RESTING STATE FUNCTIONAL MRI BASED ALZHEIMER'S DISEASE CLASSIFICATION

ECE 784: COMPUTER VISION FINAL PROJECT

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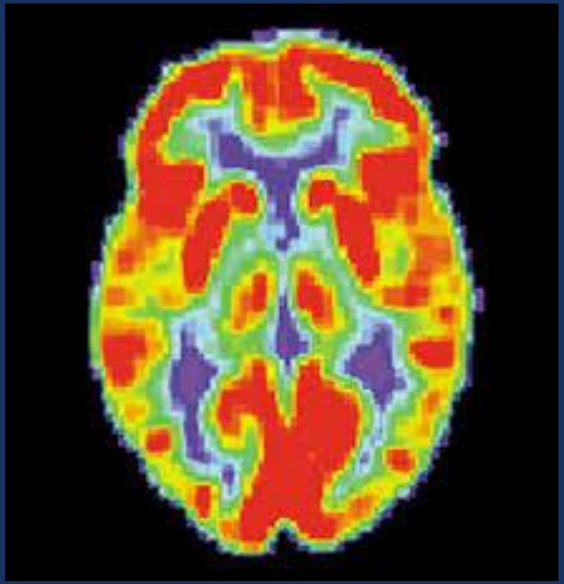
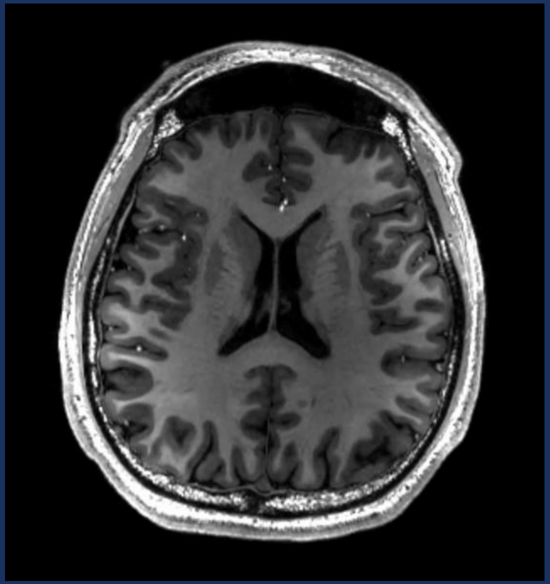


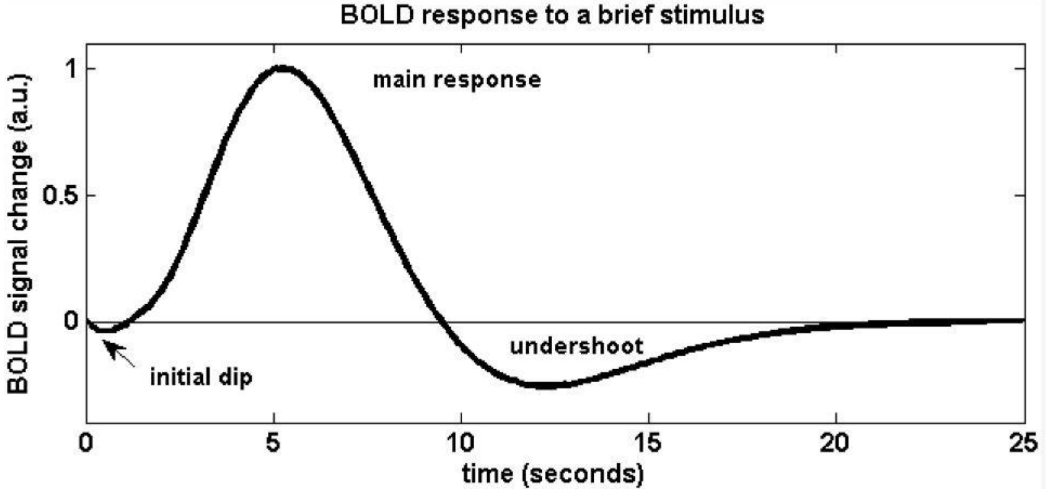


PROJECT BACKGROUND

- Alzheimer's disease (AD), biologically defined by a buildup of amyloid β plaques and tau tangles in the brain can be diagnosed with biomarkers obtained from PET scans or CSF proteomics. However, these methods are expensive and invasive, leading to most AD diagnoses being made based on cognitive tests and evidence of atrophy in the medial temporal lobe structures shown on MRI scans, such as in the hippocampus and amygdala.
- Deep learning methods with architectures such as convolutional neural networks (CNNs) have seen impressive performance in diagnosing AD from 3D structural MRI scans. Some studies have even outperformed methods currently used in clinical practice for classifying hard to detect subgroups (atypical AD) [1].
- However, relying on changes to the brain's anatomy alone for diagnosis, especially in the early stages of disease progression is not always reliable, and rs-fMRI networks have been shown to be highly sensitive to AD [2].

