

Original Article

Alzheimer's Disease Classification using a Hybrid CNN-LSTM-Quantum Learning Approach

M K V Anvesh¹, Prajna Bodapati²

^{1,2}Department of Computer Science and Systems Engineering, Andhra University, A.P, India.

¹Corresponding Author : mkvanvesh@gmail.com

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Abstract - Alzheimer's disease is a neurodegenerative disease and a primary cause of dementia. Hence, an accurate early detection method for this disease is highly important. However, most existing methods rely on a medical evaluation/clinical study or single model learning methods that cannot address complex patterns, temporal associations, or class imbalance issues associated with Alzheimer's MRI images effectively. In this regard, a CNN-LSTM-Quantum hybrid approach has been developed for the stage-wise classification of patients who have Alzheimer's disease based on their brain MRI images. Spatial features within MRI images were extracted using a ResNet-18 architecture, while a two-layer LSTM architecture was used for recognizing sequential correlations within a sequence of MRI images. Moreover, a quantum-inspired classifier helps enhance feature extraction capabilities alongside decision-making processes. In this research, a fully balanced dataset was used, including data associated with four different stages of Alzheimer's disease, allowing for an unconstrained analysis. The test accuracy of 98.9% was verified by the proposed approach, confirming that a high level of precision, recall, and class separability was reached.

Keywords - Alzheimer's Disease, ResNet-18, LSTM, Feature fusion, Hybrid quantum-classical model, Medical image classification, Disease stage prediction.

1. Introduction

Alzheimer's Disease (AD) is a degenerative brain disease that involves a gradual decline in memory, cognitive, and behavioral functions, leading to a loss of capability in performing everyday tasks. This disease is the most common type of dementia that has been associated with significant public health problems caused by the rapidly increasing number of older adults. Advancements in AD research in recent years have played a critical role in gaining an insight into molecular mechanisms, pathology, and therapy of AD, as well as highlighting the significance of correct diagnostics for successful management and treatment of the disease [1]. The 2024 Alzheimer's Disease Facts and Figures reveal that the global prevalence rate of AD has been steadily rising in recent years [2]. Pathological events related to the onset of AD occur well before the manifestation of clinical symptoms. With the continuous increase in the number of amyloid- β plaques, neurofibrillary tangles, impaired synapses, and neurodegeneration, the individual becomes affected cognitively, and the brain gets irreversibly damaged.

The cellular phase of Alzheimer's disease is seen as an important stage during which pathological changes in neurons and glial functions play an important role in causing neurodegeneration well before the occurrence of any severe symptoms clinically [3]. Thus, early detection of the disease

continues to be one of the main goals in neurology studies. Current developments in biomarker studies have led to better biological understanding and staging of AD.

The development of biomarker-based models incorporating neuroimaging data, cerebrospinal fluid biomarkers, blood biomarkers, and clinical examination has allowed for better evaluation of the progress of the disease and helps in precision medicine diagnosis and treatment [4]. In addition, neuroinflammation has also been recognized as an important factor in the pathogenesis of the disease through a complicated interplay between immune response and neuronal damage [5].

The continuous developments in the fields of basic research, diagnosis, and therapy have allowed a better understanding of AD. The recent research has emphasized efforts in increasing the accuracy of diagnosis along with the development of treatment strategies via molecular biology, neuroimaging, and computer analysis [6]. In addition, the current pipeline of drugs for AD and the clinical success of therapies designed to modify disease progression, including Lecanemab, have brought out the significance of early identification of patients in order to obtain maximum benefit from therapy [7, 8]. Magnetic Resonance Imaging (MRI) is widely recognized as a non-invasive imaging method for the



diagnosis of AD, since it enables an in-depth understanding of the anatomical structure. The expanding collection of MRI scans has supported the adoption of AI techniques along with deep learning approaches for automated disease classification.

Nonetheless, accurate classification of different stages of AD is still difficult due to minor anatomical differences among the stages, imbalanced data, inadequate feature extraction and poor generalizability of existing models. In order to resolve these shortcomings, this research work presents a hybrid deep learning framework for the classification of stages of AD through brain MRIs.

2. Literature Survey

Table 1 shows some of the recent studies carried out on the diagnosis and stage classification of AD using brain MRI images in combination with other clinical data. The existing

literature demonstrates considerable advancements in improving diagnostic accuracy. However, several problems have yet to be overcome by researchers, such as the absence of diverse datasets, imbalanced classes, overfitting, high computational cost, insufficient external validation, and generalization capability. In addition, the vast majority of current methods adopt individual learning frameworks and cannot take full advantage of the spatial and sequential information present in the MRI image. Consequently, obtaining a powerful and reliable classification framework for practical applications becomes difficult. Therefore, a major research gap emerges in the development of an integrative approach that could learn comprehensive feature representation and improve accuracy, robustness, and generalization. To fill this gap, the current work develops a hybrid CNN-LSTM-Quantum framework for accurate AD diagnosis based on brain MRI images.

