{1}{n} \sum_{j=1}^p \sum_{k=1}^K \|(\mathbf{Y}^k - \mathbf{X}^k \mathbf{B}^k) \mathbf{T}_j^k\|^2 = \frac{1}{n} \sum_{k=1}^K \|\mathbf{Y}^k - \mathbf{X}^k \mathbf{B}^k\|_F^2 = \sum_{k=1}^K \text{Tr}(\mathbf{S}^k (\mathbf{T}^k)^2)$$

where $\mathbf{S}^k = (1/n)(\mathbf{Y}^k - \mathbf{X}^k \mathbf{B}^k)(\mathbf{Y}^k - \mathbf{X}^k \mathbf{B}^k)^T$ is the sample covariance matrix.

Now suppose $\boldsymbol{\beta} = \text{vec}(\mathbf{B})$, and any subscript or superscript on \mathbf{B} will be passed on to $\boldsymbol{\beta}$. Denote by $\hat{\boldsymbol{\beta}}$ and $\hat{\Theta}$ the generic estimators given by

$$\hat{\boldsymbol{\beta}} = \arg \min_{\boldsymbol{\beta} \in \mathbb{R}^{pq}} \left\{ -2\boldsymbol{\beta}^T \hat{\boldsymbol{\gamma}} + \boldsymbol{\beta}^T \hat{\boldsymbol{\Gamma}} \boldsymbol{\beta} + \lambda_n \sum_{h \in \mathcal{H}} \|\boldsymbol{\beta}^{[h]}\| \right\} \quad (4.1)$$

$$\hat{\Theta}_j = \arg \min_{\Theta_j \in \mathbb{M}(q-1, K)} \left\{ \frac{1}{n} \sum_{k=1}^K \|\mathbf{Y}_j^k - \mathbf{X}^k \hat{\mathbf{B}}_j^k - (\mathbf{Y}_{-j}^k - \mathbf{X}^k \hat{\mathbf{B}}_{-j}^k) \boldsymbol{\theta}_j^k\|^2 + \gamma_n \sum_{j \neq j'} \sum_{g \in \mathcal{G}_y^{jj'}} \|\boldsymbol{\theta}_{jj'}^{[g]}\| \right\} \quad (4.2)$$

where

$$\hat{\boldsymbol{\Gamma}} = \begin{bmatrix} (\hat{\mathbf{T}}^1)^2 \otimes \frac{(\mathbf{X}^1)^T \mathbf{X}^1}{n} & & \\ & \ddots & \\ & & (\hat{\mathbf{T}}^K)^2 \otimes \frac{(\mathbf{X}^K)^T \mathbf{X}^K}{n} \end{bmatrix}; \quad \hat{\boldsymbol{\gamma}} = \begin{bmatrix} (\hat{\mathbf{T}}^1)^2 \otimes \frac{(\mathbf{X}^1)^T}{n} \\ \vdots \\ (\hat{\mathbf{T}}^K)^2 \otimes \frac{(\mathbf{X}^K)^T}{n} \end{bmatrix} \begin{bmatrix} \text{vec}(\mathbf{Y}^1) \\ \vdots \\ \text{vec}(\mathbf{Y}^K) \end{bmatrix}$$

with $\hat{\mathbf{T}}^k$ defined the same way using $\hat{\boldsymbol{\theta}}_j^k$ as we defined \mathbf{T}^k using $\boldsymbol{\theta}_j^k$.

Theorem 4.1. Assume fixed \mathcal{X}, \mathcal{E} and deterministic $\widehat{\mathcal{B}} = \{\widehat{\mathbf{B}}^k\}$. Also for $k = 1, \dots, K$,

(T1) $\|\widehat{\mathbf{B}}^k - \mathbf{B}_0^k\|_1 \leq v_\beta$, where $v_\beta = \eta_\beta \sqrt{\frac{\log(pq)}{n}}$ with $\eta_\beta \geq 0$ depending on \mathcal{B} only;

(T2) Denote $\widehat{\mathbf{E}}^k = \mathbf{Y}^k - \mathbf{X}^k \widehat{\mathbf{B}}^k, k \in \mathcal{I}_K$. Then for all $j \in \mathcal{I}_q$,

$$\frac{1}{n} \left\| (\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k \mathbf{T}_{0,j}^k \right\|_\infty \leq \mathbb{Q}(v_\beta, \Sigma_x^k, \Sigma_y^k)$$

where $\mathbb{Q}(v_\beta, \Sigma_x^k, \Sigma_y^k)$ is a $O(\sqrt{\log(pq)/n})$ deterministic function of \mathcal{B}, Σ_x^k and Σ_y^k .

(T3) Denote $\widehat{\mathbf{S}}^k = (\widehat{\mathbf{E}}^k)^T \widehat{\mathbf{E}}^k / n$. Then $\widehat{\mathbf{S}}^k \sim RE(\psi^k, \phi^k)$ with $Kq\phi \leq \psi/2$ where $\psi = \min_k \psi^k, \phi = \max_k \phi^k$;

(T4) Assumption (A2) holds for Σ_y^k .

Then, given the choice of tuning parameter

$$\gamma_n = 4\sqrt{|g_{\max}|} \mathbb{Q}_0; \quad \mathbb{Q}_0 := \max_{k \in \mathcal{I}_K} \mathbb{Q}(v_\beta, \Sigma_x^k, \Sigma_y^k)$$

the following holds

$$\frac{1}{K} \sum_{k=1}^K \|\widehat{\Omega}_y^k - \Omega_y^k\|_F \leq O\left(\mathbb{Q}_0 \sqrt{\frac{|g_{\max}|S}{K}}\right)$$

where $|g_{\max}|$ is the maximum group size.

Discuss tighter bound compared to vanilla JSEM

When \mathcal{X} and \mathcal{E} are random, the following propositions ensures that conditions (T2) and (T3) hold with probability approaching to 1.

Proposition 4.2. Consider deterministic $\widehat{\mathcal{B}}$ satisfying assumption (T1). Then for sample size $n \gtrsim \log(pq)$ and $k \in \mathcal{I}_K$,

1. $\widehat{\mathbf{S}}^k$ satisfies the RE condition: $\widehat{\mathbf{S}}^k \sim RE(\psi^k, \phi^k)$, where

$$\psi^k = \frac{\Lambda_{\min}(\Sigma_x^k)}{2}; \quad \phi^k = \frac{\psi^k \log p}{n} + 2v_\beta c_2 [\Lambda_{\max}(\Sigma_x^k) \Lambda_{\max}(\Sigma_y^k)]^{1/2} \sqrt{\frac{\log(pq)}{n}}$$

with probability $\geq 1 - 6c_1 \exp[-(c_2^2 - 1) \log(pq)] - 2 \exp(-c_3 n), c_1, c_3 > 0, c_2 > 1$.

2. The following deviation bound is satisfied for any $j \in \mathcal{I}_q$

$$\left\| \frac{1}{n} (\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k \mathbf{T}_{0,j}^k \right\|_\infty \leq \mathbb{Q}(v_\beta, \Sigma_x^k, \Sigma_y^k)$$

with probability $\geq 1 - 1/p^{\tau_1-2} - 6c_1 \exp[-(c_2^2 - 1) \log(pq)] - 6c_4 \exp[-(c_5^2 - 1) \log(pq)], c_4 > 0, c_5 > 1$, where

$$\begin{aligned} \mathbb{Q}(v_\beta, \Sigma_x^k, \Sigma_y^k) &= 2v_\beta^2 V_x^k + 4v_\beta c_2 [\Lambda_{\max}(\Sigma_x^k) \Lambda_{\max}(\Sigma_y^k)]^{1/2} \sqrt{\frac{\log(pq)}{n}} + \\ &c_5 [\Lambda_{\max}(\Sigma_{y,-j}^k) \sigma_{y,j,-j}^k]^{1/2} \sqrt{\frac{\log q}{n}} \end{aligned}$$

with $\sigma_{y,j,-j}^k = \mathbb{V}(E_j - \mathbb{E}_{-j}\boldsymbol{\theta}_{0,j})$, and

$$V_x^k = \sqrt{\frac{\log 4 + \tau_1 \log p}{c_x^k n}} + \max_i \sigma_{x,ii}^k; \quad c_x^k = \left[128(1 + 4\Lambda_{\max}(\Sigma_x))^2 \max_i (\sigma_{x,ii})^2 \right]^{-1}$$

The error bounds for $\hat{\Omega}_y^k, k \in \mathcal{I}_K$ follow immediately from the above two results.

