Estimating Functional Connectivity from fMRI Data Using a Frequency-Sparse Multivariate Autoregressive Model

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Introduction

Measures of functional connectivity such as partial directed coherence (PDC) derive from fitting multivariate autoregressive (MVAR) models to functional magnetic resonance imaging (fMRI) data. To regularize the ill-posed parameter estimation problem of fitting MVAR models, recent work has focused on LASSO and group LASSO-type penalties. These approaches consider the model parameters in the usual Euclidean (what we call time-based) basis. Motivated by solving inverse problems in alternative bases, we introduce LASSO-type penalty in a Fourier basis (frequency-based). Then, we propose an iterative shrinkage algorithm to solve it and report preliminary results from applying it on a fMRI dataset.

Time-based MVAR Model

MVAR Process

Let $(\mathbf{x}_t \in \mathbb{R}^n)_{1\leq t\leq N}$ be a causal and stable m-order MVAR process,

$$\mathbf{x}_t = \mathbf{A}_1\mathbf{x}_{t-1} + \mathbf{A}_2\mathbf{x}_{t-2} + \cdots + \mathbf{A}_m\mathbf{x}_{t-m} + \eta_t, \tag{1}$$

with η_t iid Gaussian, *i.e.* $\eta_t \sim \mathcal{N}(\mathbf{0}, \mu\mathbf{I})$ for $\mu > 0 \in \mathbb{R}$.

Maximum *a Posteriori* (MAP) Estimator

We want to find $\mathbf{A}_1, \ldots, \mathbf{A}_m \in \mathbb{R}^{n\times n}$, a typically ill-posed parameter estimation problem. It can be solved using a LASSO-type penalty as in [1]:

$$\operatorname*{arg\,min}_{\mathbf{A}_1,\ldots,\mathbf{A}_m\in\mathbb{R}^{n\times n}} \sum_{t=m+1}^{N} \frac{1}{2}\left\|\mathbf{x}_t - \sum_{s=1}^{m}\mathbf{A}_s\mathbf{x}_{t-s}\right\|^2 + \mu\sum_{i,j=1}^{n}\sum_{s=1}^{m}\left|[A_s]_{i,j}\right|. \tag{2}$$

Frequency-based MVAR Model

Let $\mathcal{H} = \ell^2(\mathbb{Z}_N) \otimes (\mathbb{R}^n, \|\cdot\|_2)$ such that $(\mathbf{x}_t \in \mathbb{R}^n)_{t\in\mathbb{Z}_N} \in \mathcal{H}$. Then, we are looking for a linear operator on $\mathcal{H}$, $\mathbf{A} \in \mathcal{B}(\mathcal{H})$.

Hilbert-Schmidt Operators

We consider compact Hilbert-Schmidt operators, $\mathcal{S}(\mathcal{H}) \subset \mathcal{B}(\mathcal{H})$. Let $\Phi = (\phi_\lambda)_{\lambda\in\Lambda}$ be an orthonormal basis of $\mathcal{H}$. Then,

$$\mathcal{S}(\mathcal{H}) = \left\{\mathbf{A} \in \mathcal{B}(\mathcal{H}) : \|\mathbf{A}\|_{\mathcal{S}(\mathcal{H})} < \infty\right\} \tag{3}$$

where the Hilbert-Schmidt norm is

$$\|\mathbf{A}\|^2_{\mathcal{S}(\mathcal{H})} = \sum_{\lambda\in\Lambda}\|\mathbf{A}\phi_\lambda\|^2_{\mathcal{H}}. \tag{4}$$

Orthonormal Basis of $\mathcal{H}$

Let $E = (\mathbf{e}_i)_{i=0}^{n-1}$ be any orthonormal basis of $(\mathbb{R}^n, \|\cdot\|_2)$ and $\mathcal{F} = (\mathcal{F}_k)_{k\in\mathbb{Z}_N}$ be the discrete Fourier basis of $\ell^2(\mathbb{Z}_N)$. We choose $\Phi = \mathcal{F} \otimes E$ such that $\Lambda = \mathbb{Z}_N \times \{0, \ldots, n-1\}$.

