CHAPTER 4
ARCHITECTURE OF THE PROPOSED SEGMENTATION ALGORITHM

Aging of the population will lead to more and more people developing AD. The diagnosis of AD is becoming important in aging societies. Brain changes in AD are difficult to distinguish from those in normal ageing, and this has led to the development of powerful computational methods to extract statistical information on the brain changes that are characteristic of AD, MCI and different dementia subtypes. The brains of patients with Alzheimer disease are characterized by loss of neurons in gray and white matter leading to tissue atrophy and widening of ventricles and sulci. Magnetic resonance imaging studies have been used to analyze the brain in one of two ways, segmentation and volumetry. The automatic and accurate segmentation of GM, WM and CSF are needed because manual segmentation is a time consuming and non repeatable task. Computer Aided Diagnosis (CAD) methods are powerful enough to track dementia in clinical trials, on the basis of their efficiency and sensitivity to early change, and the detail on the measures they provide. There is already a variety of computer aided diagnostic scan based investigative tools described in literature and it is possible that even superior methods may become available in the future [77]. New methods are needed to provide a probabilistic rather than a definite classification framework that adds a level of confidence to a diagnostic decision.

The objective of this study is to improve the diagnostic performance of current diagnostic methods for AD by evaluating all clinical diagnostic information with computer aided diagnostic techniques. In order to find the appropriate CAD technique for the early detection of Alzheimer’s disease is important to develop the early treatment of the disease. For this purpose, an automated image based classifier could provide an important diagnostic support to clinicians. The proposed study is used to analyze the efficacy of two different CAD systems such as VBM and classification algorithms solve the problem of separating mild to severe sporadic AD from normal aging with structural MRI. The Voxel based morphometry is a univariate approach. It includes statistical parametric mapping (SPM) which mostly focus on voxel based analysis, comparison of the value of a single image with the mean value of the graph images. The VBM with statistical map is basically used to
compare the group of images not specifically a single subject. The volume of the whole brain or its subparts can be measured by atlas based automated ROI method. The classification algorithm is a multivariate approach. The proposed study classification algorithms include an unsupervised classifier like K-Means clustering and supervised classifiers like RBFNN, GRNN, PNN, BPNN, MSVM and BFOANN classifiers to solve the problem for the discrimination of patients from the controls also tracking the progression of MCI to AD using real time MR images. The multivariate approach, focus on the analysis of the images by extracting feature and the classification of different group and classes. Neuroradiologists examination served as a gold standard (ground truth) against which classification accuracy was compared.

The proposed study analyzes the structural changes in the MR imaging of the brain using CAD approaches. This algorithm provides a detailed map of brain structure, especially useful for detecting small anatomical changes as a result of the disease process. The goal of the proposed study is to test the performance measures of the CAD techniques in the detection of gray matter density reduction and its association with global disease severity in the diagnosis of AD. This study also maps the progression of GM loss in MCI patients over time and compared progressive MCI to stable MCI subjects.

4.1 SUMMARIZED DESCRIPTION OF THE PROCESS

The strength of the present study is the first in analyzing original MR Images of AD, MCI and NCI sample derived from population based cohorts in a South Indian population especially, southern Indian province, Kerala. In the current study, we only used the MR images collected from 2009-2013 duration, which included clinical data, neuropsychological assessments, demographic information, physical and neurological examination, cognitive assessments, patient medical history and baseline and follow-up diagnosis and symptoms. The classification analysis of AD subjects using MR images was reported previously in the southern Indian population cross-sectional study. But here using original MR images of NCI, MCI and AD subjects with longitudinal and cross-sectional analysis for the early diagnosis of AD and also map the progression of GM loss in MCI patients over time and to help detect brain changes between MCI patients who may convert and may not convert to AD using various CAD based volumetric techniques. Our proposed
system shows the different steps involved in the segmentation and volumetric analysis of real MR images in a South Indian population. The main steps involved in the proposed system are depicted in the Fig.4.1.

My research contribution is applying mathematical morphology, 2D Gabor texture features and different classifiers including unsupervised K-Means classifier and supervised classifiers like Radial Basis Function Neural network, Generalized Regression Neural Networks, Probabilistic Neural Network, Back Propagation Neural Network, Multi Support Vector Machine and Bacterial Foraging Optimization tuned ANN based classifiers for the early diagnosis of AD and tracking the progression of MCI to AD. In literature no such combination of methodologies is studied for the diagnosis of AD and as such due to this approach improved performance with high accuracy of classification, sensitivity and specificity. To the best of my knowledge, there is no CAD system for the early diagnosis of AD and longitudinal prediction of MCI to AD using the optimized neural network to improve the classification accuracy of Bacterial Foraging Algorithm (BFA) with 2D Gabor features obtained by MR imaging with high performance measures. The main contributions of the thesis are in the methodology of the application of proposed supervised Bacterial Foraging Optimization tuned Artificial Neural Network (BFOANN) classifier easily identified the early diagnosis of AD and the progression of conversion from MCI to AD using real time MR images in a South Indian population. The BFO tuned ANN based classifier have identified the volumetric changes in the brain well, a comparative assessment of the results has revealed the BFOANN has outperformed the ANN and other classifier in terms of accuracy and sensitivity.

The study was approved by the Sree Chitra Tirunal Institute for Medical Science and Technology (SCTIMST) ethics committee and the study participants were recruited from the patients attending the memory & neurobehavioral clinic of SCTIMST. The spouses of the patients and some volunteers were recruited as controls. All participants, after informed consent, were subjected to clinical examination, neuropsychological and radiological investigation. Neuropsychological tests identify behavior and mental symptoms associated with brain injury or abnormal brain function, as detailed description in chapter 3.
Fig. 4.1. Block diagram of the proposed system
Neuropsychological tests have been standardized on the local population and scores on controls or norms on community based population have already been derived. Following the screening, for the purpose of this study, all participants were subjected to a baseline visit evaluation and were reclassified into one of the three clinical diagnostic categories: No Cognitive Impairment, Mild Cognitive Impairment and AD. The original set of the studied subjects was 113, including 23 controls, 49 MCI subjects and 41 subjects with AD. The MR image acquisition and further processing were described in the chapter 3 sections 3.4 and 3.5.

