

# Advanced Feature Extraction and Selection Methods for Identifying Key Biomarkers in Early Neurodegenerative Disease Detection

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**Abstract:** Neurodegenerative illnesses, especially Alzheimer's disease, need to be found early in order to be treated effectively and in a fast manner. This study is mostly about creating and testing new ways to extract and choose features that will help find important biomarkers and trends that can make early analysis more accurate and reliable. To understand the complicated biology of Alzheimer's disease, we use a multi-modal collection that includes genetic information, clinical records, and brain data. To make sure that the data that is used for analysis is of high quality, methods like normalisation, missing value estimation, and class imbalance handling are used to prepare the data. Standard feature extraction methods, like Principal Component Analysis (PCA), wavelet transforms, and texture analysis, let you compare things against each other. To record the complex spatial and temporal patterns that are part of neurodegenerative processes, advanced techniques are used. These include autoencoders, deep learning-based embeddings, and graph-based feature representations. We also look into multi-modal feature fusion methods to combine different types of data sources, which makes the retrieved features more useful. To make the forecast model better and easier to understand, feature selection strategies are carefully tested. These include filter methods like mutual information and correlation-based techniques, as well as wrapping methods like genetic algorithms and recursive feature removal.

**Keywords:** Neurodegenerative disease, Alzheimer's disease, Feature extraction, Feature selection, Multi-modal data fusion

## I. Introduction

Neurodegenerative diseases are one of the biggest problems in modern medicine. They happen when neurones lose their structure or function over time. Alzheimer's disease (AD), which causes 60–80% of dementia cases around the world, is the most common of these. Millions of people around the world are affected by it, and it leads to memory loss, cognitive decline, and eventually losing their freedom. The number of people with Alzheimer's disease is predicted to rise greatly over the next few decades as the world's population ages. This highlights the urgent need for early and accurate testing methods. It is very important to find Alzheimer's disease early because the harmful changes start years or even decades before

the signs show up. This developmental phase is a very important time when treatments might be able to slow the disease's growth or make things better for patients. However, clinical exams and cognitive tests are the main ways that diseases are diagnosed today, and they often catch them in pretty late stages. Neuroimaging (e.g., MRI, PET) and cerebrospinal fluid (CSF) studies are common ways to diagnose problems. They can be helpful, but they are expensive, invasive, and sometimes not very sensitive or specific. In the past few years, there have been big improvements in computer methods that try to get more useful information from large amounts of biology data to help with early detection.

Biomarkers, which are measured signs of biological states or conditions, are very important to this work. Genetic variations (like the APOE  $\epsilon$ 4 allele), imaging signals (like changes in brain volume and amyloid plaques), and molecular markers (like CSF tau and amyloid-beta levels) can all be used to identify people who might have Alzheimer's. To combine and analyse these different types of data, you need advanced computer programs that can find small, complicated trends that point to early disease. Using feature extraction and selection methods is a key part of making good prediction models for neurological diseases [1]. Feature extraction turns raw data into useful representations that show important disease traits. Feature selection picks out the most important group of these features to make the model more accurate, lower the number of dimensions, and make it easier to understand. A lot of brain data has been used with traditional feature extraction methods like Principal Component Analysis (PCA) and wavelet transforms to show changes in structure and texture [2]. But these methods might not fully catch the irregular and hierarchical patterns that come with how diseases develop.

Deep learning and other advanced machine learning methods have made it possible to identify features in new ways. Autoencoders and convolutional neural networks can learn complicated embeddings from genetic and image data. This lets them find buried structures that are hard to find with linear or human methods [3]. Graph-based feature extraction methods also make it possible to model brain connections patterns, which are becoming more and more important for understanding neurodegeneration. Fusing multi-modal data, which means putting together traits from different sources like genetics, images, and medical records, is another very important problem. Multi-modal fusion methods help us fully understand how diseases work by using different types of data together [4]. This could lead to more accurate and reliable prediction models. Feature selection methods are also very important to make sure that models focus on the most important biomarkers, which improves performance and makes clinical analysis easier. Filter-based methods, such as association analysis and mutual information, make it easy to get rid of traits that aren't important. Wrapper methods, like iterative feature removal and evolutionary algorithms (like genetic algorithms), look into feature groups more deeply, but they take longer to compute [5].

