Classifying Alzheimer's Disease Phases from sMRI Data Using an Adaptive Clonal Selection Approach

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***Abstract*—Structural Magnetic Resonance Imaging (sMRI) has investigated several neurological illnesses, and it has been mapped to unhealthy areas in the brain. Alzheimer's Disease (AD) individuals must be identified as soon as possible so that treatment may begin. Recent research has focused on applying Machine Learning (ML) techniques to segment the brain's structure and categorize AD. Clonal Selection (CS) theory has effectively achieved the goal of categorization and optimization. An Adaptive Clonal Selection (ACS) technique used to categorize sMRI scans into multi-class such as Cognitive Normal (CN), Mild Cognitive Impairment (MCI), and Pure AD categories. The proposed ACS characterizes essential features of the immunological response. This provides support for hypothesis that antigen can only mature inside subset of cells that receive it, as opposed to the rest of the body. Comparable to evolutionary computation relying on mutations, this method excelled at focusing on the idea of clonal expansion and the development of affinity. Proposed ACS technique introduces basic criteria from concept of clonal expansion, assist in creation of highly effective strategies for identifying template matches for aforementioned CN, MCI, and AD. The suggested ACS method outperforms the state-of-the-art methods in aspects of classification and detection accuracy by around 99%.**

***Keywords*—Alzheimer's Disease (AD), Magnetic Resonance Imaging (sMRI), Artificial Immune System (AIS), Enhanced Fuzzy K Nearest Neighbor (EFKNN), Adaptive Neuro-Fuzzy Inference System (ANFIS)**

I. Introduction

The Brain, Spinal Cord, Nerves, and so on are all victims of Neurological Diseases (ND) that impact the entire neurological system. Even a slight impairment in their performance might lead to potentially lethal physical problems. Following the most recent World Alzheimer Report, 55 million individuals throughout the globe are surviving with Alzheimer's Disease (AD) [1].

An AD is very much an irreversible ND that is the 7th largest mortality-causing factor globally. Whenever AD affects the brain, the Protein Components within the cells, referred to as Plaques, and Tangles, gradually deteriorate. When these protein building blocks are damaged, this would cause a dramatic reduction in mental capacity, resulting in devastating effects on every aspect of a human's life.

People with AD experience a wide range of difficulties, including loss of memory, mental instability, movement, and visual impairments. More education on AD among the common people seems to be a major barrier to timely diagnosis. Because of this, cognitive impairment and accompanying activities have often been misdiagnosed as signs of age or another mental health condition [2].

Patients' illnesses have been intensified because of variables including geographical isolation, a dearth of trained caretakers, as well as a shortage of specialists and cutting-edge diagnostic technologies. Thus, timely identification of AD becomes crucial to reduce hopeless patient and caregiver shortages [3]. In earlier days symptom monitoring has been the basis of AD diagnosis, and confirmation of the illness's existence which takes a very long time. Besides that, according to developments in diagnosing studies, various biomarkers such as MRI, Computed Tomography (CT), and Blood Tests have already been recognized to support earlier AD detection. Those biomarkers, together with Artificial Intelligence (AI) technology, could help clinicians make more informed diagnoses and provide better treatment for their patients [4].

Classifiers based on ML had also spread across the medical industry and have proven especially useful for identifying AD [5]. Specifically, Deep Learning (DL) approaches have spread widely in the past few years because of their accuracy in learning complete structures. Pretty much the entire model may be learned from composite data [6]. This tremendous growth in the implementation of DL techniques has unlocked new avenues for the reliable diagnosis of ND. Although applied in conjunction with DL methods, scanning reveals crucial insights into how brain function and related illnesses are perceived.

Nevertheless, there is no known cause for AD, treatments simply reduce symptoms as well as slow the

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disease's course. Psychological studies of AD are crucial for understanding its causes. In the interest of classifying AD phases, several techniques had been suggested for extracting characteristics from Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scans. Unfortunately, crucial intermediate-level data on the brain's function and structure is lacking [7]. Numerous investigations had closely concentrated on areas of the brain with dysfunctional connections but haven't retrieved the features among those regional anomalies to support diagnostic process. The definitive diagnosis and categorization of diseases might be aided by decoding the information retained in dysfunctional connections [8].

AD is linked to problems with HippoCampal (HC) functioning, which is crucial to effective cognitive processing. Many sMRI investigations have examined the ability of HC volumetric measures to differentiate between AD/ Mild Cognitive Impairment (MCI) Individuals, and Aged Subjects, providing more evidence for the usefulness of HC structure and size assessments in assisting with the identification of AD. The conventional strategy has focused on applying Machine Learning (ML) techniques to segment the brain's structure and categorize AD. These methods have shown to be sustainable when applied to small datasets with single classification but they degrade in multi-class classification which leads to major problems when using 3D sMRI images. Our review reveals that most research using MRI and ML for AD/MCI classification produces consistent results. As a seed area, HC might provide a more focused strategy for revealing connections between both the HC and also the rest of brain. Furthermore, it has the possibility of helping in the differentiation between MCI and AD.

