Prediction of Alzheimer's Disease Using Quantum Algorithms

Madhur Singh
School of Computer Science and Engineering
Vellore Institute of Technology
Chennai, India
madhur.singh2020@vitstudent.ac.in

Dr. Geetha S
School of Computer Science and Engineering
Vellore Institute of Technology
Chennai, India
geetha.s@vit.ac.in

***Abstract*— This paper explores the transformative potential of Quantum Support Vector Machines (QSVM) in the domain of Alzheimer's disease prediction, leveraging the unique properties of quantum computing. The study investigates the efficacy of QSVM in comparison to classical algorithms, showcasing the advantages derived from quantum parallelism, superposition, and entanglement. Through extensive evaluations, our research highlights the robust performance of QSVM in feature extraction and dimensionality reduction, crucial aspects in neurodegenerative disease prediction. The model's interpretability, achieved through quantum explainability tools, addresses concerns related to the transparency of quantum algorithms. While presenting promising results, we acknowledge challenges such as hardware dependency and sensitivity to noise. This work contributes to the growing intersection of quantum computing and healthcare analytics, pointing toward a future where quantum algorithms play a pivotal role in advancing predictive models for Alzheimer's disease and similar medical applications.**

Keywords— Alzheimer's Disease, Mild Cognitive Impairment, Quantum Computing, Quantum Support Vector Machines, VGG-Net, Transfer Learning

I. Introduction

Alzheimer's disease is the most prevalent form of dementia, posing a significant health challenge in our current era. Projections made by the authors in [1] anticipate that over 1% of the global population will suffer from Alzheimer's or related diseases by 2050. Alzheimer's manifests as a chronic neurodegenerative disorder in middle-to-old age people, though there are rare instances of early-onset cases affecting individuals aged 45–64 [2]. Progression of the disease causes cognitive decline symptoms, including memory impairment, language dysfunction, and diminishing cognition and judgment. Depending on the stage of the disease, individuals with symptoms may require varying levels of assistance in their daily lives, significantly impacting their quality of life (QOL) and that of their families. Studies on the economic burden of dementia and Alzheimer's highlight the substantial societal demand for elderly care, leading to increased overall socio-economic pressure.

The biological processes that lead to Alzheimer's can initiate more than two decades before symptoms manifest. Current insights into Alzheimer's pathogenesis revolve around the deposition of amyloid peptides and the accumulation and phosphorylation of tau proteins surrounding neurons, ultimately resulting in neurodegeneration and eventual brain atrophy. Factors associated with Alzheimer's include age, genetic predisposition, Down's syndrome, brain injuries, and cardiorespiratory fitness. The cognitive impairment linked to Alzheimer's spans three stages: (1) preclinical AD, where detectable changes in the brain, cerebral spinal fluid (CSF), and blood plasma are observable; (2) mild cognitive impairment (MCI) due to AD, marked by biomarker evidence of Alzheimer's-related brain changes; and (3) dementia due to AD, where noticeable alterations in the brain coincide with memory, thinking, and behavioural changes impacting daily function.

Mild cognitive impairment (MCI), the stage preceding dementia, is most commonly associated with Alzheimer's. However, not all cases of MCI progress to Alzheimer's. Various studies have examined the demographics and progression of MCI, revealing that 15–20% of individuals aged 65 or older experience MCI from various potential causes [3]. At a two-year follow-up, 15% of those with MCI developed dementia, while 32% developed Alzheimer's and 38% developed dementia at a five-year follow-up [4–6]. Early diagnosis of MCI and its subtypes allows for timely intervention, significantly impacting patient longevity and QOL [7]. Thus, gaining a deeper understanding of the condition and developing effective and precise diagnostic methods holds paramount public interest.

A. Existing Diagnostic Methods

The current standard for diagnosing Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI) relies on a comprehensive array of methods, forming an intricate diagnostic framework. Cognitive assessments, including widely used tools like the Mini-Mental State Examination (MMSE), Clinical Dementia Rating, and Cambridge Cognitive Examination, serve as foundational components. These assessments involve a series of questions designed to evaluate cognitive function. Coupled with physical and neurological examinations, they contribute to a holistic understanding of the patient's cognitive and behavioral changes, considering medical and family history, including genetic predisposition through techniques like genetic sequencing for biomarkers like the APOE-e4 allele.

Neuroimaging assumes a pivotal role in this diagnostic landscape by examining various indicators of brain changes and eliminating alternative causes. Techniques such as structural magnetic resonance and diffusion tensor imaging are routinely employed to detect signs of brain atrophy. Computed tomography (CT) in various forms is also part of the diagnostic repertoire. Positron emission tomography (PET) includes FDG-PET, assessing brain glucose metabolism, and amyloid-PET, measuring beta-amyloid levels. Single-photon emission computed tomography (SPECT), though cautiously used due to potential false-positive results, can be considered in diagnosis. It's common practice to combine multiple imaging modalities to leverage their respective strengths.

Recent advancements in diagnostics include the integration of cerebrospinal fluid (CSF) and blood plasma biomarkers like Amyloid-β42, t-tau, p-tau, neurofilament light protein (NFL), neuron-specific enolase (NSE), and HFABP. While CSF biomarkers are increasingly integral, the definitive diagnosis remains post-mortem.

In contemporary medical research, meticulous preprocessing and biomarker extraction, followed by rigorous statistical analysis, are standard practices. Studies like Gupta et al. [8] and Cui Y et al. [9] exemplify this approach, utilizing advanced methods to analyze biomarkers extracted from various imaging modalities.

