Clustering Multi-Modal Connectomes

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Summary

- Brains represented as connectomes (brain region = node, connections = edges).
- **Almost perfectly cluster test-retest scans from same subject into own group for 30 subjects** using populations of connectomes from various neuroimaging data modalities (dMRI, fMRI).
- Two models for representing population of graphs: 1) Random Dot Product Graphs (RDPG), 2) Common Subspace Independent Edge Graph (COSIE).
- Novel embedding methods for fitting the models from population of connectomes: 1) **omnibus embedding** for RDPG, 2) **multiple adjacency spectral embedding** for COSIE.
- Learn features at connectome level and node level.
- `GraSPy`- open-source Python package all algorithms implemented.

neurodata.io/graspy

Model: Random Dot Product Graphs (RDPG)

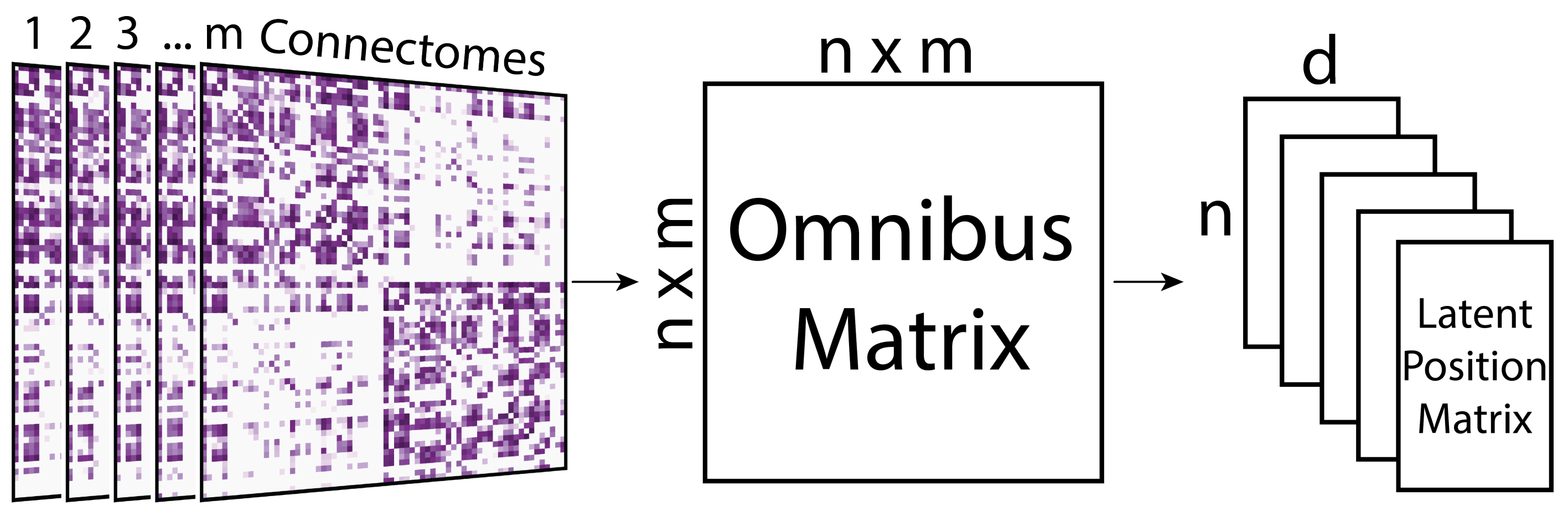
Intuition:

1. Each vertex has **latent position** vector in $\mathbb{R}^d$
2. Probability of edge occurring = dot product of two latent position vectors

Parameters:

- Latent position matrix $X_i \in \mathbb{R}^{n \times d} \forall i \in [m]$

Estimation: Omnibus Embedding


1 2 3 ... m Connectomes

n x m

n x m

Omnibus Matrix

n

d

Latent Position Matrix

Figure 1. Given multiple connectomes, an omnibus matrix combining all graphs is generated. The omnibus matrix is then decomposed using eigendecomposition to obtain a latent position matrix for each input connectome. Omnibus embedding provides a **consistent** estimate of latent positions.