In this research, deploy the latest AIS model CS theory with adaptive enhancement to classify the sMRI as CN, MCI, and AD. This was a system focused on the theory of CS and maturation of affinity, analogous to evolutionary algorithms based on mutations. This often involves the survival of the fittest evolutionary algorithm principle.

The overall structure of the paper is organized as follows: In the Section II describes about the details of the most recent works on classifying AD; Section III, it will go through over the methods and approaches that have been employed in both existing and proposed models; Section IV, it will cover the findings that we obtained by evaluating the three groups of modeling methods; and Section V, it will conclude up by looking ahead to potential future uses.

II. Related Works

Entire brain geometrical patterns would be a potentially useful discriminating trait, as suggested by the researchers in [9], who implemented a Deep Siamese Neural Network (DSNN) for classifying AD subjects. Their study's experimental results were comparable to a model trained using MRI scans that covered the entire brain. The researchers in [10] suggest a framework using Multi-Modal Data to build a model that can forecast the course of an illness over time. For the Alzheimer's Disease Neuroimaging Initiative (ADNI) database, which was specifically chosen to include both the Baseline as well as 12-month MRI, their framework attained a precision of 92.5%.

Nawaz *et al.* [11] extracted the features from brain MRI scans using the prominent Alex Net framework before classifying the data using widely-used methods like Random Forest (RF), Support Vector Machine (SVM), K-Nearest Neighbor (KNN), and so on. The suggested Alex Net method achieved high precision in the diagnosis of AD.

Chitradevi and Prabha [12] proposed a method of dissecting the Cerebral Sub-Regions in an attempt to classify AD more precisely. In the process of detecting AD, the segmentation data is passed to ML classifications, whereby, while employing the Grey-Wolf Optimization method, they achieved a diagnostic precision of 98%.

For autonomous brain tumor identification and categorization, a new Modified Adaptive Sine Cosine-Optimization Algorithm (MASCA) combined with a Particle Swarm Optimization (PSO) oriented Local Linear Radial Basis Function Neural Network (LLRBFNN) architecture has been presented [13]. The Fuzzy C-Means system-driven approaches used for segmentation perform poorly in eliminating noise within MRI scans. Therefore, this study provides a new, more efficient, and more reliable Fuzzy C-Means (FCM) method segmentation technique for removing noise and improving the smoothness of MRI scans regarding brain tumors. The accuracy of the classification outcomes generated by the suggested model is found to be higher than those generated using the existing LLRBFNN-related models.

The outcomes guarantee that the MAS technique's efficiency metrics are greater than those of previously used approaches.

CNN has been deeply and extensively reviewed for its usage in medical imaging interpretation of brain activity, lung, breast, and other organ disorders. Challenges are raised, and they are discussed constructively. According to this review, it is analyzed that the different types of ML-based prediction models are developed in the conventional works for AD classification. However, it faced challenges related to accuracy in the MCI stages. To overcome this, we propose a model to enhance the accuracy level of identifying and differentiating MCI and AD stages.

III. Methodologies

sMRI is currently applied by doctors in the diagnosis of AD at different stages since it is one of the methods of neuroimaging which offers more precise anatomical data about an individual's brain. Because sMRI may identify the shrinkage of the HC's physical structure, it is capable of being used as an assessment for AD. Volume measurements of HC seemed to be much more challenging. Certain preliminary measures need to be taken before we can classify AD in the present

research [14]. In Fig. 1, observe exactly the proposed CAD model for AD evaluation through brain sMRI datasets function in more detail.

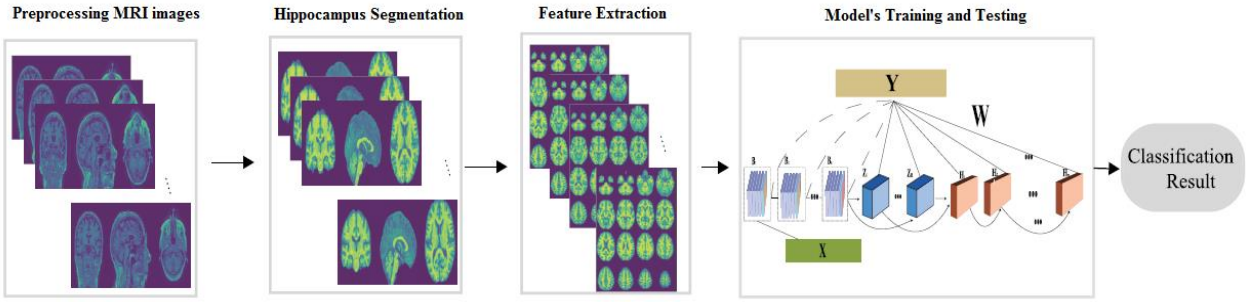


Fig. 1. Methodology for classifying AD phases.