Machine learning has become a key player in automated diagnostic algorithms, adapting to data and generalizing knowledge with reduced dependence on expert experience. Algorithms like Support Vector Machine (SVM) and penalized regression with resampling have been validated for dementia diagnosis [10,11]. Zhang et al. [12], Liu et al. [13], and Zhang et al. [14] propose innovative approaches, combining heterogeneous biomarkers for classification with linear SVM, introducing the Multifold Bayesian Kernelization (MBK) algorithm, and employing eigenbrain extraction with polynomial kernel SVM and particle swarm optimization.

Deep learning, a recent frontier, has garnered substantial interest in AD diagnostics. It integrates feature extraction and classification into neural networks, offering automated abstraction of features at various levels. Feng et al. [39] showcase the potential of deep learning in extracting biomarkers from MRI, surpassing traditional neuroimaging biomarkers in discerning amyloid and tau pathology, and neurodegeneration in prodromal AD. This collective arsenal of diagnostic methods underscores the multidimensional approach taken in the pursuit of accurate AD and MCI diagnosis.

B. *Introduction to Quantum Computing*

Quantum computing (QC) is fundamentally grounded in the principles of quantum mechanics, often elucidated through the concepts of superposition, interference, and entanglement. In the realm of quantum physics, a quantum bit, or qubit, can exist in multiple states simultaneously, representing both 1 and 0 at a given time. Exploiting this unique behavior, QC systems harness the power of qubits. Rooted in quantum physics, quantum computing holds the promise of becoming the cornerstone of future computing infrastructures, ushering in an era of immensely powerful systems capable of real-time processing of vast datasets. Researchers have recently exhibited a heightened interest in quantum computing as they seek to propel computational capabilities beyond the confines of Moore's law. However, a comprehensive and systematic survey is imperative to elucidate the potential, challenges, and pitfalls inherent in this evolving field.

C. *Applications of Quantum Computing in Healtcare*

Quantum computing (QC) stands out as exceptionally well-suited for various compute-intensive applications in healthcare, particularly within the prevalent Internet of Things (IoT) paradigm in digital healthcare. This paradigm encompasses interconnected medical devices, such as sensors, linked to the Internet or the cloud. The substantial increase in computational capacity not only benefits healthcare IoT but also holds the potential for quantum computers to drive fundamental breakthroughs in the field. Transitioning from classical bits to quantum bits (qubits) could significantly enhance healthcare pharmaceutical research. This improvement spans the analysis of protein folding, molecular structure examinations (e.g., drugs and enzymes), determination of binding strengths between biomolecules (e.g., proteins or DNA) and their ligands or binding partners (e.g., drugs or inhibitors), and acceleration of clinical trial processes. Noteworthy applications include rapid DNA sequencing, paving the way for personalized medicine, detailed modeling for therapeutic development, and the creation of efficient real-time imaging systems for clinicians. Quantum computing's capabilities extend to solving intricate optimization problems, such as devising optimal radiation plans to target cancer cells precisely. QC facilitates the study of molecular interactions at the most granular level, revolutionizing drug discovery and medical research. While whole-genome sequencing is traditionally time-consuming, qubits offer the potential to expedite this process. Quantum computing's transformative impact on healthcare extends to on-demand computing, redefined medical data security, predictive analysis of chronic diseases, and precise drug discovery methods.

II. Literature Review

The literature survey on Alzheimer's disease prediction and diagnosis encompasses a range of studies employing diverse methodologies. Visser et al. [15] and DeCarli et al. [16] identified medial temporal lobe atrophy as a predictor of Alzheimer's disease, while Walhovd et al. [17] integrated multiple modalities for enhanced diagnostic accuracy. Huang et al. [18] explored altered brain connectivity, and Zhang et al. [19] demonstrated improved classification through multimodal approaches. Wee et al. [20] and Zhang and Shen [21] investigated resting-state functional connectivity and multi-task learning, respectively. Machine learning frameworks [22,23] and deep learning techniques [24,25] were employed for predicting disease progression. Longitudinal analysis [26] and feature selection [27] provided insights into disease dynamics. Additionally, studies by Challis et al. [28], Sarraf and Tofighi [29], and Hosseini-Asl et al. [30] utilized Gaussian process classification, deep convolutional neural networks, and deeply supervised networks, respectively, for disease classification. The literature also explores the association of amyloid levels with cognitive decline [31], automated detection of mild cognitive impairment [32], and the prediction of cognitive performance based on brain network patterns [33]. Recent studies [34,35,36] highlight the predictive value of baseline structural MRI, plasma biomarkers, radiomic biomarkers, and resting-state functional connectivity. Efficient brain age prediction [37] and interpretable deep learning models [38] further contribute to the evolving landscape of Alzheimer's disease research, collectively advancing the development of accurate and early diagnostic tools.

III. Quantum Computing : History & Background

A. *Difference Between Quantum Computing and Classical Computing*

In Figure 1, a comprehensive distinction between quantum computing paradigms and classical computing approaches is presented, delineating their strengths, weaknesses, and applicability. Unlike traditional computers relying on bits, quantum computers operate using quantum bits or "qubits," which can exist in both '1' and '0' simultaneously. Quantum bits are created using quantum physical systems, such as the orientation of a photon or the spin of an electron. Quantum computers come in various types, including one-qubit, two-qubit, and higher-qubit systems, with significant advancements since the invention of the first 5-qubit quantum computer in the early 2000s. IBM's latest quantum-computing chip boasts 433 qubits, although achieving quantum supremacy, defined as the ability to solve problems beyond classical computers' capabilities in a feasible time, requires a minimum of 50 qubits.

