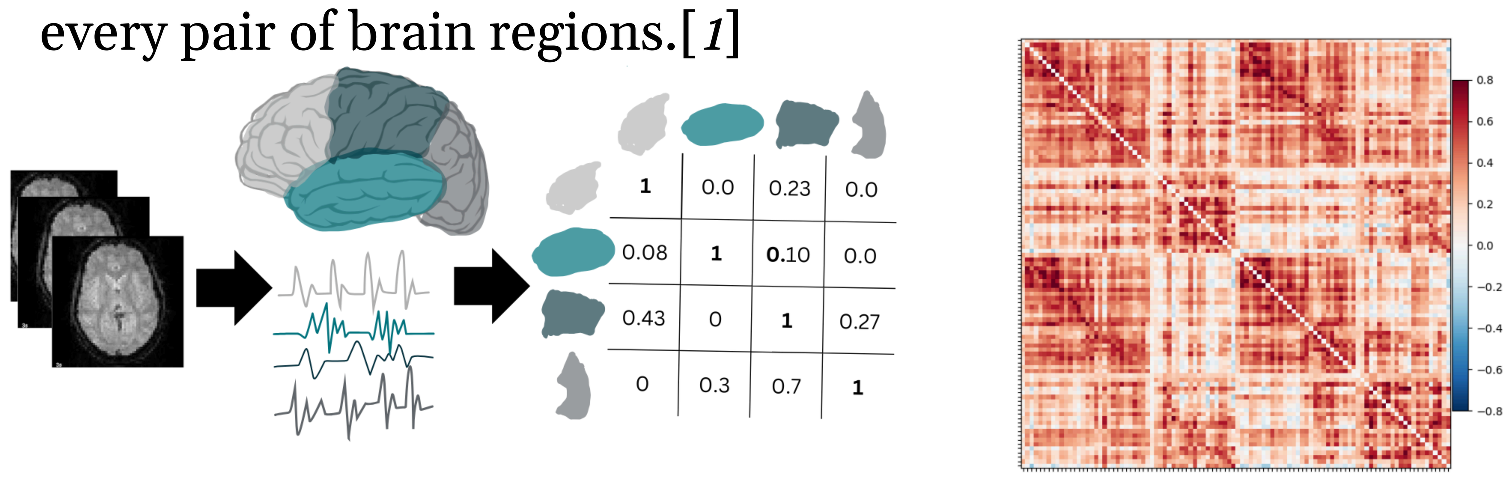
Evaluating regularized modeling methods for calculating functional connectivity

McKenzie Paige Hagen[1, 2], Ariel Rokem[1, 3], Kristofer Bouchard[2]

[1] Department of Psychology, University of Washington [3] eScience Institute, University of Washington [2] Lawrence Berkeley National Lab

Background

- Functional MRI (fMRI) is used to non-invasively study the human brain.
- **Functional connectome:** the statistical relationship between every pair of brain regions.[*1*]



- Most of fMRI literature uses Pearson correlation coefficient between brain regions to calculate the functional connectome.
  - Pearson correlation connectomes are theoretically, psychometrically, and empirically flawed.
- We investigate using the estimated model weights as alternatives to Pearson.

Do functional connectomes calculated with regularized methods overcome the drawbacks of Pearson connectomes?