Step 1: In the initial phase we acquire the sMRI images from the dataset such as Alzheimer's Disease Neuroimaging Initiative (ADNI), and KAGGLE consists of CN, MCI, and Pure AD.

Step 2: Then we launch the preprocessing phase in a second stage by inputting a sMRI and removing noise in the specified sMRI image with three separate DCT, DWT, and Median Filtration algorithms. Output to the next stage was received as the consequence of a better Peak Signal Noise Ratio (PSNR) rating.

Step 3: The preprocessed sMRI is segmented for separating the HC region by the K-means Clustering strategy in the third step after pre-processing.

Step 4: The Principal Component Analysis (PCA) has been utilized to isolate the functionalities in the fourth step after a segmenting of the hippocampus area. Features like Region of Interest (RoI) from the segmented field are extracted.

Step 5: In the next step the selection of features was used to choose the best optimal features of the feature collection selected from the previous step using Particle Swarm Optimization (PSO).

Step 6: This is the main step to classify the given sMRI input as CN, MCI, and AD. In this step, we use various classifiers, such as K-Nearest Neighbor (KNN), Enhanced Fuzzy K Nearest Neighbor (EFKNN), Alzheimer's Adaptive Neuro-Fuzzy Inference System (AANFIS), and Adaptive Clonal Selection (ACS).

Step 7: This is the final step to show the performance metrics for each classifier outcome in terms of Accuracy, and Sensitivity.

A. Enhanced Fuzzy K Nearest Neighbor (EFKNN)

The distance estimates perform a vital part in the most common application of the approaches employed to the categorization: the identification of a link between a collection of entities. Contemporary pattern classification technologies such as the KNN technique are not reliant on image compressing and are therefore a viable alternative to its limitations. The Object-Membership processes used in standard KNN grading process provide equal weight to all matched characteristics but lack several others. The EFKNN, which is based on the Fuzzy-Logic principle, exhibits not merely less variation but also more confidence when it classifies objects. The EFKNN also provides an advantageous vector between Object-Membership and Class-Membership. Our first research's goal aimed to use the EFKNN technique to find the most common way to represent a class by contrasting it against its K-closest neighbors. The EFKNN assigns Fuzzy-Membership with the sample and gives authorities discretionary decision-making power. To more accurately recognize AD's phases, this model was completely reviewed from the bottom up. This EFKNN technique was developed to categorize sMRI scans of the brain into cases of CN, MCI, and Pure AD.

ADNI's MRI collection is utilized for training the models, which are subsequently put to the test. The database includes many people who have been diagnosed with CN, MCI, and AD [15].

B. Alzheimer's Adaptive Neuro-Fuzzy Inference System (AANFIS)

In the second phase of AD classification, developed an AANFIS approach in the present research. Neuronal morphology throughout biology is the primary focus of this research. The Neuro and Fuzzy systems are employed in a dual-pathway fashion. Initially, the fuzzy-interface blocks in a NN generate the MRI characteristics. This NN could be modified to provide the desired results using the newly established model of Neuro-Fuzzy systems. In addition, FL makes advantage of the neuronal ability for training by rendering fuzzy networks more flexible to accommodate the execution of the objective. Fuzzy-Membership is employed as a decision-making framework for the provided sMRI image, and the NN has been utilized to improve its performance. There is evidence that the FL can convey the outcomes of expert analysis directly. In such a situation, it's an effort to regulate the use of certain terminology. The Member States' stance, which interprets some linguistic features numerically, requires an excessive amount of time to develop and govern. This is made feasible by combining the NN's automatic learning with the data. It improves the classifier's efficiency while decreasing training duration and costs [16].

C. Adaptive Clonal Selection (ACS)

One of the most common AIS models is the CS. AIS is a starting to emerge research topic in computer analytics science. The creation of scientific perspectives influenced by different immunological concepts has become increasingly appealing. A great deal of earlier study was performed utilizing the genetic and evolutionary estimation methods for the creation of AIS. The Genetic Algorithm (GA) and AIS are the two evolutionary algorithms, but the biggest difference between these two is the development of the species. In GA, the populations have grown by intersection and mutation. The replication of each infant created by a cell is asexual, however, in AIS it is an exact duplicate of their parents. Both algorithms utilize mutations to change cell progeny to sustain population diversity. The traditional CS was enhanced in this research through the adaptive methodology process. The ACS method was used as a final phase in this research work to identify the PSO-derived feature subset as CN, MCI, or AD.