Computer aided diagnosis methods have become very popular to classify functional or structural brain images to discriminate them into three classes: normal elderly controls or subjects with an Alzheimers disease or subjects with mild cognitive impairment. To solve this task this study has applied VBM, unsupervised and supervised clustering techniques. A block diagram of the whole detection process is shown in figure 4.1 our proposed system shows the different steps involved in the segmentation and volumetric analysis of real MR images. The general approach of CAD for AD detection in MR images involves mainly four stages. They are,

i. Preprocessing
ii. Feature Extraction
iii. Classification
iv. Volume Calculation

Preprocessing involves the major phase in medical image application and is known as skull stripping. Alzheimer's disease is the effect of shrinking volume of GM, and WM tissues. The focus of our research work is to segment the MR images and determine their volume change to detect the onset of AD in the initial stage. The segmentation and volumetric analysis of the brain images stresses the need for effective removal of extra cerebral tissues or simply the skull. Skull stripping is an indispensable primary step in the accurate analysis of brain MRI. Skull stripping removes the non cerebral tissues such as skull, scalp, veins etc. from the original MR images. In this proposed study, the skull stripping process based on the use of mathematical morphology [78]. The purpose of morphological processing is primarily to remove imperfections added during segmentation. The mathematical
morphological method can be divided into different steps. The basic operations are erosion and dilation and region filling are applied to the binary image to remove the non-cerebral tissue. The idea is to convolve the binary image with a structuring element to produce the skull stripped image. In erosion process removes the pixels on the MRI brain image’s boundaries such as the skull, scalp and meninges of non-brain regions. In the next step, the morphological dilation is applied in order to enhance and connect all the intracranial tissues within the image. The final step of mathematical morphology is to enhance the appearance of the skull-stripped brain image as region filling is used to fill in holes in the brain region. Using the basic operations we can perform opening and closing. This method has been automated and implemented under the assumption that consecutive slices have almost similar structures. Images around the mid sections of the brain will give enough idea about the possible disorder, but for accurate and early detection in volume changes. The detailed description is included in the section 4.2.

The next phase of the proposed system consists of feature extraction from brain MR images and to classify this brain image on the bases of these texture features using unsupervised and supervised classifiers. The purpose of feature extraction is to reduce the original data set by measuring certain properties or features that distinguish one input pattern from another pattern [79]. The extracted feature should provide the characteristics of the input type to the classifier by considering the description of the relevant properties of the image into a feature space. Features such as shape, texture, color, etc. are used to describe the content of the image. Texture analysis is a highly developed image processing method for extracting and measure features related to local patterns in images. In this work have chosen the 2D Gabor features for texture classification. The main advantage of the Gabor filters is that they provide optimal simultaneous resolution in both space and frequency domains [80]. The 2-D Gabor filter is easier to tune the direction and radial frequency bandwidth, and easier to tune center frequency, so they can simultaneously get the best resolution in the spatial domain and frequency domain [81]. This study, the 2D Gabor filter with different directions and frequencies can detect the slight differences between various brain regions of MR images. In normal MR brain images, the relative positions of different tissues are generally fixed, so there are certain texture patterns within one tissue and among different tissues, such as GM, WM and CSF. In this study, Gabor filters are used for extracting texture
information from the MR image. A bank of Gabor filters with different preferred orientations and wavelength is applied to the image. These filters give a two dimensional array of the same size as the input image. The output of the Gabor filters used in a filter bank for a given image pixel is combined with a vector that is associated with the considered pixel. The Gabor features were extracted with 24 orientations with a phase angle of 15 degrees. The detailed description is included in the section 4.3.

MRI brain tissue classification is a difficult task because of the effects of noise and shading artifacts and relatively low contrast-to-noise ratio between GM, WM and CSF. The subjects with Alzheimer disease have greater brain volume loss of either GM or WM, which leads to a volume increase of Cerebro-spinal fluid in cerebral sulci and lateral ventricles than elderly control subjects, which can be measured with MRI. Computer-aided diagnostic methods based on structural brain MRI may improve the early diagnosis of AD. This study objectively validates and compares methods for CAD based on structural brain MRI scans. These methods promise to fully automated, standard PC-based clinical decisions, unaffected by individual neuroradiological expertise. In this study, Neuroradiologist examination served as a gold standard against which classification accuracy was compared. This study attempted to develop two CAD methods for identification of patients with cerebral atrophy due to Alzheimer’s disease, mild cognitive stage, and normal healthy elderly controls based on a pattern recognition technique Voxel Based Morphometry and classification based on unsupervised and supervised over and above optimized ANN based classifier.

Voxel Based Morphometry is a whole-brain unbiased, objective technique has been developed for characterizing differences in the local composition of brain tissue using MR images, and can objectively map gray matter loss on a voxel-by-voxel basis also volumetric basis[82]. To the best of my knowledge, this is the first Indian study for analyzing the structural changes of brain in AD, MCI and NCI subjects using VBM with Statistical Parametric Map (SPM) and correlate the VBM with ROI based volumetry for longitudinal and cross sectional analysis for the early diagnosis and tracking the progression of AD. The volume loss of specific regions of interest in the brain can explain the observed clinical, behavioral and psychometric changes seen over time in AD patients. Both approaches assist to
localize brain regions that sustain memory and related functions in NCI, MCI and AD subjects as included in the section 4.4.1.

Clustering is a popular form of unsupervised and semi-supervised learning, and seeks to determine how the data is organized. The clustering based classification method presented in this study provides two main novelties. The first consist is an unsupervised clustering techniques, K-means and the next is supervised learning techniques. The K-means is an unsupervised classifier categorize of AD subjects from the control and MCI subjects based solely on the image statistics without availability of training samples or a-priori knowledge of the data. To overcome the drawbacks of K-means classification this study evaluates the feasibility of the early detection and tracking of Alzheimer’s disease on the basis of the analysis of real structural MRI brain data using supervised classification algorithmic approaches. The Supervised classifications are used to cluster pixels in a data set into classes corresponding to user-defined training classes. According to this model, a classifier is presented with features obtained from a selection of the objects that are to be classified, in a process known as training. The trained classifier can later label objects which were not used in its training, an ability known as generalization. The performance of classification methods depends on the type and quality of the features employed to train the classifier. The most popular classifiers were used for this proposed classification are Radial Basis Function Neural network, Generalized Regression Neural Networks, Probabilistic Neural Network, Feed Forward Neural Network, Multi Support Vector machine and BFO tuned ANN.

