Application of Symmetry Information in Magnetic Resonance Brain Image Segmentation

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Abstract

Advances in neuroimaging techniques have facilitated the study of anatomical and functional changes in the brain. In order to assist precise diagnosis and treatment, automatic image analysis methods that provide quantitative measures are of great research interests. Accurate brain tissue segmentation of magnetic resonance (MR) images has been one of the most important research areas for several years. It is an important initial step in neuroimage analysis for applications such as diagnosis of various brain diseases, treatment planning, and studies of various neurological disorders such as Alzheimer’s disease, Schizophrenia, and Multiple sclerosis (MS). However, all these potential applications are crucially dependent on the high accuracy of brain tissue segmentation.

Accurate segmentation of MR brain images is difficult since these images contain various noise artifacts. Despite the extensive research, automated analysis of neuroimages still remains a challenging problem. Recently, attention has been turned towards integration of prior knowledge based on anatomical features to improve the accuracy.

Based on the fact that the brain exhibits a high level of bilateral symmetry, in this thesis, I explore and discuss the importance of symmetry in the context of tissue classification in MRI, and develop a symmetry-based paradigm for automatic segmentation of brain tissues. Such a classification is motivated by potential radiological applications in assessing brain tissue volume, diagnosis of various brain diseases and treatment planning.

The aim of this work is two-fold: First, identifying the location of the symmetry axis or, the symmetry plane becomes imperative. Accurate identification is crucial as it is valuable for the correction of possible misalignment of radiological scans and for symmetry evaluation. In the second stage, automatic classification of brain tissues is done. In other words, the first part of this research focuses on finding the symmetry axis/plane, and the second part develops a segmentation method based on symmetry information.

Specifically, three new techniques are proposed for identifying the precise location of the brain symmetry plane in brain MR images. The first technique considers the MR
image volume as a set of axial slices and the symmetry plane is detected based on the analysis of intensity profile of each axial slice. This is a simple, and fast method when symmetry plane needs to be detected in MR T1-weighted images. Then, a novel fractal analysis based approach is proposed for detecting MSP in 3D MRI. Two methods are introduced that can perform well on MR images with different image contrasts. The proposed techniques are thoroughly validated, and have showed high level of accuracy and robustness to noise compared with the two major state-of-the-art methods. In the second stage of the thesis, an automatic method for brain tissue segmentation is devised by integrating brain symmetry information as a prior knowledge into the fuzzy c-means clustering framework. Several possible approaches are discussed, and two methods are developed where one method considers symmetry alone as spatial information while the other method takes into account symmetry as well as neighbouring spatial information. Proposed methods are compared with conventional fuzzy c-means algorithms. Experimental results show that while incorporation of symmetry information alone can greatly reduce the noise effect, when used with neighbouring spatial information, more accurate, and robust results can be achieved.

Thus, the final outcome of the thesis is a symmetry information integrated brain tissue segmentation method which can effectively handle noise artifacts. The proposed method is shown to have superior performance when compared to conventional methods.

The methods developed in this thesis for brain tissue segmentation may have a more general applicability since many other medical and non-medical images are highly symmetrical in nature.
Statement of Originality

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

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Contents

List of Figures ix

List of Tables xviii

1 Introduction 1
  1.1 Preview ......................................................... 1
  1.2 Motivation ..................................................... 1
  1.3 Contribution .................................................. 3
  1.4 Thesis Overview and Scope ............................... 4

2 Background 7
  2.1 Preview .......................................................... 7
  2.2 Imaging Modalities .......................................... 7
    2.2.1 Different imaging modalities ......................... 7
  2.3 Magnetic Resonance Imaging ............................. 8
    2.3.1 MR image contrasts ................................... 10
    2.3.2 MRI and brain disorders .............................. 12
  2.4 Brain Tissue Segmentation ............................... 14
    2.4.1 Image segmentation .................................... 14
    2.4.2 Brain anatomy .......................................... 15
    2.4.3 Brain tissue segmentation and applications .......... 15
  2.5 Motivations for Automatic Segmentation of Brain Images .... 17
    2.5.1 Neuroimages in clinical setting ...................... 17
    2.5.2 Towards an automated tissue segmentation method .... 18
  2.6 Challenges in Automatic Segmentation .................. 19
    2.6.1 Image noise .............................................. 19
    2.6.2 Partial volume averaging ................................ 19
    2.6.3 Intensity inhomogeneity ................................ 20
  2.7 Chapter Summary .............................................. 21
3 Related Work

3.1 Preview .................................................. 23

3.2 Classification-based Segmentation .................................. 23
  3.2.1 Thresholding methods ..................................... 24
  3.2.2 Statistical approach ....................................... 25
  3.2.3 Artificial neural networks .................................. 27
  3.2.4 Clustering approach ....................................... 28

3.3 Region-Based Segmentation ........................................ 30

3.4 Contour-Based Segmentation ....................................... 30
  3.4.1 Deformable models ........................................ 30

3.5 Other Approaches ............................................. 31
  3.5.1 Independent component analysis ........................... 31
  3.5.2 Atlas based segmentation ................................... 32
  3.5.3 Fuzzy connectedness ....................................... 32
  3.5.4 Rule-based methods ........................................ 33

3.6 Drawbacks of Current Methods ................................... 33

3.7 Attempts Taken Hitherto for Overcoming These Drawbacks ...... 35
  3.7.1 MRI model ................................................ 35
  3.7.2 Spatial information ........................................ 35
  3.7.3 Intensity inhomogeneity correction ......................... 36
  3.7.4 Other existing extensions to FCM .......................... 36

3.8 Chapter Summary ............................................. 38

4 Inspiration and Research Scope ..................................... 41

4.1 Preview .................................................. 41

4.2 Inspiration .................................................. 41
  4.2.1 Brain symmetry analysis .................................... 41
  4.2.2 Brain symmetry and its clinical implications .............. 42
  4.2.3 Brain symmetry analysis methods .......................... 43

4.3 Research Objectives .......................................... 45
  4.3.1 Scope of the work .......................................... 45
  4.3.2 Overview of the MR brain image segmentation framework .. 46
  4.3.3 Implementation ............................................. 46

4.4 Chapter Summary ............................................. 49

I Symmetry Plane Detection .......................................... 51

5 Symmetry Plane Detection .......................................... 53
List of Figures


2.1 A simple illustration of MR image formation. 9

2.2 Different contrasts in MRI. (a). T1, (b). T2, (c). PD. 11

2.3 Different planes of the brain images. 11

2.4 Different planes of the brain images visualized on MRI. Top row shows the different projections. (a). Axial plane, (b). Sagittal plane, (c). Coronal plane. 12

2.5 MRI has better contrast in comparison to CT. (a). CT, (b). MRI. 13

2.6 AD patient’s brain image compared to a normal brain image. (a). AD, (b). Normal. 16

2.7 A set of sagittal cross-sectional slices of a 3D brain MRI scan. The radiologist has to process and analyse a large number of images. 17

2.8 Image noise simulated using BrainWeb. Left to Right: Noise free image, image with 5% noise, image with 9% noise. 19

2.9 Partial volume effect. Left: Ideal image. Right: Acquired image [Pham et al., 2000]. 20

2.10 Intensity inhomogeneity simulated using BrainWeb. Left to right: Original image, image with 20% inhomogeneity, image with 40% inhomogeneity. Although this variation does not affect the manual procedure much, it could affect the accuracy of the automatic methods considerably. 21

3.1 A taxonomy of existing brain tissue segmentation techniques. This model is built by the author based on published categorisations on image segmentation techniques. 24

4.1 Human brain exhibits approximate bilateral symmetry. 42

4.2 Abnormality of the brain can be easily detected by comparing to the other hemisphere. 43
4.3 Work flow of the symmetry based brain tissue segmentation framework. It consists of two major parts: Brain symmetry plane detection and Symmetry integrated tissue segmentation. ............................ 47
4.4 Brain tissue substances. Extra-cranial tissues consist of skull, fat, and meninges. ............................................................. 49

5.1 Human brain axial view. Adapted from [Kelley and Petersen, 2007] with the permission from the publisher. ........................... 55
5.2 Human brain coronal view. Adapted from [Kelley and Petersen, 2007] with the permission from the publisher. ........................... 56
5.3 IF separates the two brain hemispheres. MSP is considered to be the brain symmetry plane. ........................................... 56
5.4 Common procedure of detecting brain symmetry plane .............. 62
5.5 Inter-hemispheric fissure. Graph above shows the intensity profile along a line perpendicular to IF. ................................. 63
5.6 General scheme of the similarity-based approach. .................. 65

6.1 Falx Cerebri descends vertically in the IF between the cerebral hemispheres. (a). Falx Cerebri [Wikipedia, 2013a], (b). MRI axial slice. .... 74
6.2 An example output which shows the estimated axis for each slice. These equally distanced 56 slices are taken from an image volume of 168 slices. MSP ground truth is known to be the vertical centreline of these images. Although the extreme slices show some deviation, as a whole, the median value gives the accurate estimate. .......................... 75
6.3 Distribution plot of the intensity score at each angle. MSP ground truth is at 0° ................................................................. 76
6.4 An example output which shows the estimated axis for each slice. These equally distanced 56 slices are taken from an image volume of 168 slices. Although the extreme slices show some deviation, as a whole, the median value gives the accurate estimate. .......................... 77
6.6 Robustness to noise compared with CC technique. (i). Results from MSPMethod1, (ii). Results from CC technique. (a). Noise 3%, (b). Noise 5%, (c). Noise 9%. ................................. 80
6.7 Robustness to INU compared with CC technique. (i). Results from MSPMethod1, (ii). Results from CC technique. (a). INU 20%, (b). INU 40%. 81
6.8 Robustness to pathology compared with CC technique. (i). Results from MSPMethod1, (ii). Results from CC technique. (a). Minor MS lesion model, (b). Major MS lesion model.

7.1 The famous woodblock print, “The Great Wave off Kanagawa” by the Japanese artist Katsushika Hokusai [Wikipedia, 2013b]. The fractal concept of self-similarity is used in this painting in the early 1800s.

7.2 Examples of fractals. (a). A mathematical fractal, Sierpinski triangle, (b). Romanesco broccoli, a striking example of fractals in nature. This kind of self-similarity appears in the brain.

7.3 Generation of the Koch curve.

7.4 Application of box-counting method demonstrated with the Sierpinski Triangle.

7.5 Log-log plot of a 3D MR brain image. It does show some linearity within a range of scale.

7.6 Lacunarity is a measure of inhomogeneity in the image. Left: Two textural images taken from UIUC database [Lazebnik et al., 2005]. Right: Computed lacunarity plots.

7.7 Lacunarity describes the texture by measuring the degree of non-homogeneity within an object or image. (a) has higher lacunarity than (b).

7.8 Change of lacunarity value along the sagittal direction.

7.9 Differential box counting with three boxes.

7.10 Results for real and simulated images with varying noise level, INU, and modality: (a). T1WI, (b). T1WI, (c). T1WI with added INU 20%, (d). T1WI with added Noise 5%, (e). T1WI, (f). T1WI-MS lesion, (g). PD, (d). T2WI.


7.12 Lacunarity values plotted at each sagittal location in images with varying noise. (a). No noise case, (b). Noise 5%, (c). Noise 9%.

7.13 Log-log plots of N(r) vs. r. (a). Random sagittal location, (b). Ground truth MSP location.

7.15 Experiments for the validation of our method. (a) Fractal dimension computed using the box-counting algorithm on an artificially generated fractal image [IDOLON, nd]. (b) Validation of the fractal symmetry detection method on the Sierpinski triangle. 101

7.16 Results for real images taken from IBSR database. 102

7.17 Results for real and simulated images with varying noise level, INU, and modality: (a). T1WI, (b). T1WI with added INU 20%, (c). T1WI with added Noise 9%, (d). PD, (e). T2WI, (f). T1WI-MS lesion. 102

7.18 Calculation of the deviation from the ground truth. 103

7.19 Comparison of results obtained from 3 proposed methods. MSPs are projected at axial slices of simulated images with varying noise level, and INU. (a). T1WI with added Noise 3%, (b). T1WI with added Noise 5%, (c). T1WI with added Noise 9%, (d). T1WI with added INU 20%, (e). T1WI with added INU 40%. (i). Results from MSPMethod 1, (ii). Results from MSPMethod 2, iii). Results from MSPMethod 3. 105

7.20 Comparison of results obtained from 3 proposed methods. MSPs are projected at axial slices of simulated images with different image contrast and MS lesion model. (a). T2WI, (b). PD, (c). T1WI-MS lesion. (d). Minor MS lesion model, (e). Major MS lesion model. (i). Results from MSPMethod 1, (ii). Results from MSPMethod 2, iii). Results from MSPMethod 3. 106


8.2 Performance on simulated images. MSPs projected at axial slices using simulated images from BrainWeb with various noise, INU, and modality. 111

8.3 MSPs projected at axial slices with varying slice thickness and modality. 112

8.4 Flowchart of the Edge CC method. 113

8.5 Flowchart of the KLD method. 114


8.7 Deviation from the ground truth with progressive tumor. (a). Tumor images considered, (b). Deviation from the ground truth. 117
8.8 Performance on tumor images. (i). Best performed image of each method, (ii). Worst performed image of each method. (a). Our method, (b). Edge cc method, (c). KLD method. .......................................................... 118
8.9 Deviation from the ground truth with varying noise. (a). Shepp-Logan image, (b). Contrasts changed in the Shepp-Logan image. ............. 119
8.11 Noise resistance property of our method. Figure shows loglog plots of BrainWeb Images with varying noise. ........................................ 122
8.12 Examples of images that Edge CC method produced poor results. (a). Imposed tumors on initial lower brain slices. (b). Initial edge images. (c). Estimated MSPs projected on axial slices. (i). T1-weighted image. Tumor radius:50mm. Tumor centre position: (x0=120, y0=60, z0=90), (ii). T2-weighted image. Tumor radius:40mm. Tumor centre position=(x0=60, y0=120, z0=50), (iii). PD-weighted image. Tumor radius:40mm. Tumor centre positions=(x0=110, y0=80, z0=60). ................................. 123
8.15 Edge CC method performed on with and without skull tumor embedded image. (i). Tumor imposed on with-skull image, (ii). Tumor imposed on skull stripped image. (a). Initial lower brain slice, (b). Initial edge image, (c). MSP estimate. .......................................................... 125
8.16 Examples of images that KLD method produced poor results. Left: Imposed tumor. Right: Estimated MSPs on axial slices. (a). T1-weighted image. Tumor radii=30mm and 45mm. Tumor centre position=(x0=120, z0=90) on the sagittal slice at y=80mm. (b). T2-weighted image. Tumor radius=35mm. Tumor centre position=(x0=150, z0=80) on the sagittal slice at y=100mm. (c). PD-weighted image. Tumor radii=30mm. Tumor centre positions=(x0=80, y0=80, z0=120) and (x0=160, y0=80, z0=80). ... 127
8.17 A test image with three “slices”, slices shown separately. One square represents one pixel. ......................................................... 128
8.18 Histograms for the slices in the test image shown in Figure 8.17

8.19 A sketch for illustrating the effect of head tilt. (a) The $z$ direction is aligned with the major axis of the scanner, (b) the image co-ordinate system is attached to the head, the mid-plane is shown aligned with the three co-ordinates. (c) axial slices are perpendicular to the mid-plane, (d) sagittal slices are considered in the $x$-direction, they are parallel to the mid-plane. (e) If the mid-plane is now rotated due to head tilt, a plane taken in the $x$-direction is no longer parallel to the mid-plane. This will affect the accuracy of the MSP detection method.

9.1 Whole process of the brain tissue segmentation.

9.2 Evaluation is made by using the results set and the ground truth set.

9.3 In our experiments, when our ground truth set is $(A \cup B \cup C)$, its complement is $\emptyset$.

9.4 Mirror pixel. In this illustration, when $i$th pixel value is $I(r, c)$, $j$th pixel value is $I(r, 2p - c)$.

9.5 Hemispheric symmetry analysis performed on simulated images. Results are projected on an axial slice. (i) T1W, (ii) T2W, (iii) PD. (a) A sample image slice, (b) Average symmetry value of the relevant slice, (c) Standard deviation of the symmetry values. Black pixels indicate perfect symmetry.

9.6 Hemispheric symmetry analysis performed on real images taken from IBSR database. Results are projected on an axial slice. (a) A sample image slice, (b) Average symmetry value of the relevant slice, (c) Standard deviation of the symmetry values. Black pixels indicate perfect symmetry.

9.7 Comparison of segmentation results of various synthetic greyscale images with white Gaussian noise of variance 0.03. (i) Perfectly symmetrical image, (ii) An image with non-symmetrical area, (iii) almost symmetrical image, (iv) Non-symmetrical image, (v) almost symmetrical image. (a) Original image, (b) The same image with noise, (c) Results from standard FCM, (d) Results from symFCM.

9.8 Comparison of segmentation results of a real image with added Gaussian noise. (a) Original image, (b) The same image with added Gaussian noise (var=0.01), (c) Results from standard FCM, (d) Results from symFCM.

9.9 Comparison of segmentation results of a real image with added Gaussian noise. (a) Original image, (b) The same image with added Gaussian noise (var=0.01), (c) Results from standard FCM, (d) Results from symFCM.

9.11 Comparison of segmentation results of symFCM1 and ksymFCM1 on two synthetic greyscale images with white Gaussian noise of variance 0.03. (a). Original image, (b). The same image with noise, (c). Results from symFCM1, (d). Results from ksymFCM1.

9.12 Degree of symmetry is measured considering a neighbourhood of each pixel: an example with a first-order neighbourhood.

9.13 Comparison of segmentation results of synthetic images with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.03), (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.

9.14 Comparison of segmentation results of synthetic images with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.03), (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.

9.15 Comparison of segmentation results of a synthetic image with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.03), (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.

9.16 Comparison of segmentation results of a real image with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.01), (c). Results from standard FCM, (d). Results from symFCM2, (e). Results from SFCM, (f) Results from s-symFCM2.

9.17 Comparison of segmentation results of simulated MR brain images with various levels of noise. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
9.18 Comparison of segmentation results of simulated MR brain images with various levels of noise. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information. . . . . 165

9.19 Comparison of segmentation results of simulated MR brain images with various levels of noise. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information. . . . . 166

9.20 Segmentation Accuracy vs. deviation from the ground truth. (a). MR brain image with simulated noise 5%, (b). MR brain image with simulated noise 9%. . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 170
## List of Tables

2.1 Comparison of prime imaging modalities .................................................. 8

5.1 A summary of methods for detecting brain symmetry plane/axis - 1st Part 69
5.2 A summary of methods for detecting brain symmetry plane/axis - 2nd Part 70

6.1 Description of the data set used ................................................................. 78
6.2 A comparison of the computed BD values .................................................. 80

7.1 Description of the data set used ................................................................. 94
7.2 Comparison with the cross-correlation technique ........................................ 94
7.3 Description of the data set used ................................................................. 101
7.4 Difference of the proposed method with the ground truth ............................ 104
7.5 Comparison of three proposed methods on their deviation from the
    ground truth. ......................................................................................... 105
7.6 Strong and weak points of three proposed methods for MSP detection 106

8.1 Description of the data set used ................................................................. 110
8.2 Comparison with the existing work (Tested on simulated images from
    BrainWeb) ......................................................................................... 116
8.3 Comparative results of the paired t-test ...................................................... 116

9.1 Comparative results of our symmetry measure and cross-correlation
    measure performed on 18 images ............................................................. 143
9.2 Description of the data sets used ................................................................. 147
9.3 Segmentation accuracy of synthetic images ................................................ 152
9.4 Segmentation accuracy of simulated brain images ..................................... 152
9.5 Segmentation accuracy of synthetic images ................................................ 167
9.6 Segmentation accuracy of simulated brain images ..................................... 167
9.7 Segmentation accuracy of real brain images .............................................. 168
9.8 Segmentation accuracy of of symFCM1 and s-symFCM2 169
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List of Publications

Book Chapters:


Journals:


Conferences:


Chapter 1

Introduction

1.1 Preview

This introductory chapter first looks into the context behind this research, starting with a discussion of the practical applications that motivated the study of brain tissue segmentation. This is followed by a discussion of some of the major challenges that complicate the development of automatic methods for accurate segmentation. This chapter concludes with a summary of the main contributions of this research, as well as an outline of the organisation of the remaining chapters in the thesis.

1.2 Motivation

Information technology has traversed almost every branch in the field of medical imaging. Modern imaging techniques have offered medical professionals with high resolution images which have greatly assisted clinical diagnosis, showing the potential the technology has in transforming many aspects of clinical medicine. However, in neuroimaging where three-dimensional visualizations of the data is routinely used, computer-aided diagnosis still does not play a major role despite the fact that many image analysis methods have been proposed [Hahn, 2010]. The level of accuracy and robustness of image segmentation required is often considered to be one of the main obstacles in these applications.

Segmentation of brain is an important initial step in neuroimage analysis. The task addressed in this thesis is the automatic segmentation of Magnetic Resonance Images (MRI) of the human brain. When the given input is a 3D MRI volumetric image, the output will be a labeled image in which each voxel is assigned a unique label which represents either grey matter (GM), white matter (WM) or cerebrospinal fluid (CSF).
The overall process of brain tissue segmentation is shown in Figure 1.1. Brain tissue is a complex structure and proper diagnosis of many brain disorders greatly depends upon the accurate segmentation of GM, WM, and CSF. Neurological studies analyse segmented medical images of several subjects in different populations such as normals or dementia, with the goal of characterizing the anatomical features that distinguish the populations. For instance, a recent study in Alzheimer’s disease found that by studying the density of grey matter on the MRI scans, they can get higher prediction accuracy when confirming its diagnosis [Mouton et al., 1998]. In all these applications, segmentation is a pre-processing step which is often considered the barrier for accurate image analysis.

![Figure 1.1: The task of MR brain tissue segmentation. (i). A 2D slice of the input image. (ii). Corresponding output. (a). GM, (b). WM, (c). CSF.](image)

Currently, manual procedure is used for MRI segmentation where a neuroradiological expert manually delineates the boundaries of different tissues or structures in the neuroimage. Since the number of brain diseases is vast and complex and a large number of images need to be processed by radiologist to make an accurate and definitive diagnosis, computer-aided methods can be useful. Although research on automated brain image segmentation has been done extensively over the past several decades, it still remains a difficult problem.

In automatic segmentation, the challenge lies in effective representation and use of
domain knowledge. Prior knowledge about brain anatomy can play an important role in improving the accuracy of neuroimage segmentation algorithms [Clarke et al., 1998]. However, the underlying anatomy in a neuroimage that is to be captured is complex in shape and appearance, and varies across subjects. Complexity in appearance can be due to the imaging modality or various noise artifacts. The same tissue can have different grey level appearance in different regions of the image due to distortions caused by the imaging equipment. For example, grey matter in one region of the image can be significantly brighter than grey matter in another region due to the inhomogeneity of the radio frequency (RF) coils in MRI.

Despite the challenges associated with brain tissue segmentation, human experts can learn to perform this pattern recognition task effectively. This is generally due to the fact that humans are able to combine information from a variety of sources including anatomic knowledge about shape and relative positions of structures, bilateral symmetry, and patient-specific diagnostic information [Schmidt et al., 2005]. The recent methods that encode spatial information to improve intensity-based classifications have demonstrated impressive results [Liew and Yan, 2006]. However, the ability of these systems to address the most challenging cases remains hindered due to the fact that they do not incorporate diverse forms of prior geometrical knowledge such as symmetry information from the image context.

The brain holds bilateral symmetry with only small variations. Study of brain symmetry is done by [Maes et al., 1999, Hugdahl, 2005]. The highly symmetrical distribution of brain tissue types provides an excellent opportunity for symmetry-aided image analysis. A number of researchers have been motivated by this to develop symmetry integrated methods for brain image analysis. It is a difficult task due to several reasons. First, defining approximate symmetry itself is challenging. Additionally, as mentioned above, brain images are complex in nature and depending on the imaging modality, they can be affected by various artifacts.

1.3 Contribution

The segmentation approach proposed in this thesis is based on the hypothesis that knowledge of anatomical geometry and the imaging process is crucial to the success of segmentation. The main contribution of the thesis is a novel method for the segmentation of brain images that combines knowledge of the grey-level appearance of different tissues with the knowledge of symmetry in the imaging context.

This thesis addresses the above task in two parts: First, the precise location of the brain symmetry plane is identified, and then symmetry integrated segmentation method
is developed. In order to incorporate accurate symmetry information, it is necessary to identify the precise location of brain symmetry plane. Therefore, the first part of the proposed paradigm addresses this issue. Here, a novel method based on fractal analysis which has the ability to capture the structural complexity has been proposed. In the second part of the thesis, this symmetry information is incorporated into the segmentation task. Although brain symmetry is used in tumor detection, to the best of our knowledge, this work is the first study that tries to use brain symmetry information in brain tissue segmentation into GM, WM, and CSF. The results from this thesis are applicable for performing segmentation in many other medical and non-medical images. Major novel contributions presented in this thesis can be summarized as follows.

- A thorough analysis of the importance of symmetry in neuroimage analysis.
- An extensive survey with an evaluation of the existing brain symmetry plane detection methods.
- A method for brain symmetry plane detection in MRI based on intensity profile analysis.
- Quantification of brain symmetry based on fractal dimension.
- An approach for brain symmetry plane detection in 3D MR brain images based on fractal analysis.
- A thorough validation and evaluation of the proposed methods with a comparison to two main state-of-the-art techniques.
- A modified fuzzy c-means method that integrates brain symmetry information.
- A complete brain tissue segmentation scheme based on the identification of the brain symmetry plane and integration of its location information into the fuzzy c-means framework.
- A symmetry aided fuzzy c-means algorithm which is adaptive to the level of symmetry present in the image.
- Extension of the proposed segmentation method by adapting an existing technique for neighbourhood spatial information.

1.4 Thesis Overview and Scope

Chapter 1 has introduced the problem of automatic tissue segmentation of MRI brain images along with the motivation and the contribution of this thesis. The organisation of the remaining chapters is as follows.
• **Chapter 2** attempts to give a thorough knowledge of the necessary background to understand the thesis topic: Imaging modalities, brain tissue segmentation in MRI, its applications, and challenges.

• **Chapter 3** extensively surveys the previous approaches for solving this problem. It also discusses the advantages and disadvantages of the existing methods. The fuzzy c-means algorithm is given particular attention as our proposed method is based on this algorithm.

• In **Chapter 4**, based on the main conclusions drawn from the previous chapter, a glance of the novel approach for automatic segmentation is presented by including the inspiration for choosing the methodology. The scope of the work is also highlighted.

• **Part I** of the framework goes from **Chapter 5** to **Chapter 8** where the problem of symmetry detection is addressed. In this part, **Chapter 5** explains the computational symmetry along with existing symmetry measures and a thorough survey on the previous work on brain symmetry plane detection. Existing methods are discussed by categorising them into two main approaches. It also discusses the validation techniques used in the literature.

• **Chapter 6** and **Chapter 7** presents in detail the proposed methodologies for brain symmetry plane detection which are based on two major concepts. The first one explained in **Chapter 6**, is based on the radiological and anatomical properties of MR brain images. Specifically, it is done by analysing intensity profiles in T1-weighted images. However, since this method does not perform well on T2-weighted images or proton-density images, another approach based on fractal analysis is proposed in **Chapter 7** where two new methods that exploit fractal properties are discussed. For each method, experimental results and evaluation are also demonstrated. At the end of **Chapter 7**, all proposed methods are compared and their merits and limitations are pointed out. Then, the best performing method is further be evaluated in **Chapter 8**.

• **Chapter 8** contains a thorough comparative evaluation of the proposed method with two other state-of-the-art techniques. In this chapter, the drawbacks of these two existing methods are shown through experiments. A detailed discussion and summary of Part I can also be found here.

• **Part II** consists of **Chapter 9** and **Chapter 10**. **Chapter 9** presents in detail the proposed methodology, and devise the framework for brain tissue segmentation. It also contains results and evaluation.
Chapter 10 is the discussion. Major conclusions drawn from the other chapters are presented here. Potential future directions of the research are also discussed.
Chapter 2

Background

2.1 Preview

This chapter covers the background knowledge needed for understanding the problem of brain tissue segmentation. First, it briefly discusses the different imaging modalities, MRI principle, and its applications, as MRI is the imaging modality considered in this research. Section 2.4 explains the brain tissue segmentation task. This is followed by a discussion of the motivation to automate the task of brain tissue segmentation. Section 2.6 discusses the various challenging aspects of the problem that complicate the development of automatic methods. This chapter concludes with a summary.

2.2 Imaging Modalities

Medical imaging assists the diagnosis and treatment of different diseases by producing images of the human body. Depending on the technique used, medical imaging comprises different imaging modalities.

2.2.1 Different imaging modalities

The most commonly used radiological modalities for imaging anatomy are x-ray, magnetic resonance imaging (MRI), X-ray computed tomography (CT), ultrasound, positron emission tomography (PET), and single photon emission computed tomography (SPECT).

The human body mainly consists of water, bones, and some trace elements that exist in different parts of the human body, such as iodine in the thyroid and iron in blood [Westbrook et al., 2005]. Medical imaging techniques use different properties of these
elements. The x-ray, invented by Wilhelm Rontgen in 1895, is based on the measurement of the transmission of x-ray through the body. However, a disadvantage of x-ray is the high level of radiation emitted that can cause diseases such as cancer and eye cataract. In CT, image is reconstructed from a large number of x-rays. Ultrasound measures the reflection of ultrasonic waves transmitted through the body. PET and SPECT use gamma rays. Magnetic Resonance Imaging, as the name suggests, relies on the inherent magnetic properties of molecules within the body. Resonance is a phenomenon that occurs when an object is exposed to an oscillating perturbation that has a frequency close to its natural frequency of oscillation. One of the main advantages of MRI compared with other imaging modalities is the excellent soft tissue discrimination of the images [Westbrook et al., 2005]. MRI is an important imaging technique for detecting abnormal changes in different parts of the brain in early stage, and is excellent in early detection of brain diseases. Due to its advantages, MRI has been the method of choice for imaging the brain and most of the research in brain image segmentation uses MRI images. Therefore, MRI is the primary focus of our work, although the methods developed in this study are applicable to other imaging modalities as well.

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray</td>
<td>Fast, Relatively inexpensive</td>
<td>Uses radiation, Cannot distinguish between soft tissues of similar consistency very well</td>
</tr>
<tr>
<td>CT</td>
<td>High resolution anatomical structure, Relatively fast</td>
<td>Uses radiation, Cannot provide high contrast between different tissues</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>No radiation, thus safe, Portable, and inexpensive</td>
<td>Cannot see through bone or air</td>
</tr>
<tr>
<td>MRI</td>
<td>High soft tissue contrast, No radiation, thus safe</td>
<td>Relatively expensive, Lengthy exam time</td>
</tr>
</tbody>
</table>

2.3 Magnetic Resonance Imaging

Magnetic Resonance phenomenon was discovered by Felix Bloch and Edward Purcell independently and both were awarded the Nobel Prize in Physics in 1952. Based on this principle, MRI was invented by Raymond Damadian in 1971, and has become a popular method in modern medical imaging. Moreover, it can be adapted to image brain due to the ability of MRI to record signals that can distinguish between different tissues,
such as grey matter and white matter. MRI scanning is relatively safe and unlike other medical imaging modalities, can be used as often as necessary.

