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Classifying Alzheimer's Disease Progression from Brain MRIs with Deep Learning

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***Abstract*—Alzheimer's disease is a progressive neurodegenerative disorder, and early diagnosis plays a crucial role in patient management. In this project, we explore the use of machine learning algorithms to classify brain magnetic resonance imaging (MRI) scans into four clinical categories: Cognitively Normal (CN), Early Mild Cognitive Impairment (EMCI), Late Mild Cognitive Impairment (LMCI), and Alzheimer's Disease (AD). We compare Convolutional Neural Networks (CNNs), Support Vector Machines (SVMs), and Random Forests in terms of accuracy and robustness. The methodology includes rigorous preprocessing, dimensionality reduction, and model evaluation. Our goal is to determine whether these models can provide clinically meaningful classifications and to understand the impact of data representation on performance.**

***Index Terms*—Alzheimer's Disease, MRI Classification, Machine Learning, CNN, SVM, Random Forest, Medical Imaging**

I. Deliverable 1: Project Definition

A. *Objectives*

1) To explore and preprocess the ADNI-4C MRI dataset for Alzheimer's disease classification.
2) To implement and evaluate machine learning models to classify MRI images into four categories: Alzheimer's Disease (AD), Cognitively Normal (CN), Early Mild Cognitive Impairment (EMCI), and Late Mild Cognitive Impairment (LMCI).
3) To compare model performance with baseline methods and analyze results using accuracy, precision, recall, and confusion matrices.
4) To assess the model's potential for supporting early diagnosis in clinical settings.

B. *Dataset*

The dataset used for this project is the **ADNI-4C Alzheimer's MRI Classification Dataset** [1], which contains brain MRI scans grouped into four clinical classes: CN, EMCI, LMCI, and AD.

- **Alzheimer's Disease (AD)**: 8,960 images
- **Cognitively Normal (CN)**: 6,464 images
- **Early Mild Cognitive Impairment (EMCI)**: 9,600 images
- **Late Mild Cognitive Impairment (LMCI)**: 8,960 images

II. Deliverable 2: Methodology and Algorithm Selection

A. *State of the Art*

Several recent studies have explored the use of machine learning and deep learning techniques to classify MRI data from the ADNI dataset into the four main clinical stages of Alzheimer's disease: Cognitively Normal (CN), Early Mild Cognitive Impairment (EMCI), Late Mild Cognitive Impairment (LMCI), and Alzheimer's Disease (AD).

The most common approaches involve traditional models such as Support Vector Machines (SVM) and Random Forests, often applied after dimensionality reduction techniques like PCA. More recent methods rely on deep learning, particularly Convolutional Neural Networks (CNNs), 3D ResNets, and Transformer-based models, which can automatically learn spatial features directly from the MRI scans. [2] [3]

As summarized in Table I, reported results vary depending on several factors, including the type of MRI representation (2D vs. 3D), the dataset size, and the validation strategy used. While deep models typically outperform traditional ones in raw accuracy, hybrid approaches that combine CNN-based feature extraction with classical classifiers like SVM or Random Forest are still relatively underexplored — despite showing promising results.

Note: Sensitivity refers to the proportion of actual Alzheimer's cases correctly identified (true positive rate), while specificity refers to the proportion of healthy individuals correctly identified as not having the disease (true negative rate).

*1) **Overview of Reviewed Methods**:* The following models have been used in recent literature to address the classification of Alzheimer's disease stages using MRI data. Each represents

TABLE I
SUMMARY OF REPORTED METHODS FOR MRI-BASED ALZHEIMER'S CLASSIFICATION

Method	Model Type	Classes Evaluated	Reported Performance
Traditional Clinical Diagnosis	Human Evaluation	CN, EMCI, LMCI, AD	Sensitivity: 75–85%, Specificity: 70–90%
SVM (linear) + PCA	Classical	CN, EMCI, LMCI, AD	Accuracy: 85%
CNN 2D DenseNet	Deep Learning (2D)	CN, EMCI, LMCI, AD	F1 = 0.83 (EMCI vs LMCI)
3D ResNet-50 (Transfer Learning)	Deep Learning (3D)	CN, EMCI, LMCI, AD	Accuracy: 88%
CNN Ensemble	Ensemble DL	CN, EMCI, LMCI, AD	Accuracy improvement: +3pp over best single CNN

a different strategy in terms of complexity, interpretability, and performance:

- **Traditional Clinical Diagnosis:** A human-driven approach where neurologists use cognitive tests and neuroimaging (MRI/PET) to assess patient condition. While context-aware, it is subjective and varies between clinicians.
- **SVM (linear) + PCA:** A classical machine learning pipeline where dimensionality reduction is first applied to the MRI data using Principal Component Analysis (PCA), followed by classification with a linear Support Vector Machine (SVM).
- **CNN 2D DenseNet + Attention:** A deep learning model that processes 2D slices of MRI scans using a DenseNet backbone, enhanced by attention mechanisms to focus on informative brain regions. It learns features directly from image data.
- **3D ResNet-50 with Transfer Learning:** A 3D convolutional network capable of analyzing volumetric brain scans. Transfer learning is used to benefit from pretrained features, improving convergence and performance with limited data.
- **CNN Ensemble (e.g., VGG, ResNet, DenseNet):** An ensemble strategy that combines predictions from multiple deep learning models. Ensembles are known to reduce variance and improve robustness compared to single models.

2) Advantages and Limitations of Reviewed Methods:

a) Traditional Clinical Diagnosis:

- **Advantages:**
  - **Integrates** clinical signs, cognitive tests, and patient history.
  - **Allows** contextual and holistic judgment.
- **Limitations:**
  - **Strong dependence** on physician expertise.
  - **Decision** process is time-consuming.
  - **Subject** to inter-observer variability.

b) SVM (linear) + PCA:

- **Advantages:**
  - **Simple** and interpretable implementation.
  - **Low** inference cost.
- **Limitations:**
  - **Requires** dimensionality reduction.
  - **Sensitive** to hyperparameter tuning
  - **Less effective** in overlapping or complex feature spaces.

c) CNN 2D DenseNet + Attention:

- **Advantages:**
  - **Captures** local patterns in axial slices effectively.
  - **Attention** mechanism enhances regional focus.
- **Limitations:**
  - **Loses** 3D volumetric information.
  - **Requires** extensive data augmentation.
  - **Sensitive** to overfitting in small datasets.

d) 3D ResNet-50 with Transfer Learning:

- **Advantages:**
  - **Leverages** full 3D brain volume for richer context.
  - **Skip connections** help prevent vanishing gradients.
- **Limitations:**
  - **Requires** powerful GPU resources (¿ 12 GB).
  - **Longer** training times.
  - **More complex** to fine-tune and deploy.

e) Ensemble of CNNs (e.g., VGG, ResNet, DenseNet):

- **Advantages:**
  - **Reduces** variance and increases robustness.
  - **Can** outperform individual models.
- **Limitations:**
  - **Increased** complexity in deployment and training.
  - **Requires** more memory and compute resources.
  - **Risk** of overfitting if not properly validated.

B. Selected Algorithms

1) Background: The task of classifying brain magnetic resonance images into different stages of Alzheimer's disease is a highly complex supervised learning problem, especially due to the high dimensionality of the data and the visual similarity between some classes (e.g., EMCI vs. LMCI). For this reason, the appropriate selection of algorithms is essential in order to obtain good results.

Classifying magnetic resonance images to detect different stages of Alzheimer's disease is a major challenge in this area, not only because of the high dimensionality of the images, but also because of the proximity between clinical classes. Therefore, the choice of algorithms is fundamental to guaranteeing a cohesive and clinically useful performance.

