Structural Connectome Validation using Pairwise Classification

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Motivation

— Predictive modeling using DWI-based features (in particular, structural connectomes) has become a popular subgenre of neuroimaging (Arbabshirani et al., 2016)

— The great variety of possible pre-processing steps (e.g. non-linear registration, parcellation, or tractography) leads to potential challenges in downstream application of the connectomes, for example, in a classification task.

— The performance of a particular case-control classifier may not suffice as a means of data verification due to small samples and high dimensionality

— More objective validation may be needed in addition to frequently used Intra-class Correlation Coefficient (ICC) on test-retest data

Pairwise classification

— Let's assume we have set of connectomes C^i_j, where where i-indices correspond to images and j-indices correspond to subjects and feature mapping $f : C \to \mathbb{R}^d$

— For each pair of connectome feature vectors $(f(C^{i_1}_{j_1}), f(C^{i_2}_{j_2}))$ we assign target variable 1 if they are from the same subject, 0 — else; then we construct three pairwise differences of these vectors according to l_1, l_2 and l_∞ norms

— We run linear classification on these three features and report ROC AUC score

— Two-step validation procedure. First, grid search based on a 10-fold cross-validation with a fixed random state for reproducibility. Second, evaluation of the best parameters on 100 train/test splits (test size was set to 20% of data).

Datasets: ADNI

— 227 individuals from the Alzheimers Disease Neuroimaging Initiative (ADNI2).

— Mean age at baseline visit 73.1 ± 7.4, 99 females.

— Each individual has at least 1 brain scan and at most 6 scans.

— The data include 46 people with AD (111 AD scans), 80 individuals with EMCI (247 MCI scans), 40 people with LMCI (120 LMCI scans) and 61 healthy participants (160 scans).

— 227 475 possible pairs of subjects (764 of which were labeled as 0).

More details on data: adni.loni.usc.edu

Datasets: PPMI

— 226 individuals from Parkinson's Progression Markers Initiative (PPMI).

— 159 subjects from PD cohort and 67 healthy controls.

— Mean age at the baseline visit 61.0 ± 9.8 years, 79 were females.

— Each individual has at least 1 brain scan and at most 4 scans.

— 152031 pairs from PPMI data (301 of which were labeled as 1)

More details on data: ppmi-info.org

Network construction: ADNI and PPMI

T1w Processing

Cortical reconstruction generated via FreeSurfer

Skull-stripped T1w, FreeSurfer parcellations, aligned to MNI152 space

DWI Processing

Denoise with NLSAM (PPMI-only)

Correct for motion and eddy-current distortion

Rotate b-vectors

Nonlinear correct for EPI-artifact with ANTs

Align DWI with T1w in MNI152 space

Rotate b-vectors (again)

Fit CSD at each voxel

Seed tracking at two locations per WM voxel

Dipy LocalTracking in 0.5mm increments

Filter short streamlines and those ending outside GM

Connectome normalizations and features

— **Four normalizations**: by mean, by max, binary and no normalization

— **Weighted nodes' degrees** or strength.

— **Closeness centrality.** The higher it is, the more close node to others.

— **Betweenness centrality.** Represents the degree of which nodes stand between each other.

— **Eigenvector centrality.** Measure of influence of a node in a network.

— **Local efficiency.** Measure of how efficiently node exchanges information.