Model: Common Subspace Independent Edge Graph (COSIE)

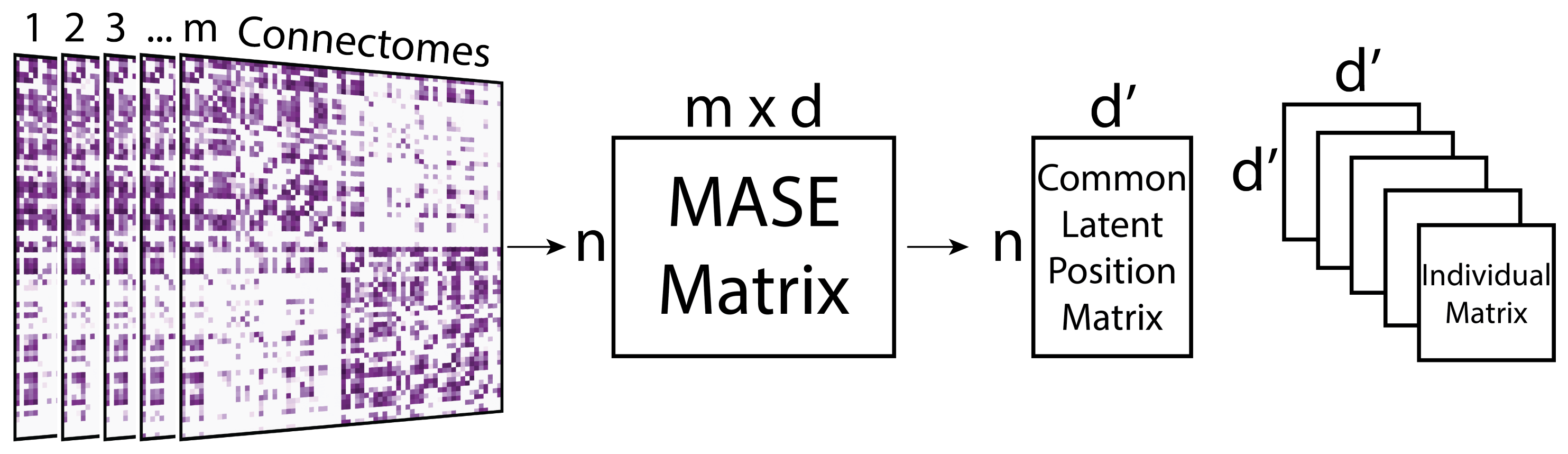
Intuition:

1. Each vertex has **latent position** vector in $\mathbb{R}^d$.
2. All graphs share a common vertex latent position matrix.
3. Individual graph is a transformation of latent position matrix.

Parameters:

1. Latent position matrix $V \in \mathbb{R}^{n \times d}$
2. Individual matrix $R_i \in \mathbb{R}^{d \times d} \forall i \in [m]$

Estimation: Multiple Adjacency Spectral Embedding (MASE)