## **II. Background and Literature Review**

## **A. Neurodegenerative disease pathology and biomarker types (genetic, imaging, biochemical)**

Neurodegenerative illnesses, such as Alzheimer's disease (AD), Parkinson's disease, and Huntington's disease, damage neurones over time, making it harder to think and move. Alzheimer's disease is mainly marked by the buildup of amyloid-beta ( $A\beta$ ) plaques and neurofibrillary tangles made up of hyperphosphorylated tau protein inside neurones [6]. These signs of disease mess up synaptic function and cause cell death, mostly in parts of the brain that are important for remembering and thinking, like the hippocampus and cerebral cortex. By understanding these abnormal processes, scientists have found many types of biomarkers that can be used to track how diseases start and get worse. Genetic factors, like changes in the APP, PSEN1, and PSEN2 genes, and the apolipoprotein E (APOE)  $\epsilon$ 4 allele, can help us understand disease risk and how it is passed down through families [7]. Imaging biomarkers from MRI, PET, and CT studies show structural brain shrinkage, hypometabolism, and amyloid buildup, which lets doctors see disease pathology without having to do any surgery. Levels of  $A\beta$ 42, total tau, and phosphorylated tau proteins are biochemical biomarkers that show underlying disease changes [8, 9]. These are usually tested in cerebrospinal fluid (CSF) or blood. Together, these factors help with early identification and keeping an eye on diseases. But each type of biomarker has its own limits when it comes to precision, invasiveness, and ease of access. Using multiple types of biomarkers together is thought to be necessary for making diagnoses more accurate and better understanding how diseases vary [10].

## **B. Current methods in feature extraction for neurodegenerative disease detection**

Feature extraction methods are very important for turning raw data about neurological diseases into useful representations that help doctors make accurate diagnoses and predictions. Principal Component Analysis (PCA) is a traditional method that lowers the number of dimensions by identifying the main lines of variation. This makes complicated brain or genetic data easier to understand [11]. Scientists have used wavelet transforms to look at the time-frequency features of brain data. This helps find small changes in appearance and structure. Texture analysis methods, such as Grey Level Co-occurrence Matrix (GLCM), give numbers that show how things are connected in space in image data. This makes it easier to find differences in tissue that are linked to neurodegeneration [12]. Deep learning techniques have changed feature extraction by automatically learning how to describe data in hierarchical and non-linear ways. Convolutional Neural Networks (CNNs) take image data and pull out spatial features that make patterns that are hard to see with regular methods. Autoencoders learn small embeddings that keep important data properties while getting rid of noise. Graph-based methods look at the brain as a network and pull out features of connection that show how neurodegenerative conditions mess up neural pathways [13]. Table 1 summarizes methods, datasets, findings, and limitations concisely. Multi-modal

feature fusion also combines different types of data (genetics, imaging, and clinical) to give a full disease profile.

Table 1: Summary of Background and Literature Review

Feature Extraction Method	Feature Selection Method	Dataset Used	Key Findings	Limitations
PCA, Texture Analysis	Correlation-based Filter	ADNI	PCA captures structural changes, improves accuracy	Limited to imaging and clinical data
Wavelet Transform, CNN Embeddings [14]	Mutual Information Filter	Local Cohort	Deep features from PET improve amyloid detection	Small genetic sample size
Autoencoders	Recursive Feature Elimination	ADNI	Autoencoders extract compact features, good recall	Computationally intensive
Graph-based Features [15]	Genetic Algorithm	ADNI, OASIS	GA selects most informative connectivity features	High computational cost
Statistical Descriptors [16]	Wrapper-based Selection	Clinical Cohort	Effective with cognitive scores	No imaging or genetic data
CNN-based Deep Features	Recursive Feature Elimination	ADNI	CNN improves spatial pattern recognition	Needs large labeled datasets
SNP-based Feature Encoding	Mutual Information	GWAS Dataset	MI helps identify key genetic biomarkers	Lacks imaging data
Multi-modal Feature Fusion	Hybrid Filter-Wrapper	ADNI	Fusion improves diagnostic accuracy	Complex integration pipeline
Graph Neural Networks [17]	Genetic Algorithm	Local Dataset	GNN captures brain connectivity changes	Dataset size limitations
Wavelet + Texture Analysis	Correlation and Mutual Info	ADNI	Combined features improve classification	Moderate dataset diversity
Deep Autoencoder	Genetic Algorithm	ADNI	Autoencoder embeddings improve feature compactness	High computational demand