Quantum Computing	Classical Computing
Calculates with Qubits, that can have values 0 o1 or both simultaneously	Calculates with transistors, that can have values either 0 or 1
Power increases exponentially in proportion to the number of Qubits	Power increases linearly with the number of transistors
Have high error rates	Have lower error rates
Operates at close to absolute zero temperature	Operates at room temperature
Much secured to work with	Less secured to work with
Suited for big/complex tasks, such as-optimization problems, data analysis and simulations	Suited for everyday processing tasks

Fig. 1. Comparison of Classical Computing and Quantum Computing

The behaviour of qubits is intricately linked to the behaviour of a spinning electron orbiting an atom's nucleus, showcasing three key quantum properties: quantum superposition, quantum entanglement, and quantum interference. Quantum superposition involves the probabilistic distribution of a spinning electron's position across all locations simultaneously, allowing qubits to exist in linear combinations of '0' and '1' states. Quantum entanglement, described by Einstein as "spooky action at a distance," enables instantaneous information transfer between highly linked pairs of systems, contributing to quantum computers' increased computational efficiency. Quantum interference, a consequence of particles' wavelike properties at the subatomic scale, is harnessed in quantum computing to manipulate probability amplitudes during qubit energy level measurements.

Quantum computing's applications span various disciplines, including communication, image processing, information theory, electronics, and cryptography. The increasing availability of quantum computers is fostering the development of practical quantum algorithms. Quantum computing holds immense potential to revolutionize verticals such as financial modelling, weather prediction, physics, and transportation (Figure 2 provides an illustrative overview of key verticals). It has already demonstrated enhancements to nonquantum algorithms in these domains. Furthermore, ongoing efforts to envision physically scalable quantum computing hardware underscore the potential for a fully realized quantum paradigm to address intractable computing challenges with existing resources.

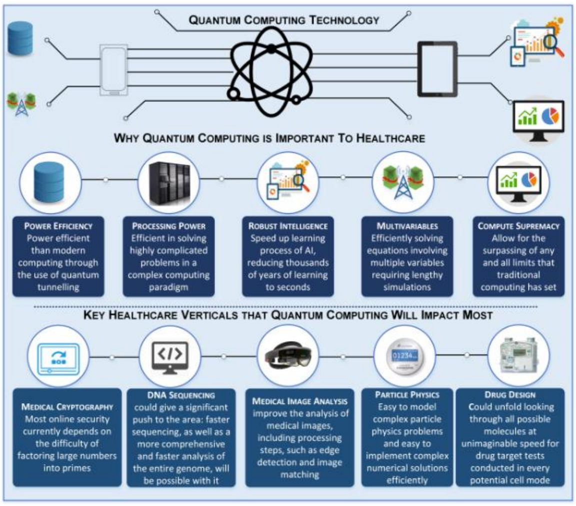

Fig. 2. Quantum Computing in Healthcare

IV. QUANTUM COMPUTING IN HEALTHCARE

Recent research indicates a distinct advantage of quantum computing over classical computing systems. Quantum computing not only offers an incremental acceleration in disease diagnosis and treatment but, in certain scenarios, can significantly reduce computation times from years to mere minutes. This technological advancement stimulates innovative approaches, enabling a higher level of proficiency in specific tasks, introducing novel architectures, and shaping new strategies. The vast potential of quantum computing extends across various healthcare applications, presenting valuable opportunities for both the broader health sector and specialized healthcare service providers. Particularly, it proves beneficial in realms such as expedited diagnoses, personalized medicine, and optimization of costs. A comprehensive literature survey underscores the discernible rise in the utilization of classical modeling and quantum-based methodologies. This surge is primarily attributed to enhanced access to global health-related data sources and increased data availability. In this context, the following section elucidates potential use cases, demonstrating the applications of quantum computing in healthcare. A visual representation of these use cases is thoughtfully presented in Figure 4.

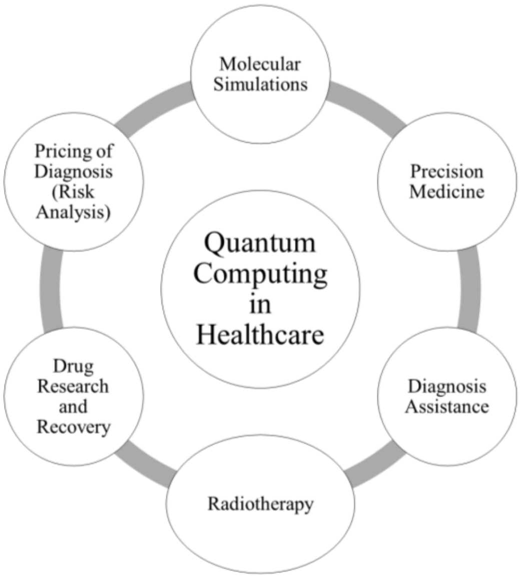

Fig. 3. Taxonomy of Quantum Computing in Healthcare

A. Precision Medicine

Precision medicine, a domain focused on tailoring prevention and treatment strategies to individuals' healthcare needs, is becoming increasingly vital as the complexity of the human biological system necessitates personalized approaches beyond standard medical treatments. Classical machine learning (ML) has demonstrated efficacy in predicting future disease risks through electronic health records. However, challenges such as data quality, noise, feature size, and intricate feature relations limit the effectiveness of classical ML. This prompts consideration of quantum-enhanced ML, offering the potential for more precise and detailed early disease detection. Quantum-enhanced ML could empower healthcare professionals to assess the impact of risks on individuals as conditions change through continuous virtual diagnosis based on real-time data streams. Ongoing research on drug sensitivity, especially at the cellular level considering genomic features of cancer cells, aims to uncover chemical properties for predicting cancer efficiency in a granular manner. Quantum-enhanced ML holds the promise of accelerating breakthroughs in healthcare, particularly in developing inference models for drug efficacy.

