**A REPORT ON**

**Projection of Progression of Alzheimer’s Disease using ML**

SUBMITTED TO

**IEEE EMBS PUNE CHAPTER**

**BY**

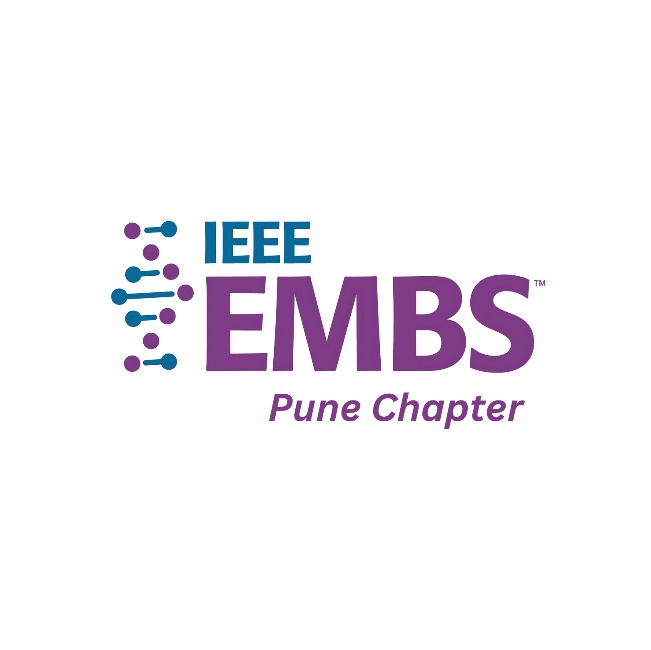
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**DECLARATION**

We, the team members

Name of the Team Members

Member 1: Aabha Jog

Member 2: Atharva Godbole

Member 3: Gargi Rahane

Hereby declare that the project work incorporated in the present project entitled “**Projection of Progression of Alzheimer’s Disease using ML”** is original work. We have properly acknowledged the material collected from secondary sources wherever required. We solely own the responsibility for the originality of the entire content.

Date: 23/06/2025

**Mr. Tushar Mane**

Place: Pune

Date: 23/06/2025

**ABSTRACT**

Alzheimer’s disease (AD) is a long-term brain disorder that mainly affects older people. It causes memory loss, confusion, and difficulty in thinking and decision-making. While there are now ways to detect Alzheimer’s in its early stages, one of the biggest challenges is predicting how fast a person’s condition will get worse over time. This process, known as prognosis, is important because it helps doctors plan better treatments, helps families prepare for future care, and supports researchers in developing new solutions.

In this project, we aim to build an intelligent system that can predict the progression of Alzheimer’s disease using deep learning. We use different types of patient data, including MRI brain scans, clinical test scores like ADAS, and genetic information. To handle this, we apply Convolutional Neural Networks (CNNs) to extract important features from MRI images. All this information is then combined and analyzed over time using advanced model like XGBoost which is adaptable for time series forecasting.

The goal is to understand whether a person’s condition will stay stable, decline slowly, or decline quickly. By combining different types of data and looking at how a person’s MRI and clinical data changes over time, this model provides useful insights for doctors and researchers. It can help with early planning, better care, and more focused clinical studies.

**SYNOPSIS**

1. **Objective**

The primary objective of this project is to accurately **predict the progression of Alzheimer’s Disease (AD)** by leveraging **longitudinal clinical and MRI data**. The system is designed using a feature based modelling approach where temporal dependencies are captured through engineered features derived from time series.

1. **Datasets Used**

The project surveyed well-established longitudinal datasets focused on Alzheimer's Disease research, including:

* **ADNI1** (Alzheimer’s Disease Neuroimaging Initiative Phase 1)
* **ADNIGO** (ADNI Grand Opportunity Extension)
* **ADNI2** (ADNI Phase 2)
* **AIBL** (Australian Imaging, Biomarkers & Lifestyle Study of Aging)

These datasets provide MRI scans, clinical test scores, and demographic/genetic information across multiple patient visits over time.

1. **Project Phases**

**Phase 1: Proof of Concept**

* **Dataset Exploration & Selection**
  + Evaluate multiple longitudinal datasets for structure and completeness.
  + Select suitable datasets based on temporal richness and modality availability.
* **Data Cleaning & Preprocessing:**

**1. Cohort Selection and Feature Identification**

A specific cohort was curated from the ADNI repository. Relevant MRI and clinical features were identified based on their importance for disease progression analysis.