Corollary 4.3. *Consider any deterministic $\hat{\mathcal{B}}$ that satisfy the following bound*

$$\|\hat{\mathbf{B}}^k - \mathbf{B}_0^k\|_1 \leq v_\beta = \eta_\beta \sqrt{\frac{\log(pq)}{n}}$$

Then, for sample size $n \gtrsim \log(pq)$ and choice of tuning parameter $\gamma_n = 4\sqrt{G_0}\mathbb{Q}_0$, there exist constants $c_1, c_3, c_4 > 0, c_2, c_5 > 1$ such that the following holds

$$\frac{1}{K} \sum_{k=1}^K \|\hat{\Omega}_y^k - \Omega_y^k\|_F \leq O\left(\mathbb{Q}_0 \sqrt{\frac{|g_{\max}|S}{K}}\right)$$

with probability $\geq 1 - 1/p^{\tau_1-2} - 6c_1 \exp[-(c_2^2 - 1)\log(pq)] - 2\exp(-c_3n) - 6c_4 \exp[-(c_5^2 - 1)\log(pq)]$.

After providing the error bounds for solutions to the subproblem (4.2), we concentrate on the subproblem (4.1). Following a similar strategy, we first get error bounds for $\hat{\beta}$ assuming everything else fixed.

Theorem 4.4. *Assume fixed \mathcal{X}, \mathcal{E} , and deterministic $\hat{\Theta} = \{\hat{\Theta}_j\}$, so that for $j \in \mathcal{I}_q$,*

(B1) $\|\hat{\Theta}_j - \Theta_{0,j}\|_F \leq v_\Theta \sqrt{\frac{\log q}{n}}$ for some v_Θ dependent on Θ .

(B2) Denote $\hat{\Gamma}^k = (\hat{\mathbf{T}}^k)^2 \otimes (\mathbf{X}^k)^T \mathbf{X}^k / n, \hat{\gamma}^k = (\hat{\mathbf{T}}^k)^2 \otimes (\mathbf{X}^k)^T \mathbf{Y}^k / n$. Then the deviation bound holds:

$$\|\hat{\gamma}^k - \hat{\Gamma}^k \beta_0\|_\infty \leq \mathbb{R}(v_\Theta, \Sigma_x^k, \Sigma_y^k) \sqrt{\frac{\log(pq)}{n}}$$

where $\mathbb{R}(v_\Theta, \Sigma_x^k, \Sigma_y^k)$ is a $O(1)$ deterministic function of Θ, Σ_x^k and Σ_y^k .

(B3) $\hat{\Gamma} \sim RE(\psi_*, \phi_*)$ with $Kpq\phi_* \leq \psi_*/2$.

Then, given the choice of tuning parameter

$$\lambda_n \geq 4\sqrt{|h_{\max}|} \mathbb{R}_0 \sqrt{\frac{\log(pq)}{n}}; \quad \mathbb{R}_0 := \max_{k \in \mathcal{I}_K} \mathbb{R}(v_\Theta, \Sigma_x^k, \Sigma_y^k)$$

the following holds

$$\|\hat{\beta} - \beta_0\|_1 \leq 48\sqrt{|h_{\max}|} s_\beta \lambda_n / \psi^* \quad (4.3)$$

$$\|\hat{\beta} - \beta_0\| \leq 12\sqrt{s_\beta} \lambda_n / \psi^* \quad (4.4)$$

$$\sum_{h \in \mathcal{H}} \|\beta^{[h]} - \beta_0^{[h]}\| \leq 48s_\beta \lambda_n / \psi^* \quad (4.5)$$

$$(\hat{\beta} - \beta_0)^T \hat{\Gamma} (\hat{\beta} - \beta_0) \leq 72s_\beta \lambda_n^2 / \psi^* \quad (4.6)$$

Proposition 4.5. Consider deterministic $\widehat{\Theta}$ satisfying assumption (B1). Assume that the matrices $(\widehat{\mathbf{T}}^k)^2, k \in \mathcal{I}_K$ are diagonally dominant. Then for sample size $n \gtrsim \log(pq)$,

1. $\widehat{\Gamma}$ satisfies the RE condition: $\widehat{\Gamma} \sim RE(\psi_*, \phi_*)$, where

$$\psi_* = \min_k \psi^k \left(\min_i \psi_t^i - dv_\Theta \right), \phi_* = \max_k \phi^k \left(\min_i \phi_t^i + dv_\Theta \right)$$

with probability $\geq 1 - 2 \exp(-c_3 n)$, $c_3 > 0$.

2. The deviation bound in (B2) is satisfied with probability $\geq 1 - 12c_1 \exp[-(c_2^2 - 1) \log(pq)]$, $c_1 > 0, c_2 > 1$, where

$$\mathbb{R}(v_\Theta, \Sigma_x^k, \Sigma_y^k) = c_2 \sqrt{\Lambda_{\max}(\Sigma_x^k)} \left(dv_\Theta \Lambda_{\min}(\Sigma_y^k) + \frac{1}{\Lambda_{\min}(\Sigma_y^k)} \right)$$

We now put both the pieces together, and prove that our alternating algorithm results in a solution sequence $\{\widehat{\mathcal{B}}^{(r)}, \widehat{\Theta}^{(r)}\}, r = 1, 2, \dots$ that lies uniformly within a non-expanding ball around the true parameter values.

5 Two-sample testing

Suppose there are two disease subtypes: $k = 1, 2$, and we are interested in testing whether the downstream effect of a predictor in X-data is same across both subtypes, i.e. if $\mathbf{b}_i^1 = \mathbf{b}_i^2$ for some $i \in \mathcal{I}_p$. For this we consider the modified optimization problem:

$$\begin{aligned} \min_{\mathcal{B}, \Theta} \frac{1}{n} \left\{ \sum_{j=1}^q \sum_{k=1}^2 \|\mathbf{Y}_j^k - \mathbf{Y}_{-j}^k \boldsymbol{\theta}_j^k - \mathbf{X}^k \mathbf{B}_j^k\|^2 + \sum_{j \neq j'} \lambda_{jj'} \|\boldsymbol{\theta}_{jj'}^*\| + \sum_{i=1}^p \eta_i \|\mathbf{B}_{i*}^*\| \right\} \\ = \min \{f(\mathcal{Y}, \mathcal{X}, \mathcal{B}, \Theta) + P(\Theta) + Q(\mathcal{B})\} \end{aligned} \quad (5.1)$$

with $n_1 = n_2 = n$ for simplicity; and $\mathbf{B}^k = (\mathbf{b}_1^k, \dots, \mathbf{b}_q^k), (\mathbf{B}_{i*}^*) \in \mathbb{R}^{q \times K}$.

In this setup, define the desparsified estimate of \mathbf{b}_i^k as

$$\widehat{\mathbf{c}}_i^k = \widehat{\mathbf{b}}_i^k + \frac{1}{nt_i^k} \left(\mathbf{X}_i^k - \mathbf{X}_{-i}^k \widehat{\boldsymbol{\zeta}}_i^k \right)^T (\mathbf{Y}^k - \mathbf{X}^k \widehat{\mathbf{B}}^k) \quad (5.2)$$

for $k = 1, 2$, where $t_i^k = (\mathbf{X}_i^k - \mathbf{X}_{-i}^k \widehat{\boldsymbol{\zeta}}_i^k)^T \mathbf{X}_{-i}^k / n$. Then we have the asymptotic joint distribution of a scaled version of the debiased coefficients for the i^{th} predictor effect.

Theorem 5.1. Define $\widehat{s}_i^k = \sqrt{\|\mathbf{X}_i^k - \mathbf{X}_{-i}^k \widehat{\boldsymbol{\zeta}}_i^k\|^2 / n}$, and $m_i^k = \sqrt{nt_i^k / \widehat{s}_i^k}$. Assume the following:

(C1) For the X-neighborhood estimators we have $\|\widehat{\boldsymbol{\zeta}}^k - \boldsymbol{\zeta}_0^k\|_1 \leq v_\zeta = \eta_\zeta \sqrt{\frac{\log p}{n}}$.

