Joint Spectral Decomposition for the Parcellation of the Human Cerebral Cortex Using Resting-State fMRI

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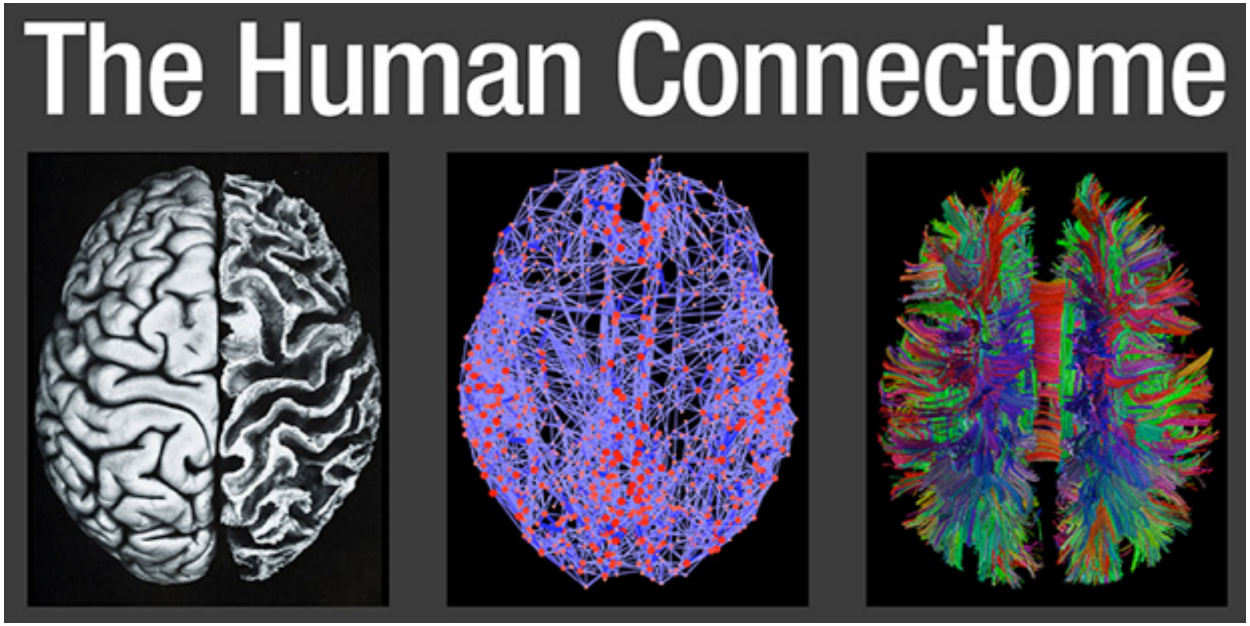
Parcellation

- Sub-division of the brain into non-overlapping subregions that share similar features
- Constitutes one of the core steps to reveal the functional organization of the brain

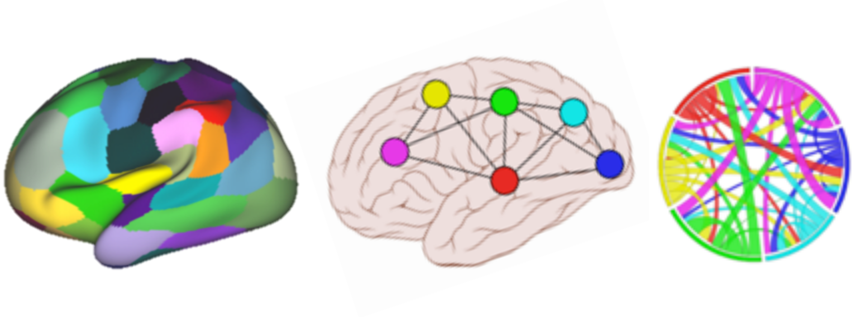


http://scimaps.org/images/maps/865W/IT_06_02_Connectome.jpg

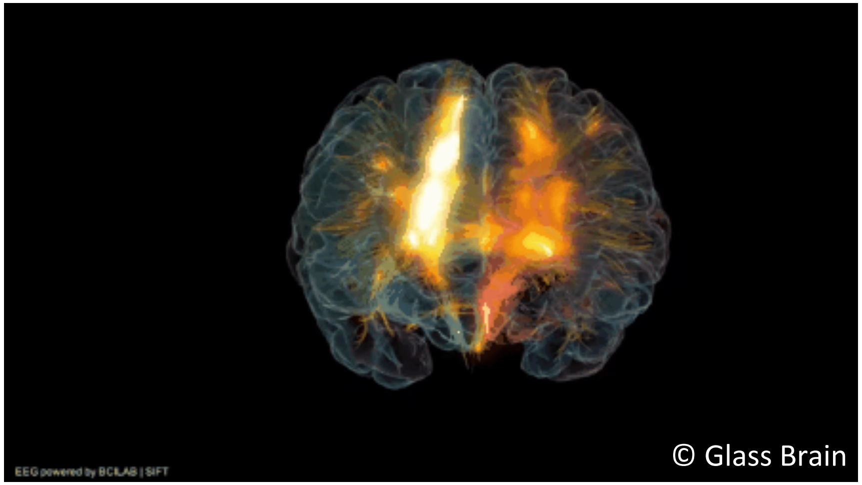
Why parcellate the brain?

Transform high dimensional data into a network

- Parcels → Network nodes
- Connections → Network edges



Neural units co-operate to perform cognitive functions



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Abstract representation

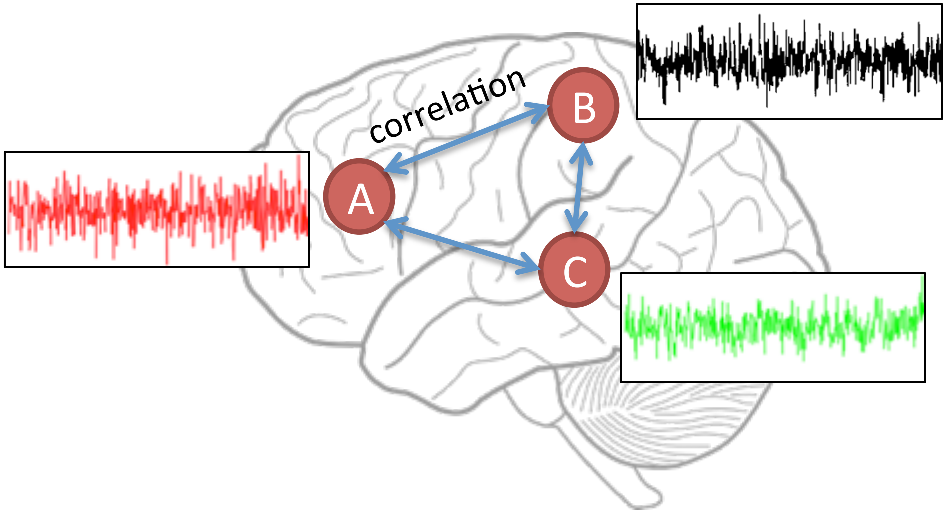
- Attempting to assemble the brain at the voxel level is not feasible