**2. Table Mapping and Data Integration**

Two datasets—MRI measurements and clinical metadata—were merged using `Subject\_ID` and `Visit` to align imaging and clinical data for each timepoint per subject

**3. Missing Data Handling**

\* Incomplete records were removed.

\* Missing feature values were imputed using mean or median strategies within diagnostic groups.

\* Highly sparse records were excluded.

**4. Deduplication and Consistency Checks**

Duplicate rows were removed based on `Subject\_ID`, `Visit`, and acquisition date. Chronological consistency and biologically valid feature ranges were verified.

* **Feature Extraction & Fusion**
  + **Clinical Data**: ADAS-Cog scores, age, etc.
  + **MRI Data**: Preprocessed through **Convolutional Neural Networks (CNNs)** to extract spatial features.
  + At each timepoint, clinical and MRI features are fused into a single **unified feature vector**.
* **Temporal Modeling**
  + Temporal data is modelled by flattening MRI and clinical features across multiple visits into structured, fixed-length vectors (e.g., Visit1\_Totscore, Visit2\_Totscore, etc.).
  + This allows the use of XGBoost, which, while not inherently temporal, effectively captures cross-visit patterns through feature-based learning.
* **3D CNN Label:**
  + **Diagnosis Class**: AD / MCI / CN
* **Predictions Output**
  + **ADAS Progression**: Stable / Slow Decline / Fast Decline

1. **Expected Outcome**

The outcome of this project is a **robust and interpretable machine learning model** that can:

* Predict Alzheimer’s cognitive decline with high accuracy
* Learn from a patient’s clinical and imaging history over time
* Provide **early warnings** for high-risk cases
* Aid in **treatment planning**, **patient monitoring**, and **clinical decision-making**

This model supports a more **personalized and proactive approach** to Alzheimer’s care and has the potential to become a valuable tool in both research and clinical settings.

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# INTRODUCTION

Alzheimer’s Disease (AD) is a brain disorder that slowly damages memory, thinking, and behavior. It mainly affects older people and is the most common cause of dementia. As the disease gets worse over time, people find it harder to do everyday tasks and live independently. Although doctors can now detect Alzheimer’s early through brain scans and clinical tests, one important challenge remains—knowing how fast the disease will progress in each person. This is known as **prognosis**, and it is very important for planning care, supporting families, and improving treatment decisions.

In recent years, the rise of digital tools and artificial intelligence (AI) in healthcare has opened new ways to study diseases like Alzheimer’s. Large datasets are now available that contain detailed information about patients collected over time. For this project, we use **longitudinal datasets** such as **ADNI (Alzheimer’s Disease Neuroimaging Initiative)** and **AIBL (Australian Imaging, Biomarkers and Lifestyle)**. These datasets include brain MRI scans, clinical test scores like MMSE and ADAS, and genetic information such as APOE status. Because they track the same patients across multiple visits, these datasets are ideal for studying how the disease progresses over time.

This project aims to build a machine learning system that can predict how a patient’s condition will change in the future. We use different models for different types of data. **Convolutional Neural Networks (CNNs)** are used to analyse MRI scans. These features are combined, formatted, concatenated with clinical data, flattened and passed to a tree-based ensemble model called **XGBoost**. The system will predict whether the patient will stay stable, decline slowly, or decline quickly.

By combining different types of data and using AI to study patient history, this model can help doctors plan better treatments and improve early intervention. It also supports ongoing research by offering a tool to understand how Alzheimer’s disease changes in different people over time.

*\_*

# CONCEPTS AND METHODS

* Development of a Machine Learning Model for Alzheimer’s Disease Prognosis requires identifying viable datasets along with the parameters.
* In the initial stages, the standardized ADNI datasets (ADNI 1, ANDI 2, ADNI GO) shall be considered as a superset of the data used for prediction.
* The input training data for prognosis model included multiple kinds of data; 3D MRI Images and numerical clinical scores.
* Each data form must be treated differently to extract the required information, but at the same time prognosis outcome requires a correlation between the individual data form outputs.
* To decode and correlate the information, a multilevel ML design is proposed.
* The multimodal fusion models were considered, with feature concatenation (early fusion)
* **Feature-Level Fusion**

In multimodal machine learning, feature-level fusion (also known as early fusion) involves combining raw or intermediate features from different data modalities before classification or prediction.

* **Fusion Mechanism:**

Feature vectors extracted from the 3D CNN (processing MRI images) are concatenated with structured clinical features (e.g., cognitive scores, demographics) to form a single, unified input vector.