(C2) The precision matrix estimators satisfy

$$\left\| (\hat{\Omega}_y^k)^{1/2} - (\Omega_y^k)^{1/2} \right\|_\infty \leq v_\Omega = \eta_\Omega \sqrt{\frac{\log q}{n}}$$

(C3) $\|\hat{\mathbf{B}}^k - \mathbf{B}_0^k\|_1 \leq v_\beta$, where $v_\beta = \eta_\beta \sqrt{\frac{\log(pq)}{n}}$ with η_β depending on \mathcal{B} only.

Then for the debiased estimators in (5.2) and sample size $n \gtrsim \log(pq)$ we have

$$\begin{bmatrix} \hat{\Omega}_y^1 & \\ & \hat{\Omega}_y^2 \end{bmatrix}^{1/2} \begin{bmatrix} m_i^1(\hat{\mathbf{c}}_i^1 - \mathbf{b}_i^1) & \\ & m_i^2(\hat{\mathbf{c}}_i^2 - \mathbf{b}_i^2) \end{bmatrix} \sim \mathcal{N}_{2q}(\mathbf{0}, \mathbf{I}) + o_P(1) \quad (5.3)$$

Based on the theorem, we have the global test for the effect of the i^{th} X-covariate.

Algorithm 1. (Global test for $H_0^i : \mathbf{B}_{0i}^1 = \mathbf{B}_{0i}^2$ at level $\alpha, 0 < \alpha < 1$)

1. Obtain the debiased estimators $\hat{\mathbf{c}}_i^1, \hat{\mathbf{c}}_i^2$ using (5.2).
2. Calculate the test statistic

$$D_i = \left\| m_i^1(\hat{\Omega}_y^1)^{1/2}\hat{\mathbf{c}}_i^1 - m_i^2(\hat{\Omega}_y^2)^{1/2}\hat{\mathbf{c}}_i^2 \right\|^2$$

3. Reject H_0^i if $D_i \geq \chi_{2q, 1-\alpha}^2$.

Given the null hypothesis is rejected, we now consider the multiple testing problem of simultaneously testing for all entrywise differences, i.e. testing

$$H_0^{ij} : b_{0ij}^1 = b_{0ij}^2 \quad \text{vs.} \quad H_1^{ij} : b_{0ij}^1 \neq b_{0ij}^2$$

for $j \in \mathcal{I}_q$. Here we use the test statistic

$$d_{ij} = \frac{\hat{c}_{ij}^1 - \hat{c}_{ij}^2}{\tau_{ij}^1/m_i^1 + \tau_{ij}^2/m_i^2} \quad (5.4)$$

with τ_{ij}^k being the $(i, j)^{\text{th}}$ element of $(\hat{\Omega}_y^k)^{-1/2}$, for $k = 1, 2$.

Now consider tests where H_0^{ij} is rejected if $|d_{ij}| > \tau$. We denote $\mathcal{H}_0^i = \{j : b_{ij}^1 = b_{ij}^2\}$ and define the false discovery proportion (FDP) and false discovery rate (FDR) for these tests as follows:

$$FDP(\tau) = \frac{\sum_{j \in \mathcal{H}_0^i} \mathbb{I}(|d_{ij}| \geq \tau)}{\max \left\{ \sum_{j \in \mathcal{I}_q} \mathbb{I}(|d_{ij}| \geq \tau), 1 \right\}} \quad FDR(\tau) = \mathbb{E}[FDP(\tau)]$$

For a pre-specified level α , we choose a threshold that ensures both FDP and FDR $\leq \alpha$ using the Benjamini-Hochberg (BH) procedure. The procedure for FDR control is now given by Algorithm 2.

Algorithm 2. (Simultaneous tests for $H_0^{ij} : b_{0ij}^1 = b_{0ij}^2$ at level $\alpha, 0 < \alpha < 1$)

1. Calculate the pairwise test statistics d_{ij} using (2) for $j \in \mathcal{I}_q$.
2. Obtain the threshold

$$\hat{\tau} = \inf \left\{ \tau \in \mathbb{R} : 1 - \Phi(\tau) \leq \frac{\alpha}{2q} \max \left(\sum_{j \in \mathcal{I}_q} \mathbb{I}(|d_{ij}| \geq \tau), 1 \right) \right\}$$

3. For $j \in \mathcal{I}_q$, reject H_0^{ij} if $|d_{ij}| \geq \hat{\tau}$.

This procedure maintains FDR and FDP asymptotically at a pre-specified level $\alpha \in (0, 1)$ under weak dependence conditions.

Theorem 5.2. Suppose $\mu_j = b_{0,ij}^1 - b_{0,ij}^2, \sigma_j = \sqrt{n} \mathbb{E}(\tau_{ij}^1/m_i^1 + \tau_{ij}^2/m_i^2)$. Assume the following holds as $(n, q) \rightarrow \infty$

$$\left| \left\{ j \in \mathcal{I}_q : |\mu_j/\sigma_j| \geq 4\sqrt{\log q/n} \right\} \right| \rightarrow \infty \quad (5.5)$$

Now Consider the conditions **C1, C1***

If (C1) is satisfied, then the following holds when $\log q = O(n^\xi), 0 < \xi < 3/23$:

$$\frac{FDP(\hat{\tau})}{(|\mathcal{H}_0^i|/q)\alpha} \xrightarrow{P} 1; \quad \lim_{n, q \rightarrow \infty} \frac{FDR(\hat{\tau})}{(|\mathcal{H}_0^i|/q)\alpha} = 1 \quad (5.6)$$

Further, if (C1*) is satisfied, then (5.6) holds for $\log q = o(n^{1/3})$.

The condition (5.5) is essential for FDR control in a diverging parameter space (Liu, 2017; Liu and Shao, 2014), while the dependence conditions (C1) and (C1*) control the amount of correlation between variables in the Y-layer.

Remark 1. Following Liu and Shao (2014), a version of Algorithm 2, where the null distribution is calibrated using bootstrap instead of normal approximation, gives asymptotic FDR control under (C1*) and $\log q = o(n^{1/2})$. We believe it is possible to obtain (5.6) under the weaker condition (C1) for $\log q = o(n^{1/2})$ by extending the framework of Liu (2017) that performs multiple testing in multiple (single layer) GGMs, with the added advantage of being generalizable to the case of $K > 2$. However, this requires a significant amount of theoretical analysis, and we leave it for future research.

Remark 2. **does within-group thresholding with FDR control for $K = 1$**

A Proofs

Proof of Theorem 4.1. The proof has three parts, where we prove the consistency of the neighborhood regression coefficients, selection of edge sets, and finally the refitting step, respectively. This is the same structure as the proof of Theorem 1 in Ma and Michailidis

(2016), where they prove consistency of the (single layer) JSEM estimates. The derivation of the first part is different from that in the JSEM proof, which we shall show in detail (in the proof of Proposition A.1). The second and third parts follow similar lines, incorporating the updated quantities from the first part. For these we provide outlines and leave the details to the reader.

Step 1: consistency of neighborhood regression. The following proposition establishes error bounds for estimated neighborhood coefficients in the Y-network.