MRI is based on the principle of Nuclear Magnetic Resonance (NMR). The principle of NMR is based on the absorption and emission of energy in the radio frequency range of the electromagnetic spectrum. The fundamental target of MRI is to map the spatial location and associated properties of specific nuclei or protons present in the object being imaged. A basic property of nuclei with odd atomic numbers or weights is the possession of angular momentum called spin. These protons carry an electric charge and spins around their axes. Due to this spinning, a magnetic field is created around these protons and therefore they act like tiny magnets, possessing both angular and magnetic moments. The magnetic moment is proportional to the spin angular moment and is related through a constant called gyro-magnetic ratio, γ, a quantum property of the proton. When each proton is spinning on its own axis, the influence of a static external magnetic field, $B_0$, produces an additional spin, or wobble of the magnetic moments. This secondary spin is called precession and causes the magnetic moments to follow a circular path around $B_0$. The speed at which they wobble around $B_0$ is called the precessional frequency. The value of the precessional frequency is governed by the Larmor equation which states that

$$\omega_0 = B_0 \times \gamma$$

(2.1)
The most abundant atom in the body is hydrogen. This is most commonly found in molecules of water and fat. The hydrogen nucleus contains a single proton that spins. Therefore, the hydrogen nucleus has a magnetic field induced around it. In the absence of an applied magnetic field, the magnetic moments of the hydrogen nuclei are randomly orientated. When placed in a strong static external magnetic field, however, the magnetic moments of the hydrogen nuclei align with this magnetic field. The net magnetic moment of hydrogen produces a significant magnetic vector that is used in clinical MRI. However, this net magnetic moment $M_0$ is not directly observable due to much stronger external magnetic field $B_0$. Therefore, for image formation, a strong static magnetic field is used to perturb magnetic moments of proton that exist in the hydrogen nucleus, and then a RF pulse having frequency equal to Larmor frequency is applied to extract $M$ as two components: longitudinal magnetization component and transverse magnetization component. When the RF pulse is turned off, the longitudinal magnetization component recovers to $M_0$ with $T_1$ relaxation time, and the transverse magnetization component decays to zero with $T_2$ relaxation time. MR images are obtained by using the information of how perturbed moments relaxes back to their equilibrium [Balafar et al., 2010]. This procedure is illustrated in Figure 2.1. By adjusting MR acquisition parameters related to $T_1$ and $T_2$, MR image can be made to contrast different tissue types.

2.3.1 MR image contrasts

An MR image has contrast depending on the signal strength. Areas of high signal appear white on the image while areas of low signal appear dark on the image. Some areas have an intermediate signal (shades of grey in between white and black). Images obtain contrast mainly through the mechanisms of $T_1$ recovery, $T_2$ decay and proton or spin density [Westbrook et al., 2005]. The proton density of a tissue is the number of protons per unit volume of that tissue. The higher the proton density of a tissue, the more signal available from that tissue.

Generally, the two extremes of contrast in MRI are fat and water. In imaging the brain, two of the most commonly used MRI images are $T_1$-weighted and $T_2$-weighted images. These weightings refer to the dominant signal (whether it be the $T_1$ time or the $T_2$ time) measured to produce the contrast observed in the image. $T_1$ is the longitudinal relaxation time. It indicates the time required for a substance to become magnetized after first being placed in a magnetic field or, alternatively, the time required to re-gain longitudinal magnetisation following an RF pulse. Areas with high fat content have a short $T_1$ time relative to water. Therefore, in the brain $T_1$-weighted scans provide good grey matter/white matter contrast with water darker and fat brighter; in other words,
T1-weighted images highlight fat deposition. On the other hand, $T2$ is the “transverse” relaxation time. It is a measure of how long transverse magnetization would last in a perfectly uniform external magnetic field. $T2$ decay is due to magnetic interactions that occur between spinning protons. Areas with high water content have a short $T2$ time relative to areas of high fat content. Like the T1-weighted scan, fat is differentiated from water, but in this case fat shows up darker, and water lighter. Figure 2.2 demonstrates an example of T1-, T2-, and PD-weighted images.

![Example of T1-, T2-, and PD-weighted images](image1.png)

*Figure 2.2: Different contrasts in MRI. (a). T1, (b). T2, (c). PD.*

Brain MRI can be viewed in three different planes such as axial plane, sagittal plane, and coronal plane (see Figure 2.3 and Figure 2.4). Axial (or transverse) views, taken from the top of the head are generally best for evaluating abnormal signal or morphology in the brain. Coronal (viewed from the back of the head) and sagittal (viewed from the side of the head) are suitable for evaluating posterior fossa of the brain. The coronal images allow left and right symmetry analysis.

![Different planes of the brain images](image2.png)

*Figure 2.3: Different planes of the brain images.*

Since magnetic resonance imaging does not ionize tissues it is considered amongst the safest of radiological techniques. Its applications are extended at almost all parts of
Figure 2.4: Different planes of the brain images visualized on MRI. Top row shows the different projections. (a). Axial plane, (b). Sagittal plane, (c). Coronal plane.

the body. MRI has good contrast in comparison to computerized CT, and is capable of providing very detailed information about soft tissues. They can differentiate between normal and abnormal tissues and may show damages missed on a CT. Therefore, it is a popular way to obtain an image of brain with high contrast. Figure 2.5 illustrates an example of CT and MRI brain images. MRI is also excellent for imaging blood flow. Functional MRI maps changes in blood flow in the brain during specific tasks. This provides valuable information about how the brain works. MRI acquisition parameters can be adjusted to give different grey levels for different tissues and various types of neuropathology. Computer manipulation of the digital data can be used to produce exact three-dimensional images of organs. As mentioned previously, a disadvantage of MRI is that the image acquisition takes considerably longer time as compared to, for example, CT.

2.3.2 MRI and brain disorders

The number of brain diseases can be quite extensive or complex, and must be visualized well to enable the radiologist to make an accurate and definitive diagnosis. As discussed above, MRI is currently the best test to evaluate any abnormalities or disorders within the brain. Here, we outline briefly several different brain diseases that can be identified with the help of MRI [Kasper et al., 2004].

- Alzheimer’s disease: Alzheimer’s disease is defined as a loss of brain function that can affect language, memory, coherence, judgment and thinking. Although certain disorders in the brain can contribute to a general diagnosis of the disease, MRI can help to differentiate the forms of Alzheimer’s disease. This information can be used as a tool to implement the best treatment plan for the patient [Tokunaga
• Aneurysm: Aneurysms are a bulging of an artery wall due to weakening. Most people who have an aneurysm are unaware of it until it ruptures. When an aneurysm ruptures, there is limited time to repair it before fatal consequences occur. An MRI is an excellent imaging tool used to detect an aneurysm before it ruptures.

• Brain Tumors: MRI can detect brain tumors in any part of the brain. It is useful even in detecting very small tumors, such as pituitary tumors. The early detection of brain tumors by MRI can help the physician plan the appropriate treatment for the patient [Clarke et al., 1998].

• Multiple Sclerosis: Multiple sclerosis, which is an autoimmune disease that affects the brain and spinal cord, can be definitively diagnosed with MRI. MRI is the test of choice to not only diagnose, but to follow the progression of multiple sclerosis. Multiple sclerosis is seen as “lesions” in the brain and the progression of the disorder or effective treatment of the disorder can be determined by an increase or decrease in the size and/or amount of these “lesions” [Johnston et al., 1996].

• Strokes: A stroke can easily be identified by an MRI. A hemorrhagic stroke is characterized by bleeding in the brain caused by a ruptured blood vessel. An ischemic stroke is when a blood vessel is obstructed or clogged, and cuts off the blood supply to the brain. Both are life-threatening and can be easily evaluated by MRI due to the changes in contrast of the surrounding tissues of the brain.
Main applications in MR brain image segmentation can be outline as follows.

Applications in MR brain image segmentation

- Measure tissue volumes
- Locate tumors and other pathology
- Diagnosis and treatment planning
- Computer guided surgery
- Study of anatomical structure
- Computer-assisted segmentation of white matter lesions in 3D MRI

2.4 Brain Tissue Segmentation

Brain tissue segmentation is an image segmentation task.

2.4.1 Image segmentation

An image is a collection of measurements in two-dimensional (2D) or three-dimensional (3D) space. In medical images, these measurements or image intensities are obtained through radiation absorption in X-ray imaging, acoustic pressure in ultrasound, or radio frequency (RF) pulse amplitude in MRI [Balafar et al., 2010]. In the 2D domain each measurement or element is called a pixel, while in 3D domain it is called a voxel. In some cases, 3D images are represented as a sequential series of 2D slices for the advantage of lower computational complexity and lesser memory.

Image segmentation is defined as the division or partitioning of an image into non-overlapping, constituent regions that are homogeneous with respect to some features like grey level or texture. With this definition, an image \( A \) can be modeled as the union of \( c \) homogeneous regions \( A_k \) [Liew and Yan, 2006].

\[
A = \bigcup_{k=1}^{c} A_k
\]  

(2.2)

The basic attribute for segmentation is image intensity for a monochrome image and colour components for a colour image. The result of image segmentation is a set of regions taken as a whole covers the entire image, or a set of contours extracted from the image. Labeling is the process of assigning a meaningful designation to each region or class [Pham et al., 2000].
Ideally, a good segmentation algorithm should produce regions which are uniform and homogeneous with respect to some characteristic such as intensity [Spirkovska, 1993]. Region interiors should be simple, without many small holes. Further, the boundaries of each segment should be spatially accurate and adjacent regions should have significantly different values with respect to the characteristics on which region uniformity is based [Haralick and Shapiro, 1985].

Image segmentation is a first and critical step in many image analysis applications. The aim of the medical image segmentation is to study anatomical structure and identify region of interest, such as tissue volumetry, tumor, lesion or any other abnormality. This will help in diagnosis and treatment planning. The focus of this thesis is on brain tissue segmentation.

2.4.2 Brain anatomy

Brain contains three major tissue types, such as, White Matter (WM), Grey Matter (GM) and Cerebrospinal Fluid (CSF). Figure 1.1 illustrates these three tissue types. Both the spinal cord and brain are covered in three continuous sheets of connective tissue, the meninges. It is necessary to measure the amount of WM, GM and CSF as well as their spatial distribution and temporal changes for diagnosis of various brain disorders [Kasper et al., 2004].

- Grey Matter: Grey matter is the masses of cell bodies. This includes cortex of the brain which contains nerve cell bodies. The grey matter is in contrast to the white matter, the part of the brain that contains myelinated nerve fibers which are white. The grey matter is so named because it appears grey.

- White Matter: This part of the brain that contains myelinated nerve fibers. The white matter is white because it is the colour of myelin, the insulation covering the nerve fibers.

- Cerebrospinal Fluid: The cerebrospinal fluid aids in the protection of the brain and spinal cord by acting as a watery cushion surrounding them to absorb the shocks to which they are exposed.

2.4.3 Brain tissue segmentation and applications

The problem this research tries to address is the automatic segmentation of brain tissues in MRI. When the input is a 3D MR brain image, the output image will have segmented brain tissues: GM, WM and CSF. We assume that each tissue class has a specific feature value based on signal intensities measured in the T1, T2, and PD weighted MR images.
Applications that use the morphological contents of MR images frequently require such segmentation of the imaged volume into different tissue types [Wells III et al., 1996]. Brain volume quantification is also important in the study of many brain diseases. Neurological diseases are complex in nature that makes them hard to diagnose. Studies have reported that severe cortical volume loss (atrophy) is a consistent neuropathological finding in many brain disorders [Mouton et al., 1998]. Absolute volumes and the spatial distribution of brain atrophy are of major interest when studying the course of neurodegenerative diseases, such as Multiple Sclerosis, Alzheimer’s disease (AD) and Schizophrenia. For example, AD is associated with the atrophy of grey matter in the cerebral cortex, which leads to a volume decrease of the cerebral cortex or a volume increase of CSF in some parts, which can be measured in MRI. Figure 2.6 compares the brain of an AD patient to a same aged normal brain. In their study [Mouton et al., 1998], Mouton et al. have measured tissue volumes of autopsy-confirmed AD cases. Their results show a strong correlation between cognitive decline and cortical atrophy in Alzheimer’s dementia. It would be important to estimate the degree of cerebral atrophy based on precisely segmented tissue regions for diagnosis of various neuro-diseases [Tokunaga et al., 2010].

Figure 2.6: AD patient’s brain image compared to a normal brain image. (a). AD, (b). Normal.

Apart from the clinical diagnosis, the identification of brain tissues or structures in MRI is very important in neuroscience and has many applications such as; mapping of functional activation onto brain anatomy, the study of brain development, and the analysis of neuroanatomical variability in normal brains [Balafar et al., 2010].
2.5 Motivations for Automatic Segmentation of Brain Images

There are a number of motivations for the development of methods for automatic brain tissue segmentation. Recent progress in imaging techniques has offered medical professionals with high resolution images which have greatly assisted clinical diagnosis. Brain image segmentation is a crucial part of clinical diagnostic tools. Accurate segmentations are needed in clinical and scientific applications.

2.5.1 Neuroimages in clinical setting

When diagnosing numerous brain diseases, accurate quantification of different brain tissues or pathologies is an important issue. While neurological studies have greatly benefited by high resolution in vivo neuroimaging, when using these images for diagnosis, visual interpretation is still the common practice used in clinical settings.

Current manual procedure for brain tissue segmentation

Current manual procedure can be described as follows: After understanding the nature of the illness the MRI radiographer who works closely with the doctor and the radiologist, perform the scan from a computer. MRI produces many pictures and medical technicians have to process a large number of images with much more details. Therefore, it takes some time for the radiologist to review. Most common procedure for analysing this image data is visual inspection on printed support. Figure 2.7 shows a picture of a radiologist doing manual segmentation.

![Figure 2.7: A set of sagittal cross-sectional slices of a 3D brain MRI scan. The radiologist has to process and analyse a large number of images.](image)

Manual segmentation is a tedious job. A typical scan which shows good contrast between soft tissues consists of nearly eight million voxels across hundreds of cross-sectional images that need to be classified. Higher accuracies on more finely detailed
volumes demand increased time from medical experts. Moreover, the image derived measurements taken by manual delineation of structures of interest by a radiologist suffer from to inter- and intra-operator variability and poor reproducibility. Studies have shown that manual segmentations vary significantly between experts as well as when an expert segments the same image at different times [Warfield et al., 2000]. Up to 15% variability has been reported in the segmentation of cortical grey matter of the brain in segmentations by different experts [Warfield et al., 2000]. These variations render the manual solution problematic in tasks such as neuroscience studies mentioned above where the desired accuracy is higher than the variability between manual segmentations, and indicates the need for reproducible and accurate automatic segmentation methods.

Furthermore, various artifacts in different imaging modalities can also compromise accurate image interpretation. It becomes important to develop objective methods for tissue segmentation, localising pathology or measuring atrophy. Accurate automatic segmentation methods could also lead to new applications, including effective content based image retrieval in large medical databases. This could allow clinicians to find similar images in historical data based on similar patterns of growth, tumor location, and extent of edema or a variety of other factors. This information could help clinicians in making decisions, in addition to being a useful research tool for exploring patterns in the historical data [Pham et al., 2000].

2.5.2 Towards an automated tissue segmentation method

Computers excel in performing certain tasks than humans. In neuroimaging, one of the questions that computers can answer more reliably than humans is about the precise quantification, like how much has changed? [Hahn, 2010]. In order to facilitate accurate detection of abnormalities and quantification, intensive research has been done on automatic medical image analysis. Advantages of an automated method include objectivity, reproducibility and the capability to process large number of images quickly [Liew and Yan, 2006, Minoshima et al., 1992].

An automatic method is defined as an approach that takes these input images and produces a final segmentation without any human interaction. This excludes operations such as manual seed selection and manual contour initialisation. However, despite several decades of research [Bezdek et al., 1993, Pham et al., 2000, Doi, 2007], automatic analysis of brain images still remains a challenging problem. Much work is still needed before many of the methods can be adopted for routine clinical use.
2.6 Challenges in Automatic Segmentation

Despite the large amount of research focusing on brain tissue segmentation in MR images, robust and automatic methods that achieve an accuracy comparable to human experts have remained out of reach. First, brain images are complex in nature. Although MRI images may visually appear uniform, intrascan intensity inhomogeneities due to radio frequency (RF) coils often affect the segmentation process. One might think differentiation between white and grey matter should be easy since these tissue types exhibit distinct signal intensities. However, in practice, the output of segmentation algorithm is affected by several main problems that can complicate the segmentation task.

2.6.1 Image noise

All MR images are affected by random noise to some extent. Noise corrupts the signal measured for each pixel. The effect of this noise is often modeled as a Gaussian random process that is independent of the underlying tissue type. Figure 2.8 demonstrates an example of a brain image with varying noise. When the level of noise is significant, tissues that are similar in contrast cannot be delineated effectively, affecting the accuracy in tissue segmentation [Liew and Yan, 2006]. This could be critical in the pathological analysis and diagnosis.

![Image noise simulated using BrainWeb. Left to Right: Noise free image, image with 5% noise, image with 9% noise.](image)

**Figure 2.8:** Image noise simulated using BrainWeb. Left to Right: Noise free image, image with 5% noise, image with 9% noise.

2.6.2 Partial volume averaging

When multiple tissues contribute to single pixel or voxel, the resultant image is blurred at boundaries of the different region or object and this effect is known as partial volume...
effect (PVE). Figure 2.9 illustrates an example of the partial volume artifact. It is the result of the finite resolution represented by acquired pixels. Since the pixels have a finite size, an individual pixel can represent more than one type of tissue, resulting in partial volume artifacts. The intensity recorded for these partial volume artifacts will be a combination of the intensities of the structures that intersect at the pixel location. Therefore, fine anatomical details will be lost. This will affect the accuracy of delineation of different tissue types.

![Figure 2.9: Partial volume effect. Left: Ideal image. Right: Acquired image [Pham et al., 2000].](image)

To deal with partial volume effect, soft segmentation is a good option [Pham et al., 2000]. In soft segmentation, regions are allowed to overlap, that is pixels are allowed to have multiple memberships with varying degree of membership coefficients in different regions.

### 2.6.3 Intensity inhomogeneity

Another major artifact that MRI suffers is the intensity inhomogeneity. It refers to variations in the recorded intensity observed within an image that can lead to a variation in the intensity values recorded for homogeneous tissues. Intensity inhomogeneities may be caused by non-uniformities in the RF field during acquisition as well as other factors [Pham et al., 2000]. This inhomogeneity artifacts cause a shading effect to appear over the images which affects the segmentation. Figure 2.10 illustrates this. Although this variation does not affect the manual procedure much, it could affect the accuracy of the automatic methods considerably, especially when this intensity variation becomes significant compared to the image contrast. Many [Wells III et al., 1996, Rajapakse and Kruggel, 1998, Liew and Yan, 2003] have modeled the inhomogeneities as a multiplicative bias field over the image assuming low-frequency intensity non-uniformity (INU) over the image, independent of the tissue classes.

Techniques based on statistical methods and fuzzy methods which gives soft segmentation results are particularly useful in overcoming this limitation [Vovk et al., 2007].
Figure 2.10: Intensity inhomogeneity simulated using BrainWeb. Left to right: Original image, image with 20% inhomogeneity, image with 40% inhomogeneity. Although this variation does not affect the manual procedure much, it could affect the accuracy of the automatic methods considerably.

2.7 Chapter Summary

This chapter has provided the background to this research. It has introduced the problem of medical image segmentation with the focus on automatic brain tissue segmentation in magnetic resonance images. The main points can be summarised as follows. There is a need for an automatic method due to the tedious and time consuming manual segmentation. Magnetic Resonance is an excellent modality for visualizing brain tissues, and there exist a large variety of current and potential applications for brain tissue segmentation in this modality. However, segmentation in MR images is complicated by noise, partial volume averaging and intensity inhomogeneity. This is further complicated by the complexity of the anatomical structure.

Computer algorithms should be developed based on the principles used by radiologists to detect abnormality or atrophy [Doi, 2007]. For example, the symmetry plane of the brain can help in identifying brain pathologies, like stroke, tumor and atrophy by comparing to healthy regions of the brain.

Although a number of algorithms have been proposed in the field of medical image segmentation, brain MR image segmentation still remains a complex and challenging problem [Clarke et al., 1995].
Chapter 3

Related Work

3.1 Preview

While there is a vast array of scientific literature focusing on the task of general image segmentation, medical image segmentation has also received significant attention due to its vital role in diagnostic applications. A large amount of research effort has focused on specific areas of the body or specific modalities, such as the segmentation of images of the brain in MR images. This chapter discusses brain tissue segmentation methods that have the best potential for MR images although many methods can also be applied to other image types and to images from other modalities. Although it would not cover in detail all of the approaches proposed for the segmentation of MR images of the brain, it provides a comprehensive survey of many of the proposed approaches for automatic brain tissue segmentation in MR images. It discusses several state-of-the-art methods in each approach. The remainder of this chapter is divided into sections based on three major categories, namely classification-based, region-based, and contour-based approaches. Fuzzy c-means (FCM) algorithm is given particular attention as it is in the centre of the techniques that have been incorporated into this work.

3.2 Classification-based Segmentation

This section first outlines several classical approaches to image segmentation, and then discuss the classification-based approaches under two main frameworks: supervised and unsupervised. Figure 3.1 illustrates this taxonomy of brain tissue segmentation techniques.
3.2.1 Thresholding methods

Thresholding is one of the oldest techniques for image segmentation. This is applied to an image to distinguish regions with contrasting intensity levels. The most widely used technique is histogram thresholding that exploits the shape properties of the histogram. An image histogram has distinct peaks, with each peak corresponding to one distinct region, and the valley as the threshold values for separating those regions. Determination of more than one threshold value is a process called multi-thresholding. These can be selected manually according to a priori knowledge or automatically through image information. In order to find threshold values, Otsu’s algorithm employs the variance property of the image. Since variance is a measure of uniformity, the larger the variance, the greater the difference between the background and the object. The segmentation is carried out by grouping all pixels with intensity between two such thresholds into one class. [Suzuki and Toriwaki, 1991] uses an iterative thresholding algorithm for segmentation of brain tissues in MR axial slices in which an optimum threshold value is decided based on a goodness measure.

The thresholding technique relies on the identification of a good threshold. Failing
to find such a threshold may lead to poor segmentation. Thresholding does not take into account the spatial characteristics of an image [Dubey et al., 2010]. Determination of a threshold satisfactorily is difficult due to overlapping of the tissue intensity and the spatial variations in MRI [Rajapakse and Kruggel, 1998]. Although the thresholding technique is simple and computationally fast, it is sensitive to noise and INU. These techniques are often used within a set of image processing operations or as an initial step in pre-processing [Gonzalez et al., 2002].

### 3.2.2 Statistical approach

Unlike simple thresholding methods, statistical classification-based methods have a rigorous mathematical foundation set up on stochastic theory. In statistical approach, a pattern is represented by a set of $n$ features viewed as an $n$-dimensional feature vector. These features are assumed to have a probability density function conditioned on the pattern class. Thus, a pattern vector $x$ belonging to class $i$ is viewed as a $p(x/i)$. Bayes theorem can be used to find a maximum likelihood or maximum a posteriori (MAP) solution for defining the decision boundary [Jain, 1989]. For instance, Bayes’ rule can be applied to determine the a posteriori conditional probability for each class for a given pixel. Bayes’ rule for pixel $i$, with feature vector $x_i$, and class $k$ is

$$P(k/x_i) = \frac{P(x_i/k)P(k)}{P(x_i)}.$$  \hspace{1cm} (3.1)

$P(k/x_i)$ is the a posteriori conditional probability that pixel $i$ is a member of class $k$, given its feature vector $x_i$. $P(k/x_i)$ gives the membership value of pixel $i$ to class $k$, where $k$ takes values between 1 and $c$ (the number of classes, while $i$ takes values between 0 and $N - 1$ (the number of pixels in the image).

A commonly used classification model in this category is the mixture model. It assumes that the pixel intensities are independent samples from a mixture of probability distributions, usually Gaussian. Classification of new data is obtained by assigning each pixel to the class with the highest posterior probability. When the data truly follows a finite Gaussian mixture distribution, the ML classifier can perform well and is capable of providing a soft segmentation composed of the posterior probabilities. Although it is a mathematically simple model that can be computed efficiently, it only uses the intensity information for segmentation without considering spatial information. Hence, it is sensitive to noise and other artifacts.

In order to integrate spatial information Markov random field (MRF) is often employed. It adds an extra term to Gaussian mixture model with prior probability distribution. MRF is said to be a model of the full joint probability distribution of a set of
random variables having the Markov property. This theory provides a way of modeling context-dependent patterns such as image pixels and correlated features [Li, 2009]. MRF modeling itself is a statistical model that can be used within segmentation methods. In this model, it is assumed that any particular pixel belonging to a region depends on the neighbourhood of the pixel. It models spatial interactions between neighbouring or nearby pixels [Kindermann and Snell, 1980]. In medical imaging, MRFs are frequently used because most pixels belong to the same class as their neighbouring pixels. In physical terms, this implies that any anatomical structure that consists of only one pixel has a very low probability of occurring under an MRF assumption. The segmentation is then obtained by maximizing the probability of the segmentation. This maximization can be achieved by iterative methods such as iterated conditional modes or simulated annealing [Li, 2009]. A limitation with MRF models is proper selection of the parameters controlling the strength of spatial interactions. A setting that is too high can result in an excessively smooth segmentation and a loss of important structural details. Despite these limitations, MRFs are widely used to model segmentation classes and also to model intensity inhomogeneities that can occur in MRIs. [Held et al., 1997] presented a Markov random field as a priori model for MR brain image segmentation.

The Expectation Maximization (EM) [Dempster et al., 1977] handles incomplete data problem. Since unsupervised segmentation of brain images can be viewed as an incomplete data problem, EM algorithm has been applied to do the segmentation [Wells III et al., 1996]. The EM algorithm applies the same clustering principles with the underlying assumption that the data follows a Gaussian mixture model. It iterates between computing the posterior probabilities and computing maximum likelihood estimates of the means, covariances, and mixing coefficients of the mixture model. In image segmentation, the observed data are the feature vectors associated with pixels, while the hidden variables are the expectations for each pixel that it belongs to each of the given clusters. In the algorithm, each iteration consists of two steps: In the expectation (E) step, the probability distribution of each hidden variable is computed from the observed values and the current estimate of the model parameters. In the maximization (M) step, the model parameters are re-estimated assuming the probability distribution computed in the E-step is true. The common disadvantage of EM algorithms is that the intensity distribution of brain images is modeled as a normal distribution, which is not true, especially for noisy images [Shen et al., 2005].

Methods in this sub-category assume a specific distribution of the features. For instance, the maximum likelihood (ML) method usually assumes multivariate Gaussian distributions. The mean and the covariance matrix for each of the tissues are estimated from a user supplied training set, usually found by drawing regions of interest (ROI)
on the images. The remaining pixels are then classified by calculating the likelihood of each tissue class, and choosing the tissue type with the highest probability. This type of methods are only useful when the feature distributions for the different classes are well known, which is not necessarily the case for MR images.

3.2.3 Artificial neural networks

Artificial neural networks (ANNs) are parallel networks of interconnected processing elements or nodes that simulate biological neurons. Each node in an ANN is capable of performing elementary computations. The main advantages of ANN are the ability to learn adaptively and the capability of performance in real time because of parallel configuration. Learning is achieved by the adaptation of weights and bias of the neurons with respect to the training procedure and training data. ANN has been widely used for segmentation and classification purposes in both supervised and unsupervised modes. Training is the main requirement of many ANN based algorithms where the classifiers need to be trained before it can be applied to segmentation and classification problem. In general, for different data sets, analysis of different images of different type and format, the whole effort of selecting training data set and training is required to be redone.

[Zijdenbos et al., 1994] examined a quantitative analysis method for MR images using artificial neural networks as the classifier. They used a similarity index for the comparison. Neuro-fuzzy systems, combinations of neural networks and fuzzy system, have also been used in image segmentation [Boskovitz and Guterman, 2002].

[Zhang et al., 2010] presented one of the most recent approaches to automatic brain segmentation in MR images. This approach used Support Vector Machines (SVMs), which is currently a popular method for performing binary classification. It is a more appealing approach than ANN models for the task of binary classification since they have more robust generalization properties and achieve a globally optimal solution. In the task of binary classification, if the classes are linearly separable in the feature space, then the logic behind SVM classification is that the best linear discriminant for classifying new data will be the one that is furthest from both classes. Binary classification with 2-class support vector machines is based on this idea of finding the linear discriminant (or hyperplane) that maximises the margin (or distance) to both classes in the feature space. The use of this margin maximizing linear discriminant in the feature space provides statistical bounds on how well the learned model will perform on pixels outside the training set.

A disadvantage of ANN is the requirement of manual interaction for obtaining training data. Training sets can be acquired for each image that requires segmentation,
but this can be time consuming and laborious. On the other hand, use of the same training set for a large number of scans can lead to biased results which do not take into account anatomical or physiological variability between different images.

### 3.2.4 Clustering approach

Clustering approaches are generally unsupervised algorithms not dependent on training data. These methods iterate between segmenting the image and characterizing the properties of the each class. Commonly used clustering techniques for MR image segmentation include k-means, and its fuzzy equivalence, fuzzy c-means (FCM) which is an extension of k-means. In these algorithms, initialisation is very important for meaningful clustering results and fast computation.

The k-means clustering algorithm clusters data by iteratively computing a mean intensity for each class and segmenting the image by classifying each pixel in the class with the closest mean. K-means algorithm produces results that correspond to hard segmentation. [Singh et al., 1996](#) employs k-means algorithm to classify grey matter in functional MRI.

The fuzzy c-means (FCM) algorithm generalises the k-means algorithm, allowing for soft segmentations based on the concept of fuzzy set theory which was formed by Zadeh [Zadeh, 1965](#). In fuzzy model, uncertainty is said to be modeled in a non-statistical way. Fuzzy clustering as a soft segmentation method has been widely studied and successfully applied to image segmentation. When \( X \) is a space of points, a Fuzzy Set \( A_k \) in \( X \) is characterized by a membership function \( m_k(x) \) which satisfies the following:

\[
0 \leq m_k(x) \leq 1, \text{ for all } k \text{ and } j \quad (3.2)
\]

\[
\sum_{k=1}^{K} m_k(j) = 1, \text{ for all } j \quad (3.3)
\]

FCM algorithm is proposed by Dunn [Dunn, 1973](#) and generalised by Bezdek [Bezdek, 1980](#), who is also one of the first to use it for medical image segmentation. The FCM algorithm, in particular, can be used to obtain a segmentation via fuzzy pixel classification. Unlike hard classification techniques which force pixels to belong exclusively to one class, FCM allows pixels to belong to multiple classes with varying degrees of membership. This idea is important in many applications where uncertainty is present due to poor contrast, limited spatial resolution and various noise artifacts. This approach allows additional flexibility in segmenting the images and has recently been widely used in the processing of MR brain images.

Mathematically, FCM aims to minimise the following objective function with respect
to the membership values $u_{ik}$ (soft partition of $X$) and the centroids $v_i$ [Bezdek, 1980].

$$J_{FCM} = \sum_{k=1}^{n} \sum_{i=1}^{c} (u_{ik})^m \|x_k - v_i\|^2$$  

(3.4)

where $x_k$ is the observation at pixel $k$, $n$ is the number of pixels in the image domain, $c$ is the number of clusters where $1 \leq i \leq c$ and $m \in [1, 0)$ is a weighting exponent on each fuzzy membership. The parameter $m$ controls the degree of “fuzziness” in the resulting membership functions. As $m$ approaches unity, the membership functions become crisper, and approach binary values. As $m$ increases, the membership values become increasingly fuzzy [Bezdek, 1981]. The total number of classes $c$ is assumed to be known. Norm operator $\|\|$ represents the standard Euclidean distance.

The membership values are constrained to be positive and to satisfy the following condition.

$$\sum_{i=1}^{c} u_{ik} = 1$$  

(3.5)

Here, the objective function is minimised when high membership values are obtained in areas where the observations are close to the centroid, and low membership values are obtained where observations are distant from the centroid.

Taking the first derivatives of equation 3.14 with respect to $u_{ik}$ and $v_i$ and setting those equations to zero yield necessary conditions for it to be minimised. Performing a Picard iteration through these two necessary conditions leads to an iterative scheme for minimizing the objective function [Bezdek, 1980, Dunn, 1973]. The resulting fuzzy segmentation can be converted to a hard or crisp segmentation by assigning each pixel solely to the region that has the highest membership value for that pixel.

A major disadvantage of FCM is that it does not incorporate information about spatial context, causing it to be sensitive to noise and other imaging artifacts. [Pham and Prince, 1999] presented an adaptive fuzzy c-means (AFCM) algorithm. Their objective function contained a multiplier field term that models the brightness variation. Recently, [Liew et al., 2000, Liew and Yan, 2003] proposed an approach taken for increasing the robustness of FCM by directly modifying the objective function for local spatial context and background intensity variation.

In fuzzy clustering, determining optimal number of clusters is a difficult problem. [Gath and Geva, 1989] showed a Fuzzy modification of the maximum likelihood algorithm (FMLE) for cluster validity. First, a fuzzy c-means clustering is performed, and then the optimal fuzzy partition was incorporated with FMLE. They implemented the
data in clustering Sleep EEG data and claimed that the algorithm performs extremely well in situations of large variability of cluster shapes, densities, and number of data points in each cluster.

In [Hall et al., 1992], a comparison of neural networks and fuzzy clustering was given. They segmented brain MR images using an artificial neural network (ANN), and compared the performance with FCM. FCM was shown to be superior on normal brains, but poor on abnormal brains with tumor, edema etc.

