Fuzzy Deep Learning for the Diagnosis of Alzheimer's Disease: Approaches and Challenges

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***Abstract*—Alzheimer's disease (AD) is the leading neurodegenerative disorder and primary cause of Dementia. Researchers are increasingly drawn to automated diagnosis of AD using neuroimaging analyses. Conventional deep learning (DL) models excel in constructing learning classifiers in early-stage AD diagnosis. However, they often struggle with AD diagnosis due to uncertainties stemming from unclear annotations by experts, challenges in data collection, like data harmonization issues, and limitations in equipment resolution. These factors contribute to imprecise data, hindering accurate analysis, interpretation of obtained results, and understanding of complex symptoms. In response, the integration of fuzzy logic into DL, forming fuzzy deep learning, effectively manages imprecise data and provides interpretable insights, offering a valuable advancement in AD. Therefore, exploring recent advancements in integrating DL with fuzzy logic is crucial for improving AD diagnosis. In this review, we explore the contributions of fuzzy logic within fuzzy DL models, focusing on fuzzy-based image preprocessing, segmentation, and classification. Moreover, in exploring research directions, we discuss the possibility of the fusion of multimodal data with fuzzy logic, addressing challenges in AD diagnosis. Leveraging fuzzy logic and membership while integrating diverse datasets such as genomics, proteomics, and metabolomics may provide an effective development of a DL classifier. Additionally, fuzzy explainable deep learning, which merges deep learning with fuzzy logic, promises more accurate and linguistically interpretable decision support systems for AD diagnosis. The primary objective of this paper is to serve as a comprehensive and authoritative resource for newcomers, researchers, and clinicians interested in employing fuzzy DL models for AD diagnosis.**

***Index Terms*—Alzheimer's Disease, Deep Learning, Fuzzy Logic, Fuzzy Deep Learning, Machine Learning, Neuroimaging.**

I. Introduction

Alzheimer's disease (AD) is a prevalent neurodegenerative disorder [1], contributing to around 70% of dementia cases [2]. This condition instigates progressive brain degeneration, predominantly impacting extensive areas of the cerebral cortex and hippocampus. The onset of abnormalities typically manifests in the frontal and temporal lobes, gradually disseminating to other neocortical regions with variable rates among individuals. It begins in the brain's learning center and causes disorientation, mood disturbances, and severe memory loss. It causes sexual dimorphism [3] and may be age-related but not dependent [4]. Approximately 6.7 million individuals aged 65 and above are currently grappling with AD, solidifying its position as the sixth-leading cause of death in the United States. The extensive economic ramifications of AD are evident, with the global cost of its management encompassing medical expenses, social welfare, and the salary loss borne by patients' families, reaching a staggering around 345 billion in the United States in 2023 [5].

AD causes brain structural and functional changes. This process takes years, turning healthy people into Alzheimer's patients [6]. Alzheimer's commonly begins with moderate cognitive impairment (MCI). Note that not all MCI patients get Alzheimer's [7]. Recent additions to the Alzheimer's Disease Neuroimaging Initiative (ADNI) Dataset [8] encompass data pertaining to significant memory concern (SMC) or subjective cognitive decline (SCD). SMC refers to a self-perceived decline in cognitive abilities lacking objective evidence of impairment. Recent research suggests that SMC may be an early indicator of more severe cognitive decline, including mild cognitive impairment (MCI) or dementia [9]. Currently, the exact causes of AD remain incompletely comprehended. However, the precise identification and diagnosis of AD are crucial in the provision of patient treatment, particularly during the first phase. Consequently, many contemporary studies have focused on formulating approaches to identify diseases at their initial phases, particularly before symptoms manifest, with the aim of impeding or halting their advancement [10, 11]. AD detection is quantified and assessed using medical imaging [12], such as magnetic resonance imaging (MRI) and positron emission tomography (PET), and new methods such as blood plasma spectroscopy [13, 14].

Machine learning (ML) has been increasingly utilized in the detection and analysis of AD using neuroimaging datasets (see Table II), offering significant advancements in the identification and understanding of this condition. Traditional ML approaches, such as support vector machines (SVM) [15], decision trees [16], and random forests [17], have been employed to analyze neuroimaging data, genetic information, and cognitive test results to distinguish between Alzheimer's patients and healthy controls [18, 19, 20, 21]. The evolution from traditional ML to deep learning (DL) has marked a significant leap in the efficiency of detecting Alzheimer's disease. DL learns complex patterns from high-dimensional brain images and automatically learns features from raw data, eliminating the need for manual feature extraction [22].

Intelligent medical applications utilizing DL encounter notable challenges, including issues of interpretability [23, 24] and the risk of overfitting or underfitting when dealing with limited medical sample sizes [25]. Additionally, classical DL, relying on crisp values, grapples with the inherent imprecision, uncertainty, and vagueness inherent in medical data,

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particularly in conditions like AD datasets used for diagnostic and therapeutic purposes. The spectrum of uncertain medical data can be broadly categorized into noise, artifacts, and high-dimensional unstructured information [26]. Instances encompass label noise, indistinct organ boundaries in images, imprecise test measurements, unstructured disease descriptions, instances of overlooked diagnostic information, and the presence of low-quality multimodal medical images [1]. Therefore, DL models relying on crisp mathematical formulations may significantly reduce the accuracy [27] of precise AD diagnoses, diminishing the model's precision and demonstrating suboptimal performance when confronted with uncertain data.

Consider a scenario in medical imaging where points exclusively belong to specific anatomical regions; challenges arise during segmentation as points with similar spatial positions may end up in different regions, leading to sharp boundary issues. Additionally, in low-frequency image segmentation, fuzzy recognition surpasses precise recognition in effectiveness. For instance, defining the threshold for diagnosing AD poses difficulties; while the essence of diagnosis is clear, determining the transition point from "diagnosed with AD" to "not diagnosed with AD" is inherently vague and fuzzy.

Fuzzy-based classifiers originate from Zadeh's fuzzy sets [28] and offer a robust capability to handle uncertain and imprecise information, presenting a novel approach to address the challenges outlined above [29, 30]. Models utilizing fuzzy logic and membership functions [31] are crucial for effectively capturing unclear medical data, particularly in the case of Alzheimer's disease. In 1969, Marinos released a research report on fuzzy logic [32], followed by Zadeh's publication in 1974 on fuzzy reasoning [33]. The focal points in fuzzy systems research involve three primary fuzzy techniques: the fuzzy set (referred to as type-1 fuzzy set) [28], the type-2 fuzzy set [34], and the linguistic variable [35]. These methodologies have gained prominence, establishing fuzzy systems as a widely discussed and explored subject.

The integration of fuzzy logic into DL gives rise to fuzzy deep learning models that utilize fuzzy logic to improve different stages of the training procedure, such as image preprocessing, segmentation, and classification. Therefore, the review is structured around these key stages: fuzzy-based image preprocessing, fuzzy-based segmentation, and fuzzy-based classification. Fuzzy DL systems have exhibited certain benefits in the realm of AD diagnosis, and this can be attributed to a minimum of three compelling reasons.

1) Diagnosing AD involves coping with uncertain and imprecise data, given the diverse symptoms that can overlap with other conditions. Traditional DL approaches relying on precise mathematics, stochastic, or probabilistic theory fall short of addressing the inherent fuzziness encountered in practice [36]. However, integrating DL and fuzzy systems offers a promising solution and mitigates the aforementioned challenges to a certain extent.
2) Further, it is crucial not only to have accurate predictions of AD but also to understand the basis of these predictions. Fuzzy DL models are compatible with human cognitive processes and can provide human-understandable and intelligible insights into what factors are influencing the prediction, which is valuable for clinicians to make informed decisions. [37, 38].
3) In the presence of noise, outliers, and fluctuations within neuroimaging or clinical data, the robustness of fuzzy systems becomes evident. Acknowledged for their resilience against such challenges, fuzzy systems exhibit the capacity to sustain reliable performance when integrated into DL frameworks. This adaptability is achieved through the utilization of membership values [39].