Convolution Operators

$\mathbf{A} \in \mathcal{S}(\mathcal{H})$ must be a convolution operator, *i.e.* non-identity and diagonal in the Φ basis,

$$\mathcal{C}(\mathcal{H}) = \left\{\mathbf{A} \in \mathcal{S}(\mathcal{H}) : \mathbf{A} = \sum_{\lambda\in\Lambda} a_\lambda \langle\cdot, \phi_\lambda\rangle\,\phi_\lambda,\ \mathbf{A} \neq \mathbf{I}\right\}. \tag{5}$$

MAP Estimator

This leads to the following generalization of (2):

$$\operatorname*{arg\,min}_{\mathbf{A}\in\mathcal{C}(\mathcal{H})} \frac{1}{2}\|\mathbf{x} - \mathbf{A}\mathbf{x}\|^2_{\mathcal{H}} + \mu\sum_{\lambda\in\Lambda}\|\mathbf{A}\phi_\lambda\|_{\mathcal{H}} \tag{6}$$

Iterative Shrinkage Algorithm

Surrogate Functional

The algorithm derives from [2], in which a surrogate functional is solved iteratively. That surrogate functional is strictly convex and asymptotically equivalent to (6). For a diagonal operator $\mathbf{D} : \mathcal{S}(\mathcal{H}) \to \mathcal{S}(\mathcal{H})$ and $\mathbf{A}, \mathbf{Z} \in \mathcal{C}(\mathcal{H})$,

$$\begin{aligned}\operatorname*{arg\,min}_{\mathbf{A}\in\mathcal{C}(\mathcal{H})}\ & \frac{1}{2}\|\mathbf{x} - \mathbf{A}\mathbf{x}\|^2_{\mathcal{H}} + \mu\sum_{\lambda\in\Lambda}\|\mathbf{A}\phi_\lambda\|_{\mathcal{H}} \\ & + \frac{1}{2}\|\mathbf{D}(\mathbf{A} - \mathbf{Z})\|^2_{\mathcal{S}(\mathcal{H})} - \frac{1}{2}\|(\mathbf{A} - \mathbf{Z})\,\mathbf{x}\|^2_{\mathcal{H}}.\end{aligned} \tag{7}$$

Algorithm

Let $\mathbf{A}^{(0)} \in \mathcal{C}(\mathcal{H})$. Then,

$$\begin{aligned} a_\lambda^{(k+1)/2} &= a_\lambda^{(k)} + \frac{\langle\mathbf{x}, \phi_\lambda\rangle_{\mathcal{H}}}{d_\lambda}\left\langle \mathbf{x} - \mathbf{A}^{(k)}\mathbf{x}, \phi_\lambda\right\rangle_{\mathcal{H}} \\ a_\lambda^{(k+1)} &= S_\mu\left(a_\lambda^{(k+1)/2}\right) \\ \mathbf{A}^{(k+1)} &= \sum_{\lambda\in\Lambda} a_\lambda^{(k+1)}\langle\cdot, \phi_\lambda\rangle\,\phi_\lambda \end{aligned} \tag{8}$$

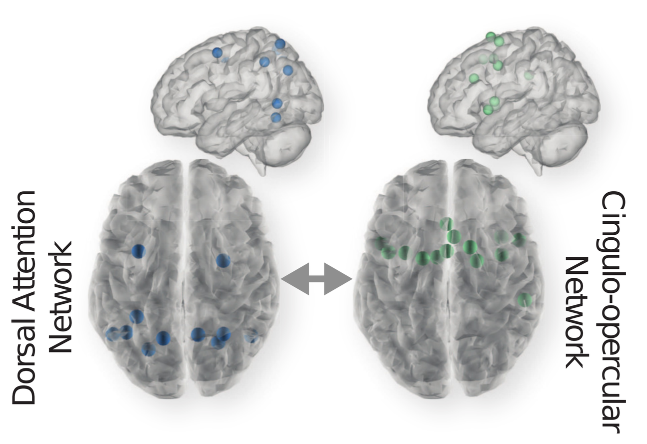
converges to the minimizer of (6) if $d_\lambda \geq |\langle\mathbf{x}, \phi_\lambda\rangle_{\mathcal{H}}|^2$ for all $\lambda \in \Lambda$. The shrinkage operator $S_\mu(\cdot)$ is defined as

$$S_\mu(x) = \begin{cases} x - \mu & x \geq \mu \\ 0 & |x| \leq \mu \\ x + \mu & x \leq -\mu \end{cases}. \tag{9}$$

