

Abstract

Resting-state functional MRI (fMRI) provides a crucial insight into brain organization, by offering a mean to measure the functional connectivity between brain regions. A popular measure, the effective functional connectivity, is derived from the precision matrix obtained by inverting the correlations between brain regions fMRI signals. This approach has been widely adopted to build brain connectomes for large populations. For small populations and single fMRI scans, however, the significant amount of noise in the fMRI scans reduces the quality of the precision matrices, and the non-invertibility of the correlation matrices calls for more sophisticated precision estimators. These issues are especially dramatic at full brain resolution. In this work, we investigate several approaches to improve full resolution precision matrices derived from single fMRI scans. First, we compare three approaches for the computation of the correlation matrix. Then, we investigate two regularized inversions, in combination with a correlation shrinkage and two spatial smoothing strategies. During these experiments, the quality of precision matrices obtained for random fMRI half scans was measured by their generalization: their fit to the unseen time points. Our experiments, using ten high resolutions scans of the Human Connectome Project, indicate that correlation shrinkage strongly improves precision generalization. The two regularizations are associated with similar generalization. Smoothing the fMRI signal before the inversion deteriorates the generalization whereas a penalty directly improving the smoothness of the precision matrix can improve the generalization, in particular for short time series and in combination with shrinkage.

Correlation Shrinkage

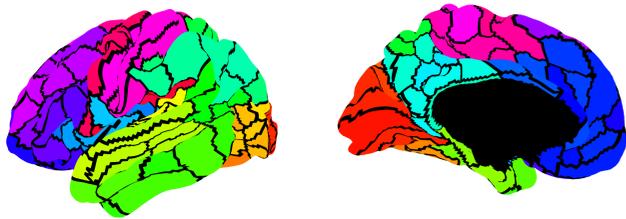
Shrinkage improves empirical correlation matrices. Several shrinkage methods exist. Linear shrinkage is parameter free, easy to implement, and doesn't require noise estimation [4].

- **Oracle Approximating Shrinkage (OAS)** [4,5,6,7]

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

$$\lambda = \frac{(1 - \frac{2}{n})\text{Trace}(\Sigma^2) + \text{Trace}^2(\Sigma)}{(t + 1 - \frac{2}{n})\left(\text{Trace}(\Sigma^2) - \frac{\text{Trace}^2(\Sigma)}{n}\right)} \quad (2)$$

when the signal is a $n \times t$ matrix



Regularized Precisions

Precision matrices are computed by solving a regularized inversion program. In this work, we compared two different regularizations

- **Tikhonov regularization** [8]

$$\max_Q [\log \det Q - \text{Trace}(Q\Sigma) - \rho \text{Trace}(Q)] \quad (3)$$

- **Riccati regularization** [1,8]

$$\max_Q \left[\log \det Q - \text{Trace}(Q\Sigma) - \frac{\rho^2}{2} \text{Trace}(Q^2) \right] \quad (4)$$

Spatial Smoothing

22 regions of the HCP parcellation [10] used to define a Laplacian matrix L

- L used to smooth the signal before the regularized inversion
- L included in the Riccati penalty [1]

Smooth Riccati Regularization

$$\max_Q \left[\log \det Q - \text{Trace}(Q\Sigma) - \frac{\rho^2}{2} \text{Trace} \left([(L + I)Q(L + I)]^2 \right) \right] \quad (5)$$

Data

In this work, we used

- the first scan of the ten unrelated Human Connectome Project subjects [2]
- processed by the ICA+FIX pipeline with MSMALL registration [9]
- band-pass filtered between 0.05 and 0.1 Hz (200 first volumes were removed)

Robust Correlations

- Pearson correlations
- Spearman's rank correlation coefficient
- Pearson correlations after Robust PCA [3]

reproducibility: inner product between extra-diagonal correlations computed for two halves of the data

Generalizability

- scans randomly divided into two halves 25 times
- precision matrix Q_a was fitted to the first half
- correlation matrix Σ_b for the second half
- **negative log-likelihood (NLL)**

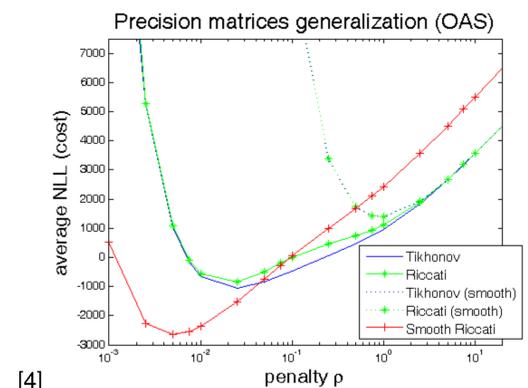
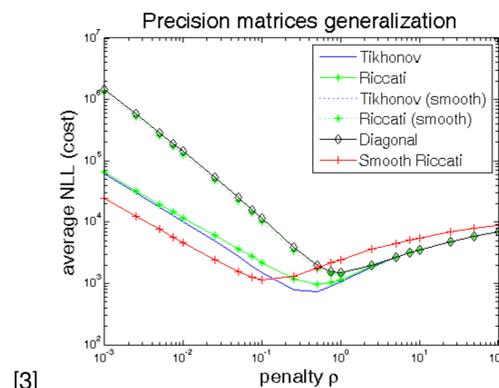
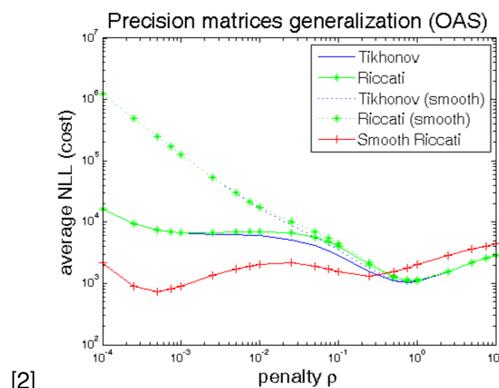
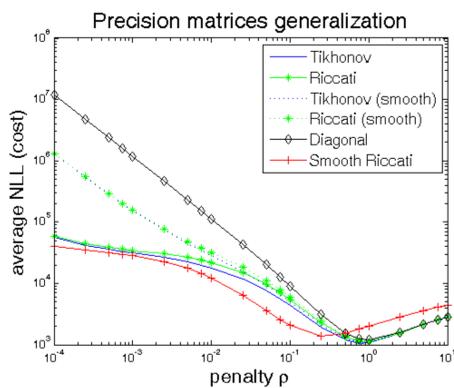
$$NLL = \text{Trace}(Q_a \Sigma_b) - \log \det Q_a$$

