Multimodal Prediction of Alzheimer's Onset

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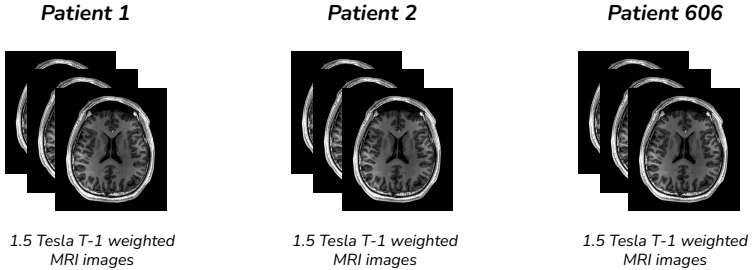
The Problem

- Alzheimer's Disease (AD) is a complex neurodegenerative disease that severely affects patients' (and their families') quality of life and is expected to cost the US **$1T by 2050** [1]
- **40%** of primary care physicians report that they are "never" or "only sometimes" comfortable diagnosing AD [1]
- Early detection can result in significantly improved outcomes [2, 3]
  - There are treatments available to slow the progression of AD, which work best in early to mid stages of disease
  - Clinical trials are available in the early stages
  - Early diagnosis can lower yearly costs by up to 20% [4]

We aim to improve health outcomes for Alzheimer's patients by enabling earlier diagnosis of the disease. Contrary to existing approaches which only use MRI data, we use genetic, cognitive, and MRI data to predict the probability of AD onset within the next 5 years.

Data Preprocessing



We used PCA to reduce 2150 measurements to 150 features (~80% of cumulative explained variance)

Final Data Structure

PTID	str	Patient identifier (012_ST_3848)
Diagnosis_at_Baseline	int	CN (0) or LCMI (1)
Age	int	Age of the patient
Gender	int	Female (0) or Male (1)
Years_of_Education	int	Years of education of the patient
Ethnicity	int	Hisp/Latino (0), Not Hisp/Latino (1), Other (2)
Race	int	Asian (0), Black (1), White (2)
APOE4	int	Number of copies of allele
MMSE	int	Most recent MMSE score
Brain_Measurement_1	float	Mindboggle brain measurement
…	…	…
Brain_Measurement_150	float	Mindboggle brain measurement

Data Exploration and Experimentation

The Task

- Predict the probability of developing AD within 3, 5, or 10 years (“horizon”)
- Existing models predict progression from CN to MCI and MCI to AD, but we opted to *not* do this due to dataset size constraints

Key Dataset Statistics:

- 59% Male, 41% Female
- 98% Not Hisp/Latino
- 93% White, 5% Black, 2% Asian
- 62% LCMI, 38% CN
- Mean Age: 75 years
- APOE4: 56% with 0 alleles, 35% with 1 allele, 9% with 2 alleles
- Train, Val, Test Size: 426, 80, 100

Experiments

- 3, 5, and 10 year time horizons for neural network, support vector machine, random forest classifier and XGBoost (multimodal and image-only)

Techniques Employed

- Oversampling, dropout layers, L1L2 regularization, early stopping, and 5-fold cross validation