Table 1. Overview of current methods for AD diagnosis

Authors	Methods & Dataset Used	Performance & Limitations
Kavitha et al. [9], 2022	Classical ML; AD dataset	83% accuracy; limited feature representation and dataset scalability.
Tiwari et al. [10], 2024	ML classifiers using CSF biomarkers	64-69% accuracy; limited predictive capability for cognitive impairment detection.
Gramkow et al. [11] 2025	Logistic Regression; Actigraphic sensor data	69% accuracy (AD), 80-89% (dementia subtypes); lower performance than imaging-based methods.
Saranya et al. [12], 2025	ML methods for MCI-to-AD prediction	95.8% (Ensemble), 91.5% (RF), 90% (KNN); small and homogeneous datasets.
Madiwalar et al. [13], 2020	SVM, RF, DT, Extra Trees; OASIS	93.14% accuracy; feature dependency and limited data.
Lazli et al. [14], 2025	PCA + SVM/FFNN/ViT; ADNI, OASIS	93.2% and 90.4% precision; relies on augmentation and large datasets.
Archana Menon et al. [15], 2024	SHAP-based interpretable ML; OASIS MRI	96% accuracy; limited validation on diverse datasets.
Bekhet et al. [16], 2025	Deep ALZNET; MRI + Clinical Data	92.2% and 90.2% accuracy; class imbalance and sampling bias.
Wang et al. [17], 2025	MRI-PET multimodal fusion; ADNI, OASIS	92.5% accuracy, 0.95 AUC; insufficient external validation.
Basanta-Torres et al. [18], 2025	AI review using T1-weighted MRI	85.93% (CNN), 82.50% (ML); overfitting and methodological variations.
Arya AD et al. [19], 2025	Review of ML/DL neuroimaging studies	Identified effective models; issues include class imbalance and small datasets.
Young et al. [20], 2025	Review of 44 DL studies	66-90% validated accuracy; data leakage affects reliability.
Heenaye-Mamode Khan et al. [21], 2024	Transfer learning models (VGG, ResNet, DenseNet, Inception, EfficientNet, MobileNet); MRI, PET, and fMRI data	Pre-trained models outperformed traditional approaches; small datasets, computational complexity, and poor generalization.
Raj et al. [22], 2025	CNN-LSTM-Attention framework; MRI images	96.6% accuracy; absence of quantum learning limits further performance enhancement.
Zadeh et al. [23], 2025	QSVM and VQC; ASD screening datasets	96.7% accuracy (QSVM); lacks hybrid learning integration and is limited to quantum classification.

3. Methodology

3.1. Dataset Description

The image collection is that of the brain MRI scans and is split into four stages of AD and includes 3,200 images belonging to the Non-Demented class, 2,240 to the Very Mild Demented class, 896 to the Mild Demented class, and 64 to the Moderate Demented class. The image collection is highly unbalanced, where most of the images belong to the Non-Demented stage, and the least belongs to the Moderate Demented stage.

Moreover, the image collection is balanced and includes an equal number of images and includes 3,200 images to make up a total of 12,800 images. Later, this balanced dataset was divided into training, validation, and testing datasets in a ratio of 70:15:15. This includes 2,240 images being used for the training dataset and 480 images used for the validation and testing datasets, making the total count of the training datasets as 8,960 images and 1,920 images for the validation and testing datasets.

3.2. Preprocessing Steps

First, in the preprocessing step, all MRI images will be converted into grayscale to eliminate information that might be extra since color has no importance in this context. Each of the images is then resized to 224×224 pixels to provide a standardized input size for the deep learning model used in the study. As a preprocessing step to improve data quality, data augmentation methods are performed on the training dataset. It includes random rotation, horizontal and vertical flipping, adjustment in brightness and contrast, slight Gaussian blurring, random cropping followed by resizing, and adding Gaussian noise.

All these operations make data more diverse, yet do not harm the medical relevance of the images. The preprocessed images are converted to tensor representations, subsequently normalized using predefined mean and standard deviation values of 0.5. At the loading of data, a sequence of three preprocessed images that belong to one class is selected and stacked to form one single input sample for the model.