1) Working principle of ACS

- The ACS defines the underlying aspects of the immune response. It points forth the theory that the antigen only develops in those cells that accept it and are chosen from those that don't.
- This was a system focused on the theory of CS and maturation of affinity, analogous to evolutionary algorithms based on mutations.
- This often involves the survival of the fittest evolutionary algorithm principle.
- The ACS method is proposed to introduce certain fundamental rules of the theory of CS, which can contribute to very powerful approaches for AD template match and optimizing issues.

The AIS has still been evolving in science, it has been seen that it can solve a broad variety of problem areas by offering a modern classification algorithm that is focused on CS theory. Owing to its versatility in simulating the clonally chosen immune system actions effectively, the CS has been more emphasized; however, until now it doesn't yet have a classified task model. The enhancement of CS was done in this research work through an adaptive process with positive findings in the classification of ADNI and KAGGLE datasets.

2) AD classification using ACS

For feature representation, the traditional CS has not been capable of multiclass classification, thus in this research, it was enhanced as ACS through the adaptive process for multiclass CN, MCI, and AD classification. The ACS has also been evaluated for the binary pattern classification problem. The focus has been on empowering Cells of the memory to be generalized to be formed which reflects the similar elements of the standard set for each model class. The genetic creation of these generalized cells facilitates proliferation. That's the valuable baseline for CS grouping. When the antigen is introduced to the antibodies one by one, then the discovery of the strongest compatible antibody often takes place.

The inheritance of DL and optimization of proposed ACS in this research are capable of classifying the sMRI and transferring it to the next generations using the temporary information acquired through the cloning and affinity maturation method. This method primarily requires the generation of memory cells that are better able to catch antigens.

The ACS classification process is mentioned in the following for recognizing the AD, MCI, and CN patterns from the PSO feature subsets of a given sMRI.

Step 1: Two repertoires like collection of antigens and a collection of antibodies have been included in the ACS.

Step 2: A randomly generated repertoire from PSO feature subsets are antibodies *Ab* which consists of two sub-sets, *Abm* ('*m*' size of repertoire in memory) and *Abr* ('*r*' size of repertoire that is remaining in memory). The output of this algorithm is the memory repertoire.

Step 3: For the number of generations that are predetermined.

Step 4: **Antigen Release:** Pick the antigen Agi from the Ag repertoire and send it to Ab.

Step 5: **Affinities:** Decide the affinities for any member of the repertoire Ab for Antigen Agi (Attracted).

Step 6: **Antibody Cloning:** Choose n maximum affinity antibodies and create a variety of independent and antigenic copies for each antibody, producing a Ci clone repertoire.

Step 7: **Maturation of Affinities:** The Ci repertoire is a maturing phase of affinity. The Maturation of Affinities is essential in a clone population mutation that is inversely related to its affinity.

Step 8: **Affinity atmosphere:** Find out the affinity of its mature clones now and pick some with the maximum affinity to join the Abm memory antibodies set.

Step 9: **Memory update:** If the above-mentioned applicant clone has an affinity greater than the Ab memory, then the Ab memory is substituted with the Ab clone cell.

Step 10: **Repertoire Updation of Antibodies:** At last, the lowest affinity antibodies in the Abr repertoire are replaced with new individuals generated randomly.

Step 11: Closing the loop **FOR**.

This prozposed ACS technique fascinates its classification work efficiency. The whole technique develops generalized memory cells with or without errors during training. The principle of KNN is used here to locate a memory cell that reflects an area of very similar classes grouped in a training set that is distant from most classes.

The ACS in this research operated as follows:

Step 1: The initial population of the antibodies is first and randomly generated.

Step 2: Besides, it is measured the affinity of any antigen and antibody. Its affinity would be proportional to the Optimal Target (F) magnitude.

Step 3: The Transient Clone (C) collection is produced with antibody clones in the community, with the Pc representing the cumulative number of father clones.

Step 4: Mostly in Clone (C) sampling, the mutation procedure has been performed by employing the Gauss Distribution, Stable Distribution, and Disordered Antibodies Distribution. Affinities serve as a way to evaluate the results of cloning and mutation. A C* subset of antibodies was therefore created at this time.

Step 5: In the latest Antibodies Collection (C*) the Affinity (F*) is determined.

Step 6: New clone entities are accompanied by the clonal selective process and the optimal refined antibodies are chosen.

Step 7: The removal procedure for the missed antibodies is conducted and the average AF fitness score is randomly chosen.

Step 8: Whereas if the current generation of AF gets greater than with preceding one, then the intermediate stage will be duplicated.

Step 9: In the ability to preserve the sample richness of the algorithm, the S% of the fresh antibody is randomly produced and the fresh antibody in the antibodies collection keeps on adding.