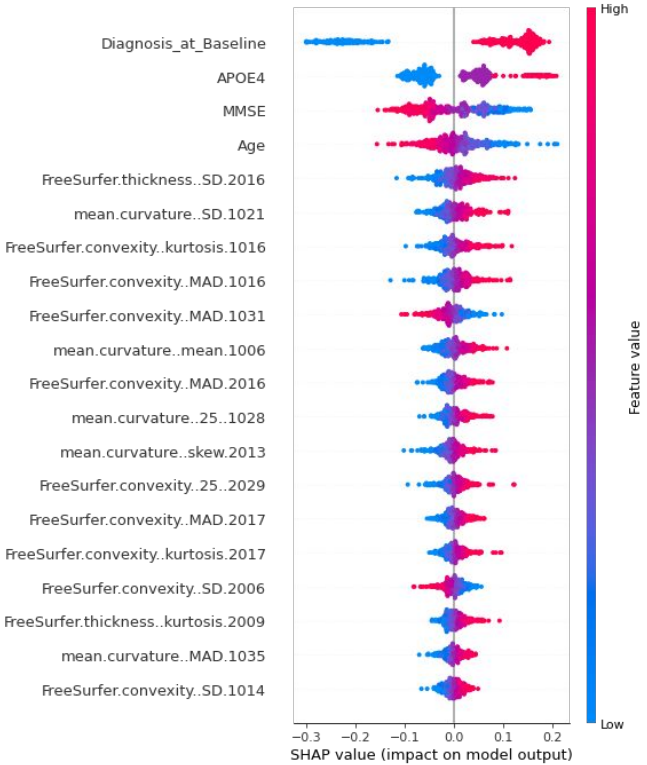
Experimental Results

	Accuracy	Precision	Recall	F1
Baseline	0.66	0	0	0
NN, multimodal	0.78	0.68	**0.68**	**0.68**
NN, image-only	0.55	0.32	0.35	0.34
SVM, multimodal	0.69	0.80	0.12	0.21
SVM, image-only	0.66	0	0	0
RFC, multimodal	**0.80**	**0.82**	0.53	0.64
RFC, image-only	0.65	0.48	0.32	0.39
XGBoost, multimodal	0.79	0.76	0.56	0.64

Our model predicts the probability of a given patient developing AD within the next 5 years

Precision, Recall, and F1 reported for positive class

Explaining Model Performance



- **Diagnosis at baseline** has a substantial impact on predictions (0=CN, 1=LMCI)
    - Removing this feature drops accuracy to 71%
- More copies of the **APOE4** allele push predictions towards 1 (AD diagnosis)
- Lower (worse) **MMSE** score push predictions towards 1
- Unexpectedly, lower **age** pushes predictions towards 1
- Larger depth of **parahippocampal sulci** (1016, 2016) push predictions towards 1 (indicative of impaired working memory)
- Larger depth of left **pericalcarine sulcus** (1021) pushes predictions towards 1 (cortical atrophy)

Deployment

Record
- id - INT NOT NULL
- patient_id - VARCHAR NOT NULL
- ad_probability - INT NOT NULL
- Diagnosis_at_Baseline - CHAR NOT NULL
- Age - FLOAT NOT NULL
- Gender - VARCHAR NOT NULL
- Years_of_Education - INT NOT NULL
- Ethnicity - VARCHAR NOT NULL
- RACE - VARCHAR NOT NULL
- APOE4 - FLOAT NOT NULL
- MMSE - FLOAT NOT NULL
- FreeSurfer_feature_1 - FLOAT NOT NULL
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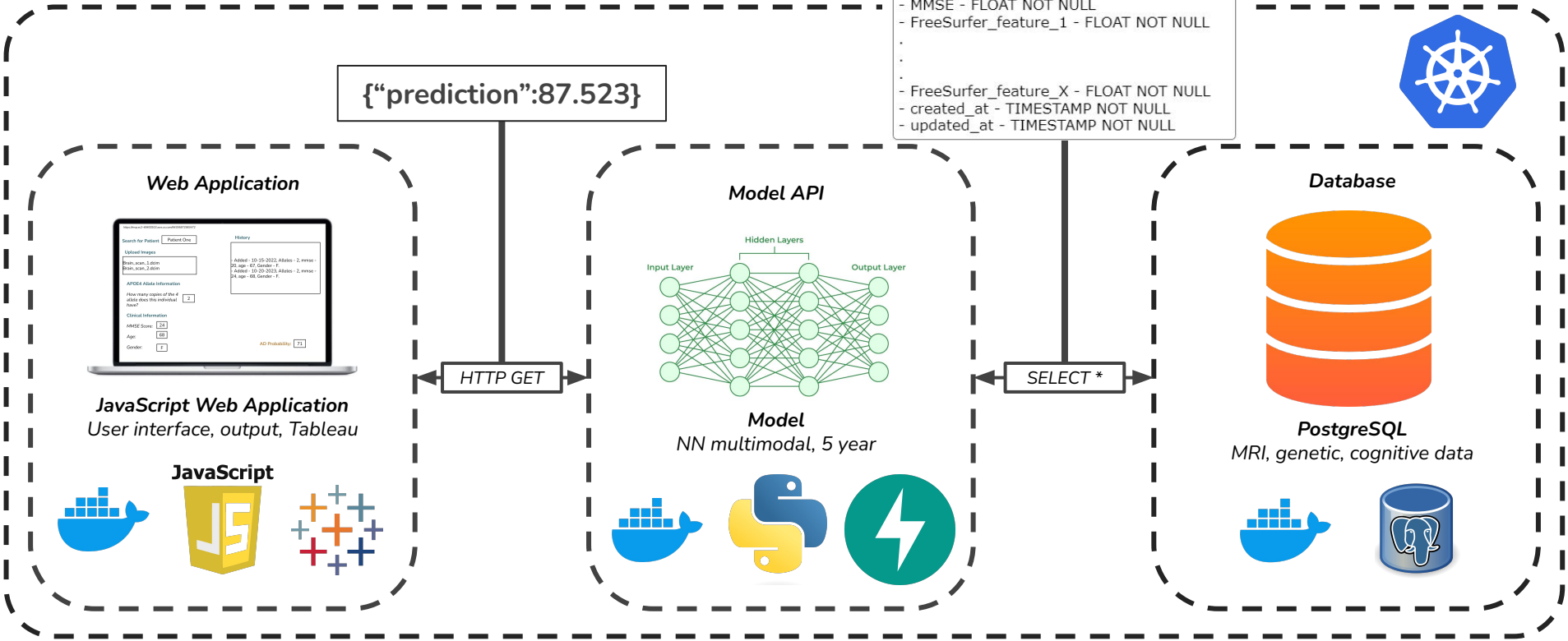
- FreeSurfer_feature_X - FLOAT NOT NULL
- created_at - TIMESTAMP NOT NULL
- updated_at - TIMESTAMP NOT NULL



