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Spring 2021
Capstone Project

Interpretable machine learning approach to identifying white matter brain differences between healthy aging and Alzheimer's onset through diffusion tensor imaging

The Problem

Alzheimer's **disease (AD)** is an incurable neurodegenerative disease whose cause is poorly understood (Burns A, 2009). What is known, is that one of the largely associated features of AD is a loss of neuronal connections within the brain (National Institute on Aging, 2021). Diffusion tensor imaging (DTI) has proved to be an effective way to estimate the white matter structure of the brain. DTI uses the anisotropic diffusion of water molecules (water tends to diffuse more freely in the direction of neural tracts rather than across them) to estimate the white matter structure of the brain (fig. 1) (Abdrabou, 2018). Fiber tractography (FT) is a 3D reconstruction technique that maps the DTI determined neural tracts. Data derived from FT scans of patients with diagnosed AD and of those without AD could hold the key to helping us better understand the onset and pathology of AD.

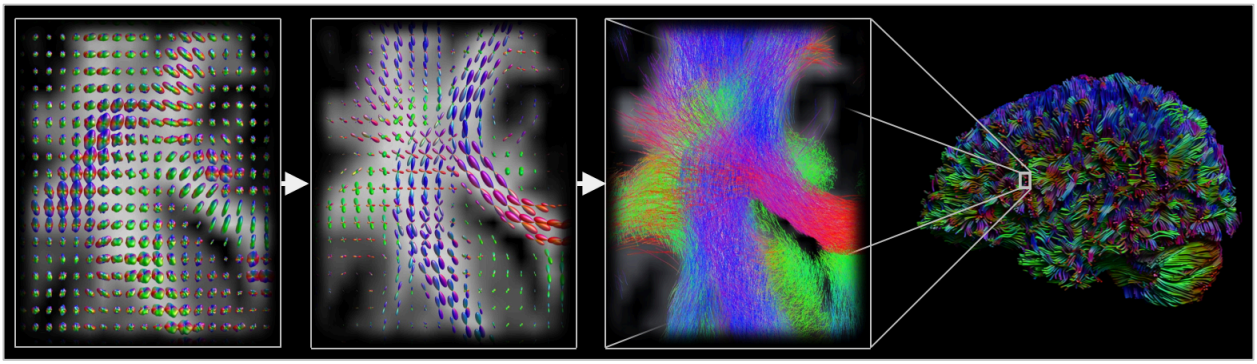

Figure 1 Diffusion Tensor Imaging and Fiber Tractography

The Methodology

My approach was to use a variety of models to classify scans of those diagnosed with AD and those without AD and look at the features the models considered important in making the classification (fig. 2). These features could reveal details about how and where AD effects the connectivity of the brain.

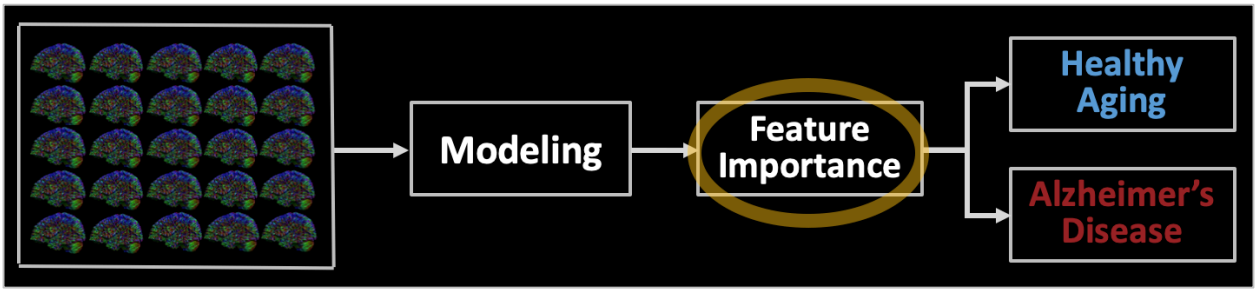

Figure 2 General Approach

The Models

I chose 5 separate models (logistic regression, support vector classification, random forest classifier, multi-layer perceptron (fully connected neural net), and gradient boosted trees classifier), that had acceptable performance in classifying AD and non-AD scans (fig 3 & 4 & table 1), from which to extract feature importance's'.

