Local White Matter Architecture Defines Functional Brain Dynamics

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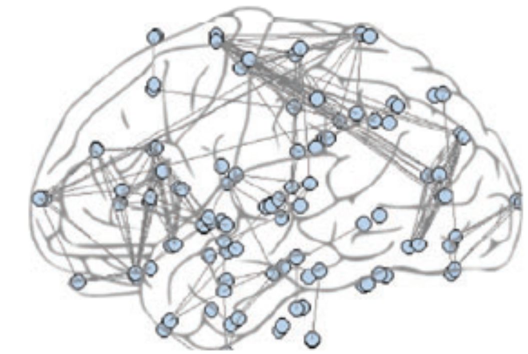
The Connectome

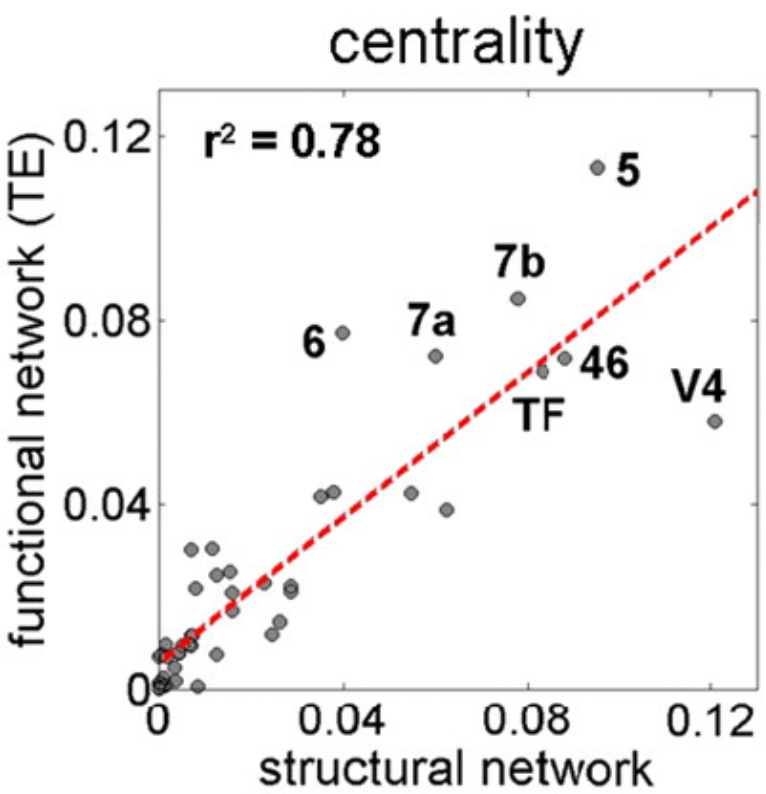


- **Structural connectivity (SC)** refers to macroscopic structural linkage, as obtained, for instance, from long-range tracing or diffusion imaging tractography.

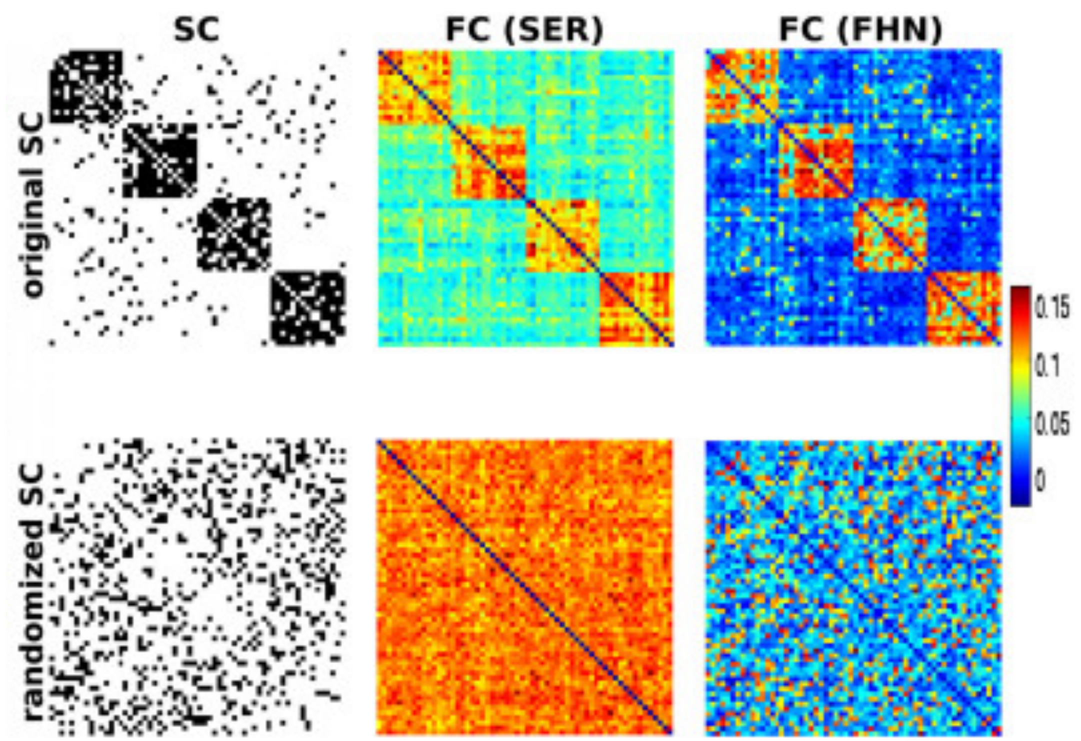
- **Functional connectivity (FC)** refers to the statistical dependence between time series describing the neural dynamics at distinct locations in the brain.

(Honey et al. 2010)

Is Function Constrained By Structural Capacity?