Challenges and Future Work

Challenges

- Differences in Tensorflow versions for AMD and ARM architectures made deployment more difficult (especially on Apple Silicon)
- Mitigating overfitting was crucial given the relatively small size of our dataset
- Models that were fed MRI data that didn't go through the pre-processing pipeline previously described never learned

Future Work

- Deploy on multiple architectures (i.e., ARM64)
- Source additional data to create a more balanced and diverse dataset
- Consult with additional potential end users regarding usability

Our Mission

Improve health outcomes for Alzheimer's patients and ease the burden of care through the use of machine learning for earlier diagnosis.

Appendix

Acknowledgements

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Previous Studies Using ADNI

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Technical Details: Models Considered

3 year horizon	Accuracy	Precision	Recall	F1
Baseline	0.72	0	0	0
NN, multimodal	**0.77**	**0.59**	0.61	**0.60**
NN, image-only	0.65	0.30	0.25	0.27
SVM, multimodal	0.72	0	0	0
SVM, image-only	0.72	0	0	0
RFC, multimodal	0.75	1.0	0.11	0.19
RFC, image-only	0.72	0.50	**0.70**	0.12

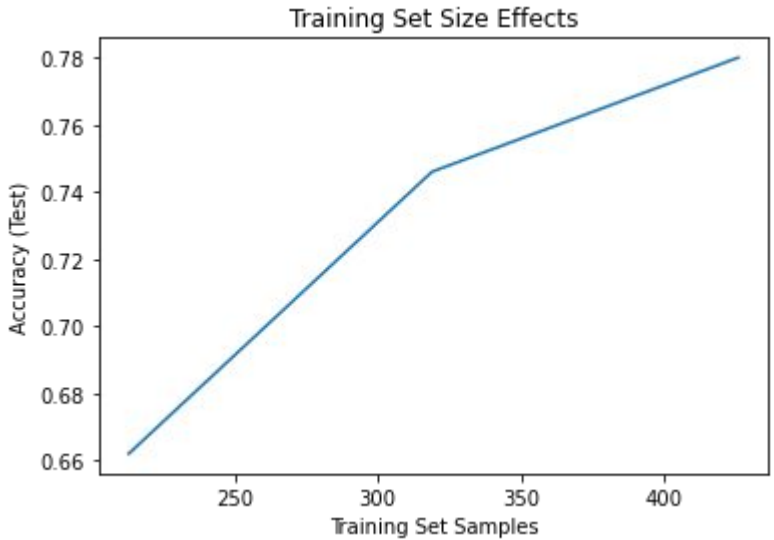
Precision, Recall, and F1 reported for positive class

Technical Details: Models Considered

10 year horizon	Accuracy	Precision	Recall	F1
Baseline	0.63	0	0	0
NN, multimodal	0.66	0.58	**0.59**	0.59
NN, image-only	0.54	0.40	0.49	0.44
SVM, multimodal	0.63	0	0	0
SVM, image-only	0.63	0	0	0
RFC, multimodal	**0.78**	**0.78**	0.57	**0.66**
RFC, image-only	0.64	0.52	0.38	0.44

