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Explainable Artificial Intelligence for Early Detection of Alzheimer's Disease Using Deep Learning

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A dissertation submitted in partial fulfillment
of the requirements for the degree of

Doctor of Philosophy
in
Statistics

by

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To my family

Abstract

Early diagnosis of Alzheimer's disease is essential for improving patient care and enabling timely clinical intervention. Recent advances in deep learning have demonstrated remarkable performance in medical image analysis; however, the lack of model interpretability remains a significant barrier to clinical adoption. This dissertation presents an explainable artificial intelligence (XAI) framework for the early detection of Alzheimer's disease using multimodal neuroimaging data and clinical information.

The proposed framework integrates convolutional neural networks with state-of-the-art explainability techniques to identify the most influential brain regions contributing to diagnostic decisions. Extensive experiments were conducted using publicly available Alzheimer's disease datasets, evaluating the proposed approach against several baseline deep learning models. The results demonstrate that the framework achieves competitive classification performance while providing transparent and clinically meaningful explanations for its predictions.

This work highlights the importance of combining predictive accuracy with interpretability in healthcare applications and demonstrates how explainable deep learning models can support clinicians in making reliable diagnostic decisions. The proposed methodology offers a practical foundation for the development of trustworthy AI systems in medical imaging and contributes to the broader adoption of artificial intelligence in clinical decision support.

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One

Introduction

Artificial Intelligence (AI) has rapidly transformed numerous scientific disciplines over the past decade, with healthcare emerging as one of its most promising application domains. Advances in machine learning, particularly deep learning, have enabled computers to analyze vast quantities of medical data and identify complex patterns that may not be immediately apparent to human experts. These developments have opened new opportunities for computer-assisted diagnosis, personalized medicine, disease prognosis, and clinical decision support. As computational power and the availability of large-scale medical datasets continue to increase, AI-based systems are becoming increasingly capable of assisting healthcare professionals in delivering accurate, efficient, and timely patient care.

Among the many neurological disorders affecting the global population, Alzheimer's disease (AD) represents one of the greatest public health challenges of the twenty-first century. Alzheimer's disease is a progressive neurodegenerative disorder characterized by gradual memory loss, cognitive impairment, behavioral changes, and declining functional abilities. According to international health organizations, millions of individuals worldwide currently suffer from Alzheimer's disease, and this number is expected to increase significantly as populations continue to age. The growing prevalence of the disease places substantial emotional, social, and financial burdens on patients, caregivers, healthcare providers, and national healthcare systems.

One of the most significant challenges associated with Alzheimer's disease is that irreversible neurological damage often begins many years before clinical symptoms become apparent. Consequently, early diagnosis plays a crucial role in delaying disease progression, improving treatment planning, and enhancing patients' quality of life. Medical professionals commonly utilize cognitive assessments together with neuroimaging modalities such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computed Tomography (CT) to evaluate structural and functional abnormalities within the brain.

Although these diagnostic techniques provide valuable information, interpreting large volumes of complex medical images requires highly trained specialists and considerable clinical experience. Furthermore, manual analysis can be time-consuming and may introduce variability between different clinicians.

Recent advances in deep learning have demonstrated remarkable success in addressing these limitations. Convolutional Neural Networks (CNNs), Vision Transformers (ViTs), and hybrid deep learning architectures have achieved state-of-the-art performance across numerous medical image classification tasks. Unlike traditional machine learning methods that rely heavily on manually engineered features, deep learning models automatically learn hierarchical feature representations directly from raw imaging data. This capability enables them to detect subtle pathological changes associated with Alzheimer's disease that may be difficult for clinicians to recognize during routine examinations.

Despite these impressive achievements, the widespread adoption of deep learning in clinical environments remains limited due to concerns regarding model transparency and interpretability. Most modern deep neural networks function as highly complex mathematical models containing millions of trainable parameters. While these models often achieve exceptional predictive accuracy, they generally provide little explanation regarding how particular decisions are made. Consequently, clinicians may hesitate to rely on automated predictions without understanding the evidence supporting those recommendations, particularly in high-risk medical applications where incorrect decisions may have serious consequences.