* **Learning from Joint Representation:**

The fused vector captures both spatial imaging patterns and clinical context, enabling downstream models (e.g., XGBoost or fully connected layers) to learn from the combined feature space.

The lower level of the proposed system utilizes a 3D Convolutional Neural Network (3D CNN) for processing MRI data. This model is specialized to extract modality-specific features that are later fused in the upper-level model for integrated prognosis.

**3D CNN (Image Feature Extractors for MRI)**

* CNNs (Convolutional Neural Networks) are deep learning models specialized for extracting hierarchical patterns in image data; they can identify features like edges, textures, shapes, and more complex structures from 2D image slices.
* For volumetric data like MRI scans, 3D CNNs are more appropriate as they apply 3D convolutional filters across the brain volume (width × height × depth), capturing spatial features across all three dimensions.
* The output of a 3D CNN is a feature embedding or classification score that represents learned spatial information from the MRI; this output feeds into the fusion model along with other modalities.
* **3D CNN Preprocessing and Data Preparation**

**Image Loading**: MRI scans were loaded in .nii format using NiBabel to access 3D voxel data.

**Cropping**: Volumes were spatially cropped to focus on the brain region and reduce computational load.

**Normalization**: Voxel intensities were scaled to [0, 1] using MinMaxScaler for consistency across samples.

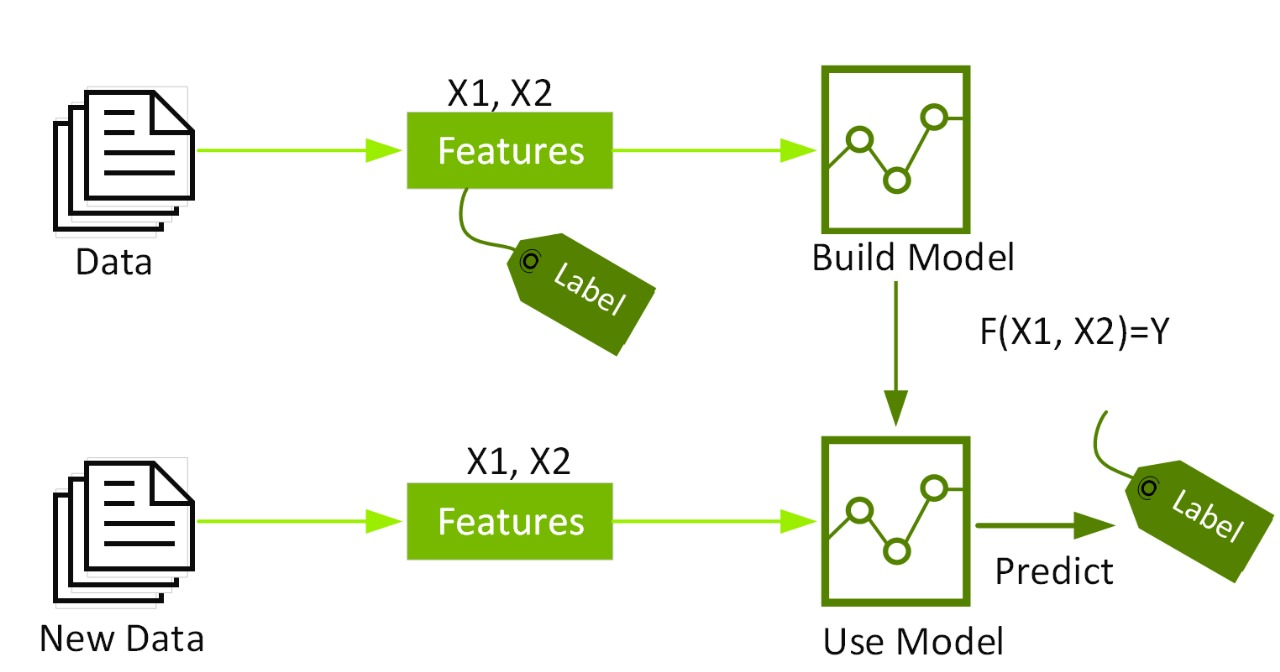
**Label Assignment**: Diagnostic labels (AD, MCI, NC) were assigned using metadata mapped by Subject\_ID and Visit.

* As the primary image-processing component of the pipeline, the 3D CNN ensures that high-resolution spatial neuroimaging data contributes directly to prognosis, capturing subtle volumetric changes in the brain across time.
* The upper-level model shall use XGBoost which takes the output of lower-level model as input and gives a prognosis. (The exact format of the output prognosis shall be decided after further research.)
* **XGBoost**

XGBoost, which stands for Extreme Gradient Boosting, is a scalable, distributed gradient-boosted decision tree (GBDT) machine learning library. It provides parallel tree boosting and is the leading machine learning library for regression, classification, and ranking problems.