DATA BACKGROUND

Figure 1. Schematic of the BOLD hemodynamic response to a brief stimulus at time zero. After the elusive “initial dip” that may arise as a result of initial oxygen uptake before hemodynamic changes occur, the blood flow effect dominates and causes the positive main BOLD response to peak after approximately 4–5 s. The return to baseline is typically preceded by a post-stimulus undershoot which can be of considerable duration.



[3]

- Functional magnetic resonance imaging (fMRI) measures small changes in blood flow over time.
- Blood-Oxygen-Level-Dependent (BOLD) indirectly measures neural activity by detecting blood oxygenation. When neurons become more active, they consume more oxygen, which triggers an influx of oxyhemoglobin.
- As local oxygen demand increases, the concentration of paramagnetic deoxy-hemoglobin decreases, BOLD signal increases. Inverse relationship, since deoxy-hemoglobin interferes with magnetic field, increases BOLD signal.
- 4D data (x, y, z, time)

THIS WORK

- In this project, we first implement common pre-processing techniques in medical image analysis with fMRIPrep: such as intensity non-uniformity (INU) correction, skull stripping, spatial normalization, and brain tissue segmentation [4]. We use this output as the starting image for rs-fMRI post processing.
- Next, we perform post-processing of the fMRI scans to extract relevant information for disease prediction:
  - Functional Connectivity (FC) Matrix
  - Mean BOLD signal
  - Amplitude of Low Frequency Fluctuations (ALFF)
  - Regional Homogeneity (ReHo)
- Finally, we will train a SVM model with these 4 metrics to classify patients from the Alzheimer's Disease Neuroimaging Initiative (ADNI) as either AD (n=49) or cognitively normal (n=17).

POST-PROCESSING

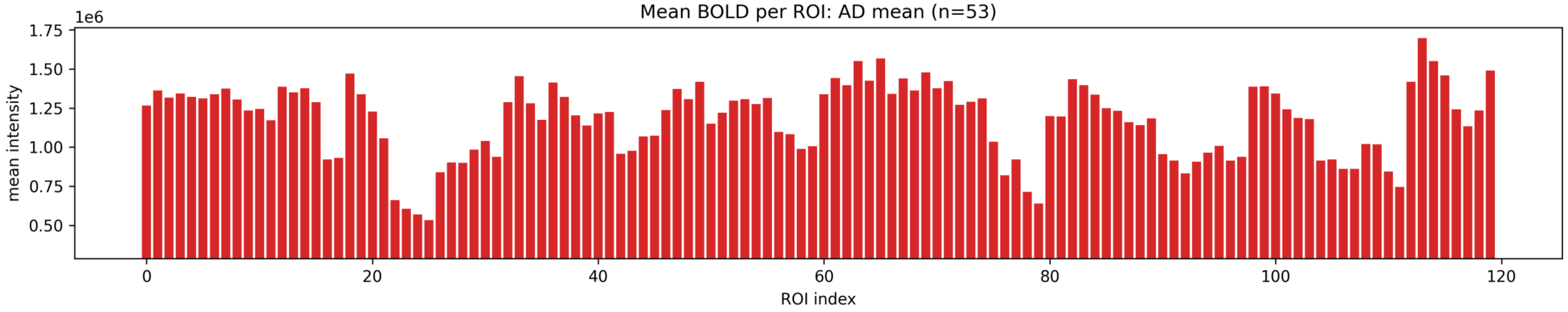
- **Functional Connectivity (FC) Matrix:** A symmetric, $N \times N$ representation of the average BOLD time series between N brain regions of interest ($N = 120$) based on the Pearson correlation coefficient. This shows how functionally connected each brain region is with every other region (fluctuates through time).
- **Mean BOLD signal:** Represents the average BOLD signal per ROI through time to serve as a baseline.
- **Amplitude of Low Frequency Fluctuations (ALFF):** Quantifies spontaneous, low frequency fluctuations of the BOLD signal. ALFF measures the square root of the power spectrum within a specific range (0.01-0.08 Hz).

