Sparse Network Modeling

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There have been many attempts to identify high-dimensional network features via multivariate approaches (Chung et al. 2013, Lerch et al. 2006, He et al. 2007, Worsley, Charil, Lerch & Evans 2005, He et al. 2008). Specifically, when the number of voxels or nodes, denoted as \( p \), are substantially larger than the number of images, denoted as \( n \), it produces an under-determined model with infinitely many possible solutions. The small-\( n \) large-\( p \) problem is often remedied by regularizing the under-determined system with additional sparse penalties.

Popular sparse network models include sparse correlations (Lee, Lee, Kang, Kim & Chung 2011, Chung et al. 2013, 2015, 2017), LASSO (Bickel & Levina 2008, Peng et al. 2009, Huang et al. 2009, Chung et al. 2013), sparse canonical correlations (Avants et al. 2010) and graphical-LASSO (Banerjee et al. 2006, 2008, Friedman et al. 2008, Huang et al. 2009, 2010, Mazumder & Hastie 2012, Witten et al. 2011). These popular sparse models require optimizing \( L_1 \)-norm penalties, which has been the major computational bottleneck for solving large-scale problems. Thus, many existing sparse brain network models in brain imaging have been restricted to a few hundreds nodes or less. 2527 MRI features used in a LASSO model for Alzheimer’s disease (Xin et al. 2015) is probably the largest number of features used in any sparse model in the brain imaging literature.

1 Why sparse network models?

If we are interested quantifying the measurements in every voxel in an image simultaneously, the standard procedure is to set up a multivariate general linear model (MGLM), which generalizes widely used univariate GLM by incorporating vector valued responses and explanatory variables (Anderson 1984, Friston et al. 1995, Worsley et al. 1996, 2004, Taylor & Worsley 2008, Chung et al. 2010). Hotelling’s \( T^2 \)-statistic is a special case of MGLM and has been mainly used for inference on surface shapes and deformations (Thompson et al. 1997, Joshi 1998, Cao & Worsley 1999, Gaser et al. 1999, Chung et al. 2001).

Let \( J_{n \times p} = (J_{ij}) \) be the measurement matrix, \( J_{ij} \) is the measurement for subject \( i \) at voxel position \( j \). The subscripts denote the dimension of matrix. We can think \( J_{ij} \) as either Jacobian determinant, fractional anisotropy values or fMRI activation. Assume there are total \( n \) subjects and \( p \) voxels of interest. The
measurement vector at the $j$-th voxel is denoted as $\mathbf{x}_j = (J_{1j}, \cdots, J_{nj})^\top$. The measurement vector for the $i$-th subject is denoted as $\mathbf{y}_i = (J_{i1}, \cdots, J_{ip})$, which is expected to be distributed identically and independently over subjects. Note that

$$J = (\mathbf{x}_1, \cdots, \mathbf{x}_p) = (\mathbf{y}_1^\top, \cdots, \mathbf{y}_n^\top)^\top.$$  

We may assume the covariance matrix of $\mathbf{y}_i$ to be

$$\mathbb{V}(\mathbf{y}_1) = \cdots = \mathbb{V}(\mathbf{y}_n) = \Sigma_{p \times p} = (\sigma_{kl}).$$  

With these notations, we set up the following MGLM over all subjects and across different voxel positions:

$$J_{n \times p} = X_{n \times k} B_{k \times p} + Z_{n \times q} G_{q \times p} + U_{n \times p} \Sigma_{p \times p}^{1/2},$$

where $X$ is the matrix of contrasted explanatory variables while $B$ is the matrix of unknown coefficients to be estimated. Nuisance covariates of non-interest are in the matrix $Z$ and the corresponding coefficients are in the matrix $G$. The components of Gaussian random matrix $U$ are independently distributed with zero mean and unit variance. The symmetric matrix $\Sigma_{1/2}$ is the square-root of the covariance matrix accounting for the spatial dependency across different voxels. In MGLM (1), we are interested in testing the null hypothesis

$$H_0 : B = 0.$$

The parameter matrices in the model are estimated via the least squares method. The resulting multivariate test statistics are called the Lawley-Hotelling trace or Roy’s maximum root. When there is only one voxel, i.e. $p = 1$, these multivariate test statistics collapses to Hotelling’s $T^2$-statistic (Worsley et al. 2004).

Note that MGLM (1) is equivalent to the assumption that $\mathbf{y}_i$ follows multivariate normal with some mean $\mu$ and covariance $\Sigma$, i.e., $\mathbf{y}_i \sim N(\mu, \Sigma)$. Then neglecting constant terms, the log-likelihood function $L$ of $\mathbf{y}_i$ is given by

$$L(\mu, \Sigma) = \log \det \Sigma^{-1} - \frac{1}{n} \sum_{i=1}^{n} (\mathbf{y}_i - \mu)^\top \Sigma^{-1} (\mathbf{y}_i - \mu).$$

By maximizing the log-likelihood, MLE of $\mu$ and $\Sigma$ are given by

$$\hat{\mu} = \bar{y}_i = \frac{1}{n} \sum_{i=1}^{n} \mathbf{y}_i$$

$$\hat{\Sigma} = \frac{1}{n} \sum_{i=1}^{n} (\mathbf{y}_i - \bar{y}_i)^\top (\mathbf{y}_i - \bar{y}_i).$$

For a notational convenience, we can center the measurement $\mathbf{y}_i$ such that

$$\mathbf{y}_i \leftarrow \mathbf{y}_i - \bar{y}_i.$$
Fig. 1: The rank of 80-nodes fMRI correlation matrices for 192 subjects published in (Qiu et al. 2015). None of correlation matrix is of full rank and not invertible. Many brain regions show pairwise correlations.