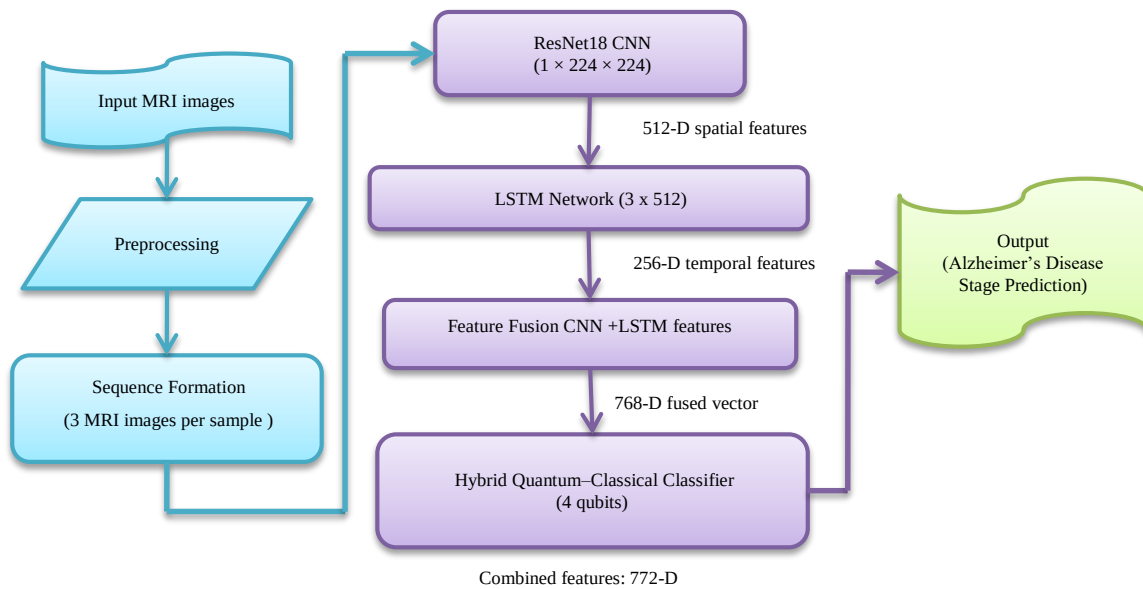


Fig. 1 Architecture of the proposed CNN-LSTM-Quantum hybrid model for AD classification

3.3. Proposed Model

The proposed system combines CNN-based spatial feature extraction, sequence learning using LSTMs, and a hybrid quantum-classical classifier for Alzheimer's disease classification. The input samples are a series of three grayscale MRI images with a $1 \times 224 \times 224$ size per image. The complete architecture of the proposed system is depicted in Figure 1.

3.3.1. Algorithm: Proposed CNN-LSTM-Quantum Framework

Input : Pre-processed MRI image sequence
Output : Alzheimer's Disease class

1. Load the pre-processed MRI image sequence.
2. Extract spatial features using the ResNet-18 network.
3. Arrange the extracted features into sequences of length three.
4. Pass the feature sequences through a two-layer LSTM network.
5. Obtain the temporal feature representation from the final LSTM layer.
6. Fuse the spatial and temporal feature representations.
7. Project the fused features into the quantum embedding space.

8. Apply parameterized quantum operations to generate quantum feature representations.
9. Concatenate the quantum features with the classical fused features.
10. The merged feature representation is processed by a fully connected neural network, and the final class prediction is generated through the Softmax activation function.
11. Return the predicted Alzheimer's disease class.

3.3.2. ResNet-18 Convolutional Neural Network (CNN)

The CNN part of the proposed model uses the ResNet-18 architecture, which is well-suited for medical image analysis, particularly those from MRI scans of the brain, due to its excellent feature extraction ability. The first layer of the CNN model was modified to suit grayscale brain MRI images, and the model weights were initialized using an ImageNet-pretrained model. Every input image for the ResNet-18 architecture is a grayscale image with dimensions of $1 \times 224 \times 224$ pixels, as illustrated in Figure 2.