Constitutes a common language

- Brodmann area 4 → the primary motor cortex

Functional connectivity captured at "rest"

- Resting-state fMRI measures neurocognitive activity from BOLD[1] signals, while the subject is at wakeful rest
- Despite of no external stimulus, the brain is still active
- BOLD signals can be used to identify the functional connectivity [Biswal et al. 1995, Magnet Reson Med]



	A	B	C
A	0	0.7	0.5
B	0.7	0	0.2
C	0.5	0.2	0

1: BOLD = Blood-oxygen-level dependent

Parcellation with rs-fMRI: Motivation

- May reflect the functional structure of the brain more effectively *than* anatomical parcellations
  [Thirion et al. 2006, Hum Brain Mapp]

- Does not need an external stimulus or a cognitive process to capture functional activity *as opposed to* task fMRI based parcellations [Smith 2013, Trends Cogn Sci]

- Does not necessarily target specific cortical areas (e.g. *motor cortex*), thus can be used for whole-brain network analysis

Parcellation methods using rs-fMRI

Resting-state network (RSN) identification

Parcellation at a very coarse level (less than hundred clusters)

[Yeo et al. 2011, J Neuroph] [G]
[Power et al. 2011, Neuron] [G]
[Van den Heuvel et al. 2008, PLoS ONE] [S/G]
[Beckmann et al. 2004, IEEE TMI] [G]
……

Node identification for connectome analysis

Parcellation at a higher resolution (typically a few hundred clusters)

[Gordon et al. 2014, Cereb Cortex] [G]
[Shen et al. 2013, NeuroImage] [S/G]
[Blumensath et al. 2013, NeuroImage] [S]
[Craddock et al. 2012, Hum Brain Mapp] [S/G]
……

Parcellations can be done at single [S] and/or group [G] levels

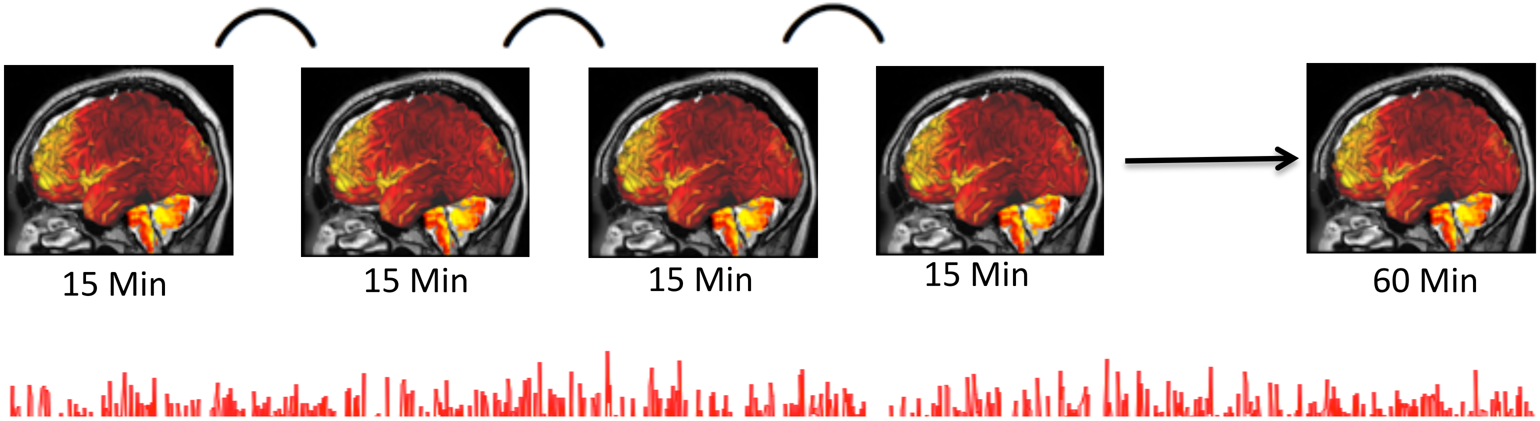
- Single-subject level: Straightforward connectivity analyses for individual subjects, also useful for the study of inter-subject variability in functional connectivity
- Group-level: Useful for exploring how the connectivity changes in a population, for example, through aging or in disease

Contributions

- Functional connectivity across the population is modeled as a multi-layer graph
- Generation of coherent groupwise and single-subject parcellations using spectral decomposition
- Parcellations better reflect the common functional characteristics across the population
- Parcellations are tolerant to the variability in functional connectivity at the single-subject level
- Increased reproducibility and functional consistency across different groups of subjects with respect to previous work