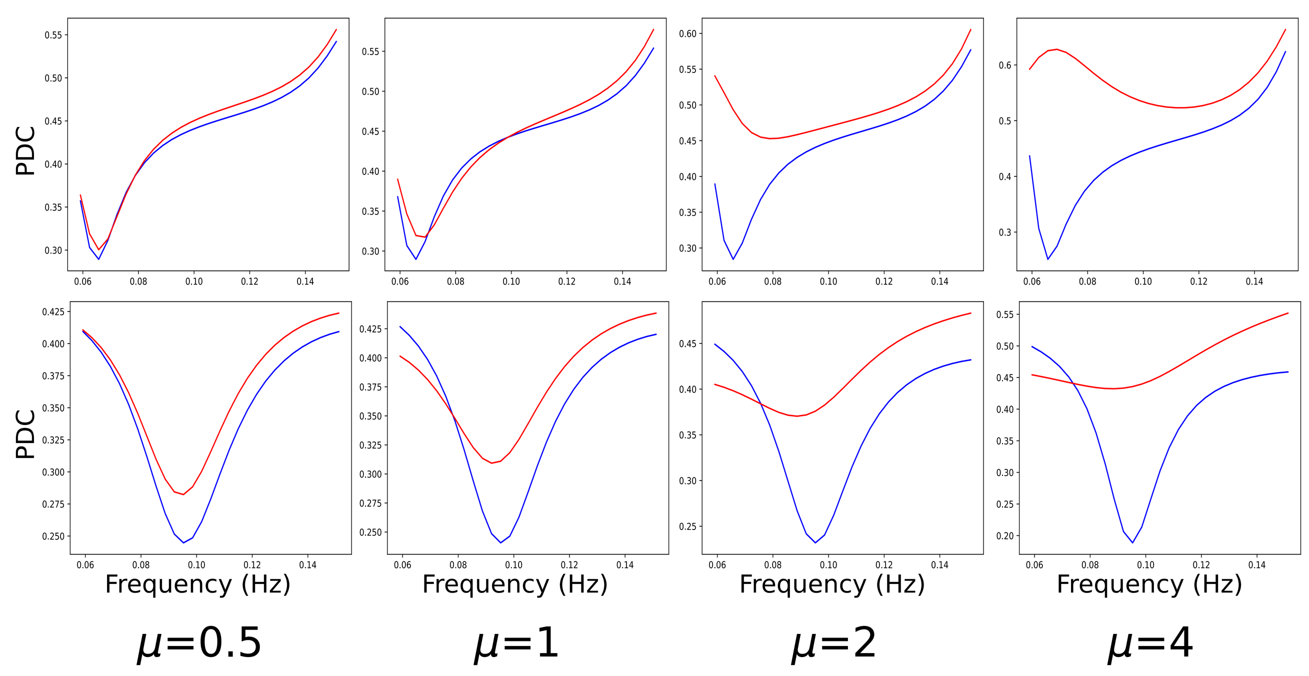
Model Order

A fixed model order can be defined as a convex set in the usual Euclidean orthonormal basis, and it can be enforced with an additional step in which $\mathbf{A}^{(k+1)}$ is projected onto that convex set.