We are basically centering the measurements by subtracting the group mean over subjects. Then MLE (3) can be written in a more compact form

\[
\hat{\Sigma} = \frac{1}{n} J_{p \times n} J_{n \times p}^\top.
\] (3)

However, there is a serious defect with MGLM (1) and its MLE (3); namely the estimated covariance matrix \(\hat{\Sigma}\) is positive definite only for \(n \geq p\) (Friston et al. 1995, Schäfer & Strimmer 2005). \(J^\top J\) becomes rank deficient for \(n < p\). In most imaging studies, there are more voxels than the number of subjects, i.e., \(n < p\). Even when \(n > p\), for various reasons, correlation and covariance matrices may not be full rank (Figure 1). When \(\hat{\Sigma}\) is singular, we do not properly have the inverse of \(\hat{\Sigma}\), which is the precision matrix often needed in partial correlation based network analyses (Lee, Lee, Kang, Kim & Chung 2011). This is the main reason MGLM was rarely employed over the whole brain region and researchers are still using mostly univariate approaches in imaging studies.

1.1 Why sparse network?

The majority of functional and structural connectivity studies in brain imaging are usually performed following the standard analysis framework (Gong et al. 2009, Hagmann et al. 2007, Fornito et al. 2010, Zalesky et al. 2010). From 3D whole brain images, \(n\) regions of interest (ROI) are identified and serve as the nodes of the brain network. Measurements at ROIs are then correlated in a pairwise fashion to produce the connectivity matrix of size \(n \times n\). The connectivity
Fig. 2: Graphical-LASSO estimation on an original singular correlation matrix from study Qiu et al. (2015). The original correlation matrix has the rank of 61 indicating approximately 19 nodes out of 80 nodes are dependent of other nodes. As the sparse parameter \( \lambda \) increases, we see more sparsity and diagonal dominance that makes the estimated sparse correlation matrix to be more positive definite.

matrix is then thresholded to produce the adjacency matrix consisting of zeros and ones that define the link between two nodes. The binarized adjacency matrix is then used to construct the brain network. Then various graph complexity measures such as degree, clustering coefficients, entropy, path length, hub centrality and modularity are defined on the graph and the subsequent statistical inference is performed on these complexity measures.

For a large number of nodes, simple thresholding of correlation will produce a large number of edges which makes the interpretation difficult. For example, for \( 3 \times 10^5 \) voxels in an image, we can possibly have a total of \( 9 \times 10^{10} \) directed edges in the graph. For this reason we used the sparse data recovery framework in obtaining a far smaller number of significant edges.

2 Sparse likelihood

Beyond sparse regression, others have proposed the likelihood methods. To remedy the small-\( n \) and large-\( p \) problem, the likelihood is regularized with a L1-norm penalty. If we center the measurements \( y_i \), the log-likelihood can be written
as

\[ L(\Sigma) = \log \det \Sigma^{-1} - \frac{1}{n} \sum_{i=1}^{n} y_i^\top \Sigma^{-1} y_i \]

\[ = \log \det \Sigma^{-1} - \text{tr}(\Sigma^{-1} S), \]

where \( S = \frac{1}{n} \sum_{i=1}^{n} y_i^\top y_i \) is the sample covariance matrix. We used the fact that the trace of a scalar value is equivalent to the scalar value itself and \( \text{tr}(AB) = \text{tr}(BA) \) for matrices \( A \) and \( B \).

To avoid the small-\( n \) large-\( p \) problem, we penalize the log-likelihood with L1-norm penalty:

\[ L(\Sigma^{-1}) = \log \det \Sigma^{-1} - \text{tr}(\Sigma^{-1} S) - \lambda \| \Sigma^{-1} \|_1, \]

(4)

where \( \| \cdot \|_1 \) is the sum of the absolute values of the elements. We made the likelihood as a function of \( \Sigma^{-1} \) to simply emphasize that we are trying to estimate the inverse covariance matrix. The penalized log-likelihood is maximized over the space of all possible symmetric positive definite matrices. (4) is a convex problem and it is usually solved using the graphical-LASSO (GLASSO) algorithm (Banerjee et al. 2006, 2008, Friedman et al. 2008, Huang et al. 2010, Mazumder & Hastie 2012). The tuning parameter \( \lambda > 0 \) controls the sparsity of the off-diagonal elements of the inverse covariance matrix. By increasing \( \lambda > 0 \), the estimated inverse covariance matrix becomes more sparse (Figure 2).