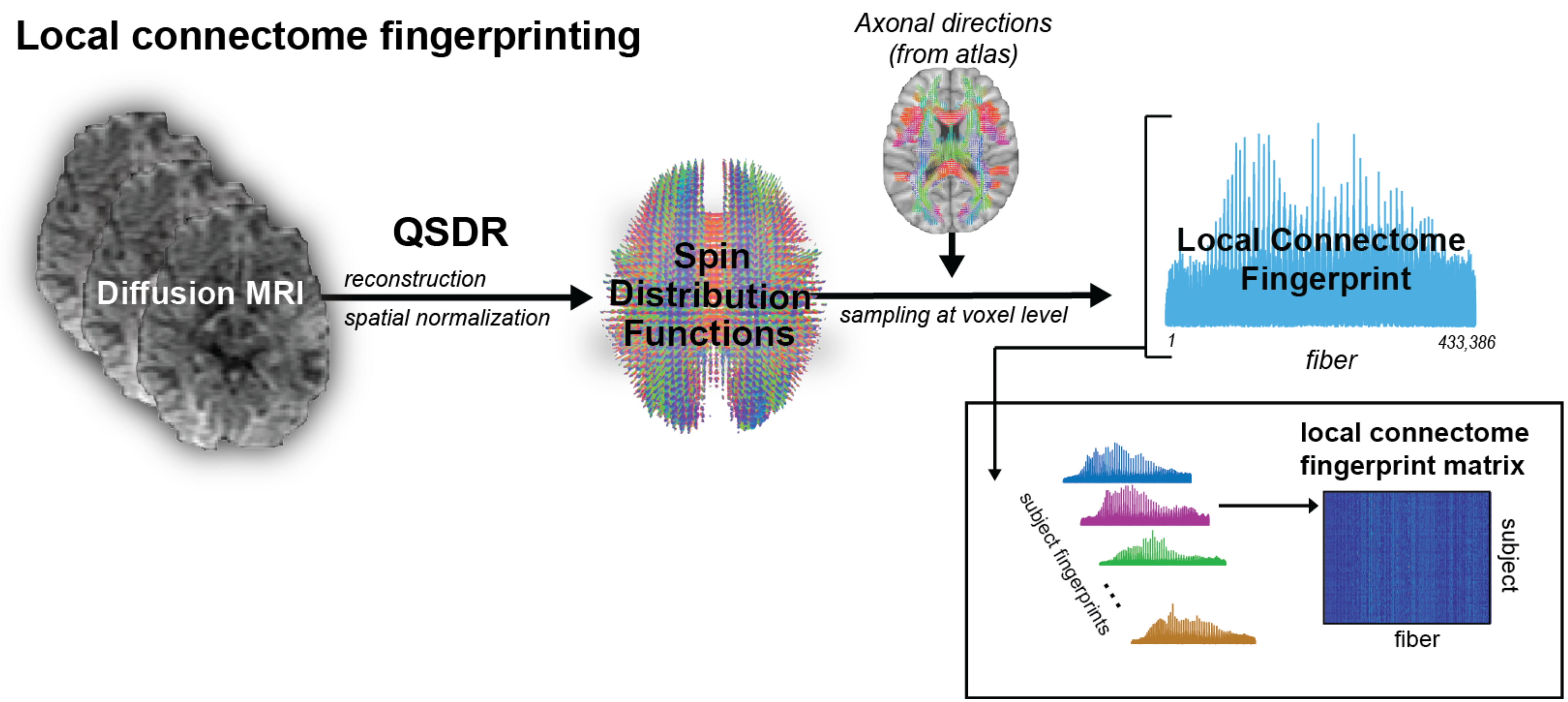
Correlation Between Centrality of Structural and Functional Networks
(Honey et al. 2007)



Simulated Connectivity Patterns for Hubbed vs. Random Networks
(Messé et al. 2015)

We are interested in not just (summaries of) the network topology, but about the actual wirings that formulate the connectome!

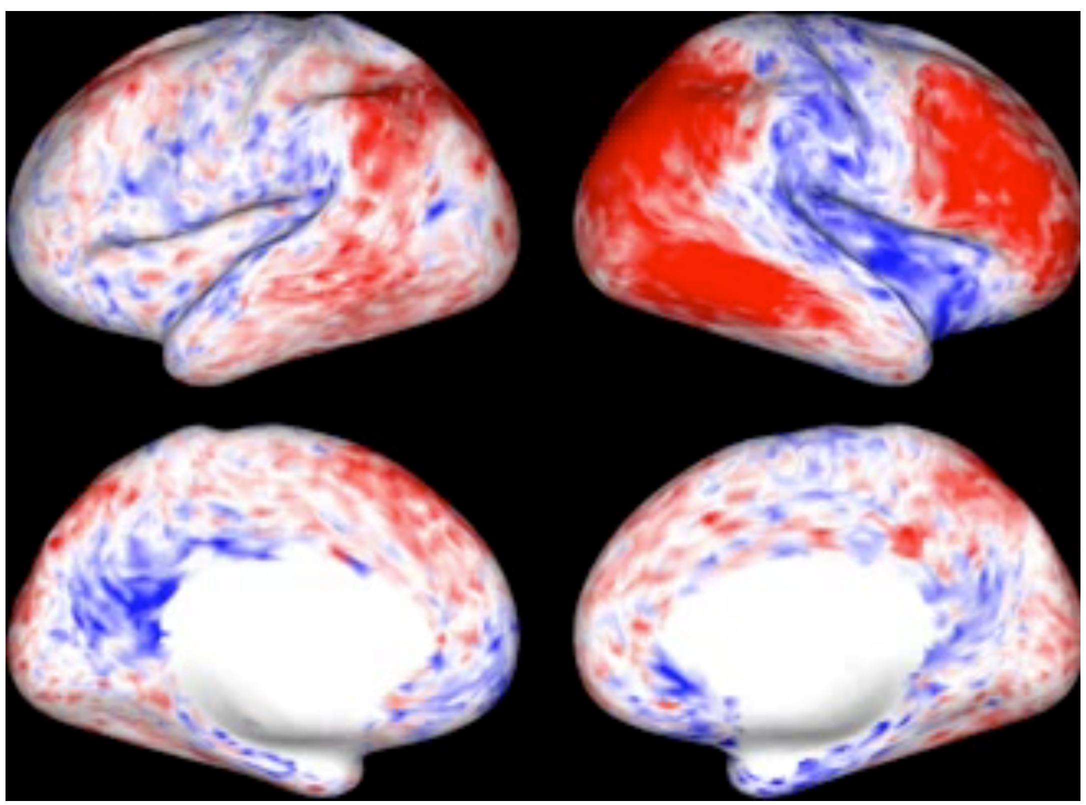
LCF Measures Local Integrity Along White Matter Bundles



Computing a local connectome fingerprint (LCF; Yeh et al. 2016).