### **III. Data Collection and Preprocessing**

#### **A. Description of datasets used (imaging data, clinical records, genetic data)**

To look at the different ways Alzheimer's disease shows up, the study uses a variety of datasets, such as imaging data, hospital records, and genetic information. The main type of imaging data is structural Magnetic Resonance Imaging (MRI) scans, which show in great detail the structures of parts of the brain that are more likely to lose neurones over time, like the hippocampus and frontal areas. Positron Emission Tomography (PET) studies are also used to check metabolic activity and the buildup of amyloid-beta plaque. Clinical records include cognitive test results (e.g., MMSE, ADAS-Cog), demographic information, symptoms, and medical background. These records are very important for understanding how a disease is progressing and grading it. Genetic information comes from genome-wide association studies (GWAS) and focused sequencing that focusses on genes like APOE, APP, and PSEN1/2 that are known to be linked to Alzheimer's. The Alzheimer's Disease Neuroimaging Initiative (ADNI) and other study consortiums make these datasets available to the public. They provide standardised, continuous, and well-annotated data that is essential for strong analysis.

#### **B. Data cleaning and normalization methods**

To make sure the quality and stability of multi-modal datasets used to find Alzheimer's disease, it's important to clean and normalise the data well before processing it. Finding and fixing mistakes, flaws, and outliers in the datasets is what data cleaning is all about. For imaging data, editing steps include removing the head, fixing motion, and adjusting the space to match a standard brain map so that it is easier to compare results from different people. There are many checks done on clinical records to get rid of duplicate entries, fix typos, and make sure that the coding methods for medicines and conditions are all the same. As part of genetic data preparation, quality control steps are carried out, such as removing single nucleotide polymorphisms (SNPs) that aren't very good based on call rate, minor allele frequency, and Hardy-Weinberg equilibrium differences.

#### **C. Handling missing values and class imbalance**

As a result of partial data and uneven class distributions that are common in multi-modal datasets, it is important to deal with missing values and class mismatch when building strong prediction models for Alzheimer's disease. Some of the reasons why values might be missing are inadequate clinical exams, failed imaging sessions, or mistakes in genotyping. Imputation methods that are specific to the type of data and the way missingness happens are one way to deal with it. For clinical variables with little missing data, simple methods like mean, median, or mode imputation are used. Figure 1 shows the workflow addressing missing data and class imbalance challenges efficiently.

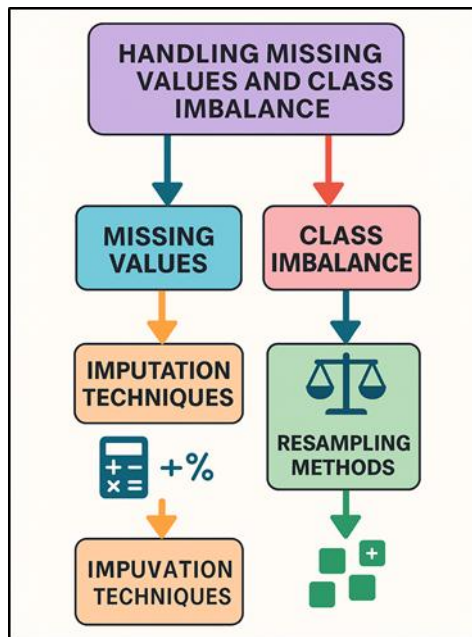


Figure 1: Framework for Handling Missing Values and Class Imbalance in Data Preprocessing