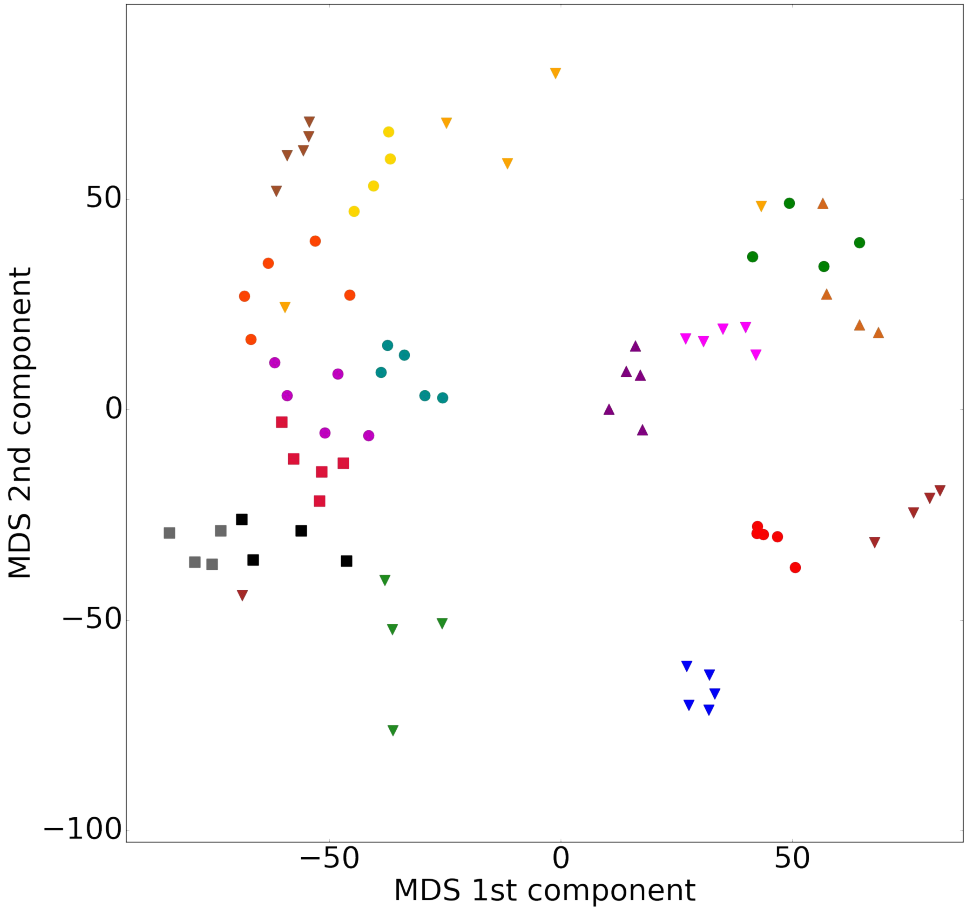
— **Clustering coefficient.** Measures degree to which nodes in a network tend to cluster together

— **Weighted number of triangles** around node.

— **PageRank** (Brin and Page, 1998). Another estimate of node's importance related to random walks on a network.

(Overview of all metrics except PageRank can be found in Rubinov and Sporns, 2009)