Step 10: The better affinities antibodies will be retained and the CS and mutation in the antibodies collection will proceed till the upper limit is reached.

By combining the local search with the global search, this enhanced ACS can rapidly and accurately determine the global optimum alternatives while omitting the need for local optimum. The ACS has indirectly enhanced the search process to point out the exact features from the PSO feature subsets. As a result, the classifying result has become more accurate and can be applied to improve diagnostic testing and administration.

IV. Results and Discussions

A. Datasets

For conducting this study, unique volumetric T1–weighted, "Magnetization Prepared Rapid Gradient Echo (MPRAGE)" sMRI images have been obtained using the open ADNI and KAGGLE datasets. A total of 2000 images of "210 (Male:105, Female:105)" with various subjects "(CN: 70, MCI 70, AD: 70)" have been used.

B. Tools

Matlab, a computational programming environment, is used in an extensive range of diagnosing imaging systems. MATrix LABoratory (MATLAB) user-friendlier interfaces make it a more rapid platform for incorporating new ideas. To evaluate all of the prototypes, we ran simulations with the Matlab software. We employed several methods, notably data generators, to enhance generalization, including "Rotating", "Intensity Modification", "Inversion", and more. The Confusion-Matrix (CM) depicts an assortment of expected and actual categories, each of which is labeled as either "True Positive (TP)", "True Negative (TN)", "False Positive (FP)", or "False Negative (FN)". The CM reveals how effectively the model performs on the training data.

C. ACS Training and Testing Phases

1) Training phase

- The repertoire reflects the knowledge while training and the repertoire Abm is an output from the training (Cells of the memory are generalized) for an Ag classification task.
- The cell size of the memory is preset and the cells of memory repertory are predefined to the classes according to the classes in the training data collection.
- When groups are assigned to the repertoire of the memory, the process of classifying commences with a training stage that generates Cells of the memory that are generalized.
- Next, it pre-processes the memory cells by arbitrarily initializing and classifying them. During the cloning method, the labels of (CN, MCI, and AD) were not modified.

The Matlab ACS training output for proposed AD detection with CAD model is shown in Fig. 2. Fig. 3 shows the storage of trained features by the proposed ACS technique.

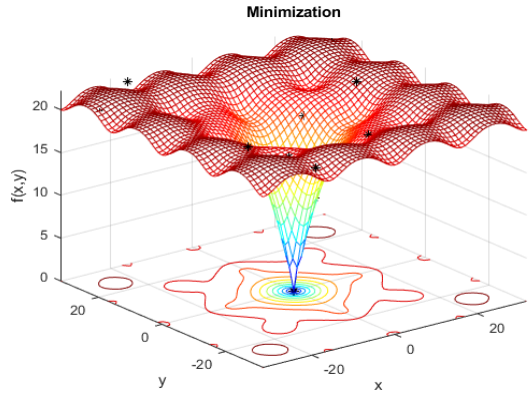


Fig. 2. ACS training.

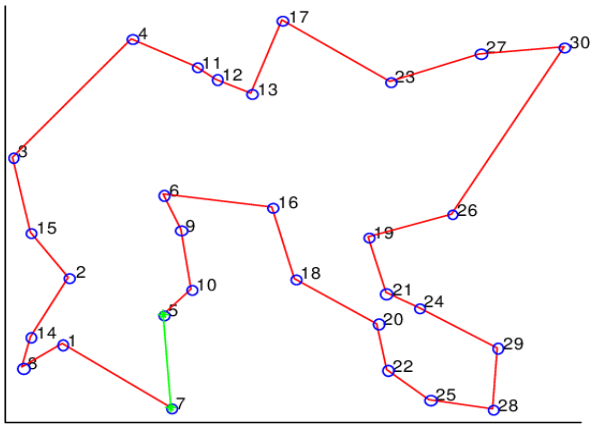


Fig. 3. ACS trained values.

2) Testing phase

- There have been 2 principles to process the testing data after the introduction of the training dataset (or antigens) into the generalized cells of the memory.
- Choose the most closely connected memory cell to the training sample (antigen). This antigen is known as the largest memory cell affinity class. The data instance is set to reclassify if memory cells in many groups have had a similar maximum affinity value.
- Using the KNN principle and detect the relations between whole memory cells to the training sample (antigen). The K memory cells only with maximum affinity poll the ranking. The significant majority decides the form category and cannot be categorized in the case of a tie.

Fig. 4 shows the proposed ACS technique output results of three classes like CN, MCI, and AD.