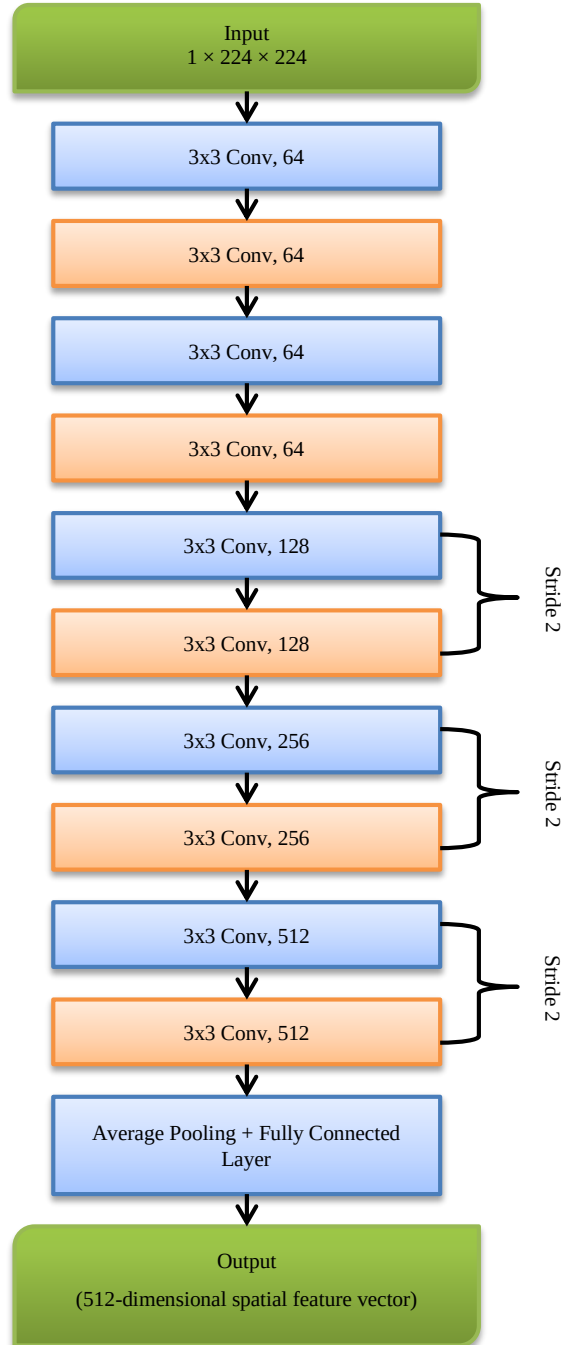


Fig. 2 ResNet-18 CNN architecture

Since the proposed system is an image sequence system, ResNet-18 processes images independently. The final output from the convolution, residue, and other layers for every image is a 512-dimensional spatial vector, which can be written as Equation (1):

$$f_i = F\theta(X_i) \quad f_i \in \mathbb{R}^{512} \quad (1)$$

The resulting 512-dimensional feature vectors extracted from each of these images are stacked together and passed on to the LSTM network. These features serve as input to learn sequences in a temporal manner, where the MRI images capture the corresponding temporal or contextual characteristics. Also, the ResNet-18 model, with the help of the residual connections, not only assists in stable training but also enhances the quality of the extracted features. It, in turn, improves the performance of the next step, consisting of LSTM networks.

3.3.3. Long Short-Term Memory Network (LSTM)

The spatial feature vectors derived from the ResNet-18 CNN are then fed into a two-layer LSTM network to capture the sequential and contextual information. The LSTM is employed in this model to capture the dependencies within a sequence by virtue of its internal memory, and this comes in handy in a situation where multiple MRI images are provided as input to the proposed model. The LSTM takes as input a sequence of feature vectors; each feature vector has 512 dimensions. As the sequence has three features, the LSTM has an input of 3×512 for each sample. The initial LSTM layer takes the features and derives the high-level information of the sequence, which the second layer then refines to form a compact representation of the features.

After processing the entire sequence, the feature vector of dimension 256 is obtained from the LSTM, which captures the context among all the MRI images in the sequence. The feature vector is obtained from the last time step of the second layer of the LSTM network, which efficiently captures all sequential information observed from the input features. The temporal feature representation can be expressed as in Equation (2):

$$h_t = f(x_1, x_2, x_3) \quad (2)$$

Where $x_1, x_2, \dots, x_T$ are the feature vectors of the sequence, and h_T is the hidden state generated after processing the whole sequence. This generated temporal feature vector is subsequently moved to the feature fusion stage, where it is fused with the spatial features derived from the CNN.

Through this integration of the temporal aspect with the spatial features, the model obtains a more holistic representation of the patterns of AD as they appear in the MRI images.

3.3.4. Feature Fusion Strategy

After the processing carried out in the LSTM, there will be two types of features to explore, and these will include the spatial features generated from the CNN as well as the temporal features generated from the LSTM. These spatial features will include structural details from the MRI images, while the temporal features will include the relationships within the images. The spatial features are calculated by averaging the 512-dimensional CNN feature vectors extracted from the three images in the sequence.

The temporal features are extracted from the final output of the LSTM, which gives an output of a 256-dimensional vector. The spatial features and the temporal features are then concatenated to form the fused feature representation with a dimensionality of 768. The fusion of the feature vector provides both anatomical and sequence information about Alzheimer's disease, thereby providing a more comprehensive representation of the data. These features are then taken forward to the hybrid quantum-classical classifier for the final prediction of the stage of the disease.

3.3.5. Hybrid Quantum-Classical Classification Model

The architecture of the Hybrid Quantum-Classical Classifier is presented in Figure 3 below. The discriminative power of the combined features extracted from CNN-LSTM is improved through the use of quantum feature encoding along with classical deep learning. First, the ResNet-18 architecture is used to extract spatial features (FCNN), while the stacked LSTM architecture is used for the extraction of temporal features (FLSTM). The fused feature representation is created through the concatenation of both feature representations, as expressed in Equation (3).

$$F_{fusion} = [F_{CNN}, F_{LSTM}] \quad (3)$$

For reducing the dimension of features prior to quantum computation, the fused feature vector is projected into a lower dimension space by means of a fully connected projection layer. The reduced feature vector is encoded in a four-qubit quantum state by means of angle encoding with the help of quantum rotation gates. The quantum state is prepared as shown in Equation (4).

$$|\psi\rangle = U(x)|0\rangle^{\otimes 4} \quad (4)$$

Where $U(x)$ refers to the quantum encoding transformation that transforms the classical inputs into the quantum states.