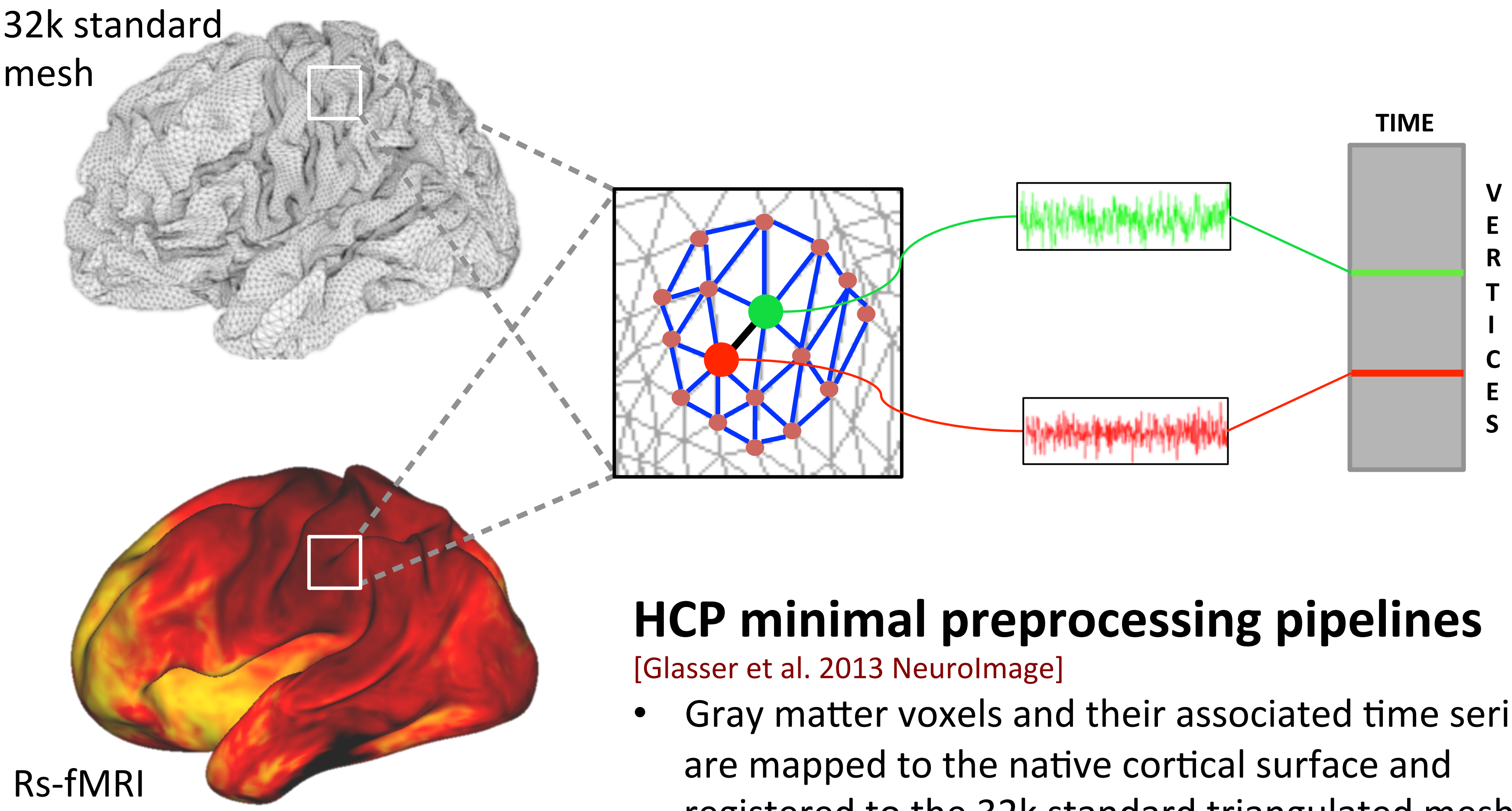
Data acquisition and preprocessing

- Rs-fMRI datasets of 40 unrelated subjects from **HCP**[1]
- Preprocessed, de-noised, and ready to analyze[2]
- Data is normalized to unit-variance and zero-mean
- Temporal concatenation of time series



[1] Van Essen et al. 2013, NeuroImage
[2] Glasser et al. 2013, NeuroImage
http://www.humanconnectome.org/

HCP cortical surface model and rs-fMRI

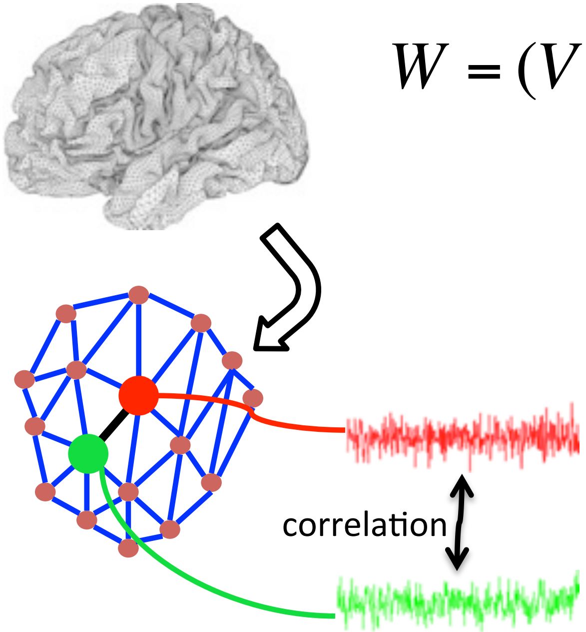


HCP minimal preprocessing pipelines

[Glasser et al. 2013 NeuroImage]

- Gray matter voxels and their associated time series are mapped to the native cortical surface and registered to the 32k standard triangulated mesh
- Enables cross-subject comparisons and multi-modal analysis of the brain