It’s vital to an understanding of XGBoost to first grasp the machine learning concepts and algorithms that XGBoost builds upon: supervised machine learning, decision trees, ensemble learning, and gradient boosting.

Supervised machine learning uses algorithms to train a model to find patterns in a dataset with labels and features and then uses the trained model to predict the labels on a new dataset’s features.



Decision trees create a model that predicts the label by evaluating a tree of if-then-else true/false feature questions, and estimating the minimum number of questions needed to assess the probability of making a correct decision. Decision trees can be used for classification to predict a category, or regression to predict a continuous numeric value. In the simple example below, a decision tree is used to estimate a house price (the label) based on the size and number of bedrooms (the features).

**Figure STYLEREF 1 \s 2. SEQ Figure \\* ARABIC \s 1 1: This is my First Figure**

# LITERATURE SURVEY

## Existing research in Alzheimer's Trajectory modelling is done by this[1] paper, using the concept of Longitudinal Siamese Neural Networks using MRI (imaging), clincal and genomic data.

## The research gap we have identified here is that the time series modelling can be improved with the help of tree based architectures

## We also considered TACDformer[2], a modified Informer based model, demonstrates the power of transformer architectures for forecasting long-sequence, multivariate time-series. The research shows that transformer architectures can handle complicated, multi-faceted feature inputs in way that conventional methods have trouble with and can potentially outperform in predictive accuracy.

## As we see that the MRI image is not a single 2D image as is the standard input for CNN, a more complex model, ie a 3D CNN may be used for the purpose of feature extraction. Existing research on the 3D MRIs in the ADNI dataset is given by this[3] paper where a pretrained encoder is used, which is ideal for our purpose.

## An alternative to Informer architecture for time series prediction[4] has also been considered, which is an LSTM - attention - LSTM based approach. The model uses two LSTM models as the encoder and decoder, and introduces an attention mechanism between the encoder and decoder. The model has two distinctive features: first, by using the attention mechanism to calculate the interrelationship between sequence data, it overcomes the disadvantage of the coder-and-decoder model in that the decoder cannot obtain sufficiently long input sequences; second, it is suitable for sequence forecasting with long time steps.

## Here we observed that our input is of varying longitudinal length (Data of only one , only two up to six timepoints) depending on the stage at which the patient is at, So for this modern complex attention based architectures are computationally expensive and inefficient. Thus we considered decision tree based classifiers for optimized output.

## The first model considered was a Growth Mixture Model (GMM) given by this [5] paper for trajectory modelling. However the implementation for the same is not well researched in python thus a more prominent and well developed machine learning library in python called XGBoost [6]

## Given the multimodal nature of our input, further experimentation is needed to check the feasibility and accuracy of any time series model on our data, thus multiple approaches have been studied.

## Reference:

## [1] Bhagwat N, Viviano JD, Voineskos AN, Chakravarty MM; Alzheimer’s Disease Neuroimaging Initiative. Modeling and prediction of clinical symptom trajectories in Alzheimer's disease using longitudinal data. PLoS Comput Biol. 2018 Sep 14;14(9):e1006376. doi: 10.1371/journal.pcbi.1006376. PMID: 30216352; PMCID: PMC6157905.

## [2] Hu, Zeyv and Jia, Zhenhong and Le, Wu and He, Congbing and Fan, Huihui and Meng, Jie, Tacdformer: An Improved Informer-Based Model for Accurate Multivariate Long-Term Time Series Forecasting. Available at SSRN: <https://ssrn.com/abstract=5303297>

## [3] E. Hosseini-Asl, R. Keynton, and A. El-Baz, "Alzheimer’s disease diagnostics by adaptation of 3D convolutional network," in *Proc. 2016 IEEE Int. Conf. Image Process. (ICIP)*, Phoenix, AZ, USA, Sep. 2016, pp. 126–130, doi:

## [4] X. Wen and W. Li, "Time Series Prediction Based on LSTM-Attention-LSTM Model," in IEEE Access, vol. 11, pp. 48322-48331, 2023,

## keywords: {Time series analysis;Predictive models;Forecasting;Data models;Logic gates;Decoding;Autoregressive processes;Time series forecasting;long short-term memory networks;encoder and decoder model;attention mechanisms},

## [5] Nguena Nguefack HL, Pagé MG, Katz J, Choinière M, Vanasse A, Dorais M, Samb OM, Lacasse A. Trajectory Modelling Techniques Useful to Epidemiological Research: A Comparative Narrative Review of Approaches. Clin Epidemiol. 2020 Oct 30;12:1205-1222. doi: 10.2147/CLEP.S265287. PMID: 33154677; PMCID: PMC7608582.