After performing the angle encoding step, the expectation value of the Pauli-Z observable is determined for each qubit to produce the quantum feature vector, as expressed in Equation (5):

$$F_Q = \langle \psi | M | \psi \rangle \quad (5)$$

Where M represents the Pauli-Z Measurement Operator, this quantum feature vector is then concatenated with the classical fusion features to give the final hybrid feature representation, as given in Equation (6):

$$F_{Hybrid} = [F_{fusion}, F_Q] \quad (6)$$

Lastly, the hybrid feature vector is provided as input to a fully connected neural network. having linear, ReLU, dropout, and output layers to get Alzheimer's disease class scores, as defined in Equation (7):

$$Y = f(F_{Hybrid}) \quad (7)$$

Where $f(\cdot)$ indicates the fully connected classification network and Y shows the class scores for the four AD categories.

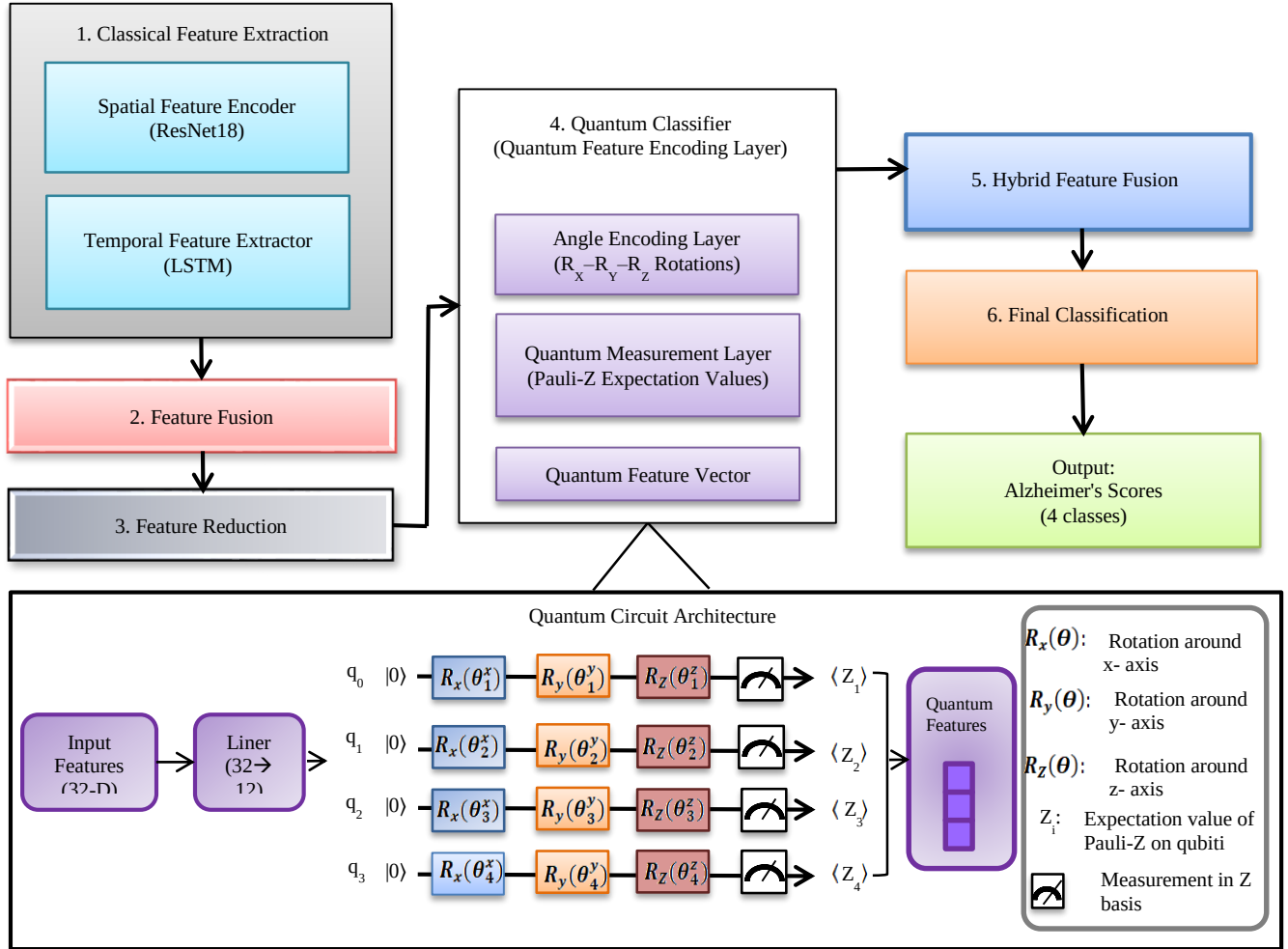


Fig. 3 Proposed hybrid quantum-classical classification framework

4. Results

The suggested model was built with the help of Python 3.10 programming language, along with the PyTorch framework for building deep neural networks. The experiments were performed within the Kaggle Notebook interface, using GPU acceleration. For the implementation, various libraries such as NumPy, OpenCV, Scikit-learn, Matplotlib, and Torchvision have been used. The overall number of parameters in the proposed framework is equal to 19,205,552. From the total number of parameters, the ResNet-

18 model with LSTM Feature Extractor has 18,782,656 parameters, while the Quantum Fusion Classifier has 422,896 parameters, as summarized in Table 2. Among the total parameters, 18,832,752 are trainable parameters, which are optimized during the training process, while 372,800 are non-trainable parameters of fixed layers. To assess the performance of the proposed CNN-LSTM-Quantum hybrid system on classification, a balanced set of brain MRI images representing different stages of AD was considered. Moreover, an identical set of samples for every stage was