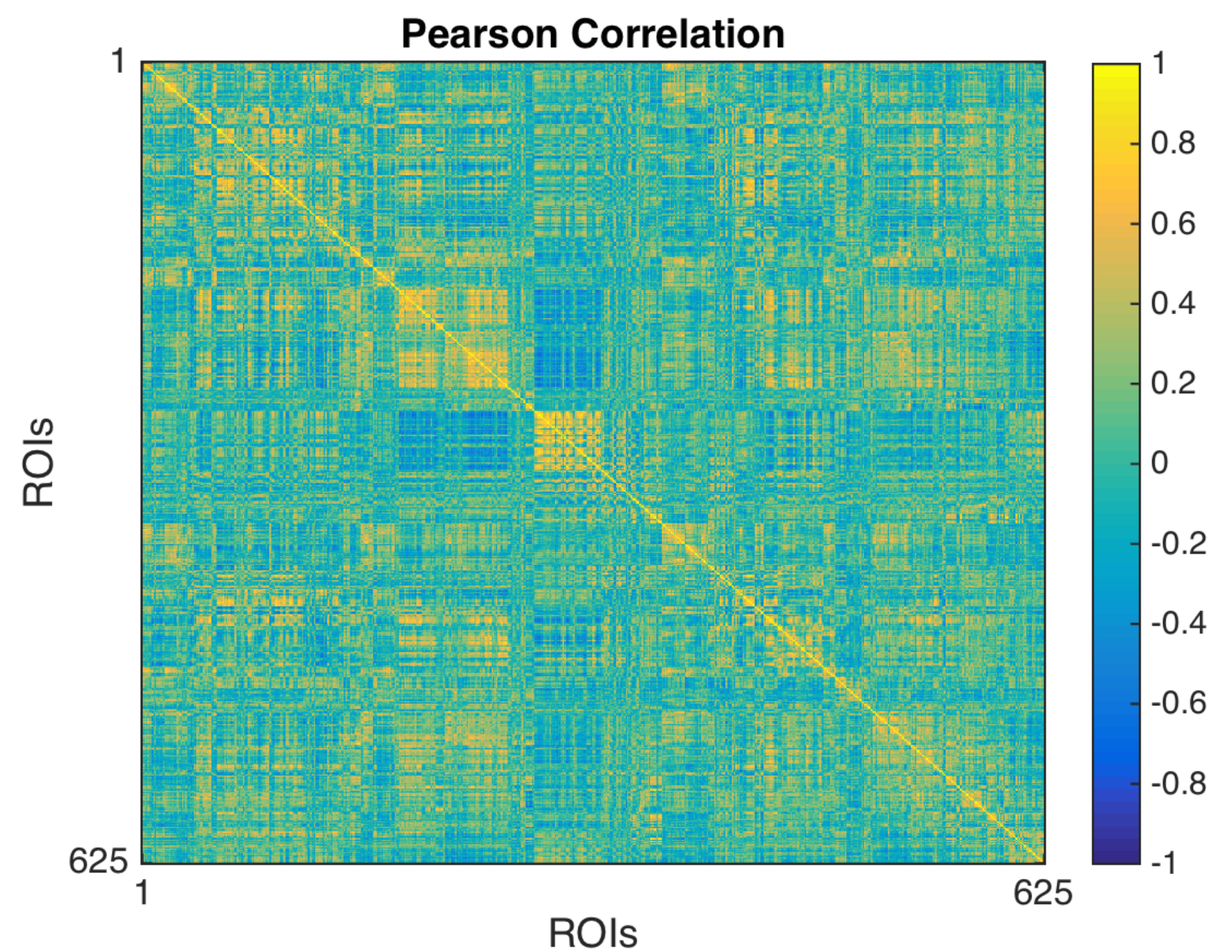
FCG Measures Functional Connectivity Patterns Across ROIs

A resting-state functional MRI



(Bhushan et al. 2016, Smith et al. 2013)

A functional connectivity graph (FCG)



Is Functional Connectivity Constrained By The Local Connectome?

The HCP Dataset

- We use 793 subjects’ dMRI and resting-state fMRI from the publicly available Human Connectome Project (HCP; Van Essen et al. 2013) dataset.
- For each subject, we compute:
    - A local connectome fingerprint (433,386 features)
    - A functional connectivity graph (195,625 features)

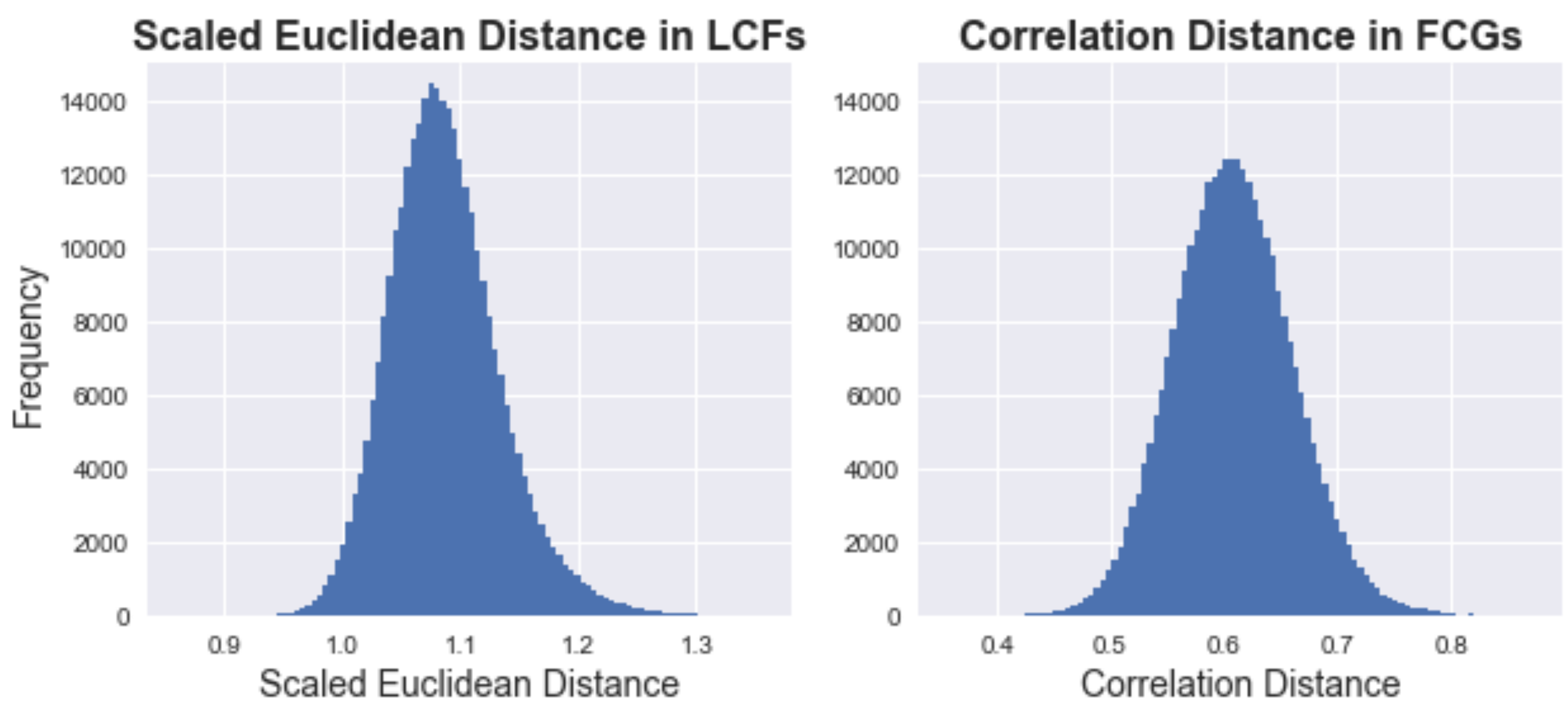
Hypothesis 1:

Similarity in the local connectome between individuals is associated with similarity in their functional connectivity patterns.

Distance-Based Correlations

- Because features are high-dimensional, we make use of the **distance** between these high-dimensional features.

