IDENTIFYING STRUCTURAL BRAIN NETWORKS FROM FUNCTIONAL CONNECTIVITY: A NETWORK DECONVOLUTION APPROACH

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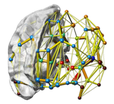
Abstract

We address the problem of identifying structural brain networks from brain signals measured by resting-state functional magnetic resonance imaging (fMRI). Functional brain activity is modeled as graph signals generated through a linear diffusion process on the unknown structural network. A network deconvolution approach is advocated to: (i) use the fMRI signals to estimate the eigenvectors of the structural network from those of the empirical covariance; and (ii) solve a convex, sparsity-regularized inverse problem to recover the eigenvalues that were obscured by diffusion. The inferred structural networks capture key patterns matching known pathology and may serve as biomarkers for further diagnosis.

Motivation and context

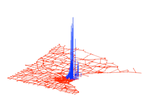
- Understanding brain function is a fundamental scientific challenge
- Network science with graph-centric tools valuable for brain analysis
- Neuroimaging studies are time-consuming and expensive
  - ⇒ Functional (FC) and structural connectivity (SC)
  - ⇒ FC and SC differ in resolution, running-time, acquisition
  - ⇒ Costly to measure FC and SC separately
- Relation between FC & SC worth exploring

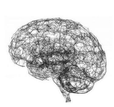


- Most previous work estimated FC from SC via
  - ⇒ Linear, parametric diffusion model relating FC and SC
  - ⇒ Large-scale simulation of nonlinear dynamics
- We take the reverse path
  - ⇒ How to infer SC from observed FC?

Graph signal processing - 101

- Network as graph $\mathcal{G} = (\mathcal{V}, \mathbf{A})$: encode pairwise relationships
- Interest here not in $\mathcal{G}$ itself, but in data associated with nodes in $\mathcal{V}$
  - ⇒ The object of study is a graph signal
- Ex: Opinion profile, buffer congestion levels, neural activity, epidemic





- Graph SP: need to broaden classical SP results to graph signals
  - ⇒ Our view: GSP well suited for brain network and signal analysis

Structural brain networks and functional signals

- Structural brain networks represent anatomical brain connections
  - ⇒ Modeled via a weighted, undirected graph $\mathcal{G} := (\mathcal{V}, \mathbf{A})$
  - ⇒ SC: Sparse and symmetric adjacency matrix $\mathbf{A} = \mathbf{V}\mathbf{\Lambda}\mathbf{V}^\top$
- Brain signals quantify level of neuronal acitivity in brain regions
- fMRI readings on N brain regions over T timepoints

$$\mathbf{X} = [\mathbf{x}_1, ..., \mathbf{x}_T] \in \mathbb{R}^{N \times T}$$

  - ⇒ FC: covariance of fMRI signals $\mathbf{\Sigma} = \mathbb{E}[\mathbf{x}\mathbf{x}^T]$
- Link SC with FC: Generative model for brain signals $\mathbf{x}$ supported on $\mathcal{G}$

Diffusion process model of functional signals

- Signal $\mathbf{x}$ generated via diffusion over structural network $\mathcal{G} := (\mathcal{V}, \mathbf{A})$

$$\mathbf{x} = \alpha_0 \prod_{l=1}^{\infty}(\mathbf{I} - \alpha_l \mathbf{A})\mathbf{w} = \sum_{l=0}^{\infty} \beta_l \mathbf{A}^l \mathbf{w}$$

  - ⇒ Zero-mean white input signal $\mathbf{w}$ with covariance $\mathbb{E}[\mathbf{w}\mathbf{w}^\top] = \mathbf{I}$
  - ⇒ SC $\mathbf{A}$ encodes one-hop interactions among brain regions
- Diffusion process induces multi-hop relations
  - ⇒ Capture indirect interactions
  - ⇒ Shape up FC structure and statistics
- From Cayley Hamilton, rewrite diffusion as

$$\mathbf{x} = \left(\sum_{l=0}^{L-1} h_l \mathbf{A}^l\right)\mathbf{w} = \mathbf{H}\mathbf{w}$$