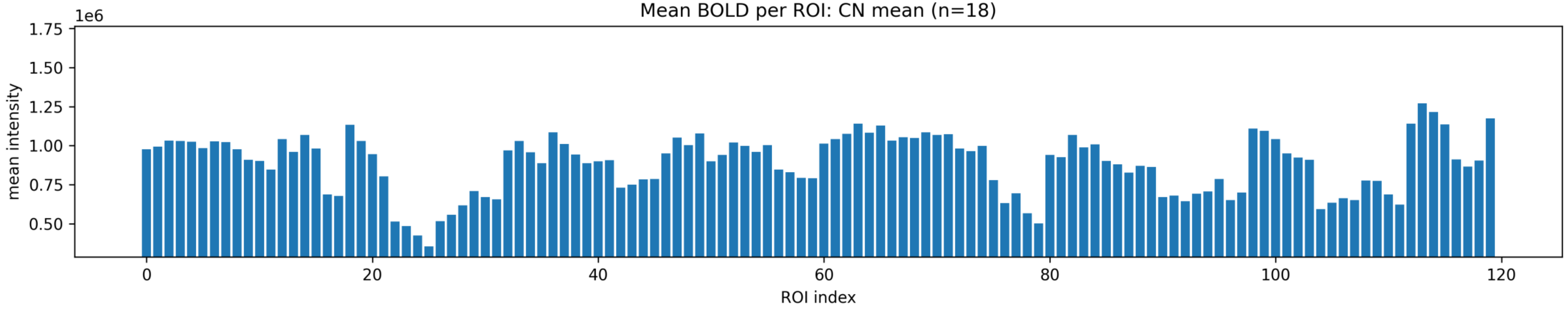
$$ALFF = \frac{1}{N}\sum_{i=1}^{N}\sqrt{S(f_i)}$$

Where N is the number of points within 0.01-0.08 Hz and $S(f_i)$ is the power at frequency f_i.

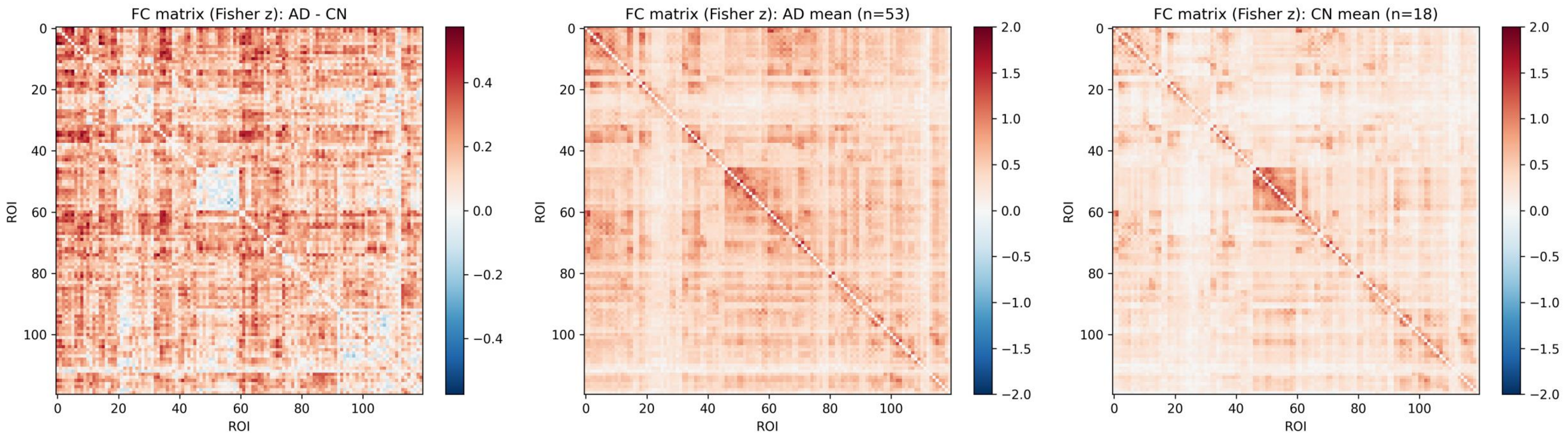
- **Regional Homogeneity (ReHo):** Captures local functional coordination, shows how synchronized nearby voxels are with each other in a localized region. Measured with the Kendall's coefficient of concordance (KCC).