Precision medicine strives to elucidate relationships between causes and treatments, predicting individualized courses of action. Traditional symptom-based diagnosis often leads to umbrella diagnoses with occasional treatment failures. Quantum computing can leverage continuous data streams to enable personalized interventions for disease prediction and relevant treatment strategies. Quantum-enhanced predictive medicine optimizes and personalizes healthcare services through continuous care. Quantum-enhanced modeling supports patient adherence and engagement in individual-level treatments. A use case of quantum-computing-based precision medicine illustrates its potential transformative impact on healthcare.

B. Radiotherapy

Radiation therapy stands as a crucial modality in cancer treatment, utilizing radiation beams to target and eliminate cancerous cells, impeding their proliferation. The intricacy of radiotherapy lies in its demand for highly precise computations, ensuring accurate delivery of the radiation beam to cancerous tissues while sparing surrounding healthy cells. Radiography, facilitated by sophisticated computers, poses a precision-driven optimization challenge, necessitating intricate simulations for optimal solutions. Quantum computing introduces a transformative dimension by enabling simultaneous simulations, providing the capability to formulate optimal plans in a significantly reduced timeframe. This quantum paradigm holds vast potential for revolutionizing the field of simulations, particularly in the context of radiography optimization.

C. Molecular Simulations

Quantum computers represent a paradigm shift in data processing, utilizing quantum bits (qubits) to operate in a fundamentally different manner compared to classical computing, where processing speed is determined by integrated circuits [50]. In contrast to classical computing's binary storage of information (0s and 1s), quantum computers leverage the phenomenon of quantum entanglement. This unique feature gives rise to quantum algorithms that counter classical computing limitations, as classical systems are not designed to harness the benefits of entanglement. In the healthcare industry, quantum computers hold the potential to leverage machine learning (ML), optimization, and artificial intelligence (AI) for the execution of intricate simulations. Healthcare processes often involve complex correlations and interconnected molecular structures with interacting electrons. The computational demands for simulations and related operations in this domain inherently grow exponentially with problem size, with time being a critical limiting factor. Thus, we posit that quantum computing-based systems are a natural and advantageous fit for such healthcare applications.

D. Diagnosis Assistance

Early disease diagnosis is crucial for improved prognosis, treatment outcomes, and reduced healthcare costs. Research indicates a fourfold decrease in treatment costs and a ninefold increase in survival rates when diseases like colon cancer are diagnosed at an early stage. However, current diagnostic and treatment approaches for many diseases are slow, costly, and prone to deviations of around 15–20%. The reliance on X-rays, CT scans, and MRIs, coupled with the rapid development of computer-aided diagnostics, introduces challenges related to noise, data quality, and replicability. Quantum-assisted diagnosis emerges as a promising solution, capable of analyzing medical images, enhancing processing steps such as edge detection, and improving image-aided diagnosis.

Current diagnostic techniques often employ single-cell methods, necessitating analytical approaches for single-cell sequencing data and flow cytometry. These methods require advanced data analytics, especially when combining datasets from different techniques. Cell classification based on biochemical and physical attributes poses a significant challenge, particularly for critical diagnoses like distinguishing cancerous cells from healthy ones. Quantum machine learning (ML) techniques, such as quantum vector machines (QVM), facilitate these classifications, enabling single-cell diagnostic methods. The identification and characterization of biomarkers open avenues for studying intricate omics datasets (metabolomics, transcriptomics, proteomics, and genomics), resulting in an expanded feature space with complex patterns and correlations that classical computational methodologies struggle to analyze.

In the diagnostic process, quantum computing can provide valuable support by offering insights that eliminate the need for repetitive diagnoses and treatments. This paradigm enables continuous monitoring and analysis of individuals' health, facilitating meta-analysis for cell-level diagnosis to determine the most effective procedures at specific times. This not only helps in cost reduction but also allows for extended data-driven diagnosis, delivering value for both medical practitioners and individuals.

E. *Drug Research and Discovery*

Quantum computing provides a groundbreaking approach for medical practitioners to model atomic-level molecular interactions, revolutionizing medical research in areas such as diagnosis, treatment, drug discovery, and analytics. With recent advancements, quantum computing allows the encoding of tens of thousands of proteins and the simulation of their interactions with drugs at an unprecedented scale, significantly outperforming conventional computing capabilities. This breakthrough empowers doctors to efficiently compare vast datasets and permutations simultaneously, identifying optimal patterns for disease-specific biomarker detection using methods like bio-barcode assays with gold nanoparticles.