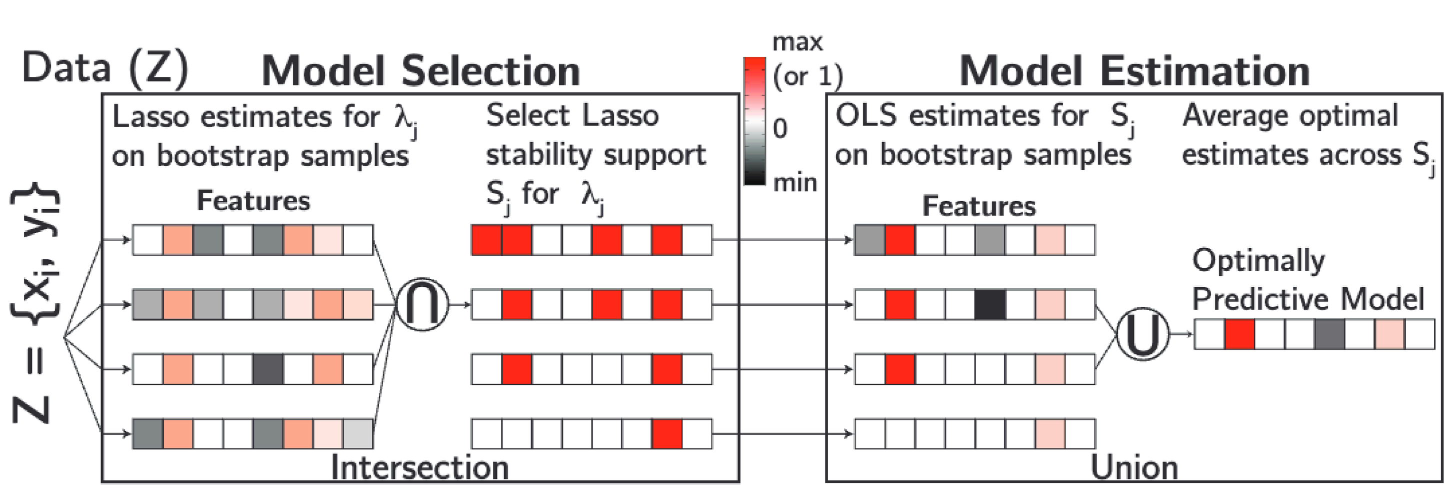
Methods

Data: Human Connectome Project - openly available, high quality MRI dataset of 1,000+ "healthy" young adults.

- Current analyses use four sessions from 100 randomly selected participants as discovery dataset.
- fMRI images processed into 100 brain regions using Schaefer atlas.

Pearson correlation: Pearson correlation between each region's timeseries represents connectivity between regions.