The foregoing discussions underscore the substantial impact of fuzzy systems on the efficacy of DL algorithms in AD diagnosis. Consequently, this article is dedicated to conducting a comprehensive review of fuzzy DL models in the context of AD diagnosis, aiming to contribute an in-depth analysis and synthesis of the current state-of-the-art research in this domain. To the best of our knowledge, this is the first review paper on fuzzy-based DL models for AD diagnosis.
The article's main contributions are summarized below.

1) Our review provides a comparative analysis of prior DL and/or ML review/survey papers on AD diagnosis, positioning our work within the existing literature. Through this analysis, we offer a comprehensive overview of advancements while emphasizing our review's unique focus on classifying fuzzy DL models according to their incorporation of fuzzy logic and structuring the review around key stages: fuzzy-based image preprocessing, segmentation, and classification.
2) We presented a comprehensive outline detailing challenges and proposed research avenues aimed at facilitating the development of new fuzzy DL-based algorithms for AD diagnosis. The challenges and research directions encompass computational complexity, multimodal fusion utilizing fuzzy logic, fuzzy explainable DL, fuzzy DL for the automatic staging of AD, an ensemble of DL using fuzzy logic, bias field correction, and noise removal.

The subsequent sections of this paper are organized as follows: Section II outlines the methodology employed for literature selection and insights gleaned from existing review/survey papers. Section III conducts an exhaustive review of existing fuzzy DL models for AD diagnosis. Challenges and prospective research directions are deliberated in Section IV, while conclusive remarks are presented in Section V.

II. Methodology for Literature Selection, Key Insights on Existing Review/Survey Papers and Publically Available Datasets for AD Diagnosis

In this section, we scrutinize the methodology employed for the selection review papers, followed by elucidating the key components of the existing state-of-the-art review and survey papers based on DL for AD diagnosis. Then we discuss the methodology of selection of technical papers and then enumerate the existing datasets for AD diagnosis.

TABLE I
PUBLISHED REVIEW PAPERS ON AD DIAGNOSIS INCORPORATING DEEP LEARNING AND/OR MACHINE LEARNING.

Reference	Year of Publication	Papers Included	Models Studied: ML/DL	Dataset coverage	Special Attention on Fuzzy based DL	Reviews Existing Surveys	Fuzzy DL for AD based Future Directions
Ebrahimighahnavieh et al. [40]	2020	Prior to Apr., 2019	No/Yes	Yes	No	No	No
Das et al. [41]	2020	Not Mentioned	No/Yes	No	Yes	No	No
Zhang et al. [1]	2020	2016 - 2019	No/Yes	Yes	No	No	No
Puente-Castro et al. [42]	2020	Not Mentioned	No/Yes	Yes	No	No	No
Tanveer et al. [43]	2020	2005 - 2019	Yes/Yes	Yes	No	No	No
Li et al. [44]	2021	Not Mentioned	Yes/Yes	Yes	No	No	No
Khojaste-Sarakhsi et al. [2]	2022	2019 - 2021	Yes/Yes	Yes	No	No	No
Sharma and Mandal [45]	2022	Not Mentioned	Yes/Yes	Yes	No	No	No
Warren and Moustafa [46]	2022	Prior to May, 2021	Yes/Yes	No	No	No	No
Saleem et al. [47]	2022	Not Mentioned	No/Yes	Yes	No	No	No
Fathi et al. [48]	2022	Prior to Feb., 2022	No/Yes	Yes	No	No	No
Ganaie et al. [49]	2022	Prior to May, 2022	No/Yes	No	No	No	No
Zheng et al. [36]	2022	1994 - 2020	No/Yes	No	Yes	No	No
Shoeibi et al. [50]	2023	2016 - 2022	No/Yes	Yes	Yes	No	No
Sharma et al. [51]	2023	2009 - 2022	No/Yes	No	No	No	No
Arya et al. [52]	2023	Not Mentioned	Yes/Yes	Yes	No	No	No
Tanveer et al. [53]	2023	Prior to Mar., 2023	No/Yes	Yes	No	Yes	No
Zheng et al. [27]	2023	2014 - 2022	No/Yes	No	Yes	No	No
Menagadevi et al. [54]	2024	2013 - 2023	Yes/Yes	Yes	No	No	No
Ours	-	2015 - 2024	No/Yes	Yes	Yes	Yes	Yes

A. Methodology for Selecting Existing Review/Survey Papers Based on DL and/or ML for AD Diagnosis and Distinguishing Features of Our Review from the Existing Ones

The identification of pertinent review/survey papers for this study involved a systematic search across reputable academic databases, including Google Scholar, Scopus, and PubMed. Keyword combinations such as “Alzheimer’s disease diagnosis”+“Fuzzy”+“Deep learning”+“Review paper”; “Alzheimer’s disease diagnosis”+“Deep learning”+“Review paper”; “Alzheimer’s disease diagnosis”+“Fuzzy”+“Deep learning”+“Survey paper” and “Alzheimer’s disease diagnosis”+“Deep learning”+“Survey paper” were utilized to refine the search results, ensuring the inclusion of comprehensive review/survey papers in the selected corpus. Initially, a pool of 51 articles was amassed through the specified search criteria. The subsequent selection process for review/survey papers employed a three-stage approach. Firstly, preference was given to review papers published on or after 2020. Secondly, titles and abstracts were scrutinized to eliminate duplicates and filter out studies lacking relevance to the study’s focus. Lastly, a thorough evaluation of the complete texts of the remaining articles was undertaken. Following this methodology, a total of 19 review/survey papers were deemed suitable for inclusion in our investigation. For detailed insights, please refer to Table I, which provides statistical information related to the published review papers included in our study.

As of the current date, numerous review and survey papers have delved into the realm of AD diagnosis, employing both ML and DL models. Table I offers a comparative analysis with previously published works to position our review within this landscape. This analysis serves a dual purpose: firstly, it consolidates the existing body of knowledge, offering a comprehensive overview of field advancements; secondly, it highlights the distinctive focus and unique contributions of our review paper.

Upon reviewing Table I, it becomes evident that the majority of existing papers exclusively concentrate on DL and ML models without incorporating a specific emphasis on fuzzy concepts. Furthermore, these papers fail to evaluate existing review papers and overlook discussions on fuzzy-based future directions. In Section I, our introductory discourse underscores the advantages of fuzzy DL over traditional DL approaches in the context of AD diagnosis. Our review stands out by presenting a broad perspective on the literature related to fuzzy DL techniques for AD diagnosis, addressing gaps left unexplored by previous works. It takes a commendable step forward by offering a focused examination of fuzzy DL and a comprehensive evaluation of its applications in the domain. To the best of our knowledge, this marks the inaugural review paper specifically dedicated to exploring fuzzy-based DL models for AD diagnosis.