In the realm of pharmaceuticals, identifying molecules that form drugs for treating or curing diseases is a critical task. Traditional drug discovery methods, often relying on fortuitous discoveries, face challenges related to climate change and emerging viruses like COVID-19. Classical computers struggle with the precise modeling of energy dissipation in chemical reactions due to the computational intensity involved in quantum behavior calculations. Quantum computers, on the other hand, reliably model properties of small molecules, such as lithium hydride, demonstrating high accuracy in simulating complex wave functions. Quantum algorithms for chemistry, estimating ground-state energies and computing molecular reaction rates, surpass their classical counterparts. Notably, research by Huggins et al. showcases the ability to accurately compute circuitry exhibiting noise using quantum chemistry on Google's 53-qubit quantum computer, simulating complex molecules like H4, molecular nitrogen, and solid diamond with up to 120 electron orbitals.

F. *Risk Analysis*

Establishing effective pricing strategies is a pivotal challenge in the intricate landscape of the healthcare ecosystem. Quantum computing plays a transformative role in pricing analysis, particularly in risk assessment by predicting an individual's current health status and susceptibility to specific diseases. This predictive capability proves invaluable for optimizing insurance premiums and pricing structures. At a population level, quantum-based risk models can contribute to finely tuned computations of financial risks and pricing models. Detection of fraud stands out as a crucial application; healthcare frauds incur substantial financial losses. While traditional data mining techniques offer insights, quantum computing elevates classification and pattern detection, enhancing the identification of fraudulent medical claims. This, in turn, aids in refining pricing models and mitigating costs associated with fraudulent activities. Quantum computing not only expedites pricing computations but also facilitates the development of customized plans, contributing to both cost reduction and improved management of pricing strategies.

V. Materials And Methods

A. *Dataset Used*

The data utilized in this research is sourced from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database, initiated in 2003 as a collaboration between the National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the Food and Drug Administration (FDA), private pharmaceutical companies, and non-profit organizations. ADNI's primary objective is to evaluate the combined use of serial MRI, PET, biological markers, and clinical and neuropsychological assessments for measuring the progression of Mild Cognitive Impairment (MCI) and early Alzheimer's Disease (AD). Led by Principal Investigator Michael W. Weiner, MD, the initiative involves numerous co-investigators from various academic institutions and private corporations, with subjects recruited from over 50 sites across the U.S. and Canada.

The initial goal of ADNI was to recruit 800 subjects, leading to subsequent phases such as ADNI-GO and ADNI-2. These protocols have collectively recruited over 1500 adults aged 55 to 90, encompassing cognitively normal older individuals, those with early or late MCI, and individuals with early AD. The follow-up duration for each group is specified in the ADNI-1, ADNI-2, and ADNI-GO protocols.

The diagnostic classification involves subjects grouped into categories: AD (Alzheimer’s Disease), NC (Normal Cognitive) and MCI (stable MCI). The detailed characteristics of the ADNI sample used in this research are provided in Table 1. This comprehensive dataset offers a diverse representation of individuals across cognitive states and serves as a valuable resource for investigating Alzheimer's disease progression and developing effective diagnostic models.

TABLE I. Characteristics of Data Used

Class Label of T1-MRI Images	Number of Images Used
AD	1124
NC	1440
CI	2590

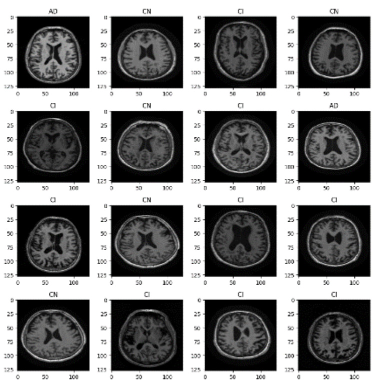

Fig. 4. Visualising MRI Images in Axial Plane

B. *Convolutional Neural Networks*

A Convolutional Neural Network (CNN) operates as a feed-forward artificial neural network, drawing conceptual inspiration from the visual cortexes of animals. Specifically designed for image processing and low-dimensional data (commonly one or two-dimensional), CNNs function by emulating the segmentation-based response mechanism observed in basic neurons. Instead of responding to the entire input, a CNN neuron aggregates activations from non-overlapping segments, generating a feature map. While CNNs yield commendable results in practical recognition tasks, the layering of networks introduces a challenge—the feature extraction process becomes increasingly opaque as layers accumulate. The extraction of high-order features tends to exhibit a degree of ambiguity, contributing to the perceived "black box" nature of the model.

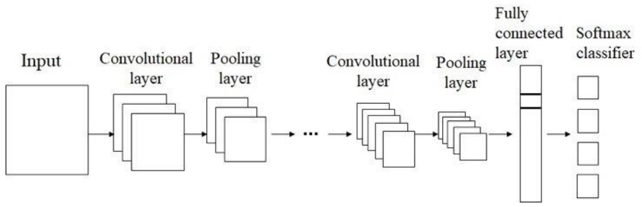

Fig. 5. Structure of Convolutional Neural Network

1) *VGG Net*

In 2013, Karen Simonyan and Andrew Zisserman introduced the VGG network, unveiling the actual model during the 2014 ImageNet Challenge. The nomenclature "VGG" pays homage to the Visual Geometry Group at the University of Oxford, the academic department they were affiliated with. This model marked a departure from preceding top-performing models, namely AlexNet-2012 and ZFNet-2013. Notably, VGG proposed the pervasive use of a small 3 x 3 receptive field (filters) with a stride of 1 pixel across the entire network, a departure from the larger receptive fields in the initial convolutional layers of its predecessors.