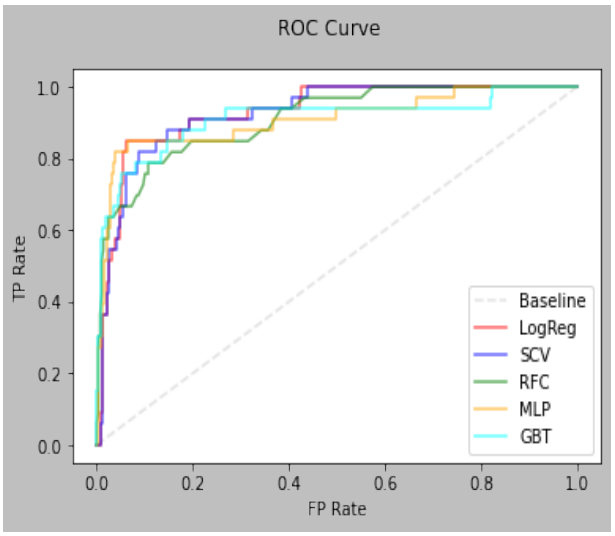

Figure 3 Model ROC Curves

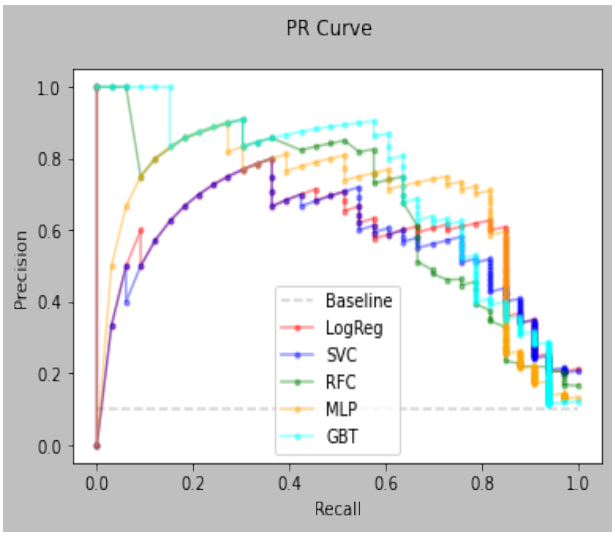

Figure 4 Model Precision Recall Curve

Model	Test ROC AUC	Average Test Precision	Test F1 Score	Model Feature Weight
Logistic Regression	0.9303	0.5911	0.5806	0.182
Support Vector	0.9261	0.5737	0.6000	0.188
Random Forest	0.9102	0.6698	0.6153	0.192
Multi-Layer Perceptron	0.9084	0.6790	0.6984	0.218
Gradient Boosted Trees	0.9102	0.7317	0.7037	0.220

Table 1 Model Test Performance

Feature Importance

A weighted committee voting system was used to weight the feature importance's of the different models. The test F1 Score (the harmonic mean of precision and recall) was used as the metric for weighting the models' features. The F1 score makes the most sense with this highly imbalanced data (1450 healthy scans – 163 AD scans). A classification accuracy based weight system could encourage models that are more conservative and tend to guess non-AD often. I would rather have models that have slightly lower overall accuracy but better performance concerning the AD scans as these are better at modeling Alzheimer's (rather than healthy).

The voting system I used was a basic voting scheme where I took the top 100 most important features from each model (in descending importance) and gave the most important feature a score of 100 * the model feature weight, the second a score of 99 * the model feature weight, and so on. Essentially if each model had the same feature as the most important it would have a score of 100. Below are the top 10 scored features (bundle and measure combinations) out of the 1521 total bundle measure combinations.