The use of supervised classifiers was investigated for classification of GM, WM and CSF variation in MR images. These different classifier models were trained to classify whether a brain region is GM or WM or CSF pattern based on quantitative image texture features. From the point of generalization RBFNN can respond well for patterns that are not used for training. The GRNN is a feed-forward neural network for supervised data. It uses nonlinear regression functions for approximation. This network does not require an iterative training procedure that is required in back propagation method. The probabilistic neural network is used for nonlinear computing which approaches the bayes optimal decision boundaries. The training manner of PNN is simple and instantaneous. The BPNN shows good classification results, because of its ability to learn through examples. The performance results based on misclassification rates and accuracy shows that BPNN
has a superior performance than the other neural network. Support vector machines applied for the detection of AD, has shown a good results in terms of reducing the false positives and false negatives. SVM models have a strong regularization property which makes it suitable for generalizing new data that are not involved in training. From the view point of classification accuracy and computational complexity, the SVM was superior to the other classifiers.

Here, feed forward neural networks that work on back propagation algorithm known as the multilayer perceptron (MLP) is proposed. This MLP classifier is thus designed with 24 input neurons, one hidden layer with 100 neurons and one neuron at the output layer. The learning rate and momentum constant was set to 0.01 and 0.9 respectively. The training was stopped when the root mean square error per training was less than 0.1 or when it reaches 100 epochs. After training, the network was evaluated with the test cases. Designing optimal neural network architecture is made by a human expert and it requires a tedious trial and error process to attain classification accuracy. To solve this problem in this study, Bacterial Foraging Optimization (BFO) algorithm has been selected and applied in the back propagation learning to optimize the initial network parameters like hidden layer neurons, learning rate and momentum constant to enhance the learning process in terms of convergence rate and classification accuracy. To increase the detection accuracy a feature extraction methodology is used to extract the texture features of the AD and MCI patient's brain tissues and NCI subjects tissues prior to classification. The optimally designed ANN has three-layer architecture: an input layer, hidden layer and an output layer. The number of neurons that structures the input layer is equal to 24 feature vector using the Gabor filter. The optimization BFOANN classifier is performed with the learning rate and the momentum constant varied from 0 to 1 and the hidden neurons varied from 31 to 200. Using the proposed algorithm an optimized ANN is achieved with Nh=152, Lr=0.2571, and Mc=0. 8963. The parameters are optimally selected thereby adjusting the connection weights and analyze the classification performance depends on the Nh, Lr and Mc. The proposed classification based segmentation which results in the subdivision of an entire image into its constituent regions such as GM, WM and CSF for the early AD diagnosis and tracking the progression in a longitudinal analysis of MCI patients.

Volumetric analysis of the brain from MR images has emerged as an important biomedical research tool to study diseases such as Alzheimer’s disease.
Segmentation of the brain parenchyma and its constituent tissue types, the gray and white matter, is necessary for volumetric information in longitudinal and cross-sectional studies. The classification approach is based on the usage of reference image as a ground truth. This allows us to calculate the performance of our brain segmentation mainly the GM, WM and CSF compared with that obtained from real MR image manually segmented (ground truth) by two-expert Neuroradiologist in this area. The volumes of GM, WM and CSF indicated important information, especially in the discrimination of AD. Hence a classification algorithmic segmentation method adopted to extract GM, WM and CSF probability maps from the source MRI data. The value of each pixel in the corresponding probability map denotes the posterior of the pixel belonging to the tissue by giving its gray intensity.

4.2 PRE-PROCESSING

Image preprocessing is necessary for the segmentation of MR brain images. It is for reducing the difficulty and computation time of the CAD algorithms. Since the image quality of the MR images fully depends on the subjects MR imaging sequences, so there is much inconsistency in the pixel value range, noise level, and background level. Different Neuro imaging applications have different requirements in the performance of the skull stripping process. MRI is a unique imaging modality for representing soft tissues with high spatial resolution and good contrast. MR brain image and their analysis based on quantitative volume, shape and size give a foresight into the possible neural disorder. The radiologist can diagnose and intervene at an early stage; this has resulted in an extensive research in the area of neuroimaging processing involving MR brain images. Alzheimer's disease is the effect of shrinking volume of GM, and WM tissues and corresponding enlargement of ventricles. The focus of our research work is to segment the MR images and determine their volume change to detect the onset of AD in the initial stage. The segmentation and volumetric analysis of the brain images stresses the need for effective removal of extra cerebral tissues or simply the skull. Skull stripping is an indispensable primary step in the accurate analysis of brain MRI.

Before applying the skull stripping algorithm, we first transform the brain volume into axial orientation and identify the axial slices that include the entire brain. We first compute the maximal intensity of each axial slice to find the top of the head and then extract only slices within a distance from the top slice. This
proposed study proposed an automated skull stripping algorithm using morphological models and unsupervised-supervised classification. Because of the tissue classification, the algorithm can be applied to images with different tissue contrasts. The purpose of morphological processing is primarily to remove imperfections added during segmentation criteria. The basic operations are erosion and dilation. Using the basic operations we can perform opening and closing.

MRI slices have both cortical and surrounding non-cortical tissues. The MR images are analyzed after extracting the cortical tissue in a process termed as skull stripping. Surrounding extra cortical tissue, such as fat, skin, eye ball is removed and separated from the brain tissues. The skull is stripping classifies the image into two classes, brain and non-brain tissues. The skull removed MR images are used for anatomical classification of structural MRI into its constituent GM, WM and CSF. We have proposed automatic methods for skull stripping, which extracts GM, WM and CSF from the MRI. Volumetric analysis of the brain can be interpreted using the slices near the mid brain. The proposed approach involves morphological operations, which include erosion and dilation for skull stripping applications. The DICOM images are used as test images in the entire algorithm. The algorithms are implemented in MATrix LABoratory (MATLAB).