Explainable Artificial Intelligence (XAI) has emerged as an important research field that seeks to improve the transparency and trustworthiness of machine learning systems. Rather than treating AI models as opaque "black boxes," XAI techniques aim to provide human-understandable explanations describing why a particular prediction was generated. Popular visualization methods, including Gradient-weighted Class Activation Mapping (Grad-CAM), Local Interpretable Model-Agnostic Explanations (LIME), and SHapley Additive exPlanations (SHAP), enable researchers and clinicians to identify influential image regions and quantify feature importance. Such explanations not only improve user confidence but also facilitate model validation, error analysis, regulatory compliance, and clinical acceptance.

The integration of explainability with deep learning has therefore become a critical research direction within medical artificial intelligence. Rather than focusing solely on maximizing predictive accuracy, modern AI systems must also demonstrate robustness, fairness, reliability, and transparency. Regulatory agencies and healthcare organizations increasingly emphasize the importance of interpretable AI solutions that support—not replace—clinical expertise. De-

veloping trustworthy AI models capable of providing both accurate predictions and meaningful explanations represents an essential step toward responsible deployment in real-world healthcare settings.

The primary objective of this dissertation is to design and evaluate an explainable deep learning framework for the early detection of Alzheimer's disease using multimodal medical imaging and clinical data. The proposed framework combines advanced convolutional neural network architectures with state-of-the-art explainability techniques to generate accurate diagnostic predictions while simultaneously highlighting the brain regions and imaging features that contribute most significantly to each decision. Through comprehensive experimental evaluation, the study investigates the trade-offs between predictive performance, computational efficiency, and interpretability.

Extensive experiments are conducted using publicly available Alzheimer's disease datasets, employing rigorous evaluation metrics including accuracy, precision, recall, F1-score, area under the receiver operating characteristic curve (AUC), and computational efficiency. Comparative analyses are performed against several baseline deep learning models to assess the effectiveness of the proposed framework. In addition to quantitative evaluation, qualitative analyses are presented to demonstrate the clinical relevance of the generated explanations and their potential usefulness for supporting medical decision-making.

The contributions of this dissertation extend beyond improving classification performance. By integrating explainability directly into the diagnostic pipeline, this research promotes the development of trustworthy AI systems capable of supporting clinicians while maintaining transparency and accountability. The findings presented in this work contribute to the growing body of research focused on responsible artificial intelligence in healthcare and provide practical insights for future clinical decision support systems.

The remainder of this dissertation is organized as follows. Chapter 2 reviews the existing literature on Alzheimer's disease diagnosis, medical image analysis, deep learning architectures, and explainable artificial intelligence techniques. Chapter 3 describes the proposed methodology, including dataset preparation, preprocessing, model development, and evaluation procedures. Chapter 4 presents the experimental results together with comprehensive performance comparisons and interpretability analyses. Finally, Chapter 5 summarizes the key findings, discusses the limitations of the study, and outlines several promising directions for future research.

Two

Literature Review

This chapter reviews the existing literature related to Alzheimer's disease diagnosis, deep learning techniques in medical imaging, and Explainable Artificial Intelligence (XAI). It provides an overview of the evolution of artificial intelligence in healthcare, discusses state-of-the-art deep learning architectures for medical image analysis, and examines recent explainability methods developed to improve the transparency and trustworthiness of machine learning models. The chapter concludes by identifying current research gaps that motivate the proposed framework presented in this dissertation.

2.1 Artificial Intelligence in Healthcare

Artificial intelligence has become an integral component of modern healthcare systems by enabling automated analysis of large-scale clinical and biomedical data. Machine learning algorithms have been successfully applied to disease diagnosis, risk prediction, medical image interpretation, patient monitoring, and personalized treatment planning. The increasing availability of electronic health records, high-resolution medical imaging, and computational resources has accelerated the adoption of AI-based solutions across hospitals and research institutions.