GLASSO is a fairly time consuming algorithm (Friedman et al. 2008, Huang et al. 2010). Solving GLASSO for 548 nodes, for instance, may take up to 6 minutes on slow desktop computers if fast algorithms like Hsieh et al. (2013) is not used. If \( \Sigma_i^{-1}(\lambda) \) is the estimated inverse sparse covariance for group \( i \) at given sparse parameter \( \lambda \), we are interested in testing the equivalence of inverse covariance matrices between the two groups at fixed \( \lambda \), i.e.,

\[ H_0 : \Sigma_1^{-1}(\lambda) = \Sigma_2^{-1}(\lambda). \]

2.1 Filtration in graphical-LASSO

The solution to graphical-LASSO has a peculiar nested topological structure. Let \( \Sigma^{-1}(\lambda) = (\sigma^{ij}(\lambda)) \) be the inverse covariance estimated from graphical-LASSO. Let \( A(\lambda) = (a_{ij}) \) be the corresponding adjacency matrix given by

\[ a_{ij}(\lambda) = \begin{cases} 1 & \text{if } \hat{\sigma}^{ij} \neq 0; \\ 0 & \text{otherwise.} \end{cases} \]

(5)

The adjacency matrix \( A \) induces a graph \( G(\lambda) \) consisting of \( \kappa(\lambda) \) number of partitioned subgraphs

\[ G(\lambda) = \bigcup_{\ell=1}^{\kappa(\lambda)} G_\ell(\lambda) \text{ with } G_\ell = \{V_\ell(\lambda), A_\ell(\lambda)\}, \]
Fig. 3: Schematic of graph filtrations obtained by sparse-likelihood (5) and sample covariance thresholding (6). The vertex set of $G(\lambda_1) = H(\lambda_1)$ consists of black nodes. For the next filtration value $\lambda_2$, $G(\lambda_2) \neq H(\lambda_2)$ since the edge sets are different. However, the partitioned vertex sets (gray colored) of $G(\lambda_2)$ and $H(\lambda_2)$ match.

where $V_l$ and $A_l$ are node and edge sets of subgraph $G_l$.

Let $S = (s_{ij})$ be the sample covariance matrix. Let $B(\lambda) = (b_{ij})$ be the adjacency matrix defined by

$$b_{ij}(\lambda) = \begin{cases} 1 & \text{if } |\hat{s}_{ij}| > \lambda; \\ 0 & \text{otherwise.} \end{cases} \quad (6)$$

The adjacency matrix $B$ similarly induces a graph with $\tau(\lambda)$ disjoint subgraphs:

$$\mathcal{H}(\lambda) = \bigcup_{l=1}^{\tau(\lambda)} H_l(\lambda) \text{ with } H_l = \{W_l(\lambda), B_l(\lambda)\},$$

where $W_l$ and $B_l$ are node and edge sets of subgraph $H_l$. Then the partitioned graphs are shown to be partially nested in a sense that the node sets exhibits persistency.

**Theorem 1.** For any $\lambda > 0$, the adjacency matrices (5) and (6) induce the identical vertex partition so that $\kappa(\lambda) = \tau(\lambda)$ and $V_l(\lambda) = W_l(\lambda)$. Further, the node sets $V_l$ and $W_l$ form filtrations over the sparse parameter:

$$V_l(\lambda_1) \supset V_l(\lambda_2) \supset V_l(\lambda_3) \supset \cdots \quad (7)$$

$$W_l(\lambda_1) \supset W_l(\lambda_2) \supset W_l(\lambda_3) \supset \cdots \quad (8)$$

for $\lambda_1 \leq \lambda_2 \leq \lambda_3 \leq \cdots$. 
Fig. 4: Left: Adjacency matrices obtained through graphical-LASSO with increasing $\lambda$ values. The persistent homological structure is self-evident. Right: Adjacency matrices are clustered as a block diagonal matrix $D$ by permutation.

From (6), it is trivial to see the filtration holds for $W_I$. The filtration for $V_I$ is proved in Huang et al. (2010). The equivalence of the node sets $V_I = W_I$ is proved in Mazumder & Hastie (2012). Note that the edge sets may not form a filtration (Figure 3). The construction of the filtration on the node sets $V_I$ (7) is very time consuming since we have to solve the sequence of graphical-LASSO. For instance, for 548 node sets and 547 different filtration values, the whole filtration takes more than 54 hours in a desktop (Chung et al. 2015).

In Figure 4, we randomly simulated the data matrix $X_{5 \times 10}$ from the standard normal distribution. The sample covariance matrix is then feed into graphical-LASSO with different filtration values. To identify the structure better, we transformed the adjacency matrix $A$ by permutation $P$ such that $D = PAP^{-1}$ is a block diagonal matrix. Theoretically only the partitioned node sets are expected to exhibit the nestedness but in this example, the edge sets are also nested as well.

3 Sparse correlation network

The problem with graphical-LASSO or any type of similar L1 norm optimization is that it becomes computationally expensive as the number of node $p$ increases. So it is not really practical for large-scale brain networks. In this section, we present a scalable large-scale network model ($p > 25000$) that yields greater computational speed and efficiency by bypassing the computational bottleneck of optimizing $L1$-penalties.

There are few previous studies at speeding up the computation for sparse models. By identifying block diagonal structures in the estimated (inverse) covariance matrix, it is possible to reduce the computational burden in the penalized log-likelihood method (Mazumder & Hastie 2012, Witten et al. 2011).
However, the method presented in this section differs from Mazumder & Hastie (2012) and Witten et al. (2011) in that we do not need to assume that the data follow Gaussianity. Subsequently, there is no need to specify the likelihood function. Further, the cost functions we are optimizing are different. Specifically, we propose a novel sparse network model based on correlations. Although correlations are often used in sciences in connection to times series and stochastic processes (Worsley, Charil, Lerch & Evans 2005, Worsley, Chen, Lerch & Evans 2005), the sparse version of correlation has been somewhat neglected.