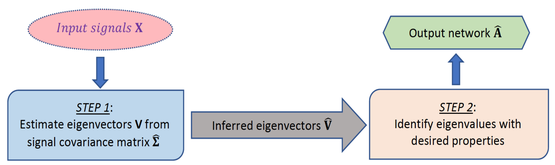
  - ⇒ Graph filter $\mathbf{H} := \sum_{l=0}^{L-1} h_l \mathbf{A}^l \in \mathbb{R}^{N \times N}$

Problem statement

Problem: Given resting-state fMRI readings $\mathbf{X} = [\mathbf{x}_1, ..., \mathbf{x}_T] \in \mathbb{R}^{N \times T}$ generated by diffusion process in the network $\mathcal{G}$, estimate the structural connectivity encoded in the sparse adjacency matrix $\mathbf{A}$

Network deconvolution

- We propose a network deconvolution approach



STEP 1: Obtaining the eigenvectors

- Recall $\mathbf{A} = \mathbf{V}\mathbf{\Lambda}\mathbf{V}^\top$, decompose graph filter as

$$\mathbf{H} = \sum_{l=0}^{L-1} h_l(\mathbf{V}\mathbf{\Lambda}\mathbf{V}^\top)^l = \mathbf{V}\left(\sum_{l=0}^{L-1} h_l \mathbf{\Lambda}^l\right)\mathbf{V}^\top$$

- Use $\mathbb{E}[\mathbf{w}\mathbf{w}^\top] = \mathbf{I}$, can write covariance matrix (FC) as

$$\mathbf{\Sigma} = \mathbb{E}[\mathbf{H}\mathbf{w}(\mathbf{H}\mathbf{w})^\top] = \mathbf{H}\mathbf{H}^\top = \mathbf{V}\left(\sum_{l=0}^{L-1} h_l \mathbf{\Lambda}^l\right)^2 \mathbf{V}^\top$$

- $\mathbf{A}$ and $\mathbf{\Sigma}$ share the same eigenvectors $\mathbf{V}$
  - ⇒ Only difference between them are eigenvalues
  - ⇒ Use $\hat{\mathbf{\Sigma}}$ obtained from signals $\mathbf{X}$ to estimate eigenvectors $\hat{\mathbf{V}}$ of $\mathbf{A}$

Ambiguity: Deconvolutoin problem is underdetermined. As long as the matrices $\mathbf{\Sigma}$ and $\mathbf{A}$ have the same eigenvectors, there exist filter coefficients $\mathbf{h}$ that generate $\mathbf{x}$ through a diffusion process on $\mathcal{G}$

- Need additional assumptions to sort out ambiguity
- Criteria for choosing eigenvalues for meaningful graph structure

STEP 2: Obtaining the eigenvalues

- To determine eigenvalues of the adjacency matrix, seek $\mathbf{A}$ that:
  - ⇒ Is optimal with respect to convex criteria $f(\mathbf{A}, \mathbf{\Lambda})$
  - ⇒ Belongs to convex set $\mathcal{S}$ of admissible adjacency matrices

$$\mathcal{S} := \{\mathbf{A} \,|\, A_{ij} = A_{ji} \geq 0, A_{ii} = 0, \textstyle\sum_j A_{j1} = 1\}$$

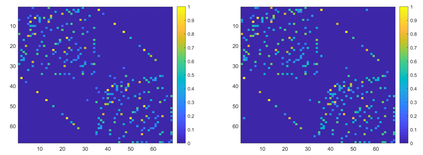
  - ⇒ Is close to $\hat{\mathbf{V}}\mathbf{\Lambda}\hat{\mathbf{V}}^T$ measured by a convex matrix distance metric
- Brain SC: sparse with fewer inter-hemisphere connections
  - ⇒ Choose a sparsity-promoting criterion $f(\mathbf{A}, \mathbf{\Lambda}) = \|\mathbf{W} \circ \mathbf{A}\|_1$
  - ⇒ $\mathbf{W}$ imposes non-uniform sparsity priors across candidate edges
- Formally, our idea is to solve the inverse problem

$$\hat{\mathbf{A}} := \underset{\mathbf{\Lambda}, \mathbf{A} \in \mathcal{S}}{\operatorname{argmin}} \ \|\mathbf{W} \circ \mathbf{A}\|_1, \quad \text{s. to } \|\mathbf{A} - \hat{\mathbf{V}}\mathbf{\Lambda}\hat{\mathbf{V}}^T\|_F^2 \leq \epsilon$$