Subject-level spectral decomposition

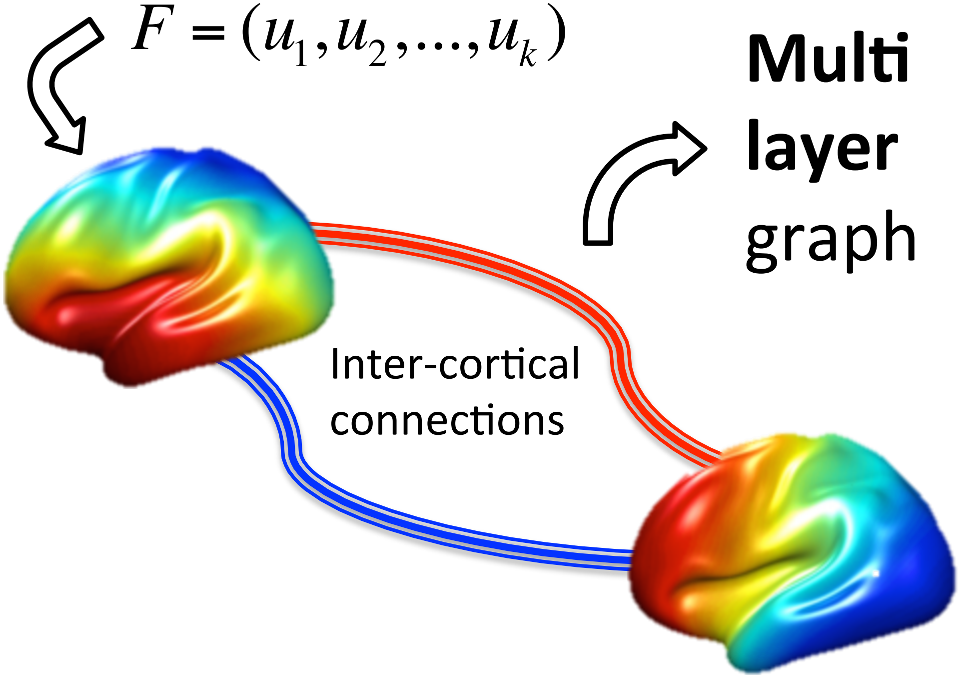


$$W = (V, E) \Longrightarrow L = D - W$$

$$L = U \Lambda U^{-1}$$

$$0 = \lambda_1 \leq \lambda_2 \leq \ldots \leq \lambda_n$$

$$F = (u_1, u_2, \ldots, u_k)$$



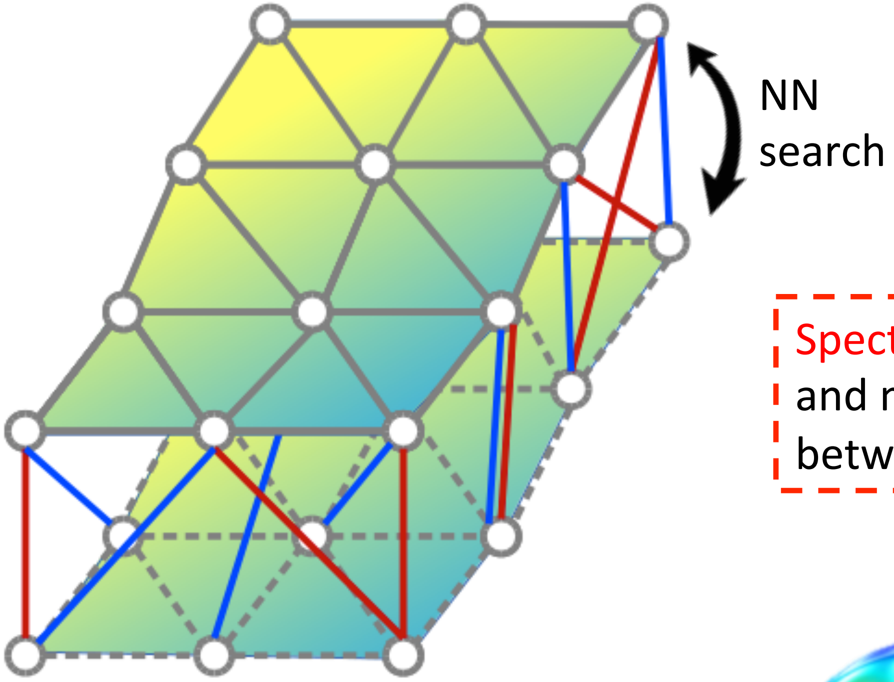
Multi layer graph

Constraint: Only connect adjacent nodes

- Ensures spatial contiguity in clusters
- Reduces computational overhead

Eigenvectors of different subjects tend to show similar characteristics.

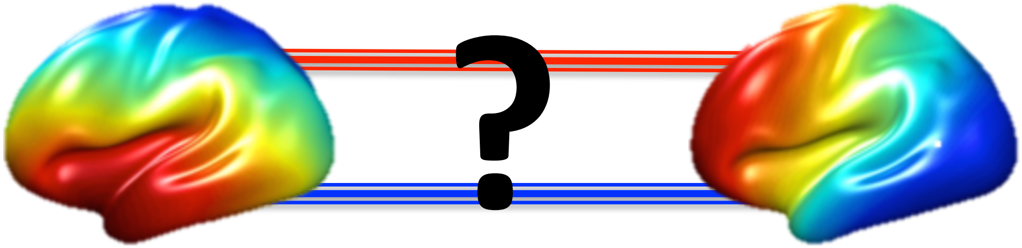
Spectral matching



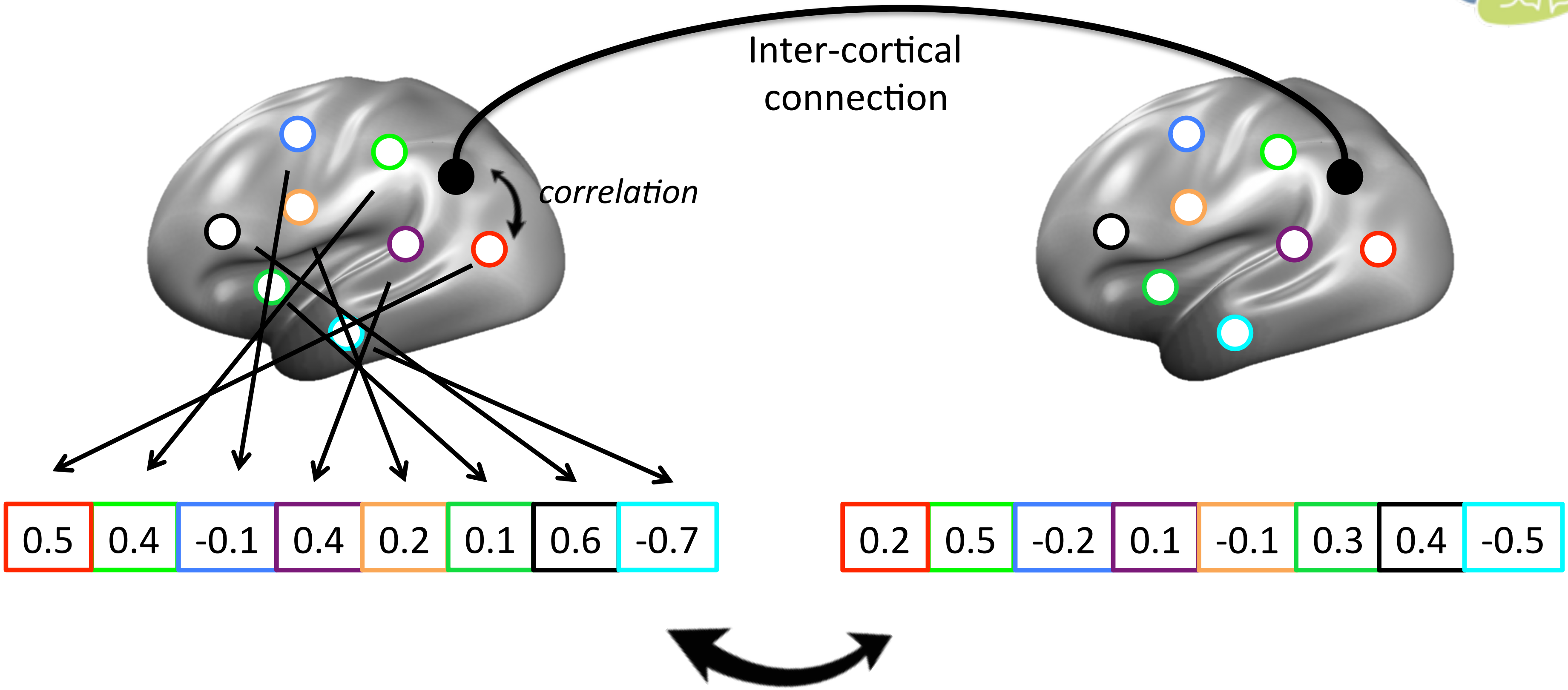
Spectral matching
[Lombaert et al. 2013, IPMI]

Spectral matching: Locate the most similar vertices in two cortical surfaces w.r.t. their spectral coordinates.