D. Performance Evaluation

1) Accuracy

Accuracy in categorizing data frequently serves as a proxy for an application's overall quality. It's an important criterion used by experts to evaluate the classification system in its entirety. This means that the more accurate the categorization, the more efficiently the entire system will function. Using the CM, we'd been able to quickly quantify the progress that was made by using all these methods, as seen by Eq. (1).

$$Accuracy = \frac{TP+TN}{TP+TN+FN+FP} \times 100\% \quad (1)$$

Fig. 5 shows the accuracy comparison of KNN, EFKNN, AANFIS, and ACS on different sMRI images. The y-axis shows accuracy, while the x-axis shows subjects for various classification methods. In this case, a total of 6 images have been examined one after another. ACS method consistently outperforms the state-of-the-art KNN, EFKNN, and AANFIS methods. The suggested ACS algorithm gives greater accuracy like 96.00%, 97.00%, 94.00%, 95.00%, 99.00%, and 99.00% for the supplied sMRI images (AD-sMRI1, AD-sMRI2, MCI-sMRI1, MCI-sMRI2, CN-sMRI1, and CN-sMRI2) as compared to the current approaches, which for KNN, EFKNN and AANFIS which provide lesser accuracy.

2) Sensitivity/Recall

According to the results of the sensitivity analysis, the method presented by Eq. (2) can correctly identify the circumstances and calculate the fractions of FN and TP classes:

$$Sensitivity = \frac{TP}{TP+FN} \times 100 \quad (2)$$

In Fig. 6, y-axis shows sensitivity, x-axis shows subjects for various classification methods on 6 images. The suggested ACS method consistently outperforms the state-of-the-art KNN, EFKNN, and AANFIS methods. The suggested ACS algorithm gives greater sensitivity like 94.00%, 95.00%, 92.00%, 93.00%, 98.00%, and 97.00% for the supplied sMRI images (AD-sMRI1, AD-sMRI2, MCI-sMRI1, MCI-sMRI2, CN-sMRI1, and CN-sMRI2).