1 2 3 ... m Connectomes

n

m x d

MASE Matrix

n

d′

Common Latent Position Matrix

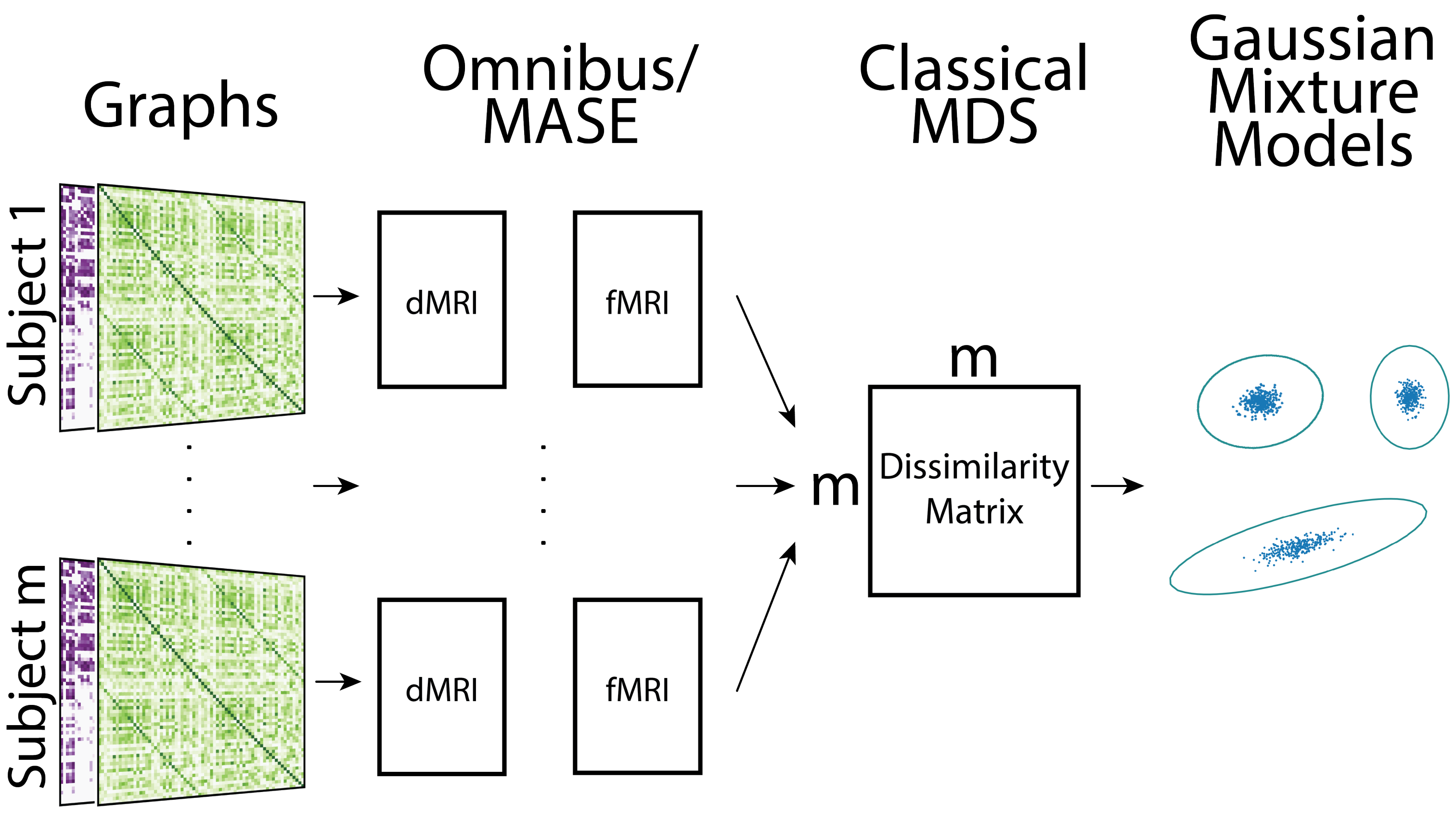
d′

d′

Individual Matrix

Figure 2. Each connectome is decomposed via eigendecomposition, and its results are concatenated to yield the MASE matrix. The MASE matrix is then decomposed via singular value decomposition to yield a latent position matrix that is shared among all input connectomes and subject matrix that is unique to each connectome. MASE provides a **consistent** estimate of common latent position matrix, and individual matrices.