3.3 Region-Based Segmentation

Region-based segmentation attempts to segment an image by identifying homogeneous regions. It extracts an image region that is connected based on some predefined criteria [Pham et al., 2000]. These criteria can be based on intensity information or edges in the image. Beginning at a seed location in the image, adjacent pixels are checked against a predefined homogeneity criterion. The possible criterion might be to grow the region until an edge in the image is met. Pixels that meet the criterion are included in the region. Continuous application of this rule allows the region to grow, defining the volume of an object in the image by identification of similar, connected pixels [Withey and Koles, 2007]. Region growing is seldom used alone but usually within a set of image processing operations, particularly for the delineation of small, simple structures such as tumors and lesions [Dubey et al., 2010]. Its main limitations is that it requires manual interaction to obtain the seed point. Region growing can also be sensitive to noise.

In [Pohle and Toennies, 2001], an adaptive region growing algorithm is proposed that learns its homogeneity criterion automatically from characteristics of the region to be segmented.

3.4 Contour-Based Segmentation

Contour-based segmentation approach assumes that the different regions of the object can be segmented by detecting their boundaries. Accordingly, these methods rely on detecting edges in the image that cause them to be sensitive to various noise artifacts.

3.4.1 Deformable models

Deformable models are artificial, closed surfaces able to expand or contract over time, within an image, and conform to specific image features. These are also called active contour models and snakes model is one example [Kass et al., 1988]. They are much more
robust to noise comparing to edge detection method, and have become an important tool in the segmentation of biomedical images.

Medical images and volumes usually contain complex and irregular structures; hence, segmentation and representation of these shapes with local descriptors are difficult. Deformable models are model-based techniques for delineating region boundaries by using closed parametric curves or surfaces that deform under the influence of internal and external forces. To delineate an object boundary in an image, a closed curve or surface must first be placed near the desired boundary and then allowed to undergo an iterative relaxation process. Internal forces are computed from within the curve or surface to keep it smooth throughout the deformation. Deformable models are extensively used in the segmentation of medical images [Dubey et al., 2010]. They are routinely used in the reconstruction of the cerebral cortex from MRIs.

The main advantages of deformable models are their ability to directly generate closed parametric curves or surfaces from images and their incorporation of a smoothness constraint that provides robustness to noise and spurious edges. Standard deformable models can also exhibit poor convergence to concave boundaries. This difficulty can be alleviated somewhat through the use of pressure forces and other modified external force models. Another important extension of deformable models is the adaptively of model topology by using an implicit representation rather than an explicit parameterization.

3.5 Other Approaches

3.5.1 Independent component analysis

Independent component analysis (ICA) is originally a method for solving the blind source separation problem to find a linear coordinate system such that the resulting signals are as statistically independent from each other as possible [Hyvärinen et al., 2001]. More specifically, in classic approach, an image is represented by a linear weighted sum of features. When $x$ and $y$ are coordinates represent horizontal and vertical addresses of an image pixel, for each incoming image $I(x, y)$, the coefficients of each feature $A_i$ in an image are denoted by $s_i$. Algebraically, we can write:

$$I(x, y) = \sum_{i=1}^{n} A_i(x, y) s_i$$ (3.6)

or in matrix form:

$$I = AS$$ (3.7)
Matrix $A$ is chosen to make each element of $S$ as independent as possible. If we assume for simplicity that the number of features $n$ equals the number of pixels, the system can be inverted.

$$Y = WI$$

(3.8)

The goal is to let $W$ get close to the inverse of the ideal matrix $A$. The mixing matrix $W$ is interactively modified so that each element of $Y$ becomes as independent as possible. If the iteration converges, $Y$ is considered to be equivalent to $S$. [Nakai et al., 2004] and [Muraki et al., 2004] have made an attempt to apply ICA to enhance the image contrast of grey and white matter. They have used T1-, T2- and proton density-weighted MR images. However, it was not a complete procedure for tissue classification. When the number of multi-spectral images (IC) is smaller than the number of tissue types (signal sources), the effectiveness of using one particular IC to characterize signal source of interest is reduced.

### 3.5.2 Atlas based segmentation

In this approach, information on anatomy, shape, size, and features of different organs and soft tissues is compiled in the form of an atlas. The atlas-guided approach is used as a reference frame for segmenting new images. It first finds a one-to-one transformation that maps a pre-segmented atlas image to the target image that requires segmentation. Since the atlas is already segmented, all structural information is transferred to the target image. Atlas-guided approaches have been widely used in MRI brain imaging for segmentation of various structures, as well as for extracting the brain volume from head scans. However, finding accurate segmentations of complex structures is difficult because of anatomical variability [Dubey et al., 2010]. An expert knowledge is required in building such a database.

[Bourouis et al., 2008] presented a fully automatic deformable level-set-model method to segment WM, GM and CFS. An anatomical atlas is used as a prior probability. They use region information (atlas-based classification step) for global segmentation and boundary information (level-set based segmentation) for refinement of previous results.

### 3.5.3 Fuzzy connectedness

The fuzzy connectedness has been used to segment the image elements using the spatio-topological considerations of their connectedness. Fuzzy connectedness has been effectively used to segment out an object in a badly corrupted image [Udupa and Samarasekera, 1996]. It permits rapid, reliable, consistent, and highly reproducible
measurement of tumor volume from MRIs with limited operator interaction. The fuzzy connected image segmentation framework developed by [Udupa and Samarasekera, 1996] assigns classification which is used for the segmentation of the target object in the image. The affinity between the two given pixels in an image is defined as a combined weighted function of the degree of coordinate space adjacency and the degree of intensity gradient space adjacency to the corresponding target object features. The goal is to capture the specific intensity patterns attached to the object of interest. The only source of variation for non-edited volume is due to the selection of seed voxels for the fuzzy connected algorithm. Seeding can change the results only if one operator selects seed points that are outside the volume obtained by the second operator. Therefore, the two operators need not choose identical seed points; rather, only seed points that are in the same included volume need to be selected. Because of this condition, application of the algorithm results in very low coefficients of variation.

3.5.4 Rule-based methods

Automatic, rule-based guidance of unsupervised image segmentation has also been explored in an attempt to improve the results from unsupervised segmentation methods and yet maintain an automated approach to the segmentation task. [Clarke et al., 1998] proposed a system that segments tumors, focusing on glioblastoma-multiformes (grade iv gliomas). They used FCM for preprocessing. Then, a rule based (information from multi-spectral and local statistics analysis) expert system was used to first separate suspected tumor areas and then again refine the segmentation in the regions containing tumor. [Hata et al., 2000] presented a framework with fuzzy inference for segmenting different tissues in the brain. In their method anatomical locations, segmentation boundaries as well as intensities are represented by fuzzy if-then rules.

3.6 Drawbacks of Current Methods

This section first briefly reviews the advantages and disadvantages of major types of approach discussed above. These can be summarized under three main categories: supervised methods that are dependent on human intervention, unsupervised methods that generally are independent on human intervention, and fuzzy methods (which might also be unsupervised) that model the uncertainty using fuzzy theory.

- Supervised methods: Supervised techniques for segmentation suffer from the drawback of manual intervention for providing a priori information. For instance, statistical approaches assume a particular intensity distribution function of the pixels which may not always accurately fit the actual image intensity distribution.
On the other hand, the methods that focus on learning a model, as in neural networks, will be effective at particular task exactly, showing good results at tasks where the different tissue classes may be very similar. However, the major disadvantage of this type of approach is that methods normally require patient-specific training. That is, the training pixels have to be from the volume to be segmented as opposed to from other volumes. When inter-patient training methods are applied, they will require large training sets.

- **Unsupervised Methods**: Unsupervised approaches are generally fast and do not require a priori information. These approaches offer the advantage that they do not rely on training data, and therefore are not subject to the degree of variation due to training bias. A disadvantage of these methods is that significant re-engineering may be required in order to apply these methods to new tasks or to use in different imaging modalities than those the system was designed for.

- **Fuzzy methods**: Fuzzy techniques allow a new perspective to model uncertainties due to the uncertainty of grey-values present in the images. The most widely used techniques in this class are the fuzzy rule based and fuzzy clustering based segmentation. The problem with fuzzy rule based image segmentation techniques is that they are application dependent with the structure of the membership functions being predefined and in certain cases, the corresponding parameters being manually determined [Karmakar et al., 2000]. Fuzzy c-means is an unsupervised technique that has been successfully applied to various tasks including medical imaging. The main disadvantage of FCM is its over-sensitivity to noise, which is also a flaw of many other intensity based segmentation methods. Also, original FCM algorithm does not consider spatial information. The number of clusters also has to be fixed initially in FCM based segmentation methods.

In designing a new system to perform automatic brain tissue segmentation in MRI images, the existing work gives a valuable source of insight into the task. It is clear that in each technique, there are a variety of different properties that can be exploited. However, since the goal of our work is to automate a task performed by medical professionals, the methods used by those experts also provide some insight into the problem. This includes knowledge of the expected appearance, location, patient-specific bilateral symmetry, and variability of normal anatomy [Schmidt, 2005]. There has been an attempt to incorporate this information into systems for automatic brain segmentation [Pham et al., 2010]. It is clear that improved results could be achieved if a system could consider a variety of sources of evidence simultaneously during segmentation.
3.7 Attempts Taken Hitherto for Overcoming These Drawbacks

As explained in the previous chapter, various artifacts in MRI images make segmentation challenging. Therefore, segmentation methods generally model these artifacts. Most frequently used technique is to model the INU as a multiplicative field.

3.7.1 MRI model

The most common model of MR image formation assumes that the noise, approximated by Gaussian probability distribution, arises from the scanner and is therefore independent of the intensity inhomogeneity field. According to this model, the acquired image $s(x)$ is obtained as:

$$s(x) = o(x)b(x) + n(x) \quad (3.9)$$

where $o(x)$ is the true signal emitted by the tissue, $b(x)$ is the intensity of inhomogeneity (or bias field), and $n(x)$ is additive noise. In this model, normally, noise is assumed to be Gaussian, which is methodologically convenient.

In another model of MR image formation, only biological noise is considered, which is scaled by the intensity inhomogeneity field so that the SNR is preserved. On the condition that the same symbol definitions as above, the MR image is expressed as:

$$s(x) = (o(x) + n(x))b(x) \quad (3.10)$$

The third MR image formation model is based on log-transformed intensities, by which the multiplicative inhomogeneity field becomes additive.

$$\log s(x) = \log o(x) + \log b(x) + n(x) \quad (3.11)$$

This model is formulated with the premise of the log-transformed noise is still assumed to be Gaussian, which is inconsistent with the first model that assumes the noise is Gaussian in the original non-logarithmic domain [Li and Zhijun, 2010].

3.7.2 Spatial information

One of the important characteristics of an image is that its neighbouring pixels are highly correlated to each other. The probability that a pixel neighbourhood will belong to the same cluster is very high. This property of the pixels is quite helpful when the image is affected by noise. However, as mentioned earlier, one disadvantage of standard FCM is not considering any spatial information in image context, which makes it very
sensitive to noise and other imaging artifacts.

### 3.7.3 Intensity inhomogeneity correction

There are two common approaches in segmenting images with intensity inhomogeneities [Pham and Prince, 1999]. One is to apply a correction algorithm separately, followed by a segmentation algorithm. Once the image has been corrected, the intensity inhomogeneities can be ignored in any subsequent processing. In [Johnston et al., 1996] a homomorphic filter was applied for removing the multiplicative effect of the inhomogeneity.

The second approach used to correct intensity inhomogeneities is to simultaneously compensate for the shading effect while segmenting the image [Pham and Prince, 1999, Sharma and Aggarwal, 2010, Liew and Yan, 2003]. This approach has the advantage of being able to use intermediate information from the segmentation while performing the correction. There are a number of researches [Pappas, 1992, Rajapakse and Kruggel, 1998], based on Markov random fields and its Gibbs’ equivalence in image segmentation algorithm that account for inhomogeneities by allowing the centroids of each class to vary independently. [Wells III et al., 1996] used an expectation-maximization (EM) algorithm that modeled the inhomogeneities as a bias field in the segmentation logarithm. However, their proposed method is supervised, requiring manual interaction to provide training data [Pham and Prince, 1999]. Recently, [Liew and Yan, 2003] have proposed a novel FCM-based adaptive segmentation method with a 3D multiplicative bias field which makes clusters spatially varying. To improve computation efficiency, the 3D log bias field is created as the estimate of a stack of 2D smoothing spline surfaces, with continuity enforced across slices [Liew and Yan, 2005]. In this method, local influence of neighbouring spatial information is considered in an adaptive manner by using a dissimilarity index. More details of this technique have been discussed in the next subsection.

### 3.7.4 Other existing extensions to FCM

The most direct way to compensate for the drawback of FCM is to smooth the image before segmentation. However, standard smoothing filters lead to a loss of important image details. Various extensions of the FCM algorithm with attempt to accommodate noise have been presented by many researchers. Toliyas and Panas post-processed the membership function to smooth the noise effect. The most popular approach for increasing the robustness of FCM to noise is to modify the objective function directly. Krishnapuram and Keller [Bezdek et al., 1999] proposed a method called possibilistic C-means (PCM), which interprets clustering as a possibilistic partition. Instead of having
one term in the objective function, a second term is included, forcing the membership to be as high as possible without a maximum limit constraint of one. However, it caused clustering being stuck in one or two clusters. [Ahmed et al., 2002] modified the objective function of the standard FCM by introducing a term that allowed the labelling of a pixel to be influenced by the labels in its immediate neighbourhood.

[Tolias and Panas, 1998] presented an approach taken for improving the results of FCM by imposing spatial constraints through a rule-based system. The number of pixels that belong to the cluster with high membership, low membership, and the maximum relative connectivity of the pixel with respect to its neighbourhood were calculated in the eight-connected neighbourhood. The set of rules suggests that the membership of the pixel examined is modified by a positive (negative) quantity that is analogous to the pixels that have high (low) membership to the cluster and belong to the same neighbourhood.

[Liew et al., 2000] proposed a spatial Fuzzy c-means Clustering (SFCM) algorithm. Their key point was the introduction of an adaptive dissimilarity index that takes into account the influence of the neighbouring pixels on the centre pixel in a 3x3 window. The algorithm is capable of suppressing the influence of the neighbouring pixels in non-homogeneous regions in the image. Since this method became an inspiration to one of our segmentation method, we also adapted this technique for incorporating neighbourhood spatial information, we discuss more details of this method below.

Fuzzy image clustering method incorporating spatial continuity

The key idea of this method is to consider the influence of neighbouring voxels on the centre voxel of interest during classification in an adaptive manner. Here we discuss this technique briefly. More details can be found in the original paper [Liew et al., 2000]. When \( \text{dist}(a, b) = \sqrt{||a - b||^2} \) denote the \( L_2 \) distance between vectors \( a \) and \( b \), for every pixel \( s(x) \) in the 3D MR image, \( L_2 \) distances are defined as follows.

\[
\partial_{xy} = \text{dist}(s(x), s(y)), \; s(y) \in N_x \tag{3.12}
\]

\[
d_{kx} = \text{dist}(s(x), v_k) \tag{3.13}
\]

where \( N_x \) is the neighbourhood of \( s(x) \), and \( v_k \) is the centroid of the \( k \)th cluster. While \( \partial_{xy} \) measures the dissimilarity of the pixel \( s(x) \) and its neighbour \( s(y) \), \( d_{kx} \) measures the affinity of the centre pixel \( s(x) \) to the cluster prototype \( v_k \). Their dissimilarity index \( D_{kx} \)
that measures the dissimilarity between $s(x)$ and $k$th cluster centroid $v_k$ is as follows.

$$D_{kx} = \frac{1}{|N_x|} \sum_{y \in N_x} \left[ d_{kx}^2 \lambda_{xy} + d_{ky}^2 (1 - \lambda_{xy}) \right]$$

(3.14)

where $|N_x|$ is the cardinality of the neighbourhood configuration, and $\lambda(\partial_{xy}) = \lambda_{xy}$, that ranges between zero and one, is the weighting factor controlling the degree of influence of the neighbouring voxels $s(y) \in N_x$. The weighting factor given in their work is a sigmoid function as follows.

$$\lambda(\partial) = \frac{1}{1 + e^{-(\partial - \mu)/\sigma}}$$

(3.15)

where the parameters $\mu$ and $\sigma$ specify the displacement of $\lambda$ from zero, and the steepness of $\lambda$, respectively. When $\partial \ll \mu$, the cluster affinity of the centre pixel is almost completely determined by the cluster affinity of its neighboring pixel. On the other hand, if $\partial \gg \mu$, the dissimilarity between $s(x)$ and $s(y)$ is significant such that the centre pixel is unlikely to belong to the same homogenous region as that of the neighboring pixels. Therefore, depending on the window is in a nonhomogeneous region or not, the influence of the neighboring pixels on the centre pixel is either suppressed or enhanced.

Even though there are many other extensions to FCM algorithm, they still have major drawbacks like inefficiency, inaccuracy, and sensitivity to extreme noise.

### 3.8 Chapter Summary

This chapter has introduced several popular approaches for the segmentation of brain images, and has discussed several efforts to employ these methodologies into MR brain tissue segmentation. It has also provided a comparison of the advantages and disadvantages of several major work. These drawbacks include inefficiency, inaccuracy, the lack of a prior, and not using robust estimators in tissue class initialisation. Based on the existing literature, several general conclusions can be drawn with respect to the elements of a segmentation system that can be used to improve performance:

- Soft segmentation retains more information about the original image by allowing the pixel to have varying degree of membership in multiple regions.

- Fuzzy clustering is an excellent method for soft segmentation and is a widely used unsupervised algorithm for the segmentation of MR images.

- Unsupervised clustering methods need better ways to specify and adjust the number of clusters, in case it is not known a priori.
• Information about shape, size, symmetry, and normal anatomic variability can be used to improve the segmentation results.

It is important to note that it is often the combination of different types of features that allows a more effective segmentation framework. In our opinion, FCM with spatial information or prior knowledge can yield better results. In this thesis, we have devised and presented a system which is predominantly based on FCM that integrates symmetry and spatial information that makes the segmentation algorithm more robust.
Chapter 4

Inspiration and Research Scope

4.1 Preview

The previous chapter has discussed a variety of approaches proposed in the literature for the task of MR brain image segmentation. Based on this previous work, it has further discussed some important points that a system should have in segmenting brain images. This leads naturally into the motivation for developing our approach, which not only incorporates several of the ideas presented in the previous work, but further explores the utility of spatial and anatomical geometry information in order to take advantage of the types of information used by human experts to perform this task.

Section 4.2 first introduces brain symmetry and its clinical implications which is the inspiration for the main methodology in this work. This is followed by the objectives and scope of the thesis.

4.2 Inspiration

The main inspiration for our work comes from the fact that the brain is roughly symmetrical (see Figure 4.1).

4.2.1 Brain symmetry analysis

Watkins et al. [Watkins et al., 2001] presented a voxel-based statistical analysis of human brain MR images. They have used 142 normal brain scans, and each of these and their mirror images are linearly transformed using a symmetrical template. Their results showed the approximate symmetry in the brain and asymmetry in certain areas. The study in [Gefen et al., 2004] has investigated the effectiveness of the symmetry feature
when applied to 3D reconstruction of mouse brain sections. The line of symmetry of each section is estimated and aligned vertically at the centre of its image support. By doing this, they have successfully created a 3D volume representation of the brain. Thirion et al. [Thirion et al., 2000] have done an extensive study of human brain’s symmetry and asymmetry analysis. By using 3D vector field operators, and the computation of 3D significance maps, the authors have evaluated normal and abnormal asymmetry of human brain. They have also determined the regions with a deficiency of symmetry which are measured and compared among several populations. In [Volkau et al., 2006b], Volkau et al. have attempted to quantify “approximate symmetry” and to classify the human brain as normal or abnormal. Their study includes 101 patients. The MSP is calculated and then J-Divergence is used to measure and analyse bilateral symmetry of both parts of the head. The results of their statistical analysis suggest the approximate symmetry of normal brains.

4.2.2 Brain symmetry and its clinical implications

Radiologists routinely use symmetry as one of the most discriminating features, in conjunction with other characters such as location, neighbourhood relationship, and shape, to assess abnormalities in brain images. It is a well-known fact that bilateral or mirror symmetry is spontaneously perceived when the axis of such symmetry is vertical [Tyler, 1996]. By looking at a medical image, a clinician identifies the symmetry axis/plane and then compares the abnormality with the healthy side of the brain [Liu, 2009]. Although the degree of asymmetry has long been thought to be helpful for
providing a diagnostic cue for clinicians [Khotanlou et al., 2009], most neuroimage analysis methods rarely incorporate the knowledge about brain symmetry to their advantage. Encoding symmetry information about the brain can be complicated by the normal variance of anatomical asymmetries. Moreover, defining symmetry itself is difficult. In order to quantify asymmetry in brain images accurately, the symmetry axis, or the symmetry plane (in 3D images), needs to be detected. Then, the amount of deviation from this symmetry can be computed. With the integration of this information into neuroimage analysis algorithms as prior knowledge, more accurate quantification would become possible that will facilitate routine clinical diagnosis.

4.2.3 Brain symmetry analysis methods

Although brain symmetry information is not yet applied in explicit brain tissue segmentation task, a number of researchers have exploited the symmetry feature in diagnostic systems. Symmetry can be helpful for diagnosis in many cases, such as Alzheimer’s Disease, tumor and schizophrenia. For example, asymmetry between left and right hippocampal volumes have been found in patients with schizophrenia [Barrick et al., 2005] and AD [Csernansky et al., 2000]. When there is an abnormality, deviation from symmetry can be observed clearly (see Figure 4.2).

Figure 4.2: Abnormality of the brain can be easily detected by comparing to the other hemisphere.

In [Clarke et al., 1998], Clark et al. presented a system with four stages that segments tumors, focusing on glioblastoma-multiformes (grade iv gliomas). The idea they have used is that each tissue has approximately the same number of pixels in each brain hemisphere while tumors often have poor symmetry. After using fuzzy c-means clustering
for pre-processing, information from multi-spectral and local statistics analysis is used in a rule based expert system which is used to first separate suspected tumor areas and then again refines the segmentation in the regions containing tumor. Khotanlou et al. [Khotanlou et al., 2009] proposed a method for segmenting brain tumors in 3D MRI. It computes the symmetry plane of the brain. By comparing the grey level characteristics of each tissue type, tumors are detected by its asymmetry with respect to the obtained plane. They have incorporated deformable models constrained by spatial relations to refine the results. Their results have shown that symmetry analysis improves the segmentation quality. In [Somasundaram and Kalaiselvi, 2010], the authors have assumed that for normal slices, CSF is symmetrical about the vertical central line. Therefore, by measuring the vertical symmetry, the presence of abnormal tissues is detected. Brain tissues of MR T2-weighted axial images are segmented using fuzzy c-means algorithm and abnormality is checked by measuring symmetry. In [Feng et al., 2008], Feng et al. described an edge detection based technique for locating brain tumors using the information of brain symmetry. A bilateral symmetry axis is defined and using an edge map, symmetrical regions are weakened and the edges that are not symmetrical are enhanced so that the unsymmetrical regions which might have been caused by a brain tumor could be detected. In [Ray et al., 2007], Ray et al. presented another region-based technique that can be used for tumor or abnormality detection, by exploiting the idea of brain’s symmetry and its disturbance in the presence of some abnormality. Sun et al. [Sun et al., 2009a] described a symmetry feature based method for detecting brain injuries from 2D MRI. Having first obtained the symmetry axis of the brain using a method based on global symmetry constellations of features [Loy and Eklundh, 2006], they then constructed a symmetry affinity matrix. Kurtosis and skewness are then computed from the symmetry affinity matrix and used for extracting asymmetric regions. They claimed that with symmetry information used in all steps of their procedure, most brain injuries were successfully extracted with a low error rate of around 10%. Another paper from the same authors [Sun et al., 2009b] proposed a region growing technique by integrating brain symmetry information for brain injury detection in 2D MR images. In [Maes et al., 1999], Maes et al. presented a procedure for the quantification of the left and right cerebral WM and GM volumes from MRI images. First, by using an atlas based method, WM and GM are segmented. Volumes for GM and WM for each hemisphere are computed by integrating the corresponding probability maps within the brain regions of interest defined by the matched template image. The method has been tested on schizophrenia data. They have obtained an excellent overlap of 95% between their segmentation and expert’s delineations.

Most of the above mentioned methods however compute the approximate brain
symmetry. The use of symmetry information for accurate tissue segmentation is complicated by the problem of identifying the precise location of the symmetry plane and the fact that the normal hemispheres of brains without pathology will also be asymmetric to some extent. It follows that an efficient algorithm for imposing a given symmetry is needed.

4.3 Research Objectives

As detailed in the previous chapter, despite the considerable amount of various approaches proposed for automatic brain tissue segmentation in MR images, these methods are still poor in accuracy and efficiency. Although the recent methods that encode spatial information do show some improvement, their ability to address the most challenging cases remains hindered [Sharma and Aggarwal, 2010]. This is due to the fact that it is not obvious how to optimally and simultaneously incorporate diverse forms of prior knowledge like bilateral symmetry or similarity to a normal brain into a system for tissue segmentation, even though it is obvious that these forms of prior knowledge are important. As discussed in the previous sections, although symmetry information from the image context can be a vital cue in brain tissue segmentation, locating symmetry plane and imposing this symmetry into the segmentation algorithm are challenging. The aim of this thesis is to look into these issues, and develop a symmetry based framework for brain tissue segmentation.

4.3.1 Scope of the work

From the conclusions drawn from the previous chapter, the primary segmentation algorithm chosen in this work is fuzzy c-means. The final goal is to enhance the performance of this algorithm by integrating the symmetry information. This can be done by exploiting left-right symmetry of the brain structure. However, in order to achieve this, the problem of identifying the precise location of brain symmetry plane needs to be investigated. The first part of the thesis addresses this issue by developing robust algorithms for brain symmetry plane detection. The integration of this symmetry information into the segmentation algorithm is tackled in the latter part of the thesis. A thorough validation of the method is done using a variety of images.

The system is further improved by using spatial neighbourhood information which plays a vital role in image segmentation. The main concept for the incorporation of this spatial information has come from the work of [Liew and Yan, 2003, Liew et al., 2000]. They have proposed a FCM based algorithm which incorporates the local spatial continuity using a dissimilarity index. Their results are superior to the conventional
FCM algorithm. However, their method can further be improved with symmetrical information taken from the image context.

The proposal of this thesis is a fully automatic framework for brain tissue segmentation in MR images that combines the strengths of some of the existing techniques with some new ideas, so that the resulting system is more robust than its individual components.

4.3.2 Overview of the MR brain image segmentation framework

This section presents the overview of the automatic MR brain image segmentation framework, which has been designed to explore and take advantage of the concepts described previously. This system performs automatic brain tissue volume segmentation in MR images in a fuzzy c-means clustering framework that incorporates symmetry information from the image context and unsupervised segmentation based on intensity and spatial information. The motivation behind this is that the clustering of pixels as being GM, WM or CSF is not based solely on intensity and spatial priors, but will additionally and simultaneously consider bilateral symmetry information. An overview of the framework is shown as a simplified flowchart in Figure 4.3.

4.3.3 Implementation

Based on the above concepts and conclusions, the main steps for implementing the framework can be outlined as follows:

- Input Image: 3D MR brain scans have predominantly been considered in this work, although any particular method can be applied into 2D images as well. Real brain images with ground truth are taken from publicly available IBSR database (http://www.cma.mgh.harvard.edu/ibsr/). Simulated brain images have been used for measuring the robustness of the algorithm to various noise levels and modalities. These phantom images are generated from the website of BrainWeb (http://www.bic.mni.mcgill.ca/brainweb). As an example, the axial T1-weighted MR brain image with 1mm section thickness can be generated using the imaging simulator. More details are given in the relevant chapters.

- Brain Symmetry Plane Detection: In order to use symmetry information, the location of the brain symmetry plane needs to be identified. Chapter 6 - Chapter 8 discusses proposed methods in detail.

- Removal of Extra-cranial Tissues (Background, muscles, meninges etc.) and Data Pre-processing:
Since the main goal is to label the entire brain into three regions (WM, GM and CSF), removal of extra-cranial tissues is an important pre-processing step. Figure 4.4 illustrates the various tissue types in a head scan. Since we are not interested in skull and outer skin etc., we have to remove those prior to the
segmentation. While thresholding is the most common method used for that purpose, a mathematical morphology related method and a deformable model based method are described in [Kapur et al., 1996] and [Smith, 2002], respectively. In this work, the method described in [Smith, 2002] has been used for its accuracy and applicability into our work.

- Initial Estimates: As mentioned earlier, in FCM, determining number of clusters is difficult. However, in this work we assume that the number of tissue types to be segmented is three, as we remove the outer region of the brain. If the cluster centroids can be initialised with optimal values, the speed of convergence can be improved. [Pham and Prince, 1999] has explained an automatic method that uses a Gaussian kernel function. This method finds the modes of a critically smoothed kernel estimator of the image histogram. However, in this work, cluster centroids are randomly initialised.

- Segmentation Stage:

  1. As explained previously, fuzzy c-means algorithm is the core of our segmentation algorithm. The main reason for choosing this technique is that fuzzy clustering methods perform soft segmentation in lesser execution time [Bezdek et al., 1993]. It can be combined with other methods to give better segmentation results. For instance, the main inspiration for spatial neighbourhood information integration is taken from the work of [Liew and Yan, 2003]. Major novel contribution to the segmentation algorithm itself is the process involved in incorporating bilateral symmetry information into the FCM objective function.

  2. Post-processing step is done so that the soft segmentation can be converted to hard segmentation by using the maximum membership classification rule.

The proposed algorithms have been implemented, and visualised in Matlab, since it is a great and fast way to test new ideas and produce demonstrations. In addition to this, the code received from [Liew and Yan, 2003] written in C, has been utilised in comparative experiments.

Synthetic images have been used to conduct an objective assessment on accuracy, robustness and reproducibility of the techniques. Proposed algorithms have been tested on both real and simulated 3D MR images obtained from IBSR (http://www.cma.mgh.harvard.edu/ibsr/) and the BrainWeb Simulated Brain Database at the McConnell Brain Imaging Centre of the Montreal Neurological Institute (MNI), McGill University (http://www.bic.mni.mcgill.ca/brainweb). Simulated brain data of varying noise
Figure 4.4: Brain tissue substances. Extra-cranial tissues consist of skull, fat, and meninges.

have been used to perform quantitative assessment of the proposed algorithm since ground truths are known for these data.

4.4 Chapter Summary

This chapter has outlined the inspiration for the work, and the proposed framework for automatic segmentation of brain MR images. Major conclusions drawn from the previous chapter has led into the main reason for choosing the core technique, which is fuzzy c-means clustering, and the necessity to incorporate prior knowledge from the brain anatomy. Moreover, inspiration for using brain symmetry information as prior knowledge has been discussed by pointing out its advantages. Finally, the overall symmetry based framework has been introduced, and put together by explaining each section briefly.
Part I

Symmetry Plane Detection
Chapter 5

Symmetry Plane Detection

5.1 Preview

Initial chapters of this thesis have dealt with the details of the brain tissue segmentation task, existing approaches, and the motivation for developing a new automatic method. Previous chapter discussed the inspiration for using brain symmetry as a prior knowledge and introduced the symmetry based segmentation framework which consists of two main parts. The first part begins with the current chapter, starting with a brief introduction of symmetry feature. This is followed by Section 5.3 where a definition to brain symmetry plane and various symmetry measures in the literature are discussed. Finally, Section 5.4 reviews existing brain symmetry plane detection methods.

5.2 Symmetry

Symmetry is fascinating to the human mind, and everyone likes objects or patterns that are in some way symmetrical [Feynman, 2006]. A certain kind of symmetry can be seen in most natural and artificial objects around us. Symmetry provides us with cues to understand our environment. A general definition of symmetry most often attributed to Hermann Weyl [Weyl, 1952], a mathematical physicist is “An object is symmetrical if one can subject it to a certain operation and it appears exactly the same after the operation. The object is then said to be invariant with respect to the given operation.” [Cantwell, 2002].

Symmetry is well known as a powerful mechanism that facilitates identifying the structure of an object. Attneave [Attneave, 1955] pointed out that symmetry is a basic feature of shapes and objects that enhances recognition and reconstruction of shapes and objects. If a group of objects exhibit symmetry, it is more likely that they are related
in some degree. Many researchers have done work on the detection of symmetries in images and shapes. Our focus is in the area of symmetry axis/plane detection and computation of the degree of symmetry so that the knowledge of symmetry could be used as a priori to enhance neuroimage analysis.