Results: ADNI MDS on bag of edges



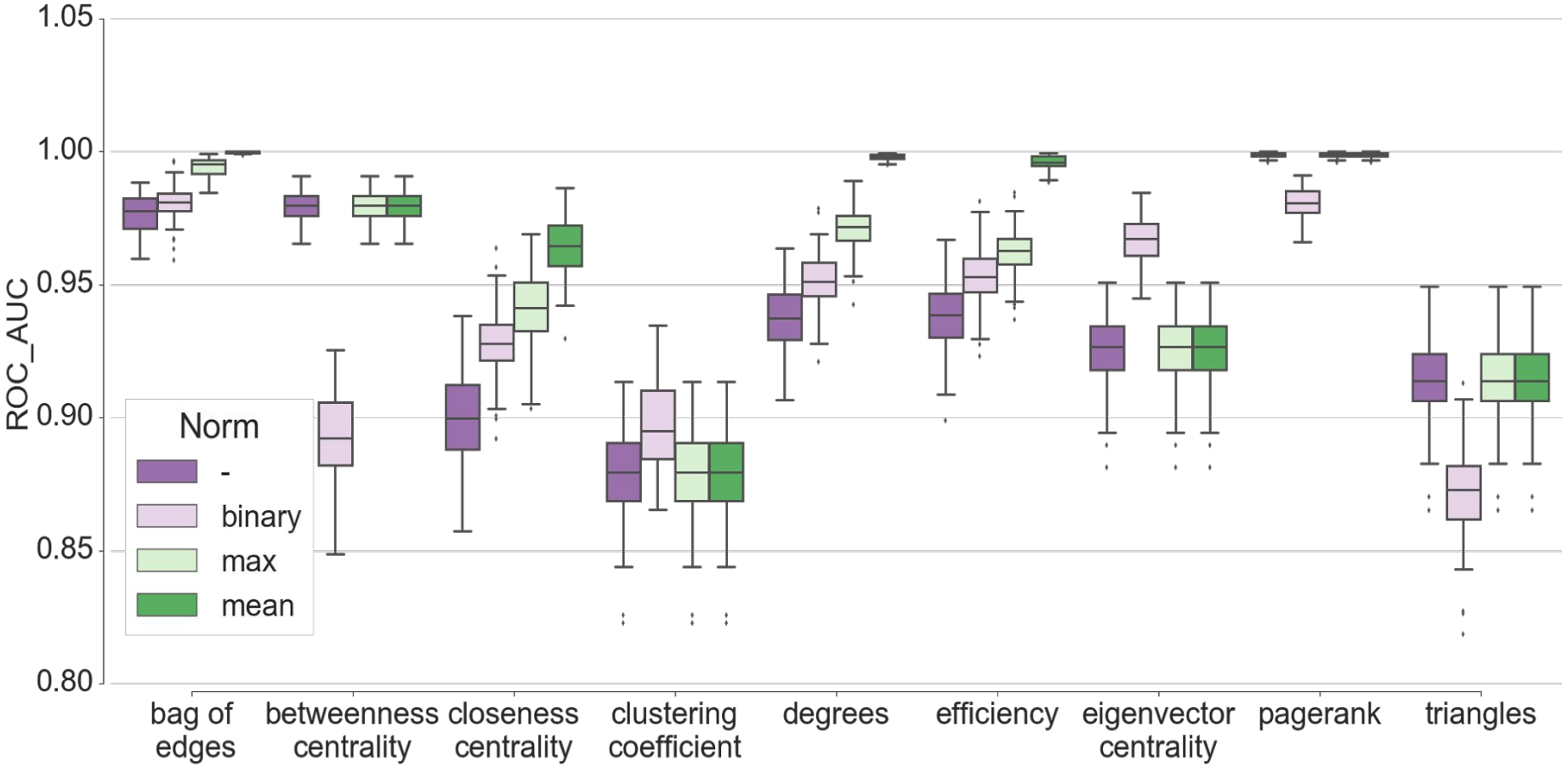
— Multidimensional scaling based on l_2-distance between bag of edges for ADNI subjects