Clustering Multi-Modal Connectomes


Graphs

Omnibus/ MASE

Classical MDS

Gaussian Mixture Models

Subject 1

Subject m

dMRI

fMRI

dMRI

fMRI

m

m

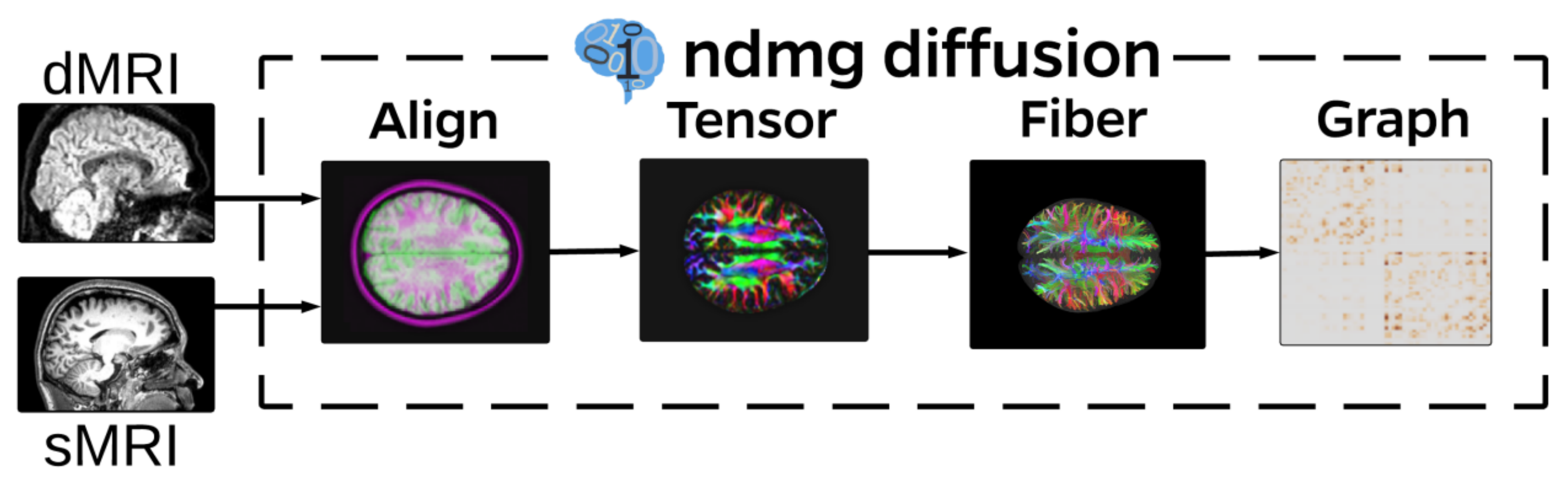
Dissimilarity Matrix

Figure 3. Given populations of graph from different modalities, graphs from each modality is embedded separately. The resulting subject matrices are then concatenated, form a dissimiliarity matrix via Euclidean distances, then embedded via classical MDS (cMDS). This results in a feature vector for each subject, which can be clustered via gaussian mixture models.

HNU1 Dataset and Preprocessing

Dataset:

- 30 subjects
- Scanned once every 5 days, 10 total scans per subject
- Preprocessed using ndmg.