Several types of symmetries such as reflection, rotation, and translation are considered in the literature and used in different areas. What we consider here is the brain’s bilateral symmetry or mirror symmetry. An image is bilaterally symmetrical when it is unchanged following a reflection about the axis of symmetry. That means that one half of the image is a mirror image of the other half. Therefore, an image \( I \) is said to have a bilateral symmetry if there exists a plane such that \( \Pi(I) = I \). Here, \( \Pi \) denotes the reflection of an image with respect to a plane. Mirror symmetry has a special status in human perception in comparison with other types of symmetry like translational or rotational symmetry [Tyler, 1996].

Symmetry of an object is usually expressed in a qualitative way referring to an object as either symmetrical or not. However, it is quite unlikely that real images have perfect symmetry. A normal human brain is largely symmetrical, although it exhibits some degree of asymmetry too: The right frontal lobe is larger than the left one, and the left occipital lobe is larger than the right one [Hugdahl, 2005]. However, two hemispheres have approximately identical anatomical properties. Therefore, the degree of symmetry needs to be defined in order to measure the similarity between the image and its reflection.

5.3 Symmetry Plane Detection

5.3.1 Brain symmetry plane

A normal human head exhibits a rough bilateral symmetry. Brain is separated into the left and right hemispheres by the inter-hemispheric fissure (IF) or the longitudinal fissure, which is a long and deep furrow (see Figure 5.1 and Figure 5.2). Located in this fissure is the falx cerebri which is a membrane or meninges. The cerebrum consists of grey matter or neuron cell bodies and white matter or myelinated axons. The largest and densest bundle of white matter fibres within the cerebrum is the corpus callosum which connects the right and left cerebral hemispheres. Anterior commissure and posterior commissure are two other important bundles of white matter fibres that cross the midline. The plane that passes vertically through this midline is considered to be the mid-sagittal plane (MSP). It is also defined as the plane that best separates two brain hemispheres, although the real separation surface between the hemispheres is not perfectly planar. The symmetry plane of the brain is often considered as a first-order
approximation to the MSP [Kruggel and Yves von Cramon, 1999].

5.3.2 Symmetry measures

Various measures that quantify the degree of similarity between an original object and its reflection have been proposed in the literature. Most of them are intensity based measures. The choice of a measure that is appropriate to each problem is based on its properties. If a 3D object possesses an exact plane of symmetry, the symmetry plane passes through the object’s centre of mass and is orthogonal to one of its ellipsoid axes [Colliot et al., 2002]. The brain is approximately symmetrical with respect to the mid-sagittal plane which approximately corresponds to the brain symmetry plane. The measures discussed in this section have provided symmetry detection methods with quantitative information for assessing the degree of symmetry. In general, all possible orientations and translations of the symmetry plane are considered when computing these measures. Since the brain is not perfectly symmetrical or anatomically homogeneous, it is usually difficult to assess the quality of a measure within and
Figure 5.2: Human brain coronal view. Adapted from [Kelley and Petersen, 2007] with the permission from the publisher.

Figure 5.3: IF separates the two brain hemispheres. MSP is considered to be the brain symmetry plane.

especially between different studies.
Correlation Coefficient

Cross-correlation (CC) is one of the most commonly used techniques in brain symmetry detection algorithms [Ardekani et al., 1997, Thirion et al., 2000, Prima et al., 2001, Liu et al., 2001, Tuzikov et al., 2003]. The correlation coefficient \( cc \) estimates the degree of statistical dependence between two distributions. \( cc \) between two images \( P \) and \( Q \) can be calculated as

\[
cc = \frac{\sum_i (P_i - \overline{P})(Q_i - \overline{Q})}{\sqrt{\sum_i (P_i - \overline{P})^2} \sqrt{\sum_i (Q_i - \overline{Q})^2}}
\]  

(5.1)

where \( P_i \) and \( Q_i \) are the intensity values in the \( i \)th pixel and \( \overline{P} \) and \( \overline{Q} \) are the respective means of the entire image. However, when the entire image is considered, the value of \( cc \) can be affected by the empty space around the brain. In [Junck et al., 1990], the cross product \( \sum_i P_i Q_i \) is used instead as it was observed to be less sensitive to empty space.

Root Mean Square Error (RMSE)

RMSE, which is frequently used, measures the difference between two sets of values \( I \) and \( I' \). It is defined as

\[
RMSE = \sqrt{\frac{1}{n} \sum_i (I_i - I'_i)^2}
\]  

(5.2)

However, RMSE is sensitive to outliers. Due to squaring of terms, large values weight more heavily than smaller ones. Normalization of \( I \) and \( I' \) prior to calculation can reduce the effect of scaling in \( RMSE \).

Stochastic Sign Change (SSC)

The SSC criterion was first described as a similarity measure by Venot et al. [Venot et al., 1986]. It is used to co-register two images. If the two images are co-registered well, the maximum random fluctuation of pixel values and zero-crossing points (sign change) are observed when the two images are subtracted. If the two images have dissimilar parts, instead of random fluctuations, those parts will exhibit groupings of all positive or negative values. When used as a symmetry measure, SSC is the total of all the sign changes in the image created by subtracting the original image from the reflected image.

Minoshima et al. [Minoshima et al., 1992] have used SSC criterion as the symmetry measure and pointed out that it is robust for registration of the images. They have modified the measure by adding a periodic pattern, so that the small differences between left and right hemisphere do not cause greatly decreased sign changes in the subtraction image.
Kurtosis

Kurtosis is also known as the normalized fourth central moment, and is used as a measure of non-Gaussianity. Kurtosis can be positive or negative. Super-Gaussian distributions typically have “spiky” or sharper peaks compared with a Gaussian one. Distributions with a negative kurtosis are called sub-Gaussian, which are flatter than a Gaussian [Hyvärinen et al., 2001]. The presence of anomalies in an image makes the distribution appear to be super-Gaussian. For a given random variable $x$, kurtosis is defined as

$$Kurtosis = \frac{\frac{1}{n} \sum_{i=1}^{n} (x_i - \bar{x})^4}{\left(\frac{1}{n} \sum_{i=1}^{n} (x_i - \bar{x})^2\right)^2}$$  \hspace{1cm} (5.3)

where $\bar{x}$ is the mean.

Sun et al. [Sun et al., 2009a] have used kurtosis of the symmetry affinity matrix to detect asymmetric regions. The idea is based on the observation that the asymmetric regions which appear brighter in the symmetry affinity matrix can be regarded as anomalies compared with the background, where symmetry affinity values of pixels are very low and smoothly distributed. However, kurtosis can be very sensitive to outliers.

Kullback-Leibler (KL) Divergence Measure

Kullback-Leibler (KL) divergence measure [Kullback and Leibler, 1951] is a non-symmetric measure of the difference between two probability distributions $P$ and $Q$. When $p_i$ and $q_i$ are the probabilities of having the $i$th state from $P$ and $Q$, respectively, then the KL divergence measure is defined as

$$D_{KL}(p||q) = \sum_i p_i \log(p_i) - \sum_i p_i \log(q_i)$$

$$= \sum_i p_i \log(p_i/q_i)$$  \hspace{1cm} (5.4)

Volkau et al. [Volkau et al., 2006a] proposed a method using the KL divergence measure for MSP detection. Probability distributions of intensities of two sagittal slices are taken as $P = \{p_i\}$ and $Q = \{q_i\}$. The authors assumed the MSP to be the plane with the maximum amount of cerebrospinal fluid amongst all sagittal slices. KL divergence measure is used as a relative measure for comparing sagittal slices with a reference slice. The sagittal slice which gives the maximum KL divergence measure is considered to be the MSP.
Jeffrey’s Divergence Measure

This technique [Volkau et al., 2006b] is based on the KL divergence measure. It measures the similarity between the intensity distributions of the left and right parts of a brain. Unlike the asymmetric KL divergence measure, the Jeffrey’s divergence measure is symmetric. It is defined as

$$J(p, q) = \sum_i p_i \log(p_i/q_i) + \sum_i q_i \log(q_i/p_i)$$  \hspace{1cm} (5.5)

$$p_i = \frac{\text{Number of voxels of intensity } i \text{ in the left part}}{\text{Total number of voxels in the left part}}$$

$$q_i = \frac{\text{Number of voxels of intensity } i \text{ in the right part}}{\text{Total number of voxels in the right part}}$$

Bhattacharyya Distance/Coefficient

Bhattacharyya distance measures the similarity of two probability distributions. For two continuous probability distributions $P$ and $Q$, Bhattacharyya coefficient $B(P, Q)$ and Bhattacharyya distance $B_D$ can be defined as follows

$$B(p, q) = \int \sqrt{p(x)q(x)} \, dx$$

$$B_D = 1 - \int \sqrt{p(x)q(x)} \, dx$$  \hspace{1cm} (5.6)

The Bhattacharyya coefficient will be in the range of 0 and 1. It will be 0 if there is no overlap in the distributions. Therefore, the distance between two fully separated distributions cannot be assessed by this measure alone.

In [Ray et al., 2007], the authors have used Bhattacharyya coefficient as a measure of symmetry for locating brain tumors.

Fuzzy Symmetry Measure

When $\mu_A$ is the membership function of $A$, the reflection of a fuzzy set $A$ is a fuzzy set $e_\Pi(A)$ defined as

$$\mu_{e_\Pi(A)}(e_\Pi(x)) = \mu_A(x) \text{ for every } x \in S.$$  \hspace{1cm} (5.7)

Colliot et al. [Colliot et al., 2002] have characterized approximate symmetries of fuzzy 3D objects. They have discussed several measures proposed in the literature of
fuzzy sets. One of the measures discussed is using t-norms and t-conorms.

\[
\sigma = \frac{\sum_{x \in S} \min(\mu_A(x), \mu_{\Pi}(x))}{\sum_{x \in S} \max(\mu_A(x), \mu_{\Pi}(x))}
\]  

(5.8)

5.4 MSP Detection Methods

Both in medical and non-medical image analysis, there are numerous situations where the detection of symmetry axis/plane becomes necessary. One of the first studies of symmetry was done by Atallah [Atallah, 1985]. He presented an algorithm for finding all the axes of symmetry of planar shapes made up of points, segments, and circles. The idea was to reduce the problem to a combinatorial question on words. An axis is rotated about the centroid and specific positions passed by the axis are represented by some symbols or codes. All occurrences are said to be found when a palindrome (a string that is same as its reverse) is made. In the case that a segment passes through the centroid and leaves the shape invariant to reflection about it, the segment is considered to be a symmetrical axis. A good review on computational symmetry can be found in [Liu et al., 2009]. In [Park et al., 2008], Park et al. presented an evaluation of three symmetry detection algorithms that are publicly available. Using 176 test images comprised of both synthetic and real images, they manually labeled ground truths as visually obvious dominant symmetries. Their conclusion is that since there is a high false positive rate in these state-of-the-art algorithms, the field is in desperate need of a good symmetry detector. However, they have not considered brain symmetry axis detection methods.

Since the brain does not possess exact symmetry, a symmetry criterion for brain often measures the degree of symmetry. A plane that maximises a symmetry criterion is called a symmetry plane. This plane is often considered as a first-order approximation to the mid-sagittal plane [Kruggel and Yves von Cramon, 1999]. In brain image analysis, the symmetry plane detection problem becomes harder because of the natural complexity and asymmetries in brain images [Smith and Jenkinson, 1999]. Furthermore, depending on the imaging modality there can be various artifacts. As explained in Chapter 2, in MRI, artifacts like intensity non-uniformity [Liew and Yan, 2006] give rise to smooth intensity variation across the image. Although it does not significantly affect visual diagnosis, it can have a major impact on automatic analysis methods due to intensity overlaps between different tissues. In detecting the symmetry plane of the brain, the goal is to have a robust estimate even when the brain image contains various noise and large asymmetry.

Even though the brain is not perfectly symmetrical about the MSP, the automatic detection of this symmetry plane itself has various applications, such as standard
registration, symmetrical probabilistic map generation and symmetry-based analysis in neuro-degenerative diseases like schizophrenia and Alzheimer’s disease. Symmetry plane helps in the process of identifying brain pathologies like stroke or tumor by comparing to healthy regions of the brain. Detection of the symmetry axis or MSP is often the first step in anatomical standardization of brain images [Ardekani et al., 1997]. It can bring different images into a common coordinate system like Talairach-Tournoux [Talairach and Tournoux, 1988], allowing radiologists to analyse brain images taken from several patients or different modalities in a standard neuroanatomical space. For example, Talairach-Tournoux framework defines principal coordinate axes based on inter-hemispheric fissure or MSP. Accurately located MSP can facilitate defining symmetrical regions of interest in the left and right hemispheres. There are also many situations in which rotation of images to a standard vertical orientation is useful for visual inspection. In MR acquisition, inter and intra-patient misalignment of the image is a common problem. For accurate brain image analysis, it is crucial to identify the MSP and to have the head scan rotated into a standard orientation. It also helps with presentation and comparison of multiple images [Junck et al., 1990].

Generally, MSP is located manually by a neuro-radiological expert. However, manual methods are operator dependent and accurate reproducibility is hard to achieve. Therefore, a robust and accurate automatic technique can be useful not only in research, but in clinical practice. However, detecting the symmetry plane is difficult due to various noise artifacts, pathologies and tilted head scans. The goal is to have robust estimates even in the tilted, pathological and noisy brain images.

Generally, two main approaches have been taken in detecting the symmetry axis in the brain. The first approach defines MSP in terms of anatomical landmarks or features of the brain. The second approach is to use the similarity of the two brain hemispheres. The basic methodology in these two approaches is demonstrated in Figure 5.4.

### 5.4.1 Feature-based approach

In this approach, the common procedure is to choose an anatomical feature/landmark and then to define the MSP around this region based on intensity or texture properties. Usually, inter-hemispheric fissure (see Figure 5.2 and Figure 5.5) is considered to be the mid-line of the brain [Brummer, 1991, Hu and Nowinski, 2003]. Others have taken as landmarks such as the corpus callosum (CC), anterior commissure (AC) and posterior commissure (PC) [Hu and Nowinski, 2003], and other anatomical and radiological features [Smith and Jenkinson, 1999, Grigaitis and Meilunas, 2007, Stegmann et al., 2005]. Generally, line/plane fitting is performed on the obtained features. These feature-based methods actually do not measure symmetry directly.
In [Brummer, 1991], Brummer presented a MSP detection technique for 3D volumetric data based on the Hough transform (HT). It detects the edge points on the structure of the inter-hemispheric fissure (IF). MSP is considered as the major plane appearing in the scans, so that it can be detected as a global maximum in a HT. A series of 2D HTs are performed for all slices on standard coronal or trans-axial scans to get straight lines. Then, these straight lines are transformed into a 2D vector on which another 2D HT is performed. This final straight line obtained is geometrically proven to be the IF-plane. Since edge images are obtained using Sobel edge detectors, its application is only limited to high contrast images like MR images. Marais et al. [Marais et al., 1996] proposed a method using B-spline snakes to detect the edge properties of inter-hemispheric fissure. A snake is initialised along a midline on one slice and allowed to propagate through the other slices under supervision. Then, a plane is fitted to these lines by orthogonal regression. Initialisation of this method requires manual
intervention. In the method by Smith and Jenkinson [Smith and Jenkinson, 1999], it is assumed that each line orthogonal to a symmetry axis has its centre on the symmetry axis. After estimating the centroid, they have considered all possible orientations for the symmetry plane. For all lines perpendicular to each candidate symmetry plane, intensity profiles are obtained and centre of symmetry is calculated. All lines’ symmetry positions are combined into a single array. From the peak in total array, location of the MSP is estimated.

Hu and Nowinski [Hu and Nowinski, 2003] presented a method by assuming that the brain is approximately symmetric in the vicinity of inter-hemispheric fissure. The brain symmetry plane is considered to be the plane formed from the majority of inter-hemispheric fissure line segments having the same orientation. Their first step is to determine suitable slices for processing based on maximum average grey level. Next, the fissure line segments in a local region around the centreline of the brain are detected. A local symmetry index is then used to compare the grey-level of pairs of lines taken from either side of the fissure line segment and the final position of the fissure line segment is refined by minimizing the local symmetry index in the searching region. A local symmetry index is used to compare the grey-level of pairs of lines taken from either side of the chosen fissure line segment. After removing outliers with the help of histogram analysis, MSP is estimated using least square error fit on the final location of the fissure line segments. However, there can be cases without local similarity near
the IF. In the method by Volkau et al. [Volkau et al., 2006a], the main idea is that due to large amount of cerebrospinal fluid (CSF), entropy of MSP is lower than that of the neighbouring sagittal slices. The authors have chosen Kullback-Leibler (KL) measure to describe the deviation from the probability distribution of MSP. First, a volume of interest (VOI) is defined around the central slice in the sagittal direction and the first slice of the VOI is taken as the reference slice. Then, KL-measure is computed on all sagittal slices in the VOI by comparing each slice to the reference slice. By taking the slice that gives the maximum KL measure as the central plane for a new smaller VOI, a new search is performed until finally the MSP is estimated. In the method by Bergo et al. [Bergo et al., 2009], it is assumed that IF contains the maximum area of CSF, when irrelevant structures such as ventricles and lesions are excluded. First, a 3D brain mask that excludes those structures is created. Then, the CSF score of each sagittal plane is obtained by computing the mean voxel intensity in the intersection between the plane and the brain mask. The plane with a reasonably large brain mask intersection and minimal intensity score is taken as the best candidate for the MSP. Finally, CSF score is calculated again for all small transformations of the chosen plane and the plane with the lowest score is considered to be the MSP. Ekin [Ekin, 2006] proposed a feature-based method for detecting IF. For each axial slice of the volumetric image, row by row image intensity analysis is performed to detect feature points that correspond to the position of IF. Then, a line is fitted onto the obtained feature points using RANSAC (Random Sample Consensus). It is only implemented on MR axial PD (proton density)-weighted images. In [Grigaitis and Meilunas, 2007], MSP is estimated by detecting falx cerebri in CT images. However, falx cerebri may not be visible in all scans.

Generally, methods in this category are robust to brain asymmetries caused by pathologies. However, existing methods are sensitive to noise, outliers and the shape of the landmark. Moreover, these methodologies are usually difficult to extend to other imaging modalities like CT, PET or SPECT, as the landmark (e.g., inter-hemispheric fissure) may not be clearly visible in those modalities.

5.4.2 Similarity-based approach

In the second approach, MSP is defined as the one that best separates the two hemispheres or the plane that maximises a defined similarity criterion. The common technique used for detecting MSP is done by iterations of measuring and optimizing the similarity of the left and right hemisphere intensity values on a given image. The idea is that the maximal left-right similarity should be obtained about the mid-sagittal plane of the brain. Usually, the image is reflected across the initial plane and the similarity is measured between the original and the reflected images. This scheme is illustrated in
Figure 5.6. These methods also rely on an initial plane computed by principal axis of inertia or edge detection.

*A number of methods first compute principal axes of inertia in order to determine the symmetry plane. For all planes passing through the centre of mass and being orthogonal to a principal axis of inertia, the plane that gives the highest degree of bilateral symmetry is taken as the symmetry plane. Most of these methods are computationally intensive. In the medical imaging domain, one of the earliest studies using symmetry was done by Minovic et al. [Minovic et al., 1992]. They presented a technique for symmetry detection and measurement of 3D medical entities. In order to deal with medical entities of arbitrary shapes, the given image is represented by an octree data structure. Principal axes are detected by solving the eigenvalue problem. According to the eigenvalues obtained from the image, types of symmetry are evaluated by computing the corresponding symmetry degrees. For example, if all eigenvalues are distinct it is said to have simple mirror symmetry. On the other hand, if two (or three) eigenvalues are equal, rotational (or spherical) symmetry is suspected. Sun and Sherrah [Sun and Sherrah, 1997] have used a method based on Extended Gaussian Image (EGI) [Horn, 1986] for 3D symmetry detection. EGI is a 3D shape representation which is defined on the unit sphere (called Gauss sphere) [Horn, 1986]. It describes the shape of an object by the distribution of object’s surface normals. The basic idea is that if the brain is symmetrical, so is the EGI. They determined the orientation of the plane of reflection symmetry and the axis and order of rotational symmetry, by using the values from 3D gradient orientation histogram. The plane that maximises the cross correlation between the EGI and its reflection along the plane is considered to be the MSP. The accuracy of the method is affected by the use of the image gradients for EGI computation and assumptions like the symmetry plane passes through the brain’s centre of mass. In the method by O’Mara and Owens [O’Mara and Owens, 1996b], the 3D image is treated*
as a binary image for detecting the dominant axis/hyperplane of bilateral symmetry. Eigenvectors of the covariance matrix for the image are computed for determining the principal axes. The bilateral symmetry is measured using intensity values of the image. It is assumed that the symmetry hyperplane is the same on the binary image and on the intensity image. In [Saha and Maulik, 2011], the authors detect symmetry axis by performing principal component analysis on the data set. They have taken the first principal axis as the symmetry line and used it for automatic clustering by using the property that the data set should be symmetrical with respect to the symmetry line. The above methods, however, are mainly tested on synthetic images and only a few brain images are used in the experiments.

Several symmetry axis detection techniques that focus on image alignment [Junck et al., 1990, Minoshima et al., 1992, Ardekani et al., 1997] have been described in the literature. Most of them work only on 2D images. Junck et al. [Junck et al., 1990] developed a method for automatic detection of the line of symmetry and rotational correction of PET and SPECT images. An image is rotated through various angles and MSP is determined by maximizing the correlation between the pixel values across the midline. An exhaustive search is performed to find the optimal alignment. This method appeared to work better than visual inspection in normal PET images. However, its assumption requiring left-right brain symmetry limits its application on images with focal brain disorders, like tumors. In the same line of research, Minoshima et al. [Minoshima et al., 1992] presented a method for detecting the MSP in 3D PET images. The measure of symmetry used in their approach is a modified stochastic sign change (SSC) criterion. The MSP is determined by iteratively optimizing similarity of the left and right hemispheres. The SSC is shown to be robust to a certain degree of asymmetry in the brain image. Ardekani et al. [Ardekani et al., 1997] presented a method to find the MSP of 3D brain images. They have applied intensity-based cross-correlation iteratively to find the plane that maximises the symmetry criterion. Similarity measure is computed for a number of plane positions. For computational efficiency, a multi-resolution approach is adopted whereby an approximate location of the MSP is constructed from smaller images of lower resolution and then located more accurately in images with higher resolution.

Tuzikov et al. [Tuzikov et al., 2003] presented an automatic method for detecting the best symmetry plane of the brain. An initial plane is obtained by using principal inertia axes, followed by an optimization using the downhill simplex method. A degree of similarity is measured using the image and its reflection along the plane. The best plane is then obtained by maximizing the similarity measure. The method by Thirion et al. [Thirion et al., 2000, Thirion, 1998] assumes that the image is roughly symmetrical.
and that a direction approximately perpendicular to the mid-plane is already known. The image is reflected about the pre-assumed symmetry plane and using their “demons algorithm” [Thirion, 1998], non-rigid image registration is performed to align the original and reflected images. In the basic demons algorithm, a velocity is defined on each pixel using intensity differences and gradient information. This velocity field is smoothed by Gaussian convolution, and iteratively used to transform the floating image to register on to the static image. Final symmetry plane is deduced from the estimated transformation by minimizing a least square criterion. The method cannot be used in cases with significant asymmetry in the image. Prima et al. [Prima et al., 2001] improved this method with a block matching procedure which finds anatomically corresponding homologous blocks for local similarity measure. They have defined the MSP as the plane that best superposing the points on one side and their counterparts on the other side by reflective symmetry. First, by taking the central plane of the image grid as the initial plane, pairs of data points are extracted from the centres of each pair of matched blocks, and then a displacement field is calculated. The best candidate plane for the MSP is estimated using least squares criterion minimizing the displacement field. The whole process is iterated until convergence. In their results, the method has worked for brain images with asymmetrical pathologies. However, the idea only holds when there is an anatomical counterpart for each data point. The method does not work for strongly tilted head scans.

Liu et al. [Liu et al., 2001] presented an edge-based method to extract MSP. It is assumed that the MSP is a planar surface, so that the orientation angle of each 2D symmetry axis should be the same for all axial or coronal slices. Initial axis is taken as the vertical centreline of each image. For all pre-processed 2D slices, the orientation of the reflection line that maximised the cross-correlation between the original image and reflection image is searched. This method gives less accurate results if the given neuroimage is strongly tilted. In [Ruppert et al., 2011], the authors have done similar work, but performing a multi-scale search to reduce time. In [Teverovskiy and Liu, 2006], Teverovskiy and Liu performed a similar edge-based cross correlation on 3D images. After pre-processing the images with anisotropic smoothing, sub-sampling and edge detection, a set of orthogonal planes located near the centroid are considered. MSP is the candidate plane that maximises the cross-correlation between the original image and its flipped copy about the plane. In the method by Stegmann et al. [Stegmann et al., 2005], MSP as well as non-planar mid sagittal surface detection was considered. They have defined a local symmetry measure based on correlation. However, quantitative validation was not performed on the results.

Similarity-based approach can be easily extended to different imaging modalities
like CT, PET and SPECT. On the other hand, since a similarity criterion is considered, they do not perform well when the brain image contains asymmetry due to pathology. Additionally, the orientation of the given image can affect the accuracy in many of these methods [Prima et al., 2001, Teverovskiy and Liu, 2006]. Another disadvantage is the high computational cost.

Brain symmetry axis/plane detection methods in the literature are summarized in Table 5.1 and Table 5.2.

5.5 Validation Methods in MSP Detection

The main goal of validation is to objectively assess the performance of an algorithm or method. Ideally, it would be desirable to compare the accuracy of a detected symmetry plane and its alignment with a “gold standard”, although no such standard exists yet. For example, as explained in [Junck et al., 1990], the gold standard may be data obtained from using a head-holding method that permits no movement in the X or Y direction and no rotation, and then the symmetry axes are marked on images by an expert radiologist. However, even the best available head-holding method permits some amount of movement. Furthermore, since no human brain exhibits perfect symmetry, and the brain size is different from person to person, it would be difficult to define a set of gold standard from real images. There is also the issue of inter-person variation when the symmetry axis is manually labelled by human experts. All these issues could affect the comparison study between two sets of results. Nevertheless, for comparative evaluations, publicly available ground truth data is still indispensable. As part of the evaluation, usually, synthetic brain images are usually used for assessing whether the algorithm is stable with respect to noise and intensity non-uniformity. Two mostly referenced databases in the literature are IBSR http://www.cma.mgh.harvard.edu/ibsr/ and BrainWeb http://mouldy.bic.mni.mcgill.ca/brainweb/. However, it should be aware that simulated images lack natural anatomical variations and various image acquisition artifacts that are frequently encountered in real images.

Validation methods can be classified into two major categories, namely qualitative and quantitative validation.

5.5.1 Qualitative validation

Obvious errors can be identified by visual inspection. Although not adequate, visual verification by an expert is often used for validating the results qualitatively. Another validation method commonly adopted in the literature is the comparison with midlines drawn by neuro-radiological experts. By measuring a correlation score or any other
<table>
<thead>
<tr>
<th>Ref</th>
<th>Method/Symmetry Measure</th>
<th>Modality</th>
<th>Dimension</th>
<th>Validation Method/Accuracy</th>
<th>Limitations</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Junck et al., 1990]</td>
<td>Rotation, correlation</td>
<td>PET, SPECT</td>
<td>2D</td>
<td>Centre of gravity &amp; Visual inspection (accuracy w/in 0.5pix)</td>
<td>Less accurate in tilted, pathological and coronal images</td>
<td>Not given</td>
</tr>
<tr>
<td>[Brummer, 1991]</td>
<td>Hough Transform</td>
<td>MRI</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Not applicable to low contrast, pathological or sagittal scans</td>
<td>20s for 40slice data on SUN-Pixar</td>
</tr>
<tr>
<td>[Minoshima et al., 1992]</td>
<td>SSC</td>
<td>PET</td>
<td>2D</td>
<td>Comparison with ground truth (Mean diff 0.37±0.28°) ssc looks more robust than cc, but still less accurate in severe pathological images and not applicable to MRI/CT</td>
<td>Not given</td>
<td></td>
</tr>
<tr>
<td>[Minovic et al., 1992]</td>
<td>Principal axes with an oc-tree model</td>
<td>CT</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Mainly tested on synthetic images</td>
<td>3min(Ref: [O’Mara and Owens, 1996b])</td>
</tr>
<tr>
<td>[O’Mara and Owens, 1996b]</td>
<td>Principal axes/Intensity difference ratio</td>
<td>MRI</td>
<td>2D,3D</td>
<td>Visual inspection</td>
<td>Not robust to asymmetries</td>
<td>4s (Pentium 133MHz) for 256²×109 MRI</td>
</tr>
<tr>
<td>[Marais et al., 1996]</td>
<td>B-spline snakes</td>
<td>MRI</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Manual intervention needed</td>
<td>Not given</td>
</tr>
<tr>
<td>[Bengo et al., 2009]</td>
<td>Correlation</td>
<td>PET, MRI</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Less accurate in pathological images</td>
<td>45s,35s (Silicon Graphics, R5000 Workst.) for 32²×18 PET &amp; 32²×14 MRI</td>
</tr>
<tr>
<td>[Sun and Sherrah, 1997]</td>
<td>EGI</td>
<td>Synthetic and CT</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Not robust to asymmetries</td>
<td>19min(on Sun Sparc10) for a 256×256×31 CT</td>
</tr>
<tr>
<td>[Smith and Jenkinson, 1999]</td>
<td>Local intensity profile ratio</td>
<td>MRI, CT, SPECT, PET</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Time-consuming</td>
<td>40min for a typical MRI on a Silicon Graphics Origin200</td>
</tr>
<tr>
<td>[Thirion et al., 2000]</td>
<td>“Demons”-Non-rigid registration</td>
<td>MRI</td>
<td>3D</td>
<td>Vector field comparison with a simulated brain</td>
<td>Less accurate in pathological images</td>
<td>Not given</td>
</tr>
<tr>
<td>Ref</td>
<td>Method/Symmetry</td>
<td>Modality</td>
<td>Dimension</td>
<td>Measure</td>
<td>Limitations Performance</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
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</tr>
<tr>
<td>Liu et al., 2001</td>
<td>Edge-based correlation</td>
<td>MRI, CT</td>
<td>3D</td>
<td>Comparison with artificial symmetric images and ground truth</td>
<td>Less accurate in strongly tilted head scans</td>
<td>7min on an SGI o2 R10000</td>
</tr>
<tr>
<td>Prima et al., 2001</td>
<td>Block-matching method</td>
<td>MRI, CT, PET, SPECT</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Method breaks for strongly tilted images</td>
<td>3min for 64 × 64 image</td>
</tr>
<tr>
<td>Tuzikov et al., 2003</td>
<td>Ellipsoid of inertia, downhill simplex</td>
<td>MRI</td>
<td>3D</td>
<td>Comparison with simulated images and visual inspection</td>
<td>Not robust to pathological images</td>
<td>3min (SUN Ultra5 350MHz workstation) for 128 × 128 × 62 image</td>
</tr>
<tr>
<td>Hu and Nowinski, 2003</td>
<td>LF line segments</td>
<td>MRI, CT</td>
<td>2D</td>
<td>Comparison with ground truth (Accuracy 0.63mm &amp; 0.4°)</td>
<td>Limit for cases with local anatomical symmetry near IF</td>
<td>6s (Pentium4, 2.4GHz) &amp; 25s (on SGI, O2)</td>
</tr>
<tr>
<td>Stegmann et al., 2005</td>
<td>Local symmetry, correlation</td>
<td>MRI</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Not applicable to low contrast images</td>
<td>Not given</td>
</tr>
<tr>
<td>Anbazhagan et al., 2006</td>
<td>Non-rigid registration &amp; Atlas</td>
<td>MRI</td>
<td>3D</td>
<td>Comparison of cerebral volumes with ground truth</td>
<td>Image results not shown, evaluation yet to be done</td>
<td>2min (on UNIX) for 256 × 256 × 198 MRI</td>
</tr>
<tr>
<td>Liu et al., 2006</td>
<td>Comparing the left-right of a sliding window in polar space</td>
<td>DWI</td>
<td>2D</td>
<td>Comparison with ground truth</td>
<td>Applied only in MR DWI</td>
<td>Not given</td>
</tr>
<tr>
<td>Ekin, 2006</td>
<td>Row-by-row intensity profiles, Ransac</td>
<td>MRI</td>
<td>3D</td>
<td>Visual inspection</td>
<td>Applied only in PDW MRI</td>
<td>Not given</td>
</tr>
<tr>
<td>Volkau et al., 2006a</td>
<td>KL measure</td>
<td>MRI, CT</td>
<td>3D</td>
<td>Comparison with ground truth (Accuracy 1.25 pixels &amp; 0.63°)</td>
<td>Less accurate in pathological and strongly tilted images</td>
<td>5s (Pentium4, 2.4GHz) for 256 × 256 × 168 image</td>
</tr>
<tr>
<td>Teverovskiy and Liu, 2006</td>
<td>Edge-based correlation</td>
<td>MRI</td>
<td>3D</td>
<td>Comparison with artificial symmetric images</td>
<td>Less accurate in noisy and pathological images</td>
<td>7min (Ref: [Ruppert et al., 2011])</td>
</tr>
<tr>
<td>Grigaitis and Meilunas, 2007</td>
<td>A line drawing technique</td>
<td>CT</td>
<td>2D</td>
<td>Visual inspection</td>
<td>Precision evaluation yet to be done</td>
<td>1s (Pentium4, 2.6GHz) for 512 × 512 images</td>
</tr>
<tr>
<td>Bergo et al., 2009</td>
<td>CSF segmentation &amp; intensity profiles</td>
<td>MRI</td>
<td>3D</td>
<td>Comparison with ground truth (Accuracy within 1.64°)</td>
<td>Applied only in T1W MRI</td>
<td>1min (1GHz, Athlon64, Linux PC)</td>
</tr>
<tr>
<td>Puspitasari et al., 2009</td>
<td>KL measure</td>
<td>CT</td>
<td>2D</td>
<td>Comparison with ground truth (Angular and distance error within 1° &amp; 1mm)</td>
<td>Less accurate in severe pathological images</td>
<td>10s for a typical CT scan on 3GHz CPU with 1GB RAM</td>
</tr>
<tr>
<td>Ruppert et al., 2011</td>
<td>Edge-based correlation</td>
<td>CT, MRI</td>
<td>3D</td>
<td>Comparison with ground truth (their MSPGTT software)</td>
<td>Less accurate in highly tilted or pathological images</td>
<td>30s (Intel Core2Quad 2.33GHz, 4GB)</td>
</tr>
</tbody>
</table>
statistical measure, the algorithm is compared with human performance.