Spectral ordering: Eigenvectors are sign-corrected and may be re-ordered to allow direct comparisons between cortical surfaces. [Lombaert et al. 2011, IPMI]



Correlations of connectivity fingerprints ✔

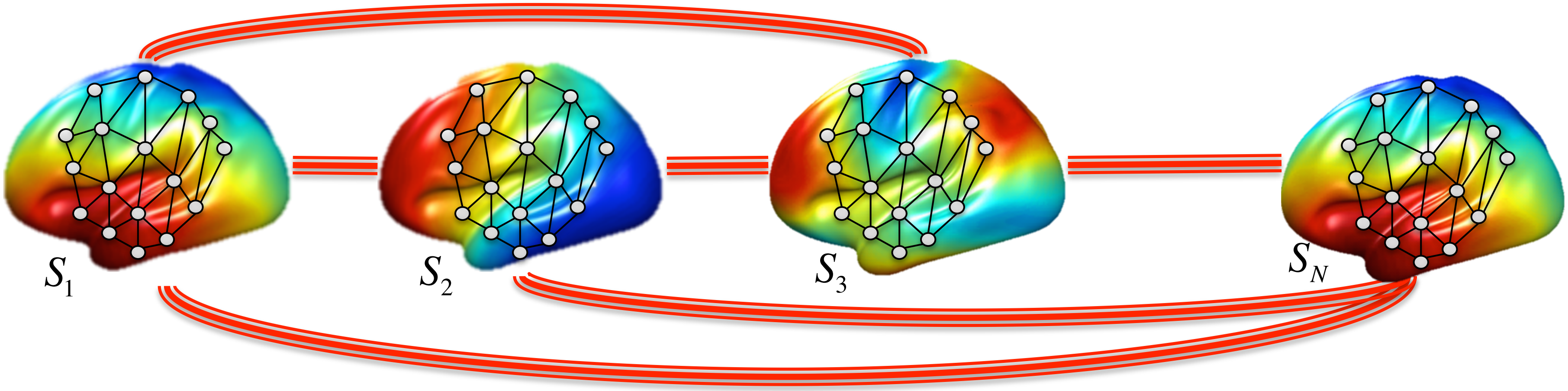


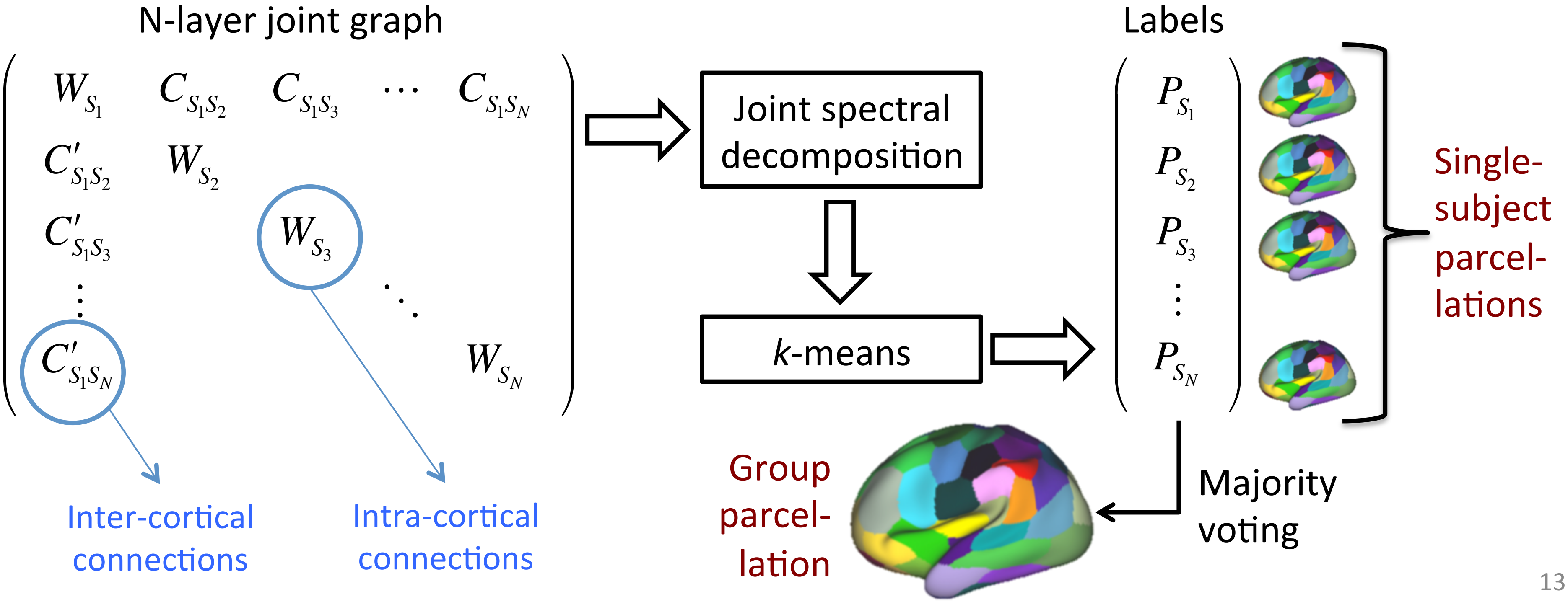
Correlation of connectivity fingerprints

0.848

- A connectivity fingerprint attributes to the functional connectivity of a vertex across the cortical surface.
- Computationally, it is a vector of correlations between the vertex time series and the time series of the other cortical vertices.

