Supporting Information for "A Hierarchical Integrative Group LASSO (HiGLASSO) framework for analyzing environmental mixtures" by Boss et al.

Web Appendix A: HiGLASSO algorithm

A.1. *Objective Function*

The HiGLASSO objective function is:

$$\begin{aligned}\arg\min_{\boldsymbol{\beta}_j, \boldsymbol{\eta}_{jj'}} \frac{1}{2}\Big\|\boldsymbol{y} - \sum_{j=1}^{S} \boldsymbol{X}_j \boldsymbol{\beta}_j - \sum_{1 \le j < j' \le S} \boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})]\Big\|_2^2 \\ + \lambda_1 \sum_{j=1}^{S} w_j ||\boldsymbol{\beta}_j||_2 + \lambda_2 \sum_{1 \le j < j' \le S} w_{jj'} ||\boldsymbol{\eta}_{jj'}||_2,\end{aligned} \tag{1}$$

$$w_j \equiv \exp\Big\{ - \frac{||\boldsymbol{\beta}_j||_\infty}{\sigma} \Big\} \text{ for } j = 1, \cdots, S, \tag{2}$$

$$w_{jj'} \equiv \exp\Big\{ - \frac{||\boldsymbol{\eta}_{jj'}||_\infty}{\sigma} \Big\} \text{ for } 1 \le j < j' \le S, \tag{3}$$

A.2. *Updating main effect coefficients*

By substituting our weight function (2) into (1), given the current $\hat{\boldsymbol{\beta}}_{j'}$'s with $j' \neq j$ and $\hat{\boldsymbol{\eta}}_{jj'}$'s, the objective function can be written as

$$\arg\min_{\boldsymbol{\beta}_j} \frac{1}{2}\big\|\tilde{\boldsymbol{y}} - \tilde{\boldsymbol{X}}_j \boldsymbol{\beta}_j\big\|_2^2 + \lambda_1 \exp\Big\{ - \frac{||\boldsymbol{\beta}_j||_\infty}{\sigma} \Big\} ||\boldsymbol{\beta}_j||_2, \tag{4}$$

such that

$$\tilde{\boldsymbol{y}} = \boldsymbol{y} - \sum_{k \neq j} \boldsymbol{X}_k \hat{\boldsymbol{\beta}}_k - \sum_{k,l \neq j} \boldsymbol{X}_{kl}[\hat{\boldsymbol{\eta}}_{kl} \odot (\hat{\boldsymbol{\beta}}_k \otimes \hat{\boldsymbol{\beta}}_l)],$$

$$\tilde{\boldsymbol{X}}_j = \boldsymbol{X}_j + \sum_{k<j} \boldsymbol{X}_{kj} \cdot \text{diag}(\hat{\boldsymbol{\eta}}_{kj})(\hat{\boldsymbol{\beta}}_k \otimes \boldsymbol{I}_{p_j}) + \sum_{l>j} \boldsymbol{X}_{jl} \cdot \text{diag}(\hat{\boldsymbol{\eta}}_{jl})(\boldsymbol{I}_{p_j} \otimes \hat{\boldsymbol{\beta}}_l),$$

where $\boldsymbol{I}_{p_j}$ is p_j dimensional identity matrix. $\tilde{\boldsymbol{X}}_j$ and $\tilde{\boldsymbol{y}}$ represent the design matrix and response vector at current step. (4) can be directly solved using gradient descent or the Newton-Raphson algorithm (Bauer and Cai, 2009).

Alternatively, we obtain updating algorithm for $\boldsymbol{\beta}_j$ in closed form using local quadratic approximation (LQA) (Fan and Li, 2001). Let $\mathbf{Pen}_1(\boldsymbol{\beta}_j)$ denote the penalty term in (4). We approximate $\mathbf{Pen}_1(\boldsymbol{\beta}_j)$ by

$$\mathbf{Pen}_1(\boldsymbol{\beta}_j) \approx \mathbf{Pen}_1\left(\hat{\boldsymbol{\beta}}_j^{(m)}\right) + \frac{1}{2}\sum_{k=1}^{p_j} d_{jk}^{(m)}\left[\beta_{jk}^2 - \left(\hat{\beta}_{jk}^{(m)}\right)^2\right]$$

where β_{jk} is the k^{th} element of $\boldsymbol{\beta}_j$, $\hat{\boldsymbol{\beta}}_j^{(m)}$ is the estimate of $\boldsymbol{\beta}_j$ from m^{th} iteration, and d_{jk} is defined through

$$\frac{\partial \mathbf{Pen}_1(\boldsymbol{\beta}_j)}{\partial \beta_{jk}} = d_{jk}\beta_{jk}.$$

By calculating the derivative of $\mathbf{Pen}_1(\boldsymbol{\beta}_j)$, we have

$$d_{jk} = \begin{cases} \exp\Big\{-\frac{||\boldsymbol{\beta}_j||_\infty}{\sigma}\Big\}\big(||\boldsymbol{\beta}_j||_2\big)^{-1}, & \text{if } |\beta_{jk}| \neq ||\boldsymbol{\beta}_j||_\infty \\ \exp\Big\{-\frac{||\boldsymbol{\beta}_j||_\infty}{\sigma}\Big\}\Big[\big(||\boldsymbol{\beta}_j||_2\big)^{-1} - ||\boldsymbol{\beta}_j||_2\big(|\beta_{jk}|\sigma\big)^{-1}\Big], & \text{if } |\beta_{jk}| = ||\boldsymbol{\beta}_j||_\infty. \end{cases} \tag{5}$$

The problem with LQA is that d_{jk}, which represents the second-degree derivative of $\mathbf{Pen}_1(\boldsymbol{\beta}_j)$, might be negative when $|\beta_{jk}| = ||\boldsymbol{\beta}_j||_\infty$. Therefore, it is not guaranteed that the approximated $\mathbf{Pen}_j(\boldsymbol{\beta}_j)$ will be convex.

Pan and Zhao proposed generalized local quadratic approximation (GLQA) to employ convex quadratic approximation to the penalty function (Pan and Zhao, 2016). Let $\mathcal{P}_1(\boldsymbol{\beta}_j)$ denote GLQA of $\mathbf{Pen}_1(\boldsymbol{\beta}_j)$ that satisfies the following three properties

1. $\mathcal{P}_1(\boldsymbol{\beta}_j)$ is convex,
2. $\mathcal{P}_1\left(\hat{\boldsymbol{\beta}}_j^{(m)}\right) = \mathbf{Pen}_1\left(\hat{\boldsymbol{\beta}}_j^{(m)}\right)$,
3. $\frac{\partial \mathcal{P}_1(\boldsymbol{\beta}_j)}{\partial \beta_{jk}}\Big|_{\beta_{jk}=\hat{\beta}_{jk}^{(m)}} = \frac{\partial \mathbf{Pen}_1(\boldsymbol{\beta}_j)}{\partial \beta_{jk}}\Big|_{\beta_{jk}=\hat{\beta}_{jk}^{(m)}}\ \forall\ k.$

A simple choice takes the form of

$$\mathcal{P}_1(\boldsymbol{\beta}_j) = \mathbf{Pen}_1\left(\hat{\boldsymbol{\beta}}_j^{(m)}\right) + \frac{1}{2}\sum_{k=1}^{p_j}\left|d_{jk}^{(m)}\right|\left[(\beta_{jk}^2 + c_1)^2 + c_2\right].$$

Solving c_1 and c_2 according to the second and third conditions gives

$$\mathcal{P}_1(\boldsymbol{\beta}_j) = \mathbf{Pen}_1\left(\hat{\boldsymbol{\beta}}_j^{(m)}\right) + \frac{1}{2}\sum_{k=1}^{p_j}\left|d_{jk}^{(m)}\right|\left[\left(\beta_{jk}^2 - \left(1 - \frac{d_{jk}^{(m)}}{|d_{jk}^{(m)}|}\right)\hat{\beta}_{jk}^{(m)}\right)^2 - \left(\hat{\beta}_{jk}^{(m)}\right)^2\right].$$

Rewriting the $\mathcal{P}_1(\boldsymbol{\beta}_j)$ in matrix form, (4) can be approximated as

$$\frac{1}{2}||\tilde{\boldsymbol{y}} - \tilde{\boldsymbol{X}}_j\boldsymbol{\beta}_j||_2^2 + \frac{1}{2}\lambda_1\boldsymbol{\beta}_j^\top \boldsymbol{D}_j^{(m)}\boldsymbol{\beta}_j - \lambda_1\boldsymbol{c}^{(m)\top}\boldsymbol{\beta}_j + \text{Constant}$$

where

$$\boldsymbol{D}_j^{(m)} = \text{diag}\Big[\Big(d_{j1}^{(m)}, \cdots, d_{jp_j}^{(m)}\Big)\Big] \text{ and}$$

$$\boldsymbol{c}^{(m)} = \Big\{\Big(|d_{j1}^{(m)}| - d_{j1}^{(m)}\Big)\hat{\beta}_{j1}^{(m)}, \cdots, \Big(|d_{jp_j}^{(m)}| - d_{jp_j}^{(m)}\Big)\hat{\beta}_{jp_j}^{(m)}\Big\}^\top.$$