Proposition A.1. *Consider the estimation problem in (4.2) and take $\gamma_n \geq 4\sqrt{|g_{\max}|}\mathbb{Q}_0$. Given the conditions (T2) and (T3) hold, for any solution of (4.2) we shall have*

$$\|\hat{\Theta}_j - \Theta_{0,j}\|_F \leq 12\sqrt{s_j}\gamma_n/\psi \quad (\text{A.1})$$

$$\sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\hat{\boldsymbol{\theta}}_{jj'}^{[g]} - \boldsymbol{\theta}_{0,jj'}^{[g]}\| \leq 48s_j\gamma_n/\psi \quad (\text{A.2})$$

Also denote the non-zero support of $\hat{\Theta}_j$ by $\hat{\mathcal{S}}_j$, i.e. $\hat{\mathcal{S}}_j = \{(j', g) : \hat{\boldsymbol{\theta}}_{jj'}^{[g]} \neq \mathbf{0}\}$. Then

$$|\hat{\mathcal{S}}_j| \leq 128s_j/\psi \quad (\text{A.3})$$

Step 2: Edge set selection. We denote the selected edge set for the k^{th} Y-network by \hat{E}^k . Denote its population version by E_0^k . Further, let

$$\tilde{\Omega}_y^k = \text{diag}(\Omega_y^k) + \Omega_{y, E_0^k \cap \hat{E}^k}^k$$

With similar derivations to the proof of Corollary A.1 in Ma and Michailidis (2016), The following two upper bounds can be established:

$$|\hat{E}^k| \leq \frac{128S}{\psi} \quad (\text{A.4})$$

$$\frac{1}{K} \sum_{k=1}^K \|\tilde{\Omega}_y^k - \Omega_y^k\|_F \leq \frac{12c_0\sqrt{S}\gamma_n}{\sqrt{K}\psi} \quad (\text{A.5})$$

following which, taking $\gamma_n = 4\sqrt{|g_{\max}|}\mathbb{Q}_0$,

$$\Lambda_{\min}(\tilde{\Omega}_y^k) \geq d_0 - \frac{48c_0\mathbb{Q}_0\sqrt{|g_{\max}|S}}{\psi} \geq (1 - t_1)d_0 > 0 \quad (\text{A.6})$$

$$\Lambda_{\max}(\tilde{\Omega}_y^k) \leq c_0 + \frac{48c_0\mathbb{Q}_0\sqrt{|g_{\max}|S}}{\psi} \leq c_0 + t_1d_0 < \infty \quad (\text{A.7})$$

with $0 < t_1 < 1$, and the sample size n satisfying

$$n \geq |g_{\max}|S \left[\frac{48c_0\mathbb{Q}_0}{\psi t_1 d_0} \right]^2; \quad \mathbb{Q}_0 := \sqrt{n}\mathbb{Q}_0$$

Step 3: Refitting. Following the same steps as part A.3 in the proof of Theorem 4.1 in Ma and Michailidis (2016), it can be proven using (A.4)–(A.7) that

$$\sum_{k=1}^K \|\hat{\Omega}_y^k - \tilde{\Omega}_y^k\|^2 \leq O(Q_0^2 |g_{\max}| S)$$

The proof is now complete by combining this with (A.5) then applying Cauchy-Schwarz inequality and triangle inequality. \square

Proof of Proposition 4.2. We drop the superscript k since there is no scope of ambiguity. For part 1, we start with an auxiliary lemma:

Lemma A.2. *For a sub-gaussian design matrix $\mathbf{X} \in \mathbb{M}(n, p)$ with columns having mean $\mathbf{0}_p$ and covariance matrix Σ_x , the sample covariance matrix $\hat{\Sigma}_x = \mathbf{X}^T \mathbf{X} / n$ satisfies the RE condition*

$$\hat{\Sigma}_x \sim RE \left(\frac{\Lambda_{\min}(\Sigma_x)}{2}, \frac{\Lambda_{\min}(\Sigma_x) \log p}{2n} \right)$$

with probability $\geq 1 - 2 \exp(-c_3 n)$ for some $c_3 > 0$.

Now denote $\hat{\mathbf{E}} = \mathbf{Y} - \mathbf{X}\hat{\mathbf{B}}$. For $\mathbf{v} \in \mathbb{R}^q$, we have

$$\begin{aligned} \mathbf{v}^T \hat{\mathbf{S}} \mathbf{v} &= \frac{1}{n} \|\hat{\mathbf{E}} \mathbf{v}\|^2 \\ &= \frac{1}{n} \|(\mathbf{E} + \mathbf{X}(\mathbf{B}_0 - \hat{\mathbf{B}})) \mathbf{v}\|^2 \\ &= \mathbf{v}^T \mathbf{S} \mathbf{v} + \frac{1}{n} \|\mathbf{X}(\mathbf{B}_0 - \hat{\mathbf{B}}) \mathbf{v}\|^2 + 2 \mathbf{v}^T (\mathbf{B}_0 - \hat{\mathbf{B}})^T \left(\frac{(\mathbf{X})^T \mathbf{E}}{n} \right) \mathbf{v} \end{aligned} \quad (\text{A.8})$$

For the first summand, $\mathbf{v}^T \mathbf{S} \mathbf{v} \geq \psi_y \|\mathbf{v}\|^2 - \phi_y \|\mathbf{v}\|_1^2$ with $\psi_y = \Lambda_{\min}(\Sigma_y)/2$, $\phi_y = \psi_y \log p / n$ by applying Lemma A.2 on \mathbf{S} . The second summand is greater than or equal to 0. For the third summand,

$$2 \mathbf{v}^T (\mathbf{B}_0 - \hat{\mathbf{B}})^T \left(\frac{(\mathbf{X})^T \mathbf{E}}{n} \right) \mathbf{v} \geq -2v_\beta \left\| \frac{(\mathbf{X})^T \mathbf{E}}{n} \right\|_\infty \|\mathbf{v}\|_1^2$$

by assumption (T1). Now we use another lemma:

Lemma A.3. *For zero-mean independent sub-gaussian matrices $\mathbf{X} \in \mathbb{M}(n, p)$, $\mathbf{E} \in \mathbb{M}(n, q)$ with parameters (Σ_x, σ_x^2) and (Σ_e, σ_e^2) respectively, given that $n \gtrsim \log(pq)$ the following holds with probability $\geq 1 - 6c_1 \exp[-(c_2^2 - 1) \log(pq)]$ for some $c_1 > 0$, $c_2 > 1$:*

$$\frac{1}{n} \|\mathbf{X}^T \mathbf{E}\|_\infty \leq c_2 [\Lambda_{\max}(\Sigma_x) \Lambda_{\max}(\Sigma_e)]^{1/2} \sqrt{\frac{\log(pq)}{n}}$$

Subsequently we collect all summands in (A.8) and get

$$\mathbf{v}^T \widehat{\mathbf{S}} \mathbf{v} \geq \psi_y \|\mathbf{v}\|^2 - \left(\phi_y + 2v_\beta c_2 [\Lambda_{\max}(\Sigma_x) \Lambda_{\max}(\Sigma_y)]^{1/2} \sqrt{\frac{\log(pq)}{n}} \right) \|\mathbf{v}\|_1^2$$

with probability $\geq 1 - 2 \exp(-c_3 n) - 6c_1 \exp[-(c_2^2 - 1) \log(pq)]$. This concludes the proof of part 1.

To prove part 2, we decompose the quantity in question:

$$\begin{aligned} \left\| \frac{1}{n} \widehat{\mathbf{E}}_{-j}^T \widehat{\mathbf{E}} \mathbf{T}_{0,j} \right\|_\infty &= \left\| \frac{1}{n} [\mathbf{E}_{-j} + \mathbf{X}(\mathbf{B}_{0,j} - \widehat{\mathbf{B}}_j)]^T [\mathbf{E} + \mathbf{X}(\mathbf{B}_0 - \widehat{\mathbf{B}})] \mathbf{T}_{0,j} \right\|_\infty \\ &\leq \left\| \frac{1}{n} \mathbf{E}_{-j}^T \mathbf{E} \mathbf{T}_{0,j} \right\|_\infty + \left\| \frac{1}{n} \mathbf{E}_{-j}^T \mathbf{X}(\mathbf{B}_0 - \widehat{\mathbf{B}}) \mathbf{T}_{0,j} \right\|_\infty \\ &\quad + \left\| \frac{1}{n} (\mathbf{B}_{0,j} - \widehat{\mathbf{B}}_j)^T \mathbf{X}^T \mathbf{X}(\mathbf{B}_0 - \widehat{\mathbf{B}}) \mathbf{T}_{0,j} \right\|_\infty + \left\| \frac{1}{n} (\mathbf{B}_{0,j} - \widehat{\mathbf{B}}_j)^T \mathbf{X}^T \mathbf{E} \mathbf{T}_{0,j} \right\|_\infty \\ &= \|\mathbf{W}_1\|_\infty + \|\mathbf{W}_2\|_\infty + \|\mathbf{W}_3\|_\infty + \|\mathbf{W}_4\|_\infty \end{aligned} \quad (\text{A.9})$$

Now

$$\mathbf{W}_1 = \frac{1}{n} \mathbf{E}_{-j}^T (\mathbf{E}_j - \mathbf{E}_{-j} \boldsymbol{\theta}_{0,j})$$

For node j in the y -network, \mathbb{E}_{-j} and $E_j - \mathbb{E}_{-j} \boldsymbol{\theta}_{0,j}$ are the neighborhood regression coefficients and residuals, respectively. Thus they are orthogonal, so we can apply Lemma A.3 on \mathbf{E}_{-j} and $\mathbf{E}_j - \mathbf{E}_{-j} \boldsymbol{\theta}_{0,j}$ to obtain that for $n \gtrsim \log(q-1)$,

$$\|\mathbf{W}_1\|_\infty \leq c_5 [\Lambda_{\max}(\Sigma_{y,-j}) \sigma_{y,j,-j}]^{1/2} \sqrt{\frac{\log(q-1)}{n}} \quad (\text{A.10})$$

holds with probability $\geq 1 - 6c_4 \exp[-(c_5^2 - 1) \log(pq)]$ for some $c_4 > 0, c_5 > 1$.