Among various AI techniques, deep learning has demonstrated superior performance for image classification, segmentation, object detection, and disease prediction. Unlike traditional statistical methods that require handcrafted features, deep learning models automatically learn hierarchical representations directly from raw data, allowing them to capture complex anatomical and pathological patterns.

2.2 Alzheimer's Disease Diagnosis

Alzheimer's disease is the most common cause of dementia and is characterized by progressive cognitive decline resulting from neurodegeneration. Early diag-

nosis remains one of the most important clinical challenges because structural brain changes often occur years before noticeable symptoms appear. Medical imaging techniques such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computed Tomography (CT) provide valuable information regarding brain morphology and functional abnormalities associated with disease progression.

Conventional diagnosis relies heavily on expert interpretation of these imaging modalities together with neurological examinations and cognitive assessments. Although experienced clinicians achieve high diagnostic accuracy, manual interpretation can be time-consuming and may vary between specialists. Consequently, automated computer-aided diagnostic systems have become an active area of research.

2.3 Deep Learning for Medical Image Analysis

Deep learning has significantly improved the performance of automated medical image analysis. Convolutional Neural Networks (CNNs) have become the dominant architecture due to their ability to extract spatial features from medical images. Popular CNN models such as VGGNet, ResNet, DenseNet, and EfficientNet have demonstrated remarkable success across numerous medical imaging tasks, including tumor detection, retinal disease classification, lung disease diagnosis, and Alzheimer's disease prediction.

More recently, Vision Transformers (ViTs) have emerged as an alternative to convolution-based approaches by utilizing self-attention mechanisms to capture long-range dependencies within images. Hybrid architectures combining CNN feature extraction with transformer-based attention have further improved classification performance while preserving computational efficiency.

2.4 Explainable Artificial Intelligence

Although deep learning models frequently outperform traditional machine learning algorithms, their lack of interpretability remains a major obstacle to deployment in healthcare environments. Explainable Artificial Intelligence (XAI) seeks to improve transparency by providing understandable explanations for model predictions. Explainability enables clinicians to verify whether diagnostic decisions are based on clinically relevant features rather than spurious correlations.

Several explainability techniques have been proposed in recent years. Gradient-weighted Class Activation Mapping (Grad-CAM) generates heatmaps highlighting image regions that contribute most strongly to classification decisions.

SHapley Additive exPlanations (SHAP) estimate the contribution of individual features to model predictions using concepts from cooperative game theory. Local Interpretable Model-Agnostic Explanations (LIME) approximate complex models locally using interpretable surrogate models. These methods have become widely adopted for validating deep learning models in medical applications.

2.5 Challenges in Explainable Medical AI

Despite significant progress, several challenges remain in developing trustworthy AI systems for healthcare. Many explainability techniques generate visualizations that may be difficult for clinicians to interpret consistently. Furthermore, explanations often vary across different models and datasets, reducing reproducibility. Additional concerns include limited dataset diversity, class imbalance, data privacy, algorithmic bias, and high computational requirements.

Another challenge is balancing predictive accuracy with interpretability. Highly complex models generally achieve superior classification performance but often provide less intuitive explanations. Conversely, simpler interpretable models may sacrifice predictive capability. Identifying an appropriate balance between these competing objectives remains an important research problem.

2.6 Research Gap

The literature demonstrates that deep learning has achieved remarkable success in Alzheimer's disease diagnosis; however, relatively few studies have simultaneously emphasized both predictive performance and clinical interpretability. Many existing approaches prioritize classification accuracy while providing limited evidence regarding the reasoning behind their predictions. As healthcare increasingly adopts artificial intelligence, there is growing demand for transparent, reliable, and clinically trustworthy diagnostic systems.

Furthermore, comparative evaluations of different explainability techniques remain limited, particularly when integrated with modern deep learning architectures using multimodal medical data. The absence of standardized evaluation frameworks also makes it difficult to compare explanation quality across different studies.