Joint spectral decomposition





N-layer joint graph

$$\begin{pmatrix} W_{S_1} & C_{S_1S_2} & C_{S_1S_3} & \cdots & C_{S_1S_N} \\ C'_{S_1S_2} & W_{S_2} & & & \\ C'_{S_1S_3} & & W_{S_3} & & \\ \vdots & & & \ddots & \\ C'_{S_1S_N} & & & & W_{S_N} \end{pmatrix}$$

Inter-cortical connections

Intra-cortical connections

Joint spectral decomposition

k-means

Labels

$$\begin{pmatrix} P_{S_1} \\ P_{S_2} \\ P_{S_3} \\ \vdots \\ P_{S_N} \end{pmatrix}$$

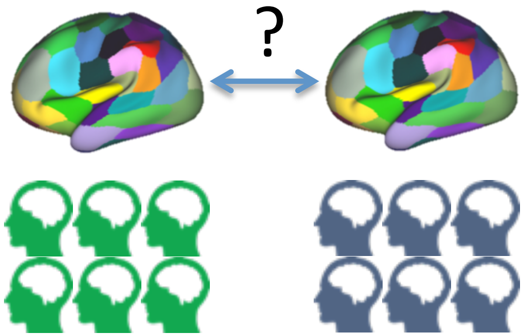
Single-subject parcellations

Majority voting

Group parcellation

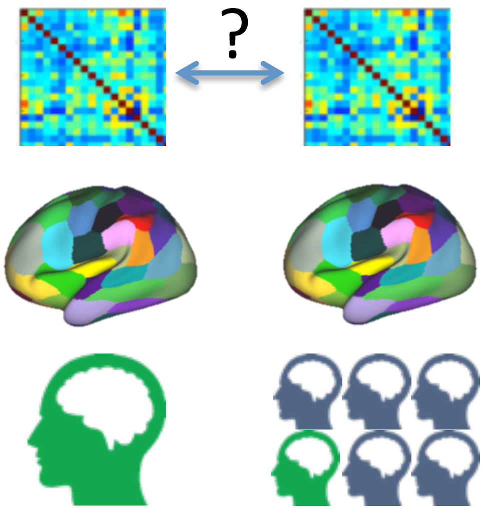
Evaluation

Reproducibility



- How reproducible are the parcellations across different groups of subjects?
- Dice scores measured from parcel overlaps

Functional consistency



- How well does a group parcellation represent the whole population?
- Change in homogeneity and connectivity networks when a subject is replaced by its group parcellation

Comparison methods

Spectral clustering based on normalized cuts (NCUTS)

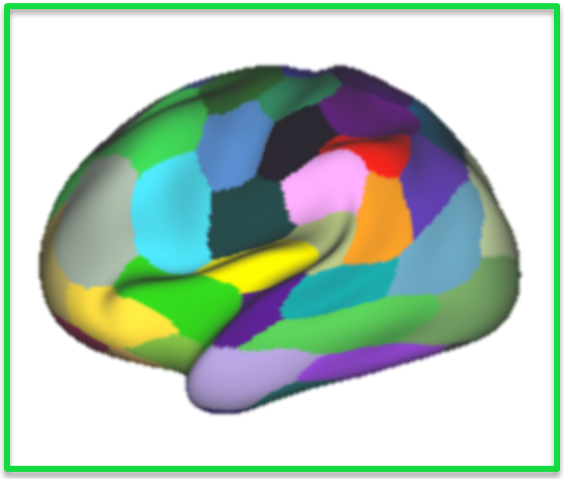
[van den Heuvel et al. 2008, PloS ONE; Craddock et al. 2012, Hum Brain Mapp]

- Two-level parcellation (Two-level)
  ① Compute individual subject parcellations with NCUTS
  ② Compute a stability graph from the parcellations
  ③ Cluster the graph to obtain the group parcellation

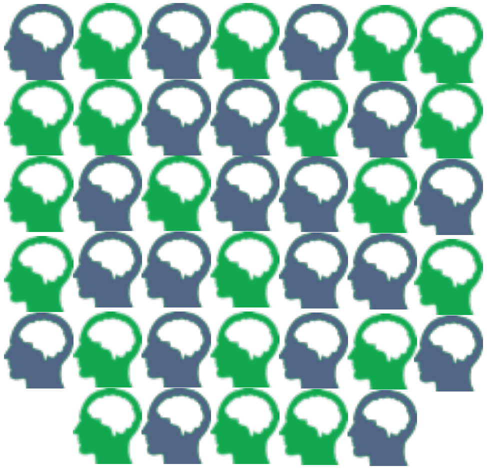
- Group average parcellation (Group-mean)
  ① Compute average of the individual adjacency matrices
  ② Cluster the average matrix with NCUTS to obtain the group parcellation

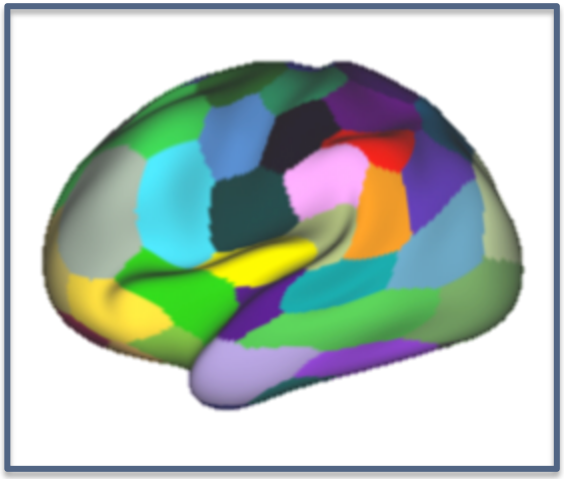
Experimental setting

- 40 subjects were separated into two equally-sized, mutually exclusive groups by random selection