Consider measurement vector $x_j$ on node $j$. If we center and rescale the measurement $x_j$ such that
\[ \| x_j \|^2 = x_j^\top x_j = 1, \]
the sample correlation between nodes $i$ and $j$ is given by $x_i^\top x_j$. Since the data is normalized, the sample covariance matrix is reduced to the sample correlation matrix.

Consider the following linear regression between nodes $j$ and $k$ ($k \neq j$):
\[ x_j = \gamma_{jk} x_k + \epsilon_j. \] (9)
We are basically correlating data at node $j$ to data at node $k$. In this particular case, $\gamma_{jk}$ is the usual Pearson correlation. The least squares estimation (LSE) of $\gamma_{jk}$ is then given by
\[ \hat{\gamma}_{jk} = x_j^\top x_k, \] (10)
which is the sample correlation. For the normalized data, regression coefficient estimation is exactly the sample correlation. For the normalized and centered data, the regression coefficient is the correlation. It can be shown that (22) minimizes the sum of least squares over all nodes:
\[ \sum_{j=1}^{p} \sum_{k \neq j} \| x_j - \gamma_{jk} x_k \|^2. \] (11)
Note that we do not really care about correlating $x_j$ to itself since the correlation is then trivially $\gamma_{jj} = 1$.

### 3.1 Sparse correlations
Let $\Gamma = (\gamma_{jk})$ be the correlation matrix. The sparse penalized version of (21) is given by
\[ F(\Gamma) = \frac{1}{2} \sum_{j=1}^{p} \sum_{k \neq j} \| x_j - \gamma_{jk} x_k \|^2 + \lambda \sum_{j=1}^{p} \sum_{k \neq j} |\gamma_{jk}|. \] (12)
The sparse correlation is given by minimizing $F(\Gamma)$. By increasing $\lambda$, the estimated correlation matrix $\hat{\Gamma}(\lambda)$ becomes more sparse. When $\lambda = 0$, the sparse
correlation is simply given by the sample correlation, i.e. \( \hat{\gamma}_{jk} = \mathbf{x}_j^\top \mathbf{x}_k \). As \( \lambda \) increases, the correlation matrix \( \Gamma \) shrinks to zero and becomes more sparse.

This is separable compressed sensing or LASSO type problem. However, there is no need to numerically optimize (23) using the coordinate descent learning or the active-set algorithm often used in compressed sensing (Peng et al. 2009, Friedman et al. 2008). The minimization of (23) can be done by the proposed soft-thresholding method analytically by exploiting the topological structure of the problem. Since \( \mathbf{x}_j^\top \mathbf{x}_j \neq \delta_{jj} \), the Dirac delta, it looks like the sparse regression is not orthogonal design and the existing soft-thresholding method for LASSO (Tibshirani 1996) is not directly applicable. However, it can be made into orthogonal design. The detail is given in the sparse cross-correlation section.

**Theorem 2.** For \( \lambda \geq 0 \), the solution of the following separable LASSO problem

\[
\hat{\gamma}_{jk}(\lambda) = \arg\min_{\gamma_{jk}} \frac{1}{2} \sum_{j=1}^{p} \sum_{k \neq j} \| \mathbf{x}_j - \gamma_{jk} \mathbf{x}_k \|^2 + \lambda \sum_{j=1}^{p} \sum_{k \neq j} |\gamma_{jk}|,
\]

is given by the soft-thresholding

\[
\hat{\gamma}_{jk}(\lambda) = \begin{cases} 
\mathbf{x}_j^\top \mathbf{x}_k - \lambda & \text{if } \mathbf{x}_j^\top \mathbf{x}_k > \lambda \\
0 & \text{if } |\mathbf{x}_j^\top \mathbf{x}_k| \leq \lambda \\
\mathbf{x}_j^\top \mathbf{x}_k + \lambda & \text{if } \mathbf{x}_j^\top \mathbf{x}_k < -\lambda
\end{cases}
\]

(13)

**Proof.** Write (23) as

\[
F(\Gamma) = \frac{1}{2} \sum_{j=1}^{p} \sum_{k \neq j} f(\gamma_{jk}),
\]

(14)

where

\[
f(\gamma_{jk}) = \| \mathbf{x}_j - \gamma_{jk} \mathbf{x}_k \|^2 + 2\lambda |\gamma_{jk}|.
\]

Since \( f(\gamma_{jk}) \) is nonnegative and convex, \( F(\Gamma) \) is minimum if each component \( f(\gamma_{jk}) \) achieves minimum. So we only need to minimize each component \( f(\gamma_{jk}) \). This differentiates our sparse correlation formulation from the standard compressed sensing that cannot be optimized in this component wise fashion. \( f(\gamma_{jk}) \) can be rewritten as

\[
f(\gamma_{jk}) = \| \mathbf{x}_j \|^2 - 2\gamma_{jk} \mathbf{x}_j^\top \mathbf{x}_k + \gamma_{jk}^2 \| \mathbf{x}_k \|^2 + 2\lambda |\gamma_{jk}|
\]

\[
= (\gamma_{jk} - \mathbf{x}_j^\top \mathbf{x}_k)^2 + 2\lambda |\gamma_{jk}| + 1.
\]

We used the fact \( \mathbf{x}_j^\top \mathbf{x}_j = 1 \).