B. Methodology for Selecting Technical Papers Based on Fuzzy DL for AD Diagnosis

To compile relevant technical literature for this study, a comprehensive search was conducted across prominent academic databases, namely Google Scholar, Scopus, and PubMed. The search spanned from Jan. 01, 2015, to Jan. 02, 2024, focusing on the keywords “Alzheimer’s disease diagnosis”+“Fuzzy”+“Deep learning”; “Alzheimer’s disease diagnosis”+“Deep learning”; “Alzheimer’s disease diagnosis”+“Fuzzy”+“Machine learning” and “Alzheimer’s disease diagnosis”+“Machine learning”. Initially, 93 technical articles were identified using the specified keywords. Subsequently, a two-stage selection process was employed to refine the list. In the first stage, titles and abstracts were scrutinized to eliminate duplicates and exclude studies not aligned with the research focus. Following this, the remaining articles underwent a thorough examination of their full texts. This selection process resulted in the inclusion of 16 technical papers that directly contributed to the objectives of our study. Graphical representations of the selection of papers are shown

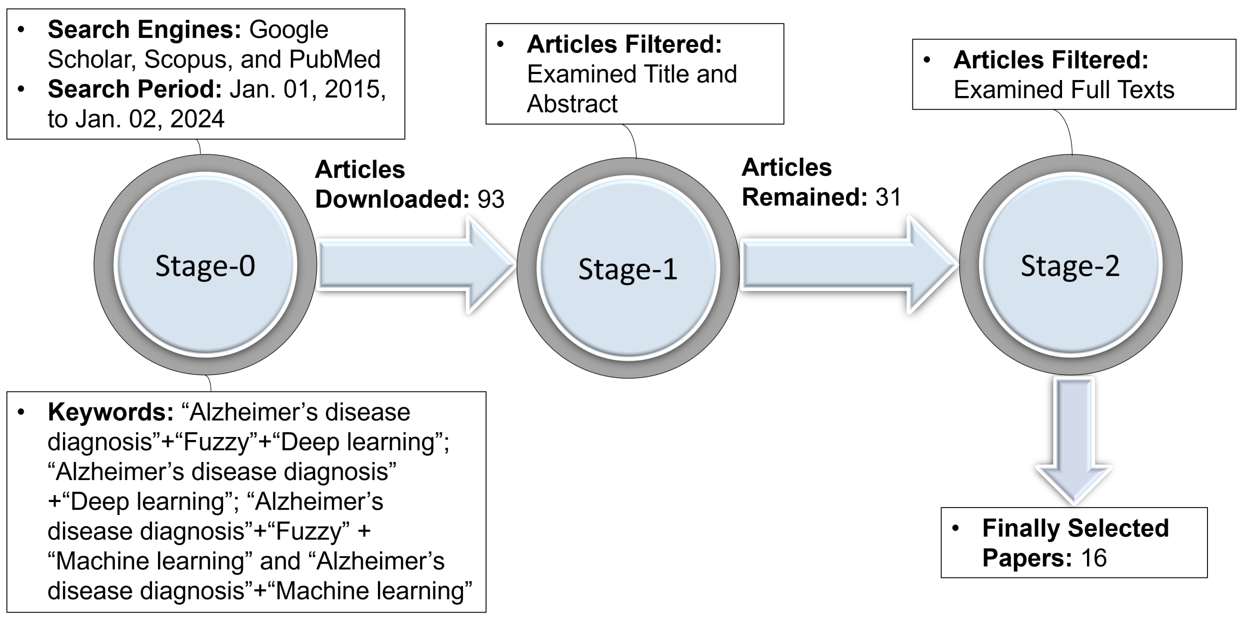

Fig. 1. Graphical representation of methodology for selecting technical papers based on fuzzy DL for AD diagnosis.

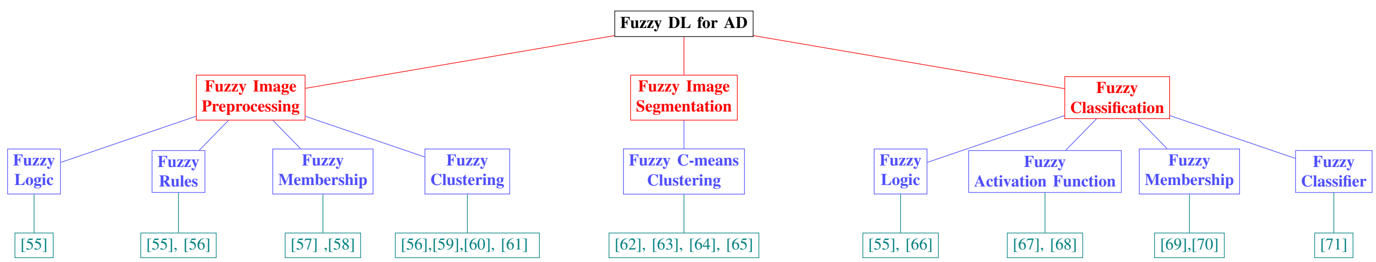

Fig. 2. Tree representation of selected articles for review, showcasing the integration of fuzzy logic with DL models for AD diagnosis in various phases, including image preprocessing, segmentation, and classification.

in Fig. 1. For a detailed overview, refer to Table III, which highlights some key points regarding the technical papers considered in this investigation.

Upon thorough examination of the articles, it became evident that a significant portion of them integrate fuzzy logic with DL for various purposes, including image preprocessing, segmentation, and classifier integration. Consequently, our literature review focuses on these key areas, exploring fuzzy preprocessing, segmentation, and classification methods to provide a comprehensive understanding of their applications in AD diagnosis. Fig. 2 represents the detailed tree representation of the selected articles for review.

C. Publically Available Datasets for AD Diagnosis

The availability of publicly accessible datasets significantly impacts the diagnosis of Alzheimer's disease (AD), facilitating research and algorithm development in this field. These datasets serve as invaluable resources, providing researchers with access to diverse clinical, imaging, and demographic data essential for training and validating AD diagnostic models. The importance of such datasets is highlighted by their role in enabling collaborative efforts and advancing the understanding and diagnosis of AD. For a comprehensive overview of the available datasets for AD diagnosis, please refer to Table II, which provides detailed information on various public datasets commonly utilized in AD research.

III. Fuzzy-Based Deep Models for AD Diagnosis

In the realm of AD diagnosis, the integration of fuzzy logic with deep learning models has yielded promising results. These models leverage fuzzy logic to enhance various stages of the diagnostic process, including image preprocessing, segmentation, and classification. This section provides a comprehensive overview of research endeavors, categorizing them into three insightful subsections, each elucidating the pivotal role of fuzzy logic in specific domains: image preprocessing, segmentation, and classification. Through a comprehensive analysis of the current literature, we aim to provide a nuanced understanding of the diverse ways in which fuzzy-based deep models contribute to enhancing the accuracy and reliability of AD diagnosis.

A. Fuzzy Image Preprocessing Techniques for AD Diagnosis

Common brain imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET), are frequently used in

TABLE II
AVAILABLE DATASETS FOR ALZHEIMER'S DISEASE DIAGNOSIS

S.No	DATASET	NO. OF SUBJECTS	MODALITY	SOURCE
1	ADNI	ADNI 1 CN: 200 MCI: 400 AD: 200	MRI (T1W,T2W,DTI,FLAIR), PET	https://adni.loni.usc.edu
		ADNI GO CN: 150 MCI: 200 AD: 150		
		ADNI 2 CN: 150 MCI: 150 AD: 150		
		ADNI 3 CN: 133 MCI: 151 AD: 87		
2	OASIS	OASIS 1 Longitudinal MRI: 416	MRI (T1W,T2W,DTISWI,ASL,TOF,FLAIR), PET	https://www.oasis-brains.org
		OASIS 2 Cross-sectional MRI: 150		
		OASIS 3 Cross-sectional MRI: 1379		
		OASIS 3_TAU Cross-sectional MRI: 451		
3	AIBL	CN: 768	MRI, PET	https://aibl.org.au
		MCI: 133		
		AD: 211		
4	J-ADNI	CN: 154	MRI, PET	https://www.alz.org
		AD: 149		
5	GARD	CN: 171	MRI, PET	https://dss.niagads.org
		AD: 81		
6	NACC	CN: 42	MRI, PET	https://naccdata.org
		aAD: 33		
		mAD: 30		
		AD: 26		

prediction of AD. However, they present challenges like biased tissue intensities due to the inhomogeneous nature of magnetic fields in scanners, and low signal-to-noise ratios necessitating preprocessing of input data for accurate prediction [66, 56, 59]. This preprocessing stage is crucial as it not only improves the overall image quality but also accentuates key features relevant to diagnosing AD. These features might include the highlighting of brain regions showing atrophy or the presence of abnormal protein deposits. As a result, the images become more suitable for in-depth analysis. In this section, we delve into the literature that leverages fuzzy-based system for the initial preprocessing of images in the context of AD diagnosis. Specifically, fuzzy logic is employed to identify the area of interest in brain images, fuzzy membership functions enhance image quality, fuzzy rules derive diagnostic outcomes, and fuzzy clustering techniques form image or set clusters.