Most of the skull stripping methods are based on intensity. Chen Yunjie et al describes the skull stripping is carried through image manipulations done on the classified Gaussian mixture model of the image [83]. Shanthi K.J study shows the outlining margins of the skull are detected and the brain tissue is extracted making use of this mask [84]. These techniques have several limitations that they cannot be used beyond the mid brain image. Standard multiple atlases are used for registration and the images are segmented for WM and GM. These images are used as masks and the CSF voxels are grown based on certain intensity and neighborhood conditions. We find in the literature different techniques are used for the skull stripping applications such as a Hybrid Watershed Algorithm (HWA), Brain Surface Extraction (BSE) and Brain Extraction Tool (BET) [85].

The proposed approach involves preprocessing using morphological operations like dilations and erosions for skull striping applications. Skull stripping is a technique for removing the skull and non brain intracranial tissues like fat, dura, skin etc; which enfold the surface of brain cortex and cerebellum in the brain. The extra-cortical voxels in MR brain images are often removed in order to help out
accurate analysis of cortical structures [86]. The morphological operations are
effective and fully automated techniques for skull stripping applications. It is based
on set theory and set in mathematical morphology representing objects in an image.
Erosion and dilation are two basic operators for gray scaled images in the area of
mathematical morphology. They are defined as Equation (4.1) and (4.2) respectively.
As erosion is a morphological process technique which uses the background and the
foreground for the processing. In Brain MRI there is a particular intensity of the
background that appears before brain image. Unfortunately, in brain MRI, the same
intensity often appears as a part of the brain and this appearance is a false
background. So in this scenario that algorithm would be unable to distinguish
between the original background and the false background. Eventually the area
around the false background will also be eroded, which causes distortion in the brain
tissues along with the skull. The dilation operation consists of eliminating all
remaining black spots on the white surface of the image. These spots are covered by
the dilation of the white parts. This process is carried out by moving a square mask
on the image and applying the logical OR operator on each of the neighboring pixels
[87].

A dilation of an image ‘I’ by the structure element ‘H’ is given by the set
operation is shown in Equation (4.1).

\[ I(+H) = \{ (b + d) / b \in I, d \in H \} \] (4.1)

An erosion of an image I by the structure element H is given by the set
operation as represented in Equation (4.2).

\[ I(-H) = \{ p \in Z^2 | ((p + q) \in I, for every q \in H) \} \] (4.2)

By applying a spherical structuring element with a suitable radius,
removal of thin connections between brain and non brain portions is achieved. We
use connectivity to isolate major structures on the eroded binarised image. The brain
can now be determined by finding the largest connected component. A binary brain
mask, then results. A reverse process of erosion termed, dilation is applied. Finally
by mapping the pixels in the extracted brain mask with that of the original image, we
obtain the actual brain. To extract the subsequent brain masks, the method described
above is followed by subtracting the current image slice from the skull of the
previous image slice. This method has been automated and implemented under the
assumption that consecutive slices have almost similar structures. Images around the mid sections of the brain will give enough idea about the possible disorder, but for accurate and early detection in volume change, all the slices need to be extracted and segmented.

In recent studies proposed a novel algorithm, based on grayscale mathematical morphology and LOGISMOS-based graph segmentation for tissue segmentation in rodent brain MRI [88]. Andre’ G.R. Balan et al studied smart histogram analysis applied to the binary mathematical morphology skull-stripping problem in T1-weighted MRI [89]. This method is highly independent of parameter tuning and very robust across considerable variations of noise ratio. Rosniza Roslan et al proposed a region growing and mathematical morphology skull stripping methods for image segmentation. The mathematical morphology method outperformed the region growing with an acceptance rate of 95.5% [78].

4.3 FEATURE EXTRACTION

Feature extraction is the technique of extracting specific features of the pre-processed images of different abnormal categories in such a way that the within-class similarity is maximized and between-class similarity is minimized. The purpose of feature extraction is to reduce the original data set by measuring certain properties or features that distinguish one input pattern from another pattern [90]. The extracted feature should provide the characteristics of the input type to the classifier by considering the description of the relevant properties of the image into a feature space. Features such as shape, texture, color, etc. are used to describe the content of the image [91]. In most cases, medical images are based on carrying less information than color images. Medical images are usually low resolution and high noise images. They are difficult to automatically analyze for extracting features. Medical images acquired with different devices, even using the same modality, may have significantly varying properties. Moreover, color and intensity are not as important in medical images as in photographs; texture analysis becomes crucial in medical image.

Three main approaches are used for the pattern recognition for feature extraction and features based classification. (1) Statistical approach (2) Syntactic or structural approach (3) Spectral approach. In case of statistical approaches, texture is defined by a set of statistically extracted features represented as vectors in
multidimensional feature space. This feature vector so generated from patterns is assigned to their specific class by probabilistic or deterministic decision algorithm. The statistical features could be based on first-order, second order, or higher-order statistics of gray level of an image [92]. A texture based on texture primitives, so this texture is spatially organized according to placement rules to generate a complete pattern. This approach is called as a syntactic approach [93]. In spectral approach, the textures are defined by spatial frequencies and are evaluated by the autocorrelation function of a texture. The transform method approach, the images are represented in the frequency domain. This method generates Fourier transform of the image and analyses the texture images by decomposing it into frequency and orientation components. One of transform domain filter, Gabor filter is shown to outperform other popular transform methods. It can achieve the optimal localization in spatial and frequency domain as well as has been successfully used in segmentation and classification of textured images [94]. The main textural feature extraction and classification methods are co-occurrence matrix method, gray level run length method, fractal texture description method and Fourier filter method [96][97][98].

Texture analysis is a highly developed image processing method for extracting and measure features related to local patterns in images. Texture analysis is a quantitative and efficient approach over a large range of spatial frequencies, giving it the potential to outperform expert visual pattern analysis in terms of diagnostic accuracy. D. Mahmoud-Ghoneim et al studies identified the application of texture analysis of MR images have yielded promising results for the segmentation of brain tumors [99]. Texture is a measurement of the variation of the intensity of a surface, quantifying properties such as regularity, smoothness and coarseness. The three principal approaches used to describe texture are structural, spectral and statistical. Texture segmentation involves accurately partitioning an image into differently textured regions. It requires simultaneous measurements in both the spatial and the spatial-frequency domains. A texture may be fine, coarse, smooth, or grained, depending upon its tone and structure, where tone is based on pixel intensity properties in primitive while structure is the spatial relationship between primitives [96].