The same bounds hold for \mathbf{W}_2 and \mathbf{W}_4 :

$$\begin{aligned} \|\mathbf{W}_2\|_\infty &\leq \left\| \frac{1}{n} \mathbf{E}_{-j}^T \mathbf{X}(\mathbf{B}_0 - \widehat{\mathbf{B}}) \right\|_\infty \|\mathbf{T}_{0,j}\|_1 \leq \left\| \frac{1}{n} \mathbf{E}^T \mathbf{X} \right\|_\infty \|\mathbf{B}_0 - \widehat{\mathbf{B}}\|_1 \|\mathbf{T}_{0,j}\|_1 \\ \|\mathbf{W}_4\|_\infty &\leq \left\| \frac{1}{n} (\mathbf{B}_{0,j} - \widehat{\mathbf{B}}_j)^T \mathbf{X}^T \mathbf{E} \right\|_\infty \|\mathbf{T}_{0,j}\|_1 \leq \left\| \frac{1}{n} \mathbf{E}^T \mathbf{X} \right\|_\infty \|\mathbf{B}_0 - \widehat{\mathbf{B}}\|_1 \|\mathbf{T}_{0,j}\|_1 \end{aligned}$$

Now since Ω_y is diagonally dominant, $|\omega_{y,jj}| \geq \sum_{j' \neq j} |\omega_{y,jj'}|$ for any $j \in \mathcal{I}_q$. Hence

$$\|\mathbf{T}_{0,j}\|_1 = \sum_{j'=1}^q |T_{jj'}| = 1 + \sum_{j' \neq j} |\theta_{jj'}| = 1 + \frac{1}{\omega_{y,jj}} \sum_{j' \neq j} |\omega_{y,jj'}| \leq 2$$

so that for $n \gtrsim \log(pq)$,

$$\|\mathbf{W}_2\|_\infty + \|\mathbf{W}_4\|_\infty \leq 4v_\beta c_2 [\Lambda_{\max}(\Sigma_x) \Lambda_{\max}(\Sigma_y)]^{1/2} \sqrt{\frac{\log(pq)}{n}} \quad (\text{A.11})$$

with probability $\geq 1 - 6c_1 \exp[-(c_2^2 - 1) \log(pq)]$ by applying Lemma A.3 and assumption (T1).

Finally for \mathbf{W}_3 , we apply Lemma 8 of Ravikumar et al. (2011) on the (sub-gaussian) design matrix \mathbf{X} to obtain that for sample size

$$n \geq 512(1 + 4\Lambda_{\max}(\Sigma_x^k))^4 \max_i(\sigma_{x,ii}^k)^4 \log(4p^{\tau_1}) \quad (\text{A.12})$$

we get that with probability $\geq 1 - 1/p^{\tau_1-2}$, $\tau_1 > 2$,

$$\left\| \frac{\mathbf{X}^T \mathbf{X}}{n} \right\|_{\infty} \leq \sqrt{\frac{\log 4 + \tau_1 \log p}{c_x n}} + \max_i \sigma_{x,ii} = V_x; \quad c_x = \left[128(1 + 4\Lambda_{\max}(\Sigma_x))^2 \max_i(\sigma_{x,ii})^2 \right]^{-1}$$

Thus with the same probability,

$$\|\mathbf{W}_4\|_{\infty} \leq \left\| \frac{\mathbf{X}^T \mathbf{X}}{n} \right\|_{\infty} \|\hat{\mathbf{B}} - \mathbf{B}_0\|_1^2 \|\mathbf{T}_{0,j}\|_1 \leq 2v_{\beta}^2 V_x \quad (\text{A.13})$$

We now bound the right hand side of (A.9) using (A.10), (A.11) and (A.13) to complete the proof, with the leading term of the sample size requirement being $n \gtrsim \log(pq)$. \square

Proof of Theorem 4.4. The proof follows that of Proposition A.1, with a different group norm structure. We only point out the differences.

Putting $\boldsymbol{\beta} = \boldsymbol{\beta}_0$ in (4.1) we get

$$-2\hat{\boldsymbol{\beta}}^T \hat{\boldsymbol{\gamma}} + \boldsymbol{\beta}^T \hat{\boldsymbol{\Gamma}} \hat{\boldsymbol{\beta}} + \lambda_n \sum_{h \in \mathcal{H}} \|\hat{\boldsymbol{\beta}}^{[h]}\| \leq -2\boldsymbol{\beta}_0^T \hat{\boldsymbol{\gamma}} + \boldsymbol{\beta}_0^T \hat{\boldsymbol{\Gamma}} \boldsymbol{\beta}_0 + \lambda_n \sum_{h \in \mathcal{H}} \|\boldsymbol{\beta}_0^{[h]}\|$$

Denote $\mathbf{b} = \hat{\boldsymbol{\beta}} - \boldsymbol{\beta}_0$. Then we have

$$\mathbf{b}^T \hat{\boldsymbol{\Gamma}} \mathbf{b} \leq 2\mathbf{b}^T (\hat{\boldsymbol{\gamma}} - \hat{\boldsymbol{\Gamma}} \boldsymbol{\beta}_0) + \lambda_n \sum_{h \in \mathcal{H}} (\|\boldsymbol{\beta}_0^{[h]}\| - \|\boldsymbol{\beta}_0^{[h]} + \mathbf{b}^{[h]}\|)$$

Proceeding similarly as the proof of Proposition A.1, with a different deviation bound and choice of λ_n , we get expressions equivalent to (B.3) and (B.4) respectively:

$$\mathbf{b}^T \hat{\boldsymbol{\Gamma}} \mathbf{b} \leq \frac{3}{2} \sum_{h \in \mathcal{H}} \|\mathbf{b}^{[h]}\| \quad (\text{A.14})$$

$$\frac{\psi^*}{3} \|\mathbf{b}\|^2 \leq \lambda_n \sum_{h \in \mathcal{H}} \|\mathbf{b}^{[h]}\| \leq 4\lambda_n \sqrt{s_{\beta}} \|\mathbf{b}\| \quad (\text{A.15})$$

Furthermore, $\|\mathbf{b}\|_1 \leq \sqrt{h_{\max}} \sum_{h \in \mathcal{H}} \|\mathbf{b}^{[h]}\|$. The bounds in (4.3), (4.4), (4.5) and (4.6) now follow. \square

Proof of Proposition 4.5. For part 1 it is enough to prove that with $\widehat{\Sigma}_x^k := (\mathbf{X}^k)^T \mathbf{X}^k / n$,

$$\widehat{\mathbf{T}}_k^2 \otimes \widehat{\Sigma}_x^k \sim RE(\psi_*, \phi_*) \quad (\text{A.16})$$

with high enough probability. because then we can take $\psi_* = \min_k \psi_*^k, \phi_* = \max_k \phi_*^k$. The proof of (A.16) follows similar lines of the proof of Proposition 1 in Lin et al. (2016), only replacing $\Theta_\epsilon, \widehat{\Theta}_\epsilon, \mathbf{X}$ therein with $(\mathbf{T}^k)^2, (\widehat{\mathbf{T}}^k)^2, \mathbf{X}^k$, respectively. We omit the details.