5.5.2 Quantitative validation

One technique used in the literature [Prima et al., 2001, Liu et al., 2001] to create a ground truth image is by finding the midline manually and then reflecting one half of the image about this line to form the other half, producing a symmetrical image. The constructed image is considered to be perfectly symmetrical and by taking it as the reference, the accuracy of the test image can be measured. Robustness of the algorithm is usually evaluated by measuring tolerance to asymmetry and noise. Most of the times, simulated images are used for this kind of evaluation. Since different methods are usually evaluated by using different datasets, fair comparison among them is not possible [Ruppert et al., 2011]. Therefore, to date there is no commonly agreed “best” method for MSP detection.

5.5.3 Comparative Evaluation

For an objective comparative evaluation of various methods, it is essential to have a well-defined quantitative symmetry measure and a publicly available ground truth image data set. However, the lack of a commonly accepted brain symmetry measure and a publicly available ground truth has prevented an objective comparison of different methodologies to be done to date. This led us to choose two of the state-of-the-art techniques from each category (feature-based and similarity based approaches), and perform a thorough comparison of those two methods along with our proposed method. This has been detailed in chapter 8.

5.6 Discussion

Pathological conditions affect the bilateral symmetry that exists in a normal brain. By exploiting this idea, researchers have been trying to use symmetry information as a prior knowledge in brain analysis algorithms. Brain symmetry plane detection is an important step and many algorithms have been proposed.

In the feature-based approach in symmetry detection, accurate localization of the feature or landmark is essential. There can be ambiguity inherent in subjective identification. Landmarks such as the falx cerebri do not offer a satisfactory feature because the curvature of the falx may be as great as several millimetres and it does not necessarily result in a centreline located midway between more lateral structures [Junck et al., 1990]. On the other hand, in similarity based approach, asymmetry due to pathology can cause errors. Consequently, there is still much room for improvements. A good definition of
symmetry is also needed for measuring approximate symmetry since the brain is known to be not perfectly symmetrical. Quantitative comparative evaluation can objectively assess the performances of different algorithms. However, as discussed in Section 5.5, to perform such evaluation, a publicly available ground truth data set, a well-defined symmetry measure and proper implementation of each method become crucial. All of these requirements are challenging and much more work is still needed. This motivated us not only to find a precise and robust method for MSP detection, but also to validate it thoroughly with extensive experiments. In addition to this, in chapter 8 we also carry out a performance evaluation of two state-of-the-art methods.

Finally, since brain is 3D, MSP extraction in 3D is expected to give better accuracy. For example, when the brain is tilted, anatomical structure may not be bilaterally symmetrical on each slice. Then, the MSP estimated by using symmetry lines on 2D slices will not be accurate. However, the computation involved in 3D symmetry analysis is expensive. In the first part of this thesis we propose a robust and accurate MSP detection method for 3D MR brain images.

\section{Chapter Summary}

This chapter has defined the bilateral symmetry feature, and MSP as brain’s symmetry plane. Although the aim of this thesis is to incorporate symmetry information into tissue segmentation algorithm, this chapter has pointed out that brain symmetry plane identification has numerous applications on its own. MSP detection is a critical initial step in brain image analysis, either done manually or automatically. Automatic extraction of the symmetry plane can provide an initial estimate for brain image registration, pathology assessment and disease diagnosis. This chapter has provided a comprehensive review on the existing methods for MSP detection under two main categories: Feature-based and Similarity-based. It has also discussed various symmetry measures in the literature.

Although a variety of works has been done in the area of MSP detection, there is no method commonly accepted as the best. Many MSP detection algorithms are variants or extensions of two main techniques based on KL-measure and edge-based cross correlation. For an algorithm to be used in clinical setting, it has to be fast, robust and accurate \cite{Hu and Nowinski, 2003}. As we have demonstrated in Chapter 8, both these techniques have drawbacks that can have severe impact on the accuracy and robustness depending on the images used. As such, existing techniques leave significant room for better applicability and accuracy. This has led us to find an accurate, robust method that can be used for MSP detection.
Chapter 6

MSP detection: Approach I

6.1 Preview

The previous chapter discussed the definitions of brain symmetry plane, various symmetry measures and the existing work in mid-sagittal plane detection. The objective of the current and the following chapter is to present the proposed approaches for identifying the precise location of MSP from volumetric MRI. In the process of trying to achieve the final goal, a theoretically simple approach based on anatomical and radiological properties was tested on T1-weighted images and found to be superior in many cases. In this chapter, we first discuss this approach. By pointing out its merits and drawbacks, in the next chapter, we proceed to the fractal analysis based method which shows superior performance on different imaging modalities.

6.2 Methodology based on Intensity Profile Analysis

The method proposed in this section is straight-forward to implement without the need for any prior segmentation. In this approach, we consider the MSP as the plane that best fits the boundary between the two hemispheres. As explained in the previous chapter, the two brain hemispheres which have similar shapes are connected by corpus callosum. In the boundary between the two hemispheres is the inter-hemispheric fissure (IF), which is a dark, deep groove (see Figure 6.1). Although the real separation surface is not perfectly planar, MSP is commonly considered as a plane passing through this boundary.

As discussed previously, due to the high contrast between different soft tissues and non-use of radiation, MRI has widely been used for studies of brain abnormalities. In MR brain images, falx cerebri can be clearly seen as a hyper-dense, pencil-thin line.
Figure 6.1: Falx Cerebri descends vertically in the IF between the cerebral hemispheres. (a). Falx Cerebri [Wikipedia, 2013a], (b). MRI axial slice.

(see Figure 6.1). It is one of the toughest meninges and it descends vertically in the IF between the cerebral hemispheres. Even though IF actually has a zigzag configuration, it is most often simplified as a planar surface. The IF contains CSF that gives a weak MR signal on T1-weighted images [Liew and Yan, 2006]. Therefore, image intensity in this region is generally low. Based on these anatomical and radiological properties, we present a method for locating mid-sagittal plane in T1-weighted MR brain images. We call this first approach MSPMethod 1.

6.2.1 MSPMethod1 algorithm

Our algorithm for detection of MSP is based upon the assumption that IF is the only major plane that appears darkest in T1-weighted MR images (see Figure 6.1). Our goal is to extract the MSP of a brain from its volumetric MRI data consisting of stacks of 2D slices. 3D data is first processed as individual 2D slices assuming that MSP is a planar surface. IF appears dark and dense in T1-weighted MR images. Although it is not clearly visible in all slices, intensity profile of each slice has a distinct intensity pattern along where the fissure is present. By exploiting this property, we analyzed the intensity profile along lines drawn in multiple angles that pass through the centroid of the image. The best possible line that fits the inter-hemispheric fissure is estimated. Each 2D slice is analyzed independently and finally the median angle is taken as the angle of the MSP to current vertical plane. Angle is measured anticlockwise from the vertical axis where the angle is taken as 0°. The overall process of the method is illustrated in Figure 6.2.

For computational efficiency and robustness towards local minima, a multi-scale approach was applied by reducing the resolution of the original image. An approximate
Figure 6.2: An example output which shows the estimated axis for each slice. These equally distributed 56 slices are taken from an image volume of 168 slices. MSP ground truth is known to be the vertical centreline of these images. Although the extreme slices show some deviation, as a whole, the median value gives the accurate estimate.

The optimal angle can be located within $1^{\circ}$ accuracy.

This multi-scale procedure can be stated as follows:

1: Read the brain volume data.
2: for each slice do
3: Compute the centroid of the image
4: Sub-scale the image slice to give an image with lower resolution.
5: for each sub-scale do
6: Rotate a straight line that passes through the centroid from 0° to 180° in 1° intervals:
7: for each angle \( k \) do
8: Measure the intensity score along the line and keep track of the angle
9: end for
10: Choose the position with the minimum score and keep track the line angle position \( l \)
11: end for
12: On the original image, perform a localised search around \( l \), between \( l-5° \) and \( l+5° \) by measuring the intensity score
13: Estimate the best-fit line by taking the minimum intensity score
14: end for
15: Estimate the best plane for the 3D volume by taking the median of the angles obtained from all slices.

For illustration, a distribution plot of intensity scores at each angle is shown in Figure 6.3.

![Distribution plot of intensity scores at each angle](image)

**Figure 6.3:** Distribution plot of the intensity score at each angle. MSP ground truth is at 0°.

### 6.2.2 Results from MSPMethod1

**Experimental data set**

In this experiment, the data set consists of 12 T1-weighted MR scans of normal and pathological cases. (See Table 6.1). The MRI datasets have been chosen from IBSR
Figure 6.4: An example output which shows the estimated axis for each slice. These equally distanced 56 slices are taken from an image volume of 168 slices. Although the extreme slices show some deviation, as a whole, the median value gives the accurate estimate.

http://www.cma.mgh.harvard.edu/ and BrainWeb http://www.bic.mni.mcgill.ca/brainweb/. The size of each image volume for IBSR data (real images) is $256 \times 256 \times Z$ ($Z$ varied from 61 to 63). In BrainWeb images, the size of each image volume is $181 \times 217 \times 181 \, 1mm^3$ voxels and slice thickness was $1\, mm$. These phantom data from BrainWeb have been used to analyse the effect of noise and intensity non-uniformity in the final results. The robustness of the algorithm to the orientation of the image has also been checked. For all data used in this study, good results have been obtained under qualitative judgment. We also have performed a quantitative evaluation comparing with commonly used cross-correlation based technique. The results obtained are shown
from Figure 6.5 to Figure 6.8.

Table 6.1: Description of the data set used

<table>
<thead>
<tr>
<th>Data source</th>
<th>Number of images</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>BrainWeb</td>
<td>9</td>
<td>Simulated images with varying noise and INU and also 2 MS-lesion models. Ground truth was available.</td>
</tr>
<tr>
<td>IBSR</td>
<td>3</td>
<td>Real images: 2 normal and 1 pathological. Ground truth was available.</td>
</tr>
</tbody>
</table>

Figure 6.5: Results of MSP detection projected on an axial slice. (a). BrainWeb image with noise. (b). BrainWeb image rotated in 30°, (c). BrainWeb image rotated in 90°, (d). IBSR image, (e). IBSR image, (f). IBSR image rotated in 60°

6.2.3 Evaluation

Qualitative Evaluation

By estimating the best-fit plane, the algorithm has succeeded in dividing the two hemispheres of all the images. When we compared the results with their ground truth, the proposed approach gave accurate results. Our approach has a key advantage of being insensitive to slow varying intensity variation which is a common problem in MR images. We have also found that the method works well for lower resolution
images as well. Our results were visually inspected by an expert and were judged to be consistently correct while 90% of the cases were scored as highly accurate. This approach does not present limitations with respect to the initial orientation of the image or the asymmetry present.

Although our method is not based on a similarity score, considering the property that the brain is approximately symmetrical along the MSP, below we provide a quantitative comparison with other similarity based techniques.

**Comparison with cross-correlation based technique**

Since cross-correlation (CC) is one of the most commonly used techniques in MSP detection algorithm, we have used this for evaluating the performance of our method. The correlation coefficient between two images $A$ and $B$ can be calculated using the equation given in Chapter 5.

For each image we rotated our estimated line in varying angle ranging from $-10^\circ$ to $10^\circ$ and computed the cross-correlation. The line that gave the maximum value of cross-correlation was compared with the line estimated by our method. Both lines coincided in some of the cases. For the rest, our approach either gave more accurate results in simulated images or showed visually better results in real images (see Figure 6.6 to Figure 6.8), despite its cc score being slightly lower. These results show the superiority of our method compared with the cross-correlation based approach. In particular, the approach is robust to pathological asymmetry as shown in Figure 6.8. Since the proposed method performs computations on each slice and then takes the median of the results to give a robust estimate, it is insensitive to pathologies that normally reside in a small part of the brain.

**Quantitative Evaluation**

If the symmetry is perfect, we expect that the histograms of intensity distribution on the left and right hemispheres will be exact replica of each other. Hence, the degree of dissimilarity between the two hemispheres separated by the estimated symmetry plane can be computed on the corresponding histograms using the Bhattacharyya distance $BD$

$$BD = 1 - \sum \sqrt{H1 \times H2}$$

where $H1$ and $H2$ are the two intensity histograms. This similarity score is in the range of 0 and 1, where 0 means that the histograms are perfectly similar.

Based on this BD measure (See Table 6.2), a paired t-test was performed to find
Figure 6.6: Robustness to noise compared with CC technique. (i). Results from MSPMethod1, (ii). Results from CC technique. (a). Noise 3%, (b). Noise 5%, (c). Noise 9%.

Table 6.2: A comparison of the computed BD values

<table>
<thead>
<tr>
<th>Image</th>
<th>( BD_{MSPMethod1} )</th>
<th>( BD_{CCmethod} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 6.5 (a)</td>
<td>0.0896</td>
<td>0.0896</td>
</tr>
<tr>
<td>Figure 6.5 (b)</td>
<td>0.0308</td>
<td>0.0315</td>
</tr>
<tr>
<td>Figure 6.5 (d)</td>
<td>0.0069</td>
<td>0.0089</td>
</tr>
<tr>
<td>Figure 6.5 (e)</td>
<td>0.0027</td>
<td>0.0015</td>
</tr>
<tr>
<td>Figure 6.5 (f)</td>
<td>0.0241</td>
<td>0.0339</td>
</tr>
<tr>
<td>Figure 6.6 (a)</td>
<td>0.0023</td>
<td>0.001</td>
</tr>
<tr>
<td>Figure 6.6 (b)</td>
<td>0.0017</td>
<td>0.0034</td>
</tr>
<tr>
<td>Figure 6.6 (c)</td>
<td>0.0072</td>
<td>0.0096</td>
</tr>
<tr>
<td>Figure 6.7 (a)</td>
<td>0.0128</td>
<td>0.0367</td>
</tr>
<tr>
<td>Figure 6.7 (b)</td>
<td>0.0274</td>
<td>0.04</td>
</tr>
<tr>
<td>Figure 6.8 (a)</td>
<td>0.0593</td>
<td>0.147</td>
</tr>
<tr>
<td>Figure 6.8 (b)</td>
<td>0.003</td>
<td>0.0397</td>
</tr>
</tbody>
</table>

Out the statistically significant difference between the mean of our method (mean = 0.0295, \( \text{stdev} = 0.0443 \)) and that of cross-correlation based method (mean = 0.0307, \( \text{stdev} = 0.0425 \)). The results (Degrees of freedom=11, t-value t = 1.834, p-value p = 0.047 and the probability value for 95% confidence level \( \alpha = 0.05 \) indicate that we have a statistically significant lower (better) mean value at 95% confidence level.

It should be noted however that above comparative analysis is based on the assump-
tion that the two hemispheres are symmetrical about MSP. This might not be true in severe pathological cases, but there is still a possibility that MspMethod1 would give accurate results as it does not assume the hemispheric similarity.

6.2.4 Advantages and disadvantages of MSPMethod1

Advantages

- It does not get easily affected by hemispheric asymmetry due to pathology.
- The method works well in tilted head scans.
- It does not need any pre-processing.

Disadvantages

- The algorithm needs modification when used for different imaging modalities.
Figure 6.8: Robustness to pathology compared with CC technique. (i). Results from MSP-Method1, (ii). Results from CC technique. (a). Minor MS lesion model, (b). Major MS lesion model.

- The method is unable to excel in T2-weighted and PD-images as in T1-weighted images.
- It cannot be used in coronal scans.

6.2.5 Summary of MSPMethod1

We have presented a novel but simple technique for detecting the mid-sagittal plane in MR images. The method exploits both anatomical and radiological properties of the inter-hemispheric fissure in T1-weighted MR brain images. It does not require any pre-processing step like removal of extra-cranial tissues. The method is robust with respect to noise, intensity non-uniformity and orientation. The algorithm has achieved good results on pathological images used in the experiment. However, the major drawback of this approach is that it is modality dependent (T1-weighted images). This has led us to find more robust method that can handle a variety of images from different imaging modalities. This is discussed in the next chapter.
Chapter 7

MSP detection: Approach II

7.1 Preview

The previous chapter discussed the first approach we took for MSP detection based on intensity profile analysis. Although this approach can achieve good results in T1-weighted images, it has one major limitation. That is its incapability to perform well in different modalities. In order to address this issue, and to achieve better robustness, this chapter presents a novel approach for symmetry plane detection in MR neuro-images based on textural information and underlying brain’s physiological structure. Although fractal geometry is capable of handling structural complexity, to the best of our knowledge no one has realised the opportunity of using it as a symmetry measure. This chapter discusses two methods based on fractal analysis; in each method fractal analysis is performed using a different technique. As a sequel to the method proposed in previous chapter, we call the methods proposed in this chapter, MSPMethod 2 and MSPMethod 3. Section 7.2 discusses the inspiration for a fractal based approach and also outlines the fractal analysis applications in the medical domain. This is followed by the basic theory in fractal analysis. In Section 7.4, MSPMethod 2 is explained with results and evaluation. Similarly, MSPMethod 3 is discussed in Section 7.5. Finally, Section 7.6 evaluates all three methods proposed for MSP detection with the merits and drawbacks of each of them. Final results show the superiority of the fractal based approach.

7.2 Motivation for a Fractal based Approach

Although a number of automatic methods have been proposed for detecting brain MSP as mentioned in Chapter 5, most of the existing literature has focused on intensity based cross-correlation without considering textural or structural information of the
brain. However, it is the brain’s structure itself which is symmetrical. To the best of our knowledge, none of the work on brain symmetry plane detection has tried to take advantage of the local self-similarity and bilateral symmetry in the structure present in brain images. In MRI, artifacts like INU give rise to smooth intensity variation across the image, thus affecting the accuracy of intensity based techniques [Liew and Yan, 2003, Liew and Yan, 2006]. Moreover, the structure and morphology of complex objects like the brain are not well described by Euclidean geometry. The fractal geometry [Mandelbrot, 1982] is used to describe self-similar sets called fractals and natural objects that are difficult to describe by using the Euclidean geometry. It has been successfully applied in a variety of areas, such as mathematics, science, biology and medicine including medical imaging [Lopes and Betrouni, 2009]. The use of a fractal dimension to describe the convolution or the complexity of a line or surface is well established in several areas of biomedical research [Free et al., 1996].

Figure 7.1: The famous woodblock print, “The Great Wave off Kanagawa” by the Japanese artist Katsushika Hokusai [Wikipedia, 2013b]. The fractal concept of self-similarity is used in this painting in the early 1800s.

7.2.1 Fractal analysis in medical applications

Fractal dimension (FD) contains information about the geometric structures of fractals. It characterizes the irregularity and the complexity of an object. One criterion of a surface being fractal is its self-similarity [Mandelbrot, 1982]. A set \( A \) is said to be self-similar when \( A \) is the union of \( N \) distinct copies of itself each of which has been
scaled down by a ratio $r (r < 1)$. Many natural structures exhibit self-similarity over a range of scales (see Figure 7.1), enabling them to be described by a fractal dimension. Since medical images are complex in nature and exhibit some similarity in different scales, fractal geometry has been applied in analysing a variety of medical images, and has played an important role in various areas of health and medical research such as differentiating pathological tissues from healthy ones [Blackledge and Dubovitskiy, 2008, Takahashi et al., 2009] and diagnosis in a broad range of diseases [Iftekharuddin, 2005, Zaia et al., 2006]. Applications of the fractal dimension to medical images have also been reported regarding quantitative texture analysis for novel understanding of brain structures [Takahashi et al., 2009]. It has also been successfully used in quantification of morphological changes in brain images [Free et al., 1996].

Kieselev et al. [Kiselev et al., 2003] has performed an analysis of the geometry of the brain cortex and their results indicate that the brain does possess some fractal property. The choice of fractal analysis on medical imaging is also motivated by the observation that FD is relatively insensitive to image scaling, and it shows a strong correlation with human judgment of surface roughness [Chaudhuri and Sarkar, 1995]. Moreover, FD has been shown to be a powerful tool for quantitative characterization of noisy medical images where the edges are usually blurred, and diagnostically important information usually lies in the texture [Oczeretko et al., 2002]. Since MR images have a degree of noise and randomness associated with the natural random texture of structure, they are said to be good candidates for characterization using fractal analysis [Iftekharuddin, 2005].

In most of the above applications however, fractal analysis is often restricted to fractal dimension as FD provides a way of quantifying the shape complexity of objects. Nonetheless, fractal dimension alone is not sufficient to fully describe the space filling-characteristics of an object. Another fractal property called lacunarity describes the texture of a fractal object and can measure how the data fills the space [Mandelbrot, 1982]. Both fractal dimension and lacunarity are successfully used for classification of different structures and textures due to their invariance to scale, rotation or translation [Zaia et al., 2006]. In this work, we apply fractal dimension and lacunarity for identifying the symmetry plane or MSP in MR brain images.

7.2.2 Approach overview

Specifically, this thesis looks into using fractal analysis for MSP detection in two ways. The first method takes into account the structural and textural differences of the region around the boundary between the two hemispheres, and considers the MSP as the plane that best fits this boundary. In the brain, MSP contains larger amounts of CSF. In
MR images, this appears as a clear textural difference. Since texture is a fundamental property that has been exploited to analyse tissues and pathologies, texture analysis using fractals could be used to differentiate structure along MSP from neighbouring tissues. This is our MSPMethod 2. Then, the MSPMethod 3 described in Section 7.5 considers fractal dimension as a symmetry measure. The idea behind this method is based on the assumption that the left and right hemispheres would be similar in structural complexity.

7.3 Fractal Analysis

A fractal is defined as a fragmented geometric shape that can be divided into smaller parts, where each part is a smaller copy of the whole [Mandelbrot, 1982]. This is an important property of the fractal called self-similarity (see Figure 7.2). Several of the best known examples of mathematical fractals are the Koch curve, the Sierpinski gasket and the Cantor set.

![Figure 7.2: Examples of fractals. (a) A mathematical fractal, Sierpinski triangle, (b) Romanesco broccoli, a striking example of fractals in nature. This kind of self-similarity appears in the brain.](image)

Some of the basic concepts of fractals can be elucidated with the Koch curve which has much of the complexity that we would see in natural objects. This is illustrated in Figure 7.3. Its construction is an iterative procedure, beginning with a straight line segment called the initiator. The initiator is partitioned into three equal segments and then the middle segment is replaced by two equal segments, forming an open equilateral triangle. This completes the basic construction step which is called the generator. Then, the procedure is repeated for every straight line segment, and in theory, the process can be continued to infinity. The result is neither a curve nor a surface but rather an infinite curve that fills the surface [Sandu et al., 2008]. Each sub-segment is an exact replica of
the original curve, thus showing the self-similarity.

Figure 7.3: Generation of the Koch curve.

When measuring the total length of the Koch curve, the result depends on the length of the scale. This leads towards a definition of the fractal dimension, related to the number of self-similar pieces that can be seen when scaling down a larger object.

7.3.1 Fractal Dimension

Fractal dimension is the most frequently used fractal measure. FD can quantify the complexity of an object, indicating how much space is filled with increasing scale [Mandelbrot, 1982]. FD is a real number that describes the structural complexity of an object. It is defined as the exponent of the number of self-similar pieces (N) with magnification factor (1/r) into which an object may be broken. The equation can be written as follows.

\[ FD = \frac{\ln(N)}{\ln(r)} \]  \hspace{1cm} (7.1)

In the case of the Koch curve, we can observe that at each step, the length of the curve grows by a factor of 4/3. By decreasing the radius to one third, the measurable length N increases by a factor of four. Therefore, the fractal dimension in the case of the Koch curve is

\[ FD = \frac{\ln(4)}{\ln(3)} = 1.2618 \]
The greater the $FD$ is, the more complex and irregular the fractal object is. Therefore, $FD$ can also be viewed as a measurement of the object’s complexity or irregularity. There are a variety of algorithms to compute the FD of a structure. The basic procedure of the most commonly used box-counting (BC) method is to systematically lay a series of grids (boxes) of decreasing side length $r$ over an image and count the number ($N(r)$) of boxes with foreground pixels in them. At each step of the procedure, the linear size $r$ is changed to progressively smaller sizes. The minimum number of boxes $N(r)$ that is necessary to cover the whole object structure is then assumed to vary according to $N(r) \approx \left(\frac{1}{r}\right)^{FD}$, where $FD$ is the fractal dimension. The logarithm of $N(r)$ versus the logarithm of $r$ gives a line whose gradient corresponds to $FD$.

Computation of FD using box-counting is demonstrated in Figure 7.4.

For a truly fractal structure the slope of the log-log graph is independent of the scale at which we observe the structure. Natural objects are not regular and are self-similar only in a statistical sense. When applying the concept of fractals to biological structures, we merely expect it to be approximately constant within some range of scale. Figure 7.5 shows a log-log plot obtained from a 3D brain MR image. FD is obtained by fitting a straight line to the plot using least square regression.

### 7.3.2 Lacunarity

When Mandelbrot [Mandelbrot, 1982] introduced the fractal geometry, he defined and used the concept of lacunarity as another complementary metric which describes the deviation from homogeneity in the texture [Pentland, 1984]. Its initial purpose was to further classify fractals and textures which had the same fractal dimension but very different visual appearance. Lacunarity, from the Latin word lacuna meaning “gap” describes the texture of an object by measuring the degree of non-homogeneity within an object or image (see Figure 7.6). If an object has large holes or gaps distributed
unevenly, it has high lacunarity. On the other hand, if an object is homogeneous with respect to the spatial arrangement of gaps or almost translationally invariant, it has low lacunarity. For instance, in Figure 7.7, left image has higher lacunarity than the right image. Lacunarity is defined quantitatively as the mean square deviation of the fluctuation of mass distribution function divided by its square mean [Tolle et al., 2008, Allain and Cloitre, 1991]. Several techniques have been proposed to estimate lacunarity. In the BC method, lacunarity $\lambda$ is calculated from the mean ($\mu$) and the standard deviation ($\sigma$) for the number of pixels within the box $r$ as

$$\lambda = \frac{\sigma^2}{\mu^2}$$

(7.2)

Lacunarity has also been taken as a quantitative measure of texture in various fields. In [Zaia et al., 2006], an approach based on lacunarity analysis on MR images is taken for studying trabecular bone structure to differentiate healthy and osteoporotic patients.
Figure 7.6: Lacunarity is a measure of inhomogeneity in the image. Left: Two textural images taken from UIUC database [Lazebnik et al., 2005]. Right: Computed lacunarity plots.

Figure 7.7: Lacunarity describes the texture by measuring the degree of non-homogeneity within an object or image. (a) has higher lacunarity than (b).
7.4 MSP Method 2

In brain MR images, MSP is visible as a distinguished pattern due to its higher amount of CSF. Going from one side towards the middle of the brain along the sagittal direction, the textural inhomogeneity increases towards the middle. This would increase the value of lacunarity. This is illustrated in Figure 7.8 with computed lacunarity values. However, there is a possibility of having images with the same lacunarity value, but different fractal dimension due to structural change. Therefore, we need to use fractal dimension as well to fully consider the structural and textural information within the image. In any given axial slice, the complexity of the structure increases near the MSP. This would increase the fractal dimension. Therefore, our method is based on calculating the lacunarity of each sagittal slice and estimating the fractal dimension of a defined region-of-interest (ROI) on the axial images.

![Figure 7.8: Change of lacunarity value along the sagittal direction](image)
7.4.1 Procedure

When pixel intensity is regarded as the height above ground plane, the intensity surface of a medical image can be regarded as a rough surface. We used a modified box-counting method called Differential Box Counting (DBC) \cite{Sarkar1994} to estimate the FD as it is well-suited for computing fractal dimension of rough images. In this method, the image of size $M \times M$ pixels is partitioned into grids of size $s \times s$ where $M/2 \geq s > 1$ and $s$ is an integer. Then, the scaling down ratio is given by $r = s/M$. Consider the image $I(x,y)$ as on a 2D $x-y$ plane and the third coordinate($z$) denoting grey level (See Figure 7.9). On each image grid there is a stack of boxes of size $s \times s \times s'$. If the total number of grey levels is $G$, then $s'$ is chosen such that $s'/G = r$. Assume that the maximum and minimum grey levels of the image in $(i,j)$th grid fall in box number $k$ and $l$ respectively. Then, $n_r(i,j) = k - l + 1$ is the contribution of $N_r$ in the $(i,j)$th grid. The contributions from all the grids is obtained by

$$N_r = \sum_{i,j} n_r(i,j)$$ \hspace{1cm} (7.3)

![Figure 7.9: Differential box counting with three boxes](image)
The main steps of our algorithm are as follows.

1. Read the 3D brain volume data $I(x, y, z)$. Positive $X$, $Y$, $Z$ coordinates correspond to head’s right, anterior and superior directions, respectively. Let the matrix size be $a \times b \times c$.

2. Compute the fractal dimension $I_{FD}(x, y, z)$ at each pixel location $(x, y, z)$ by applying the DBC method on the grayscale image. $I_{FD}$ remains the same for next two steps.

3. Working along the sagittal direction, compute the lacunarity $\lambda(x_i)$ for each sagittal slice position $x_i$ $(1 < i \leq a)$. Find the slice position $x_{i0}$ that have the maximum lacunarity value ($x_{i0} = \text{argmax}_i \lambda(x_i)$).

4. For Fine Processing: For each axial slice $j$ excluding the extreme top and bottom 20% slices; i.e., $(c/5 < j \leq 4c/5)$, define a ROI of a width of $\delta c$ pixel columns centred on $x_{i0}$ (we took $\delta c = 3$). Then, using the previously obtained $I_{FD}$, compute the averaged fractal dimension for each candidate axis using a sliding window of a width of one pixel column inside the ROI. Find the location $p(j_0)$ with the maximum fractal dimension.

5. Estimate the MSP by taking the mode of $p(j_0)$ computed over the axial slices.

7.4.2 Results

Experimental data set

The MR image data have been obtained from IBSR (http://www.cma.mgh.harvard.edu/) and BrainWeb (http://www.bic.mni.mcgill.ca/brainweb/). We have considered 20 MR scans of normal and pathological cases (See Table 7.1). T1-, T2- and PD-weighted images have been included in the data set. Simulated data from BrainWeb have been used to analyse the effect of noise, INU, and image contrast. Figure 7.10 shows some of the results obtained.