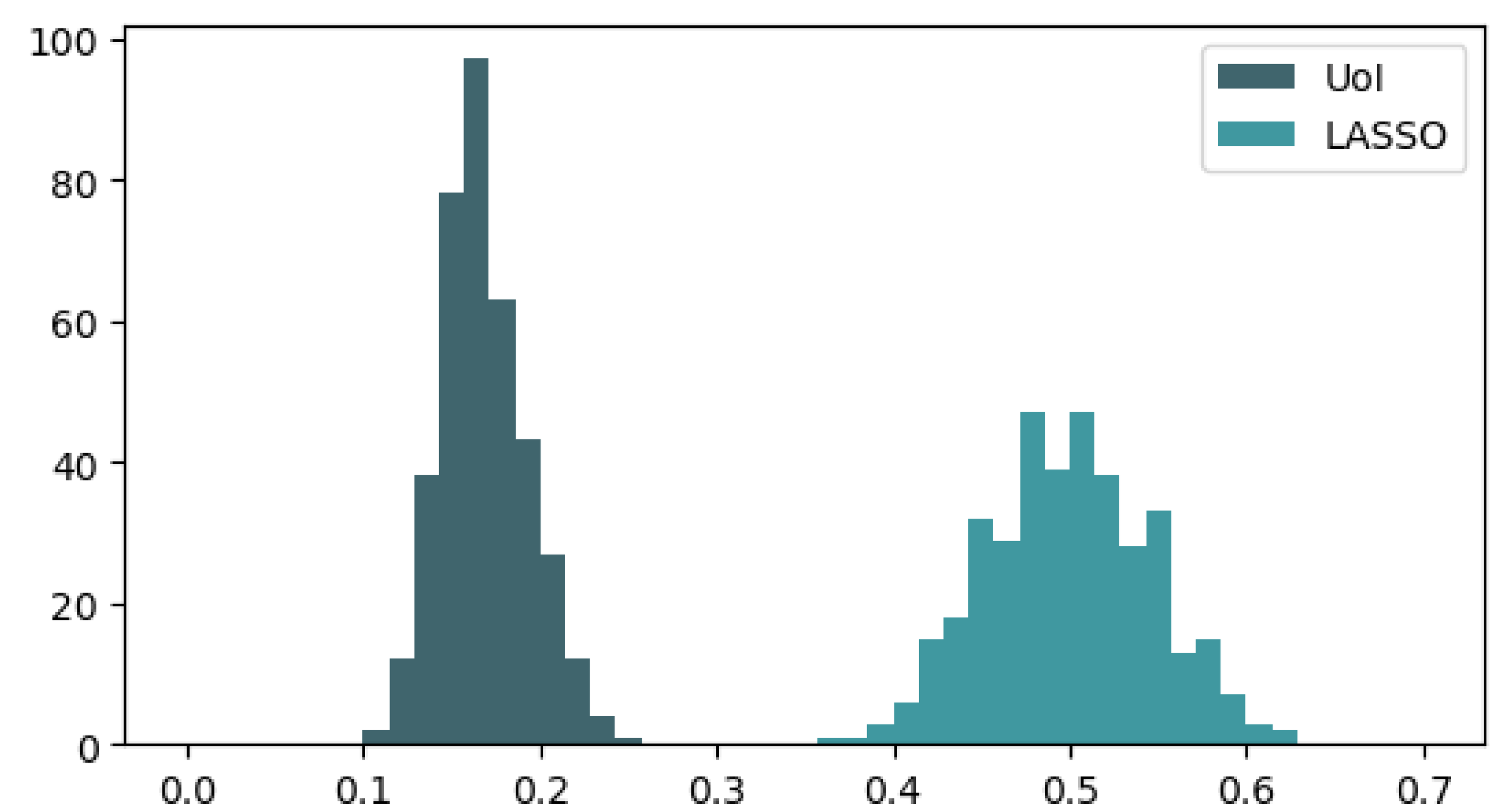
LASSO and UoI: Model beta weights fit with cross-validation predicting target region's timeseries from every other timeseries represents connectivity.