For \( \lambda = 0 \), the minimum of \( f(\gamma_{jk}) \) is achieved when \( \gamma_{jk} = \mathbf{x}_j^\top \mathbf{x}_k \), which is the usual LSE. For \( \lambda > 0 \), Since \( f(\gamma_{jk}) \) is quadratic in \( \gamma_{jk} \), the minimum is achieved when

\[
\frac{\partial f}{\partial \gamma_{jk}} = 2\gamma_{jk} - 2\mathbf{x}_j^\top \mathbf{x}_k \pm 2\lambda = 0
\]

(15)
The sign of $\lambda$ depends on the sign of $\gamma_{jk}$. Thus, sparse correlation $\hat{\gamma}_{jk}$ is given by a soft-thresholding of $x_j^T x_k$:

$$
\hat{\gamma}_{jk}(\lambda) = \begin{cases} 
    x_j^T x_k - \lambda & \text{if } x_j^T x_k > \lambda \\
    0 & \text{if } |x_j^T x_k| \leq \lambda \\
    x_j^T x_k + \lambda & \text{if } x_j^T x_k < -\lambda
\end{cases}
$$

(16)

The estimated sparse correlation (16) basically thresholds the sample correlation that is larger or smaller than $\lambda$ by the amount $\lambda$. Due to this simple expression, there is no need to optimize (23) numerically as often done in compressed sensing or LASSO (Peng et al. 2009, Friedman et al. 2008). However, Theorem 2 is only applicable to separable cases and for non-separable cases, numerical optimization is still needed.

The different choices of sparsity parameter $\lambda$ will produce different solutions in sparse model $A(\lambda)$. Instead of analyzing each model separately, we can analyze the whole collection of all the sparse solutions for many different values of $\lambda$. This avoids the problem of identifying the optimal sparse parameter that may not be optimal in practice. The question is then how to use the collection of $A(\lambda)$ in a coherent mathematical fashion. This can be addressed using persistent homology (Edelsbrunner & Harer 2008, Lee, Chung, Kang, Kim & Lee 2011, Lee et al. 2012).

### 3.2 Filtration in sparse correlations

Using the sparse solution (16), we can construct a filtration. We will basically build a graph $G$ using sparse correlations. Let $\hat{\gamma}_{jk}(\lambda)$ be the sparse correlation estimate. Let $A(\lambda) = (a_{ij})$ be the adjacency matrix defined as

$$
a_{jk}(\lambda) = \begin{cases} 
    1 & \text{if } \hat{\gamma}_{jk}(\lambda) \neq 0; \\
    0 & \text{otherwise.}
\end{cases}
$$

This is equivalent to the adjacency matrix $B = (b_{jk})$ defined as

$$
b_{jk}(\lambda) = \begin{cases} 
    1 & \text{if } |x_j^T x_k| > \lambda; \\
    0 & \text{otherwise.}
\end{cases}
$$

(17)

The adjacency matrix $B$ is simply obtained by thresholding the sample correlations. Then the adjacency matrices $A$ and $B$ induce a identical graph $G(\lambda)$ consisting of $\kappa(\lambda)$ number of partitioned subgraphs

$$
G(\lambda) = \bigcup_{l=1}^{\kappa(\lambda)} G_l(\lambda) \text{ with } G_l = \{V_l(\lambda), E_l(\lambda)\},
$$

where $V_l$ and $E_l$ are node and edge sets respectively. Note

$$
G_l \cap G_m = \emptyset \text{ for any } l \neq m.
$$
and no two nodes between the different partitions are connected. The node and edge sets are denoted as $V(\lambda) = \bigcup_{\kappa=1}^{\lambda} V_{\kappa}$ and $E(\lambda) = \bigcup_{\kappa=1}^{\lambda} E_{\kappa}$ respectively. Then we have the following theorem:

**Theorem 3.** The induced graph from the sparse correlation forms a filtration:

$G(\lambda_1) \supset G(\lambda_2) \supset G(\lambda_3) \supset \cdots$ \hspace{1cm} (18)

for $\lambda_1 \leq \lambda_2 \leq \lambda_3 \leq \cdots$. Equivalently, the node and edge sets also form filtrations as well:

$V(\lambda_1) \supset V(\lambda_2) \supset V(\lambda_3) \supset \cdots$

$E(\lambda_1) \supset E(\lambda_2) \supset E(\lambda_3)$.

The proof can be easily obtained from the definition of adjacency matrix (17).