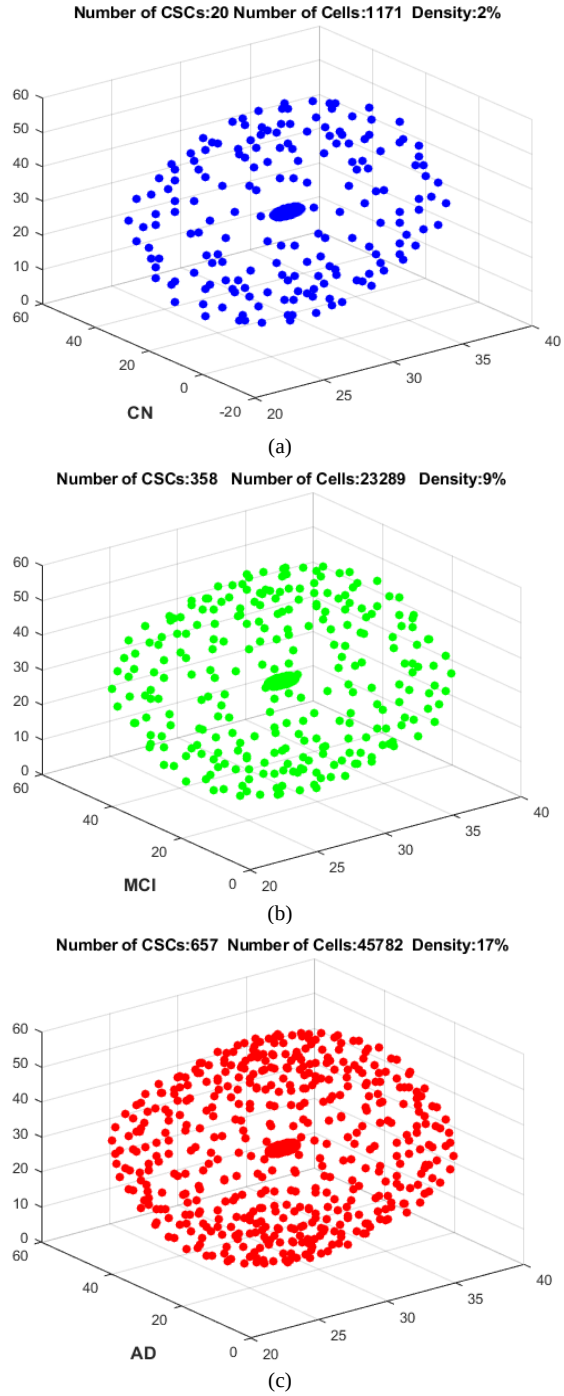
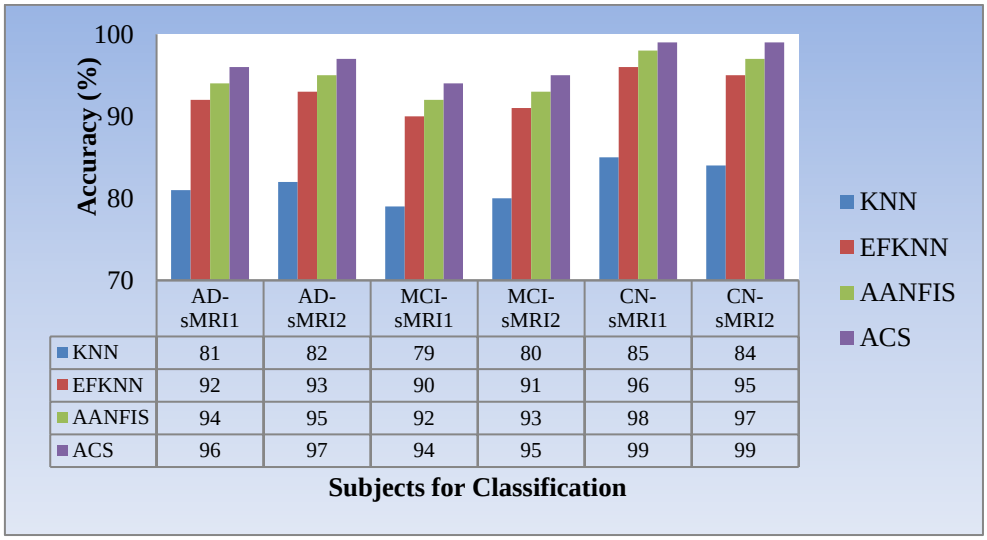
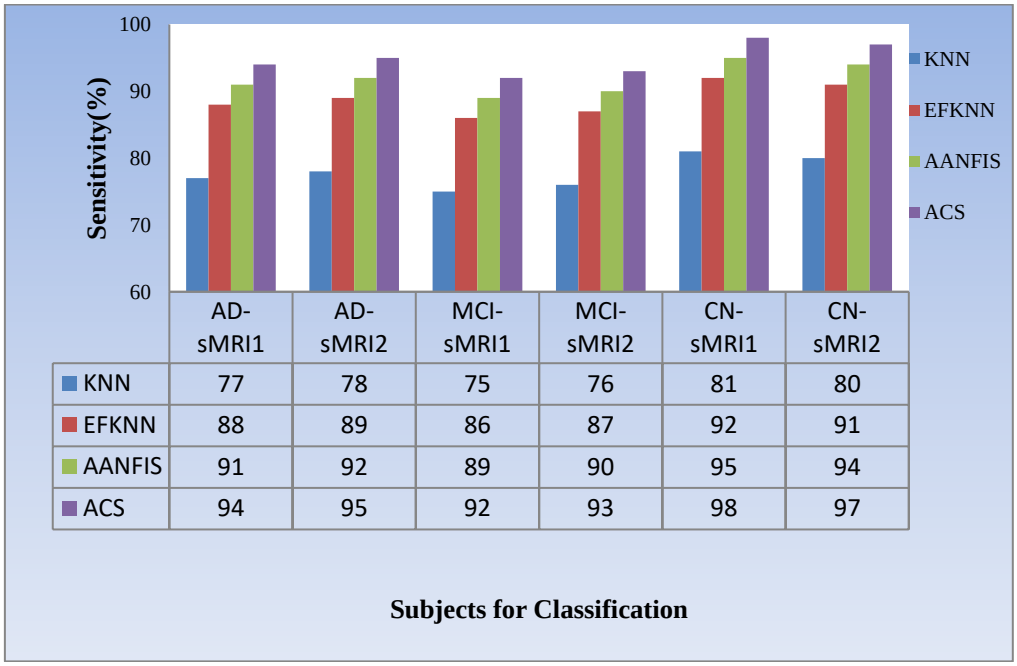


Fig. 4. ACS Classification results on classes; (a). Output for CN, (b). Output for MCI, (c) Output for AD.



	AD-sMRI1	AD-sMRI2	MCI-sMRI1	MCI-sMRI2	CN-sMRI1	CN-sMRI2
KNN	81	82	79	80	85	84
EFKNN	92	93	90	91	96	95
AANFIS	94	95	92	93	98	97
ACS	96	97	94	95	99	99

Fig. 5. Accuracy comparison.



	AD-sMRI1	AD-sMRI2	MCI-sMRI1	MCI-sMRI2	CN-sMRI1	CN-sMRI2
KNN	77	78	75	76	81	80
EFKNN	88	89	86	87	92	91
AANFIS	91	92	89	90	95	94
ACS	94	95	92	93	98	97

Fig. 6. Sensitivity comparison.