## [6] @inproceedings{Chen\_2016, series={KDD ’16}, title={XGBoost: A Scalable Tree Boosting System},url={http://dx.doi.org/10.1145/2939672.2939785},DOI={10.1145/2939672.2939785}, booktitle={Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining}, publisher={ACM}, author={Chen, Tianqi and Guestrin, Carlos}, year={2016}, month=aug, pages={785–794}, collection={KDD ’16} }

# PROJECT PLAN

The Alzheimer’s Prognosis Prediction System we propose leverages a multimodal structure so as to be able to combine 3D MRI scans, clinical assessments and potentially genomic data for comprehensive understanding of the patient's condition.

In the implementation of this system we identify the following phases:

1. **Identify Ideal Subject**
2. **Identify CNN to Be Used**
3. **Identify Model to Be Used**
4. **Build End-to-End Pipeline**
5. **Phase Goals**
6. **Identify Ideal Subjects**Select patients with aligned MRI, past ADAS history, and future ADAS scores.
7. **Identify CNN to Be Used**Choose or design a 3D CNN to extract spatial brain features from MRI.
8. **Identify Model to be used**

Experiment with various gradient boosting python implementations of classification machine learning models which take time series inputs in the form of 2D array of features and labels for prediction of categorical labels.

1. **End to end pipeline**Integrate all components into a trainable model that predicts rate of decline.

Now let us consider the tasks which need to be done with respect to these phase

**Phase 1:**

1. In the **ADNI** dataset, identify the patients satisfying following criteria

* Having MRI data at at least 3 timepoints
* Having corresponding ADAS scores at the same timepoint as the MRI
* Having ADAS scores at at least 3 timepoints after the last MRI timepoints.

1. Create folder containing .nii 3D MRI files of the identified patients
2. Create proper csv as required of the ADAS scores
3. Collect and store metadata of the selected patients (age, sex, medical history)

**Phase 2:**

1. Prepare 2-3 options of pretrained 3D CNNs for feature extraction of MRIs
2. Determine size of output feature vector
3. Create code pipeline for the same

**Phase 3:**

1. Combine the clinical score of each timepoint with feature extracted from 3D CNN
2. Adjust data composition as per specific model requirement
3. From the given ADAS scores from each patient calculate analysis classes for prognosis

**Phase 4:**

1. Test multiple models for label classification
2. Create code pipeline for the same

**Timeline**

Structured timeline cannot be pre decided due to academic commitments and lack of experience and multiple concurrent commitments however all proposed phases will be completed on schedule.

Note on resource allocation: -

Primary resources are intern developers and available time; hence they will be managed to the best of the interns’ ability.

# PROPOSED SOLUTION

**Final Work:**

The proposed system combines multimodal data to predict Alzheimer’s Disease progression. MRI scans are processed through a Convolutional Neural Network (CNN) to extract key structural features. These features are fused with clinical time-series data, that is ADAS scores, at each timepoint to create a unified feature vector. The resulting sequence of vectors is then fed into a XGBoost model, which captures temporal patterns and long-term dependencies. This integrated architecture supports robust, personalized prognosis in Alzheimer’s Disease.

**Key Features:**

The proposed solution has the following key features:

* **Multimodal Data Integration**: merges clinical scores and MRI data to capture complementary aspects of disease progression.
* **Longitudinal Time-Series Modeling**: incorporates data from multiple visits to predict trends rather than one-time classifications.
* **CNN-based MRI Feature Extraction**: leverages deep CNNs to automatically learn disease-relevant brain structural features in the form of second to last layer of 64 features.
* **Architecture for Temporal Forecasting**: uses the adapted XGBoost model to handle long patient histories and irregularly spaced follow-ups along with variable length inputs more efficiently.
* **Feature Fusion Strategy**: builds a unified feature vector at each timepoint by combining MRI and clinical features via mapping the extracted feature vector to the clinical data, improving prediction performance.
* **Scalability**: the framework is designed so that additional data sources (e.g., PET scans, blood biomarkers, or lifestyle data) can be added by concatenating outputs of particular models considered as per data form.
* **Personalized Prognosis**: supports a precision-medicine approach by providing forecasts tailored to each individual’s disease pattern.