Evaluation

Since cross-correlation (CC) is one of the most commonly used techniques in MSP detection, we compared the performance of our method with the CC technique. For each image we rotated the ground truth line in 1 degree intervals from $-5^\circ$ to $5^\circ$ and
Table 7.1: Description of the data set used

<table>
<thead>
<tr>
<th>Data source</th>
<th>Number of images</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>BrainWeb</td>
<td>12</td>
<td>Simulated images with varying noise and INU and also 2 MS-lesion models. Ground truth was available.</td>
</tr>
<tr>
<td>IBSR</td>
<td>8</td>
<td>Real images: 4 normal and 4 pathological. Ground truth was available for 3 (2 normal and 1 pathological) images.</td>
</tr>
</tbody>
</table>

Table 7.2: Comparison with the cross-correlation technique

<table>
<thead>
<tr>
<th>Methods</th>
<th>$\alpha_{mean}$</th>
<th>$\alpha_{stdev}$</th>
<th>$d_{mean}$</th>
<th>$d_{stdev}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our method</td>
<td>0.4</td>
<td>0.39</td>
<td>0.32</td>
<td>0.47</td>
</tr>
<tr>
<td>CC Technique</td>
<td>1.3</td>
<td>0.48</td>
<td>0.77</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Figure 7.10: Results for real and simulated images with varying noise level, INU, and modality: (a). T1WI, (b). T1WI, (c). T1WI with added INU 20%, (d). T1WI with added Noise 5%, (e). T1WI, (f). T1WI-MS lesion, (g). PD, (d). T2WI.

Figure 7.11: Comparison of intensity based CC between the original image and its flipped version. The line that gave the maximum CC was compared with the line estimated by our method. We also computed the cc value for our estimate, and found out that the cc value for our method was lower than the maximum cc value. As shown in Figure 7.11, despite its slightly lower cc value our approach gave visually better results.

For a quantitative comparison, we measured the angular deviation ($\alpha$, in degrees) and the deviation of the Euclidean distance ($d$, in millimeters) of the end points between each method’s estimated MSPs and the ground truth lines. Summary of the results are shown in Table 7.2.
Figure 7.11: Comparison of the proposed method with CC method on MRI with varying artifacts and contrast: (i). Our method. (ii). CC method. (a). T1-Noise 5%, (b). T1-INU 40%, (c). PD, (d). T2.

Figure 7.12: Lacunarity values plotted at each sagittal location in images with varying noise. (a). No noise case, (b). Noise 5%, (c). Noise 9%

As shown in Figure 7.11, our method was robust to noise, INU and different modalities, while CC method was sensitive to these factors. We believe this is due to the fact that our method does not rely on a maximization of pixel-wise grayscale similarity of the two hemispheres. Instead, we compare the structural complexity and the homogeneity by using fractal dimension and lacunarity. Moreover, when the CC as a similarity measure is performed slice-by-slice, it gives less accurate results if the given neuroimage is strongly tilted, as then the left-right similarity breaks.

7.4.3 Discussion

In this section 7.4, we have presented a novel approach based on fractal analysis for detecting the MSP in MR neuroimages. In contrast to many existing methods that mea-
sure the similarity of the two brain hemispheres using intensity-based cross-correlation, our method assumes that the MSP has the most complex and inhomogeneous structure amongst all sagittal slices and this structural complexity shows up as a textural difference on MR images. We have used a combination of fractal dimension and lacunarity as a measure to characterize the structural complexity associated with the mid-sagittal plane.

The proposed method has been tested on various MR images and is robust to different imaging modalities, noise and INU artifacts. Experimental results show the effectiveness of our approach. In comparison with the most frequently used cross-correlation method, the performance of our fractal analysis based method is very encouraging.

However, this method has to perform the computation in two parts in sagittal and axial slices, which is computationally expensive. Additionally, lacunarity is sensitive to extreme level of noise (see Figure 7.12), and in such a condition, if the ROI window considered in the second stage is not chosen carefully, the method may give less accurate results. These limitations motivated us to find a method that can be implemented in 3D brain volume (without performing slice-wise computations), and to find a suitable symmetry measure based on fractal analysis. The next section discusses the proposed method with a significant improvement in accuracy, robustness, and implementation simplicity.

### 7.5 MSPMethod 3

As explained in previous sections, fractal dimension provides a way to quantify the shape complexity of objects using a single numerical value. It has proven to be a useful measure in describing the structure of a wide range of mathematical and naturally occurring objects and patterns [Iftekharuddin, 2005, Uemura et al., 2000]. This section presents a novel method that uses the concept of fractal dimension as a quantitative measure for identifying symmetry plane in 3D MR brain images. It differs from the MSPMethod 2 for a number of reasons. First, it is based on a novel symmetry measure which considers the structural complexity. MSPMethod 2 on the other hand was based on the inhomogeneity and the complexity of the MSP with respect to the other sagittal planes. Then, the current method computes the FD using box-counting method and later uses lacunarity for fine processing if higher accuracy is needed. While most of the existing methods in MSP detection are based on 2D projections of 3D MRI, our MSPMethod 3 considers the information in the 3D volume.

As explained in Chapter 5, various measures that quantify the degree of similar-
It has been proposed in the literature. Anatomical complexity of the brain has made defining symmetry measure for MSP detection a particularly challenging task. As discussed earlier, many methods have considered either the CC [Liu et al., 2001, Prima et al., 2001, Tuzikov et al., 2003] or the KLD as a symmetry measure. To recapitulate, in cross-correlation, the image is reflected across the estimated plane and the \( cc \) is measured between the original and the reflected images. Besides being computationally demanding, CC approach is highly sensitive to asymmetry in brain images. KLD [Volkau et al., 2006a] has been defined as a symmetry measure for MSP detection by assuming that the MSP contains maximum amount of CSF amongst all sagittal slices.

In this method, we propose fractal dimension based symmetry index for detecting MSP directly from 3D MRI. The idea behind our approach is based on the assumption that the left and right hemispheres would be similar in structural complexity. As mentioned previously, it has been shown that two objects with the same fractal dimension can be different in appearance [Taguchi, 1987]. Lacunarity has the ability to differentiate this and even small differences in texture can result in measurably different lacunarity values [Dougherty and Henebry, 2001]. In our experiments we found that the average lacunarity value of the MSP was greater than the immediate neighbouring slices (see Figure 7.14). However, using maximum lacunarity alone as in MSPMethod 2 was not reliable enough, especially for images with pathology or strong noise due to its sensitivity to these factors. Hence, MSPMethod 3 uses a FD based symmetry measure to identify the MSP and lacunarity is later used for obtaining higher accuracy on given a restricted volume of interest.

7.5.1 Procedure

In our method we assume that both the left and right hemispheres have similar FD. Once the 3D brain is divided into two parts in the sagittal direction, the difference of FD of the two parts should be at a minimum when the division is chosen to be at the MSP. Figure 7.13 demonstrates the log-log plots taken at any random sagittal location which is not MSP (left image) and at the MSP ground truth (right image). At the location of the ground truth, the left and right plots nearly coincide.

Based on the observation that the FD difference between the left and right hemispheres would be at a minimum for the MSP, we define a new symmetry criterion. Let the FD of the whole image, the left part, and the right part be denoted as \( F_{DW}, F_{DL}, \) and \( F_{DR} \), respectively, our symmetry measure \( \alpha \) is defined by

\[
\alpha = \frac{F_{DL} - F_{DR}}{F_{DW}}
\]  

(7.4)
Figure 7.13: Log-log plots of $N(r)$ vs. $r$. (a). Random sagittal location, (b). Ground truth MSP location.

Figure 7.14: (a). (i). Sagittal slice left to MSP, (ii). Sagittal slice at MSP, (iii). Sagittal slice right to MSP. (b). Lacunarity value of MSP ground truth and two immediate neighbouring slices.
Computation of fractal dimension and lacunarity

In this method, we used the box-counting method [Russell et al., 1980] to compute the fractal dimension due to its power in representing structural complexity, applicability to objects with little self-similarity, and its easy implementation [Kilic and Abiyev, 2011]. Box-counting method counts the number of cubes of size $r$ needed to cover the non-zero elements of the image data. This procedure can be stated as follows.

1. BEGIN Box-Counting
2. Initialise the cube sizes $r$.
3. for each cube size $r$, $r$ increasing at each iteration do
4. Count the number of cubes $N(r)$ needed to cover the image.
5. end for
6. Estimate $FD$ as the slope of the least squares linear fit to the data.
7. END

In the BC method, lacunarity $\lambda$ is calculated [Nekka, 2002] from the mean ($\mu$) and the standard deviation ($\sigma$) of the number of pixels within the boxes of side length $r$ using Equation 7.2.

Algorithm

Steps for the MSP detection algorithm can be summarized as follows.

1. Read 3D brain data $I(x, y, z)$. $X$, $Y$, $Z$ be the left-right, anterior-posterior and top-bottom axes, respectively.
2. Estimate the FD, $FD_W$ for the whole image.
3. Select the sagittal region $\Omega$ of the image $I$ by ignoring the extreme 20% end slices.
4. For each sagittal location $c$ in the region $\Omega$
   - Estimate the FD, $FD_L$ for the portion of $\Omega$ to the left of $c$.
   - Estimate the FD, $FD_R$ for the portion of $\Omega$ to the right of $c$.
   - Compute $\alpha(c)$ by Equation 7.4 using $FD_W$, $FD_L$, and $FD_R$.
5. By considering all candidate planes, find the $c^*$ that gives the minimum $\alpha$. 

99
6. Assign $c^*$ to be an estimate for the sagittal location for MSP.

To refine the estimated MSP position using lacunarity:

7. Consider a region of interest (ROI) centred on $c^*$, and select sagittal planes $s$ within the ROI centred on $c^* \pm \delta$. When creating these planes, only the co-ordinate in the sagittal direction is changed while keeping the other two co-ordinates similar to those of $c^*$. So, if the co-ordinates of $c^*$ can be given as $(c^*, y^*, z^*)$, co-ordinates of the candidate planes will be $(s, y^*, z^*)$, where $s \in [c^* \pm 1]$. We took $\delta$ as 0.5mm.

8. Compute the average lacunarity values $\lambda(s)$ for the chosen planes $s$. The average lacunarity is obtained by taking the mean of the lacunarity values for all boxes of side length $r$.

9. By considering all candidate planes within the ROI, find the $s_0$ that gives the maximum average value for $\lambda$.

10. Assign $s_0$ to be the sagittal location for MSP.

Although the method is for 3D images, when applying the method on axial or coronal 2D images (in the case that the test image is 2D), computing $\alpha$ is straightforward. When calculating lacunarity, small rectangular regions within the ROI were considered.

Before implementing the method on brain MRI, it was validated by using simulated images with a known fractal dimension. As shown in Figure 7.15, the computed $FD$ was close to the true or theoretical value, showing the reliability of the method. We also tested the accuracy of our symmetry measure method by applying the algorithm on a mathematical fractal image ‘Sierpinski Triangle’. Figure 7.15(b) validates our symmetry measure.

7.5.2 Results

Experimental data set

The MR image data sets have been obtained from IBSR (http://www.cma.mgh.harvard.edu/) and BrainWeb (http://www.bic.mni.mcgill.ca/brainweb/). Although we have considered more than 100 images for validating this method (See Table 7.3), this section shows an evaluation based on 20 scans of normal and pathological cases (See image description in Table 7.1). More thorough evaluation has been done in the next chapter with extensive experiments. T1-, T2- and PD-weighted images have been included in
Figure 7.15: Experiments for the validation of our method. (a) Fractal dimension computed using the box-counting algorithm on an artificially generated fractal image [IDOLON, nd]. (b) Validation of the fractal symmetry detection method on the Sierpinski triangle.

this 20 image data set. Phantom data from BrainWeb were used to analyse the effect of noise and intensity non-uniformity. The size of each 3D image is $181 \times 217 \times 181 (mm^3)$. The robustness of the algorithm to the modality (T1, T2 and PD) of the image has also been checked. Figure 7.16 and Figure 7.17 show some of the results obtained projected on the axial or coronal slices.

<table>
<thead>
<tr>
<th>Data source</th>
<th>Number of images</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>BrainWeb</td>
<td>43</td>
<td>Ground truth was available for all images. These datasets were used to analyse the effect of noise, INU, slice thickness, and rotation.</td>
</tr>
<tr>
<td>IBSR</td>
<td>53</td>
<td>Ground truth was available for 38 images.</td>
</tr>
<tr>
<td>AANLIB</td>
<td>08</td>
<td>Ground truth was available for 4 images.</td>
</tr>
<tr>
<td>Clinical data</td>
<td>36</td>
<td>Ground truth was not available. These images were used to test the applicability of the method, and were visually assessed by a medical doctor.</td>
</tr>
</tbody>
</table>

Visual evaluation

The results were visually assessed by a medical doctor and were judged to be consistently correct. As can be seen in Figure 7.16 and Figure 7.17, the accuracy of our
Figure 7.16: Results for real images taken from IBSR database.

Figure 7.17: Results for real and simulated images with varying noise level, INU, and modality: (a). T1WI, (b). T1WI with added INU 20%, (c). T1WI with added Noise 9%, (d). PD, (e). T2WI, (f). T1WI-MS lesion.
method does not get affected by noise, INU, and different imaging contrasts. This could be understood as both left and right ROIs considered are affected by nearly equal amounts of noise and INU thus cancelling their effects. Our method gives good results in pathological cases as well. We postulate that this is because in the pathological brain the abnormality resides only in a localized area and it does not affect the overall results of our box-counting FD estimation method.

Quantitative evaluation

In order to compare our method with human performance we had the ground truth MSPs manually marked by a medical expert. On five of the IBSR image data, we randomly selected three widely-separated slices from each axial scan for getting the MSP manually marked by an expert. Since the output of our algorithm is a sagittal plane, the expert first judged the accuracy qualitatively, and then, manually marked results on axial slices. Then, we measured the angular deviation ($\theta$, in degrees) and average deviation of the distance ($d$, in pixels) of the end points between the estimated MSPs and the ground truth lines according to Figure 7.18 and Equation 7.5. Summary of the results is shown in Table 7.4.

$$d = \frac{\sqrt{(xt_g - xt_e)^2 + (yt_g - yt_e)^2} + \sqrt{(xb_g - xb_e)^2 + (yb_g - yb_e)^2}}{2}$$  \hspace{1cm} (7.5)
Table 7.4: Difference of the proposed method with the ground truth

<table>
<thead>
<tr>
<th>θ (in degrees)</th>
<th>d (in pixels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>stdev</td>
</tr>
<tr>
<td>0.08</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Comparative evaluation

A thorough comparative evaluation of this method with the existing techniques has been carried out in the next chapter along with a comprehensive discussion.

7.5.3 Discussion

This section proposed a novel method based on fractal dimension for automatically detecting the symmetry plane in 3D MR images. We tested the method on various 3D MR images from different imaging modalities, and got some excellent results. The method is also robust with respect to strong noise, intensity non-uniformity and pathology in the brain.

7.6 Comparative Evaluation of the Three Methods Proposed for MSP Detection

So far, we proposed three methods for MSP detection. In this section we evaluate these methods for pointing out the advantages and disadvantages of each method. In order to assess the robustness of each method to noise, modality, and INU we used 10 simulated images taken from BrainWeb database.

These results are shown in Figure 7.19 and Figure 7.20. We also performed a quantitative comparison as explained in previous sections, by measuring the deviation of the Euclidean distance ($d$, in millimeters) of the end points between each method’s estimated MSPs and the ground truth lines. For MSPMethod1 we also measured the angular deviation (in degrees) although it was not necessary for the other two methods, as the two methods performed computations in the sagittal direction on the simulated images that were already centred. Table 7.5 depicts these results.

However, it should be noted that our goal has been to identify the precise location of MSP. In some of these examples, the difference is about 0.5 mm. According to a radiologist we talked with, in manual delineation, having constant accuracy of less than 1mm is challenging, especially when processing a large number of images.

The merits and drawbacks of these three proposed methods are summarized in Table 7.6.
Table 7.5: Comparison of three proposed methods on their deviation from the ground truth.

<table>
<thead>
<tr>
<th>Image</th>
<th>MSPMethod 1</th>
<th>MSPMethod 2</th>
<th>MSPMethod 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 7.19 (a)</td>
<td>0.30, (1°)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Figure 7.19 (b)</td>
<td>0.13, (1°)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Figure 7.19 (c)</td>
<td>0.10, (0°)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Figure 7.19 (d)</td>
<td>0.04, (1°)</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Figure 7.19 (e)</td>
<td>2.30, (0°)</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Figure 7.20 (a)</td>
<td>1.27, (5°)</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Figure 7.20 (b)</td>
<td>1.07, (5°)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Figure 7.20 (c)</td>
<td>1.07, (0°)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Figure 7.20 (d)</td>
<td>0.93, (0°)</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>Figure 7.20 (e)</td>
<td>0.19, (5°)</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Mean          0.84      0.8      0.25
Stdev          0.71      0.63     0.26
Average computational time 7s 4min 2min

Figure 7.19: Comparison of results obtained from 3 proposed methods. MSPs are projected at axial slices of simulated images with varying noise level, and INU. (a). T1WI with added Noise 3%, (b). T1WI with added Noise 5%, (c). T1WI with added Noise 9%, (d). T1WI with added INU 20%, (e). T1WI with added INU 40%. (i). Results from MSPMethod 1, (ii). Results from MSPMethod 2, (iii). Results from MSPMethod 3.
Figure 7.20: Comparison of results obtained from 3 proposed methods. MSPs are projected at axial slices of simulated images with different image contrast and MS lesion model. (a). T2WI, (b). PD, (c). T1WI-MS lesion. (d). Minor MS lesion model, (e). Major MS lesion model. (i). Results from MSPMethod 1, (ii). Results from MSPMethod 2, iii). Results from MSPMethod 3.

Table 7.6: Strong and weak points of three proposed methods for MSP detection

<table>
<thead>
<tr>
<th>Method</th>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSPMethod1</td>
<td>Robustness to tilted head scans, not easily affected by minor hemispheric asymmetry</td>
<td>Does not perform well in T2 or PD images</td>
</tr>
<tr>
<td>MSPMethod2</td>
<td>Robustness to different image contrasts and INU</td>
<td>Computationally expensive, sensitivity to extreme noise</td>
</tr>
<tr>
<td>MSPMethod3</td>
<td>Robustness to noise, INU, and pathologies</td>
<td>Becomes less accurate when the pathology becomes larger</td>
</tr>
</tbody>
</table>
From the above results it can be seen that MSPMethod 3 shows superior results in terms of accuracy, robustness, and computational cost.

7.7 Chapter Summary

This Chapter has discussed the proposed fractal based approach for MSP detection. Based on this approach two methods have been proposed. Each method has been explained in detail with evaluation. We have found out that while intensity based similarity measure methods can be severely affected by pathologies and hemispheric dissimilarity due to tilted head scans, our methods are less sensitive to such asymmetry. Finally, all three proposed methods for MSP detection have been compared. Since the MSPMethod 3 has shown superior results, in the next chapter, we focus on this method and perform extensive experiments and a thorough evaluation of this method.
Chapter 8

Evaluation, Discussion and Summary

8.1 Preview

The previous two chapters introduced the intensity profile and fractal based methods for MSP detection, and discussed the advantages and disadvantages of all three proposed methods. A conclusion could be drawn that MSP Method 3 which is based on fractal based symmetry measure was superior to the other two methods. The objective of this chapter is to investigate this method further with extensive experiments and comparison with two state-of-the-art methods taken from each category described in Chapter 5. Section 8.2 shows the results from a number of experiments to assess the robustness of the method to image contrast, pathology, and noise. This is followed by a comprehensive discussion in Section 8.3, where comparative studies with the two chosen state-of-the-art methods are discussed. This chapter concludes with a summary of Part I.

8.2 Evaluation

The MR image data sets were provided by the Centre for Morphometric Analysis at Massachusetts General Hospital and is available at http://www.cma.mgh.harvard.edu/ibsr/ [IBSR, nd]. Data sets from AANLIB (http://www.med.harvard.edu/) [AANLIB, nd], and BrainWeb (http://www.bic.mni.mcgill.ca/brainweb/) [BrainWeb, nd, Coscosco et al., 1997] databases have also been used for analysing the robustness of the method. A total of 104 MR scans of normal and pathological cases in T1-, T2- and PD-weighted images were included in the data set (See Table 8.1). Simulated data from
BrainWeb have been used to analyse the effect of noise and intensity non-uniformity. The size of each 3D image is $256 \times 256 \times z$ ($z$ varied from 60 to 64) for IBSR data and $181 \times 217 \times 181$ for BrainWeb simulated images. AANLIB images are $256 \times 256$ 2D images. The robustness of the algorithm to the modality (T1, T2 and PD) of the image has also been checked. The slice thickness varied between 1mm and 9 mm.

<table>
<thead>
<tr>
<th>Data source</th>
<th>Number of images</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>BrainWeb</td>
<td>43</td>
<td>Simulated data. Ground truth was available for all images. These datasets were used to analyse the effect of noise, INU, slice thickness, and rotation.</td>
</tr>
<tr>
<td>IBSR</td>
<td>53</td>
<td>Real data. Ground truth was available for 38 images.</td>
</tr>
<tr>
<td>AANLIB</td>
<td>08</td>
<td>Real data. Ground truth was available for 4 images. These images were used for analysing the effect of range of pathologies.</td>
</tr>
</tbody>
</table>

### 8.2.1 Evaluation of robustness to variety of images

Figure 8.1 to Figure 8.3 illustrate sample results obtained projected on the axial or coronal slices. Figure 8.1 shows some of the results for the clinical images that include both normal and pathological images obtained from IBSR and AANLIB. In order to analyse the effect of noise, INU, slice thickness, and modality; simulated images from BrainWeb have been chosen and these results are shown in Figure 8.2 and Figure 8.3.

Figure 8.2: Performance on simulated images. MSPs projected at axial slices using simulated images from BrainWeb with various noise, INU, and modality.
8.2.2 Comparative Evaluation with the two state-of-the-art methods

We have chosen the two most frequently-used state-of-the-art techniques from each category (feature-based and similarity based approaches) discussed in Chapter 5 to perform a comparative evaluation with our proposed method. The two methods are edge based cross-correlation (Edge CC) method [Liu et al., 2001, Ruppert et al., 2011, Teverovskiy and Liu, 2006] and the Kullback-Leibler divergence based method (KLD) [Volkau et al., 2006a, Volkau et al., 2006b, Puspitasari et al., 2009]. The edge based CC method is different from most common intensity based CC technique in that it performs the cross correlation on an edge image that captures the anatomical structures of the brain and skull ignoring intensity fluctuations. We have implemented the two methods according to their original papers [Liu et al., 2001] and [Volkau et al., 2006a], respectively. Flowcharts of these two methods are shown in Figure 8.4 and Figure 8.5. For the edge based CC method, we have used the canny edge detector as mentioned in [Liu et al., 2001].

Figure 8.3: MSPs projected at axial slices with varying slice thickness and modality.
Figure 8.4: Flowchart of the Edge CC method.

Read the brain volume data and reduce the size of each slice repeatedly by a factor of 2 until the shortest side is between 32 and 64 pixels in length.

Compute binary edge images from the reduced slices.

Pick one of the lowest 2-D brain slices.

Reflect the image about the current vertical centre line and compute the cc sampled every 5°, in the range of [-90° 90°].

Find initial estimate for symmetry axis orientation by taking the angle that gives the maximum cc.

Taking it as the initial estimate, find symmetry axis orientation on each 2-D slice sampled every 1° in the range of [-10° 10°].

Find the mean angle using a robust estimate.

Compute image offsets by finding the maximum cc of each angle-corrected 2D slice and its vertical reflection.

Using the angle and offset, estimate MSP using least median of squares (LMS).
Read the brain volume data

Identify the central slice in the volume along the sagittal direction.

Define a volume of interest (VOI) in the range of ±2 cm around the central slice in the sagittal direction.

Choose the first slice of the VOI as the reference slice, \( S_r \).

Compute the KLD for all slices in the VOI with respect to \( S_r \).

Assign cMSP to the slice with the maximum KLD.

Perform a localized search around cMSP considering a smaller VOI.

Take the slice with the maximum KLD as MSP.

Figure 8.5: Flowchart of the KLD method.
Performance on Simulated Images

In order to perform a quantitative comparison, we used 34 images from the BrainWeb database, and measured the average deviation \( d \) (in pixels) along the sagittal direction. Since the simulated images we considered were centred, and all of these methods gave a result in sagittal direction, there was no need to calculate the angle deviation. In order to compare the mean computational time, all methods were executed on the same machine (Intel Core2 duo CPU p8700 2.53GHz 3.45GB RAM). The proposed method took 3 minutes for a \( 181 \times 217 \times 181 \) image. These results are summarized in Table 8.2. Even the fractal dimension alone in our method gave very good results, once refined using lacunarity, the method gave very accurate results most of the time.

![Figure 8.6: Comparison with the current state-of-the-art techniques. (i). Our method, (ii). CC method, (iii). KLD method. (a). MS Lesion model, (b). Noise 9%, (c). PDW, (d). T2W.](image)

A paired t-test was performed to reveal the statistically reliable difference between the mean value of our method and that of the other two methods. The comparison results with the edge based cc method and the KLD method for the probability value for a 95% confidence level are shown in Table 8.3. These results indicate that we have a statistically significant lower mean value.
Table 8.2: Comparison with the existing work (Tested on simulated images from BrainWeb)

<table>
<thead>
<tr>
<th></th>
<th>$d_{mean}$</th>
<th>$d_{stdev}$</th>
<th>Computational time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our method (FD only)</td>
<td>0.41</td>
<td>0.19</td>
<td>1 min</td>
</tr>
<tr>
<td>Our method (refined using $\lambda$)</td>
<td>0.22</td>
<td>0.25</td>
<td>2 min</td>
</tr>
<tr>
<td>Edge CC method</td>
<td>0.54</td>
<td>0.19</td>
<td>7 min</td>
</tr>
<tr>
<td>KLD method</td>
<td>0.52</td>
<td>0.12</td>
<td>8 s</td>
</tr>
</tbody>
</table>

Table 8.3: Comparative results of the paired t-test

<table>
<thead>
<tr>
<th></th>
<th>FD only with $\lambda$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t-value</td>
</tr>
<tr>
<td>With Edge CC method</td>
<td>3.020</td>
</tr>
<tr>
<td>With KLD method</td>
<td>3.187</td>
</tr>
</tbody>
</table>

Performance on pathological images

The robustness of the algorithm to pathological images was checked using 6 tumor images with progressive history taken from IBSR data. For each image of size $256 \times 256 \times 28$, average pixel deviation from the ground truth was measured. Figure 8.7 shows a comparison with the two state-of-the-art techniques. Although the accuracy is affected by the from the ground truth was only 2.5 pixels. Figure 8.8 shows the best and worst case scenario of each method. Although the edge based method gives excellent results on simulated images with artificial tumors, the method performed poorly in the real images we tested here. The edge based method relies on the initial estimate taken from a lower brain axial slice. In its worst case image, the initial estimate gives incorrect results, thus severely affecting the final results. KLD method performs better in most cases, but still is sensitive to the changes due to pathology as the maximum KLD appears to be at a location different to the MSP’s in those images where the method performed poorly.
Figure 8.7: Deviation from the ground truth with progressive tumor. (a). Tumor images considered, (b). Deviation from the ground truth.
Tolerance to Noise

One of the main strengths we saw in our fractal based method was its robustness to noise. In order to investigate this property further, we made a comparison of the performance of these different techniques on an image with varying Gaussian noise. For this, we used the Shepp-Logan phantom image [Schabel, nd] which is a well-known standard imitation of the human brain. For the cross correlation technique we considered both the intensity based CC and the edge based CC methods. For the edge based CC method, we used the canny edge detector as mentioned in [Liu et al., 2001]. As the KLD technique and the edge based CC technique fail to locate the accurate symmetry plane in the noise free Shepp-Logan phantom image (see Figure 8.9 (a)), we modified the Shepp-Logan image by changing the contrasts of the ellipses in the middle of the image to a darker value (see Figure 8.9 (b)), so that all methods performed equally well in the noise-free image. We did this modification in this way as the edge based method relies on the initial edge image and the KLD method assumes that the maximum KLD occurs at a sagittal slice in the region of 20 mm apart from the medial slice. When this change is applied to the image, the edge image showed the structures in the middle better and the maximum KLD occurred at the midline position.

Plots in Figure 8.9 demonstrate the performance of each method. 30 samples were used for each noise level tested. Since the deviation of our method from the ground truth was zero all the time, it is not visible in the plot. KLD method deviates from the ground truth as it is quite difficult to identify the mid-plane when there are can be
multiple positions with maximum KLD, especially in a noisy image (this has further been discussed in Section 8.3). Both cross correlation methods get affected by noise as they consider intensity/edge based similarity between the two sides. The fractal method, on the other hand, gives excellent results as the technique does not depend on the image intensity itself, but rather it measures the complexity of organisation of image pixels. Figure 8.10 shows the results obtained when each of these methods was applied.
on another phantom brain image with gradient and noise taken from IBSR database.

![Figure 8.10: Performance on a phantom brain image. (a). Phantom brain image, (b). Our method, (c). KLD method, (d). Edge based CC method, (e). Intensity based CC method.]

### 8.3 Discussion

Our analysis showed that the estimation of MSP in MR brain scans by means of fractal analysis is highly robust and accurate. Our method uses FD and lacunarity to locate the MSP as FD alone may not completely characterize the differences in structural inhomogeneity. It is possible that two objects can have the same fractal dimension, but different appearances. In such cases, lacunarity becomes helpful in differentiating objects with the same FD values. During our experiments, in many cases we saw that MSP had maximum average lacunarity value in comparison with the other sagittal slices. However, lacunarity alone was not sufficient; especially in pathological or noisy images as average lacunarity value can be sensitive to these factors. Our method combining lacunarity and fractal dimension was able to give very accurate results. There are various methods to compute FD besides box-counting. We have also experimented with differential box-counting method (DBC) as in MSPMethod 2 described in Chapter 7 [Sarkar and Chaudhuri, 1994]. Besides being computationally more expensive, it was not robust in the presence of strong noise. Brain structure can also be regarded as a mixture of different fractals [Oczeretko et al., 2002]. In that case, multifractal analysis can give the distribution of the fractal dimension. However, for our purpose, the simple box-counting method gives good results.

#### 8.3.1 Advantages of a fractal analysis based method over existing techniques

As mentioned in Chapter 7, a distinct feature of the brain is local self-similarity and the structural similarity of the two hemispheres. However, existing work has not taken advantage of these properties. Most of the methods either consider cross correlation as a symmetry measure or assume that the MSP contains a higher amount of CSF that can be distinguished in a neuroimage. These two approaches suffer from several shortcomings. First, as mentioned previously, the common procedure in the cross correlation technique
is to reflect the image across the estimated plane and to measure the CC between the original and the reflected image. This is a computationally demanding process and the result can easily be affected by the normal or abnormal hemispheric asymmetry. In MRI, artifacts like intensity non-uniformity (INU) give rise to smooth intensity variation across the image which can have a major impact on such intensity based methods [Liew and Yan, 2003, Liew and Yan, 2006]. Although the CSF appears dark in T1-weighted images, on other imaging modalities it appears differently. Ventricles which have a large amount of CSF and the contrast of pathologies on the image can affect the accuracy of a method which assumes that MSP has the maximum amount of CSF. Furthermore, these methods can also be affected by strong noise and low image resolution. There are several advantages of using a fractal based method in brain MSP detection. First, as mentioned in previous sections, fractal geometry is well recognized for having the ability to capture the structural complexity of an object. Second, its scale invariance property allows it to perform well on images with different resolutions or strong noise. The computed log-log plots of images with different noise (see Figure 8.11) demonstrate the noise resistance property of our fractal method. Moreover, as discussed earlier, since our method compares the structural similarity of left and right hemispheres which are affected by nearly equal amounts of noise and INU, performance does not get affected by such artifacts.

8.3.2 Analysis of the two-state-of-the-art methods

While the edge based CC method and the KLD method gave excellent results in simulated images, they did not perform well in real pathological images. In order to investigate this, we superimposed artificial pathologies in simulated brain images as described in [Liu et al., 2001]. When X, Y and Z coordinate axes pointing to the anterior, right and superior directions, respectively, we superimposed spherical “lesions” in the image volume by specifying the centre position (x0, y0, z0), radius and intensity value. Some of the results where these methods performed poorly are shown in Figure 8.12 and Figure 8.16. Below, each of these two methods has been investigated separately.