RESULTS- MEAN BOLD

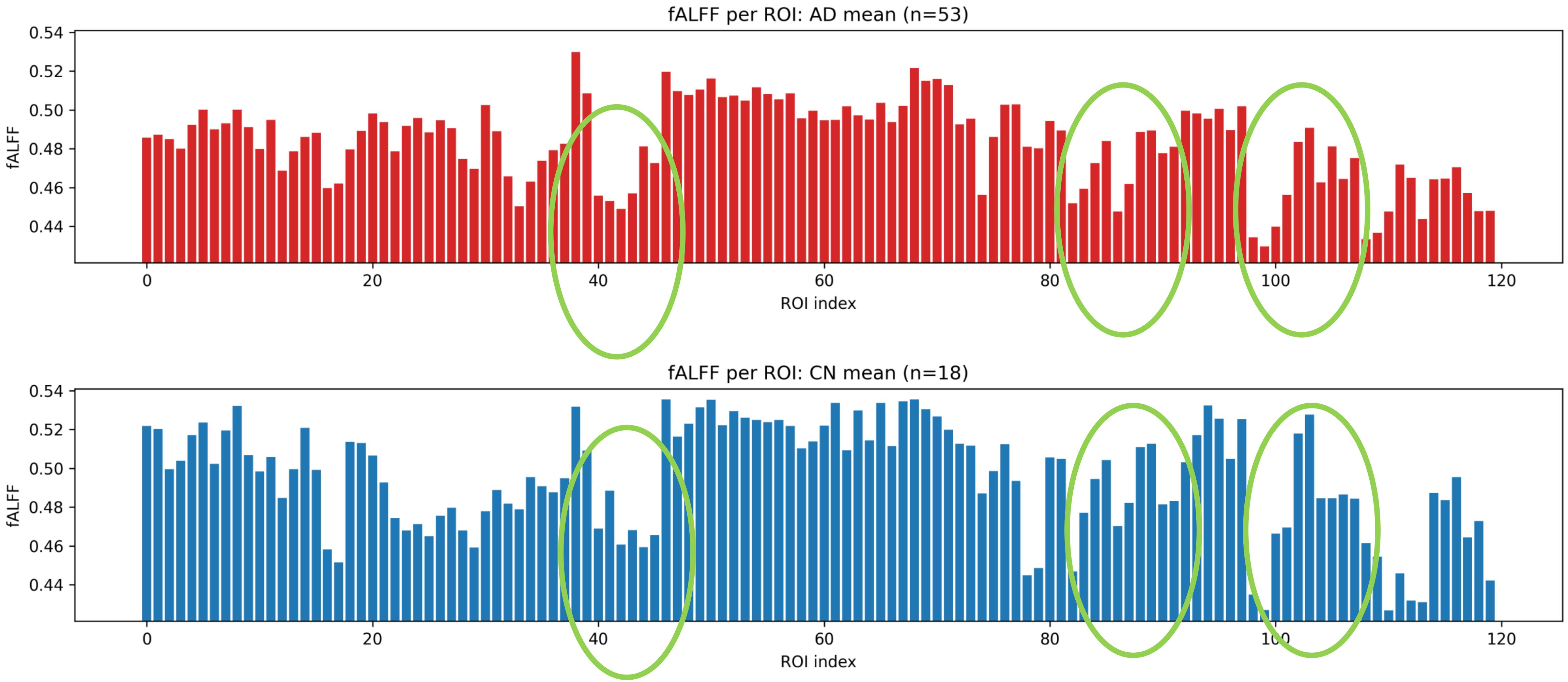




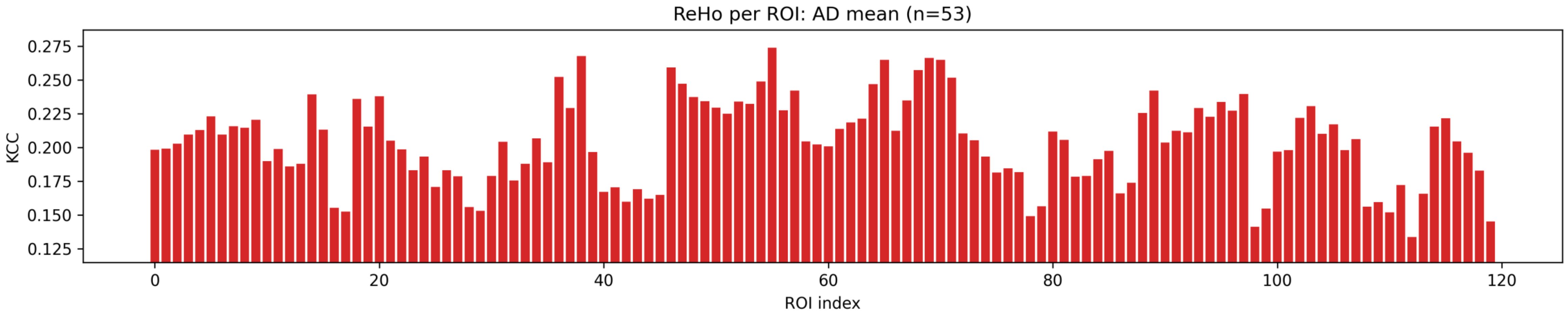
RESULTS- FC MATRIX

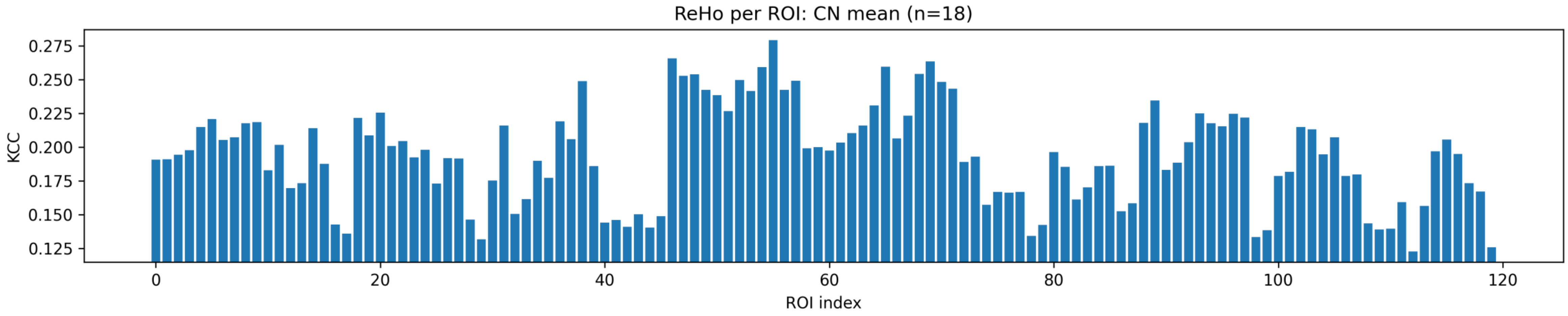


RESULTS- ALFF



RESULTS- REHO





MODELING WITH SUPPORT VECTOR MACHINE

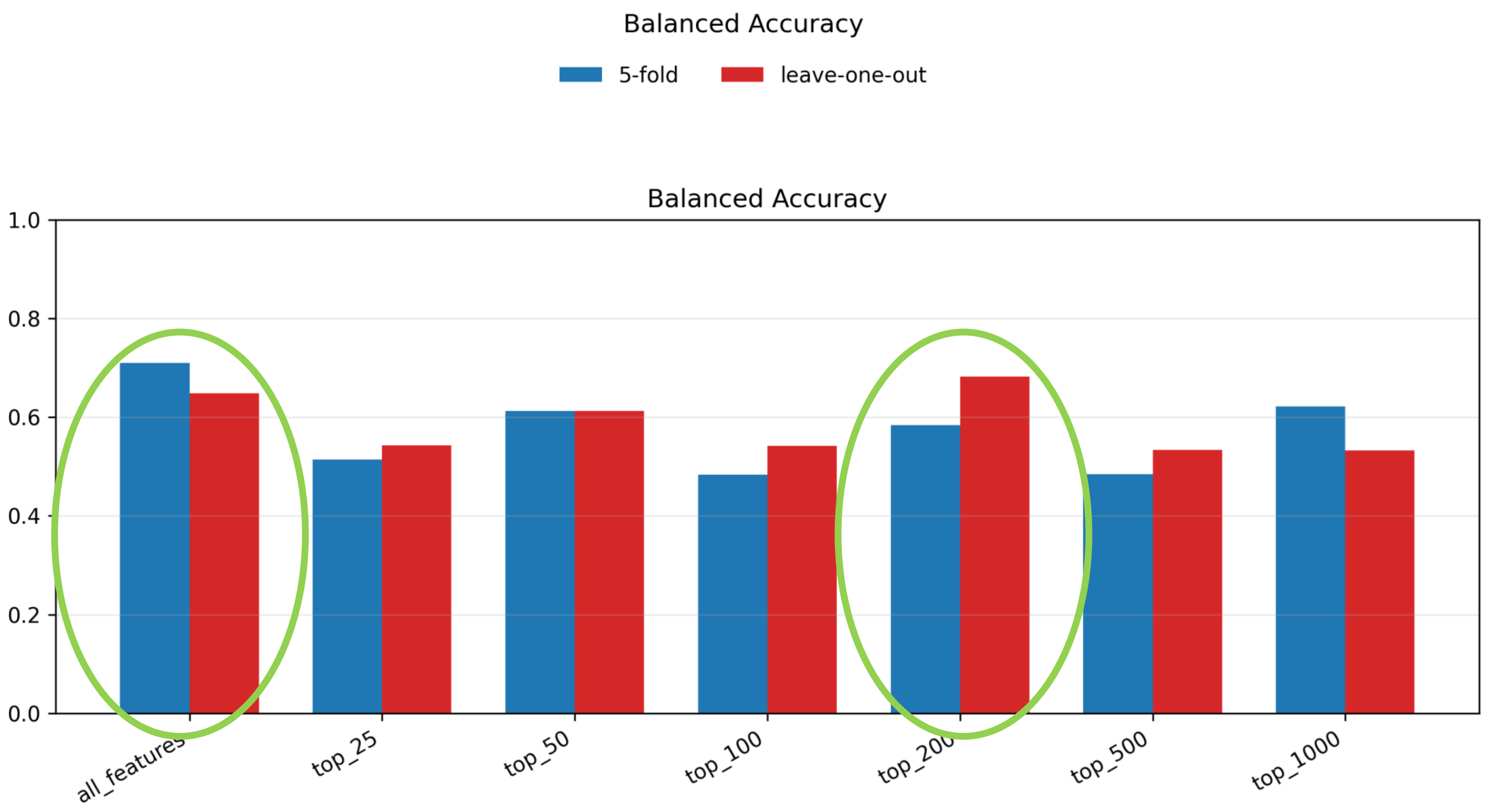
- We use the Support Vector Machine (SVM) architecture for this task due to its known ability to work well on high dimensional feature spaces with a low number of samples.
- SVM finds an optimal decision boundary that separates data points of different classes with the maximum possible margin in high dimensional space. The support vectors lie closest to the decision boundary.
- For each subject we concatenate the 120 mean BOLD, f/ALFF, ReHo, Fisher-z FC upper triangular matrix into a single vector of length 7,620 after removing duplicates (120 * 5) + (120 * 120) / 2
- We also train an SVM on a reduced set of selected features using the SelectKBest selection algorithm on K = 25, 50, 100, 200, 500, 1000 most statistically significant features to drastically reduce the feature space complexity.