### 3.3 Sparse cross-correlations

We can extend the sparse correlation framework to the sparse cross-correlations. Let $V = \{v_1, \cdots, v_p\}$ be a node set where data is observed. We expect the number of nodes $p$ to be significantly larger than the number of images $n$, i.e., $p \gg n$. Let $x_k(v_i)$ and $y_k(v_i)$ be the $k$-th paired scalar measurements at node $v_i$. They can be twins, longitudinal scans or even multimodal images. Denote
Fig. 6: The schematic of hyper-network construction on paired image vectors $\mathbf{x}$ and $\mathbf{y}$. The image vectors $\mathbf{y}$ at voxel $v_j$ is modeled as a linear combination of the first image vector $\mathbf{x}$ at all other voxels. The estimated parameters $\beta_{ij}$ give the hyper-edge weights.

$$\mathbf{y}(v_j) = \sum_{i,j=1}^{p} \beta_{ij} \mathbf{x}(v_i) + \mathbf{e}$$

$x(v_i) = (x_1(v_i), \ldots, x_n(v_i))^T$ and $y(v_i) = (y_1(v_i), \ldots, y_n(v_i))^T$ be the paired data vectors over $n$ different images at voxel $v_i$. Center and scale $\mathbf{x}$ and $\mathbf{y}$ such that

$$\sum_{k=1}^{n} x_k(v_i) = \sum_{k=1}^{n} y_k(v_i) = 0,$$

$$\|\mathbf{x}(v_i)\|^2 = \mathbf{x}^T(v_i)\mathbf{x}(v_i) = \|\mathbf{y}(v_i)\|^2 = \mathbf{y}^T(v_i)\mathbf{y}(v_i) = 1$$

for all $v_i$. The reasons for centering and scaling will soon be obvious.

We set up a hyper-network by relating the paired vectors at different voxels $v_i$ and $v_j$:

$$\mathbf{y}(v_j) = \sum_{i=1}^{p} \beta_{ij} \mathbf{x}(v_i) + \mathbf{e}$$

for some zero-mean noise vector $\mathbf{e}$ (Fig. 6). The parameters $\beta = (\beta_{ij})$ are the weights of the hyper-edges between voxels $v_i$ and $v_j$ that have to be estimated.

We are constructing a physically nonexistent artificial network across different images. For fMRI, (19) requires estimating over billions of connections, which is computationally challenging. In practice however, each application will likely to force $\beta$ to have a specific structure that may reduce the computational burden.

For this section, let us set up a linear model between $\mathbf{x}(v_i)$ and $\mathbf{y}(v_j)$:

$$\mathbf{y}(v_j) = b_{ij} \mathbf{x}(v_i) + \mathbf{e},$$

(20)
where $\mathbf{e}$ is the zero-mean error vector whose components are independent and identically distributed. Since the data are all centered, we do not have the intercept in linear regression (20). The least squares estimation (LSE) of $b_{ij}$ that minimizes the L2-norm

$$
\sum_{i,j=1}^{p} \| y(v_j) - b_{ij} x(v_i) \|^2
$$

is given by

$$
\hat{b}_{ij} = x^T(v_i) y(v_j),
$$

which are the (sample) cross-correlations (Worsley, Charil, Lerch & Evans 2005, Worsley, Chen, Lerch & Evans 2005). The cross-correlation is invariant under the centering and scaling operations. The sparse version of L2-norm (21) is given by

$$
F(\beta; x, y, \lambda) = \frac{1}{2} \sum_{i,j=1}^{p} \| y(v_j) - \beta_{ij} x(v_i) \|^2 + \lambda \sum_{i,j=1}^{p} |\beta_{ij}|.
$$

The sparse cross-correlation is then obtained by minimizing over every possible $\beta_{ij} \in \mathbb{R}$:

$$
\hat{\beta}(\lambda) = \arg\min_{\beta} F(\beta; x, y, \lambda).
$$

The estimated sparse cross-correlations $\hat{\beta}(\lambda) = (\hat{\beta}_{ij}(\lambda))$ shrink toward zero as sparse parameter $\lambda \geq 0$ increases. The direct optimization of (23) for large $p$ is computationally demanding. However, there is no need to optimize (23) numerically using the coordinate descent learning or the active-set algorithm as often done in sparse optimization (Peng et al. 2009, Friedman et al. 2008). We can show that the minimization of (23) is simply done algebraically.

**Theorem 4.** For $\lambda \geq 0$, the minimizer of $F(\beta; x, y, \lambda)$ is given by

$$
\hat{\beta}_{ij}(\lambda) = \begin{cases} 
    x^T(v_i) y(v_j) - \lambda & \text{if } x^T(v_i) y(v_j) > \lambda \\
    0 & \text{if } |x^T(v_i) y(v_j)| \leq \lambda \\
    x^T(v_i) y(v_j) + \lambda & \text{if } x^T(v_i) y(v_j) < -\lambda
\end{cases}.
$$