**Target Audience:**

This system is intended for:

* **Clinicians and Neurologists**, who need to predict the likely progression of Alzheimer’s in their patients to plan interventions.
* **Researchers** and **Data Scientists** , who require reliable progression models for participant selection in clinical trials.

**Uniqueness compared to Existing Solutions:**

* While many current machine learning systems focus only on classifying AD from healthy controls or MCI, few address the **temporal progression** of the disease. Even fewer integrate multimodal data over multiple visits.
* **Multimodal Data Integration**: merges clinical scores and MRI data to capture complementary aspects of disease progression.
* **Adaptive Prediction Mechanism**: XGBoost model performs well on prediction based on single point input as well as multi-point time series input without retraining.
* **End-to-End Design**: a pipeline capable of going from raw MRI scans to interpretable cognitive decline predictions.
* **Personalized Predictions**: tailored forecasts rather than population-average estimates, helping move toward precision medicine.
* **Extensible Architecture**: designed to incorporate future data modalities with minimal effort.

In this way, the proposed system goes beyond simple classification and provides a meaningful, patient-cantered prognosis framework for Alzheimer’s Disease, aligning with the future direction of digital healthcare and personalized medicine.

# Results

**Dataset Summary**

**Dataset Used:**

The dataset used for this project is derived from the **Alzheimer’s Disease Neuroimaging Initiative 1 (ADNI1)** cohort. The ADNI dataset includes multimodal measurements collected from participants across various stages of cognitive decline, including cognitively normal individuals, those with mild cognitive impairment, and those diagnosed with Alzheimer’s disease.

Research groups considered:

 CN: Cognitively Normal

 MCI: Mild Cognitive Impairment

 AD: Alzheimer’s Disease

For this work, we focus on cross-sectional (single timepoint) data, including:

* Clinical and Cognitive scores (such as the Alzheimer’s Disease Assessment Scale, ADAS)

**Dataset Splits:**

The number of 3D MRI NIfTI files (.nii) used in each phase of the 3D CNN training was as follows:

* **Training set**: *24* files
* **Validation set**: *6* files
* **Testing set**: *10* files

**Data Preprocessing Steps:**

**Note:** We downloaded .nii images from the ADNI 1 Standardized 3Yr 3T List which is publicly available on the ADNI website under image collections and it contains 60 subjects.

1. **Data Loading and Organization**
   * The pipeline loads NIfTI-format MRI scans using the nibabel library.
   * It traverses the MRI directory structure to collect file paths and matches subject identifiers with corresponding clinical metadata (containing diagnosis groups: Alzheimer’s Disease (AD), Mild Cognitive Impairment (MCI), and Cognitively Normal (CN)).
   * It removes duplicate subjects to ensure only one scan per subject is included.
2. **Resizing / Resampling**
   * Each MRI volume is resized to a fixed target shape of (155, 155, 95) using skimage.transform.resize.
   * This resampling step guarantees consistent input dimensions across all samples, which is a prerequisite for 3D convolutional neural networks.
3. **Intensity Normalization**
   * After resizing, each volume undergoes intensity normalization to achieve zero mean and unit variance.
   * This process ensures stable and faster convergence during training.
4. **Channel Formatting**
   * Since Keras 3D convolution layers require a channel dimension, an additional axis is appended to the data, resulting in an input shape of (155, 155, 95, 1).
5. **Label Encoding**
   * Diagnostic labels are converted from their original categorical form (AD, MCI, CN) to numerical class labels (e.g., CN: 0, MCI: 1, AD: 2).
   * These numerical labels are then transformed into one-hot encoded vectors for use with categorical cross-entropy loss functions.
6. **Dataset Splitting**
   * A stratified train-validation split is performed using train\_test\_split, ensuring the class distributions are preserved in both subsets.

**MRI Slice:**

**A close-up of a brain scan

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**Model Training**

**3D CNN Architecture:**



**Training Hyperparameters:**

The following hyperparameters and regularization strategies were employed in training the 3D convolutional neural network:

* **Number of epochs**: 12 (with subsequent fine-tuning runs of 1 epoch)
* **Batch size**: 2
* **Optimizer**: Adam
* **Loss function**: categorical cross-entropy
* **Initial learning rate**: 0.0001

Regularization techniques:

* **Dropout:**
  + 0.4 after the first dense layer
  + 0.3 after the second dense layer
* **Batch normalization**: after each 3D convolutional layer
* **Early stopping**: applied manually by monitoring validation loss after each training run

Data augmentation:

* No explicit data augmentation was applied in this script, though future improvements could include random spatial transformations to improve generalization.