considered to remove imbalanced classification. Also, it was ensured that an identical set of samples corresponding to every stage was considered for validation. This adopted approach helps to minimize biases during both train and validation stages. This would allow a fair assessment of system performance. Under these circumstances, the proposed system was able to attain a final accuracy of 98.88% during testing.

Table 2. Parameter summary of the proposed CNN-LSTM quantum model

Component	Total Parameters
ResNet-18 + LSTM Feature Extractor	18,782,656
Quantum Fusion Classifier	422,896
Total Parameters	19,205,552

4.1. Training and Validation Performance

Figure 4 below is a graph that depicts the training and validation loss trends of the proposed CNN-LSTM-Quantum model as it trains through each epoch. The training loss drops dramatically during the initial stages of training, and this indicates a proper capture of distinctive feature information within the MRI image sequences.

Additionally, with continued training of the model, there is a steady drop in the training loss until it levels off. The same applies to the validation loss that steadily drops with every epoch of training and is lower compared to the training loss. This indicates a proper test of the model with no overfitting. The proximity of the two curves indicates a proper training of the model.

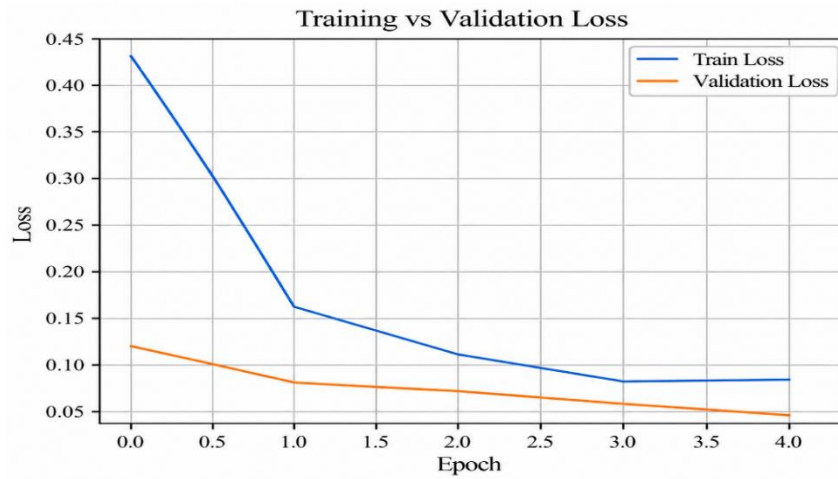


Fig. 4 Training and validation loss trends of the CNN-LSTM-Quantum hybrid framework

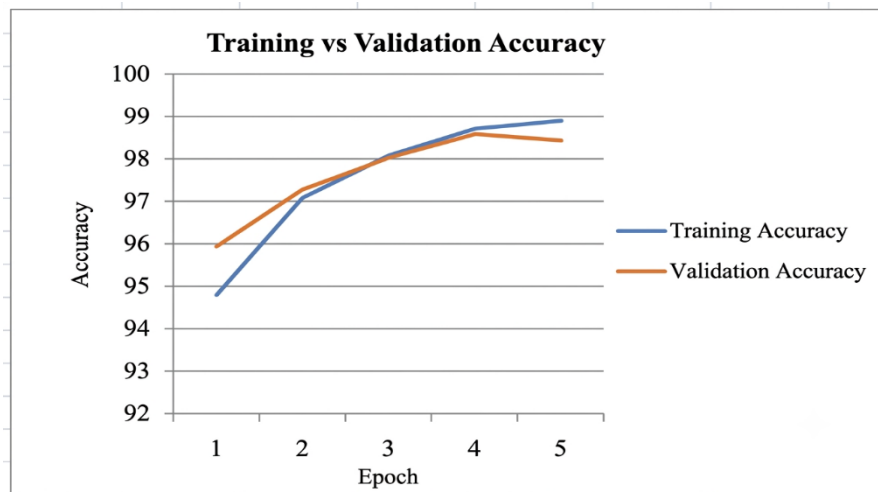


Fig. 5 Training and validation accuracy graph of the proposed CNN-LSTM-Quantum hybrid model across training epochs

Figure 5 illustrates the training and validation accuracy curves of the proposed model over five training epochs. There is a steady rise in both the accuracies, which clearly indicates that the model effectively learns the discriminative features.