The innovation lies in the uniform application of 3 x 3 filters, providing flexibility in creating effective receptive fields. The amalgamation of two consecutive 3 x 3 filters, for instance, results in a receptive field of 5 x 5, and three filters yield a receptive field of 7 x 7. This strategic combination enables a synthesis of multiple 3 x 3 filters to substitute for larger receptive areas, emphasizing the model's adaptability.

Contrary to concerns about increased complexity, the approach offers advantages. Incorporating three convolution layers with three corresponding non-linear activation layers enhances discriminative decision functions, promoting faster convergence during training. Additionally, the strategy significantly reduces the number of weight parameters in comparison to a single 7 x 7 layer, concurrently acting as a regularization mechanism and mitigating the risk of overfitting.

Addressing the possibility of smaller receptive size filters, it is affirmed that 3 x 3 is deemed the minimal size essential for capturing spatial relationships effectively, ensuring a comprehensive understanding of left-to-right and top-to-down features in the image. The consistent utilization of 3 x 3 convolutions throughout the network underscores VGG's simplicity, elegance, and user-friendly characteristics, making it an influential and accessible model in the field of convolutional neural networks.

C. *Quantum Support Vector Machines*

Quantum Support Vector Machines (QSVMs) operate on the foundational principle of classical Support Vector Machines (SVMs), aiming to discover a hyperplane within a high-dimensional space that maximally segregates distinct classes. Nevertheless, QSVMs diverge by leveraging the computational capabilities of quantum computers to execute the optimization necessary for identifying the hyperplane. This optimization process entails minimizing the objective function, defined as the sum of squared distances between points and the hyperplane, while adhering to specific constraints.

The quantum optimization in QSVMs is orchestrated by the quantum gradient descent algorithm, a quantum variant of the classical gradient descent, which iteratively fine-tunes the hyperplane parameters to minimize the objective function. The inherent parallelism of quantum computers endows the quantum gradient descent algorithm with faster convergence compared to classical counterparts.

A pivotal aspect of QSVMs revolves around the concept of the kernel function, a metric gauging the similarity between two points. This function is instrumental in mapping points from the original space to a higher-dimensional feature space, facilitating the identification of the hyperplane. Commonly employed kernel functions in QSVMs encompass the linear kernel, polynomial kernel, and radial basis function (RBF) kernel.

Another fundamental element in QSVMs is the margin, denoting the distance between the hyperplane and the closest points. The margin serves as an indicator of the model's generalization capability, with a larger margin correlating with enhanced generalization. In QSVMs, the optimization problem is configured to maximize the margin while adhering to specified constraints.

In summary, QSVMs harness the computational prowess of quantum computers to optimize the identification of a hyperplane for maximal class separation. This process involves the application of the quantum gradient descent algorithm and kernel functions to map points to a higher-dimensional feature space. The maximization of the margin within the optimization constraints results in a model with robust generalization abilities.

Quantum Support Vector Machines are superior to their classical counterpart due to variety of reasons. Few of these are enumerated below.

1. Faster Training Times: QSVMs exhibit accelerated training times compared to classical SVMs, a consequence of the heightened computational efficiency afforded by quantum computers. This attribute proves particularly advantageous for large-scale machine learning tasks where training time is a critical bottleneck.
2. Improved Generalization Performance: Empirical evidence suggests that QSVMs outperform classical SVMs in terms of generalization, showcasing superior predictive accuracy on unseen data. This superiority stems from QSVMs' capacity to discern more intricate patterns in the data, facilitated by the utilization of higher-

dimensional feature spaces enabled by quantum kernel functions.

3. Handling Non-linear Data Effectively: QSVMs excel in handling non-linear data, surpassing classical SVMs in this aspect. This prowess is attributed to the utilization of quantum kernel functions, which proficiently map data into higher-dimensional spaces where linear separability is achievable. Classical SVMs, constrained by linear kernel functions, lack this flexibility in handling non-linear data structures.

VI. Proposed Solution

A. Block Diagram

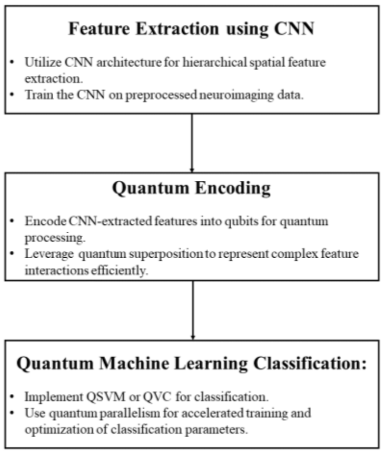

Fig. 6. Block Diagram of Proposed Methodology

In the proposed methodology, Convolutional Neural Networks (CNNs) are employed for feature extraction from MRI images, leveraging a pre-trained model such as VGG16. To adapt the CNN to the specific characteristics of brain images, a fine-tuning process is undertaken on the dataset. Subsequently, quantum feature encoding techniques are explored to represent the CNN-extracted features in a quantum state. This involves investigating methods like amplitude encoding, quantum embeddings, and other quantum feature maps to encode relevant information. Moving forward, a Quantum Support Vector Machine (QSVM) is implemented using a quantum computing library, such as Qiskit. The quantum states obtained from the preceding step are encoded as inputs to the QSVM, which is then trained on the encoded features for the three classes—Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI), and Normal Control (NC). This integrated approach aims to harness the strengths of classical and quantum methods for enhanced accuracy in classifying Alzheimer's disease stages from MRI data.