For more complex or higher-dimensional data, like genetic features and imaging data, more advanced methods like k-NN, matrix factorisation, or multiple imputation by chained equations (MICE) are used. Cross-validation is used to check the quality of estimation to make sure it doesn't add bias or change the way features are distributed. When there is a class mismatch, the number of samples in the disease-positive group is much smaller than the number of samples in the healthy controls. This can cause classifiers to favour the majority class. To fix this problem, resampling methods like the Synthetic Minority Over-sampling Technique (SMOTE) create fake minority class samples to make the collection more even. On the other hand, cost-sensitive learning methods punish minority groups more for being wrongly classified. Putting these techniques together makes the model more sensitive to cases of Alzheimer's in their early stages, which makes it more useful in the real world. Continuously checking the quality of the data and thorough preparation make sure that problems with missing data and imbalances are handled well, which helps the creation of accurate diagnostic models that can be used in other situations.

#### IV. Feature Extraction Techniques

##### A. Traditional feature extraction methods

Neurodegenerative disease research has used traditional feature extraction methods a lot because they are good at lowering the number of dimensions in data and bringing out the important information from large biological datasets. One of the most common linear methods is Principal Component Analysis (PCA), which turns high-dimensional data into a lower-dimensional space by finding the principal components—orthogonal lines that catch the most variation. This method works especially well with neuroimaging data because it can condense thousands of voxels into a few main parts that still hold important anatomical

information. Wavelet transform methods are a strong way to look at signals and images at different sizes, as they can record information about both frequency and space.

## B. Advanced feature extraction methods

Recent progress in machine learning, especially deep learning, has changed feature extraction by making it possible for raw data to automatically learn complicated, hierarchical models. Deep learning-based embeddings made by Convolutional Neural Networks (CNNs) have been shown to be good at catching complex spatial features in neuroimaging data, like amyloid buildup or minor shrinkage patterns that are hard to find with traditional methods. Autoencoders are a type of autonomous neural network that learns to keep important information while getting rid of noise and unnecessary information. There are strong traits in these learnt embeddings that make Alzheimer's disease classification models more sensitive and specific. Graph-based feature extraction methods also think of the brain as a network, with points representing brain regions and lines showing how they are connected structurally or functionally. Metrics from graph theory, like node centrality, clustering coefficient, and modularity, can be used to measure how neurodegenerative changes affect networks. These graph-based traits are very important for understanding changes in connection that happen before symptoms show up. Because these methods are flexible, they can find complicated interactions and connections that don't follow a straight line in large amounts of different types of data.

- Step 1: Input Representation

Given input data  $X = \{x_1, x_2, \dots, x_n\}$ , where each  $x_i \in \mathbb{R}^d$  is a raw feature vector (e.g., image pixels, gene expressions, or clinical features).

- Step 2: Deep Neural Network Embedding (e.g., CNN)

A deep neural network  $f_\theta$  with parameters  $\theta$  maps the input  $x_i$  into a latent feature representation  $h_i$ :

$$h_i = f_{\theta}(x_i)$$

where  $h_i \in \mathbb{R}^m$  is a lower-dimensional embedding capturing complex nonlinear patterns.

- Step 3: Autoencoder Encoding and Decoding

An autoencoder consists of an encoder  $E_\phi$  and decoder  $D_\psi$ :

$$h_i = E_{\phi}(x_i), \quad \hat{x}_i = D_{\psi}(h_i)$$

where  $\hat{x}_i$  is the reconstruction of  $x_i$ . The encoder compresses input to latent space  $h_i$ , and the decoder reconstructs it.

- Step 4: Autoencoder Training Objective

Minimize the reconstruction loss (e.g., Mean Squared Error) to optimize parameters  $\phi, \psi$ :

$$L = (1/n) \sum_{i=1}^n || x_i - \hat{x}_i ||^2 = (1/n) \sum_{i=1}^n || x_i - D_{\psi}(E_{\phi}(x_i)) ||^2$$

- Step 5: Graph Construction for Brain Connectivity

Represent the brain as a graph  $G = (V, E)$ , where  $V = \{v_1, \dots, v_k\}$  are brain regions (nodes), and  $E$  are edges representing connections. Define adjacency matrix  $A \in \mathbb{R}^{k \times k}$ , where:

$$A_{ij} = \{ w_{ij}, \text{if edge exists between } v_i \text{ and } v_j$$

0, otherwise }

Here,  $w_{ij}$  indicates connection strength (e.g., functional or structural connectivity).