Although it is not obvious, Theorem 4 is related to the orthogonal design in LASSO (Tibshirani 1996) and the soft-shrinkage in wavelets (Donoho et al. 1995). To see this, let us transform linear equations (20) into a index-free matrix equation:

$$
\begin{bmatrix}
    y(v_1) & \cdots & y(v_1) \\
    y(v_2) & \cdots & y(v_2) \\
    \vdots & \ddots & \vdots \\
    y(v_p) & \cdots & y(v_p)
\end{bmatrix}
\begin{bmatrix}
    \mathbf{b}_{11} x(v_1) & \mathbf{b}_{21} x(v_2) & \cdots & \mathbf{b}_{p1} x(v_p) \\
    \mathbf{b}_{12} x(v_1) & \mathbf{b}_{22} x(v_2) & \cdots & \mathbf{b}_{p2} x(v_p) \\
    \vdots & \vdots & \ddots & \vdots \\
    \mathbf{b}_{1p} x(v_1) & \mathbf{b}_{2p} x(v_2) & \cdots & \mathbf{b}_{pp} x(v_p)
\end{bmatrix}
= 
\begin{bmatrix}
    \mathbf{e} & \cdots & \mathbf{e}
\end{bmatrix}
$$

$$
+ 
\begin{bmatrix}
    \mathbf{e} & \cdots & \mathbf{e}
\end{bmatrix}.
Fig. 7: Schematic showing the equivalence of binary graph construction using the sparse cross-correlations and soft-thresholding. Top: The sparse cross-correlations are estimated by minimizing the $L_1$ cost function (23) for 4 different sparse parameters $\lambda$. The edge weights shrinked to zero are removed. Bottom: the equivalent binary graph can be obtained by soft-thresholding, i.e., simply thresholding the sample cross-correlations at $\lambda$.

The above matrix equation can be vectorized as follows.

$$
\begin{bmatrix}
y(v_1) \\
\vdots\\
y(v_p)
\end{bmatrix}
= 
\begin{bmatrix}
x(v_1) & \cdots & 0 \\
\vdots & \ddots & \vdots \\
0 & \cdots & x(v_1)
\end{bmatrix}
\begin{bmatrix}
b_{11} \\
\vdots\\
b_{p1}
\end{bmatrix}
+ 
\begin{bmatrix}
e \\
\vdots\\
e
\end{bmatrix}
\begin{bmatrix}
1 & 1 & \cdots & 1 \\
\vdots & \ddots & \vdots & \vdots \\
1 & 1 & \cdots & 1
\end{bmatrix}
$$

The above equation can be written in a more compact form. Let

$$
X_{n \times p} = [x(v_1) \; x(v_2) \cdots x(v_p)] \\
Y_{n \times p} = [y(v_1) \; y(v_2) \cdots y(v_p)] \\
I_{a \times b} = 
\begin{bmatrix}
1 & 1 & \cdots & 1 \\
\vdots & \ddots & \vdots & \vdots \\
1 & 1 & \cdots & 1
\end{bmatrix}_{a \times b}
$$

Then the matrix equation can be written as

$$
1_{p \times 1} \otimes \text{vec}(Y) = X_{np^2 \times p^2} \text{vec}(b) + 1_{np^2 \times 1} \otimes e, \quad (26)
$$
where \textit{vec} is the vectorization operation. The block diagonal design matrix \(X\) consists of \(p\) diagonal blocks \(I_p \otimes x(v_1), \ldots, I_p \otimes x(v_p)\), where \(I_p\) is \(p \times p\) identity matrix. Subsequently, \(X^\top X\) is again a block diagonal matrix, where the \(i\)-th block is

\[
[I_p \otimes x(v_i)]^\top [I_p \otimes x(v_i)] = I_p \otimes [x(v_i)^\top x(v_i)] = I_p.
\]

Thus, \(X\) is an orthogonal design. However, our formulation is not exactly the orthogonal design of LASSO as specified in (Tibshirani 1996) since the noise components in (26) are not independent. Further in standard LASSO, there are more columns than rows in \(X\). In our case, there are \(n\) times more rows. Still the soft-thresholding method introduced in (Tibshirani 1996) is applicable and we obtain the analytic solution, which speed up the computation drastically compared to existing LASSO-based numerical optimization (Figure 8) (Peng et al. 2009, Friedman et al. 2008).

Theorem 4 generalizes the sparse correlation case given in Chung et al. (2013). Figure 7-top displays an example of obtaining sparse cross-correlations from the initial sample cross-correlation matrix

\[
X^\top Y = \begin{pmatrix}
\times & 0.4 & 0.5 & -0.7 \\
\times & \times & 0.3 & -0.1 \\
\times & \times & \times & 0.9
\end{pmatrix}
\]
using Theorem 4. Due to directional nature of the cross-correlation matrix, only the upper triangle part of the sample cross-correlation is demonstrated.

4 Partial correlation network

Let \( p \) be the number of nodes in the network. In most applications, the number of nodes is expected to be larger than the number of observations \( n \), which gives an underdetermined system. Consider measurement vector at the \( j \)-th node

\[
x_j = (x_{1j}, \ldots, x_{nj})^T
\]

consisting of \( n \) measurements. Vector \( x_j \) are assumed to be distributed with mean zero and covariance \( \Sigma = (\sigma_{ij}) \). The correlation \( \gamma_{ij} \) between the two nodes \( i \) and \( j \) is given by

\[
\gamma_{ij} = \frac{\sigma_{ij}}{\sqrt{\sigma_{ii}\sigma_{jj}}}
\]

By thresholding the correlation, we can establish a link between two nodes. However, there is a problem with this simplistic approach in that it fails to explicitly factor out the confounding effect of other nodes. To remedy this problem, partial correlations can be used in factoring out the dependency of other nodes (He et al. 2007, Marrelec et al. 2006, Huang et al. 2009, 2010, Peng et al. 2009).