It should be noted that the images analyzed are divided into four sets: **AD** (Alzheimer's Disease), **CN** (Cognitively Normal), **EMCI** (Early Mild Cognitive Impairment), and **LMCI** (Late Mild Cognitive Impairment).

2) Algorithms: **After a group assessment of the algorithms to be used for analysis and comparison, we prioritized the following:**

*a) **1. Convolutional Neural Networks (CNN)**:* Convolutional Neural Networks (CNNs) are a class of deep learning models specifically designed to process visual data. Unlike traditional neural networks, CNNs include convolutional layers that allow the network to automatically learn spatial hierarchies of features from raw image pixels. Their main advantage lies in their ability to extract and learn complex visual patterns with minimal preprocessing, making them particularly suitable for high-dimensional data such as magnetic resonance images. Given their proven success in image classification tasks, CNNs are especially appropriate for this project, where subtle anatomical differences between classes must be detected and distinguished.

*b) **2. Support Vector Machines (SVM)**:* SVM is a linear classifier that seeks to find the best boundary separating the classes with the largest possible margin. Although it was originally a binary classifier, it can be extended to multiclass using the 'one-vs-rest' technique. In the case of images, it is often used after dimensionality reduction, such as PCA, to avoid the problem known as 'curse of dimensionality'.

*c) **3. Random Forests**:* Random Forest is an algorithm based on multiple decision trees trained on random subsets of data. It is effective in contexts where the data may contain noise. In this project, it will be used as a baseline, allowing the performance of simpler models to be compared with more advanced neural networks.

*d) **Comparison and Justification**:* The choice of these three models aims to cover approaches with different levels of complexity: from rule-based models (Random Forest), through classical mathematical methods (SVM), to deep learning architectures capable of learning hierarchical visual representations (CNN). Comparing them will allow us not only to see which model performs best, but also to gain insights into the influence of pre-processing and the dimensionality of the data.

It should be noted that at the end of our project, we intend to combine the three selected algorithms in order to evaluate whether an ensemble approach can improve classification performance. While implementation details will be presented in Deliverable 3, the combination may involve techniques such as using CNNs for feature extraction followed by classification with SVM and Random Forest, or ensemble strategies like hard voting (majority rule) and soft voting (average of predicted probabilities). Our goal is to determine whether it is possible to identify, with a high degree of accuracy, the stage of Alzheimer's disease (CN, EMCI, LMCI, AD) using machine learning algorithms applied to MRI images.

C. Data Processing Methodology

*1) **Data Preprocessing**:* To ensure that the algorithms work properly and produce consistent results, we have defined a set of preprocessing steps that will be applied to the MRI images:

- **Intensity Normalisation**: Pixel values will be normalised to the [0,1] interval, minimising variations caused by different image acquisition protocols.
- **Resizing**: All images will be resized to 224×224 pixels, maintaining an adequate resolution for analysis and reducing the computational load.
- **Noise Reduction**: Mild Gaussian filtering will be applied in order to reduce noise without eliminating relevant anatomical details.
- **Selection of Axial Sections**: The most relevant slices of each exam will be selected, excluding images that do not contain useful diagnostic information.
- **Data Augmentation**: To address class imbalance, data augmentation techniques will be applied (e.g., small rotations of ±10°, horizontal inversions, and slight contrast variations), mainly in the less represented classes.

*2) **Feature Extraction**:* Feature extraction will be adapted to the algorithm used:

- **Convolutional Neural Networks (CNN)**: Features will be learned automatically during training through convolutional and pooling layers, allowing the model to extract complex spatial patterns from the raw images.
- **Support Vector Machines (SVM) and Random Forests**: These models will rely on explicit feature extraction techniques, including:
  - **PCA (Principal Component Analysis)**: Dimensionality reduction preserving 95% of the variance.
  - **Textural Descriptors (Haralick)**: Extraction of texture-based features, useful for distinguishing subtle patterns of brain atrophy.
  - **Regional Statistics**: Calculation of metrics (mean, standard deviation, entropy) in critical brain regions such as the hippocampus and entorhinal cortex.
  - **Morphological Characteristics**: Quantitative measures of the shape and volume of relevant anatomical structures.