Gabor filters are well recognized in the recent past as a joint spatial/spatial-frequency representation of textures. Segmentation based on textural
feature methods gives more reliable results; therefore, texture based analysis is extensively used in the analysis of medical images [97]. Gabor filters are defined by harmonic functions modulated by a Gaussian distribution. The use of the 2D Gabor filter in computer vision was introduced by Daugman in the late 1980s. Since that time it has been used in many computer vision applications including image compression, edge detection, texture analysis, object recognition and facial recognition. A 2D Gabor filter is a Gaussian kernel function modulated by a sinusoidal plane wave in the spatial domain. All the Gabor filters are self-similar and are generated from one mother wavelet by dilation and rotation [100]. Features are extracted using a set of Gabor filters with different frequencies and orientations. The various parameters of the Gabor filter play a major role in deciding the output image. The size, phase, orientation and frequency of the output image are selected by the Gabor filter. The image features are measured by employing an appropriate Gabor filter with adaptively chosen size, orientation, frequency and phase for each pixel. An image property called phase divergence is used for the selection of the appropriate filter size. Characteristic features related to the change in brightness, texture and position are extracted for each pixel at the selected size of the filter. A Gabor filter is a linear filter whose impulse response is defined by a harmonic function multiplied by a Gaussian function is revealed in Equation (4.3).

\[ h(x, y) = g(x, y)s(x, y) \]  \hspace{1cm} (4.3)

Where \( s(x, y) \) is a complex sinusoid, known as carrier and \( g(x, y) \) is a Gaussian shaped function, known as an envelope. The Gabor filters are self-similar, i.e.; all filters can be generated from one mother wavelet by dilation and rotation. The Gabor filters are self-similar, i.e.; all filters can be generated from one mother wavelet by dilation and rotation. Since the Gaussian function is a complex function so on convolving Gabor filter with input image the output obtained can be used in various ways. Two ways of manipulating the output of Gabor filter to extract features are described in Equation (4.4) and Equation (4.5).

\[ h(x, y; \lambda, \phi, \sigma_x, \sigma_y) = \frac{1}{2\pi \sigma_x \sigma_y} \exp \left\{ -\frac{1}{2} \left[ R_1^2/\sigma^2 + R_2^2/\sigma^2 \right] \right\} \exp \left( \frac{2\pi R_1}{\lambda} \right) \]  \hspace{1cm} (4.4)

Where

\[ R_1 = x \cos \phi + y \sin \phi, \]
\[ R_2 = -x \sin \phi + y \cos \phi, \]

Where

\[ \sigma \] – is the spatial spread
\[ \lambda \] – is the frequency
\[ \phi \] – is the orientation

\[ h(x, y; \lambda, \phi, \sigma_x, \sigma_y) = C \exp \left\{ -2\pi^2 (\sigma^2 (F1 - 1/\lambda)^2 + \sigma_y^2 (F2)^2) \right\} \]  

(4.5)

Where

\[ F1 = u \cos \phi + c \sin \phi, \]
\[ F2 = -u \sin \phi + v \sin \phi, C = \text{constant} \]

The 2-D Gabor filter is easier to tune the direction and radial frequency bandwidth, and easier to tune center frequency, so they can simultaneously get the best resolution in the spatial domain and frequency domain. The Gabor filter outputs can be modeled as Gaussian’s and develop an algorithm for selecting optimal filter parameters [101]. A 2-D Gabor function is an oriented complex sinusoidal grating modulated by a 2-D Gaussian function. The parameters of the Gabor function are specified by the frequency, the orientation of the sinusoid (or represented by the center frequency), and the scale of the Gaussian function. Local orientations and spatial frequencies explicit in Gabor filters are therefore used as the key features for texture processing. The input image is generally filtered by a family of Gabor filters tuned to several resolutions and orientations. However, it may not be computationally convenient or feasible to apply a large number of filters responding at multiple resolutions and orientations to an image [102].

In the conventional Gabor filter design approaches, the best filter parameters are generally selected so that the corresponding energy is a maximum for each specific texture. Here we consider the design of a single Gabor filter to segment multiple textures based on a maximum principle. There are several approaches to texture segmentation. Commonly, the segmentation process consists of two major steps, namely feature vector extraction and feature vector clustering. In feature vector extraction, several textural features are extracted from localized regions in the image. All features extracted from the same localized region comprise a single feature vector. In feature vector clustering, the feature vectors extracted from all localized
regions are grouped into several groups. Ideally, all vectors belonging to the same group should correspond to visually similar local texture regions.

In summary, this set of features is based on extracting features from real parts and imaginary parts of the output of Gabor filters. For this set of features we don’t process the outputs further as we did in earlier technique rather we use the outputs as it is, as our feature extracted. One thing to note is that whenever the image is convolved with Gabor Filter the size of output is similar to size of input image we have taken.

4.3.1 Texture feature extraction using Gabor features

Gabor filter has tunable orientation and radial frequency bandwidths, tunable center frequencies, allowing them to optimally achieve joint resolution in the spatial and frequency domains. This section presents the Gabor filter analysis of the brain regions of GM, WM and CSF of MR image for extracting the texture features. Gabor wavelets capture the local structure corresponding to spatial frequency (scales), spatial localization, and orientation selectivity they are widely applied in many research areas, such as texture analysis and image segmentation [103].

In the proposed study, Gabor filter analysis is used to extract the texture features of magnetic resonance brain images into GM, WM and CSF differentiate between AD, MCI and NCI subjects. Gabor filter with different orientations and various frequencies is performed with contrast-enhanced T1-weighted MR images to extract the discriminant feature. A classification model is built based on the extracted features. Experiments show that the proposed method, which uses mathematical morphological skull stripping analysis, Gabor filter analysis, unsupervised and supervised classifier and final volumetric analysis, can distinguish different diagnostic categories of MR images.

For any supervised or unsupervised classification scheme, the choice of features is very crucial. In this work, we have chosen the 2D Gabor features for texture classification. The main advantage of the Gabor filters is that they provide optimal simultaneous resolution in both space and frequency domains. Gabor wavelets capture the local structure corresponding to spatial frequency (scales), spatial localization, and orientation selectivity, they are widely applied in many research areas, such as texture analysis and image segmentation [104]. The process of texture segmentation using Gabor filters involves proper design of a filter bank.
tuned to different spatial-frequencies and orientations to cover the spatial-frequency space, decomposing the image into a number of filtered images; extraction of features from the filtered images; and the clustering of pixels in the feature space to produce the segmented image. Both supervised and unsupervised approaches were used in texture segmentation [105]. Supervised approaches rely on training methods and reference segmentations for performance assessment, while unsupervised approaches mainly rely on subjective assessment.