The validation accuracy is 98.44%, whereas the training accuracy attains a value of 98.9% in the fifth epoch. The overlapping nature of the curves clearly indicates stable convergence and good generalization ability.

4.2. Confusion Matrix Evaluation

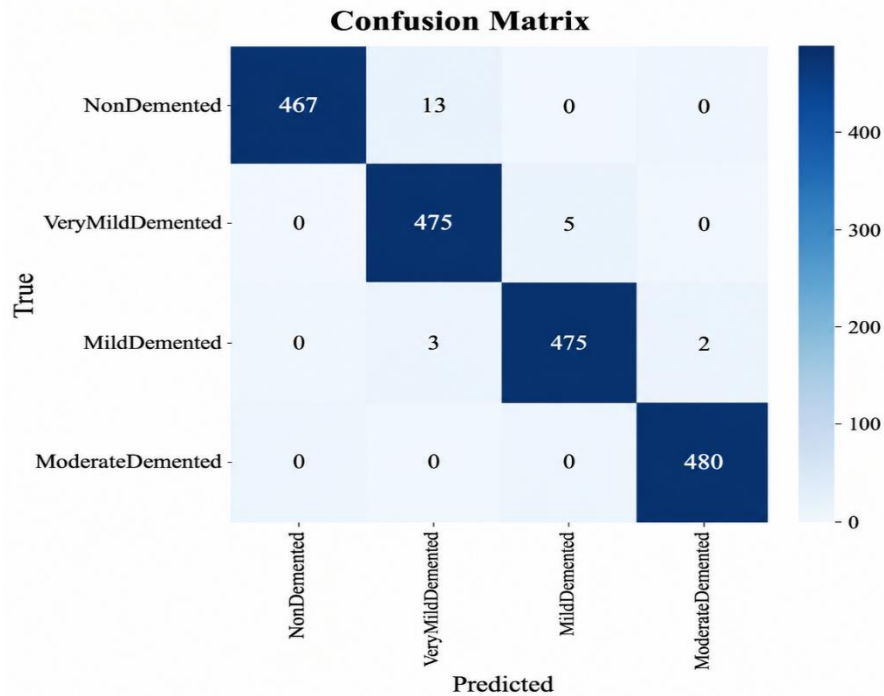


Fig. 6 Confusion matrix of the proposed CNN-LSTM-Quantum hybrid model

Figure 6 presents the confusion matrix obtained for the CNN-LSTM-Quantum hybrid model evaluated on the test dataset. Each row indicates the actual class of Alzheimer's disease, and each column represents the predicted class. One may notice that strong values exist on the diagonal, indicating the correct classification of most MRI images. Specifically, 467 Non-Demented, 475 Very Mild Demented, 475 Mild Demented and 480 Moderate Demented images are correctly predicted. Only a few misclassifications between clinical

stages are noticed, such as a few Non-Demented subjects being predicted into Very Mild Demented, along with minor confusion between Very Mild and Mild Demented classes. Apparently, no misclassifications occur in the Moderate Demented class. Overall, the confusion matrix indicates excellent performance of the classifier, showing very balanced and excellent classification of the model within all the classes regarding distinguishing the different stages of Alzheimer's disease.