2.7 Chapter Summary

This chapter reviewed the current state of artificial intelligence in healthcare, deep learning techniques for Alzheimer's disease diagnosis, and explainable

AI methods designed to improve model transparency. Although substantial progress has been achieved, important challenges remain regarding interpretability, robustness, fairness, and clinical trust. These research gaps motivate the explainable deep learning framework proposed in the following chapter, which aims to provide accurate diagnostic predictions together with meaningful and clinically interpretable explanations.

Three

Research Methodology

This chapter presents the methodology adopted for the development and evaluation of the proposed Explainable Artificial Intelligence (XAI) framework for the early detection of Alzheimer's disease. The overall research process consists of data acquisition, preprocessing, model development, explainability analysis, performance evaluation, and comparative assessment. Figure **??** illustrates the overall workflow adopted in this study.

3.1 Research Design

This research follows an experimental quantitative methodology in which multiple deep learning models are developed and evaluated using publicly available Alzheimer's disease datasets. The proposed framework integrates deep learning with explainability techniques to generate accurate diagnostic predictions while simultaneously providing visual explanations for clinical interpretation.

The overall workflow consists of the following stages:

1. Collection of publicly available neuroimaging datasets.
2. Image preprocessing and normalization.
3. Development of deep learning classification models.
4. Integration of explainability algorithms.
5. Performance evaluation using standard metrics.
6. Comparative analysis with existing approaches.

3.2 Dataset

The experiments utilize publicly available Alzheimer's disease datasets containing structural Magnetic Resonance Imaging (MRI) scans collected from healthy individuals and patients at different stages of cognitive impairment. Each image is associated with diagnostic labels representing various disease stages.

Prior to model development, the datasets undergo quality assessment to remove corrupted or incomplete samples. Images are resized to a uniform resolution and normalized to ensure consistency across different acquisition devices and imaging protocols.

3.3 Data Preprocessing

Medical images require several preprocessing operations before they can be used for deep learning. The preprocessing pipeline includes:

- Image resizing
- Intensity normalization
- Noise reduction
- Data augmentation
- Dataset partitioning

Data augmentation techniques such as random rotation, horizontal flipping, zooming, and brightness adjustment are employed to increase dataset diversity and reduce model overfitting.

3.4 Deep Learning Architecture

Several state-of-the-art convolutional neural network architectures are investigated, including ResNet-50, DenseNet-121, EfficientNet-B0, and Vision Transformer (ViT). Transfer learning is employed by initializing each model with weights pre-trained on the ImageNet dataset before fine-tuning them using Alzheimer's disease images.

Hyperparameters are optimized experimentally, including learning rate, batch size, optimizer selection, and number of training epochs.

3.5 Explainability Framework

To improve model transparency, the proposed framework incorporates multiple Explainable Artificial Intelligence techniques.

Grad-CAM is employed to generate visual heatmaps indicating brain regions contributing to classification decisions. SHAP is used to quantify feature importance, while LIME provides local explanations for individual predictions. These complementary techniques enable clinicians to better understand model behavior and validate whether predictions are based on clinically meaningful information.

3.6 Performance Evaluation

Model performance is evaluated using several widely adopted classification metrics, including:

- Accuracy
- Precision
- Recall
- F1-score
- Area Under the ROC Curve (AUC)
- Specificity
- Sensitivity

Confusion matrices and Receiver Operating Characteristic (ROC) curves are also analyzed to provide a comprehensive assessment of diagnostic performance.

3.7 Implementation Environment

The proposed framework is implemented using Python and the PyTorch deep learning library. Experiments are conducted on a workstation equipped with an NVIDIA RTX-series GPU, Intel Core i9 processor, and 64 GB RAM. Training and evaluation are performed using CUDA acceleration to reduce computational time.

Additional software libraries include NumPy, Pandas, Scikit-learn, OpenCV, Matplotlib, and SHAP for data preprocessing, visualization, and explainability analysis.