- The choice of a distance metric is determined by how effectively the metric identifies unique individual characteristics.



Statistical Inference with Distance-Based Correlations

$$H_0 : \mathcal{R}(\mathbf{x}, \mathbf{y}) = 0 \quad \text{and} \quad H_1 : \mathcal{R}(\mathbf{x}, \mathbf{y}) > 0$$

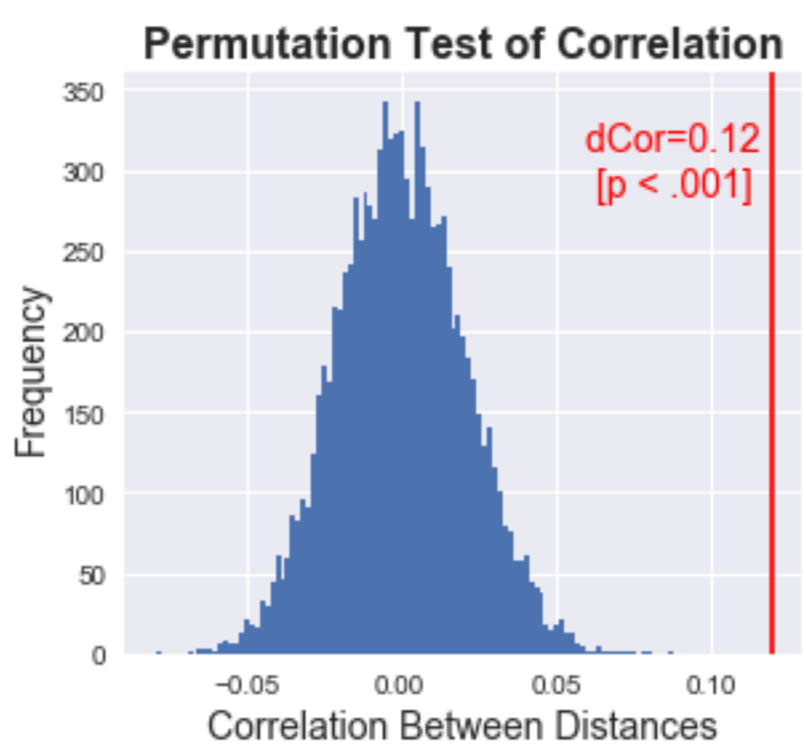
where

$$\begin{aligned}\mathcal{R}(\mathbf{x}, \mathbf{y}) &= \rho(d_{\mathcal{X}}(\mathbf{x}, \mathbf{x}'), d_{\mathcal{Y}}(\mathbf{y}, \mathbf{y}')) \\ &= \frac{\mathsf{Cov}\left(d_{\mathcal{X}}(\mathbf{x}, \mathbf{x}'), d_{\mathcal{Y}}(\mathbf{y}, \mathbf{y}')\right)}{\sqrt{\mathsf{Var}\left(d_{\mathcal{X}}(\mathbf{x}, \mathbf{x}')\right)}\sqrt{\mathsf{Var}\left(d_{\mathcal{Y}}(\mathbf{y}, \mathbf{y}')\right)}}\end{aligned}$$

Similarity in Local Connectome Is Correlated With Similarity in Functional Activity

TABLE II: Summary of Statistical Inference Results ($n = 793$)

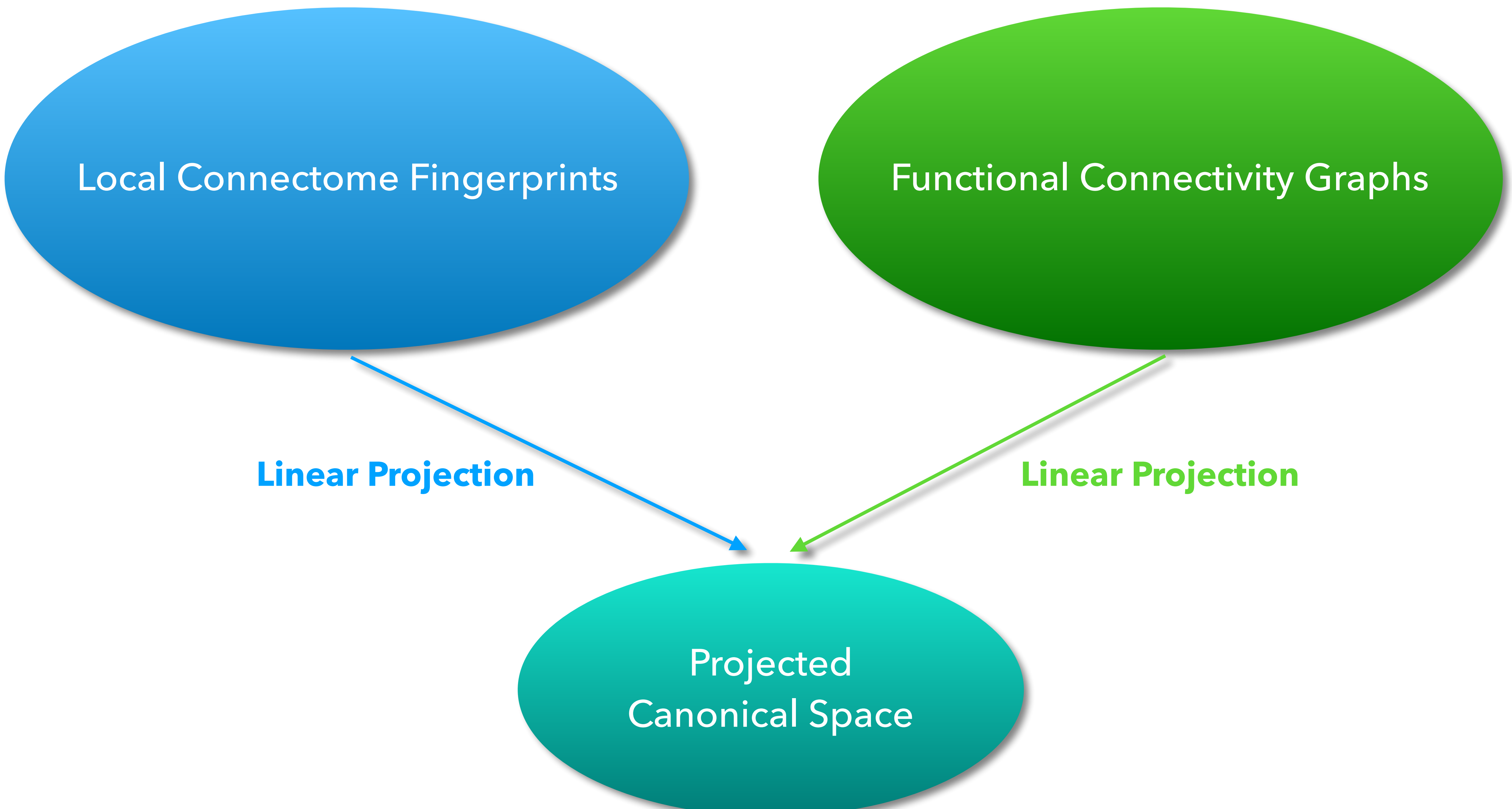
Method	Correlation	Result Type	Result
Permutation (6)	0.120	p-value	$< \mathbf{0.001}^{***}$
dCor t**-test** [16]	0.252	p-value	$< \mathbf{0.001}^{***}$
Subsampling	0.120	95% conf. int.	$\mathbf{(0.098,\ 0.141)}^{+}$



Hypothesis 2:

Variability in specific segments of the local connectome is associated with patterns of functional connectivity in specific circuits.

