Poster 4091

Reproducible and Efficient Computation of Functional Partial Correlations for the Entire Brain

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Introduction

Resting-state functional MRI (rs-fMRI) is a prominent tool for brain mapping. The correlations between the time series acquired during rs-fMRI scans are commonly used for measuring brain connectivity. In order to control for the connectivity with the rest of the brain when computing the connectivity between two brain regions, correlations can be transformed into partial correlations. Clean partial correlations can be obtained using sparse inverse covariance matrix method penalizing an L1 or L21 norm of the inverse correlation matrix [7]. To date however and despite impressive efforts, these methods would require several dozens of minutes per scan for computing whole brain connectivity [5,6]. This concern was mitigated by parcellating the brain for reducing the dimension of the correlation matrices, but many parcellation methods exist and their results are still debated [8].

In this work, we explore an alternative path recently opened by Honorio and Jaakkola [1]. Noticing that under Tikhonov penalization the analytical form of the inverse covariance matrix is known and can be computed very efficiently by performing a singular value decomposition (SVD) of the rs-fMRI data, they propose a similar method based on a Riccati penalization. In this work, we investigate two improvements of this approach: (1) random projections (RP) [4] for accelerating the SVD and (2) correlations shrinkage (OAS) [3] for reducing the noise in the correlation matrix prior to the application of [1]. We demonstrate with a sample of 850 scans part of the Philadelphia Neurodevelopment Cohort (PNC) [2] that, in addition to computation speed, these extensions improve the reproducibility of the partial correlations.

Tikhonov and Riccati Penalties

For a matrix X of time series, of size $N \times T$, associated with the covariance $\Sigma = XX^T$, Honorio and Jaakkola investigated two regularized inverse covariance problems of the form [1]:

$$\mathtt{argmax}_{Z \succ 0}[\log \det Z - \langle \Sigma, Z \rangle - R(Z)]$$

They show that if the Singular Value Decomposition (SVD) of X is denoted by USV^T, the regularized inverse covariance $Q = (q_{i,j})_{i,j}$ has the following form:

$$Q = U \Omega U^T + \gamma I \quad ; \quad \Omega = diag(\omega_1, \ldots \omega_t, \ldots \omega_T) \quad ; \quad \omega_t = g(s_t^2)$$

Partial correlations are computed from Q as follows: $p_{ij} = \frac{-q_{ij}}{\sqrt{q_{ii} q_{jj}}}$

penalties investigated in [1]

- **Tikhonov** $R(Z) = \rho^{Tikhonov} Tr(Z)$
  $g(x) = \frac{-x}{\rho^{Tikhonov}(x + \rho^{Tikhonov})}$ and $\gamma = \frac{1}{\rho^{Tikhonov}}$
- **Riccati** $R(Z) = \frac{\rho^{Riccati}}{2} ||Z||_2^2$
  $g(x) = \sqrt{\frac{1}{\rho^{Riccati}} + \frac{x^2}{4{\rho^{Riccati}}^2}} - \frac{x}{2\rho^{Riccati}} - \frac{1}{\sqrt{\rho^{Riccati}}}$
  $\gamma = \frac{1}{\sqrt{\rho^{Riccati}}}$

Contributions

We propose **correlation shrinkage** and **random projections** prior to the computation of the regularized inverse for reducing the influence of noise. The combinations of processings were **scaled** for comparison.

Correlation Shrinkage

Under the assumption that the data are Gaussian, shrinkage estimators improve the empiricial estimation of covariance matrices. Here, under a simplifying assumption, we used the Oracle Approximating Shrinkage (OAS) estimator [3] for reducing the noise introduced by the empirical estimation of rs-fMRI correlation matrices. The correlation matrices Σ were replaced by a shrinked $\overline{\Sigma}$. We found that shrinkage can be introduced in the analytical framework at almost no computational cost.

$$\overline{\Sigma} = (1 - \lambda)\Sigma + \lambda I$$

$$\lambda = \frac{(1 - \frac{2}{N}) Tr(\Sigma^2) + N^2}{(T + 1 - \frac{2}{N})(Tr(\Sigma^2) - N)}$$

Random Projections

Random projections have been proposed for reducing the dimension of a matrix X prior to a SVD [4]. In practice, they approximately cut the spectrum of X for keeping only the most prominent singular values. These properties, singular values filtering and reduction of the computational burden of the SVD, are both particularly interesting for preparing rs-fMRI correlation matrices to a regularized inversion.