— Only 17 subjects shown for purpose of visualisation

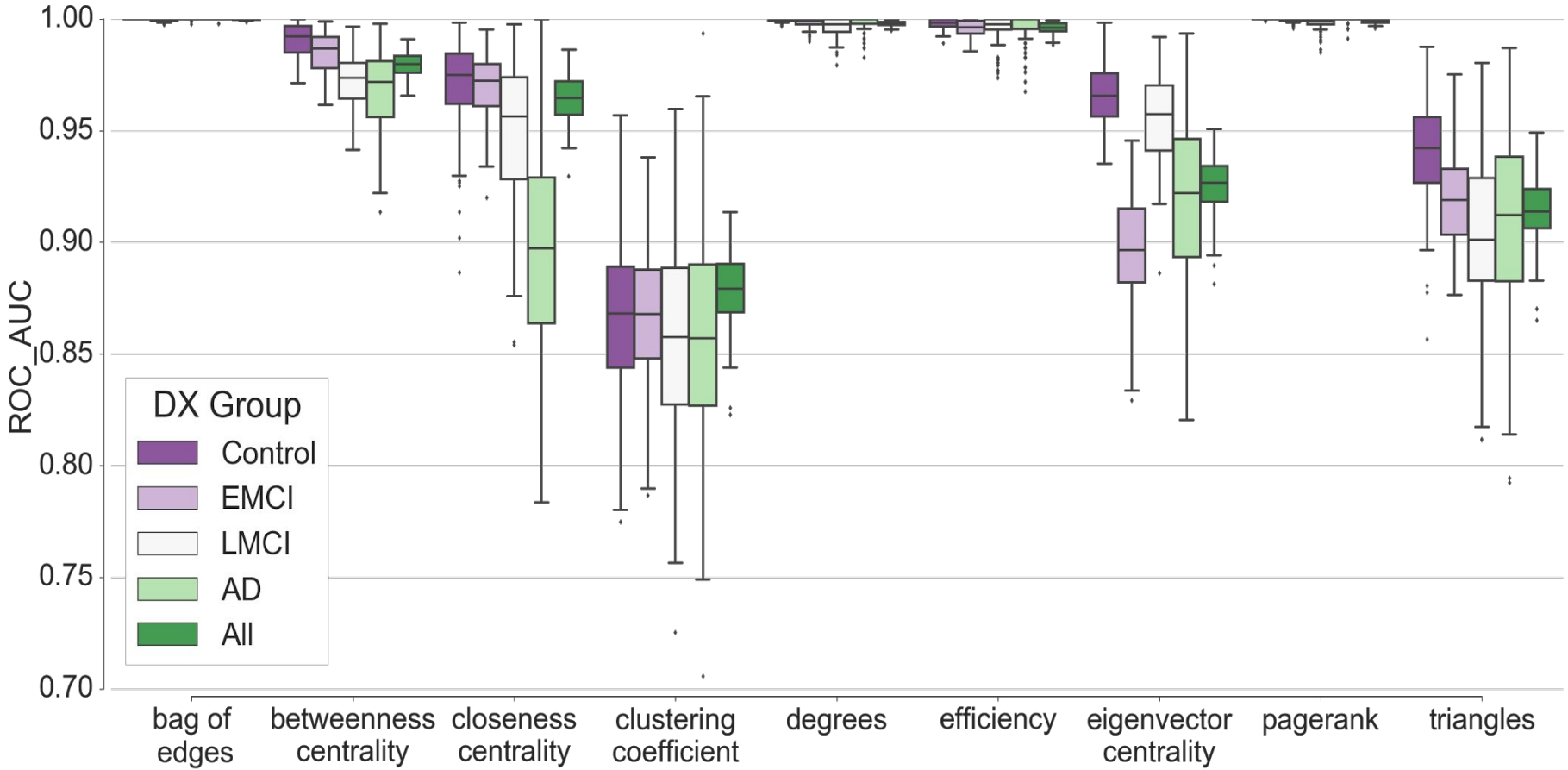
— Different colors represent different subjects