a) Fuzzy Logic: The system proposed by [55] extracts the area of interest from brain images using fuzzy logic. Specifically, three input linguistic variables are defined: empty space volume, beta-amyloid volume, and TAU (Tubulin Associated Unit) protein volume. These variables are characterized by different intervals each consisting of three subsets with triangular membership function: small, medium, and large. The volume of empty space is determined by stripping the outer skull from an MRI and calculating the volume of black voxels. Beta-amyloid volume is computed by identifying yellow and red voxels from PET (Florbetaben) images, while TAU Protein volume is calculated by measuring the volume of red and yellow voxels from PET (Flortaucipir) images. Subsequently, a rule-based mechanism is employed to derive diagnostic outcomes.

b) Fuzzy Rules: The systems proposed by [55] and [56] utilize rule-based systems to derive diagnostic outcomes from the extracted area of interest. [55] focus on empty space, Beta-amyloid volume, and TAU Protein volume, while [56] utilize dominant sets.

c) Fuzzy Membership: In studies such as [57] and [58], alongside preprocessing techniques like DeepDream, Hyper-column, or CLAHE (Contrast Limited Adaptive Histogram Equalization), the Fuzzy Color Image Enhancement technique is employed to enhance MRI images. FCIE consists of three stages: converting images from grayscale to fuzzy levels, adjusting fuzzy level parameters to enhance the image, and converting back to grayscale based on the assigned membership degree per pixel. This technique is particularly effective for enhancing color images with low contrast, thereby improving their overall contrast quality.

d) Fuzzy Clustering: Some studies employ a fuzzy approach to associate images/dominant sets with their class centroids or anchors. Apart from other preprocessing techniques [60], [61] and, [56] also employ fuzzy clustering of images and dominant sets. Unlike traditional clustering methods, Fuzzy C-means (FCM) assigns each image vector to a set of membership values, one for each cluster, instead of assigning vectors to a single cluster in [60]. Similarly in [59], in addition to standard preprocessing techniques, the data undergoes fuzzy amplification using methods such as Gaussian, median, and bilateral blurring. Subsequently, enhanced anchors are derived through fuzzification. Specifically, instead of designating only one augmented image as a positive sample and the rest as negatives, a fuzzy supervised contrastive strategy treats all samples from the same class as positive and the others in a batch as negative. Furthermore, fuzzy smoothing is applied to labels to reduce their rigidity.

B. Fuzzy Image Segmentation Techniques for AD Diagnosis

In this subsection, we discuss the frontier of research where fuzzy-based deep models are employed for AD diagnosis, focusing particularly on studies that introduce novel segmentation schemes. Accurate segmentation of brain structures is a critical step in AD diagnosis, as it facilitates the identification of region-specific abnormalities indicative of the disease. Additionally, we also discuss some key steps of the undertaken work.

In [62], Sathiyamoorthi et al. developed a computer-aided diagnosis (CAD) system for the prediction of AD using MRI images. The system consists of four main components: MRI image preprocessing, segmentation, feature extraction, and classification. The MRI images are preprocessed using 2D adaptive bilateral filter (2D-ABF) and 2D adaptive histogram adjustment (2D AHA) to eliminate noise and enhance image quality and contrast. After that, the processed images are segmented to identify the region of interest, which is crucial for accurate diagnosis. The segmentation process involves the adaptive mean shift modified expectation maximization (AMS-MEM) algorithm. AMS-MEM algorithm integrates the adaptive mean shift clustering approach with the modified expectation maximization technique to effectively segment MRI images. The adaptive mean shift component allows for the adaptive clustering of image data based on local data densities, while the modified expectation maximization component enables the estimation of the underlying data distribution and the identification of clusters representing different tissue types or abnormalities. In the AMS-MEM algorithm, fuzzy logic is employed to determine the optimal threshold for image segmentation by taking into account the fuzzy membership values of pixels. This approach enables the algorithm to effectively handle complex image distributions and variations in pixel intensities, leading to more accurate and robust segmentation results. Overall, the AMS-MEM algorithm provides a powerful and adaptive approach for segmenting MRI images, particularly in the context of identifying abnormal regions associated with AD. The gray-level co-occurrence matrix (GLCM) is used for feature extraction and texture analysis. Finally, the deep convolutional neural network (DCNN) is the classification technique implemented to classify AD.

In [63], Raghavaiah and Varadaraja also proposed a CAD system for AD diagnosis using MRI data. The key steps of the work are: segmentation, feature extraction, and classification. In the context of segmentation, the paper introduces a new segmentation method, temporally consistent black widow optimization (BWO) combined fuzzy c-means clustering (FCM) segmentation. This method addresses the temporal changes in intensity homogeneities in brain tissues by considering the bias field and intensity means of each tissue. The key features of the temporally consistent BWO-FCM segmentation are as follows. 1) Temporal consistency: The method incorporates temporal consistency constraints into the FCM algorithm, allowing for the consideration of temporal changes in intensity homogeneities in brain tissues over multiple time points [72]. 2) FCM: The FCM algorithm is utilized as the basis for the segmentation process, providing a fuzzy logic-based approach to assign membership values to each pixel in the image, indicating the degree to which the pixel belongs to different tissue classes (e.g., white matter, gray matter, cerebrospinal fluid) [73, 74]. 3) BWO: The BWO approach is employed to optimize the FCM clustering process [75, 76]. BWO is a metaheuristic optimization algorithm inspired by the predation behavior of black widow spiders. It is used to enhance the efficiency and effectiveness of the FCM algorithm by iteratively searching for optimal solutions and avoiding local optima. Overall, the temporally consistent BWO-FCM segmentation method represents an innovative approach to MRI-based tissue segmentation, specifically tailored for AD diagnosis systems. For feature extraction, a hybrid Texture, Edge, Color, and Density (TECD) method is proposed that combines texture, color, edge irregularities, tissue densities, and statistical color features to enhance the discerning capability of every pattern. Further, a hybrid feature deep neural network (HF-DNN) is proposed for classification. The HF-DNN combines a deep stacked autoencoder (DSAE) and a rotation forest (RF) classifier for classifying the extracted features into AD, MCI, and NC groups.