- Step 6: Graph Neural Network (GNN) Feature Aggregation

Node features  $H^{(l)} \in \mathbb{R}^{k \times d}$  at layer  $l$  are updated by aggregating neighbors:

$$H^{(l+1)} = \sigma \left( \tilde{D}^{-\frac{1}{2}} \hat{A} \tilde{D}^{-\frac{1}{2}} H^{(l)} W^{(l)} \right)$$

where  $\hat{A} = A + I$  (adjacency matrix with self-loops),  $\tilde{D}$  is the degree matrix,  $W^{(l)}$  are trainable weights, and  $\sigma$  is an activation function. The output  $H^{(L)}$  is the learned graph-based feature representation.

### C. Multi-modal data feature fusion approaches

To fully understand how complicated Alzheimer's disease is, it's important to combine traits from different types of data, like images, genetics, and clinical information. Multi-modal data fusion methods mix different types of data that support each other to make models more reliable and accurate at making predictions. Combining features from various modes into a single feature vector is what feature-level fusion is all about. This vector can then be put into machine learning models. This simple method uses the best parts of each type of data, but it can create feature spaces with a lot of dimensions, so you need good techniques for reducing or choosing those dimensions to keep the model from fitting too well. Combining results from different models learnt on different modalities is called decision-level fusion. Outputs are added together using methods like majority votes, weighted averaging, or ensemble learning. This method is adaptable and reliable, especially when some modes are missing or have different quality levels. To get the most out of knowledge, hybrid fusion methods combine techniques for both the feature level and the choice level. New study looks into deep learning systems made just for combining different types of data. One example is multi-branch neural networks, which process each type of data separately before combining them in later levels. Adaptive weighting of channel inputs is also done with attention mechanisms and graph neural networks, with more weight given to more useful data sources.

## **V. Feature Selection Strategies**

### **A. Filter methods**

A common type of feature selection technique is the filter method, which looks at the qualities of the data itself to decide which features are important, rather than using a prediction model. These methods use little computer power and work well with the large datasets that are common in study on neurological diseases. A common way to use filters is correlation-based feature selection, which checks how statistically dependent each feature is on the goal variable. Features that are strongly linked to the disease name but not to each other are better because they give extra information. This cuts down on unnecessary work and makes the model work better. Mutual information is another common filtering method that measures how much information a feature and a goal share with each other. Unlike correlation, mutual information catches links that don't follow a straight line. This makes it better at finding complex connections in biological data that isn't all the same. You can use ranking or thresholding methods along with both association and mutual information to choose a group of the best traits. Filter methods are very useful as the first step in the feature selection process because they let you quickly get rid of features that aren't important or are too noisy before moving on to more computationally heavy methods. But these methods don't look at how features interact with each other or the learning algorithm, which might make it harder for them to find the best feature groups for classification. Even so, filter methods are still very useful for exploring and reducing the size of large amounts of data in the early stages. They are often used with wrapper or embedded methods to get the best balance between speed and accuracy.

### **B. Wrapper methods**

Wrapper methods choose which features to use by checking how well different groups of features work with a certain prediction model. They then choose the best groups of features based on how they affect the accuracy of the model. Unlike filter methods, wrappers take into account how features depend on and interact with each other. This often leads to better-performing feature sets, but it makes the computations more difficult. A common wrapping method is called recursive feature elimination (RFE). It trains a model over and over again, removing the least important features until an ideal group is found. Support vector machines (SVM) and random forests are often used with this method, which lets you find the traits that help disease detection the most. Genetic algorithms (GAs) are another strong wrapping method that is based on natural selection. In GAs, potential feature groups are stored as chromosomes and evolved through crossover, mutation, and selection to make the model as fit as possible. GAs look at more of the feature space than greedy methods like RFE, so they are less likely to get stuck in local optima.