$$ANOVA = \frac{between\ group\ variance}{within\ group\ variance}$$

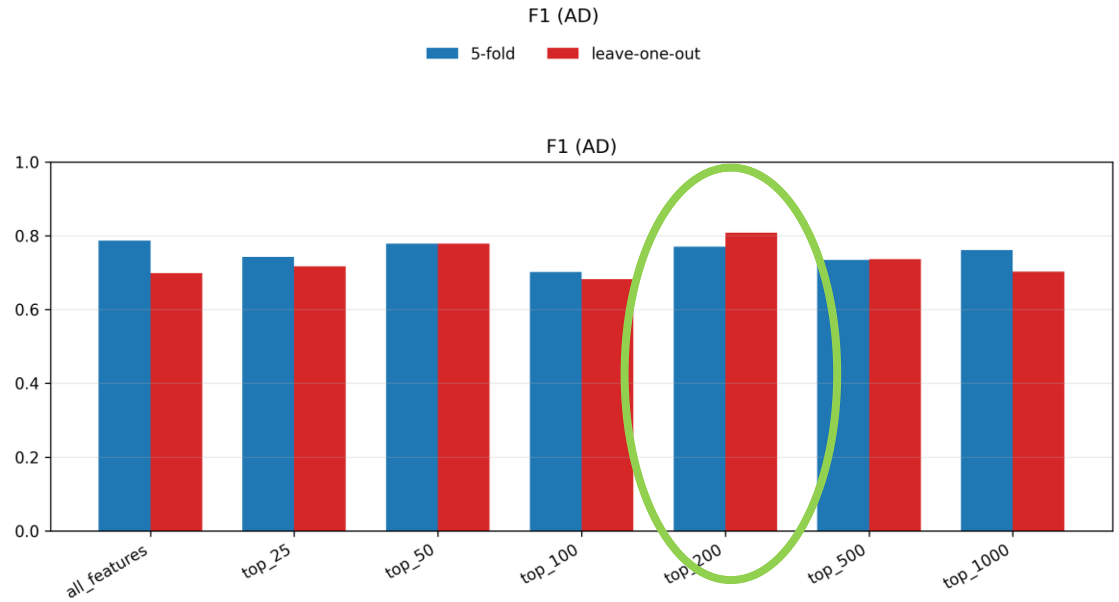
$$L(y, f(x)) = \max(0, 1 - y * f(x)) : y \in \{-1, 1\}$$