Canonical Correlation Analysis



CCA in High Dimensions

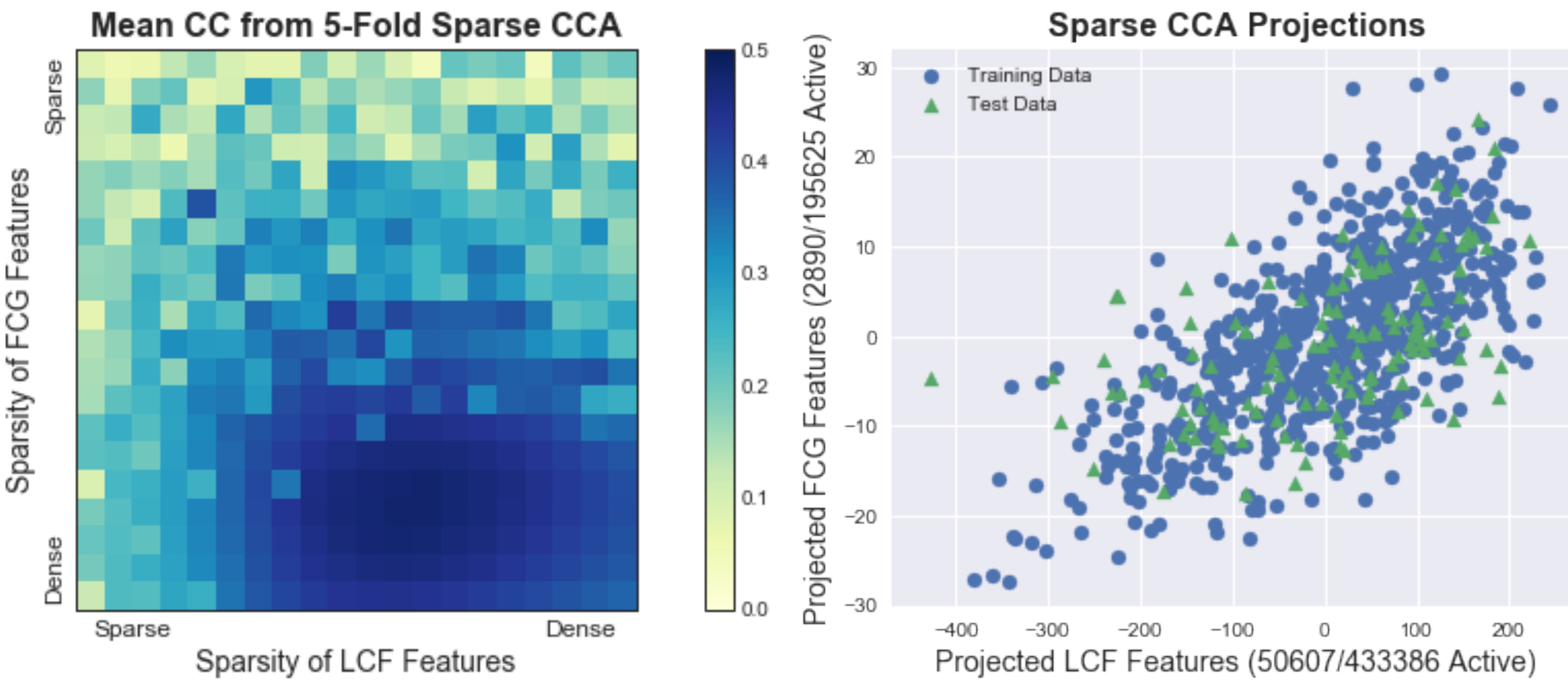
- Classical CCA doesn't quite work in high dimensions, because (from Gao et al. 2015):

    1. The number of features makes each feature **difficult to interpret**,

    2. It is typically **impossible to consistently estimate** the canonical projections ("alignments") without additional structural assumptions.

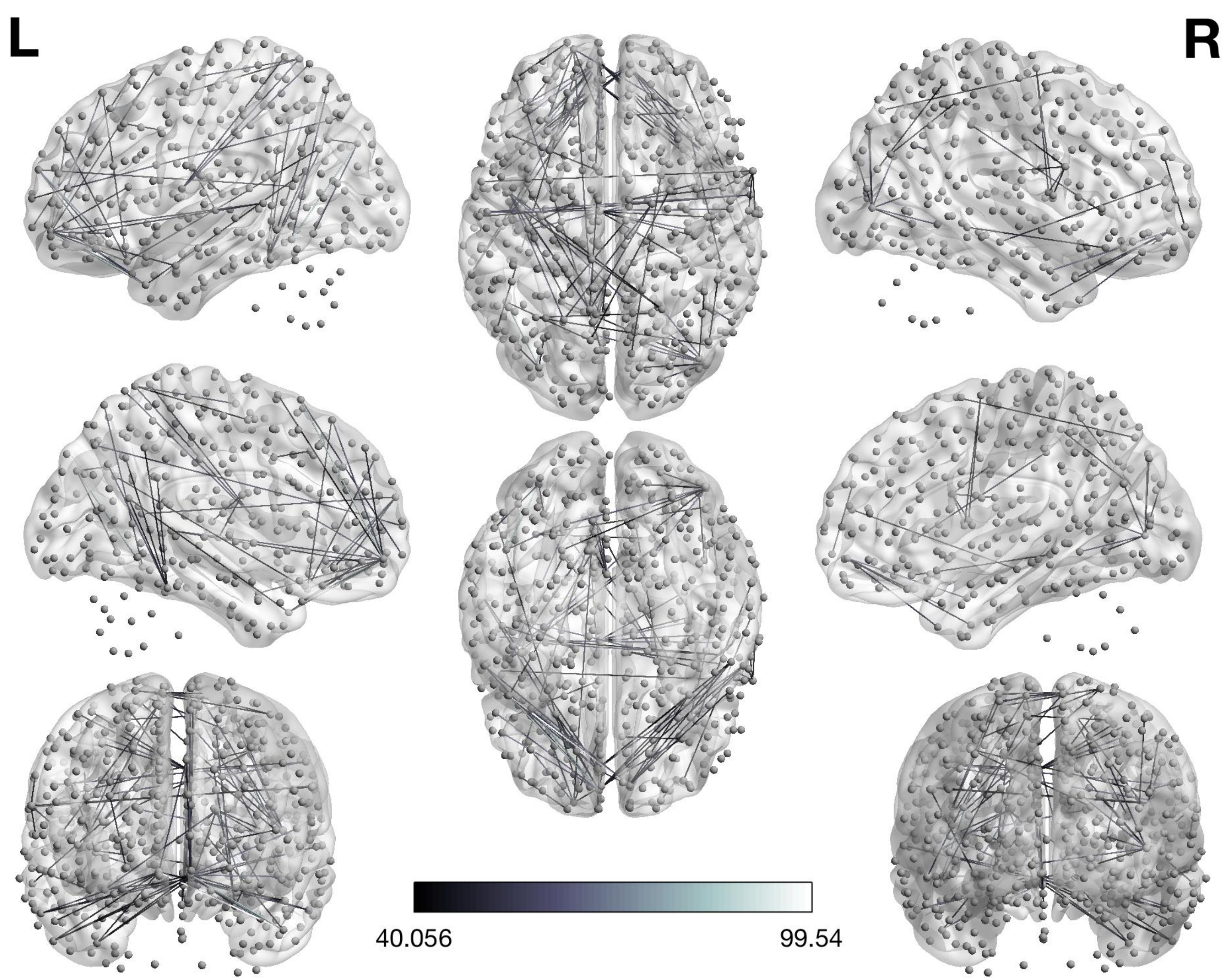
➡ Induce **sparsity** in learned projections with the L1 penalty!