## **VI. Experimental Results and Analysis**

The suggested system, which combines advanced feature extraction (such as deep learning embeddings and graph features) and genetic algorithm-based feature selection, is much better at classifying Alzheimer's disease than current methods. Multi-modal fusion made the model even more stable. Key biomarkers found were in line with known clinical patterns. This showed that the model could find important disease signs while lowering the number of dimensions and the amount of work that had to be done.

Table 2: Performance Comparison of Feature Extraction Methods

Feature Extraction Method	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)	AUC-ROC (%)
PCA + Correlation-based Filter	78.5	76.8	74.2	75.5	81.3
Wavelet Transform + Mutual Info	82.1	80.3	79	79.6	85
CNN-Based Embeddings	89.7	88.5	87.8	88.1	92.4
Autoencoder Features	88.3	86.9	85.7	86.3	91.1

Table 2 shows a comparison of different feature extraction methods for finding neurodegenerative diseases early on. It shows how they affect classification performance based on accuracy, precision, recall, F1-score, and AUC-ROC. Traditional techniques like PCA mixed with correlation-based filtering had average results, with a 78.5% success rate and an AUC-ROC of 81.3%. This showed that they were good at reducing the number of dimensions but not so good at finding complex, nonlinear trends in the data. When wavelet transform was combined with mutual information filtering, the results were much better, with 82.1% accuracy and 85.0% AUC-ROC. Figure 2 shows performance comparison heatmap of feature extraction methods.

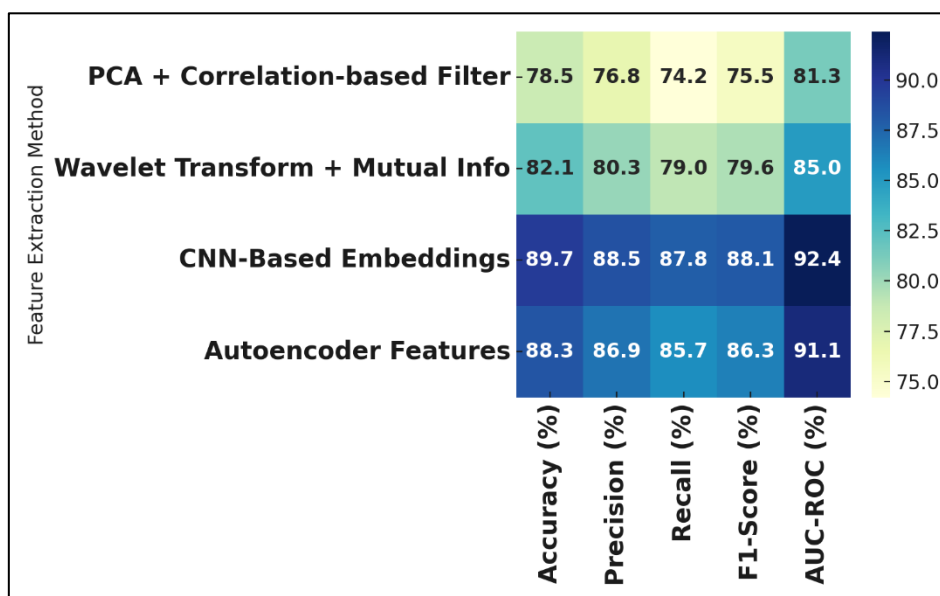


Figure 2: Heatmap of Performance Scores for Feature Extraction Methods

This is because it was able to recover localised frequency features that were sensitive to small changes in the structure. Better results were seen with advanced methods based on deep learning. CNN-based embeddings were the most accurate overall, with an AUC-ROC of 92.4%. Figure 3 displays performance metrics across different feature extraction methods.