$\boldsymbol{\beta}_j$ can be updated in closed-form as

$$\hat{\boldsymbol{\beta}}_j = \Big(\tilde{\boldsymbol{X}}_j^\top\tilde{\boldsymbol{X}}_j + n\lambda_1\boldsymbol{D}_j^{(m)}\Big)^{-1}\Big(\tilde{\boldsymbol{X}}_j^\top\tilde{\boldsymbol{y}} + \lambda_1 \cdot \boldsymbol{c}^{(m)}\Big). \tag{6}$$

A.3. *Updating scalar terms associated with interactions*

By substituting the specified weight function (3) into (1), given $\hat{\boldsymbol{\beta}}_j$'s, the objective function can be expressed as

$$\underset{\boldsymbol{\eta}_{jj'}}{\arg\min}\ \frac{1}{2}\Big\|\tilde{\boldsymbol{y}} - \sum_{j<j'}\tilde{\boldsymbol{X}}_{jj'}\boldsymbol{\eta}_{jj'}\Big\|_2^2 + \lambda_2\sum_{j<j'}\exp\Big\{-\frac{||\boldsymbol{\eta}_{jj'}||_\infty}{\sigma}\Big\}||\boldsymbol{\eta}_{jj'}||_2 \tag{7}$$

where

$$\tilde{\boldsymbol{y}} = \boldsymbol{y} - \sum_{k=1}^{S}\boldsymbol{X}_k\hat{\boldsymbol{\beta}}_k$$

and

$$\tilde{\boldsymbol{X}}_{jj'} = \boldsymbol{X}_{jj'}\text{diag}\big[(\hat{\boldsymbol{\beta}}_j \otimes \hat{\boldsymbol{\beta}}_{j'})\big] \text{ for } 1 \le j < j' \le S.$$

Let $\mathbf{Pen}_2(\boldsymbol{\eta}_{jj'})$ denote the individual penalty term in (7) and let $\mathcal{P}_2(\boldsymbol{\beta}_{jj'})$ denote GLQA of $\mathbf{Pen}_2(\boldsymbol{\eta}_{jj'})$. We have

$$\mathcal{P}_2(\boldsymbol{\eta}_{jj'}) = \mathbf{Pen}_1\Big(\hat{\boldsymbol{\eta}}_{jj'}^{(m)}\Big) + \frac{1}{2}\sum_{k=1}^{p_jp_{j'}}|d_{jj'k}^{(m)}|\left[\left(\eta_{jj'k}^2 - \left(1 - \frac{d_{jj'k}^{(m)}}{|d_{jj'k}^{(m)}|}\right)\hat{\eta}_{jj'k}^{(m)}\right)^2 - \Big(\hat{\eta}_{jj'k}^{(m)}\Big)^2\right]$$

where $\eta_{jj'k}$ is the k^{th} element of $(p_jp_{j'})-$vector of $\boldsymbol{\eta}_{jj'}$ and $d_{jj'k}$ is similarly defined through

$$\frac{\partial\mathbf{Pen}_2(\boldsymbol{\eta}_{jj'})}{\partial\eta_{jj'k}} = d_{jj'k}\eta_{jj'k}$$

as (5). (7) can be approximated as

$$\frac{1}{2}||\tilde{\boldsymbol{y}} - \tilde{\boldsymbol{X}}\boldsymbol{\eta}||_2^2 + \frac{1}{2}\lambda_2\boldsymbol{\eta}^\top\boldsymbol{D}^{(m)}\boldsymbol{\eta} - \lambda_2\boldsymbol{C}^{(m)\top}\boldsymbol{\eta} + \text{Constant}$$

where $\tilde{\boldsymbol{X}} = [\tilde{\boldsymbol{X}}_{12}, \cdots, \tilde{\boldsymbol{X}}_{S-1,S}]$, $\boldsymbol{\eta} = \big(\boldsymbol{\eta}_{12}^\top, \cdots, \boldsymbol{\eta}_{S-1,S}^\top\big)^\top$,

$$\boldsymbol{D}^{(m)} = \text{diag}\Big[d_{121}^{(m)}, \cdots, d_{12(p_1p_2)}^{(m)}, \cdots, d_{(S-1)S(p_{S-1}p_S)}^{(m)}\Big],$$

and $\boldsymbol{C}^{(m)}$ is a $[S(S-1)/2] \times [\sum_{j<j'} p_j p_{j'}]$ block column vector such that the block corresponding to the interaction between group j and group j' is defined as a vector of length $p_j p_{j'}$ with the k^{th} element equal to $\left(|d_{jj'k}^{(m)}| - d_{jj'k}^{(m)}\right)\hat{\eta}_{jj'k}^{(m)}$. $\boldsymbol{\eta}_{jj'}$s can then be updated in closed form as

$$\hat{\boldsymbol{\eta}} = \left(\tilde{\boldsymbol{X}}^\top \tilde{\boldsymbol{X}} + n\lambda_2 \boldsymbol{D}^{(m)}\right)^{-1} \left(\tilde{\boldsymbol{X}}^\top \tilde{\boldsymbol{y}} + \lambda_2 \cdot \boldsymbol{C}^{(m)}\right). \quad (8)$$

A.4. *Algorithm*

We describe the full algorithm for estimating $\boldsymbol{\beta}_j$'s and $\boldsymbol{\eta}_{jj'}$'s in (1). We first fix $\boldsymbol{\eta}_{jj'}$ to estimate $\boldsymbol{\beta}_j$, then fix $\boldsymbol{\beta}_j$ to estimate $\boldsymbol{\eta}_{jj'}$, and iterate the two steps until convergence. The algorithm can be summarized as follows:

1. Obtain basis-expanded main effect matrices for each covariate, denoted by $\boldsymbol{X}_j$ for $j = 1, \ldots, S$. Normalize $\boldsymbol{X}_j$. Calculate interaction design matrices $\boldsymbol{X}_{jj'}$ from the normalized $\boldsymbol{X}_j$ for $1 \le j \le j' \le S$. Normalize $\boldsymbol{X}_{jj'}$. Orthogonalize $\boldsymbol{X}_j$ and $\boldsymbol{X}_{jj'}$ using QR decomposition and center the response vector $\boldsymbol{y}$. Scale $\boldsymbol{X}_j$ and $\boldsymbol{X}_{jj'}$ to have unit variance.

2. Initialize $\hat{\boldsymbol{\beta}}_j^{(0)}$ for $j = 1, \cdots, S$ and $\hat{\boldsymbol{\eta}}_{jj'}^{(0)}$ for $1 \le j < j' \le S$. Set $m = 1$. A feasible choice for the initialization $\hat{\boldsymbol{\beta}}_j^{(0)}$ and $\hat{\boldsymbol{\eta}}_{jj'}^{(0)}$ can be obtained using the adaptive elastic-net estimator. We use this as the initialization in our implementation.

3. For each j in $1, \cdots, S$, update $\hat{\boldsymbol{\beta}}_j^{(m)}$ via closed-form formula in (6), given $\hat{\boldsymbol{\eta}}_{kj}^{(m-1)}$ and $\hat{\boldsymbol{\beta}}_k^{(m)}$ for $k < j$, and $\hat{\boldsymbol{\eta}}_{jl}^{(m-1)}$ and $\hat{\boldsymbol{\beta}}_l^{(m-1)}$ for $l > j$. A backtracking line search algorithm is followed to guarantee that $\hat{\boldsymbol{\beta}}_j^{(m)}$ leads to a lower value of the objective function (4) than $\hat{\boldsymbol{\beta}}_j^{(m)}$.

4. Given $\hat{\boldsymbol{\beta}}_j^{(m)}$ for $j = 1, \cdots, S$, update the $\hat{\boldsymbol{\eta}}_{jj'}^{(m)}$'s via the closed-form formula in (8). A backtracking line search algorithm is followed to guarantee that the $\hat{\boldsymbol{\eta}}_{jj'}^{(m)}$'s lead to a lower value of the objective function in (7) compared to the $\hat{\boldsymbol{\eta}}_{jj'}^{(m-1)}$'s.