B. Process Flow

1) Data Preprocessing

The MRI images obtained from the ADNI dataset were pre-processed prior to being fed to the CNN model for feature extraction. Input shape of the images was set to be (224,224) akin to VGG-16s input layer. The MRI images are then converted to grayscale for simplification, consistency, and enhanced interpretability. Grayscale representation reduces the image to a single intensity channel, facilitating the implementation of image processing algorithms with reduced computational complexity. Grayscale images also provide improved contrast, making them suitable for visualizing specific anatomical details or abnormalities. Min-Max normalization is also applied to scale pixel values between 0 and 1, ensure consistent scale and mitigate intensity variations.

2) Data Augmentation

Data augmentation serves as a pivotal preprocessing step in the analysis of medical images, encompassing diverse transformations like flips or rotations to artificially amplify dataset diversity. The significance of this augmentation lies in its capacity to bolster the resilience and generalization of machine learning models, particularly when trained on limited datasets. By introducing variations within the training set, augmented data aids the model in effectively capturing the inherent variability in medical images, thereby mitigating overfitting and enhancing the model's performance on previously unseen data. In the realm of MRI images, data augmentation plays a crucial role in advancing the development of robust and accurate models, particularly for tasks such as disease classification or segmentation, where challenges stemming from variations in patient positioning and imaging conditions are prevalent.

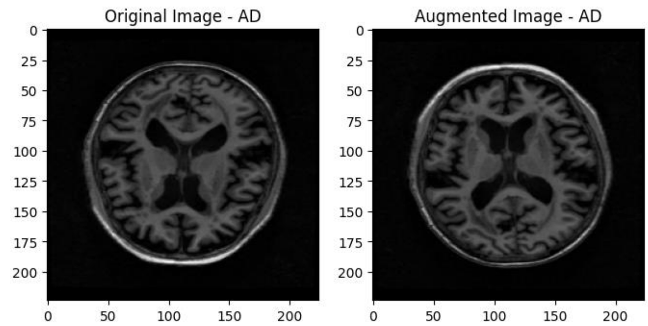

Fig. 7. Example of an Augmented Image

3) Feature Extraction

The VGG16 architecture is leveraged for feature extraction from medical imaging data. The VGG16 model, pre-trained on large-scale image datasets, is utilized as a convolutional neural network (CNN) with 16 layers. By passing MRI images through the VGG16 network, hierarchical and abstract features are automatically extracted at multiple convolutional layers. The obtained features serve as high-level representations capturing intricate patterns and structures within the images. This process enhances the ability of the model to discern discriminative features relevant to the task at hand, contributing to the development of a robust and effective framework for subsequent stages of medical image analysis, such as disease classification or segmentation. The use of VGG16 for feature extraction aligns with its proven efficacy in diverse image recognition tasks, establishing a foundation for comprehensive and accurate feature representation in the context of medical imaging research.

ConvNet Configuration					
A	A-LRN	B	C	D	E
11 weight layers	11 weight layers	13 weight layers	16 weight layers	16 weight layers	19 weight layers
input (224 × 224 RGB image)					
conv3-64	conv3-64 **LRN**	conv3-64 **conv3-64**	conv3-64 conv3-64	conv3-64 conv3-64	conv3-64 conv3-64
maxpool					
conv3-128	conv3-128	conv3-128 **conv3-128**	conv3-128 conv3-128	conv3-128 conv3-128	conv3-128 conv3-128
maxpool					
conv3-256 conv3-256	conv3-256 conv3-256	conv3-256 conv3-256	conv3-256 conv3-256 **conv1-256**	conv3-256 conv3-256 **conv3-256**	conv3-256 conv3-256 conv3-256 **conv3-256**
maxpool					
conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512 **conv1-512**	conv3-512 conv3-512 **conv3-512**	conv3-512 conv3-512 conv3-512 **conv3-512**
maxpool					
conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512	conv3-512 conv3-512 **conv1-512**	conv3-512 conv3-512 **conv3-512**	conv3-512 conv3-512 conv3-512 **conv3-512**
maxpool					
FC-4096					
FC-4096					
FC-1000					
soft-max					

Fig. 8. VGG-16 Model Architecture

4) *Quantum Kernel*

Quantum kernel machine learning represents a groundbreaking approach aimed at harnessing the power of quantum feature maps for the kernel trick. In essence, this involves the creation of a quantum kernel by mapping classical feature vectors, denoted as $\vec{x}$ into a Hilbert space through the utilization of a quantum feature map $\phi(\vec{x})$. This can be represented mathematically as,

$$K_{ij} = \left|\langle \phi(\vec{x}_i) | \, \phi(\vec{x}_j) \rangle\right|^2$$

where,

K_{ij} is the kernel matrix

$\vec{x}_i, \vec{x}_j$ are the n dimensional inputs

$\phi(\vec{x})$ denotes the quantum feature map

The distinctive capability of quantum kernels lies in their versatility, seamlessly integrating with conventional classical kernel learning algorithms like Support Vector Machines (SVMs) or clustering algorithms. Additionally, novel quantum kernel methods, exemplified by the QSVC class provided by Qiskit, exemplify the frontier of this paradigm, opening avenues for innovative and powerful quantum-assisted machine learning techniques.