Part 2 follows the proof of Proposition 2 in Lin et al. (2016). \square

Proof of Theorem 5.1. Let us define the following:

$$\begin{aligned} \widehat{\Omega}_y &= \text{diag}(\widehat{\Omega}_y^1, \widehat{\Omega}_y^2) \\ \mathbf{M}_i &= \text{diag}(m_i^1, m_i^2) \\ \widehat{\mathbf{C}}_i &= \text{diag}(\widehat{\mathbf{c}}_i^1, \widehat{\mathbf{c}}_i^2) \\ \widehat{\mathbf{D}}_i &= \text{diag}(\widehat{\mathbf{b}}_i^1, \widehat{\mathbf{b}}_i^2) \\ \mathbf{D}_i &= \text{diag}(\mathbf{b}_{0,i}^1, \mathbf{b}_{0,i}^2) \\ \mathbf{R}_i^k &= \mathbf{X}_i^k - \mathbf{X}_{-i}^k \widehat{\mathbf{C}}_i^k; k = 1, 2 \end{aligned}$$

Then from (5.2) we have

$$\mathbf{M}_i(\widehat{\mathbf{C}}_i - \widehat{\mathbf{D}}_i)^T = \frac{1}{\sqrt{n}} \begin{bmatrix} \frac{1}{\widehat{s}_i^1} (\mathbf{R}_i^1)^T \widehat{\mathbf{E}}^1 \\ \frac{1}{\widehat{s}_i^2} (\mathbf{R}_i^2)^T \widehat{\mathbf{E}}^2 \end{bmatrix} \quad (\text{A.17})$$

We now decompose $\widehat{\mathbf{E}}^k$:

$$\begin{aligned} \widehat{\mathbf{E}}^k &= \mathbf{Y}^k - \mathbf{X}^k \widehat{\mathbf{B}}^k \\ &= \mathbf{E}^k + \mathbf{X}^k (\mathbf{B}_0^k - \widehat{\mathbf{B}}^k) \\ &= \mathbf{E}^k + \mathbf{X}_i^k (\mathbf{b}_{0,i}^k - \widehat{\mathbf{b}}_i^k) + \mathbf{X}_{-i}^k (\mathbf{B}_{0,-i}^k - \widehat{\mathbf{B}}_{-i}^k) \end{aligned}$$

Putting them back in (A.17) and using $t^k = (\mathbf{R}^k)^T \mathbf{X}^k / n$,

$$\begin{aligned} \mathbf{M}_i(\widehat{\mathbf{C}}_i - \widehat{\mathbf{D}}_i)^T &= \frac{1}{\sqrt{n}} \begin{bmatrix} \frac{1}{\widehat{s}_i^1} (\mathbf{R}_i^1)^T \mathbf{E}^1 \\ \frac{1}{\widehat{s}_i^2} (\mathbf{R}_i^2)^T \mathbf{E}^2 \end{bmatrix} + \mathbf{M}_i(\mathbf{D}_i - \widehat{\mathbf{D}}_i)^T + \frac{1}{\sqrt{n}} \begin{bmatrix} \frac{1}{\widehat{s}_i^1} (\mathbf{R}_i^1)^T \mathbf{X}_{-i}^1 (\mathbf{B}_{0,-i}^1 - \widehat{\mathbf{B}}_{-i}^1) \\ \frac{1}{\widehat{s}_i^2} (\mathbf{R}_i^2)^T \mathbf{X}_{-i}^2 (\mathbf{B}_{0,-i}^2 - \widehat{\mathbf{B}}_{-i}^2) \end{bmatrix} \\ \Rightarrow \widehat{\Omega}_y^{1/2} \mathbf{M}_i(\widehat{\mathbf{C}}_i - \mathbf{D}_i)^T &= \frac{\widehat{\Omega}_y^{1/2}}{\sqrt{n}} \begin{bmatrix} \frac{1}{\widehat{s}_i^1} (\mathbf{R}_i^1)^T \mathbf{E}^1 \\ \frac{1}{\widehat{s}_i^2} (\mathbf{R}_i^2)^T \mathbf{E}^2 \end{bmatrix} + \frac{\widehat{\Omega}_y^{1/2}}{\sqrt{n}} \begin{bmatrix} \frac{1}{\widehat{s}_i^1} (\mathbf{R}_i^1)^T \mathbf{X}_{-i}^1 (\mathbf{B}_{0,-i}^1 - \widehat{\mathbf{B}}_{-i}^1) \\ \frac{1}{\widehat{s}_i^2} (\mathbf{R}_i^2)^T \mathbf{X}_{-i}^2 (\mathbf{B}_{0,-i}^2 - \widehat{\mathbf{B}}_{-i}^2) \end{bmatrix} \quad (\text{A.18}) \end{aligned}$$

At this point, we drop k in the subscripts, and prove the following:

Lemma A.4. *Given conditions (C1) and (C2), the following holds for sample size n such that $n \gtrsim \log(pq)$ and $\sigma_{x,i,-i} - n^{-1/4} - v_\zeta^2 V_x > 0$:*

$$\frac{1}{\sqrt{n\widehat{s}_i}} \widehat{\Omega}_y^{1/2} \mathbf{E}^T \mathbf{R}_i \sim \mathcal{N}_q(\mathbf{0}, \mathbf{I}) + \mathbf{S}_{1n};$$

$$\|\mathbf{S}_{1n}\|_\infty \leq \frac{v_\Omega \sqrt{\Lambda_{\max}(\Sigma_e)}}{\sigma_{x,i,-i} - n^{-1/4} - v_\zeta^2 V_x} \left[c_7 \sqrt{\sigma_{x,ii} \log q} + c_9 (1 + v_\zeta^2) \sqrt{\Lambda_{\max}(\Sigma_{x,-i}) \log(pq)} \right] \quad (\text{A.19})$$

with probability larger than or equal to

$$1 - 6c_6 e^{-(c_7^2 - 1) \log q} - 6c_8 e^{-(c_9^2 - 1) \log(pq)} - \frac{1}{p^{\tau_1 - 2}} - \frac{\kappa_i}{\sqrt{n}} \quad (\text{A.20})$$

for some $c_6, c_8 > 0, c_7, c_9 > 1$, and $\kappa_i := \mathbb{V}[(X_i - \mathbb{X}_{-i} \zeta_{0,-i})^2]$. Additionally, given condition (C3)

$$\left\| \frac{1}{\sqrt{n\widehat{s}_i}} \mathbf{R}_i^T \mathbf{X}_{-i} (\mathbf{B}_{0,-i} - \widehat{\mathbf{B}}_{-i}) \widehat{\Omega}_y^{1/2} \right\|_\infty \leq \frac{v_\beta (\Lambda_{\min}(\Sigma_y)^{1/2} + v_\Omega)}{\sigma_{x,i,-i} - n^{-1/2} - v_\zeta^2 V_x} \times \left[c_{11} \sqrt{(\sigma_{x,i,-i} \Lambda_{\max}(\Sigma_{x,-i})) \log p} + \sqrt{n} v_\zeta V_x \right] \quad (\text{A.21})$$

with probability $\geq 1 - 6c_{10} \exp[-(c_{11}^2 - 1) \log(p - 1)] - (1/p)^{\tau_1 - 2} - \kappa_i/\sqrt{n}$ for some $c_{10} > 0, c_{11} > 1$.