Cross-Validated Sparse CCA



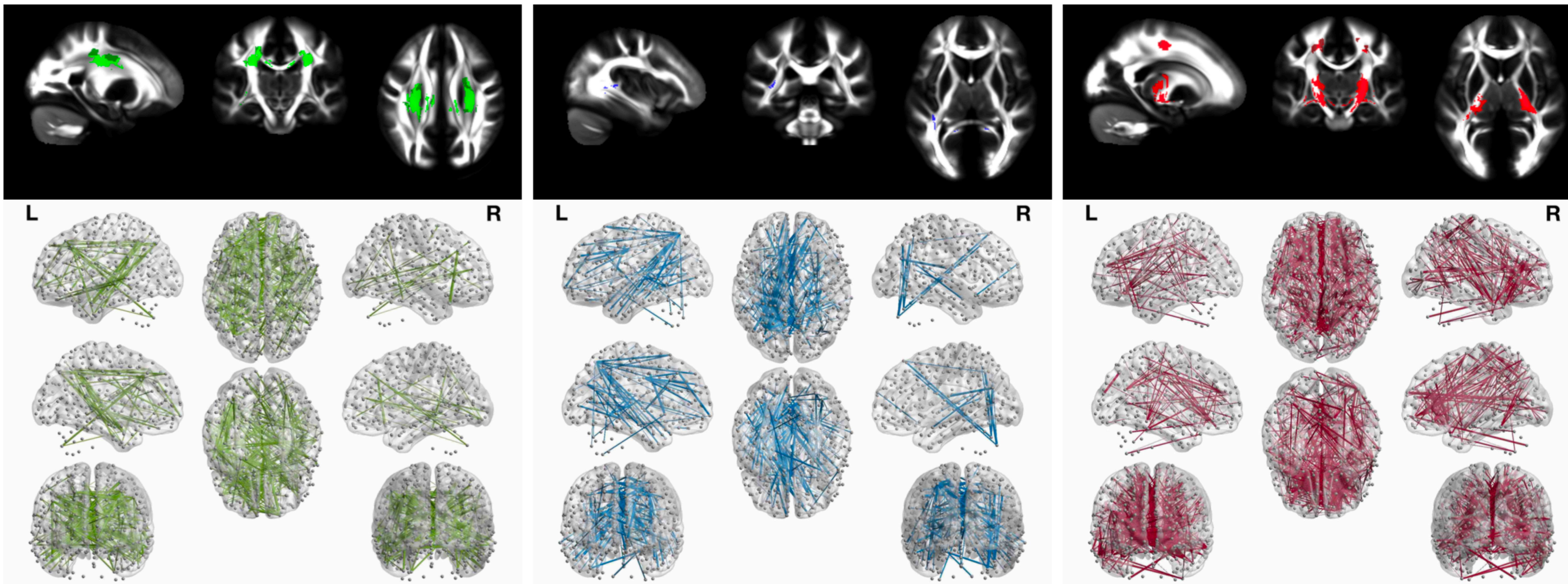
Canonically Correlated Features Selected by Sparse CCA

Structural Features



Functional Features

Canonically Correlated LCF & FCG Sub-clusters



Association Pathways | Ventral Visual Pathways | Projection Pathways

*Sub-clustering of selected features performed with hierarchical clustering.

Conclusion

Variability in the local white matter architecture is associated with global patterns of functional dynamics.

1. A hypothesis test of distance-based correlations showed a statistically significant correlation between similarities of structural and functional connectome.

2. Individual variability in the white matter architecture along major pathways correlates with individual differences in functional dynamics within specific class of brain networks, consistently with existing neuroanatomical knowledge.