In contrast to [62, 63], Ansingkar et al. [64] proposed an innovative methodology for the early prediction of AD using a hybrid equilibrium optimizer with a capsule autoencoder. The proposed methodology involves several key steps, including image pre-processing with skull stripping and normalized linear smoothing and median joint (NLSMJ) filtering, segmentation of brain regions using adaptive fuzzy-based atom search optimization, feature extraction using improved Zernike features (IZF) and hybrid wavelet Walsh features (HWWF). After that, features are selected using adaptive rain optimization (ARO), and finally, a hybrid equilibrium optimizer with capsule autoencoder is utilized for multi-class AD detection. In this work, fuzzy logic is utilized in the segmentation process. Specifically, it is employed in the adaptive fuzzy-based atom search optimization (AFASO) technique to assess the degree of membership of pixels to different clusters or regions within the brain images. This membership degree is used to characterize the uncertainty associated with the assignment of pixels to specific brain tissue types, such as grey matter, white matter, and cerebrospinal fluid. AFASO works by iteratively optimizing the positions of a set of atoms within the image, with the goal of minimizing a fitness function that measures the difference between the segmented regions and the actual regions of interest. The adaptive nature of the algorithm allows it to adjust its parameters based on the characteristics of the image being segmented. This enables it to effectively handle images with varying levels of complexity and noise.

To further improve the accuracy and reduce the misclassification of noisy pixels, Sasikala [65] proposed a novel CAD system for AD diagnosis. The proposed system includes a pre-processing stage using the statistical parametric mapping (SPM) tool, a segmentation stage using the iteratively reweighted adaptive spatial fuzzy c-means (IRW-ASFCM) technique, and a feature extraction stage using the 2-level selective wavelet kernel (2LS-WaveCNN) ensemble approach. The segmentation process using IRW-ASFCM is a key component of the proposed CAD system, contributing to the reliable identification and delineation of brain tissue regions essential for AD diagnosis. The IRW-ASFCM technique incorporates geographical information into the membership function, allowing for more accurate segmentation of brain tissue. By substituting the fixed fuzzifier value with a fuzzy linguistic fuzzifier value, the technique reduces the misclassification of noisy pixels. This approach aims to address the challenges associated with traditional segmentation methods and improve the accuracy of tissue segmentation in MRI images. Finally, the Wave CNN networks built from hidden layers are trained using deep tree training (DTT) for AD classification.

C. Fuzzy Classification for AD Diagnosis

This section discusses various classification algorithms that are employed within the framework of fuzzy-based deep-learning (DL) models for diagnosing AD.

A deep non-iterative random vector functional link (RVFL) neural network was developed by Sharma et al. [67] to detect AD at the early stage. In which, a pre-trained DL model, ResNet-50 is used to extract the features of the MRI images. Then, the classification of these extracted features is carried out using a non-iterative RVFL network initialized with random vectors. The weights and biases between the input layer and enhancement nodes of the RVFL network are randomly generated. MRI images may include various outliers such as motion artifacts, bias field correction artifacts, noise, and other irregularities. The Fuzzy Activation Function (s-FAF) is implemented within the hidden layer of the RVFL neural network to transform the features into a non-linear space, aiming to mitigate the impact of outliers present within the features of the MRI images. Then, feeding the combined enhanced and original features into the output layer for classification results in faster and significantly more accurate classification outcomes. To mitigate computational complexity, the s-FAF method employs only three linguistic variables: low, medium, and high. For further enhancement of approximation capability, increased generalization, and expedited RVFL classification, Sharma et al. [68] introduced a convolutional neural network-based ensemble RVFL classifier for AD diagnosis. The proposed methodology involves several preprocessing steps to prepare MRI and PET scans for suitable input. Statistical Parametric Mapping (SPM) is employed as a preprocessing tool to standardize both MRI and PET data. Preprocessing of MRI and PET scans involves several steps, including image realignment to eliminate motion artifacts, intra-modal registration for aligning all MRI and PET scans within the same modality, and inter-modal co-registration to ensure precise fusion of MRI features with PET features. After co-registration, significant middle slices are extracted from both MRI and PET scans. Wavelet packet transform (WPT) is used for slice fusion to obtain decent, accurate, and high-quality images. The fused scans from the WPT are then fed into the CNN network. Eight-layered CNN networks are employed, extracting features from each max-pooling layer following every convolutional block, excluding the first two hidden layers and the terminal layer of the network. The primary objective of max pooling is to decrease the dimensionality of the feature space derived from the MRI and PET slices while simultaneously incorporating translation invariance. This results in more abstract training features of MRI and PET images, leading to an improvement in the efficacy of model learning. The extracted features are subsequently input into an ensemble of the RVFL model for classification. The RVFL network integrates the s-FAF as an activation function, aiding in mitigating the impact of outliers. The outputs from all customized RVFL classifiers are averaged and then fed into the RVFL classifier to determine the final decision for AD classification. In contrast to [67, 68], Sajid et al. [69] proposed the fuzzy broad learning system (F-BLS) model for the diagnosis of AD. F-BLS assigns fuzzy membership value to each training point aids in mitigating the influence of noise and outliers present in the medical dataset such as the AD dataset. As a result, samples near the class center receive higher weightage, while those farther from the class center receive lower weightage. Consequently, it effectively addresses the issue of outliers present in the datasets. Intuitionistic fuzzy BLS (IF-BLS) is further proposed, leveraging a kernel function to assign intuitionistic fuzzy (IF) numbers to each sample in the high-dimensional feature space. IF-BLS utilizes membership and non-membership functions to facilitate this assignment process, allowing for a more comprehensive representation of uncertainty in the data. Based on the IF number, a fuzzy score is ultimately assigned to each sample in the dataset. IF sets offer a broader representation of uncertainty compared to traditional fuzzy theory, enabling efficient handling of noise and outliers within the ADNI dataset.

In [70], ML and DL algorithms incorporate a fuzzy-based classifier with a deep residual neural network as a feature extractor. The ResNet-101 network is employed for feature extraction. ResNet-101 is a deep neural network comprising 101 layers, drawing inspiration from the VGG-19 network but incorporating skip connections between the fundamental neural blocks. The objective behind incorporating residual blocks, or layers, is to mitigate the problem of vanishing gradients. This is achieved by reusing activations from the preceding layer until the current layer has sufficiently learned its weights. All the features extracted by the network, following the global pooling layer, are inputted into the fully connected layer. The fully connected layer flattens the extracted features, creating a feature vector. Finally, the output of the fully connected layer is inputted into the fuzzy hyperplane-based least square twin support vector machine (FLS-TWSVM) classifier. FLS-TWSVM generates the two nonparallel hyperplanes to classify the data points. The hyperplane positions are determined by implementing a triangular membership function, chosen for its capacity to encompass the distribution of data points or support vectors within a triangular region. Triangular functions efficiently position the data points with respect to the drawn hyperplane, indirectly enhancing the model's accuracy by accommodating outliers for a specific class. Fuzziness implies that the decision boundary around a given point is less explicit, whereas reduced fuzziness indicates a more clearly defined boundary. Haouas et al. [55] develop approaches to predict Alzheimer's disease within the pretreatment of brain images. The Fuzzy logic method is employed for AD identification and classification. The fuzzy logic method relies on a logical system with three linguistic input variables: volume of Beta-Amyloid and volume of Tau protein, volume of empty space, and linguistic output variable. It is based on 8 logical rules and utilizes maximum average defuzzification logic and function. This method incorporates 3D MRI, 3D PET Florbetaben, and 3D PET Flortaucipir images.

A Computer-Aided Diagnosis (CAD) system has been deployed using Magnetic Resonance Imaging (MRI) data sourced from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database [66]. A normalization procedure is applied to every three-dimensional MRI image to establish them in the

MNI/ICBM atlas space. Subsequently, the extraction process focuses on isolating the grey matter region of the brain. The feature extraction process involves utilizing a two-dimensional Gabor filter across three scales and eight orientations. An optimal deep neural network (DNN) classifier is employed to categorize the images into three groups: Cognitive normal (CN), Alzheimer's disease (AD), and Mild Cognitive Impairment (MCI). The efficiency of the DNN model is highly sensitive to its weight parameters due to their direct correlation with the objective function. Hence, it's crucial to optimize and select these parameters effectively. The classification accuracy of the deep stacked sparse auto-encoder is improved by employing the enhanced squirrel search algorithm (ESSA) algorithm to select optimal weight parameters. The intention is to enhance the squirrel search algorithm (SSA) by incorporating fuzzy logic to achieve improved solutions. Within the SSA framework, the gliding constant plays a pivotal role in regulating both exploration and exploitation within the search space. Adapting this parameter dynamically is essential for achieving improved outputs. Fuzzy logic is employed to dynamically adjust the parameters according to each iteration's circumstances.