Correlations Reproducibility

	Pearson correlations	Spearman correlations	robust PCA
full half scan	(SEM)		
mean reproducibility	0.957 (0.0037)	0.952 (0.0041)	0.957 (0.0038)
time (seconds)	0.705 (0.0089)	0.813 (0.0104)	6.698 (0.0499)
100 time points			
mean reproducibility	0.818 (0.0143)	0.800 (0.0152)	0.735 (0.0222)
time (seconds)	0.031 (0.0002)	0.097 (0.0006)	0.335 (0.0035)

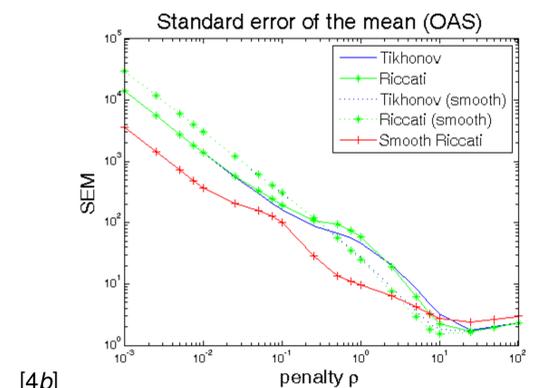
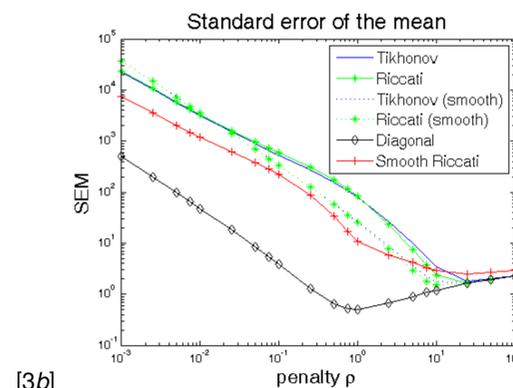
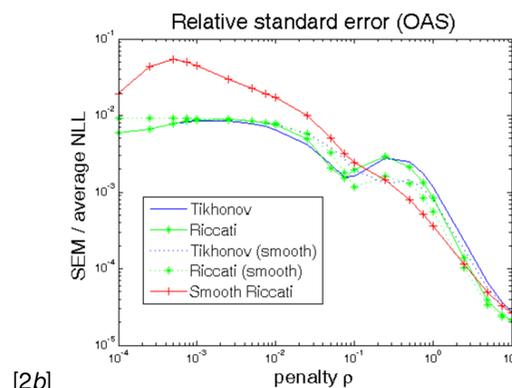
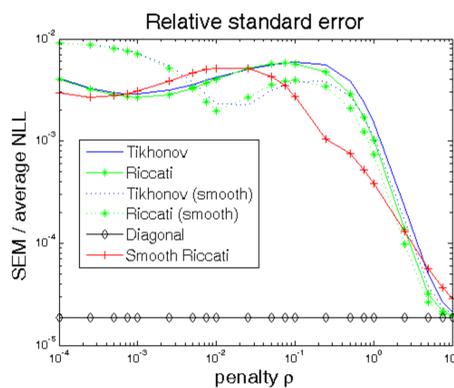
Reproducibility and computational time for the three correlations

Precision Generalizability



Generalizability measured by the average NLL for all the types of precisions. [1] without Oracle Approximating Shrinkage (OAS) of the signal [2] after OAS. Smooth Riccati precisions are obtained by solving (5), while "Riccati (smooth)" indicates the precision obtained by performing a Riccati regularized inversion of the signal smoothed by the Laplacian (spatial downsampling to 1188 nodes).

Generalizability for half scans shortened to 100 time points. [3] without Oracle Approximating Shrinkage (OAS) of the signal [4] after OAS (spatial downsampling to 1485 nodes).



Standard error of the means associated with the average precision matrices NLL (1-4).

Conclusion

- for short scans Pearson correlations are the most robust
- Oracle Approximating Shrinkage strongly improves the quality of the precision matrices
- Smoothing the fMRI signal before the computation of the precisions deteriorates the generalization
- smooth Riccati penalty in combination with OAS shrinkage generates the most reproducible precisions

Future work

- test other precision smoothing strategies
- use the smooth Riccati precision matrices to define effective networks
- extract features from these effective networks, for clinical applications (diagnosis/prognosis)

References

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