V. Conclusion and Future Work

In this research, we deploy the latest AIS model CS theory with adaptive enhancement to classify the sMRI as CN, MCI, and AD. This was a system focused on the theory of CS and maturation of affinity, analogous to evolutionary algorithms based on mutations. This proposed ACS technique fascinates its classification work efficiency. The whole technique develops generalized memory cells with or without errors during training. The principle of KNN is used here to locate a memory cell that reflects an area of very similar classes grouped in a training set that is distant from most classes. In terms of the accuracy and sensitivity in classification, the outcomes of the comparison reveal that the suggested ACS technique excels over the state-of-the-art KNN, EFKNN, and AANFIS techniques. Based on our findings, a dysfunctional HC connection could represent a valuable sMRI biomarker for speeding the preliminary identification of AD and MCI. In conclusion, key findings of the long-term goal of this project became to assess the generalization ability of categorization systems in hopes of accelerating the translation of findings from the experiments into the treatment center. While we narrowed our attention to AD identification during this phase of research, we believe that future application areas could improve considerably from the categorization of other mental disorders, which would provide advantages in terms of both the disclosure of pathological distinctions across diseases and the improvement of the precision with which they are diagnosed. This expansive field of study requires more investigation because of difficulties associated with

massive multiple illness databases and complex categorization algorithms.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Mathews Emmanuel: Conceptualization, Methodology, Writing, Original Draft and Formal analysis; J. Jabez: Writing, Review and Editing, Interpretation of Data; all authors had approved the final version.

REFERENCES

[1] S. Gauthier, P. R. Neto, J. A. Morais, and C. Webster, "World Alzheimer report 2021," *Journey through the diagnosis of dementia, Alzheimer's Disease International*, pp. 1–313, 2021.

[2] L. Jia *et al.*, "Dementia in China: Epidemiology, clinical management, and research advances," *The Lancet Neurology*, vol. 19, no. 1, pp. 81–92, 2020.

[3] G. Mirzaei and H. Adeli, "Machine learning techniques for diagnosis of Alzheimer disease, mild cognitive disorder, and other types of dementia," *Biomedical Signal Processing and Control*, vol. 72, pp. 1–28, 2022.

[4] K. R. Bhatele and S. S. Bhadauria, "Brain structural disorders detection and classification approaches: A review," *Artificial Intelligence Review*, vol. 53, pp. 3349–3401, 2022.

[5] M. Tanveer *et al.*, "Machine learning techniques for the diagnosis of Alzheimer's disease: A review," *ACM Transactions on Multimedia Computing, Communications, and Applications (TOMM)*, vol. 16, pp. 1–35, 2020.

[6] M. Mahmud *et al.*, "Deep learning in mining biological data," *Cognitive Computation*, vol. 13, pp. 1–33, 2021.

[7] Y. N. Ou *et al.*, "FDG-PET as an independent biomarker for Alzheimer's biological diagnosis: A longitudinal study," *Alzheimer's Research and Therapy*, pp. 1–11, 2019. doi: 10.1186/s13195-019-0512-1

[8] Z. Fan*et al.*, "Classification of Alzheimer's disease based on brain MRI and machine learning," *Neural Computing and Applications*, vol. 32, pp.1927–1936, 2020.

[9] C. F. Liu *et al.*, "Using deep Siamese neural networks for detection of brain asymmetries associated with Alzheimer's disease and mild cognitive impairment," *Magnetic Resonance Imaging*, vol. 64, pp.190–199, 2019.

[10] C. Ostertag *et al.*, "Predicting brain degeneration with a multimodal Siamese neural network," in *Proc. 2020 Tenth International Conference on Image Processing Theory, Tools and Applications (IPTA)*, pp.1–6, 2020.

[11] H. Nawaz *et al.*, "A deep feature-based real-time system for Alzheimer disease stage detection," *Multimedia Tools and Applications*, pp. 35789–35807, 2021.

[12] D. Chitradevi and S. Prabha, "Analysis of brain sub regions using optimization techniques and deep learning method in Alzheimer disease," *Applied Soft Computing*, vol. 86, pp. 1–31, 2020.

[13] S. Mishra, P. Sahu, and M. R. Senapati, "MASCA–PSO based LLRBFNN model and improved fast and robust FCM algorithm for detection and classification of brain tumor from MR image," *Evolutionary Intelligence*, vol. 12, pp. 647–663, 2019.

[14] M. Emmanuel and J. Jabez, "A brief survey on different methods employed in each module for diagnosing Alzheimer disease in the early stage," *International Journal of Health Sciences*, vol. 6, 2022.

[15] M. Emmanuel and J. Jabez, "An enhanced fuzzy based KNN classification method for Alzheimer's disease identification from SMRI images," *Journal of Algebraic Statistics*, pp. 89–103, 2022.

[16] M. Emmanuel and J. Jabez, "An advanced adaptive neuro-fuzzy inference system for classifying Alzheimer's disease stages from SMRI images," in *Proc. 2023 Advanced Computing and Communication Technologies for High Performance Applications (ACCTHPA)*, 2023.