Performance evaluation of the edge based CC method

Figure 8.12 demonstrates some example images with embedded tumors in which the edge based CC method did not perform well. After further experiments, several relevant observations were found regarding this. In edge detection, simulated images show stronger edges in the skull area, so there is a lesser possibility of these edges getting affected by inner regions, even when an artificial tumor is imposed on to the image. However, in real images, the skull area does not show edges as strong as in simulated
images. Some examples are shown in Figure 8.13, Figure 8.14, and Figure 8.15. Moreover, the edge based CC method relies on the initial estimate of the MSP taken from a lower brain slice. If the edge image of the lower brain slice fails to show a strong symmetry about the MSP due to pathology, for example, the method can break down. Although the edge based CC method is said to be applicable to scans in both axial and coronal formats, we found that the method performs poorer on the coronal slices.

*Figure 8.11: Noise resistance property of our method. Figure shows loglog plots of BrainWeb Images with varying noise.*

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122
Figure 8.12: Examples of images that Edge CC method produced poor results. (a). Imposed tumors on initial lower brain slices. (b). Initial edge images. (c). Estimated MSPs projected on axial slices. (i). T1-weighted image. Tumor radius:50mm. Tumor centre position: (x0=120, y0=60, z0=90), (ii). T2-weighted image. Tumor radius:40mm. Tumor centre position=(x0=60, y0=120, z0=50), (iii). PD-weighted image. Tumor radius:40mm. Tumor centre positions=(x0=110, y0=80, z0=60).
Figure 8.13: Performance of Edge CC method on simulated images and real images: Axial view. (i). Simulated image example from BrainWeb, (ii). Real image example taken from IBSR. (a). Initial lower brain slice, (b). Initial edge image, (c). MSP estimate.

Figure 8.14: Simulated images vs. real images: Coronal view. (i). Simulated image example from BrainWeb, (ii). Real image example taken from IBSR. (a). Initial lower brain slice, (b). Initial edge image, (c). MSP estimate.
Figure 8.15: Edge CC method performed on with and without skull tumor embedded image. (i). Tumor imposed on with-skull image, (ii). Tumor imposed on skull stripped image. (a). Initial lower brain slice, (b). Initial edge image, (c). MSP estimate.
Performance evaluation of the KLD method

According to our experimental results, KLD method produced quite good results although its search region should be restricted. KLD method tries to find the sagittal slice that gives maximum divergence measure with respect to a reference slice. In this method, it is assumed that the MSP contains larger amount of CSF and smaller amount of WM compared to the sagittal slice at 20 mm away from the MSP which has a large manifestation of WM. Therefore, in comparison with the reference slice, MSP is observed to produce a significant peak at CSF and a lower peak at WM. As discussed earlier in Chapter 5, when \( p_i \) and \( q_i \) denote the probability of occurrence of pixels with intensity \( i \) in the comparing sagittal slice and the reference slice, respectively, \( p = p_i \) and \( q = q_i \) are their discrete probability distributions of intensities. Using the KL measure, the change in the probability of the intensity in the two slices is computed.

\[
D_{KL}(p||q) = \sum_i p_i \log \left( \frac{p_i}{q_i} \right)
\]  

(8.1)

In order to understand why the KLD method sometimes fails to give accurate results, we analyzed several experiments on images with artificially embedded tumors. The results are shown in Figure 8.16, projected on axial slices. It can be seen that depending on the pathology and its contrast, there is a possibility that the method does not give expected results.

In order to exemplify this, consider the example shown in Figure 8.17. In this test example, assume that black, dark grey, light grey, and white squares represent the background, CSF, GM, and WM, respectively. If we are trying to find the slice that has higher CSF and lower WM compared to the reference slice, it should be slice P1. Fig. 18 demonstrates the histograms for the three slices. We computed the KL-measure for slice P1 and slice P2 with respect to the reference slice Q. We get \( D_{KL}(p1||q) \) as 0.358 and \( D_{KL}(p2||q) \) as 0.360, thus resulting in the P2.

Therefore, for a given slice, if a pathological state makes enough deviation in any of the tissue contrasts with respect to the reference slice, the KLD method would not be able to detect the MSP accurately. Also, since the method throws away zero values for the denominator to provide continuity of \( p_i \) with \( q_i \), there is a possibility of missing important information. If a reference sagittal slice ever exists with zero occurrence of the CSF contrast, the method would not be able to detect the MSP.

8.3.3 Limitations of the proposed method

Although our method was robust to pathological images in comparison with the other existing techniques, the proposed algorithm still requires a certain degree of symmetry
between the left and right hemispheres. Therefore, it may not give accurate results on images with severe global asymmetry like substantial hemispheric removal. However, this is also a limitation for all existing methods.

Since MSPMethod3 considers sagittal scans, if the initial orientation is either axial or coronal, we have to first get the sagittal slices. This is illustrated in Figure 8.19. For instance, if we have axial scans and the head tilt is large, we have to get an initial estimate of the rotation angle. For this we used MSPMethod1 to estimate large tilt angle.
Then, we can generate sagittal slices taking into account the estimated tilt angle and apply our method to accurately detect the MSP.

As already mentioned, the MSP detected as a straight line or a plane has numerous applications. It also provides symmetry information that can be incorporated into brain tissue segmentation algorithm. However, MSP or IF is not exactly planar. There might
Figure 8.19: A sketch for illustrating the effect of head tilt. (a). The $z$ direction is aligned with the major axis of the scanner, (b). the image co-ordinate system is attached to the head, the mid-plane is shown aligned with the three co-ordinates. (c). axial slices are perpendicular to the mid-plane, (d). sagittal slices are considered in the $x$-direction, they are parallel to the mid-plane. (e). If the mid-plane is now rotated due to head tilt, a plane taken in the $x$-direction is no longer parallel to the mid-plane. This will affect the accuracy of the MSP detection method.

be applications where it becomes advantageous if the non-planar surface that separates the two hemispheres could also be detected [Stegmann et al., 2005]. Although [Lee and Liu, 2012] has started working in this direction, this particular problem of MSP detection has not been fully addressed yet. A possible future work is to extend the fractal based method for detecting non-planar MSP.
8.3.4 Possible future directions

Our goal for identifying the precise location of MSP was based on our aim to integrate brain symmetry information in a segmentation framework. However, as discussed in Chapter 5, MSP detection itself has numerous applications. Another related avenue for future work is to use the location of symmetry plane for asymmetry analysis of pathological brains.

8.4 Summary of Part I

In the first part of this thesis, we have discussed the importance of brain symmetry in brain image analysis and did an extensive survey of the existing work on brain mid-sagittal plane detection, categorising them into the class of feature-based approach or similarity-based approach. We have also discussed different symmetry measures and validation strategies used in existing algorithms.

In Chapter 6 and Chapter 7, we have proposed three methods for accurate localization of the MSP. Each method has been analyzed separately with results and at the end all three methods have been compared by pointing out the strengths and weaknesses. Since the MSP detection in direct 3D images using a fractal-based symmetry measure gave superior results in comparison with the other methods, in this Chapter we have provided a rigorous analysis and extensive experimentation comparing it to two other state-of-the-art methods. We have also discussed the merits and drawbacks of our fractal based method, and have pointed out the strengths and weaknesses of the two-state-of-the-art methods by evaluation on various images. Finally, possible future directions have also been discussed.

Although knowing the location of MSP has numerous applications, in this thesis we aim to integrate this symmetry information into a fuzzy c-means based segmentation algorithm. This is discussed in detail in the next chapter.
Part II

Symmetry Integrated Segmentation
Chapter 9

Proposed Methods for Symmetry Integrated Brain Tissue Segmentation

9.1 Preview

The first part of this thesis dealt with precise identification of the location of brain symmetry plane, so that this information could be incorporated into a brain tissue segmentation framework. As the second phase, the objective of the current chapter is to devise this symmetry integrated method based on a fuzzy c-means clustering framework. As explained in Chapter 4, the main reason for choosing fuzzy c-means clustering as the core technique of our segmentation algorithm is its capability to perform soft segmentation. In the process of achieving our final goal, we have looked into ways of symmetry integration in several different ways, and each of these methods has been discussed here separately. This chapter begins with a brief introduction to symmetry integrated tissue segmentation in Section 9.2. This is followed by the details of the conventional fuzzy c-means algorithm, and the details of the proposed methods. In experiments, synthetic greyscale images have been used to validate the method, and then the performance has been investigated further on simulated brain images to assess the robustness of the method against noise. All proposed methods have been compared with the conventional fuzzy c-means algorithms. The results show the viability of a symmetry based approach, and its robustness against the standard FCM.
9.2 Introduction to Symmetry Integrated Segmentation

As detailed in Chapter 2, many clinical diagnosis and research applications using MR brain images require a segmentation of neuroimages into different tissue classes. However, brain image segmentation is a complex and challenging task. Despite the number of segmentation methods in the literature [Liew and Yan, 2006, Bezdek et al., 1993], the use of automated methods in clinical practice is still limited. Since various noise artifacts, such as random noise, INU and partial volume effect (PVE) has made brain tissue segmentation in MRI a challenging task [Liew and Yan, 2003, Liew and Yan, 2006, Pham and Prince, 1999], it is crucial to take advantage of anatomical features of the brain as a priori information for accurate segmentation.

As described in Chapter 3, fuzzy c-means algorithm as a soft segmentation method is one of the most used techniques for brain image segmentation as it can handle uncertainty by incorporating fuzziness for the belongingness of each image pixel. Therefore, in comparison with crisp or hard segmentation methods, FCM can retain more information from the original image. However, conventional FCM does not consider any spatial information from the image context, which makes it sensitive to noise. Numerous other methods have been proposed by exploiting spatial information and modifying the standard FCM objective function [Liew and Yan, 2003, Ahmed et al., 2002]. These are mostly to incorporate immediate neighbourhood information of a pixel. A previous work based on region-growing algorithm [Sun and Bhanu, 2012] has exploited bilateral symmetry information for image segmentation. However, they have not considered brain image segmentation. Despite the fact that the human brain exhibits approximate bilateral symmetry, to the best of our knowledge, our work is the first attempt to use bilateral symmetry information for brain tissue segmentation.

Specifically, our first step is to accurately identify the brain symmetry plane. Part I of this thesis was devoted for proposing a method to accurately identify the location of the brain symmetry plane which is generally approximated by MSP. Therefore, now we have a robust and effective method to estimate MSP. Having this information in hand, our next objective is to present a novel modified fuzzy c-means algorithm with symmetry information to reduce the effect of noise in MR brain image segmentation. We incorporate symmetry information as an additional term to the conventional FCM method. This whole process is illustrated in Figure 9.1. In conventional FCM algorithms, the classification of each pixel is either determined by its own intensity value or additionally, integrating intensity values of its neighbourhood. However, in our proposed method, the classification of each pixel has been influenced by the pixel in a symmetrical position with respect to the global symmetry axis. We call this pixel a mirror pixel (see Figure 9.4. The primary objective of this chapter is to show the improvement in accuracy.
and robustness of the FCM algorithm with the integration of symmetry information. We extend the method further by incorporating the neighbourhood information using a technique described in [Liew et al., 2000]. In experiments, both synthetic and simulated brain images were used to assess the performance of the new method in comparison with the conventional FCM.

9.2.1 Evaluation

In order to perform a quantitative analysis of our proposed methods we looked into several evaluation techniques. Assessing the performance of an automatic method for brain segmentation is not trivial due to the lack of a standard data set, and the lack of availability of implementations of existing methods [Schmidt, 2005]. In our quantitative experiments, we have used images with ground truth segmentations. There are a few standard evaluation methods reported in the literature, and they all try to measure the accuracy of segmentation with respect to the ground truth segmentation.

Misclassification rate (MCR)

This measure can be used to compare the accuracy of different algorithms. It measures the percentage of misclassified pixels present in a cluster. In an experiment to measure the robustness against noise, we first find the number of pixels in each cluster on our noise-free synthetic images. After that, we add noise to the image and calculate the number of pixels which are misclassified. Finally the percentage of misclassified pixels is calculated using the following formula.

$$\text{MCR} = \frac{\text{Number of misclassified pixels}}{\text{Total number of pixels}} \times 100\%$$

(9.1)

Jaccard similarity index

Jaccard similarity index is another measure that can be found in the literature, which measures the overlap of two sets. This can be expressed in terms of the true positive (TP), false positive (FP), and false negative (FN) sets (Figure 9.2) as follows.

$$J = \frac{TP}{FP + TP + FN}$$

(9.2)

If the two sets do not have common members at all, the Jaccard index is zero. It is one if they are identical. Higher numbers indicate better agreement in the sets, so when we apply this index to evaluate the agreement of brain tissue segmentation results, the goal is to get as close to 1 as possible. For instance, in order to quantitatively assess the
quality of automatic segmentation of each tissue type in comparison to the ground truth (or a manual segmentation), Jaccard index can be used as follows.

\[ J(A, M) = \frac{A \cap M}{A \cup M} \] (9.3)
Figure 9.2: Evaluation is made by using the results set and the ground truth set

where $A$ represents the pixels belonging to a particular class in the automatic segmentation. $M$ represents the pixel belong to the same class in the reference (or the ground truth).

**Segmentation accuracy (SA)**

Another similar form is called segmentation accuracy, and it is given by

$$SA = \frac{Number \ of \ correctly \ classified \ pixels}{Total \ number \ of \ pixels} \times 100\% \quad (9.4)$$

In our experiments, we applied this segmentation accuracy in order to measure the quality of the segmentation performance quantitatively. Since we either discard background pixels or take them as a separate cluster, $TN = 0$.

Figure 9.3: In our experiments, when our ground truth set is $(A \cup B \cup C)$, its complement $= \phi$
9.3 Clustering Method

As mentioned above, our symmetry based segmentation framework has been devised by using fuzzy c-means as the core algorithm. We have conducted experiments with both standard FCM and the kernelized FCM, which we explain briefly in the following subsections.

9.3.1 Conventional fuzzy c-means (FCM) algorithm

The FCM algorithm [Dunn, 1973, Bezdek, 1981] assigns pixels to each category by using fuzzy memberships. This gives the flexibility to express that data points can belong to more than one cluster. Furthermore, these membership degrees offer a much finer degree of detail of the data model [Oliveira and Pedrycz, 2007]. Let \( X = \{x_i, i = 1, 2, \ldots N\} \) denotes an image with \( N \) pixels to be partitioned into \( c \) clusters. \( x_i \) is the intensity value of pixel \( i \). The FCM algorithm is an iterative optimisation that classifies \( X \) into \( c \) fuzzy clusters by minimizing the following objective function with respect to the membership function \( u \) and centroid values \( v \)

\[
J_{FCM} = \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m d_{ik}^2
\]  

(9.5)

where

\[ d_{ik} = \|x_k - v_i\|. \]

Here, \( u_{ik} \) is the fuzzy membership value of pixel \( i \) in cluster \( k \), \([u_{ik}] = U\) representing a partition matrix, \( U \in M \) which satisfies,

\[
M\{u_{ik} \in [0, 1] \mid \sum_{i=1}^{c} u_{ik} = 1 \forall k \text{ and } 0 < \sum_{k=1}^{N} u_{ik} < N \forall N\}
\]

(9.6)

\( v_i, i = 1, \ldots c \), \( \{v_i\}_{i=1}^{c} \) (namely cluster prototypes or cluster centres), denotes the average intensity value in cluster \( i \). \( \| \| \) is a norm metric, and we have considered Euclidean distance here. The parameter \( m \) is a weighting exponent on each fuzzy membership and determines the amount of “fuzziness” of the resulting classification. \( m > 2 \), and generally, \( m = 2 \), and it is used in this study.

This objective function is minimised when pixels close to the centroid of their clusters are assigned high membership values while pixels far from the centroid are assigned low membership values. The objective function can be minimised by taking the first derivatives of \( J_{FCM} \) with respect to \( u_{ik} \), and \( v_i \) and then setting them to zero that results in two necessary conditions for it to be at a local extrema. In the following subsections, we derive these two conditions which can be used as update equations in the clustering
process.

Membership evaluation

The constrained optimisation mentioned above is solved using one Lagrange multiplier.

\[
F_{FCM} = \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m d_{ik} - \lambda \left( \sum_{i=1}^{c} u_{ik} - 1 \right) \tag{9.7}
\]

Taking the derivative of \(F_{FCM}\) with respect to \(u_{ik}\) and setting the result to zero, we get

\[
\frac{\partial F_{FCM}}{\partial u_{ik}} = m u_{ik}^{m-1} d_{ik}^2 - \lambda = 0
\]

Solving for \(u_{ik}\) we have

\[
u_{ik} = \left( \frac{\lambda}{m} \right)^{1/m-1} \times \frac{1}{(d_{ik}^2)^{1/m-1}} \tag{9.8}
\]

Since \(\sum_{t=1}^{c} u_{tk} = 1 \forall k\)

\[
\sum_{t=1}^{c} \left( \frac{\lambda}{m} \right)^{1/m-1} \times \frac{1}{(d_{tk}^2)^{1/m-1}} = 1
\]

or

\[
\left( \frac{\lambda}{m} \right)^{1/m-1} = \sum_{t=1}^{c} (d_{tk}^2)^{-1/m-1}
\]

Substituting this into above Equation 9.8, we get the updating equation for membership values.

\[
u_{ik} = \frac{1}{\sum_{t=1}^{c} (d_{ik}^2)^{2/m-1}} \tag{9.9}
\]

Cluster prototype updating

In the following derivation, we use the standard Euclidean distance which is used in our study. Taking the derivative of \(F_{FCM}\) in Equation 9.7 with respect to \(v_i\), and setting the result to zero, we get

\[
\frac{\partial F_{FCM}}{\partial v_i} = \sum_{k=1}^{N} u_{ik}^m (x_k - v_i) = 0
\]
Solving this for \( v_i \), we get the updating equation for cluster prototypes.

\[
v_i = \frac{\sum_{k=1}^{N} u_{ik}^m x_k}{\sum_{k=1}^{N} u_{ik}^m}
\]  

(9.10)

In addition to above standard fuzzy c-means algorithm, there are a few other main variations like possibilistic FCM. However, accurate initialisation is critical for it to perform well, so details are omitted here.

9.3.2 Kernel-based fuzzy clustering

Standard FCM algorithm generally applies Euclidean distance to measure similarity among image pixels. Hence, it is effective in clustering “spherical” data. In order to cluster more general data set, a kernel-based fuzzy c-means (KFCM) algorithm is proposed [Zhang and Chen, 2004, Girolami, 2002] by exploiting kernel function to measure data’s similarities. KFCM can perform a nonlinear mapping to a high dimensional feature space via a kernel function to replace Euclidean distance in the standard FCM algorithm.

In a similar fashion to standard FCM, and using similar parameters, the KFCM algorithm classifies \( X \) into \( c \) fuzzy clusters by minimizing the following objective function.

\[
J_{KFCM} = \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m \| \Phi(x_k) - \Phi(v_i) \|^2
\]

(9.11)

where \( \Phi(x) \) is an implicit nonlinear map function defined as \( \Phi : x \rightarrow \Phi(x) \in L, x \in X \). \( L \) is a transformed feature space with a higher dimension. The principle behind this is usually called “kernel trick” and its aim is to turn the original nonlinear problem in the input space into potentially a linear one in rather high dimensional feature space as it would facilitate problem solving as proved by Cover [Cover, 1965].

Then, \( \| \Phi(x_k) - \Phi(v_i) \|^2 = K(x_k, x_k) + K(v_i, v_i) - 2K(x_k, v_i) \)

where \( K(x, y) = \Phi(x)^T \Phi(y) \). While Gaussian, polynomial, and sigmoid kernel functions are the three most commonly used kernel functions in the literature, in our experiments we use the Gaussian kernel. In this case, \( K(x, y) = \exp(-\|x-y\|^2 / \sigma^2) \), so, \( K(x, x) = 1 \). \( \sigma \) is width of the Gaussian kernel function. Then, the KFCM objective function in Equation 9.11 can be simplified as follows.

\[
J_{KFCM} = 2 \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m (1 - K(x_k, v_i))
\]

(9.12)

In a similar way to the standard FCM algorithm, the objective function \( J_{KFCM} \) can
be minimised under the constraint of \( U \).

\[
F_{KFCM} = 2 \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m (1 - K(x_k, v_i)) - \lambda \left( \sum_{i=1}^{c} u_{ik} - 1 \right)
\]

By taking the first derivatives of \( F_{KFCM} \) with respect to \( u_{ik} \) and \( v_i \), and zeroing them, respectively, two necessary conditions for \( J_{KFCM} \) to be at its local extrema are obtained as follows.

\[
u_{ik} = \frac{1}{\sum_{t=1}^{c} \left( \frac{(1 - K(x_t, v_i))}{(1 - K(x_k, v_t))} \right)^{1/m-1}}
\]

\[
v_i = \frac{\sum_{k=1}^{N} u_{ik}^m K(x_k, v_i) x_k}{\sum_{k=1}^{N} u_{ik}^m K(x_k, v_i)} \tag{9.14}
\]

However, similar to FCM, KFCM method does not consider spatial information which makes it susceptible to noise. Additionally, KFCM is computationally expensive.

### 9.4 Symmetry Information Incorporated Image Segmentation

As we have explained previously, the integration of spatial information from the image context is important for accurate image segmentation. When segmenting symmetrical or nearly symmetrical image objects, this symmetry information can be utilized to have better segmentation in noisy images, which is our main focus of this study. When modifying FCM, we assume that the location of the global symmetry plane of the symmetrical/approximate symmetrical image is known. As mentioned previously, in brain tissue segmentation this symmetry plane is the MSP. Then, for each pixel a degree of symmetry value is computed. Although various symmetry measures can be used here [O’Mara and Owens, 1996b], we defined a new symmetry measure as follows.

\[
\zeta_i = \frac{d_{ij}}{\text{maxd}} \tag{9.15}
\]

where \( d_{ij} = \| x_i - x_j \| \), when \( j \) is the mirror pixel of \( i \) in the image context (see Figure 9.4.

where maxd is the maximum value of \( d_{ij} \) for \( i = 1, .. N \).

In this way, we can obtain a continuous symmetry value for each pixel in the image. Here, 0 represents perfect symmetry.

In addition to the above metric, we used cross-correlation for a comparative evaluation of symmetry measures, and the hemispheric symmetry. These experiments are detailed in the following subsection.
9.4.1 Analysis of hemispheric symmetry

In order to demonstrate the efficacy of using symmetry as a priori knowledge, first we analyzed the hemispheric symmetry of a number of simulated as well as real brain images. In the first experiment, we used 18 simulated images (each with the size 181 × 217 × 181) from the BrainWeb database, and computed a symmetry value for each pixel in the image using Equation 9.15, and then calculated the averaged symmetry values and their standard deviations. Then, we also performed the same computations on 18 real MR brain images taken from IBSR database. In real images, we performed an image registration for scaling and rotation using our MSP detection algorithm so that the symmetry plane for each image is centred. Figure 9.5 and Figure 9.6 demonstrate these results. In these figures, black pixels indicate perfect symmetry.

Next, we compared our symmetry measure with the cross-correlation based method. These results are shown in Table 9.1. In order to have a more than 99 percent confidence that the mean hemispheric symmetry value for a normal image would be above 0.8, we performed a $t$-test (since sample size < 30). As summarized in Table 9.1, since the computed $t$-values are larger than the critical $t$-value, we have evidence that the mean symmetry value for a normal image would be at least 0.8. Since our metric $\zeta$ has a larger $t$-value than the cross-correlation based measure, it gives better confidence in the symmetry value, and so we proceeded with $\zeta$.

From the above results, we can see that there is a high hemispheric symmetry in MR brain images.
Table 9.1: Comparative results of our symmetry measure and cross-correlation measure performed on 18 images

<table>
<thead>
<tr>
<th>Image No.</th>
<th>Correlation Coefficient</th>
<th>$\zeta$ in Equation 9.15</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.8183</td>
<td>0.9086</td>
</tr>
<tr>
<td>2</td>
<td>0.8813</td>
<td>0.8922</td>
</tr>
<tr>
<td>3</td>
<td>0.8258</td>
<td>0.8459</td>
</tr>
<tr>
<td>4</td>
<td>0.8804</td>
<td>0.8737</td>
</tr>
<tr>
<td>5</td>
<td>0.8691</td>
<td>0.8756</td>
</tr>
<tr>
<td>6</td>
<td>0.8648</td>
<td>0.8495</td>
</tr>
<tr>
<td>7</td>
<td>0.8317</td>
<td>0.8379</td>
</tr>
<tr>
<td>8</td>
<td>0.8255</td>
<td>0.8269</td>
</tr>
<tr>
<td>9</td>
<td>0.8128</td>
<td>0.8308</td>
</tr>
<tr>
<td>10</td>
<td>0.8244</td>
<td>0.8199</td>
</tr>
<tr>
<td>11</td>
<td>0.8680</td>
<td>0.8595</td>
</tr>
<tr>
<td>12</td>
<td>0.8075</td>
<td>0.8242</td>
</tr>
<tr>
<td>13</td>
<td>0.8864</td>
<td>0.8912</td>
</tr>
<tr>
<td>14</td>
<td>0.8595</td>
<td>0.8569</td>
</tr>
<tr>
<td>15</td>
<td>0.8392</td>
<td>0.8509</td>
</tr>
<tr>
<td>16</td>
<td>0.8612</td>
<td>0.8795</td>
</tr>
<tr>
<td>17</td>
<td>0.8695</td>
<td>0.8807</td>
</tr>
<tr>
<td>18</td>
<td>0.8387</td>
<td>0.8597</td>
</tr>
</tbody>
</table>

Mean: 0.8480, $\zeta$: 0.8591

Stdev: 0.025755, $\zeta$: 0.025811

Alternative Hypothesis: $\mu > 0.8, \mu > 0.8$

$t$-value: 7.685, 9.439

Critical $t_{0.001,17}$: 3.646, 3.646
9.5 Modified FCM with Symmetry Information: symFCM1

As mentioned previously, in our algorithm, we assume that the location of the global symmetry plane of the symmetrical/approximate symmetrical image is known. Then, for each pixel a degree of symmetry value is computed. Based on the symmetry metric we defined in Equation 9.15, we define the degree of symmetry for $k$th pixel, $\beta_k \in [0, 1]$ as follows.

$$\beta_k = 1 - \frac{\lambda_{kj}}{\max(\lambda)}$$  \hspace{1cm} (9.16)
Figure 9.6: Hemispheric symmetry analysis performed on real images taken from IBSR database. Results are projected on an axial slice. (a) A sample image slice, (b) Average symmetry value of the relevant slice, (c) Standard deviation of the symmetry values. Black pixels indicate perfect symmetry.

where \( \lambda_{kj} = \text{abs}(\bar{x}_k - \bar{x}_j) \), and \( j \) is the mirror pixel of current pixel \( k \). \( \max(\lambda) \) is the maximum value of \( \lambda_{kj} \) for \( k = 1, \ldots, N \). \( \bar{x}_t \) is the median of the neighbours within a specified window around \( x_t \).

Based on this symmetry information, our modified FCM (symFCM1) objective function can be defined as follows.

\[
J_{\text{symFCM1}} = c \sum_{i=1}^c \sum_{k=1}^N u_{ik}^m \|x_k - v_i\|^2 + \frac{\beta_k u_{ik}^m \|x_j - v_i\|^2}{\alpha_{kj}}
\] (9.17)

Here \( \alpha_{kj} \) is computed from the absolute intensity difference between pixel \( k \) and pixel \( j \), defined by \( 1 + \text{abs}(x_k - x_j) \).

Thus, the update equations for minimizing \( J_{\text{symFCM1}} \) with the necessary conditions can be derived in the same fashion described in Section 9.3.

\[
F_{\text{symFCM1}} = c \sum_{i=1}^c \sum_{k=1}^N u_{ik}^m (\|x_k - v_i\|^2 + \frac{\beta_k \|x_j - v_i\|^2}{\alpha_{kj}}) - \lambda \left( \sum_{i=1}^c u_{ik} - 1 \right)
\]

\[
\frac{\partial F_{\text{symFCM1}}}{\partial u_{ik}} = m u_{ik}^{m-1} (\|x_k - v_i\|^2 + \frac{\beta_k \|x_j - v_i\|^2}{\alpha_{kj}}) - \lambda = 0
\]

\[
u_{ik} = \left( \frac{\lambda}{m} \right)^{1/m-1} \times \frac{1}{(\|x_k - v_i\|^2 + \frac{\beta_k \|x_j - v_i\|^2}{\alpha_{kj}})^{1/m-1}}
\]

Since \( \sum_{t=1}^c u_{tk} = 1 \forall k \)

\[
\sum_{t=1}^c \left( \frac{\lambda}{m} \right)^{1/m-1} \times \frac{1}{(\|x_k - v_i\|^2 + \frac{\beta_k \|x_j - v_i\|^2}{\alpha_{kj}})^{1/m-1}} = 1
\]
Therefore, we get the updating equation for membership values as follows.

\[ u_{ik} = \frac{1}{\sum_{t=1}^{c} \left( \frac{\|x_k - v_t\|^2 + \frac{\beta_k}{\alpha_{kt}} \|x_j - v_t\|^2}{\|x_k - v_i\|^2 + \frac{\beta_k}{\alpha_{kt}} \|x_j - v_i\|^2} \right)^{1/m-1}} \]  

(9.18)

Similarly, considering the standard Euclidean distance, and taking the derivative of \( F_{symFCM1} \) with respect to \( v_i \), and setting the result to zero, we get

\[ \frac{\partial F_{symFCM2}}{\partial v_i} = \sum_{k=1}^{N} u_{ik}^m (x_k - vi + \frac{\beta_k}{\alpha_{kj}} (x_j - vi)) = 0 \]

Solving this for \( v_i \), we get the updating equation for cluster prototypes.

\[ v_i = \frac{\sum_{k=1}^{N} u_{ik}^m (x_k + \frac{\beta_k x_j}{\alpha_{kj}})}{\sum_{k=1}^{N} u_{ik}^m (1 + \frac{\beta_k}{\alpha_{kj}})} \]  

(9.19)

This modified symFCM1 for brain tissue segmentation can be summarized in the following steps. The procedures are as follows:

1: Read the brain volume data.
2: Pre-compute the degree of symmetry matrix for the entire image.
3: Set the number of tissue classes \( c \), select initial cluster centroids, and set the \( \epsilon \) to a small value.
4: Update fuzzy membership \( u_{ik} \) using Equation 9.18.
5: Update cluster centroids \( v_k \) using Equation 9.19.
6: If \( \|U_{new} - U_{old}\| \leq \epsilon \), proceed to step 7, else return to step 4.
7: Get the final segmentation results using the maximum fuzzy membership value of each pixel.

Since the degree of symmetry can be pre-computed, the algorithm is efficient.

9.5.1 Results

A summary of the experimental data set is depicted in Table 9.2. Before proceeding to the experiments with MR brain images, we run the method on simple synthetic images as well as nearly symmetrical natural images. These results are shown in Figure 9.7, Figure 9.8, and Figure 9.9.
Table 9.2: Description of the data sets used

<table>
<thead>
<tr>
<th>Data</th>
<th>Number of images</th>
</tr>
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<tbody>
<tr>
<td>Synthetic images</td>
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<tr>
<td>Natural images</td>
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</tr>
<tr>
<td>Simulated images (BrainWeb)</td>
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<td>Simulated images (IBSR)</td>
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<tr>
<td>Real images (IBSR)</td>
<td>32</td>
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</table>

**Synthetic images**

In order to verify the validity of our approach, we used 2D synthetic greyscale images which have either a global symmetry axis or a global approximate symmetry axis. Figure 9.7 shows these results. It can be seen that the standard FCM (Figure 9.7 (c)) is greatly affected by noise. In comparison, our symFCM1 (Figure 9.7 (d)) is far more robust to noise.

**Real images**

In addition to the above images, we also performed some experiments on real images taken from the UCB database (The Berkeley segmentation dataset and benchmark) [Ren et al., 2006, Martin et al., 2001]. Figure 9.8 and Figure 9.9 show these results.