In this study, Gabor filters are used for extracting texture information from the MR image. A bank of Gabor filters with different preferred orientations and wavelength is applied to the image. These filters give a two dimensional array of the same size as the input image. The output of the Gabor filters used in a filter bank for a given image pixel is combined with a vector that is associated with the considered pixel. The Gabor features were extracted with 24 orientations with a phase angle of 15 degrees. In this study, we consider filters having equal spread in both directions. The response of the filter is determined by the spread parameter ‘σ’ of the Gaussian and the radial frequency of the modulating sinusoid. The orientation ‘∅’ of the Gabor filter is determined by the parameter. The important issue in the design of Gabor filters for texture classification is the choice of filter parameters; radial frequency, the spread of the filters and the orientation of the filter.

In a recent study, Jianfeng Li et al (2010) proposed tongue image texture segmentation based on Gabor filters plus the normalized cut is proposed in this paper. The experiments show that the overall rate of correcting for this method exceeds 81% [106]. In 2012 Heng Liu et al investigated force field convergence map and Log-Gabor filter, used for multi-view ear feature extraction approach is proposed. Experimental results and comparisons show the efficiency and the superiority of the proposed convergence map with the log-Gabor filter method [107]. Chuanzhen Li et al (2011) study proposed an improved energy feature decided by the scale of Gabor kernel and PCA as the dimension reduction method and K-means algorithm as clustering algorithm for simplicity [108]. From the experimental results using several features, it can be seen that this feature can improve the separability of texture boundaries and irregular textures. J. Dheeba et al (2012) proposed an improved decision support system for the detection of lesions in mammograms using differential evolution optimized wavelet neural network. A Gabor feature extraction methodology is used to extract the texture features of the abnormal breast tissues and
normal breast tissues prior to increase the classification accuracy. The result shows that this proposed algorithm has a sensitivity of 96.9% and specificity of 92.9% [109].

4.4 CLASSIFICATION

Segmentation of tissues and structures from medical images has an important role in the early diagnosis of AD, the development of treatment plans and evaluation of disease progression. Segmentation of Brain MRI is the process of separating the brain MR images into three brain tissues GM, WM and CSF. These segmented tissues can be used to determine the volume of the brain tissues from the 3D images obtained from the MRI. The segmentation and volumetric analysis of the brain tissues can easily identify the fact that diseases affect specific tissues or structures, atrophy or volume loss and abnormalities. Manual segmentation, although prone to rater drift and bias, is usually accurate, but is impractical for large datasets because it is tedious and time consuming. Consequently, an accurate, reliable, and automatic segmentation of these tissues and structures can improve diagnosis and treatment of diseases. Two main novelties of a CAD system for the automatic segmentation for classifying the AD patients from controls and also analyze the longitudinal progression of AD in MCI subjects. The whole-brain unbiased, objective technique, known as Voxel Based Morphometry and classification algorithms include unsupervised K-means classifier, Supervised RBFNN, GRNN, PNN, BPNN, MSVM and BFO tuned ANN based classifier to build a fully automatic and accurate brain MR image classification. The proposed algorithm is applied to challenging applications in the gray matter, white matter and CSF segmentation of real datasets MR images in a South Indian population.

4.4.1 CAD system based on Voxel Based Morphometry

Morphometry analysis has become a common tool for computational brain anatomy studies. It allows a comprehensive measurement of structural differences within or across groups, not only in specific structures but throughout the entire brain. Voxel based morphometry was a computational approach to Neuro-anatomy that measures differences in local concentrations of brain tissue, through a voxelwise comparison of multiple brain images [50]. The VBM procedure involves the three dimensional (3D) MR images were normalized to the same standard
stereotactic space. The normalized images were then portioned into GM, WM and CSF based on the priori probability maps. A 12 mm FWHM Gaussian kernel was used to smooth the GM images to correct the noise and small variation and finally voxel-wise statistical test. The areas of significant GM loss in AD patients were obtained according to the general linear model and random field theory using two sample tests. The computation of a given contrast provides a statistical parametric map, which is threshold according to the random field theory. The result of the SPM analysis for VBM is the identification of clusters of voxels that show significant effects. The detailed description of analysis and results is presented in Chapter.6. For instance, VBM analysis studies identified that the discrimination of AD and control subjects, the volumetric atrophy of the grey matter in areas of neocortex [110][12].

4.4.2 CAD System based on Classification algorithms

This study proposes an automated approach for the identification of AD from MRI of the brain using classification algorithmic approaches and also these techniques applied in the baseline and multiple follow-up MRI scans of participants with MCI, in order to investigate the potential of predicting short term conversion to AD on an individual basis. Extensive studies have been performed for identification of AD using various classification techniques in automated manner [51]. This proposed study using three different classification models, unsupervised K-means classifier and supervised classifiers like Radial Basis Function Neural network, Generalized Regression Neural Networks, Probabilistic Neural Network, Feed Forward Neural Network, Multi Support Vector Machine and Bacterial Foraging Optimization tuned ANN based classifiers. Moreover, the proposed approach identifies the performance measures of these classifiers with the use of 2D Gabor texture features as compared to existing approaches.

4.4.2.1 Unsupervised K-means classifier

Segmentation may also be addressed as a classification task, which can be accomplished by supervised or unsupervised learning. In this study, clustering techniques group similar voxels in an unsupervised way, according to a similarity criterion. Unsupervised learning uses no external teacher and is based upon only local information. It is also referred to as self-organization, in the sense that it self-organizes data presented to the network and detects their emergent collective
properties. This classifier categorize of AD subjects with images based solely on the image statistics without availability of training samples or a-priori knowledge of the data. K-means is a kind of unsupervised clustering algorithm has been extensively applied in the segmentation of gray level images. This classifier provides no information to the algorithm on which data points belong to which clusters. In this study, after feature selection K-means clustering algorithms is applied to the dataset and finally partitioning of a data set into groups (clusters) such that similar objects are grouped together. The classification method presented in this study provides an unsupervised technique to segment the structural MRI images, in order to delimitate the three main tissues GM, WM and CSF. The K-means method aims to reduce the sum of squared distances between all points and cluster center. In this study investigated the efficacy of K-means unsupervised classifier using 2D Gabor filter texture features for the early diagnosis and prediction of conversion from MCI to AD in terms of accuracy and volumetric analysis. The detailed discussion is included in chapter 7.