In [71], two novel hybrid deep-learning architectures were developed and assessed for detecting AD progression. The models are constructed by integrating multiple deep bidirectional long short-term memory (BiLSTM) models. The initial architecture constitutes an interpretable multitask regression model, forecasting seven pivotal cognitive scores for patients 2.5 years following their last observations. The projected scores are leveraged to construct an interpretable clinical decision support system, grounded on a transparent glass-box model. This architecture endeavors to investigate the efficacy of multitasking models in generating more stable, resilient, and precise outcomes. In the second architecture, a hybrid model is implemented wherein the deep features extracted from the BiLSTM model are employed to train multiple machine learning classifiers which include DT [77], RF [78, 79], SVM [15], NB [80] and FL models (FURIA [81], DL model (SoftMax) and MOEFC [82]). The LSTM model will be utilized for feature engineering tasks, leveraging time series data, while the fuzzy model will be employed for the classification task. The two primary components of a fuzzy classifier consist of: (1) Knowledgebase (KB): This encompasses the rule base along with the database of membership functions utilized to represent linguistic labels. (2) Reasoning mechanism: This denotes the approach employed to classify examples, drawing upon the knowledge base. Developing a deep learning model that leverages the interpretability features offered by fuzzy classifiers. Two prominent data-driven fuzzy classifiers are employed: FURIA and MOEFC. These techniques offer a balance between the accuracy and linguistic interpretability of the resultant models. Moreover, the key components of these systems, such as fuzzy partitions and knowledge bases (KBs), are automatically extracted from the training data. FURIA is a contemporary fuzzy classifier that extends and adapts the RIPPER rule induction algorithm [83]. Empirical evidence demonstrates that FURIA surpasses the accuracy of numerous machine learning algorithms [84]. FURIA employs soft boundaries to learn rules and generates an unordered rule set utilizing a one-vs-rest strategy. In case a new instance is not covered by any rule from the rule base, a rule stretching technique is utilized. Also, MOEFC builds a fuzzy classifier through the implementation of the widely used NSGA-II elitist Pareto-based multi-objective evolutionary algorithm [85]. NSGA-II is employed to optimize the two conflicting objectives of maximizing accuracy and minimizing complexity, specifically reducing the number of fuzzy rules.

D. Summary and Insights from the Existing Literature

The aforementioned literature on fuzzy DL for AD diagnosis yields valuable perspectives on integrating fuzzy logic into DL models to enhance the accuracy and reliability of AD diagnosis. Here are the key summary points and insights gleaned from the existing literature:

a) Diverse Methodologies: The reviewed literature showcases a wide array of approaches that amalgamate fuzzy logic with DL models across various phases of the diagnostic process, including image preprocessing, segmentation, and classification. This diversity vividly illustrates the adaptability and flexibility of fuzzy-based approaches in tackling distinct facets of AD diagnosis.

b) Tool and Dataset Variability: The literature presents a myriad of tools and datasets employed in the evolution of fuzzy DL models for AD diagnosis. While certain studies concentrate on particular tools or algorithms, others delve into an array of methodologies across diverse datasets. This diversity suggests a broad exploration of techniques in the utilization of fuzzy DL for AD diagnosis, reflecting a wide-ranging and thorough investigation into the subject matter.

c) Performance and Interpretability: Fuzzy DL models offer the potential for developing more interpretable AI systems for AD diagnosis. Unlike traditional DL models that often function as black boxes, fuzzy DL models can provide insights into how decisions are made. In the realm of constructing fuzzy DL models for AD diagnosis, achieving a delicate equilibrium between performance and interpretability is paramount. Performance metrics serve as pivotal yardsticks for evaluating the effectiveness and accuracy of fuzzy DL models in diagnosing AD. While the attainment of superior performance holds significant importance, the interpretability of the model is equally critical. In the medical domain, particularly in diagnosing complex conditions like AD, interpretability plays a significant role in gaining acceptance from healthcare practitioners. Understanding the rationale behind the model's determinations can foster this trust and expedite its acceptance within clinical practice.

d) Additional Benefits of Fuzzy DL: The application of Fuzzy DL in AD diagnosis offers several additional benefits beyond mere performance appraisals. Fuzzy DL models demonstrate adaptability to the intricacies of medical data, encompassing noise, outliers, and fluctuations commonly encountered in AD datasets. Through the integration of fuzzy logic, these models adeptly capture and process uncertain information, leading to more robust and reliable diagnostic outcomes. Further, fuzzy DL models have the potential to enhance feature extraction capabilities, allowing them to identify relevant patterns and relationships in complex medical data. This enhanced feature extraction can lead to more accurate and informative diagnostic predictions, improving the overall effectiveness of AD diagnosis.

In summary, the advantages of fuzzy DL in AD diagnosis, such as improved handling of uncertainty, enhanced feature extraction capabilities, and the potential for more interpretable AI systems, make these models valuable tools for advancing the accuracy and reliability of diagnostic processes in AD. By leveraging fuzzy logic within DL frameworks, researchers can address key challenges in AD diagnosis and pave the way for more effective and interpretable diagnostic solutions.

IV. Challenges and Future Scope

Although the fuzzy deep learning for AD diagnosis has arrived at a certain degree of maturity, our critical study has revealed multiple research areas that still need to be investigated more. Referring to fig. 3, we discussed a thorough outline of the challenges and suggested possible research directions that may help the researchers to develop new algorithms.

A. Multimodal Data Fusion

AD causes a set of changes in the brain, including structural, functional, metabolic, etc. The need to incorporate various forms of data beyond conventional clinical evaluations and neuroimaging grows in tandem with the growing knowledge of AD. Omics data (genomics, proteomics, metabolomics), retinal images, and neuroimaging biomarkers are examples of new data modalities that provide important insights into the development and processes of disease. For AD characterization, it is crucial to incorporate these data modalities via fuzzy logic to enhance generalization and supplement feature analysis.

Based on the significance of each modality, different fuzzy membership functions will be given to the features of each modality. Fuzzy logic can be used for the efficient fusion of multimodality data. Multiomics data integration, including genomes, proteomics, and metabolomics, offers a comprehensive AD perspective. Fusing mutiomics data using fuzzy logic can improve AD prediction by utilizing the weightage of each modality to get better information. Brain imaging, including MRI, PET, and fMRI, provides extensive information on structural, metabolic, and functional connections, respectively. Using all this information will enhance AD diagnosis. Fuzzy logic can combine structural, metabolic, and functional data by giving each modality a membership value. This allows relevant features from different imaging modalities to be extracted. The set of models can capture complementary elements of AD-related alterations, enhancing disease characterization and prediction. The retina, an anatomical outgrowth of the brain, shares similarities with the retina, including embryologic origin, neurotransmitter pathophysiology, neural cell layer, blood vessels, microvasculature, and microglia. Researchers discovered protein aggregation in the retina of AD patients and structural alterations including decreased choroidal thickness, increased macular thickness and volume, and thicker retinal nerve fiber layer. Combining retinal biomarkers with neuroimaging modalities employing fuzzy logic can help to detect and monitor AD.