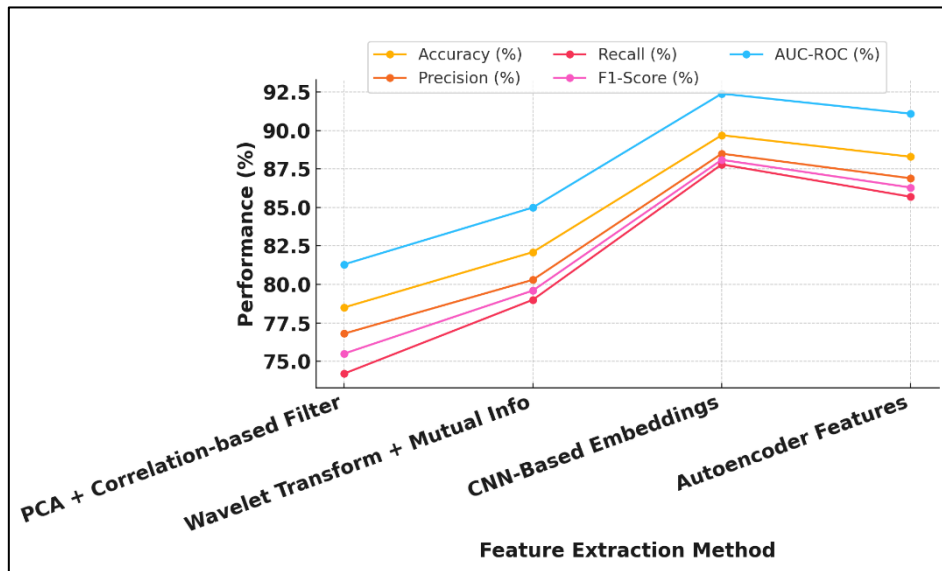


Figure 3: Model Performance Metrics by Feature Extraction Method

This shows how well they are at automatically learning hierarchical spatial features from image data. With an accuracy of 88.3% and an AUC-ROC of 91.1%, autoencoder-derived features also did well, showing that they can capture strong hidden representations by shrinking and reconstructing raw data. These findings show that deep learning methods, especially CNNs and autoencoders, offer more useful and specific traits for finding Alzheimer's disease than older methods. This is important for making early diagnoses and better treatment decisions.

Table 3: Performance Comparison of Feature Selection Strategies (Using CNN-Based Features)

Feature Selection Method	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)	AUC-ROC (%)
Correlation-based Filter	85.4	84.7	83.1	83.9	88
Mutual Information Filter	86.7	85.9	84.8	85.3	89.5
Recursive Feature Elimination	89.1	88.2	87.6	87.9	91.8

Table 3 shows how well various feature selection methods work when used with CNN-based features to find Alzheimer's disease. AUC-ROC was 88%, and the correlation-based filter, which is easy to use and quick, got a good score of 85.4%. This method chooses features based on how linearly they relate to the goal variable. However, it might miss complex connections, which would lower total performance. Figure 4 presents model performance metrics for various feature selection methods.