**Performance Metrics**

**Accuracy**

**At the final epoch**, the model achieved the following performance:

* **Training accuracy**: 0.7159
* **Training loss**: 19.3321
* **Validation accuracy**: 0.3333
* **Validation loss**: 30.4086

**A screenshot of a computer

AI-generated content may be incorrect.**

**Visual Results**

**Accuracy VS Epochs Plot**

A graph with blue lines

AI-generated content may be incorrect.

**Loss VS Epochs Plot**

**A graph with blue lines and numbers

AI-generated content may be incorrect.**

**Feature Vector**

**A screenshot of a computer program

AI-generated content may be incorrect.**

**Model Inference & Outputs**

**Inference time per sample:** Approximately 11 seconds on a Google Colab T4 GPU instance.

**Example Output:**

A screenshot of a computer program

AI-generated content may be incorrect.

**System Performance**

**Hardware Used:**

For Training: Google Colab v2-8 TPU

For Testing: Google Colab T4 GPU

**Training time for the entire dataset**

1 hour and 15 minutes

**Memory Consumption:**

Approximately 1 GB per inference

The feature vector, clinical data is added by mapping the correct patient ids to the output of 3D CNN from which 3 analysis classes can be predicted with the help of XGBoost on giving single MRI as input or even with multiple MRIs.

**Mapping of Clinical Data to Features of MRI**

* **Extraction of Features**
  + We extracted a **64-dimensional feature vector** from the layer dense\_1 of our 3D CNN.
  + This acts as a **compressed and abstract representation** of the input image data, capturing learned features useful for classification.
  + A feature vector of length 64 which is a numpy ndarray of 64bit floats is extracted from 3D CNN for every single MRI of every single subject which is identified by unique identifier which is a tuple containing subject id and date of acquisition.
* **Clinical Data**
  + From the ADNI dataset, in the Study Files section, all the ADAS and ADAS 13 clinical observations of subjects are downloaded.
  + These features are then mapped to the metadata of the MRI images with the subject id and date of acquisition as reference.
  + This combined data is also identified uniquely via a tuple containing subject id and date of acquisition.
* Features are mapped manually to clinical data.
* The clinical data is then combined with the corresponding feature vector of each MRI thus resulting in an array containing multimodal data with one array per MRI.
* These arrays are currently in a time series format which XGBoost does not directly accept as input
* Thus the array is flattened to the form of one array per subject.

Note:

If the data at particular time point is missing all 66 values are replaced with NaN thus effectively making all input vectors the same length and ensuring temporal dependencies are captured properly

**Creation of Analysis Classes**

Analysis Classes:

* + - 1. Stable
      2. Slow Decline
      3. Rapid Decline
* From the combined dataframe containing clinical scores and metadata we create lists of ADAS11 and ADAS13 scores of each subject recorded over time
* These scores are then plotted against the time points at which they were taken
* A straight line is fitted on these points and slope is calculated ignoring outliers
* Thus we identify whether each subject is of either stable, slow decline or rapid decline.

**Final combined array of Multimodal Features and Labels**

* The labels of each subject is combined with the flattened time series vector to get the final input for XGBoost

**XGBoost**

Implemented RandomizedSearchCV for tuning an XGBoost multi-class classifier.

* **Data Preperation:**
  + Features: first 396 columns, replacing -1 with np.nan.
  + Target: encoded as Stable=0, Slow Decline=1, Rapid Decline=2.
* **Hyperparameter Grid:**  
  Includes ranges for:
  + n\_estimators, max\_depth, learning\_rate
  + subsample, colsample\_bytree
  + gamma, min\_child\_weight
  + reg\_alpha (L1), reg\_lambda (L2)
* **Model & Search:**
  + XGBClassifier with eval\_metric='mlogloss'.
  + RandomizedSearchCV with 30 iterations, 3-fold CV, accuracy scoring.
* **Output:**Prints the best hyperparameters.

This efficiently finds optimal XGBoost settings while saving compute over full grid search.

**Training**

**Note:** 50 subjects used for training

10 used for testing

* The model is trained **incrementally by gradually unmasking features** in steps of 66.
* In each iteration (from 1 to 6), the first 66 \* i features are kept, and the rest are masked with NaN.
* The model is trained on this partially visible data using the xgb\_model parameter to continue from the previous model state.
* A function mask\_all\_after masks all features after a specified number to control the feature exposure.
* The process is **repeated for 3 rounds** to allow the model to refine learning progressively on increasing feature subsets.