B. Fuzzy Explainable Deep Learning

Explainable and interpretable deep networks is a new and emerging field of deep learning that shows the important features of the image used for the classification. Explainable deep learning open black box models, improve model knowledge, and explain individual estimations. Explainable deep learning will be beneficial for AD diagnosis to show the most significant brain area affected due to degeneration. The goal of explainable deep learning is to create tools and ways to simplify network decisions, recommendations, and assistance for decision-makers. These justifications can shed light on the decision-making process behind an action or the assignment of a certain classification to an object. The study [86] shows the advantages of fuzzy systems over the current frameworks for explainable learning models, such as transparency, understanding, and comprehensibility.

Interpretability in deep learning is the capacity to convey information in a way that an individual can comprehend. The interpretability of fuzzy deep learning is a technique that combines deep learning with fuzzy systems to create a decision support system that is more accurate and interpretable. A human-interpretable structure, on the other hand, requires careful consideration of a wide range of factors. First, the natural language-like fuzziness of fuzzy linguistic rules as a basic description mechanism and the inherent understandability of that system. The second consideration is how easy it is to comprehend and use the rule-based system and the inference technique. By utilising interpretable support systems, researchers can gain insight into human reasoning processes, learn more about the system in question, and improve problem-solving abilities through the comprehensibility of the intended solutions.

C. Automatic Staging of Alzheimer's Disease

There are usually seven stages to the gradual progression of AD: early, medium, and late, ranging from normal, very mild, mild, moderate, severe, moderate, severe decline, and AD. As there is no cure for neurodegeneration due to AD, early diagnosis of AD at a particular stage can help to slow down the progression of the disease with proper medications. Although there is no clear demarcation between mild and moderate stages, the alterations are typical over time. However, changes in the brain start 10–15 years before the visible symptoms due to AD. However, these changes are too small to be captured by conventional deep-learning networks. Therefore, the grading of AD, or the staging of AD, is very important in reducing the mortality rate due to AD.

Fuzzy deep learning algorithms can be developed for prediction, staging, estimation, or regression problems for AD diagnosis. New approaches that integrate state-of-the-art fuzzy tools with deep learning can be suggested for AD diagnosis at an early stage. To enhance the model's performance, the regularisation parameters are set using the fuzzy logic method. Further, information regarding the level of uncertainty in the membership is provided during the description of fuzzy image data. The integration of cutting-edge fuzzy tools with deep learning will produce better image analysis results, improve

TABLE III
SUMMARY OF THE KEY CHARACTERISTICS OF THE LITERATURE REVIEWED IN THE MANUSCRIPT.

Year	Reference	Preprocessing	Segmentation	Feature extraction	Feature Selection	Classifier
2020	[66]	Bias correction, Normalization, Segmentation, Spatial smoothing	FWHM	2D Gabor filter	—	An optimal DNN is utilized, and the SSA algorithm is employed to select the optimal weight perimeter, incorporating fuzzy logic to achieve an enhanced solution.
2020	[71]	KNN, Data normalization, SMOTE	—	BiLSTM-based longitudinal feature extraction	—	Two hybrid DL architectures are developed for AD detection, which incorporates two prominent fuzzy classifiers: FURIA and MOEFC.
2020	[60]	Gaussian Filter, Fuzzy C-means (clustering) - assigns each image vector to a set of membership values.	Otsu threshold Algorithm	Gray Level Co-occurrence Matrix (GLCM)	—	CNN
2021	[62]	2D-ABF and AHA	AMS-MEM algorithm is utilized to determine the optimal threshold for image segmentation by considering the fuzzy membership values of pixels.	GLCM	—	Deep CNN
2021	[70]	VBM, data normalization, realignment and registration, slice extraction	—	ResNet-101 based Deep Network	—	Fuzzy hyperplane-based LS-TWSVM is used to enhance the robustness against outliers.
2021	[67]	Slice selection	—	ResNet-50	—	RVFL is utilized, in which a fuzzy activation function is employed in the hidden layer to map the features to the output space.
2021	[61]	Bias correction, atlas registration, slice selection, Fuzzy C-means (FCM) - assigns each image vector to a set of membership values.	FCM, Otsu, PSO, Traditional CS, and Modified CS	GLCM	PCA	SVM
2021	[57]	DeepDream, FCIE - enhance color images with low contrast using fuzzy membership, Hypercolumn	—	Visual Geometry Group-16 (VGG-16)	—	SVM
2021	[55]	Fuzzy logic extracts area of interest	—	—	—	A fuzzy logic method is used for classification.
2022	[63]	Bias correction, Image Normalization, Segmentation, Spatial smoothing	Temporally consistent BWO-FCM is used, in which the FCM algorithm is utilized to assign fuzzy logic-based membership values to each pixel.	A hybrid Texture, Edge, Color and density (TECD) method is employed.	—	HF-DNN
2022	[64]	Skull stripping and NLSMJ filter	AFASO algorithm is utilized, in which fuzzy logic assesses pixel membership degrees to different brain regions, characterizing uncertainty in pixel-to-tissue assignments.	Improved Zernike features (IZF) and hybrid wavelet Walsh features (HWWF) are employed.	ARO	HEOCAE
2022	[58]	CLAHE, FCIE - enhance color images with low contrast using fuzzy membership, Hypercolumn	—	—	—	SVM classifier
2023	[68]	Image realignment, normalization, registration and co-registration.	—	CNN	—	An ensemble of RVFLs is integrated to classify the features. Additionally, the s-membership fuzzy function serves as the activation function for each RVFL.

TABLE III
(CONTINUED) SUMMARY OF THE KEY CHARACTERISTICS OF THE LITERATURE REVIEWED IN THE MANUSCRIPT.

Year	Reference	Preprocessing	Segmentation	Feature extraction	Feature Selection	Classifier
2023	[59]	Data slicing, tiling, and interpolation, Intensity normalization, Fuzzy amplification and augmentation of data	—	HAM, maximum pooling modules, L1-L4, double CNN	—	Multilayer perception with contrastive loss
2023	[69]	—	—	Voxel based morphometry (VBM) and Volume based morphometry (VolBM)	—	F-BLS and IF-BLS are used, which employ membership and non-membership functions to mitigate the impact of noise and outliers.
2024	[65]	Intensity normalization, tissue segmentation, spatial registration, SPM, VBM	IRW-ASFCM technique is used, allowing for more accurate segmentation of brain tissue. It reduces the misclassification of noisy pixels by substituting fixed fuzzifier values with a fuzzy linguistic fuzzifier value.	2LS-WaveCNN ensemble	—	DTT

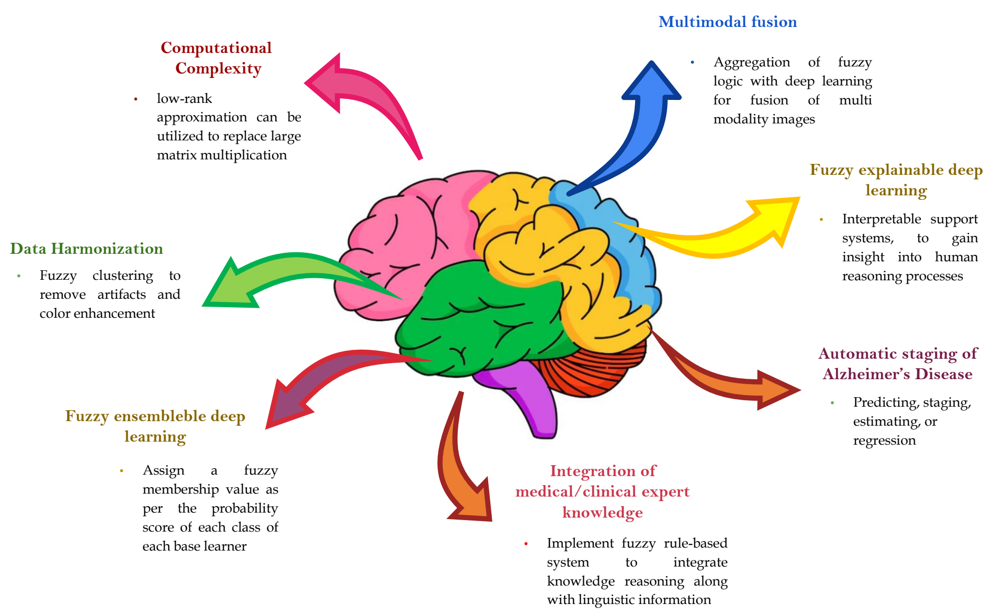

Fig. 3. Graphical representation of challenges and future directions of Fuzzy Deep Learning for AD diagnosis.

the intelligent decision-making method for medical auxiliary diagnosis in terms of rationality and precision, and shorten decision-making times.