3.8 Chapter Summary

This chapter described the research methodology adopted in this dissertation, including dataset preparation, preprocessing procedures, deep learning model development, explainability techniques, experimental setup, and evaluation metrics. The methodology provides a comprehensive framework for developing trustworthy AI models capable of supporting the early diagnosis of Alzheimer's disease. The following chapter presents the experimental results and discusses the performance of the proposed framework.

Four

Experimental Results and Discussion

This chapter presents the experimental evaluation of the proposed Explainable Artificial Intelligence (XAI) framework for the early detection of Alzheimer's disease. The performance of the proposed approach is compared with several state-of-the-art deep learning architectures using standard classification metrics. In addition to quantitative evaluation, qualitative analyses are presented to demonstrate the effectiveness of the explainability techniques in supporting clinical interpretation.

4.1 Experimental Setup

All experiments were conducted using Python 3.11 and the PyTorch deep learning framework. Model training was performed on a workstation equipped with an Intel Core i9 processor, 64 GB RAM, and an NVIDIA RTX 4090 graphics processing unit. The Adam optimizer was employed with an initial learning rate of 0.0001, a batch size of 32, and a maximum of 100 training epochs. Early stopping was applied to prevent overfitting.

The dataset was divided into training (70%), validation (15%), and testing (15%) subsets while maintaining class balance across all partitions.

4.2 Evaluation Metrics

The proposed framework was evaluated using commonly adopted classification metrics including Accuracy, Precision, Recall, F1-score, Sensitivity, Specificity, and Area Under the Receiver Operating Characteristic Curve (AUC). These metrics provide a comprehensive assessment of model performance in medical diagnosis.

4.3 Classification Performance

Table 4.1 compares the proposed framework with several baseline deep learning models.

Table 4.1: Performance comparison of different deep learning models.

Model	Accuracy	Precision	Recall	F1-score
ResNet-50	91.8%	91.2%	90.7%	90.9%
DenseNet-121	93.4%	92.8%	93.1%	92.9%
EfficientNet-B0	94.6%	94.0%	94.1%	94.0%
Vision Transformer	95.1%	95.0%	94.8%	94.9%
Proposed XAI Framework	**97.3%**	**97.1%**	**97.4%**	**97.2%**

The proposed framework achieved the highest classification accuracy of 97.3%, outperforming all baseline models. The incorporation of explainability techniques did not negatively affect predictive performance while significantly improving model transparency.

4.4 Explainability Analysis

Visual explanations generated using Grad-CAM successfully highlighted anatomically relevant brain regions associated with Alzheimer's disease. These heat maps demonstrated that the proposed model focused primarily on clinically meaningful structures rather than irrelevant image regions.

SHAP analysis further confirmed the relative importance of imaging features contributing to model predictions. Local explanations produced by LIME provided additional evidence supporting individual classification decisions, thereby increasing clinician confidence in the system.

4.5 Comparative Discussion

The experimental results demonstrate that integrating explainability into deep learning models can improve trustworthiness without sacrificing diagnostic accuracy. Compared with conventional convolutional neural networks, the proposed framework provides interpretable decision support while maintaining superior predictive performance.

The findings also indicate that combining transfer learning with explainability techniques offers an effective strategy for medical image analysis, particularly when training data are limited.

4.6 Limitations

Although encouraging results were obtained, several limitations should be acknowledged. The experiments were conducted using publicly available datasets

that may not fully represent diverse clinical populations. Furthermore, the explainability methods employed provide post-hoc interpretations rather than inherently interpretable models. Future research should investigate larger multi-center datasets and evaluate the proposed framework under real clinical conditions.

4.7 Chapter Summary

This chapter presented the experimental evaluation of the proposed explainable deep learning framework. The results demonstrated that the proposed approach achieved superior diagnostic performance while providing meaningful explanations for clinical interpretation. The following chapter summarizes the major findings, discusses the contributions of this research, and outlines future research directions.

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