dMRI

sMRI

ndmg diffusion

Align

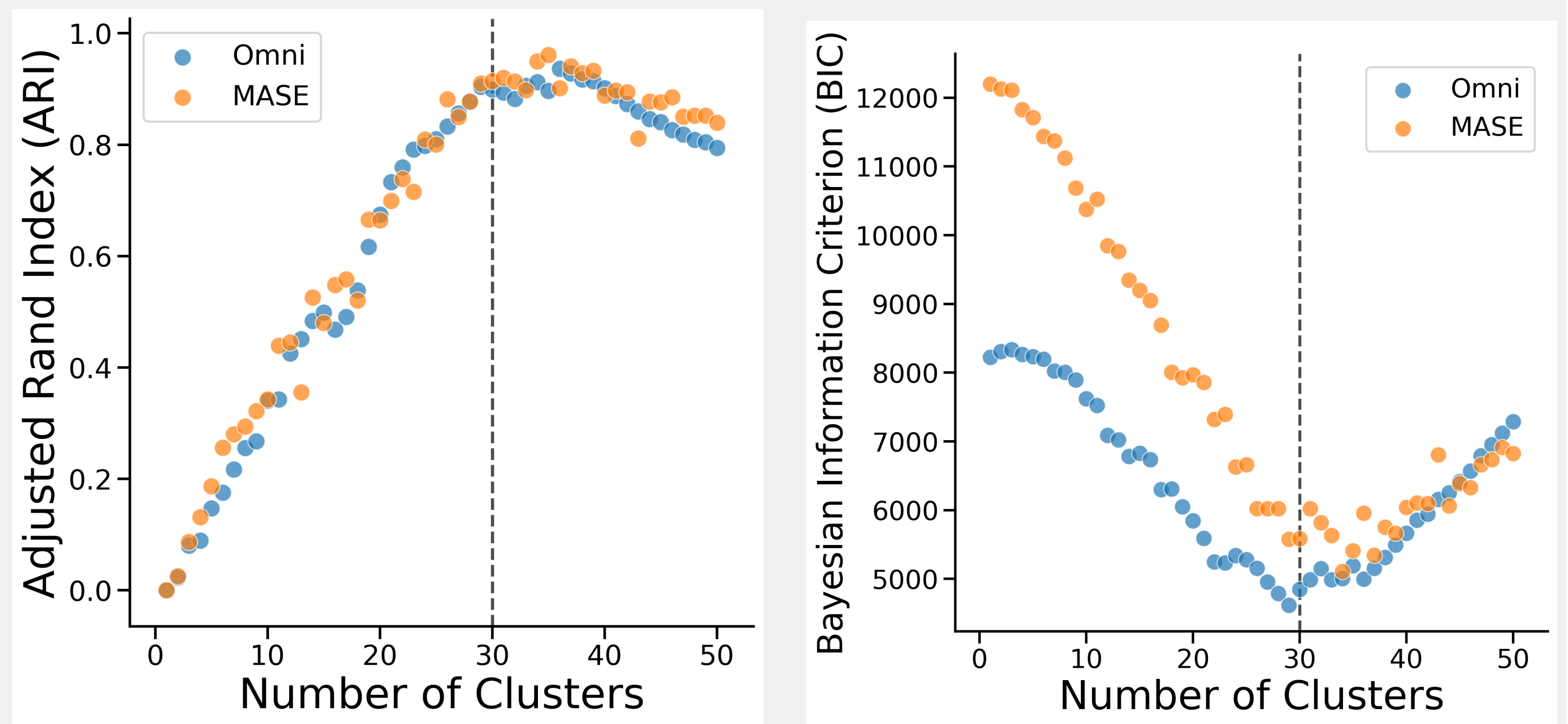
Tensor

Fiber

Graph

Figure 4. Outline of the *ndmg* (https://ndmg.neurodata.io) pipeline. Image taken from [3].

Clustering Results

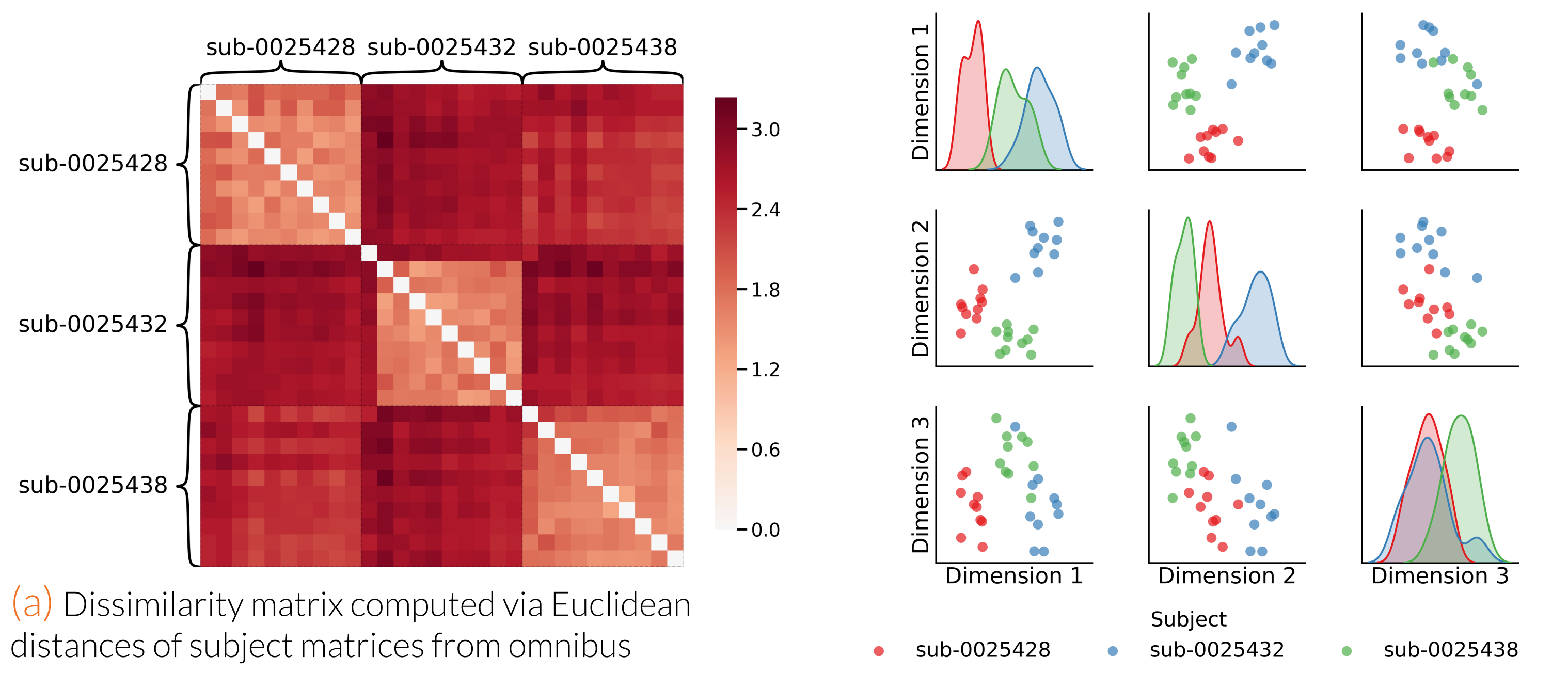


(a) Adjusted rand index (ARI) measures the goodness of estimated clusters given ground truth. ARI of 0 means chance clustering, and ARI of 1 means perfect clustering. Dashed vertical line represents 30 clusters. At 30 clusters, ARI is at about 0.9, meaning that the each of the resulting clusters almost perfectly resemble scans from the same subject.