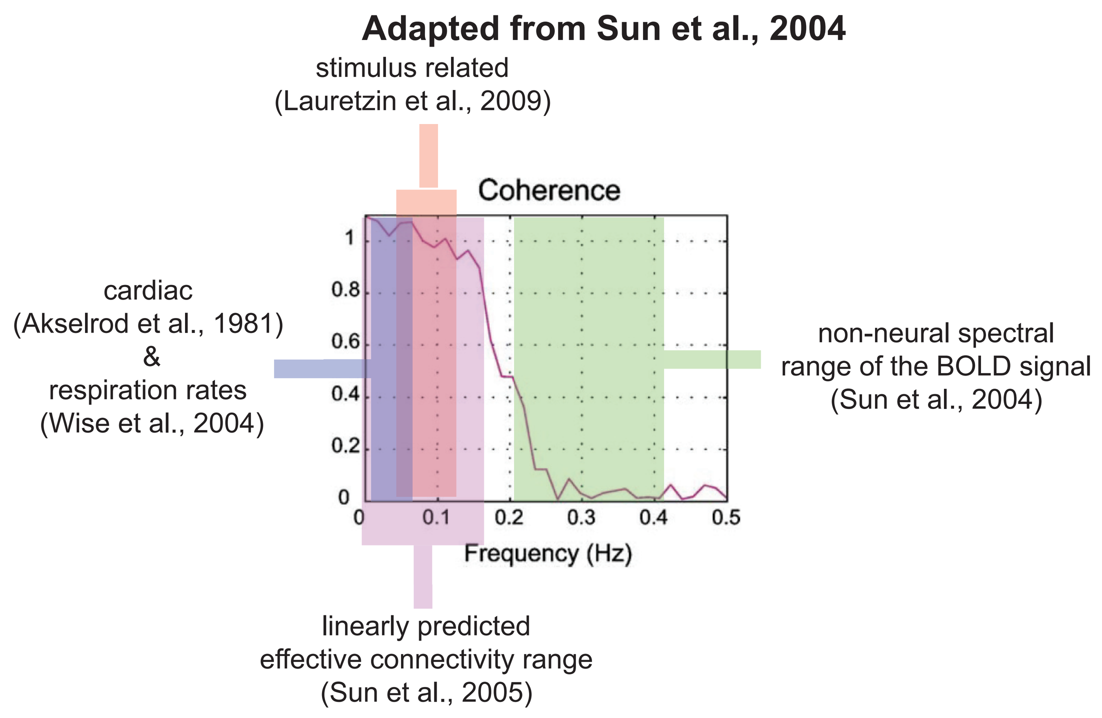
Results



(a) The dorsal attention (blue) and cingulo-opercular (green) networks had the strongest connectivity across frequency. Here, the networks are plotted on a common brain template.



(b) Functional connectivity (PDC) from a dorsal attention network to cingulo-opergular network plotted as a function of frequency using time-based (red) and frequency-based (blue) sparsity penalties. Results are shown for two subjects across different sparsity parameters (μ). As expected, increasing the time-based sparsity penalty results in smearing of the connectivity in the frequency domain.



(c) Previous fMRI research has shown that specific frequency bands of the BOLD response are susceptible to non-neural contamination, such as respiration, heart-rate, and general vascular properties of the brain. A small portion of this research is summarized above.

On-going Analysis

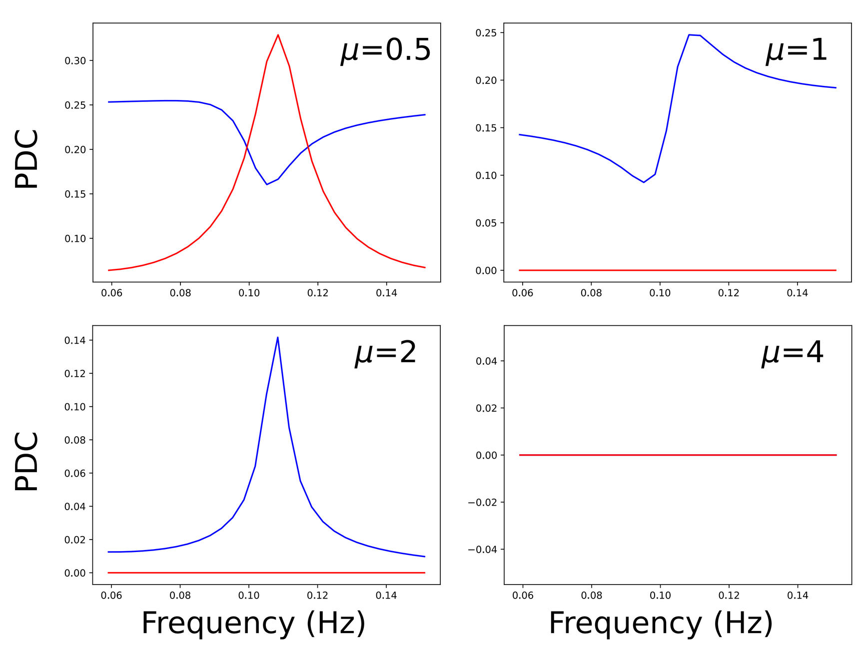


Figure: Preliminary analysis yielded unexpected results such as high sensitivity to the sparsity parameter in some subjects as well as high intersubject variability. The results from one subject are shown above in which PDC shows high sensitivity to both time- and frequency-based sparsity penalties.

Methods

- Task-based fMRI data in which participants made speeded responses to letter stimuli
- fMRI voxels clustered into thirteen functional systems ($n = 13$) derived from a task-free network approach
- Functional connectivity derived from PDC:

$$\rho_{i,j}(\omega) \propto \sum_{t\in\mathbb{Z}_N}[\mathbf{A}_t]_{i,j}\,e^{2\pi i\omega t} \tag{10}$$

- fMRI frequency responses (0.0625-0.1458 Hz) [3]
- model order of ten ($m = 10$)

Conclusion

Preliminary analysis suggests that time-based sparsity penalties may smear important functional connectivity features, especially if not optimally tuned.

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