4.3. Feature Visualization using t-SNE

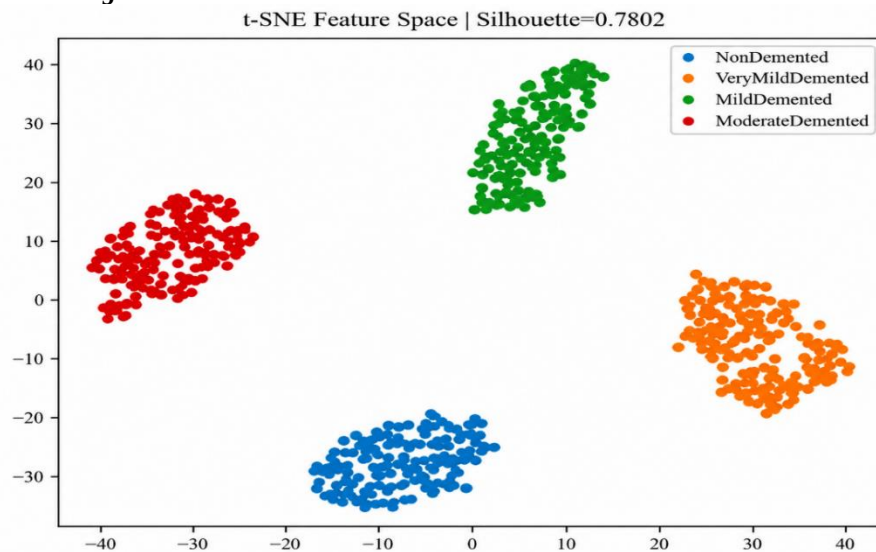


Fig. 7 t-SNE visualization of feature separation across Alzheimer's disease stages

Figure 7 represents the t-SNE plot obtained for the feature learning capability of the hybrid CNN-LSTM-Quantum model. The points in the graph indicate feature vectors derived from the MRI image sequences, which are color-coded based on their stages of AD. The compact and separated clusters for the different classes demonstrate that the model is successful in learning distinctive features.

There is no overlapping region between the clusters, which represents high separability among the stages of AD. This is also evident from the silhouette value of 0.7802.

4.4. Performance Evaluation and Comparative Analysis

The classification report shown in Table 3 highlights the overall performance of the proposed framework across the different stages of AD is evaluated. The model achieves high

precision, recall, and F1-score for each class, demonstrating its correct and well-balanced performance. Non-Demented patients perform exceedingly well, requiring minimal misclassification, and for the Very Mild and Mild Demented classes, the predictions are correct with a score of 0.980 and 0.990, respectively. Moderate Demented class patients are correctly classified. Overall, the proposed model attains a performance of approximately 99% for the test images of 1,920.

Table 4 presents a comparative analysis of the proposed model with recent studies on AD classification. The proposed CNN-LSTM-Quantum hybrid model secured the best classification accuracy rate of $98.9\% \pm 0.7$, indicating the efficiency of the proposed hybrid approach for classifying AD at various stages.

Table 3. Classification report of the proposed CNN-LSTM-Quantum hybrid model on the test dataset

Alzheimer's Class	Precision	Recall	F1 -Score	Support
Non Demented	1.00	0.97	0.99	480
Very Mild Demented	0.97	0.99	0.98	480
Mild Demented	0.99	0.99	0.99	480
Moderate Demented	1.00	1.00	1.00	480
Accuracy	-	-	0.99	1920

Table 4. Comparison of the proposed CNN-LSTM-Quantum hybrid model with recent AD detection methods

Author	Models used	Dataset	Accuracy
Zadeh et al. (2025) [23]	Quantum Support Vector Machine (QSVM)	ASD Tests Dataset	96.7%
Jumaili et al. (2025) [24]	Deep learning ensemble model	OASIS	86.0%
Ali et al. (2024) [25]	EfficientNet-B0 + MobileNet-V2	MRI Dataset	94.7%
Mmadumbu et al. (2025) [26]	Custom CNN-based model	ADNI	96.19%
Srijeet Goswami et al. (2025) [27]	Custom 12-Layer CNN	MRI Dataset	97.80%
Proposed Model	CNN-LSTM-Quantum Hybrid Model	Balanced MRI Dataset	$98.9\% \pm 0.7$

4.5. Discussion of Model Robustness and Generalization

The hybrid approach of CNN-LSTM-Quantum achieves robust and stable performance when classifying multiclass Alzheimer's disease cases. Combining the benefits of spatial, sequence, and quantum-based feature learning allows the model to differentiate among subtle differences in the disease's progression while achieving reliable classification results. Stable results across all performance metrics indicate good generalization of the approach on the test data. The experimental findings indicate that the proposed model performs Alzheimer's disease classification with high effectiveness.

5. Conclusion

In this paper, a hybrid CNN-LSTM-Quantum model is presented for performing the classification of AD using MRI images of the brain. By exploring both spatial features and temporal sequences with quantum-inspired classification, it overcomes certain limitations regarding class imbalance, the unavailability of temporal modeling, and poor generalization.

Performance evaluation on the fully balanced dataset exhibited an excellent performance with a test accuracy of 98.9%, as well as high precision, recall, and clear class separability.

The results indicated that the proposed hybrid framework provided a feasible and effective approach for the timely and reliable identification of AD. It would have promising implications for future clinical decision-making systems.

The future work will concentrate on utilizing advanced feature engineering and data balancing approaches in order to achieve an even greater robustness of the suggested framework. An extensive ablation study is going to be performed in order to estimate the impact of each part of the hybrid CNN-LSTM-Quantum architecture. In addition, Explainable AI techniques, such as SHAP and LIME, will be incorporated to improve the explainability of the proposed framework. Finally, the proposed framework will be tested on large public benchmarks, such as ADNI and OASIS.

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