Thank You

Acknowledgements

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Distance Metrics

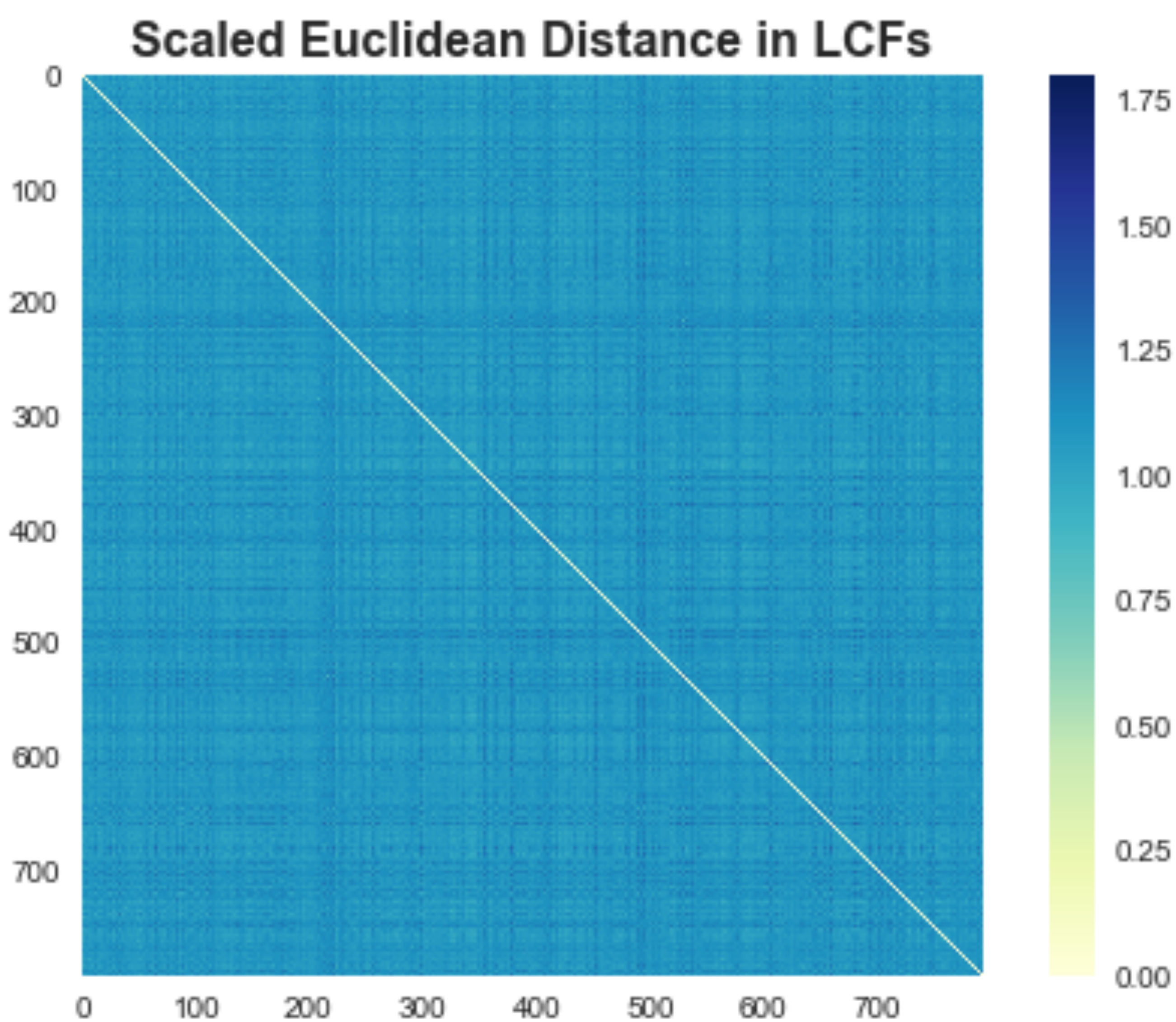
Scaled Euclidean Distance

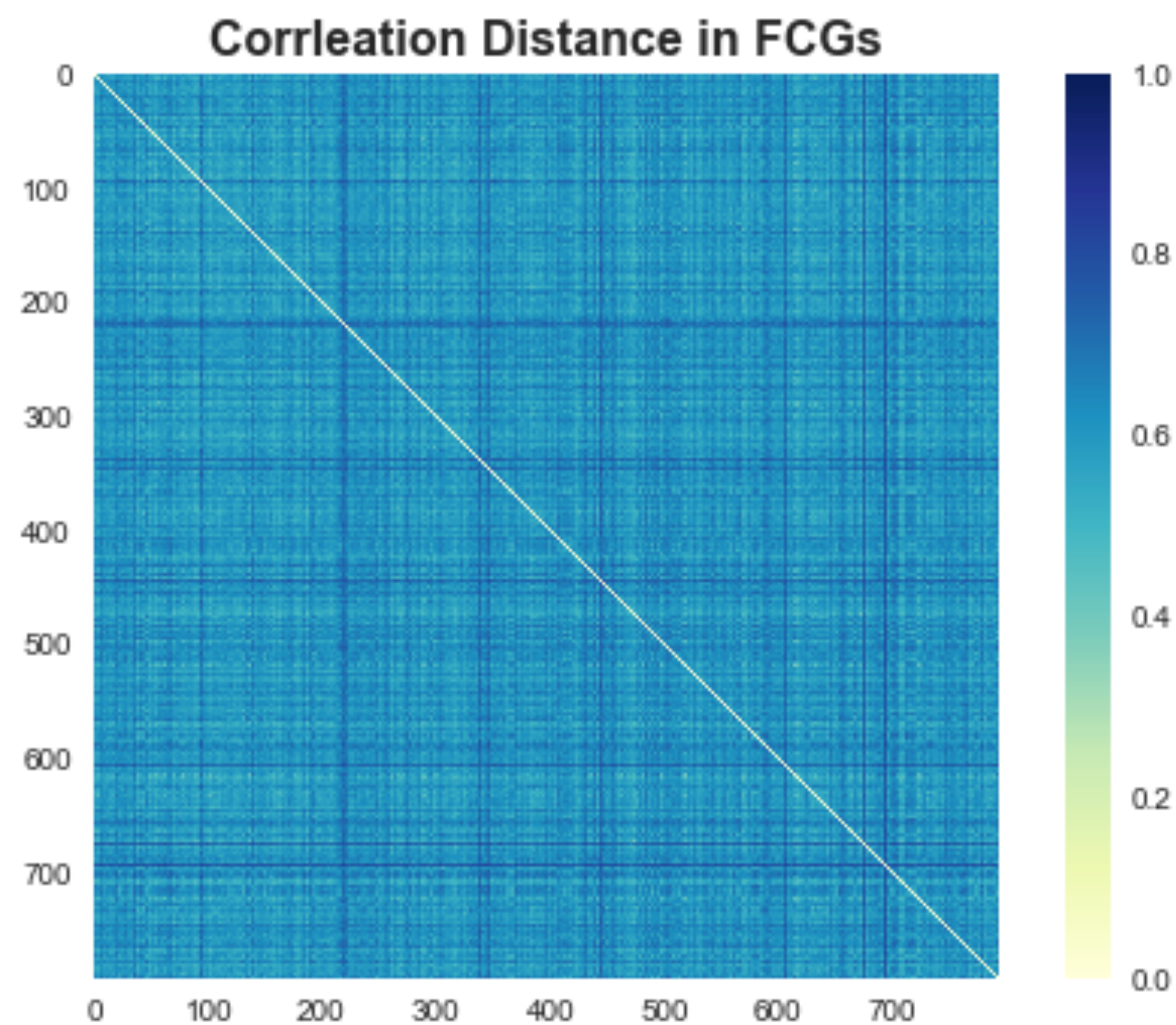
$$d_{\mathcal{X}}(\mathbf{x}, \mathbf{x}') = \frac{1}{p} \|\mathbf{x} - \mathbf{x}'\|_2 = \frac{1}{p} \sqrt{\sum_{k=1}^{p} (x_k - x'_k)^2}$$

Correlation "Distance"

$$\begin{aligned} d_{\mathcal{Y}}(\mathbf{y}, \mathbf{y}') &= 1 - \rho(\mathbf{y}, \mathbf{y}') \\ &= 1 - \frac{\sum_{l=1}^{q} (y_l - \overline{\mathbf{y}})(y'_l - \overline{\mathbf{y}'})}{\sqrt{\sum_{l=1}^{q} (y_l - \overline{\mathbf{y}})^2} \sqrt{\sum_{l=1}^{q} (y'_l - \overline{\mathbf{y}'})^2}} \end{aligned}$$