4.4.2.2 Supervised Classifier

In supervised classification, the network user assembles a set of training data based on the cluster pixels in a data set into classes. According to this model, a classifier is presented with features obtained from a selection of the objects that are to be classified, in a process known as training. The training data contain patterns of inputs together with the corresponding outputs, and the network learns to infer the relationship between the two. The trained classifier can later label objects which were not used in its training, an ability known as generalization. The performance of classification methods depends on the type and quality of the features employed to train the classifier. The performance analysis done with the unsupervised classifiers was not found to be much more remarkable. Hence, to improve the classification performance, supervised classifiers are used. Further, the use of supervised classifiers like RBFNN, GRNN, PNN, BPNN and MSVM was investigated for the segmentation and classification of AD, MCI and controls from MR images. These different classifier models were trained to classify whether a brain region is GM, WM or CSF and also find GM regions is atrophied or not based on quantitative image texture features and volumetric analysis.
Artificial Neural Networks (ANN) are a powerful tool for the classification and discrimination of AD patients from controls and MCI patients from healthy elderly controls. The artificial neural network is known as universal approximates with specific characteristics such as the ability to learn or adapt, to organize or to generalize data. SVM models have a strong regularization property which makes it suitable for generalizing new data that are not involved in training. SVMs gain flexibility and SVMs can be robust, even when the training sample has some bias. The results obtained from testing demonstrated that the kernel based SVM classifier yielded the best performance, outperforming neural network classifiers. The detailed discussion is included in chapter 8.

4.4.2.3 Supervised Bacterial Foraging Optimization tuned ANN based classifier

This thesis focuses mainly on designing a CAD system based on the optimized neural network parameters evaluated using evolutionary approaches to improve the classification accuracy in the early diagnosis and classification of AD and also analyze the conversion status of MCI to AD thereby reducing the misclassification rate. The BFO algorithm is swarm intelligence technique which simulates the foregoing policies of the E. coli bacteria as a distributed optimization process. By utilizing the bacterial foraging algorithm, the parameters of the ANN are optimized.

The process of ANN is represented by obtaining one bacterium. Designing optimal neural network architecture is made by a human expert and it requires a tedious trial and error process to attain classification accuracy. To solve this problem in this study, Bacterial Foraging Optimization (BFO) algorithm has been selected and applied in the back propagation learning to optimize the initial network parameters like hidden layer neurons, learning rate and momentum constant to enhance the learning process in terms of convergence rate and classification accuracy. To increase the detection accuracy a feature extraction methodology is used to extract the texture features of the AD and MCI patient's brain tissues and NCI subjects tissues prior to classification. The performance evaluation demonstrates that the result of the optimized artificial neural network classifier is generally better than that of the non-optimized ANN. Overall classification accuracy is the most important measure of performance.
4.5 VOLUME CALCULATION AND MANUAL VALIDATION

Early detection of AD is seen as important because treatment may be more efficacious if introduced as early as possible. Recently in the early diagnosis of AD studies under the consideration of imaging cost and non invasive requirement there has been a realization that MRI may add positive predictive value to a diagnosis of Alzheimer’s disease [111]. The detection of changes in brain tissues that reflect the pathological processes of MCI would prevent or postpone the disease progresses either from normal control to MCI or from MCI to AD. If MCI can be diagnosed at an early stage and effectively intervened, then it is possible to reduce the advanced damages.

A standard segmentation problem within MRI is the task of labeling voxels according to their tissue type that are white matter, gray matter and CSF. Image segmentation provides volumetric quantification of cortical atrophy and thus helps in the diagnosis of Neuro degenerative diseases such as Alzheimer’s disease. Diagnosing these disorders need very accurate determination of volumetric changes of GM, WM and CSF. Use of imaging methods for quantitative volume estimation such as manual, semi-automated and automated methods can provide the capability to reliably detect and identify general and specific structural abnormalities of the brain and monitoring the progression of the disease. Quantitative measures of the brain atrophy can be clinically relevant and much work has been carried out to establish the diagnosis of AD [112]. The simplest but the most time consuming method is a slice-by-slice manual tracing. This operator-dependent method is still being used, mainly as a ‘gold-standard’ reference method for whole brain and GM/WM/CSF segmentations. Manual measurements of these structures on MR images are time-consuming and do not capture the full pattern of atrophy.

In this study, the segmentation evaluation approach and volumetric analysis are based on the use, manually segmented reference image as a ground truth by two experts Neuroradiologist in this field. This allows us to compute the performance of our brain segmentation mainly the GM, WM and CSF. The volumes of GM, WM and CSF indicated important information, especially in the discrimination of AD. In contrast to the volume features which are extracted from the whole three dimensional volume. In this study, we compare the volumetric results to those obtained by radiologists. A binary diagnostic classification was made by two radiologists with different levels of experience in the same scans and information
that had been analyzed with classification approaches. All the resulting images in the study were validated by a neurologist at SCTIMST, Trivandrum. There are semi automatic segmentation methods and fully automatic methods to replace the time intensive manual segmentation. There has been recent interest in the application of computer aided diagnosis techniques to neuroimaging based diagnosis. These methods promise to fully automated, standard PC-based clinical decisions, unbiased by variable radiological expertise. In the proposed approach, unsupervised clustering algorithm based on K-means clustering and supervised classification based on ANN and BFOANN are used to classify GM, WM and CSF and to separate sporadic Alzheimer’s disease from normal ageing and from other dementia.

Diagnostic criteria for AD are currently based on clinical and psychometric assessment. The main procedures for the evaluation of probable AD patients are neuropsychological tests. In clinical, magnetic resonance imaging is a very important tool in diagnosing AD because it can qualitatively measure the neuronal loss by the shrinkage of the structures-of-interest more easily. Consequently, MRI has demonstrated that volumetric atrophy appears in the early stages of AD. In addition, the enlargement of the ventricles is also a significant characteristic of AD due to neuronal loss. The ventricles are filled with CSF and surrounded by GM and WM. As a result, by measuring the CSF volumetry rate shows higher correlation with the disease progression when compared to the medial temporal lobe atrophy rates, and reveals significant variation between normal individuals and AD.