Given Lemma A.4, the first and second summands on the right hand side of (A.18) are bounded above by applying each of (A.19) and (A.21) twice, respectively. This completes our proof. \square

Proof of Theorem 5.2. \square

B Proof of auxiliary results

Proof of Proposition A.1. In its reparametrized version, (4.2) becomes

$$\widehat{\mathbf{T}}_j = \arg \min_{\mathbf{T}_j} \left\{ \frac{1}{n} \sum_{k=1}^K \|(\mathbf{Y}^k - \mathbf{X}^k \widehat{\mathbf{B}}^k) \mathbf{T}_j^k\|^2 + \gamma_n \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\mathbf{T}_{jj'}^{[g]}\| \right\} \quad (\text{B.1})$$

with $\mathbf{T}_{jj'}^{[g]} := (T_{jj'}^k)_{k \in g}$. Now for any $\mathbf{T}_j \in \mathbb{M}(q, K)$ we have

$$\frac{1}{n} \sum_{k=1}^K \|(\mathbf{Y}^k - \mathbf{X}^k \widehat{\mathbf{B}}^k) \widehat{\mathbf{T}}_j^k\|^2 + \gamma_n \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\widehat{\mathbf{T}}_{jj'}^{[g]}\| \leq \frac{1}{n} \sum_{k=1}^K \|(\mathbf{Y}^k - \mathbf{X}^k \widehat{\mathbf{B}}^k) \mathbf{T}_j^k\|^2 + \gamma_n \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\mathbf{T}_{jj'}^{[g]}\|$$

For $\mathbf{T}_j = \mathbf{T}_{0,j}$ this reduces to

$$\sum_{k=1}^K (\mathbf{d}_j^k)^T \widehat{\mathbf{S}}^k \mathbf{d}_j^k \leq -2 \sum_{k=1}^K (\mathbf{d}_j^k)^T \widehat{\mathbf{S}}^k \mathbf{T}_{0,j}^k + \gamma_n \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \left(\|\mathbf{T}_{jj'}^{[g]}\| - \|\mathbf{T}_{jj'}^{[g]} + \mathbf{d}_{jj'}^{[g]}\| \right) \quad (\text{B.2})$$

with $\mathbf{d}_j^k := \widehat{\mathbf{T}}_j^k - \mathbf{T}_{0,j}^k$ etc. For the k^{th} summand in the first term on the right hand side, since $\mathbf{d}_{jj}^k = 0$, $\widehat{\mathbf{E}}^k \mathbf{d}_j^k = \widehat{\mathbf{E}}_{-j}^k \mathbf{d}_{-j}^k$. Thus

$$\begin{aligned} \sum_{k=1}^K \left| (\mathbf{d}_j^k)^T \widehat{\mathbf{S}}^k \mathbf{T}_{0,j}^k \right| &= \sum_{k=1}^K \left| \mathbf{d}_j^k \cdot \frac{1}{n} (\widehat{\mathbf{E}}^k)^T \widehat{\mathbf{E}}^k \mathbf{T}_{0,j}^k \right| \\ &\leq \sum_{k=1}^K \left\| \frac{1}{n} (\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k \mathbf{T}_{0,j}^k \right\|_{\infty} \|\mathbf{d}_{-j}^k\|_1 \\ &\leq \mathbb{Q}_0 \sqrt{|g_{\max}|} \sum_{j \neq j', g \in \mathcal{G}} \|\mathbf{d}_{jj'}^{[g]}\| \end{aligned}$$

by assumption (T2). For the second term, suppose $\mathcal{S}_{0,j}$ is the support of $\Theta_{0,j}$, i.e. $\mathcal{S}_{0,j} = \{(j', g) : \boldsymbol{\theta}_{jj'}^{[g]} \neq 0\}$. Then

$$\begin{aligned} \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \left(\|\mathbf{T}_{jj'}^{[g]}\| - \|\mathbf{T}_{jj'}^{[g]} + \mathbf{d}_{jj'}^{[g]}\| \right) &\leq \sum_{(j', g) \in \mathcal{S}_{0,j}} \left(\|\mathbf{T}_{jj'}^{[g]}\| - \|\mathbf{T}_{jj'}^{[g]} + \mathbf{d}_{jj'}^{[g]}\| \right) - \sum_{(j', g) \notin \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \\ &\leq \sum_{(j', g) \in \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| - \sum_{(j', g) \notin \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \end{aligned}$$

so that by choice of γ_n (B.2) reduces to

$$\begin{aligned} \sum_{k=1}^K (\mathbf{d}_j^k)^T \widehat{\mathbf{S}}^k \mathbf{d}_j^k &\leq \frac{\gamma_n}{2} \left[\sum_{(j', g) \in \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| + \sum_{(j', g) \notin \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \right] + \gamma_n \left[\sum_{(j', g) \in \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| - \sum_{(j', g) \notin \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \right] \\ &= \frac{3\gamma_n}{2} \sum_{(j', g) \in \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| - \frac{\gamma_n}{2} \sum_{(j', g) \notin \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \\ &\leq \frac{3\gamma_n}{2} \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\mathbf{d}_{jj'}^{[g]}\| \quad (\text{B.3}) \end{aligned}$$

Since the left hand side is ≥ 0 , this also implies

$$\sum_{(j', g) \notin \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \leq 3 \sum_{(j', g) \in \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \Rightarrow \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\mathbf{d}_{jj'}^{[g]}\| \leq 4 \sum_{(j', g) \in \mathcal{S}_{0,j}} \|\mathbf{d}_{jj'}^{[g]}\| \leq 4\sqrt{s_j} \|\mathbf{D}_j\|_F$$

with $\mathbf{D}_j = (\mathbf{d}_j^k)_{k \in \mathcal{I}_K}$. Now the RE condition on $\widehat{\mathbf{S}}^k$ means that

$$\sum_{k=1}^K (\mathbf{d}_j^k)^T \widehat{\mathbf{S}}^k \mathbf{d}_j^k \geq \sum_{k=1}^K (\psi_k \|\mathbf{d}_j^k\|^2 - \phi_k \|\mathbf{d}_j^k\|_1^2) \geq \psi \|\mathbf{D}_j\|_F^2 - \phi \|\mathbf{D}_j\|_1^2 \geq (\psi - Kq\phi) \|\mathbf{D}_j\|_F^2 \geq \frac{\psi}{2} \|\mathbf{D}_j\|_F^2$$

by assumption (T3).

Thus we finally have

$$\frac{\psi}{3} \|\mathbf{D}_j\|_F^2 \leq \gamma_n \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\mathbf{d}_{jj'}^{[g]}\| \leq 4\gamma_n \sqrt{s_j} \|\mathbf{D}_j\|_F \quad (\text{B.4})$$

Since

$$(\mathbf{D}_j)_{j',k} = \widehat{T}_{jj'}^k - T_{0,jj'}^k = \begin{cases} 0 & \text{if } j = j' \\ -(\widehat{\theta}_{jj'}^k - \theta_{0,jj'}^k) & \text{if } j \neq j' \end{cases}$$

The bounds in (A.1) and (A.2) are obtained by replacing the corresponding elements in (B.4).

For the bound on $|\widehat{\mathcal{S}}_j|$, notice that if $\widehat{\boldsymbol{\theta}}_{jj'}^{[g]} \neq 0$ for some (j', g) ,

$$\begin{aligned} \frac{1}{n} \sum_{k \in g} \left| ((\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k (\widehat{\mathbf{T}}_j^k - \mathbf{T}_{0,j}^k))^{j'} \right| &\geq \frac{1}{n} \sum_{k \in g} \left| ((\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k \widehat{\mathbf{T}}_j^k)^{j'} \right| - \frac{1}{n} \sum_{k \in g} \left| ((\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k \mathbf{T}_{0,j}^k)^{j'} \right| \\ &\geq |g| \gamma_n - \sum_{k \in g} \mathbb{Q}(v_\beta, \Sigma_x^k, \Sigma_y^k) \end{aligned}$$

using the KKT condition for (4.2) and assumption (T2). The choice of γ_n now ensures that the right hand side is $\geq 3|g|\gamma_n/4$. Hence

$$\begin{aligned} |\widehat{\mathcal{S}}_j| &\leq \sum_{(j',g) \in \widehat{\mathcal{S}}_j} \frac{16}{9n^2 |g|^2 \gamma_n^2} \sum_{k \in g} \left| ((\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k (\widehat{\mathbf{T}}_j^k - \mathbf{T}_{0,j}^k))^{j'} \right|^2 \\ &\leq \frac{16}{9\gamma_n^2} \sum_{k=1}^K \frac{1}{n} \left\| (\widehat{\mathbf{E}}_{-j}^k)^T \widehat{\mathbf{E}}^k (\widehat{\mathbf{T}}_j^k - \mathbf{T}_{0,j}^k) \right\|^2 \\ &= \frac{16}{9\gamma_n^2} \sum_{k=1}^K (\mathbf{d}_j^k)^T \widehat{\mathbf{S}}^k \mathbf{d}_j^k \\ &\leq \frac{8}{3\gamma_n} \sum_{j \neq j', g \in \mathcal{G}_y^{jj'}} \|\mathbf{d}_{jj'}^{[g]}\| \leq \frac{128s_j}{\psi} \end{aligned}$$

using (B.3) and (B.4). □

Proof of Lemma A.2. This is same as Lemma 2 in Appendix B of Lin et al. (2016) and its proof can be found there. □