— Shapes of markers represent diagnostic group: □ — AD, ▲ — MCI, ▼— EMCI, ○ — HC

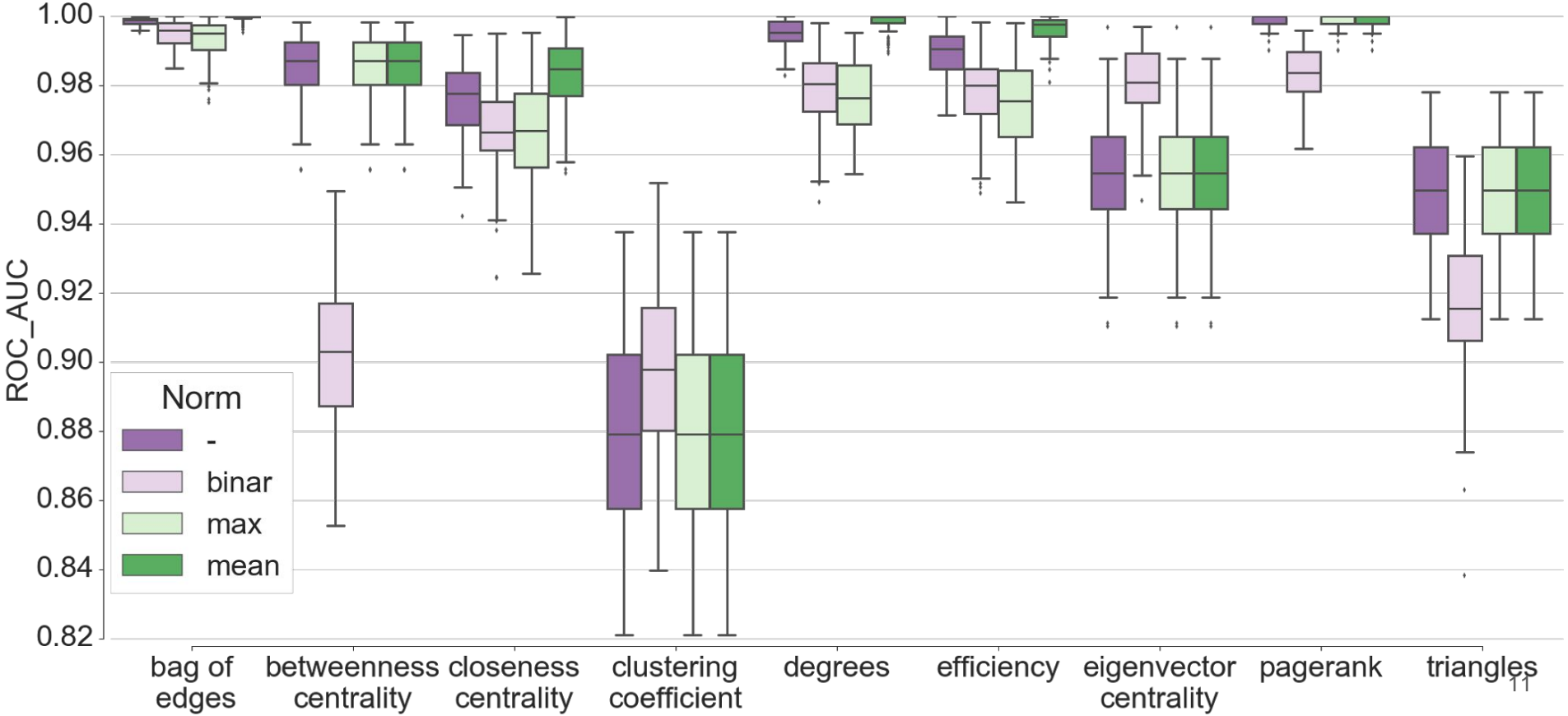
Results: ADNI by norms and features



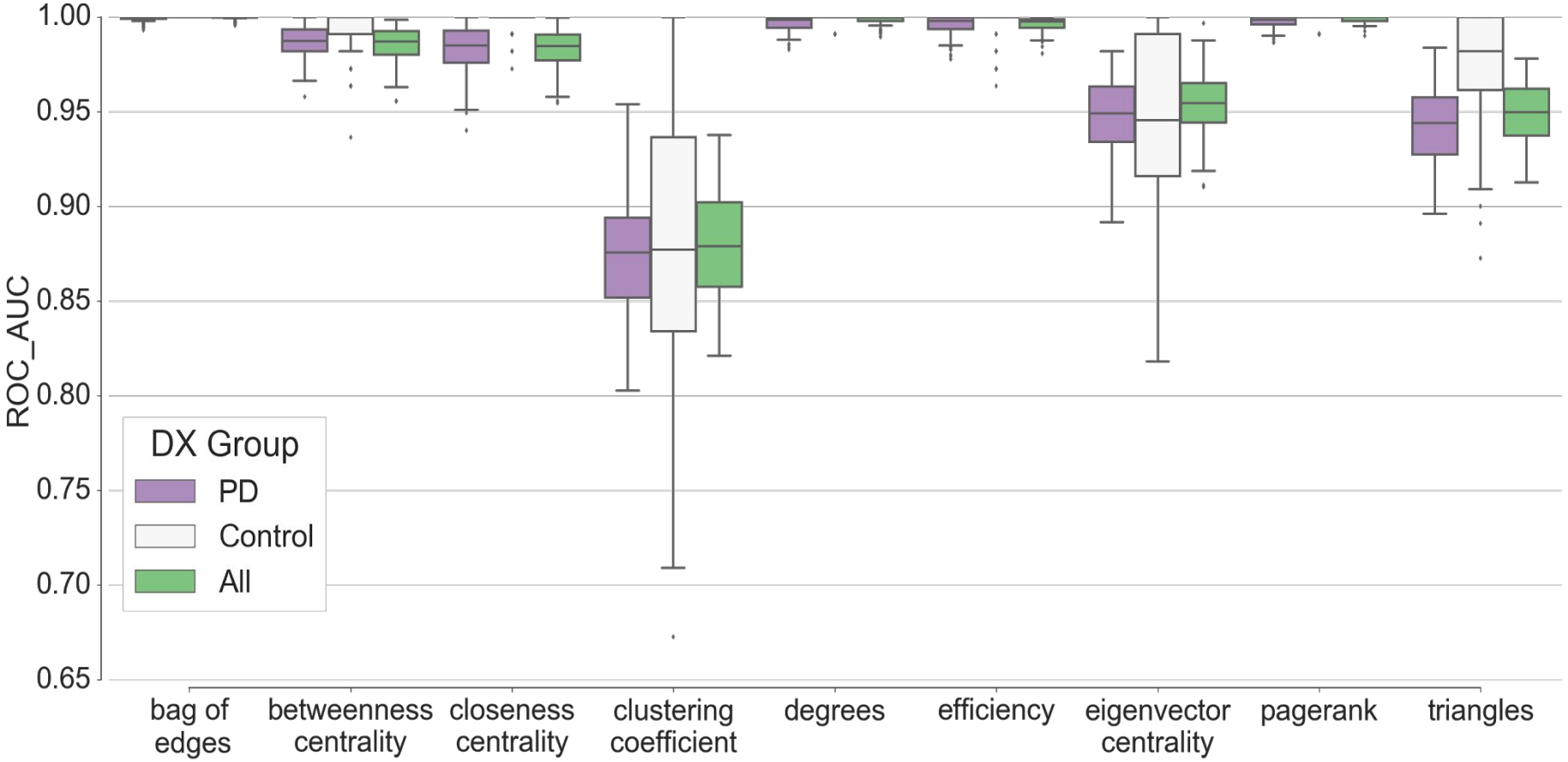
Results: ADNI by DX groups and features



Results: PPMI by norms and features



Results: PPMI by DX group and features



Conclusion

— Pairwise classification may be useful for comparison of preprocessing pipelines and particular features

— Results consistent across two datasets and inside diagnostic groups

— Images for both ADNI and PPMI data were obtained with time difference at least a year. We can’t be sure that subject connectomes didn’t change due to some reasons (i.e. disease progression)

— Pairwise classification is not a feature selection technique for classification tasks in a common sense.

Related work

— Finn, Emily S., et al. "Functional connectome fingerprinting: identifying individuals using patterns of brain connectivity." *Nature neuroscience* (2015). Similar work for fMRI data. Authors successfully identified subjects based on fMRI connectivity. Results were consistent across scan sessions and even between task and rest conditions.

— Yeh, Fang-Cheng, et al. "Quantifying Differences and Similarities in Whole-brain White Matter Architecture Using Local Connectome Fingerprints." *PLOS Computational Biology* 12.11 (2016). Authors used a local structural connectome, different features, datasets and connectome construction pipelines and arrived at similar conclusions.

Possible extensions

— Evaluation of different connectome building pipelines using both pairwise classification and Intraclass Correlation Coefficient on test-retest data (done, under review).

— Investigation of how pairwise classification changes with each pre-processing and connectome building step.

— Time difference regression on connectome pairs.

— Structural/functional connectome pairs classification.

Links and acknowledgements

Source code:

github.com/neuro-ml/structural-connectome-validation-pairwise

Library for creating and curating reproducible pipelines:

github.com/neuro-ml/reskit

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Thank you!

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