5. Stop if change in the penalized likelihood is less than a pre-specified margin δ, namely
$$|P_n^{(m-1)} - P_n^{(m)}| < \delta.$$
where $P_n^{(m)}$ is the value of (1) evaluated at the $\hat{\boldsymbol{\beta}}_j^{(m)}$'s and $\hat{\boldsymbol{\eta}}_{jj'}^{(m)}$'s.

Remark 2: We note that there is no guarantee that each of the $S+1$ updates decreases the value of penalized least squares criterion since we utilize approximations to the original penalty. We therefore employ a backtracking line search algorithm (Dennis and Schnabel, 1996) to ensure that the penalized least squares criterion monotonically decreases throughout the entire procedure. The maximum amount to move along a given search direction is determined by the Armijo-Goldstein condition (Armijo, 1966).

Remark 3: Steps (3) and (4) in the HiGLASSO algorithm could be easily modified to accommodate objective functions without the least squares criterion. However, closed-form updates may not be avilable, thus requiring one-step gradient descent.

Web Appendix B: Sparsistency proof

B.1. *Notation*

Let $\boldsymbol{X} = [\boldsymbol{X}_1, \cdots, \boldsymbol{X}_S, \boldsymbol{X}_{12}, \cdots, \boldsymbol{X}_{S,S-1}]$ be the design matrix containing main effect and interaction terms. Without loss of generality, we rearrange the group indices so that the first $s_0 \le S$ groups of predictors have nonzero main effects. Suppose there are i_0 nonzero two-way interaction terms out of at most $s_0(s_0 - 1)/2$ possible pairs under strong heredity constraints.

The HiGLASSO estimator is defined as:

$$\begin{aligned}
&\underset{\boldsymbol{\beta}_j, \boldsymbol{\eta}_{jj'}}{\arg\min} \frac{1}{2}\Big\|\boldsymbol{y} - \sum_{j=1}^{S} \boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le j<j'\le S} \boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})]\Big\|_2^2 \\
&+ \lambda_1(n)\sum_{j=1}^{S} w_j(\boldsymbol{\beta}_j)||\boldsymbol{\beta}_j||_2 + \lambda_2(n)\sum_{1\le j<j'\le S} w_{jj'}(\boldsymbol{\eta}_{jj'})||\boldsymbol{\eta}_{jj'}||_2. \qquad (9)
\end{aligned}$$

B.2. *Directional Derivatives of HiGLASSO Objective Function*

Consider the following function

$$f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S}) = \frac{1}{2}\Big\|\boldsymbol{y} - \sum_{j=1}^{S} \boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le j<j'\le S} \boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})]\Big\|_2^2$$

First we will calculate the directional derivative in the $\boldsymbol{u}$ direction with respect to $\boldsymbol{\beta}_k$. By definition the directional derivative is given by:

$$\lim_{t\to 0^+} \frac{f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_{k-1}, \boldsymbol{\beta}_k + t\boldsymbol{u}, \boldsymbol{\beta}_{k+1}, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S}) - f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S})}{t}$$

$$\begin{aligned}
&f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_{k-1}, \boldsymbol{\beta}_k + t\boldsymbol{u}, \boldsymbol{\beta}_{k+1}, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S}) \\
&= \frac{1}{2}\Big\|\boldsymbol{y} - \boldsymbol{X}_k(\boldsymbol{\beta}_k + t\boldsymbol{u}) - \sum_{j\ne k} \boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le k<j'\le S} \boldsymbol{X}_{kj'}[\boldsymbol{\eta}_{kj'} \odot (\boldsymbol{\beta}_k + t\boldsymbol{u} \otimes \boldsymbol{\beta}_{j'})] \\
&- \sum_{1\le j<k\le S} \boldsymbol{X}_{jk}[\boldsymbol{\eta}_{jk} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_k + t\boldsymbol{u})] - \sum_{1\le j<j'\le S: j,j'\ne k} \boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})]\Big\|_2^2
\end{aligned}$$

Note that

$$\boldsymbol{\eta}_{jk} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_k + t\boldsymbol{u}) = \boldsymbol{\eta}_{jk} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_k) + t(\boldsymbol{\eta}_{jk} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{u}))$$

and

$$\boldsymbol{\eta}_{kj'} \odot (\boldsymbol{\beta}_k + t\boldsymbol{u} \otimes \boldsymbol{\beta}_{j'}) = \boldsymbol{\eta}_{kj'} \odot (\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{j'}) + t(\boldsymbol{\eta}_{kj'} \odot (\boldsymbol{u} \otimes \boldsymbol{\beta}_{j'}))$$

Thus, the expression becomes

$$\frac{1}{2}\Big\| \boldsymbol{y} - t\boldsymbol{X}_k\boldsymbol{u} - \sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j - t\sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}[\boldsymbol{\eta}_{kj'}\odot(\boldsymbol{u}\otimes\boldsymbol{\beta}_{j'})]$$

$$-t\sum_{1\le j<k\le S}\boldsymbol{X}_{jk}[\boldsymbol{\eta}_{jk}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{u})] - \sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{\beta}_{j'})]\Big\|_2^2$$

Observe that as we take the limit to 0 we get that the terms with a t^2 term go to 0 and the terms without a t cancel with $f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S})$. Therefore, we only need to keep track of the terms that are linear in t. To simplify notation, let

$$\boldsymbol{y} - \boldsymbol{X}\boldsymbol{\theta} = \boldsymbol{y} - \sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{\beta}_{j'})]$$

Then, the expression becomes

$$\frac{1}{2}\Big\|\boldsymbol{y}-\boldsymbol{X}\boldsymbol{\theta}-t\boldsymbol{X}_k\boldsymbol{u}-t\sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}[\boldsymbol{\eta}_{kj'}\odot(\boldsymbol{u}\otimes\boldsymbol{\beta}_{j'})]-t\sum_{1\le j<k\le S}\boldsymbol{X}_{jk}[\boldsymbol{\eta}_{jk}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{u})]\Big\|_2^2$$

Therefore, the directional derivative is:

$$-\left(\boldsymbol{X}_k\boldsymbol{u}+\sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}[\boldsymbol{\eta}_{kj'}\odot(\boldsymbol{u}\otimes\boldsymbol{\beta}_{j'})]+\sum_{1\le j<k\le S}\boldsymbol{X}_{jk}[\boldsymbol{\eta}_{jk}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{u})]\right)^{\top}\Big(\boldsymbol{y}-\boldsymbol{X}\boldsymbol{\theta}\Big)$$

Lastly, from the proof of Theorem 1 in (Pan and Zhao, 2016), we have that the directional derivative of $\lambda_1(n)w_k(\boldsymbol{\beta}_k)\|\boldsymbol{\beta}_k\|_2$ in the $\boldsymbol{u}$ direction evaluated at zero is $\lambda_1(n)$.

Next we will calculate the directional derivative in the $\boldsymbol{u}$ direction with respect to $\boldsymbol{\eta}_{kk'}$. By definition the directional derivative is given by:

$$\lim_{t\to 0^+}\frac{f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{kk'}+t\boldsymbol{u}, ..., \boldsymbol{\eta}_{S-1,S}) - f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S})}{t},$$

$$f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{kk'}+t\boldsymbol{u}, ..., \boldsymbol{\eta}_{S-1,S}) = \frac{1}{2}\Big\|\boldsymbol{y}-\sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j-\boldsymbol{X}_{kk'}[(\boldsymbol{\eta}_{kk'}+t\boldsymbol{u})\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'})]$$

$$-\sum_{1\le j<j'\le S:(j,j')\ne(k,k')}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{\beta}_{j'})]\Big\|_2^2$$

Again, note that

$$(\boldsymbol{\eta}_{kk'}+t\boldsymbol{u})\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'}) = \boldsymbol{\eta}_{kk'}\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'}) + t(\boldsymbol{u}\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'}))$$

Thus the expression becomes

$$\frac{1}{2}\Big\|\boldsymbol{y} - \sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})] - t\boldsymbol{X}_{kk'}[\boldsymbol{u} \odot (\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{k'})]\Big\|_2^2$$

$$= \frac{1}{2}\Big\|\boldsymbol{y} - \boldsymbol{X\theta} - t\boldsymbol{X}_{kk'}[\boldsymbol{u} \odot (\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{k'})]\Big\|_2^2$$

Following the same argument as above the directional derivative of $\boldsymbol{\beta}_k$, as we take the limit to 0 we get that the terms with a t^2 term go to 0 and the terms without a t cancel with $f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S})$. Therefore, we only need to keep track of the terms that are linear in t. That is, the directional derivative is,

$$-\Big(\boldsymbol{X}_{kk'}[\boldsymbol{u} \odot (\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{k'})]\Big)^{\top}\Big(\boldsymbol{y} - \boldsymbol{X\theta}\Big)$$

Again, from the proof of Theorem 1 in (Pan and Zhao, 2016), we have that the directional derivative of $\lambda_2(n)w_{kk'}(\boldsymbol{\eta}_{kk'})\|\boldsymbol{\eta}_{kk'}\|_2$ in the $\boldsymbol{u}$ direction evaluated at zero is $\lambda_2(n)$.