If we denote the inverse covariance matrix as \( \Sigma^{-1} = (\sigma^{-1}) \), the partial correlation between the nodes \( i \) and \( j \) while factoring out the effect of all other nodes is given by (Peng et al. 2009)

\[
\rho_{ij} = -\frac{\sigma_{ij}}{\sqrt{\sigma_{ii}\sigma_{jj}}}, \quad (27)
\]

Equivalently, we can compute the partial correlation via a linear model as follows. Consider a linear model of correlating measurement at node \( j \) to all other nodes:

\[
x_j = \sum_{k \neq j} \beta_{jk} x_k + \epsilon_k. \quad (28)
\]

The parameters \( \beta_{jk} \) are estimated by minimizing the sum of squared residual of (28)

\[
L(\beta) = \sum_{j=1}^{p} \|x_j - \sum_{k \neq j} \beta_{jk} x_k\|^2 \quad (29)
\]

in a least squares fashion. If we denote the least squares estimator by \( \hat{\beta}_{jk} \), the residuals are given by

\[
r_j = x_j - \sum_{k \neq j} \hat{\beta}_{jk} x_k. \quad (30)
\]

The partial correlation is then obtained by computing the correlation between the residuals (He et al. 2007, Lerch et al. 2006, Peng et al. 2009):

\[
\rho_{ij} = \text{corr} (r_i, r_j).
\]
4.1 Sparse partial correlations

There is a serious problem with the least squares estimation framework discussed in the previous section. Since \( n \ll p \), this is a significantly underdetermined system. This is also related to the covariance matrix \( \Sigma \) being singular so we cannot just invert the covariance matrix. For this, we need sparse network modeling.

The minimization of (29) is exactly given by solving the normal equation:

\[
x_j = \sum_{k \neq j} \beta_{jk} x_k,
\]

which can be turned into standard linear form \( y = A\beta \) (Lee, Lee, Kang, Kim & Chung 2011). Note that (31) can be written as

\[
x_j = \begin{bmatrix} x_1, \ldots, x_{j-1}, 0, x_{j+1}, \ldots, x_p \end{bmatrix} \begin{pmatrix} \beta_{j1} \\ \beta_{j2} \\ \vdots \\ \beta_{jp} \end{pmatrix},
\]

where \( 0_{n \times 1} \) is a column vector of all zero entries. Then we have

\[
\begin{pmatrix} x_1 \\ x_2 \\ \vdots \\ x_p \end{pmatrix} = \begin{pmatrix} X_{-1} & 0 & \cdots & 0 \\ 0 & X_{-2} & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & X_{-p} \end{pmatrix} \begin{pmatrix} \beta_{1} \\ \beta_{2} \\ \vdots \\ \beta_{p} \end{pmatrix},
\]

where \( A \) is a block diagonal matrix and \( 0_{n \times p} \) is a matrix of all zero entries. We regularize (32) by incorporating \( l_1 \) LASSO-penalty \( J \) (Tibshirani 1996, Peng et al. 2009, Lee, Lee, Kang, Kim & Chung 2011):

\[
J = \sum_{i,j} |\beta_{ij}|.
\]

The sparse estimation of \( \beta_{ij} \) is then given by minimizing \( L + \lambda J \). Since there is dependency between \( y \) and \( A \), (32) is not exactly a standard compressed sensing problem (Peng et al. 2009, Lee, Lee, Kang, Kim & Chung 2011). It should be intuitively understood that sparsity makes the linear equation (31) less underdetermined. The larger the value of \( \lambda \), the more sparse the underlying topological structure gets. Since

\[
\rho_{ij} = \beta_{ij} \sqrt{\frac{\sigma_{ii}}{\sigma_{jj}}},
\]

the sparsity of \( \beta_{ij} \) directly corresponds to the sparsity of \( \rho_{ij} \), which is the strength of the link between nodes \( i \) and \( j \) (Peng et al. 2009, Lee, Lee, Kang, Kim & Chung 2011). Once the sparse partial correlation matrix \( \rho \) is obtained, we can simply link nodes \( j \) and \( j \), if \( \rho_{ij} > 0 \) and assign the weight \( \rho_{ij} \) to the edge. This way, we obtain the weighted graph.
4.2 Limitations

However, the sparse partial correlation framework has a serious computational bottleneck. For $n$ measurements over $p$ nodes, it is required that we solve a linear system with an extremely large $A$ matrix of size $np \times p^2$, so that the complexity of the problem increases by a factor of $p^3!$. Consequently, for a large number of nodes, the problem immediately becomes almost intractable for a small computer. For example, for 1 million nodes, we have to compute 1 trillion possible pairwise relationships between nodes. One practical solution is to modify (28) so that the measurement at node $i$ is represented more sparsely over some possible index set $S_i$:

$$x_i = \sum_{S_i} \beta_{ij} x_j + \epsilon_i.$$ 

making the problem substantially smaller.

An alternate approach is to simply follow the homotopy path, which adds network edges one by one with a very limited increase of computational complexity so there is no need to compute $\beta$ repeatedly from scratch (Donoho & Tsaig 2006, Plumbley 2005, Osborne et al. 2000). The trajectory of the optimal solution $\beta$ in LASSO follows a piecewise linear path as we change $\lambda$. By tracing the linear path, we can substantially reduce the computational burden of reestimating $\beta$ when $\lambda$ changes.

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