(b) Bayesian information criterion (BIC) measures the goodness of model by penalizing the number of estimated parameters. BIC allows for automated cluster selection by choosing the model with lowest BIC. Dashed vertical line represents 30 clusters. BIC for Omni is minimized at 29 clusters and BIC for MASE is minimized at 34 clusters. Minimized BIC around 30 cluster means that our method forms correct number of clusters, and each cluster is meaningful.

Figure 5. Clustering results from HNU1 dataset using 30 subjects with Omni and MASE.

Visualizations of Intermediate Steps



(a) Dissimilarity matrix computed via Euclidean distances of subject matrices from omnibus embedding for 3 out of 30 subjects. Matrix is subsampled only for visualization purposes. Diagonal blocks corresponds to test-retest scans for a subject and have lower dissimilarity. Off-diagonal blocks correspond to test-retest scans across subjects and have higher dissimilarity.

(b) Visualization of embedding of dissimilarity matrix. Same 3 subjects are subsampled for visualization purposes. Each point represent a feature vector for a scan. Points from the same subject are closer together suggesting that test-retest scans from same subject are very similar to each other.

Figure 6. Visualizations of outputs from Classical MDS. The resulting feature vectors from Classical MDS is used for clustering.

Conclusion

- Two new models for representing population of connectomes (RDPG, COSIE).
- Omnibus embedding and multiple adjacency spectral embedding for estimating parameters of RDPG and COSIE, respectively.
- **Estimated parameters can be used for any downstream tasks (e.g. hypothesis testing, clustering, classification).**
- Clustering on HNU1 data shows near perfect clustering of test-retest scans into correct subject cluster.
- Can be applied to any population of connectomes.

Code and Data

All analysis was performed using an open-source package **GrasPy** (https://graspy.neurodata.io). All dMRI images are open-source and provided by Hangzhou Normal University (`http://fcon_1000.projects.nitrc.org/indi/CoRR/html/hnu_1.html`).

NeuroData Workshop

NeuroData is hosting a week long workshop for all of our neuroscience and statistical tools.

Date	Tool	Description
8/19	mgc	High dimensional hypothesis testing
8/20	RerF	Decision forest for classification, regression
8/21	GraSPy	Statistical Inference on graphs
8/22	reggie	Non-linear registration
8/23	ndmg	fMRI and dMRI processing

neurodata.io/workshop

Come join us at Baltimore, MD USA!

References

[1] Avanti Athreya, Donniell E. Fishkind, Minh Tang, Carey E. Priebe, Youngser Park, Joshua T. Vogelstein, Keith Levin, Vince Lyzinski, Yichen Qin, and Daniel L Sussman.
Statistical inference on random dot product graphs: a survey.
Journal of Machine Learning Research, 18(226):1–92, 2018.

[2] Jaewon Chung, Benjamin D Pedigo, Eric W Bridgeford, Bijan K Varjavand, and Joshua T Vogelstein.
Graspy: Graph statistics in python.
arXiv preprint arXiv:1904.05329, 2019.

[3] Gregory Kiar, Eric Bridgeford, Will Gray Roncal, , Vikram Chandrashekhar, Disa Mhembere, Sephira Ryman, Xi-Nian Zuo, Daniel S Marguiles, R Cameron Craddock, Carey E Priebe, Rex Jung, Vince Calhoun, Brian Caffo, Randal Burns, Michael P Milham, and Joshua Vogelstein.
A high-throughput pipeline identifies robust connectomes but troublesome variability.
bioRxiv, 2018.

[4] Keith Levin, Avanti Athreya, Minh Tang, Vince Lyzinski, and Carey E Priebe.
A central limit theorem for an omnibus embedding of random dot product graphs.
arXiv preprint arXiv:1705.09355, 2017.

[5] Mu Zhu and Ali Ghodsi.
Automatic dimensionality selection from the scree plot via the use of profile likelihood.
Computational Statistics & Data Analysis, 51(2):918–930, 2006.

[6] Xi-Nian Zuo, Jeffrey S Anderson, Pierre Bellec, Rasmus M Birn, Bharat B Biswal, Janusch Blautzik, John CS Breitner, Randy L Buckner, Vince D Calhoun, F Xavier Castellanos, et al.
An open science resource for establishing reliability and reproducibility in functional connectomics.
Scientific data, 1:140049, 2014.