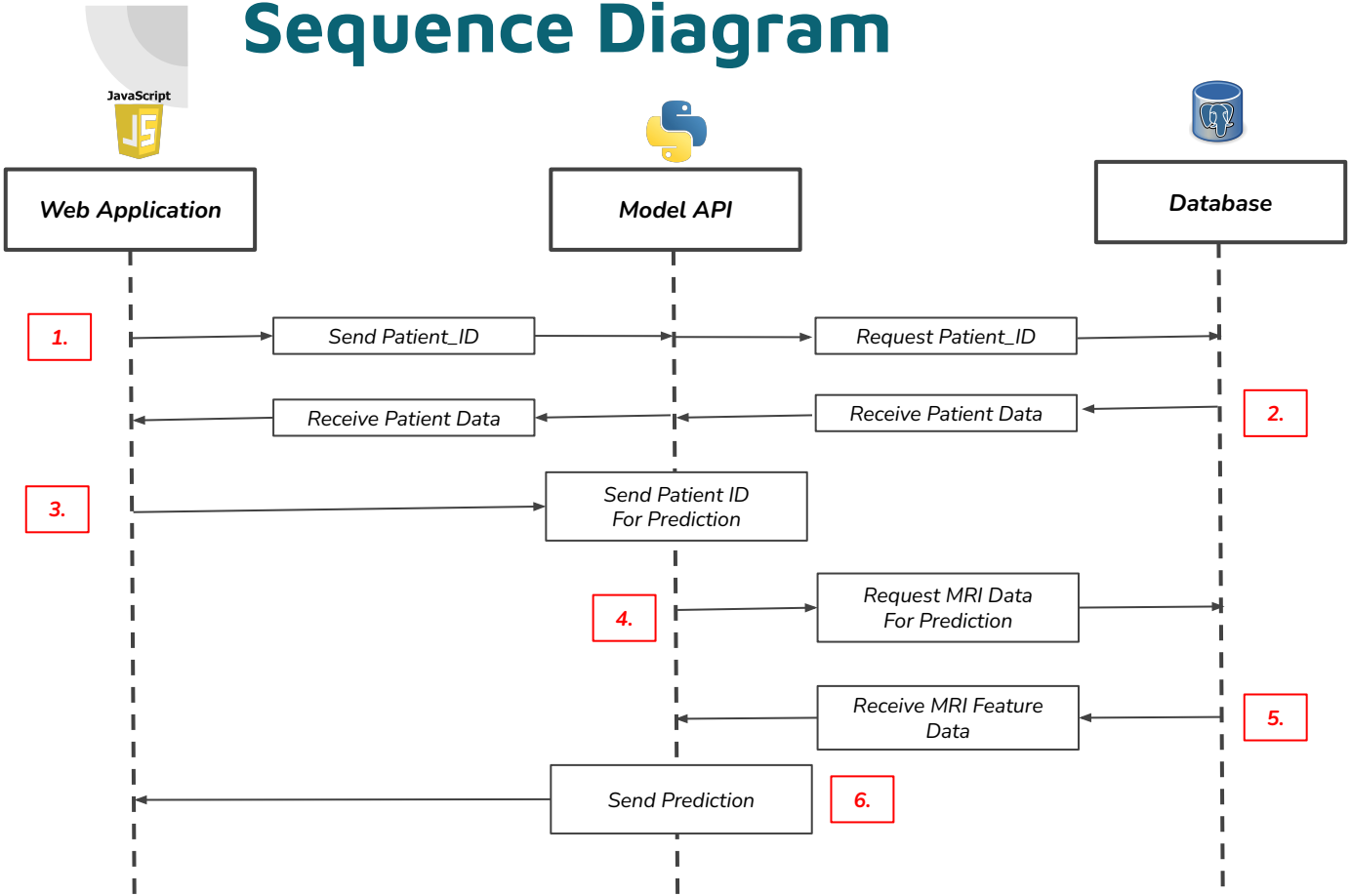
Precision, Recall, and F1 reported for positive class

Training Size Effects



- For the model that we have selected:
  - **Train size**: 426
  - **Val size**: 80
  - **Test size**: 100
  - **Test Accuracy**: 0.78
- To further improve performance, we would search for additional data
  - Architectural modifications might have a positive effect on performance, but given the limited size of the dataset could result in overfitting

Sequence Diagram



List of Endpoints:

- GET /predict
- GET /patient
- POST /patient
- GET /patient/record
- POST /patient/record