D. Integration of Medical/Clinical Expert Knowledge

Expert knowledge, information, and expertise, encompassing both qualitative and quantitative elements, can make healthcare decisions more accurate for real-time assessments. Diagnostic decisions based on clinicians' knowledge of the patient may include lifestyle factors, medical history, genetic factors, blood test results, clinical tests, and various image modalities like an MRI, PET, or CT scan. Many different processes contribute to the development of AD. By combining medical knowledge-driven features with data-driven features, new disease mechanisms, therapeutic targets, and treatment approaches can be better understood and developed.

Future work can be explored by using expert clinician preferences in a fuzzy rule-based system that implements knowledge reasoning along with linguistic information to improve diagnostic performance. A fuzzy inference system can predict the grades of severity for different information provided by the clinicians and deep learning will classify the subject into a particular stage of AD. Integrating fuzzy deep learning along with knowledge-driven features will lower the rate of medical mistakes while simultaneously raising the bar for healthcare quality and efficiency.

E. Fuzzy Ensemble Deep Learning

Deep learning models may face the issue of overfitting or underfitting. Sometimes the data set used to train deep learning networks is too small to train the network. One such solution is ensemble learning, which combines the judgment scores of numerous classifiers to forecast the final input sample's class label. The goal of using an ensemble model is to improve performance more than that of using separate base classifiers by including the most important aspects of each model. Such models are stable because ensembling reduces the bias or variance of the base models' predictions. A homogeneous ensemble deep learning model is one in which all of the base classifiers use the same deep learning network. When several base learners use different deep learning networks, the ensemble model is called heterogeneous. The ensembling of deep learning networks can be done using bagging or boosting. Stacking, one of the most well-known ensembling techniques, acquires knowledge from several different base models and then aggregates the results of those models by training a meta-model. Moreover, stacking generates models with distinct viewpoints on the input data by employing multiple base algorithms on the same data simultaneously.

The incorporation of fuzzy logic in ensemble deep learning can attract researchers to develop new models for AD diagnosis. Fuzzy logic can determine the extent to which each observation fits into each of the fuzzy sets. To incorporate fuzzy logic in ensemble deep learning, a homogeneous or heterogeneous ensemble model can be proposed. Each base learner's decision can be assigned a fuzzy membership function based on their probability scores. A base learner will assign a fuzzy membership value to the likelihood of each class it predicts. When calculating a fuzzy membership function, non-linear functions such as the $tanh$ or exponential functions can be used. Finally, the predicted final score can be obtained by fusing the membership functions of all of the base learners. Both the accuracy and sensitivity of the results regarding the presence of AD disease can be improved by utilizing the fusion of membership values in the prediction process.

F. Data Harmonization

During the acquisition of MRI or PET data, undesirable artifacts may arise due to patient movement or an improper acquisition arrangement. These artifacts must be removed since they drastically reduce the quality of MR images and make it impossible to see important anatomical and physiological details. The major known causes of these artifacts include variations in the scanner, patient anatomy, and radio frequency field non uniformity. Bias field correction uses a filtering-based or bias field model-based strategy to lessen the non-uniformity of MR image intensity. Researchers have suggested intensity standardization-based techniques to correct the discrepancy between intensity distributions in various MRI scans. The conventional method for dealing with noise is noise filtering, which aims to reduce noise by reducing the intensity of images inside a certain tissue area while keeping the borders of that area intact.

Integrating clinical features retrieved from data gathered by various scanners and protocols to enhance stability and robustness has long been a concern in large-scale digital healthcare studies aimed at removing the bias and artifacts of multicenter data. The study [87] reviewed the various data harmonization methods used in the digital healthcare domain, covering topics such as assessment criteria grounded in various theories, harmonization procedures, and data about multiple modalities. Data harmonization techniques were categorized in this review according to four main areas: distribution-based methods, image processing, synthesis, and invariant feature learning.

When fuzzy logic is used in preprocessing, it can let the labels of a pixel or voxel close by affecting their labels. This can make up for differences and artifacts. To update the current centre pixel and eliminate noisy pixels, a fuzzy membership value will be applied to nearby pixels. This value combines local contextual information to provide the matching anisotropic weight. Further, to reduce the color variation, fuzzy logic can be utilized to control the contrast enhancement and modify the color coefficients. The color variations in the MRI and PET images may also be reduced using rough sets and fuzzy clustering algorithms.

G. Computational Complexity

Fuzzy systems could add more parameters to the learning structure of deep learning, which already has a complex design. The complex structure and learning style will lead to an increase in computing costs. The fuzzy membership functions might cause computational complexity, and thus fuzzy deep learning could lead to a complicated modeling structure.

To decrease the computational complexity in deep learning networks, a low-rank approximation can be utilized to replace a large matrix multiplication with two or more smaller matrices. The deep learning network can be made sparser to reduce computational requirements for inferencing. Pruning, low-rank compression, and quantization are methods that can do this. Further, minimize the number of layers and neurons in each layer of the deep learning network. As a result, the network may train more quickly and with fewer parameters.

V. Conclusion

The most prevalent kind of dementia, Alzheimer's disease (AD), causes progressive loss of cognitive function over time in elderly people. There is no cure for AD at this time; therefore, early diagnosis is crucial for physicians to help with treatment planning. Doctors will be able to track the disease's development more precisely with the use of computer-aided diagnostic techniques. While researchers have long used deep learning networks for AD diagnosis, recent developments in fuzzy deep learning have significantly enriched the deep learning architectures by enhancing model robustness, generalization, and accuracy. This review focuses on the application of fuzzy deep learning networks used for AD diagnosis, which are categorized into three categories: image preprocessing, segmentation, and classification of AD disease. This review intends to provide a gentle introduction to fuzzy deep learning for interested researchers for accurate AD diagnosis. Although the study discusses several existing uses of fuzzy deep-learning approaches for AD diagnosis, many unexplored opportunities remain. We discussed about the challenges and possible solutions for fuzzy DL research, including fuzzy explainable DL, automatic AD staging, fuzzy ensemble learning, data harmonization, fuzzy DL for multimodal fusion, integrating knowledge-driven features, and computational complexity.

Computational biomedical researchers are increasingly focusing on fuzzy systems and deep learning as an important step in big multicenter investigations. There has been tremendous theoretical progress in this area, but the community as a whole needs to be aware that there is still a long way to go before fuzzy deep learning is fully developed and useful for AD diagnosis, according to many of the points made in this review. Inspiring challenges and future scope that embrace the multiplicity of fuzzy deep learning methodologies to revolutionize AD and biomedical research, we hope this review article has stimulated ideas on fuzzy deep learning across different disciplines.

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