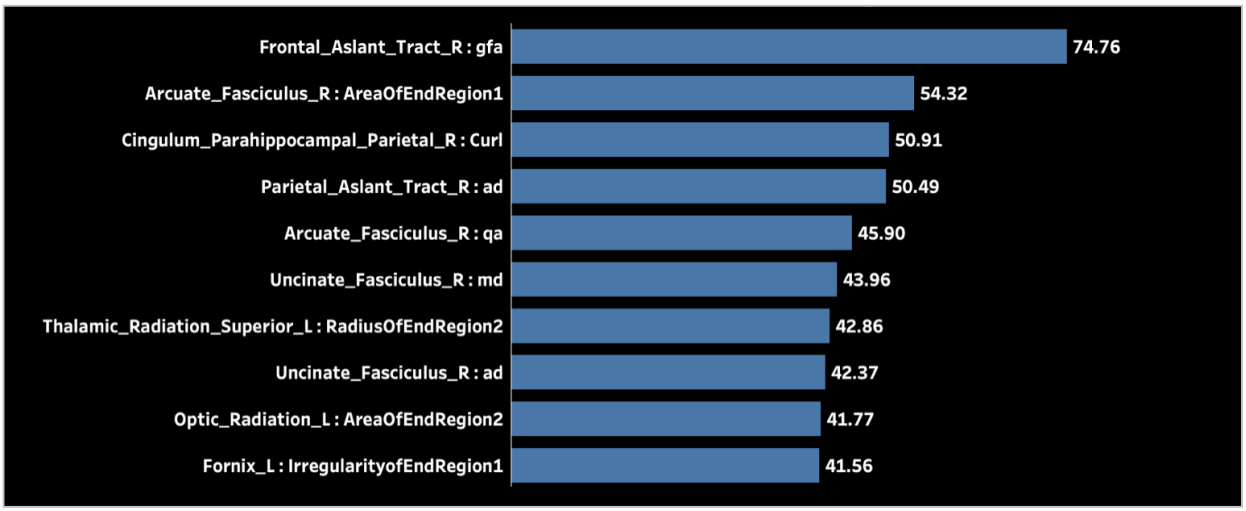

Figure 5 Top Ten Most Important Features (Bundle : Measure) and Their Scores

I also wanted to look at what specific measures are most important to the models and what specific bundles are. This could help shed light on what kind of white matter measures are important in AD and what regions of the brain could be of interest in future AD research.

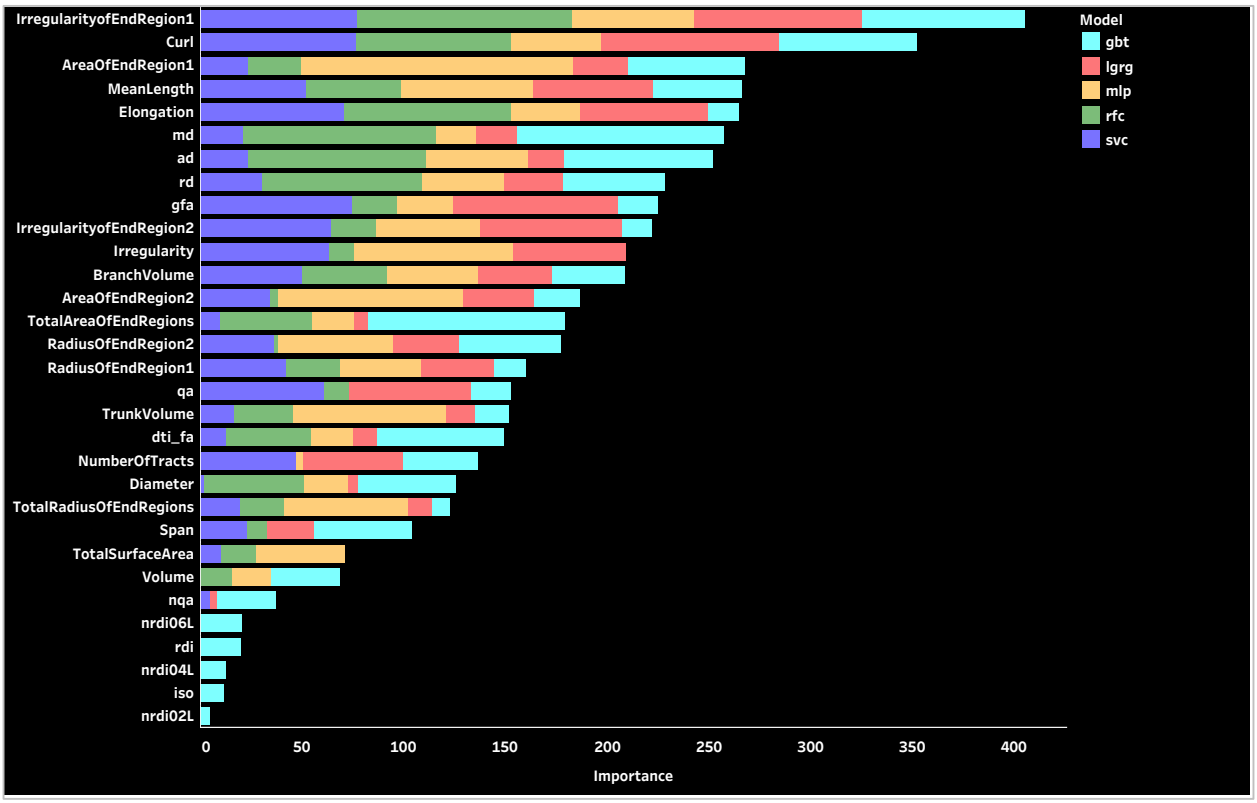

Figure 6 Combined Measure Importance's

The measure importance's indicate that some shape features that tend to be important are concerned with the end region 1 of bundles (its irregularity and area). My models also agree that curl, mean length, and elongation also tend to be important for all bundles (fig 6).