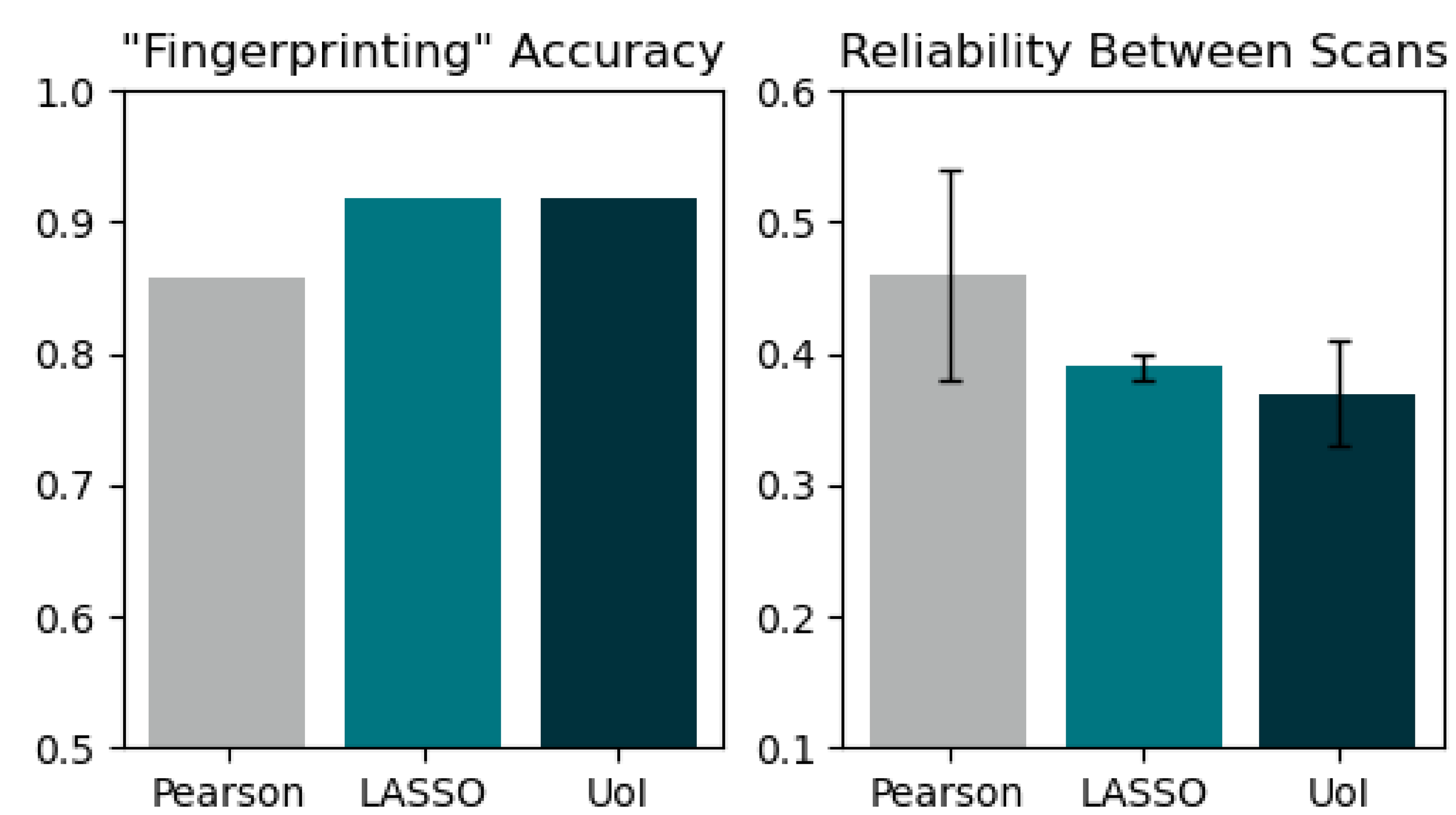
LASSO models fit with L1 regularization penalizing sum of the absolute value of beta weights. UoI models fit with a combination of model selection and estimation with resampling. Figure from [*2*].