Cranial volume is an important measurement in the study of abnormalities of cranial size and shape. Changes in the composition of GM, WM and CSF in the whole volume or within specific regions can be used to characterize physiological processes and disease entities or to characterize disease severity. Quantitative analysis of MR images is increasingly important [34]. The patients suffering from Alzheimer’s disease are mainly characterized by the loss of neurons in GM and WM leading to brain tissue atrophy and subsequently the widening of ventricles and sulci filled with CSF [113]. Neuroimaging techniques have confirmed the loss of brain tissues, especially GM, increased CSF and WM abnormalities. Given that Neuro degeneration primarily affects gray matter, we first extracted GM segments from T1-weighted brain scans and normalized them into standard anatomical space. Such segments contain several thousand voxels. After pre-
processing, each voxel reflects the magnitude of the local GM volume. Atrophy typically starts in the medial temporal and limbic areas, subsequently extending to parietal association areas, and finally to frontal and primary cortices. Early changes in the GM structure of the brain in the hippocampus and entorhinal cortex have been demonstrated with the help of MRI, and these changes are consistent with the underlying pathology of MCI and AD.

The analysis was carried out by finding the total brain pixels comprising of GM, WM and CSF. In AD affected person there is a reduction in the number of pixels of GM and WM and a corresponding increase in the number of pixels of CSF. The reduction in the number of WM and GM pixels causes the reduced space to be filled with the fluid i.e.; CSF. Hence a reduction in number of WM and GM pixels means an increase in the number of pixels in CSF. This acts as a deterministic factor in recognizing AD. Hence it is very appropriate to use the relative ratio of brain pixels of GM and WM pixels of the real MR images. The comparison of this ratio helps a radiologist in identifying an AD affected brain. The images were first skull stripped. The skull stripped image was segmented to extract GM, WM and CSF separately. In the baseline image compared follow-up MRI image, have some subtle changes in the volume of the follow up tissue can be visually interpreted by the neurologist. The algorithm aids and helps the neurologist in detecting AD in the earlier stage.

We therefore undertook a direct prospective, blinded comparison of diagnostic accuracy between radiologists and the automated classification method using the same scans and associated clinical information. The 3D segmentation of MR brain images resulting in an excellent discrimination of soft tissues which enables quantitative volumetric analysis of brain tissues. Proper volumetric analysis finds applications to perform quantitative analysis of various brain structures. The different methods developed have been discussed and the results of each of the methods are analyzed in the respective chapters. In this section, the segmentation is applied over the real MR data set and a decisive conclusion on the classification of AD. A comparative study of the brain images obtained at different periods of time such as baseline and follow up time gives an idea about the variation in volume of the brain. The decrease in the volume of the brain tissues is an indication of the beginning of AD [114].
The volume calculation is made by finding the number of nonzero pixels in an image and grouping them in a rectangular array of size \( M \times N \). The successful segmentation and accurate computation of the volume of the MRI depends on the accuracy of the skull stripping. Skull stripping should extract only the brain tissue from the surrounding non-brain tissues. Any extra tissue it carries will drastically affect the accuracy of the volume calculation. Early detection of AD before the disease can manifest itself depends on ability to detect these changes immediately in the beginning, for early and effective treatment. One set of skull stripped images is displayed and the volume of the brain tissue on the whole is computed. The skull stripped images are validated manually by carefully looking for the extra tissue. Manual validation of the WM and GM, pixel by pixel is very labor intensive and hence avoided. This study designed an MRI-based classification framework to distinguish the patients with MCI and AD from normal individuals using different classifiers and features. In this proposed study, an MRI-based classification framework was proposed to distinguish the patients with AD and MCI from normal participants by using supervised and unsupervised classification approaches.

The volumes of brain tissues such as GM, WM, and CSF indicate important information, especially in brain degeneration diseases. A clustering based segmentation algorithm provided to extract GM, WM and CSF probability maps from whole-brain MRI data. The value of each pixel in the corresponding probability map denotes the posterior of the pixel belonging to the tissue by giving its gray intensity. The intensities of voxels belonging to each of these clusters conform to a normal distribution which can be described by a mean, a variance, and the number of voxels belonging to the distribution. Here, the volumes of GM, WM, CSF, are calculated by volume tissue as represented in Equation (4.6), Equation (4.7) and Equation (4.8) [115].

\[
\text{Volume}_{\text{CSF}} = \sum_\forall i \left( (C_{\text{csf}} / 0.5 \leq f(i)) \right) \text{\,1.5} \quad (4.6) \\
\text{Volume}_{\text{GM}} = \sum_\forall i \left( (C_{\text{gray}} / 1.5 \leq f(i)) \right) \text{\,2.5} \quad (4.7) \\
\text{Volume}_{\text{WM}} = \sum_\forall i \left( (C_{\text{white}} \geq f(i)) \right) \text{\,2.5} \quad (4.8)
\]

Where, ‘\( i \)’ is any pixel of the MRI data and \( f(i) \) stands for the gray level of \( i \). ‘\( C \)’ means the cluster tissue stands for the parts of GM, WM, or CSF.
Finally, the algorithm was tested for symptoms of AD of a particular patient on the MR images acquired at two different times, at SCTIMST. All the images used in the work were provided by SCTIMST, with patient information undisclosed. Unlike the western countries, the people here are not well aware of the disease AD. This reduces the chance for a wide database. A comparison based on an automated brain volume calculation would yield meaningful results. The volumetric changes in the brain tissues are an indication of AD advancing in the patient. These subtle changes in the volume of the tissue cannot be visually interpreted by the neurologist. The volumetric evaluation based on the computer aided diagnosis aids and helps the neurologist in detecting AD in the earlier stage.

4.6 SUMMARY

In this chapter, we will report on the works we have done to evaluate the feasibility of the early detection and tracking the progression of Alzheimer’s disease on the basis of the analysis of real structural MRI brain data using voxel based morphometric analysis and different classifier techniques. This chapter presents preprocessing steps prior to segmentation of the brain tissues based on the mathematical morphological operations and a feature extraction process using Gabor filter and finally brain volume is calculated by classifying the brain tissues.