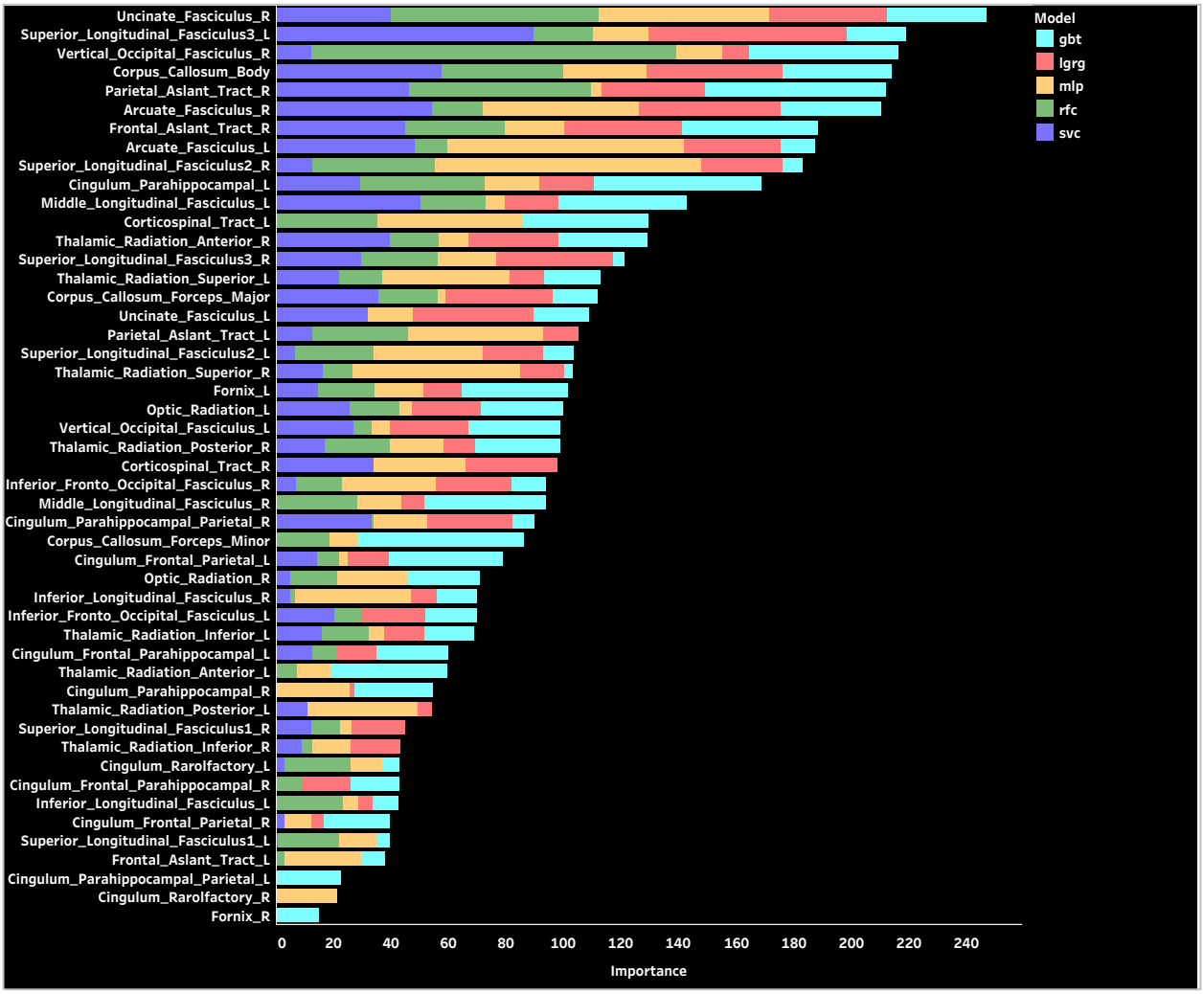

Figure 7 Combined Bundle Importance's

The Uncinate Fasciculus (right) white matter bundle is deemed most important by the committee of models. This is particularly interesting because there is evidence that this region of the brain is important in terms of AD, "consistent abnormalities in the **uncinate fasciculus** are found in **Alzheimer's disease**, semantic dementia, and temporal lobe epilepsy" (Von der Heide, R; Skipper, L; Klobusicky, E; Olson, IR, 2013). This inspires some confidents in my models and my committee method for determining feature importance.

What I've Learned

It has been a fantastic experience working with some very interesting data and developing a novel approach to a real-world problem. Bridging the gap between data science and biology is a passion of mine and it has been a great experience to get to do test it out in an area as interesting as neuro-science. It has also been a pleasure working with some brilliant people on such an interesting project.

Acknowledgements

I would like to recognize and thank Dr. Kurt Schilling, Cailey Kerley, Leon Cai, & Yuzhi (Nino) Yao for their endless support during this project!

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