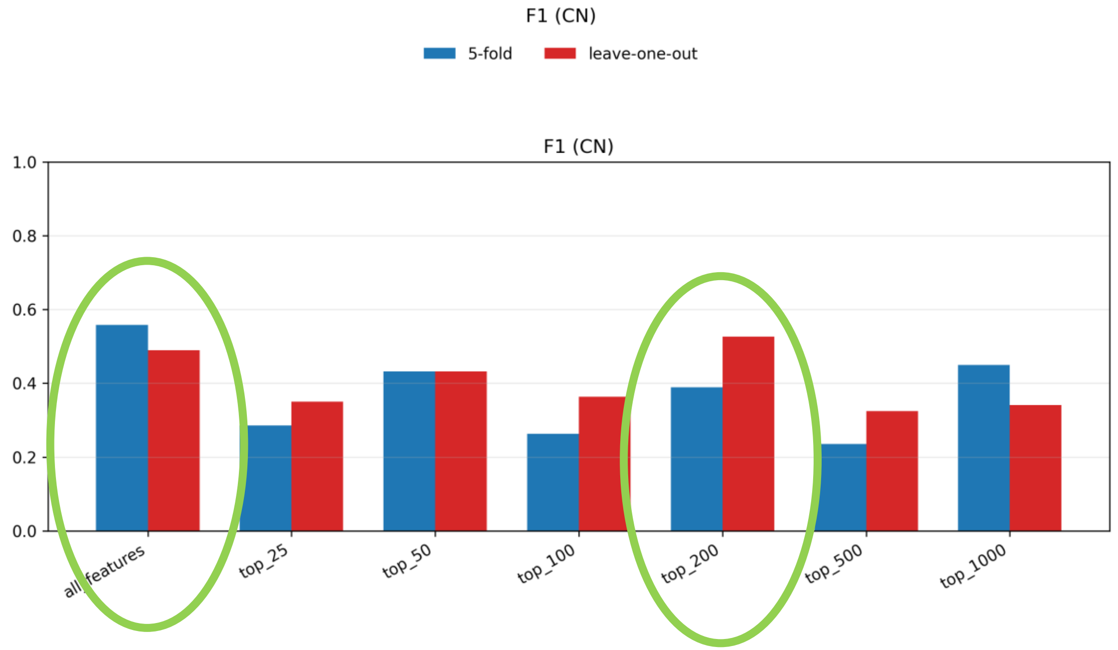
- The Analysis of Variance (ANOVA) F-value is the ratio of the variance between groups to the variance within groups to rank how strongly each feature differs between the 2 classes and uses these features to train the SVM.

RESULTS- BALANCED ACCURACY



RESULTS- F1 SCORE





RESULTS- METRICS

Model	Validation	Acc	Bal Acc	F1 CN	F1 AD
All Features	5-fold	0.71	**0.71**	**0.59**	0.79
All Features	Leave one out	0.62	0.64	0.49	0.70
K=25	5-fold	0.62	0.63	0.29	0.74
K=25	Leave one out	0.61	0.56	0.35	0.72
K=100	5-fold	0.58	0.48	0.26	0.70
K=100	Leave one out	0.58	0.54	0.36	0.68
K=200	5-fold	0.67	0.58	0.39	0.77
K=200	Leave one out	**0.73**	0.68	0.53	**0.81**
K=500	5-fold	0.61	0.48	0.24	0.73
K=500	Leave one out	0.62	0.53	0.32	0.74
K=1000	5-fold	0.67	0.62	0.45	0.76
K=1000	Leave one out	0.73	0.53	0.34	0.70