5) *Classification*

Kernel methods constitute a suite of pattern analysis algorithms that leverage kernel functions to operate within high-dimensional feature spaces. Among these methods, Support Vector Machines (SVMs) stand out as widely recognized tools for supervised learning, particularly in classification tasks. SVMs aim to discern decision boundaries that effectively segregate a given dataset into distinct classes. In scenarios where the data spaces lack linear separability, the integration of kernels proves invaluable for identifying these boundaries.

In a formal context, decision boundaries manifest as hyperplanes within a high-dimensional space. The kernel function plays a pivotal role by implicitly mapping input data into this augmented space, simplifying the resolution of the initial problem. In essence, kernels possess the transformative capability to convert non-linearly separable data distributions into linearly separable problems, a phenomenon aptly termed the "kernel trick."

VII. Results And Discussion

In this section, we present the key outcomes of our investigation, highlighting the main findings and observations derived from the experiments and analyses conducted.

A. *Evaluation Metrics*

We evaluated the performance of our proposed Quantum Support Vector Machine (QSVM) model for Alzheimer's prediction using a comprehensive set of metrics. These metrics include accuracy, precision, recall, and F1-score, providing a holistic view of the model's classification performance. The overall accuracy for the model with Quantum SVM was found to be 98.2% which was more than 93.5% for when standard SVM was used with Quantum Kernel.

TABLE II. Evaluation Metrics of All Classes

Metric	AD	MCI	NC
True Positives	2164	2165	2154
True Negatives	4334	4323	4332
False Positives	3	14	6
False Negatives	5	4	14
Precision	99.8%	99.3%	99.7%
Recall	99.7%	99.8%	99.3%
F1 Score	99.8%	99.5%	99.5%

B. *Feature Importance and Quantum Advantage*

1. Quantum Feature Extraction: Quantum SVM leverages quantum computing's unique ability for parallelism and superposition to perform feature extraction. We investigated the importance of quantum-derived features in distinguishing between different cognitive states, providing insights into the quantum advantage.
2. Dimensionality Reduction: The quantum nature of the QSVM allows for efficient dimensionality reduction in the feature space. We explored how this reduction impacts model training time and generalization performance compared to classical SVMs, shedding light on the quantum model's scalability.
3. Quantum Parallelism: Quantum algorithms inherently leverage parallelism, processing multiple possibilities simultaneously. In the context of Alzheimer's prediction, this allows for the exploration of numerous feature combinations concurrently, potentially leading to more comprehensive and efficient model training.
4. Quantum Entropy: Quantum algorithms can exploit quantum entropy to explore a broader solution space. This capability is advantageous for optimizing model parameters and improving the robustness of Alzheimer's prediction models.
5. Inherent Quantum Advantage: Quantum algorithms, by nature, offer advantages in specific computational tasks. In scenarios where classical algorithms may struggle, such as complex feature extraction and high-dimensional data analysis, quantum algorithms, including QSVM, hold the potential to provide novel solutions and insights

VIII. Limitations And Future Work

Despite the promising results, our QSVM model has certain limitations, such as dependency on quantum hardware availability and potential sensitivity to noise. These limitations necessitate ongoing research to enhance the model's robustness and applicability. To address the identified limitations, future research directions include investigating noise-resistant quantum algorithms, exploring hybrid quantum-classical approaches, and further refining feature extraction techniques for Alzheimer's prediction. We plan on extending out research to explore the development and optimization of Quantum Convolutional Neural Networks (QCNNs) specifically designed for AD prediction, investigating novel architectures and quantum-inspired feature hierarchies. We will also focus on hybrid models, integrating classical and quantum components to leverage the strengths of both, and explore quantum algorithms for preprocessing tasks. Further optimization efforts will be directed towards quantum circuit depth, considering dynamic adaptation and mitigating errors. Emphasis will be placed on enhancing quantum model interpretability through feature attribution and visualizations. As quantum computing technologies advance, we plan to scale our quantum algorithms for AD prediction to larger quantum hardware and establish standardized benchmarks. Additionally, our research will explore the fusion of quantum predictions with classical modalities and ensemble approaches, aiming to capitalize on the strengths of each model for more robust and accurate AD predictions. Overall, these future endeavours contribute to advancing the field of quantum-enhanced healthcare analytics in AD prediction.

IX. Conclusion

In conclusion, our research explores the innovative application of Quantum Support Vector Machines (QSVM) in the realm of Alzheimer's prediction, marking a significant stride at the intersection of quantum computing and healthcare. The findings of our study underscore the unique advantages offered by quantum algorithms, demonstrating their potential to revolutionize the landscape of neurodegenerative disease prediction. The results showcase the robust performance of the QSVM model, leveraging quantum parallelism, superposition, and entanglement to extract intricate features crucial for Alzheimer's prediction. The ability of quantum algorithms to efficiently handle high-dimensional data and provide dimensionality reduction presents a promising avenue for developing more accurate and scalable predictive models.

While our study demonstrates promising results, we acknowledge certain limitations, including dependence on the availability of quantum hardware and sensitivity to noise. These challenges pave the way for future research avenues aimed at refining quantum algorithms and addressing practical considerations in healthcare applications. As we look ahead, the integration of quantum computing into healthcare analytics, particularly for neurodegenerative disease prediction, holds immense potential. The synergy between quantum algorithms and medical research marks the beginning of a transformative era, promising more accurate, efficient, and interpretable models for improving patient outcomes in Alzheimer's disease and beyond.

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