*3) **Data Division Strategy**:* To avoid bias and ensure a reliable evaluation of model performance, the dataset will be divided into three subsets:

- **Training Data**: 70%
- **Validation Data**: 15%
- **Test Data**: 15%

We chose this three-way split to ensure that the proportion of each class (CN, EMCI, LMCI, AD) is maintained across all subsets, preserving balance and enabling fair comparison across models.

*4) **Class Imbalance Treatment**:* The CN (Cognitively Normal) class has a lower number of images (6,464) compared to the other classes. To address this imbalance and prevent the model from being biased toward the majority classes, the following strategies will be applied:

- **Weighted Cost Function**: Assigning higher training weights to the CN class to penalize misclassifications more heavily.
- **Targeted Data Augmentation**: Applying more aggressive augmentation techniques (e.g., rotations, contrast shifts, flips) specifically to CN samples to artificially increase their representation.
- **Stratified Sampling**: Ensuring a balanced class distribution is maintained across training, validation, and test sets.

*5) **Evaluation Metrics:*** Model performance and comparison will be assessed using the following evaluation metrics, selected to provide both global and class-level insights:

- **Overall Accuracy**: The total percentage of correct classifications across all classes.
- **Confusion Matrix**: A detailed analysis of misclassifications between classes, with particular attention to the distinction between EMCI and LMCI.
- **Precision, Recall, and F1-Score per Class**: Class-specific evaluation metrics, emphasizing the importance of avoiding false negatives in AD and false positives in CN.
- **Training and Inference Time**: Analysis of the time required to train the models and to make predictions, considering the practical applicability in a clinical setting.

*6) **Cross-Validation Strategy:*** To ensure the robustness of the models and minimize the risk of overfitting, the following strategies will be adopted:

- **Stratified k-Fold Cross-Validation (k = 5)**: Ensures that the class proportions are preserved in each fold, allowing fair and balanced evaluation.
- **Hold-Out Validation**: A classic 70/15/15 train/validation/test split will be applied in parallel with k-fold to validate model performance consistency.
- **Repetition with Different Random Seeds**: Multiple runs with varied seeds will help reduce the impact of initialization randomness and sampling variability.
- **Learning Curves**: Used to detect signs of overfitting or underfitting and guide the tuning of model hyperparameters accordingly.

*7) **Final Conclusion:*** The methodological approach defined in this work combines technical rigour with a practical focus, ensuring that the models can be applied in real-world clinical contexts. The use of three distinct algorithms — Convolutional Neural Networks (CNN), Support Vector Machines (SVM), and Random Forest — allowed us to explore multiple paradigms of supervised learning, from classical statistical models to modern deep learning architectures.

Robust preprocessing, targeted feature extraction, class imbalance handling, and cross-validation strategies were employed to ensure that the comparison between models was fair, unbiased, and replicable. Furthermore, the evaluation based on diverse metrics — including per-class accuracy, confusion matrices, and training/inference times — provides a comprehensive assessment of each algorithm's performance.

These strategies form the foundation for a rigorous and meaningful analysis of the models' effectiveness in classifying brain MRI images in the context of Alzheimer's disease. With the conclusion of our project, we aim to answer our initial research question through objective results and evidence-based insights.

III. ML Use Disclosure

Machine Learning tools were used to assist in the preparation of this document and throughout the development of the project. Specifically, ChatGPT [4] was used to rephrase and clarify certain sentences, assist in summarizing technical content, and suggest structure and methodology relevant to Alzheimer's disease classification. Whenever possible, references were provided to the model or requested from it, and all information was manually verified for coherence and accuracy.

In addition, ChatGPT and similar tools have been (and will continue to be) used to support implementation tasks, including code generation, preprocessing pipelines, model development, and performance evaluation — always under human supervision and with critical validation at each step.

References

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