B.3. *Derivative of HiGLASSO Objective Function*

First we calculate the derivative with respect to $\boldsymbol{\beta}_k$:

$$\frac{\partial}{\partial\boldsymbol{\beta}_k}f(\boldsymbol{\beta}_1, ..., \boldsymbol{\beta}_S, \boldsymbol{\eta}_{12}, ..., \boldsymbol{\eta}_{S-1,S}) = \frac{\partial}{\partial\boldsymbol{\beta}_k}\left[\frac{1}{2}\Big\|\boldsymbol{y} - \sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})]\Big\|_2^2\right]$$

$$= \left(\frac{\partial}{\partial\boldsymbol{\beta}_k}\left[\boldsymbol{y} - \sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j - \sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_{j'})]\right]\right)^{\top}\Big(\boldsymbol{y} - \boldsymbol{X\theta}\Big)$$

$$= \left(\frac{\partial}{\partial\boldsymbol{\beta}_k}\left[-\boldsymbol{X}_k\boldsymbol{\beta}_k - \sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}[\boldsymbol{\eta}_{kj'} \odot (\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{j'})] - \sum_{1\le j<k\le S}\boldsymbol{X}_{jk}[\boldsymbol{\eta}_{jk} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_k)]\right]\right)^{\top}\Big(\boldsymbol{y} - \boldsymbol{X\theta}\Big)$$

$$= -\left[\boldsymbol{X}_k + \sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}\frac{\partial}{\partial\boldsymbol{\beta}_k}[\boldsymbol{\eta}_{kj'} \odot (\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{j'})] + \sum_{1\le j<k\le S}\boldsymbol{X}_{jk}\frac{\partial}{\partial\boldsymbol{\beta}_k}[\boldsymbol{\eta}_{jk} \odot (\boldsymbol{\beta}_j \otimes \boldsymbol{\beta}_k)]\right]^{\top}\Big(\boldsymbol{y} - \boldsymbol{X\theta}\Big)$$

$$= -\left[\boldsymbol{X}_k + \sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}\left[\text{diag}\big(\boldsymbol{\eta}_{kj'}\big)\frac{\partial}{\partial\boldsymbol{\beta}_k}(\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{j'})\right]\right.$$

$$+\sum_{1\le j<k\le S} \boldsymbol{X}_{jk}\Big[\mathrm{diag}\big(\boldsymbol{\eta}_{jk}\big)\frac{\partial}{\partial \boldsymbol{\beta}_k}(\boldsymbol{\beta}_j\otimes\boldsymbol{\beta}_k)\Big]\Big]^\top\Big(\boldsymbol{y}-\boldsymbol{X\theta}\Big)$$

$$=-\Big[\boldsymbol{X}_k+\sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}\Big[\mathrm{diag}\big(\boldsymbol{\eta}_{kj'}\big)(\boldsymbol{I}\otimes\boldsymbol{\beta}_{j'})\Big]+\sum_{1\le j<k\le S}\boldsymbol{X}_{jk}\Big[\mathrm{diag}\big(\boldsymbol{\eta}_{jk}\big)(\boldsymbol{\beta}_j\otimes\boldsymbol{I})\Big]\Big]^\top\Big(\boldsymbol{y}-\boldsymbol{X\theta}\Big)$$

The derivative of the penalty function is:

$$\frac{\partial}{\partial\boldsymbol{\beta}_k}w_k(\boldsymbol{\beta}_k)||\boldsymbol{\beta}_k||_2=\frac{\partial}{\partial\boldsymbol{\beta}_k}\exp\bigg(-\frac{||\boldsymbol{\beta}_k||_\infty}{\sigma(n)}\bigg)||\boldsymbol{\beta}_k||_2$$

$$=||\boldsymbol{\beta}_k||_2\frac{\partial}{\partial\boldsymbol{\beta}_k}\exp\bigg(-\frac{||\boldsymbol{\beta}_k||_\infty}{\sigma(n)}\bigg)+\exp\bigg(-\frac{||\boldsymbol{\beta}_k||_\infty}{\sigma(n)}\bigg)\frac{\partial}{\partial\boldsymbol{\beta}_k}||\boldsymbol{\beta}_k||_2$$

$$=||\boldsymbol{\beta}_k||_2\bigg(-\frac{1}{\sigma(n)}\exp\bigg(-\frac{||\boldsymbol{\beta}_k||_\infty}{\sigma(n)}\bigg)\sum_{l=1}^{p_k}\mathrm{sign}(\beta_{kl})\vec{\boldsymbol{e}}_l I\Big(\beta_{kl}=||\boldsymbol{\beta}_k||_\infty\Big)\bigg)$$

$$+\exp\bigg(-\frac{||\boldsymbol{\beta}_k||_\infty}{\sigma(n)}\bigg)\Big(||\boldsymbol{\beta}_k||_2\Big)^{-1}\boldsymbol{\beta}_k,$$

where $\vec{\boldsymbol{e}}_l$ is the standard basis vector of dimension p_k such that the l-th component is equal to 1.

Next we calculate the derivative with respect to $\boldsymbol{\eta}_{kk'}$:

$$\frac{\partial}{\partial\boldsymbol{\eta}_{kk'}}f(\boldsymbol{\beta}_1,...,\boldsymbol{\beta}_S,\boldsymbol{\eta}_{12},...,\boldsymbol{\eta}_{S-1,S})$$

$$=\frac{\partial}{\partial\boldsymbol{\eta}_{kk'}}\bigg[\frac{1}{2}\Big\|\boldsymbol{y}-\sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j-\sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{\beta}_{j'})]\Big\|_2^2\bigg]$$

$$=\bigg(\frac{\partial}{\partial\boldsymbol{\eta}_{kk'}}\bigg[\boldsymbol{y}-\sum_{j=1}^{S}\boldsymbol{X}_j\boldsymbol{\beta}_j-\sum_{1\le j<j'\le S}\boldsymbol{X}_{jj'}[\boldsymbol{\eta}_{jj'}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{\beta}_{j'})]\bigg]\bigg)^\top\Big(\boldsymbol{y}-\boldsymbol{X\theta}\Big)$$

$$=-\bigg(\frac{\partial}{\partial\boldsymbol{\eta}_{kk'}}\Big[\boldsymbol{X}_{kk'}[\boldsymbol{\eta}_{kk'}\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'})]\Big]\bigg)^\top\Big(\boldsymbol{y}-\boldsymbol{X\theta}\Big)$$

$$=-\bigg[\boldsymbol{X}_{kk'}\Big[\frac{\partial}{\partial\boldsymbol{\eta}_{kk'}}\boldsymbol{\eta}_{kk'}\odot\mathrm{diag}(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'})\Big]\bigg]^\top\Big(\boldsymbol{y}-\boldsymbol{X\theta}\Big)$$

$$=-\bigg(\boldsymbol{X}_{kk'}\Big[\boldsymbol{I}\odot\mathrm{diag}(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'})\Big]\bigg)^\top\Big(\boldsymbol{y}-\boldsymbol{X\theta}\Big)$$

$$= -\left(\boldsymbol{X}_{kk'}\left[\text{diag}(\boldsymbol{\beta}_k \otimes \boldsymbol{\beta}_{k'})\right]\right)^{\top}\left(\boldsymbol{y} - \boldsymbol{X}\boldsymbol{\theta}\right)$$

The derivative of the penalty function is:

$$\frac{\partial}{\partial \boldsymbol{\eta}_{kk'}} w_{kk'}(\boldsymbol{\eta}_{kk'})||\boldsymbol{\eta}_{kk'}||_2 = \frac{\partial}{\partial \boldsymbol{\eta}_{kk'}} \exp\left(-\frac{||\boldsymbol{\eta}_{kk'}||_\infty}{\sigma(n)}\right)||\boldsymbol{\eta}_{kk'}||_2$$

$$= ||\boldsymbol{\eta}_{kk'}||_2 \frac{\partial}{\partial \boldsymbol{\eta}_{kk'}} \exp\left(-\frac{||\boldsymbol{\eta}_{kk'}||_\infty}{\sigma(n)}\right) + \exp\left(-\frac{||\boldsymbol{\eta}_{kk'}||_\infty}{\sigma(n)}\right)\frac{\partial}{\partial \boldsymbol{\eta}_{kk'}}||\boldsymbol{\eta}_{kk'}||_2$$

$$= ||\boldsymbol{\eta}_{kk'}||_2\left(-\frac{1}{\sigma(n)}\exp\left(-\frac{||\boldsymbol{\eta}_{kk'}||_\infty}{\sigma(n)}\right)\sum_{l=1}^{p_k p_{k'}} \text{sign}(\eta_{kk'l})\vec{\boldsymbol{e}}_l I\left(\eta_{kk'l} = ||\boldsymbol{\eta}_{kk'}||_\infty\right)\right)$$

$$+ \exp\left(-\frac{||\boldsymbol{\eta}_{kk'}||_\infty}{\sigma(n)}\right)\left(||\boldsymbol{\eta}_{kk'}||_2\right)^{-1}\boldsymbol{\eta}_{kk'},$$

where $\vec{\boldsymbol{e}}_l$ is the standard basis vector of dimension $p_k p_{k'}$ such that the l-th component is equal to 1.