Group parcellation 1



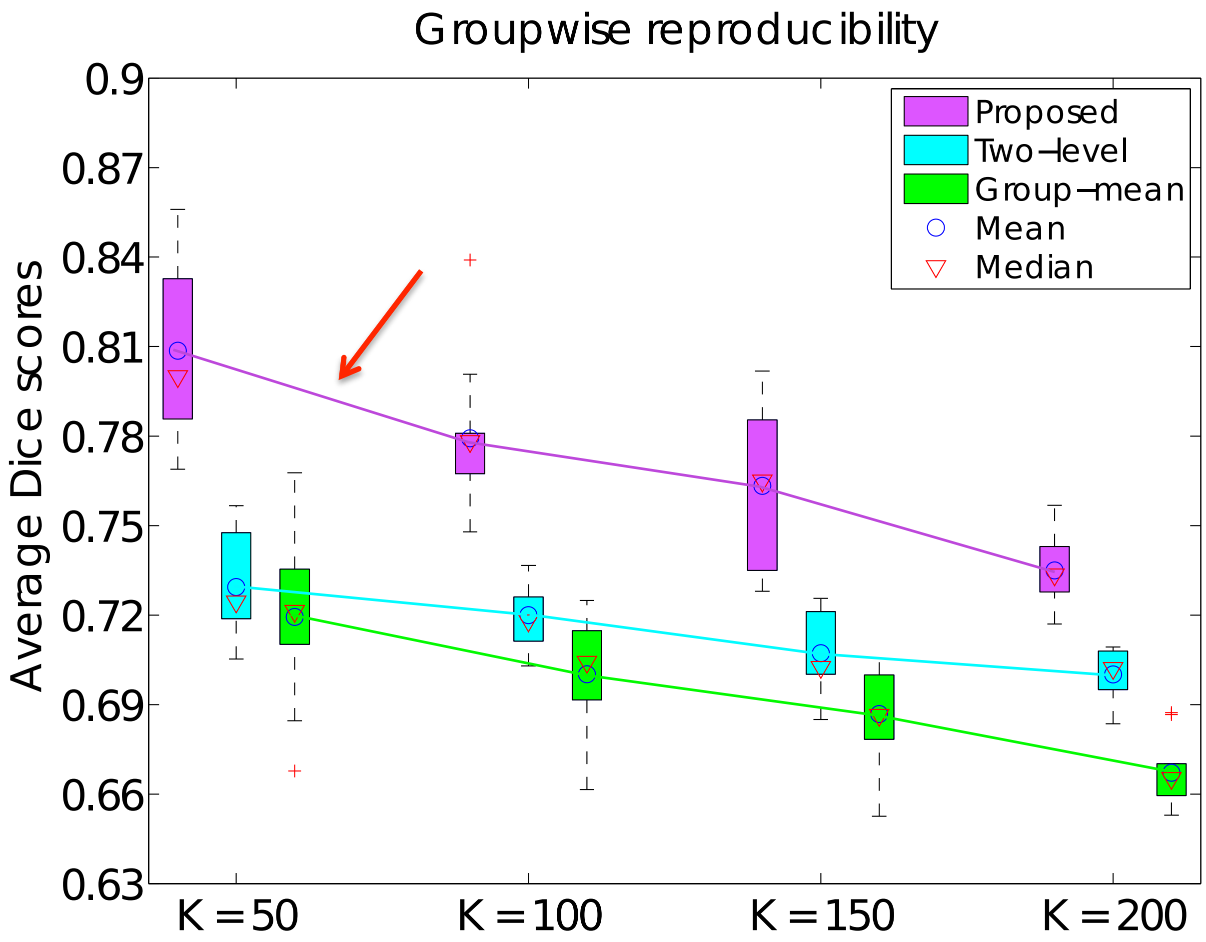


Group parcellation 2

repeat the process

×10

Reproducibility

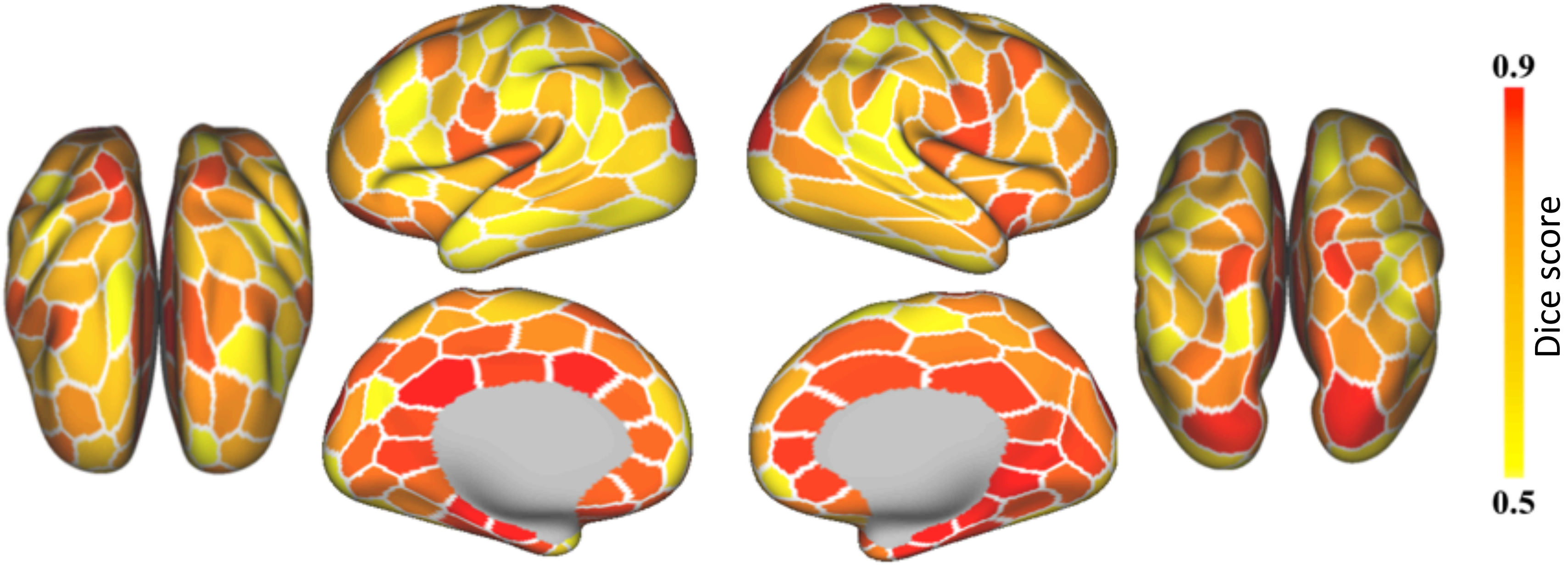


Proposed approach is able to obtain more reproducible parcellations, with at least an average Dice score of 0.72.

Statistical significance is tested with the two-sided Wilcoxon signed rank test. $p < 0.005$ for all resolutions.