Preliminary Results

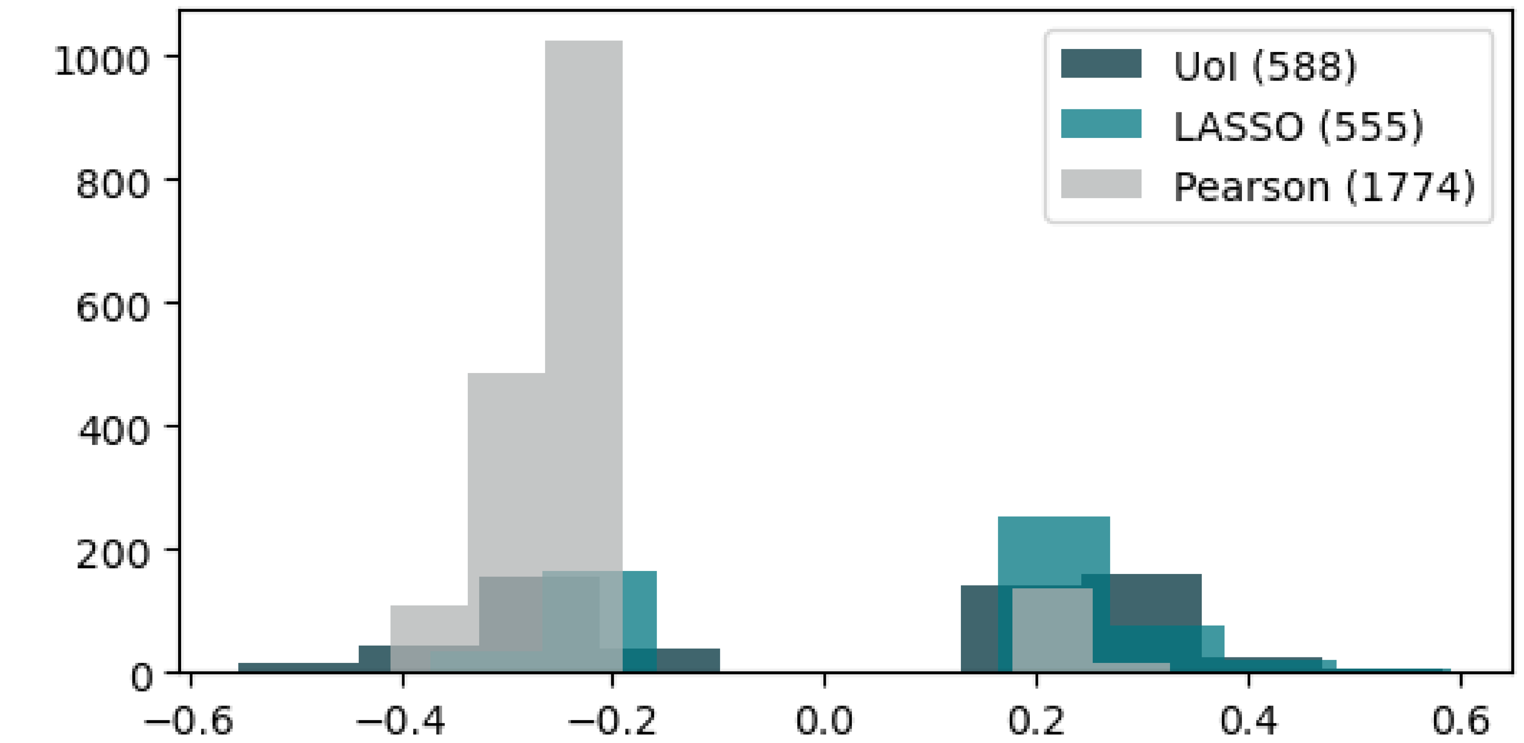
Connectomes evaluated using characteristics desirable for empirical analyses using functional connectomes: sparsity, reliability, identifiability ("fingerprinting"), correlation with motion ("qcfc").



Selection ratio. The proportion of selected edges by each model for each participant. Pearson connectomes not shown since all edges are selected. UoI selects far fewer edges than LASSO, demonstrating biologically-realistic sparsity.



Psychometric Properties. UoI and LASSO perform equally well as Pearson correlation on participant identification and repeat reliability (error bars: 95% CI).



Edge correlation with motion. Pearson connectomes have more edges that are significantly correlated with particpant motion during scanning, indicating that they are not capturing true connectivity, but motion-induced spurious correlations.

High Performance Computing

- UoI computationally demanding for long scans and large sample sizes, but "embarrassingly parallel"
- "Datalad" (distributed data management) used to minimize long-term storage demands
- Strict naming conventions helpful for data organization and sharing: Brain Imaging Data Structure Extention Project (BIDS-BEP17) used formalize file format and naming convention for connectomes

Conclusions

- Regularized connectomes show promise for correcting the flaws of Pearson connectomes.
- Regularized connectomes are sparse, reliable, and empirically valid.

Future Directions:

- Confirm current findings with whole HCP dataset, other large datasets.
- Other metrics to evaluate connectomes are phenotypic predictions and robustness to processing pipeline variabilty.
- Re-evaluate previous studies with LASSO/UoI to determine the robustness of their findings with regularized modeling methods.

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References

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2. P. S. Sachdeva *et al.*, *J. Neurosci. Methods* (2021).

Contact: mphagen@uw.edu