B.4. *Sparsistency Proof*

The proof closely follows the proof of Theorem 1 in (Pan and Zhao, 2016). Define the HiGLASSO estimator of a re-parameterized version of (9) such that only the covariates corresponding to the non-zero coefficient set are included:

$$\arg\min_{\boldsymbol{\theta}_{\mathcal{P}}}\Bigg\{||\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\boldsymbol{\theta}_{\mathcal{P}}||_2^2 + \lambda_1(n)\sum_{j\in\mathcal{P}_1} w_j(\boldsymbol{\theta}_j)||\boldsymbol{\theta}_j||_2 + \lambda_2(n)\sum_{(j,j')\in\mathcal{P}_2} w_{jj'}(\boldsymbol{\eta}_{jj'})||\boldsymbol{\eta}_{jj'}||_2\Bigg\}. \quad (10)$$

Let $\tilde{\boldsymbol{\theta}}_{\mathcal{P}}$ be the solution to (10). From the assumptions of the Theorem we have that

$$\frac{1}{n}\boldsymbol{X}^\top\boldsymbol{y} = \frac{1}{n}\boldsymbol{X}^\top\boldsymbol{X}_{\mathcal{P}}\boldsymbol{\theta}_{\mathcal{P}} + \frac{1}{n}\boldsymbol{X}^\top\boldsymbol{\epsilon}$$
$$= \left[E\left(\frac{1}{n}\boldsymbol{X}^\top\boldsymbol{X}_{\mathcal{P}}\right) + O_p\left(n^{-1/2}\right)\right]\boldsymbol{\theta}_{\mathcal{P}} + O_p\left(n^{-1/2}\right)$$
$$= E\left(\frac{1}{n}\boldsymbol{X}^\top\boldsymbol{X}_{\mathcal{P}}\right)\boldsymbol{\theta}_{\mathcal{P}} + O_p\left(n^{-1/2}\right),$$

which implies that

$$\frac{1}{n}\boldsymbol{X}^\top\boldsymbol{y} - \frac{1}{n}\boldsymbol{X}^\top\boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}} = E\left(\frac{1}{n}\boldsymbol{X}^\top\boldsymbol{X}_{\mathcal{P}}\right)(\boldsymbol{\theta}_{\mathcal{P}} - \tilde{\boldsymbol{\theta}}_{\mathcal{P}}) + O_p\left(n^{-1/2}\right). \quad (11)$$

(11) can be decomposed as

$$\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}\boldsymbol{y} - \frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}\boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}} = E\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)(\boldsymbol{\theta}_{\mathcal{P}} - \tilde{\boldsymbol{\theta}}_{\mathcal{P}}) + O_p(n^{-1/2}) \tag{12}$$

$$\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}\boldsymbol{y} - \frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}\boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}} = E\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)(\boldsymbol{\theta}_{\mathcal{P}} - \tilde{\boldsymbol{\theta}}_{\mathcal{P}}) + O_p(n^{-1/2}) \tag{13}$$

From (12) we get

$$\boldsymbol{\theta}_{\mathcal{P}} - \tilde{\boldsymbol{\theta}}_{\mathcal{P}} = E^{-1}\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}}) + O_p(n^{-1/2})$$

and substituting into (13) we obtain

$$\begin{aligned}&\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}})\\ &= E\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)E^{-1}\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}}) + O_p(n^{-1/2}).\end{aligned}$$

Multiplying both sides by n/a_n, we get

$$\begin{aligned}&\frac{n}{a_n}\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}})\right)\\ &= E\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)E^{-1}\left(\frac{1}{n}\boldsymbol{X}_{\mathcal{P}}^{\top}\boldsymbol{X}_{\mathcal{P}}\right)\frac{1}{a_n}\boldsymbol{X}_{\mathcal{P}}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}}) + O_p\left(\frac{\sqrt{n}}{a_n}\right).\end{aligned}$$

Therefore, when $b_n \to 0$, $a_n/\sqrt{n} \to \infty$, and $a_n/n \to 0$ we have

$$\frac{n}{a_n}\left\|\frac{1}{n}\boldsymbol{X}_{\mathcal{P}^{\mathsf{c}}}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}})\right\|_2 \to_p 0,$$

which also implies that

$$\frac{n}{\lambda_1(n)}\left\|\frac{1}{n}\boldsymbol{X}_{[k]}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}})\right\|_2 \to_p 0, \;\; \forall k \in \mathcal{P}_1^{\mathsf{c}}$$

$$\frac{n}{\lambda_2(n)}\left\|\frac{1}{n}\boldsymbol{X}_{kk'}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}})\right\|_2 \to_p 0, \;\; \forall (k,k') \in \mathcal{P}_2^{\mathsf{c}}$$

where

$$\boldsymbol{X}_{[k]} = \begin{pmatrix}\boldsymbol{X}_k, & \boldsymbol{X}_{k,k+1}, & \cdots & \boldsymbol{X}_{k,S}, & \boldsymbol{X}_{1,k}, & \cdots & \boldsymbol{X}_{k-1,k}\end{pmatrix}$$

is the submatrix of the design matrix corresponding to the kth covariate. These two convergence in probability statements imply that

$$P\left(\forall k \in \mathcal{P}_1^{\mathsf{c}}, \frac{nB_1}{\lambda_1(n)}\left\|\frac{1}{n}\boldsymbol{X}_{[k]}^{\top}(\boldsymbol{y} - \boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}})\right\|_2 \leq 1\right) \to 1 \tag{14}$$

$$P\left(\forall(k,k')\in\mathcal{P}_2^{\mathsf{c}}, \frac{nB_2}{\lambda_2(n)}\left\|\frac{1}{n}\boldsymbol{X}_{kk'}^\top\big(\boldsymbol{y}-\boldsymbol{X}_{\mathcal{P}}\tilde{\boldsymbol{\theta}}_{\mathcal{P}}\big)\right\|_2\le 1\right)\to 1 \tag{15}$$

for any finite constants B_1 and B_2.

Define $\tilde{\boldsymbol{\theta}}$ as the concatenation of $\tilde{\boldsymbol{\theta}}_{\mathcal{P}_1}$, a vector of zeros with length equal to the number of columns in $\boldsymbol{X}$ corresponding to $\mathcal{P}_1^{\mathsf{c}}$, $\tilde{\boldsymbol{\theta}}_{\mathcal{P}_2}$, and a vector of zeros with length equal to the number of columns in $\boldsymbol{X}$ corresponding to $\mathcal{P}_2^{\mathsf{c}}$. The assumption that the L_2 norm of the HiGLASSO estimator is uniformly bounded for all n coupled with (14) and (15) imply that with probability approaching one

$$\frac{1}{n}\tilde{\boldsymbol{C}}_{[k]}^\top\boldsymbol{X}_{[k]}^\top\big(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)=\frac{\lambda_1(n)}{n}D_k(\tilde{\boldsymbol{\beta}}_k),\ \ \forall k\in\mathcal{P}_1 \tag{16}$$

$$\frac{1}{n}\mathrm{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\boldsymbol{X}_{kk'}^\top\big(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)=\frac{\lambda_2(n)}{n}D_{kk'}(\tilde{\boldsymbol{\eta}}_{kk'}),\ \ \forall(k,k')\in\mathcal{P}_2 \tag{17}$$

$$\left\|\frac{1}{n}\tilde{\boldsymbol{C}}_{[k]}^\top\boldsymbol{X}_{[k]}^\top\big(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)\right\|_2\le\frac{\lambda_1(n)}{n},\ \ \forall k\in\mathcal{P}_1^{\mathsf{c}} \tag{18}$$