  - ⇒ $\mathcal{O}(N^3)$ complexity, scales to brain atlas with ~ 100 regions
  - ⇒ More efficient than traditional non-linear simulations

Numerical tests: simulated signals on known graph structure

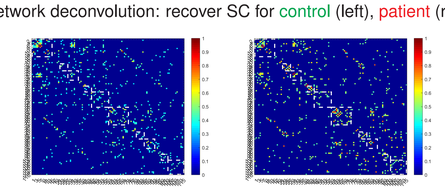
- Ground-truth preprocessed structural brain network $\mathcal{G}_0$ (left)
- Generate synthetic signals via diffusion model with Gaussian inputs
- Network deconvolution to recover structural network $\mathcal{G}_r$ (right)



- Edge normalized and thresholded to maintain connected graphs
- Recovery error of 11.1% over 10 Monte Carlo realizations

ADHD data group-level analysis: Network recovery

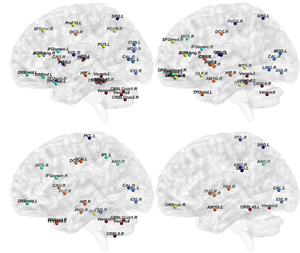
- Data: Preprocessed BOLD signals from ADHD-200 dataset
  - ⇒ 182 healthy subjects and 107 ADHD type-1 patients
  - ⇒ Signals registered on AAL-116 brain atlas
- Concatenate brain signals of subjects in each group into
  - ⇒ $\mathbf{X}_c \in \mathbb{R}^{116 \times 182T}$ for the control group
  - ⇒ $\mathbf{X}_p \in \mathbb{R}^{116 \times 107T}$ for the patient group
- Network deconvolution: recover SC for control (left), patient (right)



- For patients, edges more clustered in diagonal blocks
  - ⇒ *Frontal, Occipital, Parietal, Temporal and Cerebellum*
  - ⇒ Loss of long-range connection
  - ⇒ Increased local connection

ADHD data group-level analysis: Network comparison

- Quantitatively analyze recovered SCs across groups
- Network analytic methods: compare node-level graph metrics
  - ⇒ Clustering coefficient, closeness, degree, local efficiency
    - ⇒ Combo: graph metric of a node, e.g. *degree of Frontal*



- 105 combos found with ***significantly*** larger metrics in patient group
  - ⇒ *e.g. degree of left paracentral lobule, closeness of right caudate*
  - ⇒ *e.g. local efficiency of right paracentral, degree of right fusiform*

ADHD data subject-level analysis: Classification

- Data: Processed BOLD signals of 30 controls, 29 patients
- Goal: Perform subject-level patient-control classification
- Method: Recover $A \in \mathbb{R}^{116 \times 116}$ for each subject, and
  - ⇒ Compute above 4 metrics for each of the 116 nodes
  - ⇒ Concatenate and obtain feature vector $\mathbf{f}_1 \in \mathbb{R}^{464}$ per subject
  - ⇒ Extract 105 combos identified above from $\mathbf{f}_1 \to \mathbf{f}_2 \in \mathbb{R}^{105}$
  - ⇒ Sequential forward selection to reduce dimension to 6
  - ⇒ Machine learning classifier models on feature vector inputs

	ACC	AUC	TPR	TNR
$\mathbf{f}_2 \in \mathbb{R}^{105}$ with selection	**0.774**	**0.836**	**0.767**	**0.782**
$\mathbf{f}_1 \in \mathbb{R}^{464}$ with selection	0.678	0.737	0.733	0.621
Method in [Feizi et al'13]	0.492	0.493	0.522	0.459

- 105 identified combos help improve classification accuracy
  - ⇒ Network deconvolution model accurately infers SC
  - ⇒ Recovered SC captures key patterns in brain networks
- More general diffusion model and sparsity promotion
- Competitive with results of ADHD-200 global competition

Discussion and road ahead

- **Network deconvolution** framework to identify SC from fMRI signals
- Built upon **linear diffusion model** between FC and SC
- Group-level and subject-level analysis match existing results
- Identified brain regions with discriminative power for patient diagnosis
- Envisioned research topics
  - ⇒ Further validate recovery of SC from observed signals
  - ⇒ Exploring graph frequency domain for discriminative features
  - ⇒ Subject-level network inference and disease diagnosis

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