Structural & Functional Distances





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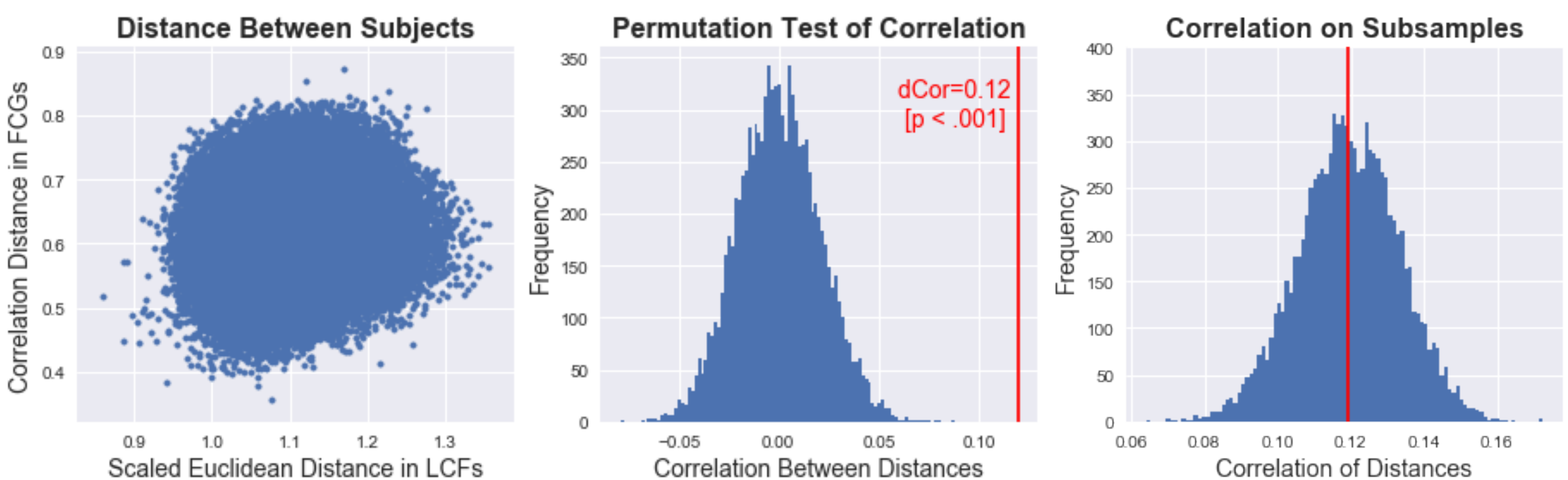
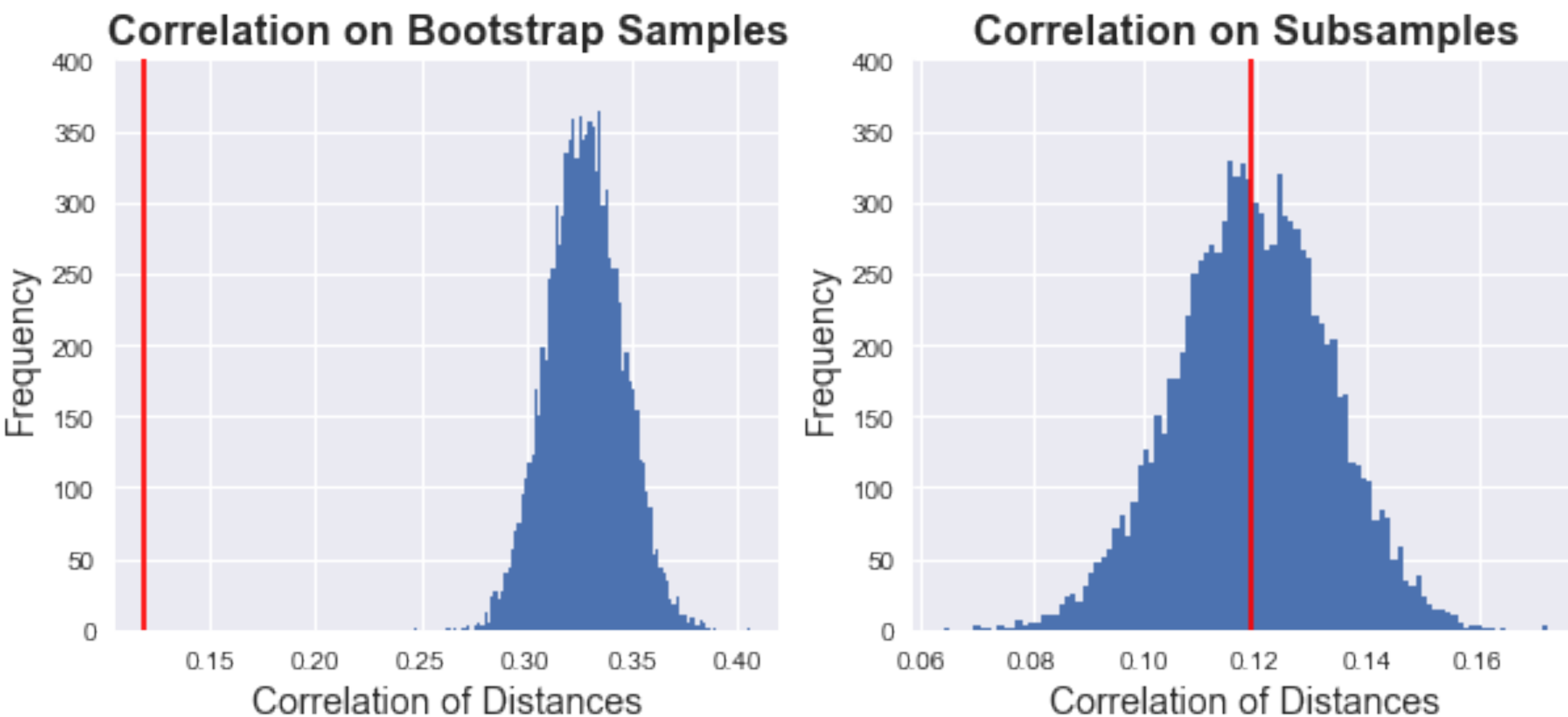


Bootstrap vs. Subsampling



Sparse CCA

Classical CCA

$$\begin{aligned} \underset{\mathbf{u}\in\mathbb{R}^p, \mathbf{v}\in\mathbb{R}^q}{\text{maximize}} \quad & \langle \mathbf{X}\mathbf{u}, \mathbf{Y}\mathbf{v} \rangle \\ \text{subject to} \quad & \|\mathbf{X}\mathbf{u}\|_2^2 \leq 1 \\ & \|\mathbf{Y}\mathbf{v}\|_2^2 \leq 1 \end{aligned}$$

L1 Penalty

$$\|\mathbf{u}\|_1 \leq c_1 \quad \text{and} \quad \|\mathbf{v}\|_1 \leq c_2$$