Scaling

Riccati and Tikhonov penalties can not be compared directly because their effects are different (penalization of the diagonal versus all the matrix components). In order to compare the different combinations of penalties and processings fairly we scaled the penalties for obtaining the same diagonal term γI in the regularized inverse correlation matrix for all the methods. The diagonal term of the original Riccati regularized inverse was chosen as a reference.

after scaling the penalties

- **Ricatti penalty**
  $g(x) = \sqrt{\frac{1}{\rho} + \frac{x^2}{4\rho^2}} - \frac{x}{2\rho} - \frac{1}{\sqrt{\rho}}$
  $\gamma = \frac{1}{\sqrt{\rho}}$
- **Tikhonov penalty**
  $g(x) = \frac{-x}{\sqrt{\rho}(x + \sqrt{\rho})}$
  $\gamma = \frac{1}{\sqrt{\rho}}$
- **Ricatti penalty after shrinkage**
  $g(x) = \sqrt{\frac{1}{\tau} + \frac{((1-\lambda)x + \lambda)^2}{4\tau^2}} - \sqrt{\frac{1}{\rho} + \frac{\lambda^2}{4\tau^2}} - \frac{(1-\lambda)x}{2\tau}$
  $\tau = \rho - \lambda\sqrt{\rho}$
  $\gamma = \frac{1}{\sqrt{\rho}}$
- **Tikhonov penalty after shrinkage**
  $g(x) = \frac{-(1-\lambda)x}{\sqrt{\rho}((1-\lambda)x + \sqrt{\rho})}$
  $\gamma = \frac{1}{\sqrt{\rho}}$

Results

- **Data** 850 scans part of the Philadelphia Neurodevelopment Cohort (PNC) [2] randomly grouped by 25 ⇒ 34 concatenations of 3000 timepoints
- **Experiments** DMN extraction by using a same seed in the PCC, correlations between connectivity matrices, correlation between extracted DMN

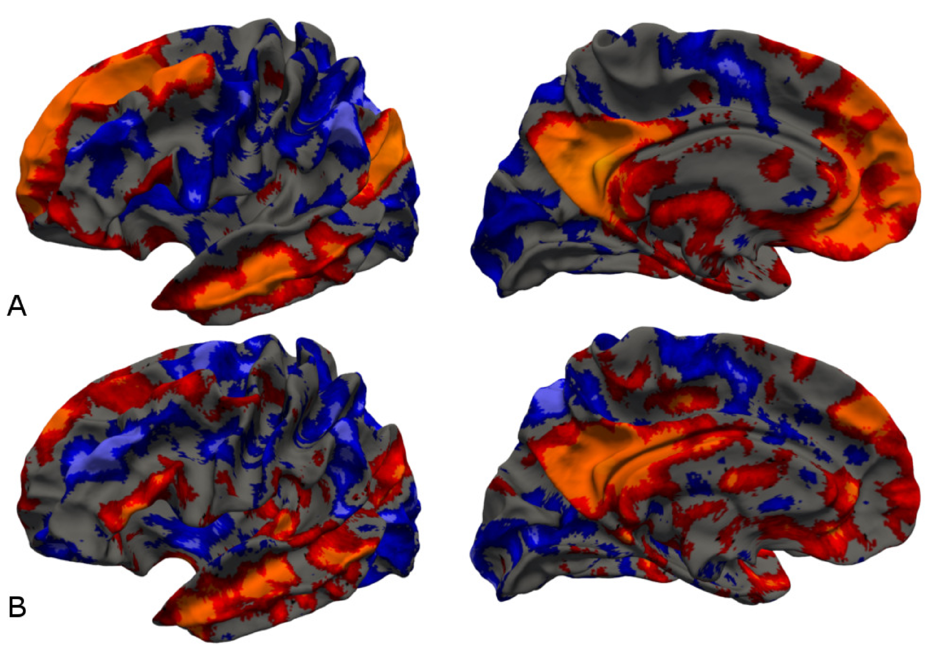

Figure 1. DMN extracted for the left hemisphere (A) using Pearson correlations and (B) using one of the partial correlations considered in this work. Left: lateral original cortical surface. Right: medial original cortical surface.