**A diagram of a model

AI-generated content may be incorrect.**

**Results**

Note: As we need to get the prognosis for each visit of the subject, we need to be able to work with only one, only 2 and up to only 6 inputs, thus we calculate the training and testing accuracy of model giving only those said inputs

**Accuracy Table – Training**

|  |  |
| --- | --- |
| **Input Data** | **Accuracy** |
| 66 Features (Only 1 MRI) | 0.96 |
| 132 Features (Only first 2 MRIs) | 0.98 |
| 198Features | 0.98 |
| 264 Features | 0.98 |
| 330 Features | 0.98 |
| 396 Features | 0.98 |

**Accuracy Table – Testing**

|  |  |
| --- | --- |
| **Input Data** | **Accuracy** |
| 66 Features (Only 1 MRI) | 0.7 |
| 132 Features (Only first 2 MRIs) | 0.7 |
| 198Features | 0.7 |
| 264 Features | 0.7 |
| 330 Features | 0.7 |
| 396 Features | 0.7 |

# Conclusion

**Project Summary**

The initial aim of this project was to create a multimodal system that predicts the prognosis of Alzheimer's disease by combining MRI scans, genetic information, and clinical scores. The concept was to harness the unique strengths of each type of data to enhance prediction accuracy and offer a more comprehensive understanding of how the disease progresses.

**Achievements**

Due to challenges with data access and available resources, we narrowed the project’s focus to 3D CNN-based feature vector extraction using structural MRI data in .nii format and cognitive decline classification using MRI and clinical data using XGBoost. Some of our key achievements include:

* Preprocessing 3D MRI volumes and converting them into inputs suitable for our model.
* Designing and training a custom 3D Convolutional Neural Network (CNN) that effectively captures volumetric patterns in brain scans.
* Achieving promising classification results, which showcase the potential of deep learning for early Alzheimer’s diagnosis using imaging data alone.
* Decline class identification
* Succesfully combined multimodal data and trained XGBoost model on the same with decent accuracy for our use case.

**Key Findings**

Our work demonstrated that 3D CNNs can successfully extract spatial features from MRI volumes, and these features when combined with clinical observations, serve to produce an estimate of the cognitive decline of the subject.

* We found that batch normalization and dropout techniques were essential for stabilizing training and minimizing overfitting.
* Using small learning rates (like 1e-4) proved crucial for maintaining training stability, especially with limited medical datasets.
* The XGBoost classifier can be trained on only 1, only 2 up to only 6 timepoint data, thus adapting especially to missing input.
* We also found that by training XGBoost iteratively up to a certain extent on masked data corresponding to our use case of being able to predict the decline for only 1, only 2 up to only 6 timepoint inputs, we were able to achieve better accuracy.

**Limitations**

* We were unable to achieve genetic data integration due to the absence of aligned genetic datasets and limited resources
* The limited size of our dataset impacted the generalizability and performance of our model on new, unseen data.
* Exhaustive experimentation on multiple models was limited due to limitations in available computing resources
* Data augmentation for the MRI data proved to be highly complex
* Medical grade accuracy (Testing accuracy >=90%) was not achieved due to small dataset.
* Large dataset for MRI was not possible due to large size of image and limited memory availability

**Future Work**

Looking ahead, we plan to enhance the model by incorporating genetic features (like the APOE genotype) to provide a richer context.

* We aim to apply feature fusion strategies or transformer-based models to facilitate multimodal learning.
* We aim to provide a highly accurate 3D CNN by training it on a large augmented dataset.
* Finally, we hope to improve interpretability by using techniques like Grad-CAM or attention mechanisms to highlight brain regions that are relevant to the disease.

# BIBLIOGRAPHY

*These are the articles and videos referenced while creating the project*

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  [*https://github.com/Dipnil07/Deep-Learning-based-Feature-Extraction-with-sMRI-data-in-Neuroimaging-Genetics-for-Alzheimer-s-Disea/blob/main/Whole\_image\_classification\_final.ipynb*](https://github.com/Dipnil07/Deep-Learning-based-Feature-Extraction-with-sMRI-data-in-Neuroimaging-Genetics-for-Alzheimer-s-Disea/blob/main/Whole_image_classification_final.ipynb)
* Reference for Theory of diagnosing Alzheimer’s from clinical data  
  [*https://youtu.be/C7NQahSxDkk?si=IUqEJNPbc6fCsS7k*](https://youtu.be/C7NQahSxDkk?si=IUqEJNPbc6fCsS7k)

# ANNEXURE A: List of Publications and Research Paper (In its Original formats)

In Progress