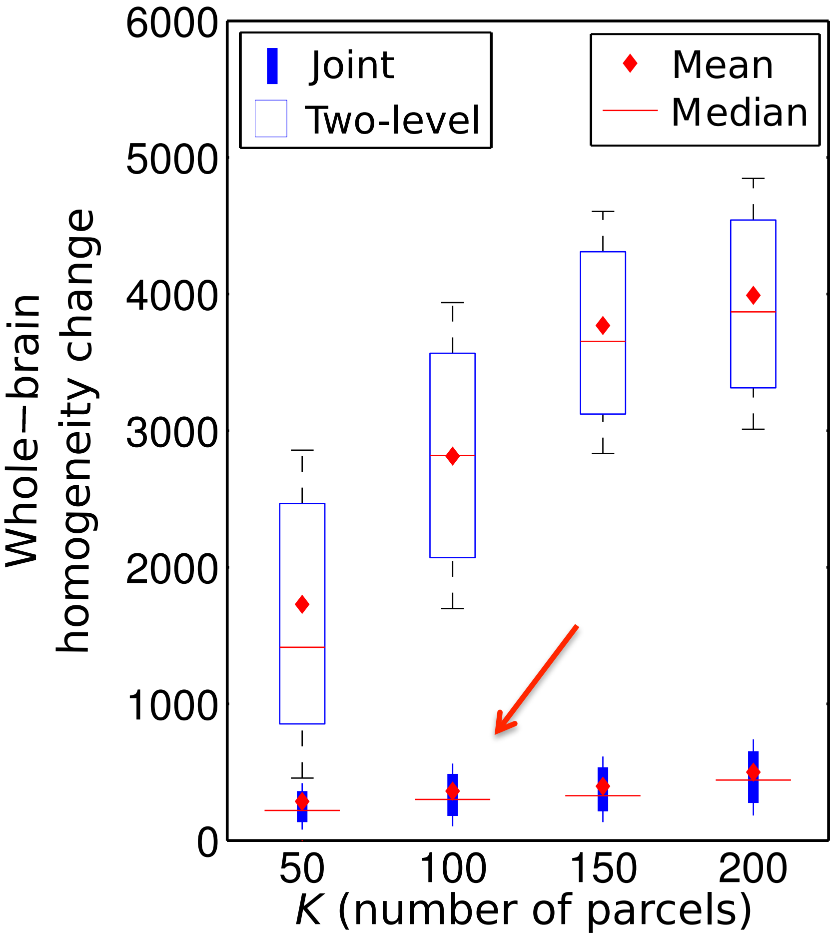
A decreasing trend in reproducibility is observed with the increasing parcellation resolution.

Visual results (K=100)



Due to high functional inter-variability across different individuals and the varying levels of SNR in cortical subregions, it is not possible to parcellate all parts of the cortical surface equally consistently.

Functional consistency – 1



Whole-brain homogeneity change

- Homogeneous (reliable) parcellations are expected to accommodate parcels with alike time series
- **Homogeneity**: Sum of the Euclidean distances between a parcel's time series and their average [Shen et al. 2013, NeuroImage]

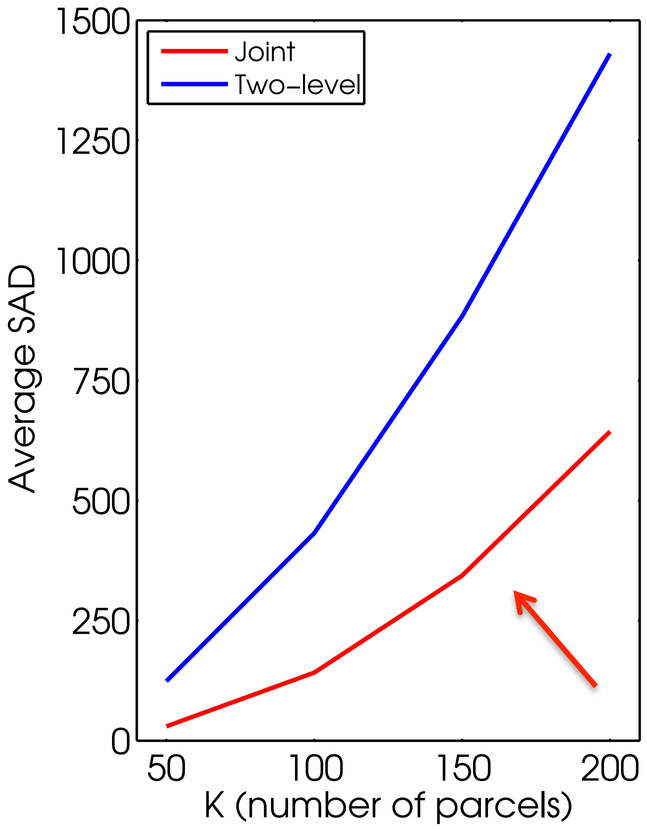
← How parcellation homogeneity changes?

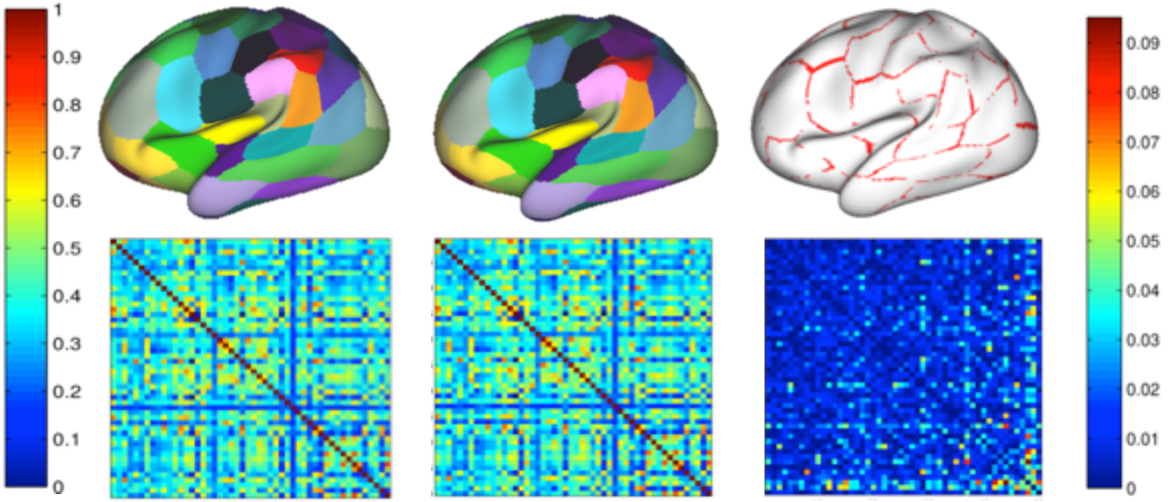
Homogeneity levels between group- and single-level parcellations obtained by our approach are **highly consistent** across different runs and at varying resolutions.

Functional consistency – 2

Average sum of absolute differences (SAD)

- Compute connectivity networks (correlation profiles) by cross-correlating parcels
- Two networks using subject's rs-fMRI data
- Compute sum of absolute differences between the networks





Subject Group Differences

Our approach computes more consistent networks compared to the other method.

Conclusions

- We presented a joint spectral decomposition technique for cortical parcellation using resting-state fMRI
- Parcellations with higher reproducibility and functional consistency
- Ability to reflect functional features shared by multiple subjects
- Parcellations obtained by our approach can be reliably used to identify the nodes in a group-wise network analysis
- Application: Divide subjects into subgroups based on age, analyze how network connectivity changes through aging
- Future work: Run method with different modalities (e.g. diffusion) and/or different clustering approaches

Thanks for your attention!

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