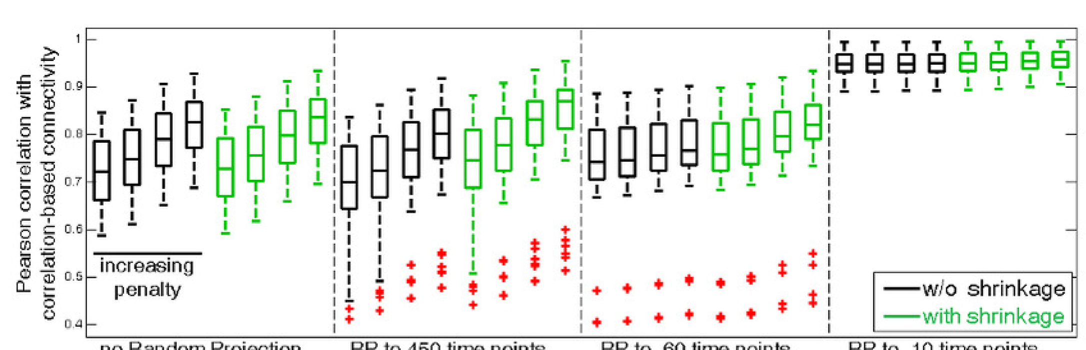

Figure 2. Similarity between the cortical connectivity measured by Pearson correlations and the cortical connectivity measured by all the partial correlations considered in this work. For each random projection, partial correlations produced without correlation shrinkage are presented first. For each method, four increasing penalties were imposed. For the sake of clarity, the results obtained for both hemispheres and for Tikhonov and Riccati penalties were grouped into single boxplots. The large similarity observed (always significant) indicates that correlations and partial correlations capture similar brain networks. For moderate random projections, however, partial correlation seem to contain additional information.

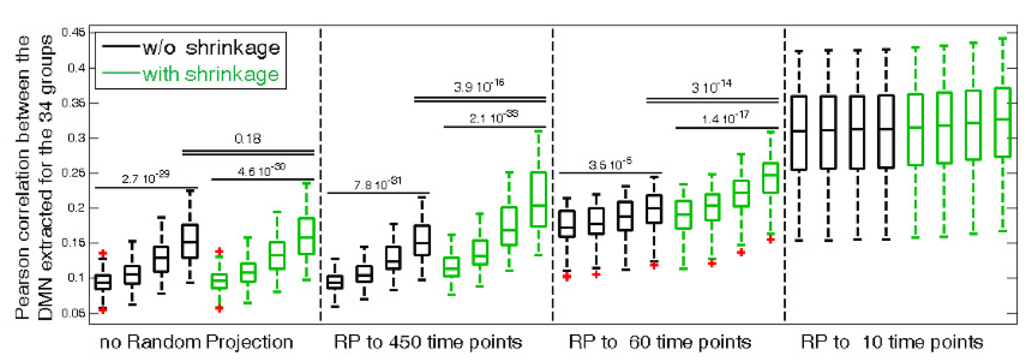

Figure 3. Reproducibility of a seed based DMN extraction (for left hemisphere) from the partial correlation matrices computed during this work. For all the random projections tested, we present first the partial correlations obtained without correlation shrinkage. For each method four increasing penalties were imposed. Each boxplot reports the similarity between the DMN extracted for the first group of scans and the DMN extracted for the other 33 groups, for Tikhonov and Riccati penalties. All the p-values are associated with unpaired two-smaples t-tests. We observe in particular significant improvements of reproducibility when the penalty is increased (single lines) and when shrinkage is performed (double lines). Random projections tend also to increase the reproducibility of the results.

Conclusion

- efficient computation of regularized partial correlations under an **analytical form**
- Tikhonov and Riccati penalties produce very similar results (not shown here)
- correlation shrinkage improves a little the reproducibility of DMN detection.
- Random Projections are the most useful. They efficiently cut the smallest (noisy) eigenvalues of the correlation matrices and they reduce the computational time required for the SVD, which further accelerate the computation of the partial correlations.
- Ongoing work adopt a test-retest approach (ICC) for measuring the stability of the regularized partial correlations and fixing the penalty ρ and the number of random projections

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