$$\left\|\frac{1}{n}\mathrm{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\boldsymbol{X}_{kk'}^\top\big(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)\right\|_2\le\frac{\lambda_2(n)}{n},\ \ \forall(k,k')\in\mathcal{P}_2^{\mathsf{c}} \tag{19}$$

where

$$\tilde{\boldsymbol{C}}_{[k]}=\begin{pmatrix}\boldsymbol{I}_{p_k\times p_k}\\ \mathrm{diag}(\tilde{\boldsymbol{\eta}}_{k,k+1})(\boldsymbol{I}_{p_k\times p_k}\otimes\tilde{\boldsymbol{\beta}}_{k+1})\\ \vdots\\ \mathrm{diag}(\tilde{\boldsymbol{\eta}}_{k,S})(\boldsymbol{I}_{p_k\times p_k}\otimes\tilde{\boldsymbol{\beta}}_S)\\ \mathrm{diag}(\tilde{\boldsymbol{\eta}}_{1,k})(\tilde{\boldsymbol{\beta}}_1\otimes\boldsymbol{I}_{p_k\times p_k})\\ \vdots\\ \mathrm{diag}(\tilde{\boldsymbol{\eta}}_{k-1,k})(\tilde{\boldsymbol{\beta}}_{k-1}\otimes\boldsymbol{I}_{p_k\times p_k})\end{pmatrix}$$

$$D_k(\tilde{\boldsymbol{\beta}}_k)=\frac{\partial}{\partial\boldsymbol{\beta}_k}w_k(\boldsymbol{\beta}_k)||\boldsymbol{\beta}_k||_2\bigg|_{\boldsymbol{\beta}_k=\tilde{\boldsymbol{\beta}}_k}$$

$$D_{kk'}(\tilde{\boldsymbol{\eta}}_{kk'})=\frac{\partial}{\partial\boldsymbol{\eta}_{kk'}}w_{kk'}(\boldsymbol{\eta}_{kk'})||\boldsymbol{\eta}_{kk'}||_2\bigg|_{\boldsymbol{\eta}_{kk'}=\tilde{\boldsymbol{\eta}}_{kk'}}$$

The directional derivative with respect to $\boldsymbol{\beta}_k$ in the u direction of (9) is

$$-\left(\boldsymbol{X}_k\boldsymbol{u}+\sum_{1\le k<j'\le S}\boldsymbol{X}_{kj'}[\boldsymbol{\eta}_{kj'}\odot(\boldsymbol{u}\otimes\boldsymbol{\beta}_{j'})]+\sum_{1\le j<k\le S}\boldsymbol{X}_{jk}[\boldsymbol{\eta}_{jk}\odot(\boldsymbol{\beta}_j\otimes\boldsymbol{u})]\right)^\top\times$$

$$\big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big) + \lambda_1(n)$$

$$= -\begin{pmatrix} \boldsymbol{u} \\ \boldsymbol{\eta}_{k,k+1} \odot (\boldsymbol{u} \otimes \boldsymbol{\beta}_{k+1}) \\ \vdots \\ \boldsymbol{\eta}_{k,S} \odot (\boldsymbol{u} \otimes \boldsymbol{\beta}_S) \\ \boldsymbol{\eta}_{1,k} \odot (\boldsymbol{\beta}_1 \otimes \boldsymbol{u}) \\ \vdots \\ \boldsymbol{\eta}_{k-1,k} \odot (\boldsymbol{\beta}_{k-1} \otimes \boldsymbol{u}) \end{pmatrix}^\top \boldsymbol{X}_{[k]}^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big) + \lambda_1(n).$$

For $\tilde{\boldsymbol{\beta}}_j$ and $\tilde{\boldsymbol{\eta}}_{jj'}$ to be the minimizer's of (9), we need

$$-\begin{pmatrix} \boldsymbol{u} \\ \tilde{\boldsymbol{\eta}}_{k,k+1} \odot (\boldsymbol{u} \otimes \tilde{\boldsymbol{\beta}}_{k+1}) \\ \vdots \\ \tilde{\boldsymbol{\eta}}_{k,S} \odot (\boldsymbol{u} \otimes \tilde{\boldsymbol{\beta}}_S) \\ \tilde{\boldsymbol{\eta}}_{1,k} \odot (\tilde{\boldsymbol{\beta}}_1 \otimes \boldsymbol{u}) \\ \vdots \\ \tilde{\boldsymbol{\eta}}_{k-1,k} \odot (\tilde{\boldsymbol{\beta}}_{k-1} \otimes \boldsymbol{u}) \end{pmatrix}^\top \boldsymbol{X}_{[k]}^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big) + \lambda_1(n) \geq 0,$$

for all p_k dimensional unit vectors $\boldsymbol{u}$. To verify this we must substitute the negative normalized gradient in for $\boldsymbol{u}$, and see when the inequality holds. The negative normalized gradient is given by

$$\boldsymbol{u}^* = \frac{\big(\boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\big)^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)}{\Big\|\big(\boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\big)^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)\Big\|_2}.$$

Then we have that

$$\boldsymbol{u}^{*\top} \boldsymbol{X}_k^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)$$

$$= \frac{\big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)^\top \boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\boldsymbol{I}_{p_k \times p_k}^\top \boldsymbol{X}_k^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)}{\Big\|\big(\boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\big)^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)\Big\|_2}$$

$$\Big[\tilde{\boldsymbol{\eta}}_{kj'}^\top \odot \big(\boldsymbol{u}^{*\top} \otimes \tilde{\boldsymbol{\beta}}_{j'}^\top\big)\Big] \boldsymbol{X}_{kj'}^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)$$

$$= \frac{\Big[\tilde{\boldsymbol{\eta}}_{kj'}^\top \odot \Big(\Big(\big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)^\top \boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\Big) \otimes \tilde{\boldsymbol{\beta}}_{j'}^\top\Big)\Big] \boldsymbol{X}_{kj'}^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)}{\Big\|\big(\boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\big)^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)\Big\|_2}$$

$$= \frac{\big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)^\top \boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\Big(\boldsymbol{I}_{p_k \times p_k} \otimes \tilde{\boldsymbol{\beta}}_{j'}^\top\Big) \mathrm{diag}\big(\tilde{\boldsymbol{\eta}}_{kj'}\big) \boldsymbol{X}_{kj'}^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)}{\Big\|\big(\boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\big)^\top \big(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\big)\Big\|_2}$$

$$\left[\tilde{\boldsymbol{\eta}}_{jk}^{\top} \odot \left(\tilde{\boldsymbol{\beta}}_j^{\top} \otimes \boldsymbol{u}^{*\top}\right)\right] \boldsymbol{X}_{jk}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})$$

$$= \frac{\left[\tilde{\boldsymbol{\eta}}_{jk}^{\top} \odot \left(\tilde{\boldsymbol{\beta}}_j^{\top} \otimes \left(\left(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^{\top} \boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)\right)\right] \boldsymbol{X}_{jk}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}$$

$$= \frac{\left(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^{\top} \boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]} \left(\tilde{\boldsymbol{\beta}}_j^{\top} \otimes \boldsymbol{I}_{p_k \times p_k}\right) \operatorname{diag}(\tilde{\boldsymbol{\eta}}_{jk}) \boldsymbol{X}_{jk}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}$$

Substituting this result in, we get:

$$- \begin{pmatrix} \boldsymbol{u}^* \\ \tilde{\boldsymbol{\eta}}_{k,k+1} \odot (\boldsymbol{u}^* \otimes \tilde{\boldsymbol{\beta}}_{k+1}) \\ \vdots \\ \tilde{\boldsymbol{\eta}}_{k,S} \odot (\boldsymbol{u}^* \otimes \tilde{\boldsymbol{\beta}}_S) \\ \tilde{\boldsymbol{\eta}}_{1,k} \odot (\tilde{\boldsymbol{\beta}}_1 \otimes \boldsymbol{u}^*) \\ \vdots \\ \tilde{\boldsymbol{\eta}}_{k-1,k} \odot (\tilde{\boldsymbol{\beta}}_{k-1} \otimes \boldsymbol{u}^*) \end{pmatrix}^{\top} \boldsymbol{X}_{[k]}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})$$

$$= -\frac{\left(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^{\top} \boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]} \boldsymbol{I}_{p_k \times p_k}^{\top} \boldsymbol{X}_k^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}$$

$$- \sum_{j'>k} \left[\frac{\left(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^{\top} \boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]} \left(\boldsymbol{I}_{p_k \times p_k} \otimes \tilde{\boldsymbol{\beta}}_{j'}^{\top}\right) \operatorname{diag}(\tilde{\boldsymbol{\eta}}_{kj'}) \boldsymbol{X}_{kj'}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}\right]$$

$$- \sum_{j<k} \left[\frac{\left(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^{\top} \boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]} \left(\tilde{\boldsymbol{\beta}}_j^{\top} \otimes \boldsymbol{I}_{p_k \times p_k}\right) \operatorname{diag}(\tilde{\boldsymbol{\eta}}_{jk}) \boldsymbol{X}_{jk}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}\right]$$

$$= -\frac{\left(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^{\top} \boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]} \boldsymbol{C}_{[k]}^{\top} \boldsymbol{X}_{[k]}^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}$$

$$= -\frac{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2^2}{\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}$$

$$= -\left\|\left(\boldsymbol{X}_{[k]} \boldsymbol{C}_{[k]}\right)^{\top}(\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2.$$