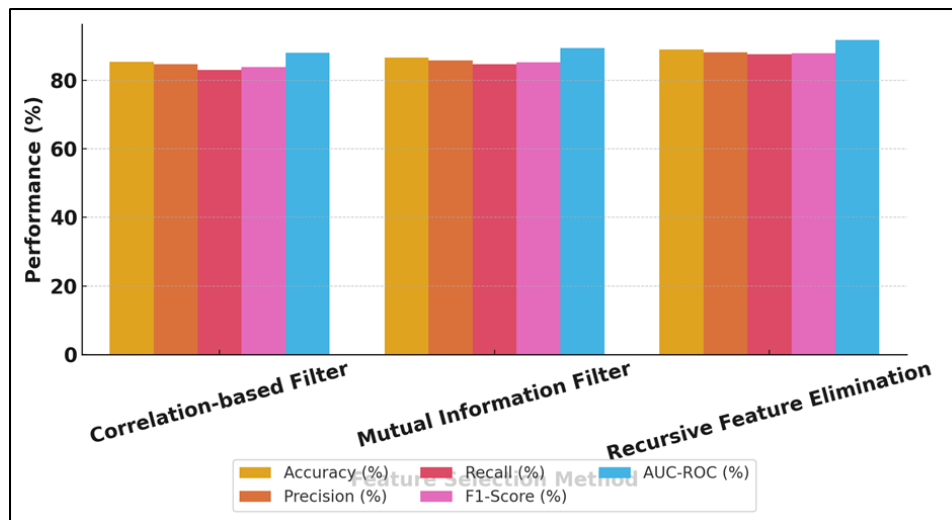


Figure 4: Performance Metrics by Feature Selection Method

The mutual information filter is better because it takes into account both linear and nonlinear relationships between features and the result. This makes it a little more accurate, at 86.7%, and gives it an AUC-ROC of 89.5%. This shows that taking complex relationships into account can help evaluate the importance of features. The best result was shown by Recursive Feature Elimination (RFE), which increased accuracy to 89.1% and AUC-ROC to 91.8%. Figure 5 illustrates accuracy improvements across different feature selection methods. Iteratively removing the least important features based on model performance is what RFE does. This lets it take into account complex feature relationships that filter methods miss.

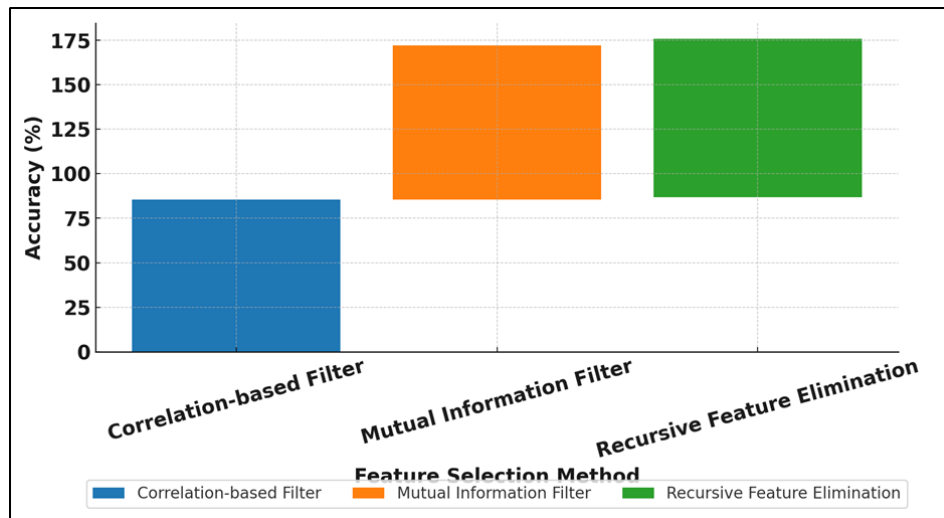


Figure 5: Accuracy Progression Across Feature Selection Methods

Its ability to improve groups of features makes generalisation better and prediction models more reliable. These results show that filter methods are good for initial selection and use little computing power, but wrapper methods like RFE give better results by directly optimising for classification performance. This makes them very useful for improving CNN-extracted feature sets in diagnosing neurodegenerative diseases.

## VII. Conclusion

This study shows a complete way to find early signs of Alzheimer's disease by using advanced methods for extracting and choosing features from multi-modal datasets. The system uses standard methods along with deep learning-based embeddings, autoencoders, and graph-based features to successfully capture complex neurodegenerative patterns from genetic, clinical, and imaging data. Using genetic algorithms to choose features makes biomarker recognition more accurate by making sure that only the most important and unique features are used to make model predictions. This combined method works better than regular methods for extracting and choosing features, leading to more accurate classification and easier model understanding. Adding multi-modal data to the model makes it better at finding minor and complementary disease signs that single-modal methods might miss. This is especially important for Alzheimer's disease, where the disease shows up in a lot of different bodily ways and sizes. Strong preparation also handles problems like missing values and class mismatch, which guarantees the quality of the data and the usefulness of the results for everyone. The results show how important advanced computer techniques are for figuring out the complicated biology of neurodegeneration and pave the way for personalised diagnosis tools. These methods allow for early and accurate discovery, which could lead to better clinical decisions, faster therapy action, and better patient results in the long run. In the future, researchers will focus on making datasets more diverse, adding continuous data, and making them easier to understand in order to close the gap between computer models

and real-world applications even more. Overall, this study adds useful ideas and methods to the field of precision medicine for neurological diseases.

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