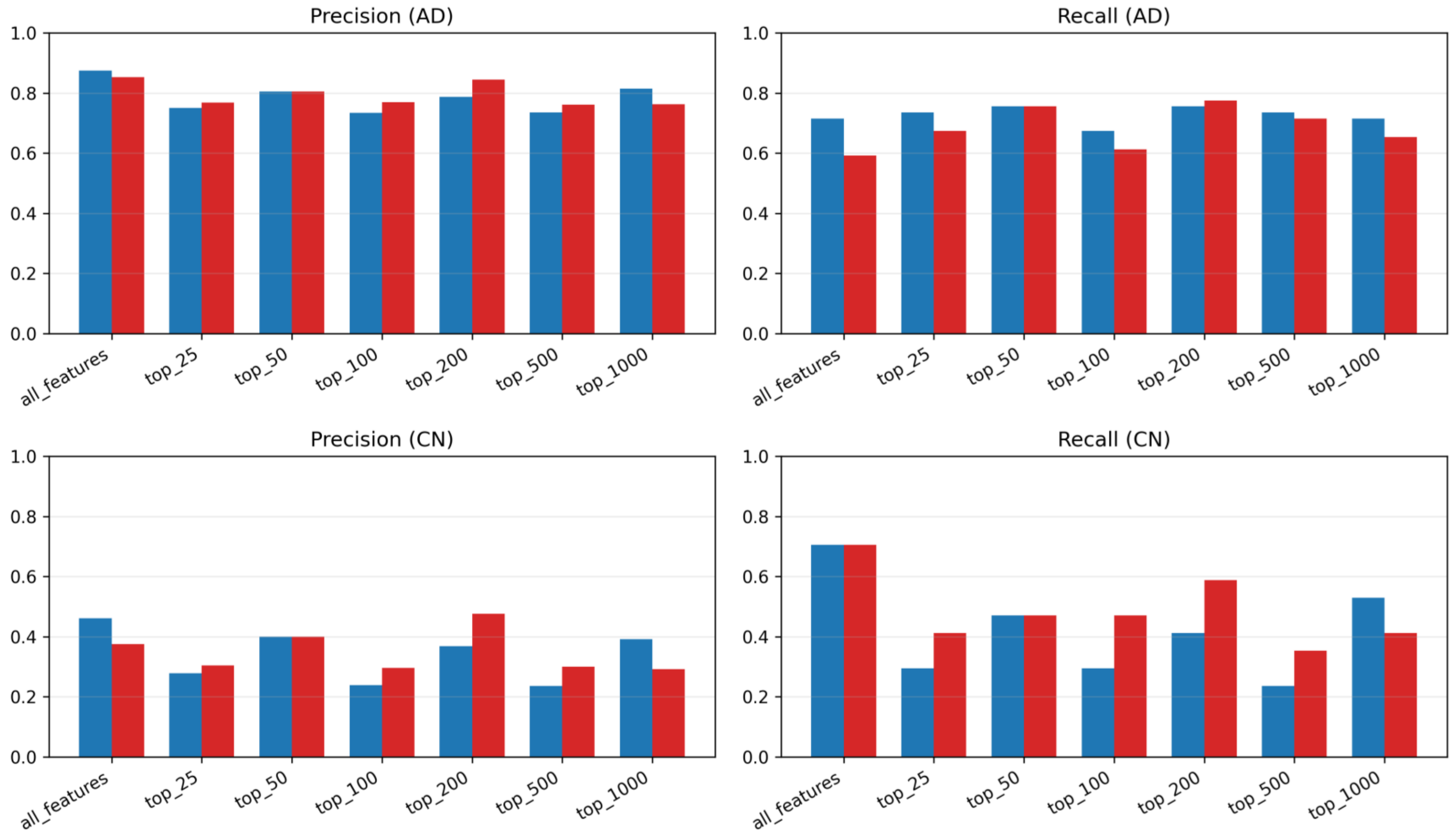
RESULTS- METRICS

Precision: TP / TP + FP

Recall: TP / TP + FN

CN class has better recall than precision, so it is more prone to predict CN when it is not CN (has high FP) than it is to miss a real CN case.

AD class has better precision than recall, so it is more likely to miss a real AD case than to incorrectly predict AD for a CN case.



CONCLUSION AND FUTURE WORK

- In this project, we first implemented common pre-processing techniques in medical image analysis with fMRIPrep and extracted relevant information from the scans for disease prediction:
  - Functional Connectivity (FC) Matrix
  - Mean BOLD signal
  - Amplitude of Low Frequency Fluctuations (ALFF)
  - Regional Homogeneity (ReHo)
- Then, we trained an SVM model with these 4 metrics to classify patients as AD vs CN on both the full feature set and a statistically significant reduced subset of the full feature space.
- Our model achieves up to a balanced accuracy score of 71% using the full feature set on 5-fold cross validation. To mitigate the effects of our 3:1 class imbalance, we also record leave one out metrics and achieve a balanced accuracy of 68% using the K=200 feature set.
- **In the future:** It would be useful to increase the dataset size, as performance suggests that it will continue improving with more data. We would also like to explore the literature to find a baseline expected performance for SVM classification from similar rs-fMRI features. Lastly, changing analysis to the network level rather than ROI level could be more clinically relevant.

REFERENCES

- [1] Witherow, Megan A., et al. "Machine learning-enhanced non-amnestic Alzheimer's disease diagnosis from MRI and clinical features." *arXiv preprint arXiv:2601.15530* (2026).
- [2] Hojjati, Seyed Hani, Ata Ebrahimzadeh, and Abbas Babajani-Feremi. "Identification of the early stage of Alzheimer's disease using structural MRI and resting-state fMRI." *Frontiers in neurology* 10 (2019): 904.
- [3] Barth, Markus, and Benedikt A. Poser. "Advances in high-field BOLD fMRI." *Materials* 4.11 (2011): 1941-1955.
- [4] Esteban, Oscar, et al. "fMRIPrep: a robust preprocessing pipeline for functional MRI." *Nature methods* 16.1 (2019): 111-116.