Therefore, for $\tilde{\boldsymbol{\beta}}_j$ and $\tilde{\boldsymbol{\eta}}_{jj'}$ to be the minimizer's of (9), we need

$$-\left\|\left(\boldsymbol{X}_{[k]}\boldsymbol{C}_{[k]}\right)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right\|_2+\lambda_1(n)\geq 0,$$

which implies that

$$\left\|\frac{1}{n}\boldsymbol{C}_{[k]}^\top\boldsymbol{X}_{[k]}^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right\|_2\leq\frac{\lambda_1(n)}{n}. \tag{20}$$

The directional derivative with respect to $\boldsymbol{\eta}_{kk'}$ in the u direction of (9) is

$$-\Big(\boldsymbol{X}_{kk'}[\boldsymbol{u}\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'})]\Big)^\top\left(\boldsymbol{y}-\boldsymbol{X}\boldsymbol{\theta}\right)+\lambda_2(n)$$

For $\tilde{\boldsymbol{\beta}}_j$ and $\tilde{\boldsymbol{\eta}}_{jj'}$ to be the minimizer's of (9), we need

$$-\Big(\boldsymbol{X}_{kk'}[\boldsymbol{u}\odot(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})]\Big)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)+\lambda_2(n)\geq 0,$$

for all $p_kp_{k'}$ dimensional unit vectors $\boldsymbol{u}$. To verify this we must substitute the negative normalized gradient in for $\boldsymbol{u}$, and see when the inequality holds. The negative normalized gradient is given by

$$\boldsymbol{u}^*=\frac{\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)}{\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right\|_2}.$$

Substituting this into our expression for the we get

$$-\Big(\boldsymbol{X}_{kk'}[\boldsymbol{u}^*\odot(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})]\Big)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)$$

$$=-\frac{\left[\left(\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\boldsymbol{X}_{kk'}^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right)\odot(\boldsymbol{\beta}_k\otimes\boldsymbol{\beta}_{k'})\right]^\top\boldsymbol{X}_{kk'}^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)}{\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right\|_2}$$

$$=-\frac{\left(\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\boldsymbol{X}_{kk'}^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right)^\top\boldsymbol{X}_{kk'}^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)}{\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right\|_2}$$

$$=-\frac{\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)^\top\boldsymbol{X}_{kk'}\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\boldsymbol{X}_{kk'}^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)}{\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k\otimes\tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top\left(\boldsymbol{y}-\boldsymbol{X}\tilde{\boldsymbol{\theta}}\right)\right\|_2}$$

$$= -\frac{\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k \otimes \tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top (\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2^2}{\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k \otimes \tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top (\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2}$$

$$= -\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k \otimes \tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top (\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2.$$

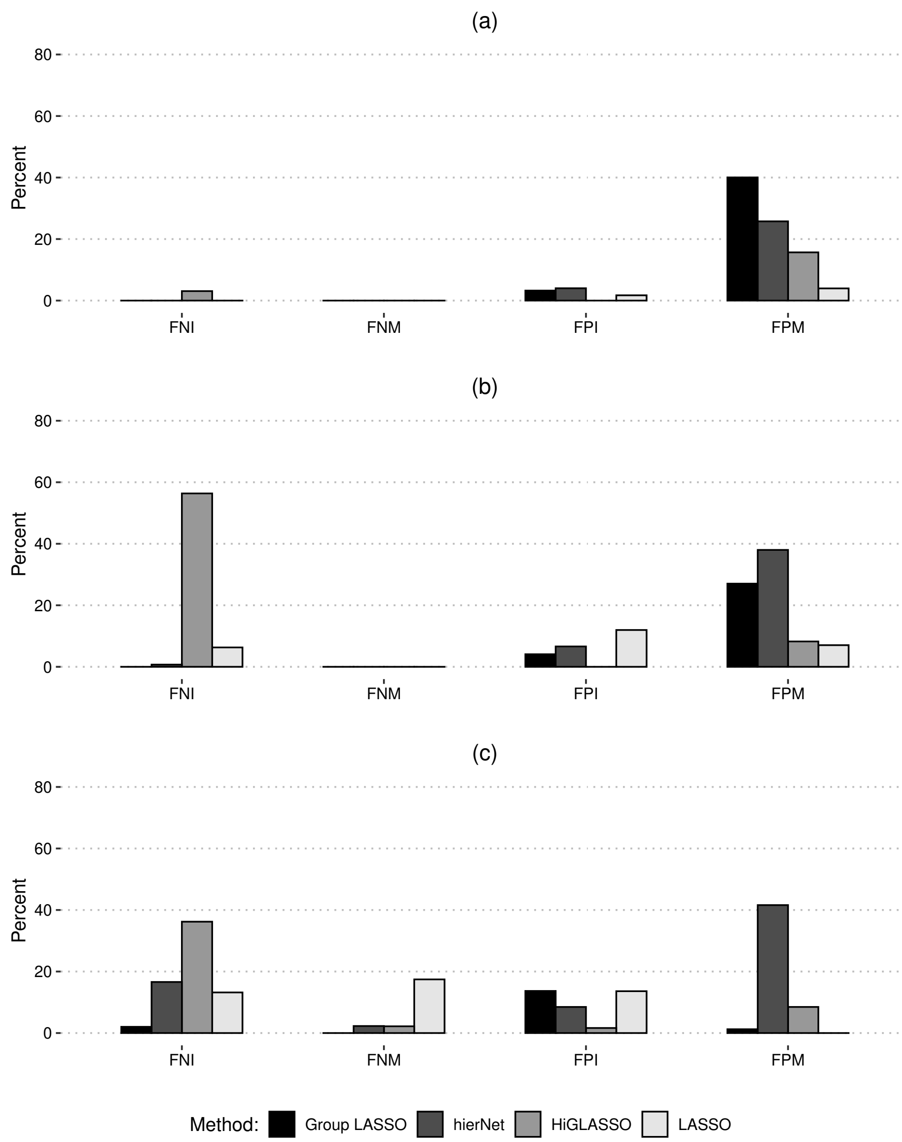
Therefore, for $\tilde{\boldsymbol{\beta}}_j$ and $\tilde{\boldsymbol{\eta}}_{jj'}$ to be the minimizer's of (9), we need

$$-\left\|\left(\boldsymbol{X}_{kk'}\left[\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k \otimes \tilde{\boldsymbol{\beta}}_{k'})\right]\right)^\top (\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2 + \lambda_2(n) \geq 0,$$