Proof of Lemma A.3. This is a part of Lemma 3 of Appendix B in [Lin et al. \(2016\)](#), and is proved therein. \square

Proof of Lemma A.4. To show (A.19) we have

$$\frac{1}{\sqrt{n\hat{s}_i}}\hat{\Omega}_y^{1/2}\mathbf{E}^T\mathbf{R}_i = \frac{1}{\sqrt{n\hat{s}_i}}(\hat{\Omega}_y^{1/2} - \Omega_y^{1/2})\mathbf{E}^T\mathbf{R}_i + \frac{1}{\sqrt{n\hat{s}_i}}\Omega_y^{1/2}\mathbf{E}^T\mathbf{R}_i$$

The second summand is distributed as $\mathcal{N}_q(\mathbf{0}, \mathbf{I})$. For the first summand,

$$\begin{aligned} \frac{1}{\sqrt{n}} \left\| (\hat{\Omega}_y^{1/2} - \Omega_y^{1/2})\mathbf{E}^T\mathbf{R}_i \right\|_\infty &\leq \frac{1}{\sqrt{n}} \left\| \hat{\Omega}_y^{1/2} - \Omega_y^{1/2} \right\|_\infty \left\| \mathbf{E}^T\mathbf{R}_i \right\|_1 \\ &\leq \sqrt{nv\Omega} \frac{1}{n} \left[\left\| \mathbf{E}^T(\mathbf{X}_i - \mathbf{X}_{-i}\boldsymbol{\zeta}_i) \right\|_1 + \left\| \mathbf{E}^T\mathbf{X}_{-i}(\hat{\boldsymbol{\zeta}}_i - \boldsymbol{\zeta}_{0,i}) \right\|_1 \right] \\ &\leq \sqrt{nv\Omega} \frac{1}{n} \left[\left\| \mathbf{E}^T\mathbf{X}_i \right\|_\infty + \left\| \mathbf{E}^T\mathbf{X}_{-i} \right\|_\infty \left\{ \left\| \boldsymbol{\zeta}_i \right\|_1 + \left\| \hat{\boldsymbol{\zeta}}_i - \boldsymbol{\zeta}_{0,i} \right\|_1 \right\} \right] \\ &\leq \sqrt{nv\Omega} \left[\frac{1}{n} \left\| \mathbf{E}^T\mathbf{X}_i \right\|_\infty + \frac{1 + v\zeta^2}{n} \left\| \mathbf{E}^T\mathbf{X}_{-i} \right\|_\infty \right] \end{aligned} \quad (\text{B.5})$$

because Ω_x is diagonally dominant implies $\left\| \boldsymbol{\zeta}_i \right\|_1 = \sum_{i' \neq i} |\omega_{x,ii'}|/\omega_{x,ii} \leq 1$, and using assumption (C1). Applying Lemma A.3 twice we have for $n \gtrsim \log(pq)$,

$$\frac{1}{n} \left\| \mathbf{E}^T\mathbf{X}_i \right\|_\infty \leq c_7 [\sigma_{x,ii} \Lambda_{\max}(\Sigma_e)]^{1/2} \sqrt{\frac{\log q}{n}} \quad (\text{B.6})$$

$$\frac{1}{n} \left\| \mathbf{E}^T\mathbf{X}_{-i} \right\|_\infty \leq c_9 [\Lambda_{\max}(\Sigma_{x,-i}) \Lambda_{\max}(\Sigma_e)]^{1/2} \sqrt{\frac{\log((p-1)q)}{n}} \quad (\text{B.7})$$

with probability $\geq 1 - 6c_6 \exp[-(c_7^2 - 1) \log q] - 6c_8 \exp[-(c_9^2 - 1) \log((p-1)q)]$ for some $c_6, c_8 > 0, c_7, c_9 > 1$.

On the other hand

$$s_i := \frac{1}{n} \left\| \mathbf{X}_i - \mathbf{X}_{-i}\boldsymbol{\zeta}_i \right\|^2 \leq \hat{s}_i + \frac{1}{n} \left\| \mathbf{X}_{-i}(\hat{\boldsymbol{\zeta}}_i - \boldsymbol{\zeta}_{0,i}) \right\|^2 \leq \hat{s}_i + \left\| \hat{\boldsymbol{\zeta}}_i - \boldsymbol{\zeta}_{0,i} \right\|_1^2 \left\| \frac{1}{n} \mathbf{X}_{-i}^T \mathbf{X}_{-i} \right\|_\infty$$

By applying Lemma 8 of [Ravikumar et al. \(2011\)](#),

$$\left\| \frac{1}{n} \mathbf{X}_{-i}^T \mathbf{X}_{-i} \right\|_\infty \leq \left\| \frac{1}{n} \mathbf{X}^T \mathbf{X} \right\|_\infty \leq V_x \quad (\text{B.8})$$

with probability $\geq 1 - 1/p^{\tau_1-2}$, $\tau_1 > 2$, and

$$n \geq 512(1 + 4\Lambda_{\max}(\Sigma_x))^4 \max_i (\sigma_{x,ii})^4 \log(4p^{\tau_1}) \quad (\text{B.9})$$

On the other hand, by Chebyshev inequality, for any $\epsilon > 0$

$$P(|s_i - \sigma_{x,i,-i}| \geq \epsilon) \leq \frac{\mathbb{V}s_i}{\epsilon^2} = \frac{\kappa_i}{n\epsilon^2}$$

Taking $\epsilon = n^{-1/4}$, we have $s_i \geq \sigma_{x,i,-i} - n^{-1/4}$ with probability $\geq 1 - \kappa_i n^{-1/2}$. Then, for n satisfying (B.9) and $\sigma_{x,i,-i} - n^{-1/4} > v_\zeta^2 V_x$, we get the bound with the above probability:

$$\frac{1}{\widehat{s}_i} \leq \frac{1}{\sigma_{x,i,-i} - n^{-1/4} - v_\zeta^2 V_x} \quad (\text{B.10})$$

Combining (B.5), (B.6), (B.7) and (B.10) gives the upper bound for the right hand side of (A.19) with the probability condition (A.20).

To prove (A.21) we have

$$\frac{1}{n} \|\mathbf{R}_i^T \mathbf{X}_{-i}\|_\infty \leq \frac{1}{n} \|(\mathbf{X}_i - \mathbf{X}_{-i} \boldsymbol{\zeta}_{0,i})^T \mathbf{X}_{-i}\|_\infty + \frac{1}{n} \|\mathbf{X}_{-i}^T \mathbf{X}_{-i} (\widehat{\boldsymbol{\zeta}}_i - \boldsymbol{\zeta}_{0,i})\|_\infty \quad (\text{B.11})$$

Applying Lemma A.3, for $n \gtrsim \log(p-1)$ we have

$$\frac{1}{n} \|(\mathbf{X}_i - \mathbf{X}_{-i} \boldsymbol{\zeta}_i)^T \mathbf{X}_{-i}\|_\infty \leq c_{11} [\sigma_{x,i,-i} \Lambda_{\max}(\Sigma_{x,-i})]^{1/2} \sqrt{\frac{\log(p-1)}{n}} \quad (\text{B.12})$$

with probability $\geq 1 - 6c_{10} \exp[-(c_{11}^2 - 1) \log(p-1)]$ for some $c_{10} > 0, c_{11} > 1$. By (B.8), the second term on the right side of (B.11) is bounded above by $v_\zeta V_x$ with probability $\geq 1 - 1/p^{\tau_1-2}$ and n satisfying (B.9). The bound of (A.21) follows by conditions (C2), (C3) and (B.10). \square

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