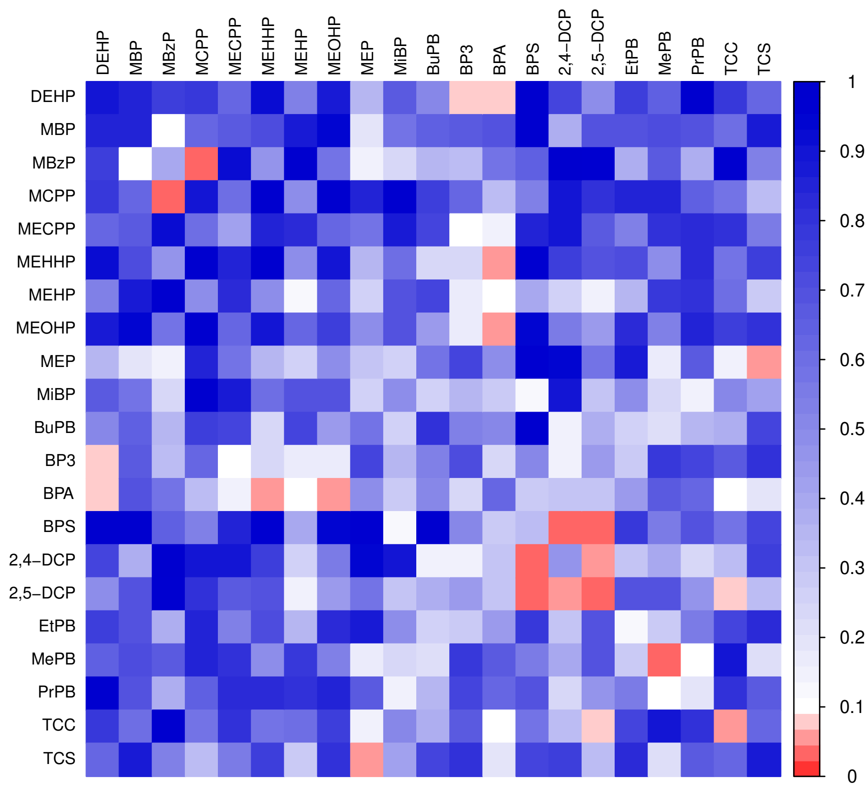
which implies that

$$\left\|\frac{1}{n}\operatorname{diag}(\tilde{\boldsymbol{\beta}}_k \otimes \tilde{\boldsymbol{\beta}}_{k'})\boldsymbol{X}_{kk'}^\top (\boldsymbol{y} - \boldsymbol{X}\tilde{\boldsymbol{\theta}})\right\|_2 \leq \frac{\lambda_2(n)}{n}. \tag{21}$$

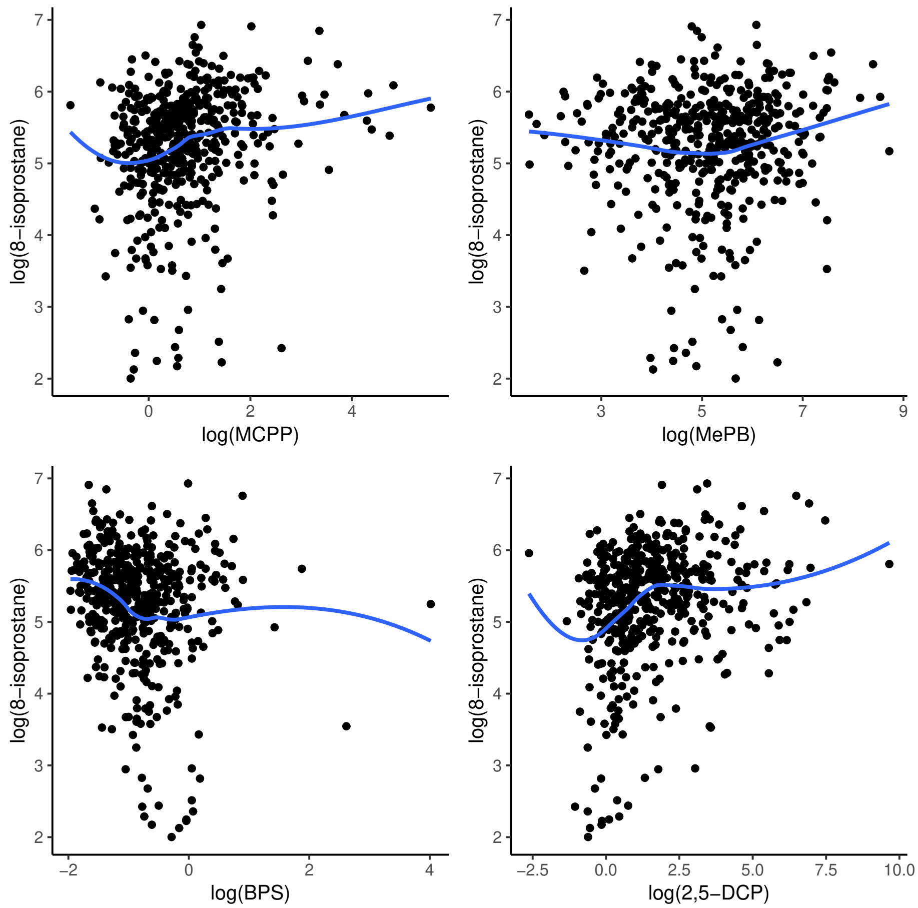
Since (20) is equivalent to (18) and (21) is equivalent to (19), this concludes the proof.



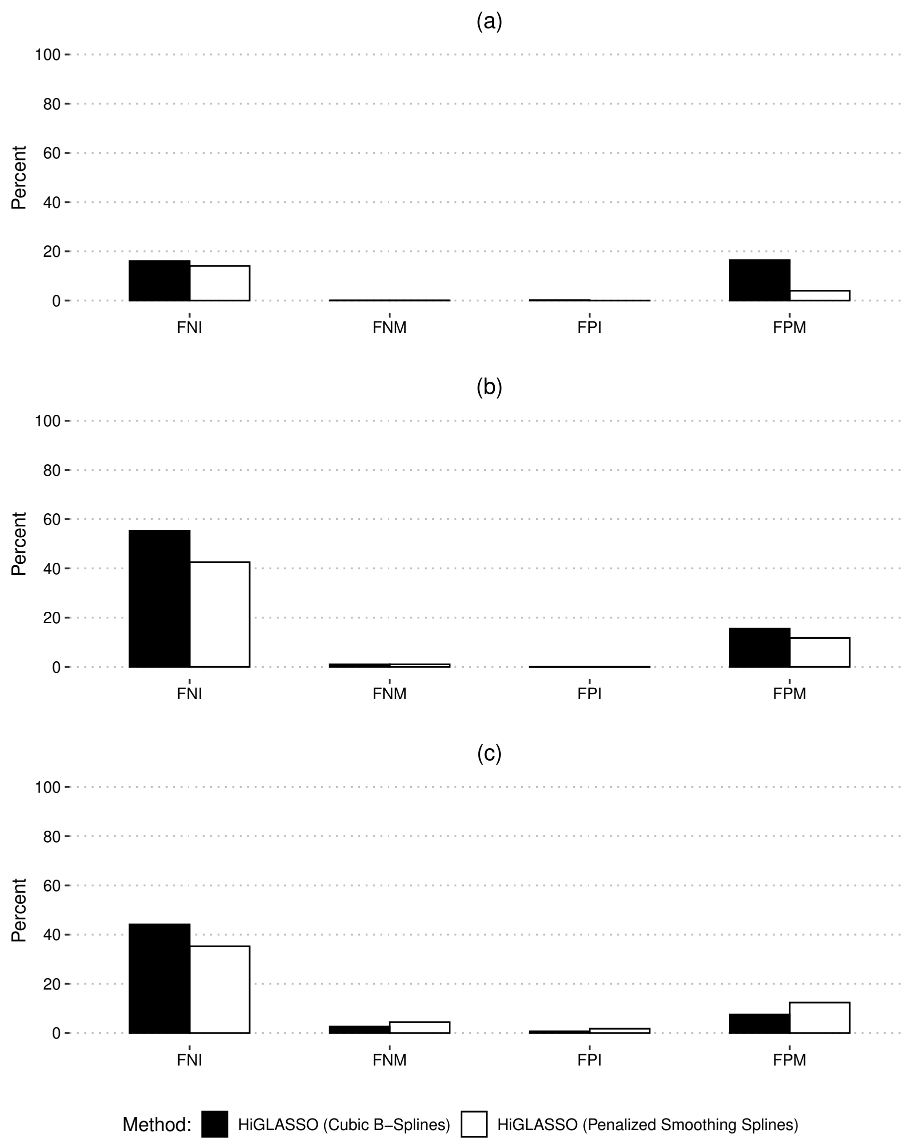
Web Figure 1: Simulation Results for the $n = 10000$ and $p = 10$ cases: (a) Linear main and interaction effects (b) Piecewise linear main and interaction effects (c) Nonlinear main and interaction effects. FNI, FNM, FPI, and FPM are defined in Section 4.2.



Web Figure 2: Heatmap for Wald test p-values corresponding to all pairwise linear interactions. Each p-value is obtained from a multiple regression model with 21 exposure main effect terms and a single pairwise linear interaction term. Diagonal elements indicate the addition of a squared term instead of an interaction.



Web Figure 3: Scatterplots between four exposures and 8-isoprostane superimposed with a Locally Weighted Scatterplot Smoothing (LOWESS) curve. The four exposures are mono(3-carboxypropyl) phthalate (MCPP), methyl paraben (MePB), Bisphenol S (BPS), and 2,5-Dichlorophenol (2,5-DCP).



Web Figure 4: Simulated comparison between HiGLASSO with cubic B-splines and HiGLASSO with penalized smoothing splines for the $n = 1000$ and $p = 10$ cases: (a) L10 (b) PL10 (c) NL10. FNI, FNM, FPI, and FPM are defined in Section 4.2 of the main text.

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