**Results for brain images**

Our brain image data set comprises the T1-weighted MR scans of normal cases. The simulated MR brain images were obtained from the BrainWeb database of the McConell Brain Imaging Center at the Montreal Neurological Institute, McGill University [BrainWeb, nd, Cocosco et al., 1997] (http://www.bic.mni.mcgill.ca/brainweb/). The size of each image volume was 181x217x181 (in mm) and slice thickness was 1mm. Phantom data with zero INU were simulated from the true model in order to analyse the effect of noise. In addition, INU corrected real brain images with available ground truth have been obtained from IBSR (http://www.cma.mgh.harvard.edu/). Prior to segmentation, the extra-cranial tissues such as skull and meninges were removed from all images. Then, the brain images were classified into three tissue classes: GM, WM, and CSF. These results are shown in Figure 9.10.
Figure 9.7: Comparison of segmentation results of various synthetic greyscale images with white Gaussian noise of variance 0.03. (i). Perfectly symmetrical image, (ii). An image with non-symmetric area, (iii). almost symmetrical image, (iv). Non-symmetrical image, (v). almost symmetrical image. (a). Original image, (b). The same image with noise, (c). Results from standard FCM, (d). Results from symFCM1.
Figure 9.8: Comparison of segmentation results of a real image with added Gaussian noise. (a). Original image, (b) The same image with added Gaussian noise (var=0.01), (c). Results from standard FCM, (d). Results from symFCM1.
Figure 9.9: Comparison of segmentation results of a real image with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.01), (c). Results from standard FCM, (d). Results from symFCM1.
Figure 9.10: Comparison of segmentation results of simulated MR brain images with various levels of noise. (i). Noise 1%, (ii). Noise 3%, (iii). Noise 5%, (iv). Noise 9%. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM1.
Table 9.3: Segmentation accuracy of synthetic images

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<th>symFCM1</th>
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Table 9.4: Segmentation accuracy of simulated brain images

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9.5.2 Evaluation

Qualitative evaluation

In Figure 9.7–Figure 9.10, segmentation results are compared with the segmentation obtained from standard FCM. When a qualitative comparison is made, it can be seen that the proposed method shows better segmentation in these images. When a non-symmetrical image is used as in Figure 9.7 (iv), although there is a misclassified region due to the consideration of symmetry, it still achieves better overall segmentation. Note that the only new knowledge we integrated here is the symmetry information. We hypothesise that the accuracy can further be improved when used along with other spatial information like neighbourhood context.

Quantitative evaluation

In order to measure the quality of the segmentation performance quantitatively, we also apply segmentation accuracy measure, \( SA \) given in Equation 9.4.

Table 9.3 and Table 9.4 depict the SA of the proposed method and the standard FCM when applied to synthetic images and simulated brain images, respectively. The SA column shows that as the percentage of noise is increased, the accuracy for both methods decreases. Our method, however, consistently performs better under all noise conditions than the conventional FCM.

Kernelized version of our algorithm

In order to investigate whether a kernelized version of our algorithm could perform better, we modified the objective function using the kernel method as described in
Section 9.3.2. The modified objective function is as follows.

\[ J_{ksymFCM1} = 2 \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m (\|\phi(x_k) - \phi(v_i)\|^2) + \gamma (\|\phi(x_k') - \phi(v_i)\|^2) \]  

(9.20)

Here, \( k' \) is the mirror pixel, and \( \gamma = \beta/\alpha \) as similar to symFCM1, and explained in Equation 9.16 and Equation 9.17. \( \phi \) is an implicit nonlinear mapping as explained previously, and we have considered Gaussian kernel.

\[
\|\phi(x_k) - \phi(v_i)\|^2 = (\phi(x_k) - \phi(v_i))^T (\phi(x_k) - \phi(v_i))
\]
\[
= \phi(x_k)^T \phi(x_k) - \phi(v_i)^T \phi(x_k) - \phi(x_k)^T \phi(v_i) + \phi(v_i)^T \phi(v_i)
\]
\[
= K(x_k, x_k) + K(v_i, v_i) - 2K(x_k, v_i)
\]
\[
= 2(1 - K(x_k, v_i)) \quad \text{← Gaussian kernel considered}
\]

In a similar way to previous explanations, the objective function \( J_{ksymFCM1} \) can be minimised under the constraint of \( U \). Specifically, taking the first derivatives of \( F_{ksymFCM1} \),

\[
F_{ksymFCM1} = 2 \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m (1 - K(x_k, v_i) + \gamma (1 - K(x_k', v_i))) - \lambda \sum_{i=1}^{c} u_{ik} - 1
\]

with respect to \( u_{ik} \) and \( v_i \), and zeroing them, respectively, two necessary conditions for \( J_{ksymFCM1} \) to be at its local extrema can be obtained as follows.

\[
u_{ik} = \frac{1}{\sum_{t=1}^{c} \left( \frac{1 + \gamma - K(x_k, v_i) - \gamma K(x_k', v_i)}{1 + \gamma - K(x_k', v_i)} \right)^{1/m-1}}
\]

(9.21)

\[
v_i = \frac{\sum_{k=1}^{N} u_{ik}^m x_k K(x_k, v_i) + \gamma x_k' K(x_k', v_i)}{\sum_{k=1}^{N} u_{ik}^m K(x_k, v_i) + \gamma K(x_k', v_i)}
\]

(9.22)

The steps for implementing this algorithm are similar to symFCM1, but the Equation 9.21 and Equation 9.26 are used as update equations. Although results of this kernelized version shows slight improvement in the segmentation accuracy, computational time (12s for 2D image shown in Figure 9.11) is much higher than the symFCM1 (1s for the same image). Figure 9.11 shows some comparison results. Since the improvement is negligible, we proceeded with normal symFCM1 in our further validations.
9.5.3 Conclusion for symFCM1

In this section, we presented a modified fuzzy c-means algorithm that incorporates symmetry information in order to improve the segmentation results. Degree of symmetry was computed for each pixel/voxel about the global symmetry axis/plane. This information was transformed into a weighting function which was incorporated into the objective function. The new method was tested on synthetic images as well as simulated brain MRI. The results showed that the effect of noise in segmentation was considerably less with the new algorithm than with the conventional FCM.

Although this method gives impressive results in symmetrical images, it does not perform well if there is any large asymmetrical area in the image. However, this does not seem to have affected normal brain images which exhibit high symmetry, we wanted to find a method that is more adaptive to the image context. Details of this second method (symFCM2) are given in the next section.

9.6 Modified FCM with Symmetry Information: symFCM2

The basic idea behind this approach is similar to previous method where we compute the degree of symmetry for each pixel with respect to a global symmetry axis of the image, and then this information is integrated into the objective function of the standard FCM algorithm. However, by taking the inspiration from [Liew et al., 2000] we have designed a weighting function which is adaptive to the image content in a way that
the influence from the symmetrical pixel is increased if the degree of symmetry value is larger and vice versa. After showing the feasibility and robustness of the algorithm with the addition of symmetry information, in order to show the improvement of the method, we then further extend the algorithm by considering neighbourhood spatial information.

With a slight modification to the symmetry measure we defined in Equation 9.15, we define the degree of symmetry for the th pixel,

\[ \beta_k = 1 - \gamma_k \]  

(9.23)

Here,

\[ \gamma_k = \frac{1}{N_R + 1} \left( \|x_k - x_{k'}\| + \sum_{r \in N_k} \|x_r - x_{r'}\| \right) \]  

(9.24)

\[ = \|\overline{x}_k - \overline{x}_{k'}\| \]  

(9.25)

where \( x_t = \frac{1}{N_R + 1}(x_t + \sum_{r \in N_t} x_r) \)

\( \beta_k \) is the degree of symmetry for the th pixel, and \( k' \) is the mirror pixel of \( k \) (see Figure 9.12). \( N_k \) stands for the set of neighbours in the considering window and \( N_R \) is the cardinality of \( N_k \).

![Figure 9.12: Degree of symmetry is measured considering a neighbourhood of each pixel: an example with a first-order neighbourhood.](image)

We propose our modification to FCM by introducing an additional term that allows the labeling of a pixel to be influenced by the label of its mirror pixel. Here, we define a weighting function as follows.

\[ \alpha(\beta) = \frac{1}{1 + e^{-(\beta - \mu)/\sigma}} \]  

(9.26)

\( \mu \) is the global averaged symmetry value of the image. \( \sigma \) controls the influence of the mirror pixel, and here we have used the standard deviation of the degree of symmetry values. By setting a threshold value to \( \mu \), the symmetry influence can completely be
turned off, if \( \mu < \text{threshold} \).

In a certain pixel, if the degree of symmetry \( \beta \) is large, then \( \alpha \rightarrow 1 \) whereas for small \( \beta \), \( \alpha \rightarrow 0 \). Since the weighting function can be pre-computed, the computation time of the algorithm can greatly be reduced.

Based on this symmetry information, our modified FCM (symFCM2) objective function can be defined as follows.

\[
J_{\text{symFCM2}} = \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m \|x_k - v_i\|^2 + \alpha_k u_{ik}^m \|x_{k'} - v_i\|^2
\]  
(9.27)

As before, the update equations for minimizing \( J_{\text{symFCM2}} \) with the necessary conditions can be derived as follows.

\[
F_{\text{symFCM2}} = \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m (\|x_k - v_i\|^2 + \alpha_k \|x_{k'} - v_i\|^2) - \lambda \left( \sum_{i=1}^{c} u_{ik} - 1 \right)
\]

\[
\frac{\partial F_{\text{symFCM2}}}{\partial u_{ik}} = m u_{ik}^{m-1} (\|x_k - v_i\|^2 + \alpha_k \|x_{k'} - v_i\|^2) - \lambda = 0
\]

\[
u_{ik} = \left( \frac{\lambda}{m} \right)^{1/m-1} \times \frac{1}{\left( \|x_k - v_i\|^2 + \alpha_k \|x_{k'} - v_i\|^2 \right)^{1/m-1}}
\]

Since \( \sum_{i=1}^{c} u_{ik} = 1 \forall k \)

\[
\sum_{i=1}^{c} \left( \frac{\lambda}{m} \right)^{1/m-1} \times \frac{1}{\left( \|x_k - v_i\|^2 + \alpha_k \|x_{k'} - v_i\|^2 \right)^{1/m-1}} = 1
\]

Therefore, the updating equation for membership values becomes

\[
u_{ik} = \frac{1}{\sum_{i=1}^{c} \left( \|x_k - v_i\|^2 + \alpha_k \|x_{k'} - v_i\|^2 \right)^{1/m-1}}
\]  
(9.28)

Similarly, updating equation for cluster prototypes can be obtained by solving the \( F_{\text{symFCM2}} \) for \( v_i \) considering the standard Euclidean distance.

\[
v_i = \frac{\sum_{k=1}^{N} u_{ik}^m (x_k + \alpha_k x_{k'})}{\sum_{k=1}^{N} u_{ik}^m (1 + \alpha_k)}
\]  
(9.29)

This modified symFCM2 for image segmentation can be summarized in the following steps.
Read the brain volume data.
Pre-compute the degree of symmetry matrix for the entire image based on the symmetry plane.
Set the number of tissue classes $c$, select initial cluster centroids, and set the $\epsilon$ to a small value ($1 \times 10^{-5}$).
Update fuzzy membership $u_{ik}$ using Equation 9.28.
Update cluster centroids $v_i$ using Equation 9.29.
If $\|U_{new} - U_{old}\| \leq \epsilon$, proceed to step 7, else return to step 4.
Get the final segmentation results using the maximum fuzzy membership value of each pixel.

9.6.1 Extended symFCM2 with neighbouring information integration (s-symFCM2)

Since the pixels on an image are highly correlated, neighbouring spatial information becomes important in image segmentation. Therefore, in order to improve our symmetry integrated method further, we incorporated neighbourhood information as an additional term to the symFCM2 objective function. We adapted the spatial continuity incorporated clustering method described in [Liew et al., 2000]. As explained previously, this technique is based on an adaptive dissimilarity index that takes into account the influence of the neighbouring pixels in a $3 \times 3$ window. Its adaptive index is capable of enhancing the influence of the neighbouring pixels on the centre pixel depending on whether the neighbourhood window is in a homogeneous region or not.

Incorporating this spatial continuity condition into our symFCM2, we define the new objective function s-symFCM2 as follows.

$$J_{s-symFCM2} = \sum_{i=1}^{c} \sum_{k=1}^{N} u_{ik}^m \|x_k - v_i\|^2 + \alpha_k u_{ik}^m \|x_{k'} - v_i\|^2 + \lambda_k u_{ik}^m \|x_k - v_i\|^2$$

(9.30)

where $\bar{x}_k = \frac{1}{N_R} \sum_{r \in N_k} x_r$. Here, for computational efficiency, we have used the mean value of the neighbours ($\bar{x}_k$) by assuming that the number of edges are small in comparison with the smoothed region.

$\lambda$ is the dissimilarity index explained in [Liew et al., 2000], and here we have adapted the parameters as follows.

$$\lambda = \frac{1}{1 + e^{(\partial - \mu)/\sigma_s}}$$

(9.31)

Here, $\partial (k) = \left( \frac{1}{N_R} \sum_{r \in N_k} \|x_k - x_r\|^2 \right)$ for $r \in N_k$, and
\[ \mu_s = \frac{1}{N} \sum_{k=1}^{N} \hat{O}(k) \]

For the steepness parameter \( \sigma_{sk} \), we used the standard deviation of the distances \( \| x_k - x_r \| \) in the neighbouring window.

As in a similar fashion to previous updating equations, equations for \( u_{ik} \) and \( v_i \) for \( J_{s-symFCM2} \) can be obtained as follows.

\[
u_i = \frac{\sum_{k=1}^{N} \frac{u_{ik}^n (x_k + \alpha_k x_k' + \lambda_k \bar{x}_k)}{\sum_{k=1}^{N} u_{ik}^n (1 + \alpha_k + \lambda_k)}}{\sum_{k=1}^{N} u_{ik}^n (1 + \alpha_k + \lambda_k)}
\]

The steps in the extended algorithm are similar to procedure in symFCM2, except for computing a mean filtered image and the parameter \( \lambda \) for neighbourhood term. Membership values and centroids are updated using Equation 9.32 and Equation 9.33, respectively.

9.6.2 Results

A summary of the experimental data set is depicted in Table 9.2. Similar to symFCM1, in order to evaluate the validity of our method, first we used 2D synthetic greyscale images which have either global symmetry axis or a global approximate symmetry axis. This was followed by experiments performed on simulated brain images obtained from the McConell Brain Imaging Center at the Montreal Neurological Institute, McGill University. (http://www.bic.mni.mcgill.ca/brainweb/) [BrainWeb, nd, Cocosco et al., 1997]. The size of each image volume was \( 181 \times 217 \times 181 \) (in mm) and slice thickness was 1mm. Various noise images with zero INU were simulated for the experiment in order to analyse the effect of noise. In addition, real brain images with available ground truth have been obtained from IBSR (http://www.cma.mgh.harvard.edu/). As before, prior to segmentation, the extra-cranial tissues such as skull and meninges were removed from all images. Then, the brain images were supposed to be classified into three tissue classes: GM, WM, and CSF.

Synthetic images

The figure below illustrates the clustering results of two synthetic images corrupted by Gaussian noise with variance 0.03. Figure 9.13 (i) is a perfectly symmetrical image. As demonstrated in the figure, standard FCM (Figure 9.13 (i)-(c)) is greatly affected
by noise (SA=98.91%). In comparison, our method symFCM2 (Figure 9.13 (i) (d)) is far more robust to noise (SA=99.94%). Although the method SFCM with neighbourhood information described in [Liew et al., 2000] removes most of the noise (Figure 9.13 (i) (e)), the result is still not perfect (SA=99.97%). Adopting this neighbourhood information into our algorithm, the extended s-symFCM2 method (see Figure 9.13 (i) (e)) gives perfect results (SA=100.00%). We also applied the same algorithms to a few other synthetic images which include non-symmetrical images. These results are illustrated in Figure 9.13, Figure 9.14, and Figure 9.15.

**Real images**

Furthermore, for testing the performance on natural images, we used several real images taken from the UCB database (The Berkeley segmentation dataset and benchmark) [Ren et al., 2006, Martin et al., 2001]. Figure 9.16 shows these results.

**Results for brain images**

The results for simulated MR brain images with varying noise are shown in Figure 9.17, Figure 9.18, and Figure 9.19. It can be seen that the performance of the standard FCM is greatly affected by noise. While both SFCM and symFCM2 display a slightly better accuracy, when both are combined together, s-symFCM2 shows a significant improvement in robustness to noise.
Figure 9.13: Comparison of segmentation results of synthetic images with added Gaussian noise. (a). Original image, (b). the same image with added Gaussian noise (var=0.03), (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
Figure 9.14: Comparison of segmentation results of synthetic images with added Gaussian noise. 
(a). Original image, (b). The same image with added Gaussian noise (var=0.03), (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
Figure 9.15: Comparison of segmentation results of a synthetic image with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.03), (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
Figure 9.16: Comparison of segmentation results of a real image with added Gaussian noise. (a). Original image, (b). The same image with added Gaussian noise (var=0.01), (c). Results from standard FCM, (d). Results from symFCM2, (e). Results from SFCM, (f) Results from s-symFCM2.
Figure 9.17: Comparison of segmentation results of simulated MR brain images with various levels of noise. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
Figure 9.18: Comparison of segmentation results of simulated MR brain images with various levels of noise. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
Figure 9.19: Comparison of segmentation results of simulated MR brain images with various levels of noise. (a). MR image with noise, (b). Ground truth, (c). Results from standard FCM, (d). Results from symFCM2 only with symmetry information, (e). Results from SFCM, (f). Results from s-symFCM2 with both symmetry and neighbourhood information.
Table 9.5: Segmentation accuracy of synthetic images

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<th>SFCM</th>
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Table 9.6: Segmentation accuracy of simulated brain images

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9.6.3 Evaluation

Qualitative evaluation

According to the results shown from Figure 9.13 to Figure 9.19, when a qualitative comparison is made, it can be seen that the proposed method shows better segmentation in comparison with the results obtained from standard FCM. Furthermore, extended method with neighbouring information (s-symFCM2) shows better results than the SFCM. Even when non-symmetrical images are used, although there are some misclassified regions due to the consideration of symmetry, symFCM2 still achieves better overall segmentation in comparison with FCM, and s-symFCM2 shows further improved results.

Quantitative evaluation

Table 9.5 and Table 9.6 depict the segmentation accuracy SA of the proposed methods (symFCM2 and s-symFCM2), the standard FCM and SFCM when applied to synthetic images, and brain simulated images, respectively. SA value is computed by averaging the segmentation accuracy over 30 runs. The SA columns show that as the percentage of noise is increased, the accuracy for all methods also decreases. symFCM2, however, is much more robust to increased noise than the conventional FCM. s-symFCM2 performs better than the other methods under all noise conditions.

Results for real brain images are depicted in Table 9.7. It can be observed that s-symFCM2 exhibits a significant improvement in comparison with the standard FCM. However, in practice, before applying our method in clinical images several other artifacts such as INU and pathological asymmetry need to be tackled.
Table 9.7: Segmentation accuracy of real brain images

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<thead>
<tr>
<th>Real Brain Images</th>
<th>FCM</th>
<th>symFCM2</th>
<th>SFCM</th>
<th>s-symFCM2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Image 1</td>
<td>70.48%</td>
<td>71.59%</td>
<td>70.60%</td>
<td>71.81%</td>
</tr>
<tr>
<td>Image 2</td>
<td>88.85%</td>
<td>89.25%</td>
<td>89.47%</td>
<td>89.54%</td>
</tr>
<tr>
<td>Image 3</td>
<td>70.59%</td>
<td>72.28%</td>
<td>70.63%</td>
<td>71.95%</td>
</tr>
</tbody>
</table>

9.6.4 Conclusion for symFCM2

In this section, we presented another modified fuzzy c-means algorithm that incorporates symmetry information in order to improve the noise sensitivity in image segmentation. The difference between this method and the symFCM1 described in the previous section is that the new method is adaptive to the asymmetry present in the image. The method was tested on both synthetic and real images. Results showed that the noise sensitivity was considerably reduced in segmentation in comparison with the conventional FCM. We further improved the algorithm with the addition of neighbourhood spatial information. Our results show that symmetry information compliments the spatial continuity information, thus showing improved accuracy and robustness.

9.7 Comparison of the Two Proposed Methods symFCM1 and s-symFCM2

Both methods proposed above possess far more robustness to noise than the standard FCM. symFCM2 was developed so that it could be more adaptive to the asymmetry found in images. This is especially useful when segmenting natural images. Comparison results of the symFCM1 and s-symFCM2 are summarized in Table 9.8. Note that in symFCM1, only symmetry information is considered while in s-symFCM2, both symmetry and neighbourhood information is taken into account. Although, symmetry information alone gave more accurate results than the standard FCM results, the accuracy can further be improved with the incorporation of neighbourhood information.

9.8 Limitations

In this symmetry based approach, small errors in the initial detection of the symmetry plane might weaken the accuracy of the segmentation algorithm. This is the reason for conducting extensive trials with a thorough analysis to validate the MSP detection method in Chapter 8. Nevertheless, in order to demonstrate the performance of the segmentation with respect to the accuracy of the symmetry axis estimates, segmentation accuracy was computed for varying deviations (from $-5^\circ$ to $5^\circ$) from the ground truth.
Table 9.8: Segmentation accuracy of symFCM1 and s-symFCM2

<table>
<thead>
<tr>
<th>Image</th>
<th>symFCM1</th>
<th>s-symFCM2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Image 1</td>
<td>99.96%</td>
<td>100.00%</td>
</tr>
<tr>
<td>Synthetic Image 2</td>
<td>99.62%</td>
<td>100.00%</td>
</tr>
<tr>
<td>Synthetic Image 3</td>
<td>98.38%</td>
<td>98.70%</td>
</tr>
<tr>
<td>Synthetic Image 4</td>
<td>96.36%</td>
<td>98.74%</td>
</tr>
<tr>
<td>Synthetic Image 5</td>
<td>96.98%</td>
<td>99.03%</td>
</tr>
<tr>
<td>Synthetic Image 5</td>
<td>96.98%</td>
<td>99.03%</td>
</tr>
<tr>
<td>MR brain image with Noise 5%</td>
<td>97.08%</td>
<td>97.12%</td>
</tr>
<tr>
<td>MR brain image with Noise 7%</td>
<td>95.73%</td>
<td>96.40%</td>
</tr>
<tr>
<td>MR brain image with Noise 9%</td>
<td>94.43%</td>
<td>95.49%</td>
</tr>
</tbody>
</table>

This is illustrated in Figure 9.20.

It can be observed that when the noise level is low (5%), symmetry incorporated method performs poorly when the deviation from the ground truth symmetry axis is larger than $2^\circ$. However, when the noise level is high (9%), the symmetry integrated method still manages to give better results in comparison with the standard FCM.

9.9 Chapter Summary

This Chapter has discussed the proposed symmetry integrated approach for MR brain tissue segmentation. Based on this approach, two methods have been proposed. In method 2, we also incorporated neighbourhood information to further improve the results. Each method has been explained in detail with evaluation. We have observed that while the standard FCM could be severely affected by noise, our methods are far more robust to noise. Finally, both proposed methods for brain tissue segmentation have been compared. Although symmetry information alone can reduce the noise effect, both symmetry and neighbourhood integrated method demonstrates superior results. These results indicate that symmetry information compliments the spatial continuity information, thus showing improved accuracy and robustness.
Figure 9.20: Segmentation Accuracy vs. deviation from the ground truth. (a). MR brain image with simulated noise 5%, (b). MR brain image with simulated noise 9%.
Chapter 10

Discussion

10.1 Preview

This thesis has discussed the problem of automatic brain tissue segmentation in MR images. It is an interesting, but a challenging task which can ultimately have a major impact on early diagnosis of neurodegenerative diseases like Alzheimer’s disease.

This chapter begins with a summary of the thesis and the novel contributions presented in this thesis. This is followed by a discussion of potential future directions of research that directly follow from this work. The chapter ends with the conclusion of the thesis.

10.2 Summary

In this thesis we have looked into the utilisation of symmetry information in MR brain tissue segmentation. As a consequence of the task of brain tissue segmentation being motivated from practical concerns, necessary background knowledge and application areas were discussed in Chapter 2. The existing techniques were surveyed and their merits and limitations were pointed out in Chapter 3. One of the main conclusions that could be drawn from the discussion of existing literature was that using anatomical information such as shape, size, and symmetry as prior knowledge could improve segmentation results. The main objective of this thesis was to explore symmetry feature in brain image analysis, and to incorporate symmetry as a prior knowledge to the existing brain tissue segmentation algorithms. Inspiration and the main framework for exploiting brain symmetry were introduced in Chapter 4. In order to use symmetry information in brain tissue segmentation, the symmetry plane needs to be correctly identified. In Chapter 5, a thorough review of the existing approaches for brain sym-
metry plane detection was given. It also pointed out the limitations of the existing approaches. Chapter 6 proposed a novel method to detect brain symmetry plane or MSP in T1-weighted MR brain images. Fractal analysis was introduced in Chapter 7 for accurate and robust identification of MSP in images with varying contrasts, noise artifacts, and pathology. Chapter 8 evaluated the performance of this method with various challenging images, and compared the performance with two major state-of-the-art techniques. It also contained a discussion and a summary of the first part of this thesis. Finally, in Chapter 9, automatic brain tissue segmentation framework that integrates symmetry information was devised, and implemented. It also evaluated the performance of the method by comparing it to the conventional fuzzy c-means algorithms. Results demonstrated that symmetry knowledge could play a key role in reducing the noise sensitivity.

10.3 Contribution

The primary contribution of this thesis is to study and use symmetry information as a spatial prior knowledge for facilitating the automatic segmentation of brain tissues in MR images. The major contribution of this work involved the following three aspects.

First, a simple, but robust method based on anatomical and radiological properties has been proposed for extracting the brain symmetry plane or MSP in T1-weighted MRI. The main strength of this method is its robustness to tilt of the head scan. Then, this method has been extended to other imaging modalities. Here, we have claimed that fractal analysis can be used as a symmetry measure for robust identification of brain symmetry plane. Based on the fact that the structural similarity of the two brain hemispheres outperforms their intensity based similarity, a novel approach has been proposed for detecting the MSP. The proposed method has proven to be robust to extreme noise, and pathology.

Second, a thorough analysis and a discussion has been made for using brain symmetry plane as a spatial prior knowledge for brain tissue segmentation.

The third contribution involved devising a fuzzy c-means based framework for incorporating symmetry information. Two methods have been proposed by modifying the standard FCM objective function. Results have demonstrated that the symmetry information integrated method is far more noise resistant in comparison with the conventional FCM. We have further improved the algorithm with the addition of neighbourhood spatial information. Our results have proved that symmetry information compliments the spatial continuity information, thus demonstrating improved accuracy and robustness.
10.4 Limitations and Future Work

One potential problem with the approach presented here is that the accuracy of symmetry information seems to rely on the precision of the symmetry plane detection algorithm. In other words, small errors in the initial detection of the symmetry plane might weaken the accuracy of the segmentation algorithm. Therefore, we conducted extensive trials with a thorough analysis in order to validate our method for MSP detection.

While we understood symmetry information could certainly improve segmentation results, there are several possible extensions. Quantification of continuous symmetry during tissue segmentation can be improved with a deeper analysis based on the tissue type and a probabilistic atlas. For instance, we could observe that WM as a whole exhibits less symmetry than GM. Therefore, by combining a probabilistic atlas with a tissue dependent symmetry measure, the segmentation accuracy can further be improved.

Another important direction for future work involves the extension of our final segmentation algorithms to deal with the bias field. As mentioned in Chapter 3, for some of our experiments that needed bias field estimation we used a prior work based on multiplicative MR image formation model [Liew and Yan, 2003]. However, we can combine these two methods, so that the final system can handle intensity non-uniformity while giving accurate and robust results.

A practical application of the proposed framework requires an efficient user interface. Therefore, one of the necessary future work is to combine all image processing tasks together to build a graphical user interface that can be used to display, analyse, and manage the results.

Another avenue is to use this symmetry information for identifying various pathological brain tissues.

Finally, the symmetry integrated segmentation methods presented in this thesis can be employed in other non-medical applications such as segmentation of mirror symmetrical images.

10.5 Conclusion

Although experts use symmetry as one of the discriminating features to manually analyse brain images, it is not exploited in existing automated methods. The symmetry based paradigm proposed in this thesis is grounded on the hypothesis that symmetry information can play a key role in improving the existing brain tissue segmentation algorithms. Integrating symmetry information as a prior knowledge has the potential
to strengthen the robustness of a brain tissue segmentation algorithm. This thesis has thoroughly analysed the importance of symmetry. The novel segmentation approach taken in this work consists of two major parts. First, the precise location of brain symmetry plane has been determined. Then, this symmetry information has been integrated into a fuzzy c-means clustering framework to improve the accuracy of brain tissue segmentation in MRI. All proposed methods have been evaluated on various challenging tasks. Results have proved the effectiveness and robustness of our approaches, thus demonstrating that the integration of symmetry information promises to enhance the algorithm performance in brain tissue segmentation. These results set the stage for future research aimed at ultimately providing medical experts with a reliable method to quantify brain tissues with high accuracy. This can make a significant contribution towards the improvement of diagnostic capability of brain imaging.
Glossary

- **Active Contour**: A boundary that adaptively adjusts itself based on the image data.
- **ANN**: Artificial Neural Network, a learning method consisting of a set of nodes, where each node may apply a mathematical operation to its inputs, and there exists (adjustable) weights along the connections between nodes.
- **Atrophy**: Decrease in size or wasting away of a body part or tissue.
- **Bayes Theorem**: A method to optimally calculate conditional probabilities, given prior probabilities.
- **B-spline**: A piecewise polynomial function that can be recursively defined.
- **Bias Field**: A field that varies spatially over an image and that describes the deviation at each pixel from its uncorrupted value.
- **Brain Masking**: The segmentation of the brain from surrounding tissues.
- **Classification**: The task of assigning a class (from a finite set) to examples based on a set of measured features.
- **Conditional Probability**: The probability of an event, given the known information.
- **CSF**: Cerebro-spinal Fluid, normal fluid present within the brain.
- **CT**: Computer Tomography, an X-Ray based method for producing three-dimensional volumes.
- **Edema**: Swelling (excess water).
- **Edge Detection**: Processing of an image to highlight/detect edges.
- **EM**: Expectation Maximization, a general approach to learning with hidden variables.
- **Entropy**: An information content measure that considers the likelihoods of individual events occurring.
- **fMRI**: Functional Magnetic Resonance Imaging, a technique for assessing activation of different parts of the brain.
- **FD**: Fractal dimension, an index for quantifying the complexity of fractal patterns/objects as a ratio of the change in detail to the change in scale.
- **Gaussian Distribution**: Synonym for ‘normal distribution’, a parametric distribution characterized by its mean and standard deviations.
- **ICM**: Iterated Condition Modes, a method of inference in Random Fields.
- **IF**: Inter-hemispheric fissure, the deep groove that separates the two brain hemispheres.
- **INU**: Intensity Non-uniformity, a smooth intensity variation across the image.
- **Jaccard Measure**: A similarity measurement between two sets.
- **Knowledge-Based Approaches**: A segmentation strategy that consists of manually engineering rules and/or processing steps that will lead to a segmentation.
- **KNN**: K-Nearest Neighbours, a classification method that assigns instances to the class label of the k closest training instances in the feature space.
- **Lacunarity**: Lacunarity, from the Latin lacuna meaning “gap”, is a measure of how patterns, especially fractals, fill space, where patterns having more or larger gaps generally have higher lacunarity.
- **Least Squares**: A regression method that minimizes the sum of the squared distance from the model to the training data.
- **Level Set**: An active contour method that is convenient for modelling three-dimensional objects.
- **Markov Random Field**: A statistical model that takes into account dependencies in the labels of neighbouring instances, in addition to dependencies between features and labels.
- **MAP**: Maximum a posteriori, MAP estimation involves calculating the parameters that maximize the likelihood of the data occurring, given the model chosen and a prior probability over the model parameters.
- **ML**: Maximum Likelihood, ML estimation involves calculating the parameters that maximize the likelihood of the data occurring, given the model chosen.
- **Modality**: An imaging medium. For example, T1-weighted MR images, or CT images.
- **MR**: Magnetic Resonance, the physical property being measured in MRI.
- **MRI**: Magnetic Resonance Imaging, a technique to visualize parts of the human body based on water/fat content.
- **MSP**: Mid-sagittal plane, a vertical plane through the midline of the body. In this thesis it is predominantly the plane that divides left and right brain hemispheres.
- **Slice**: An orthogonal view of the body part being visualized by the MRI.
- **Supervised Learning**: A framework that employs a set of measured features and labeled training examples to learn a model that maps from the values of the features to the labels.
• **SVM**: Support Vector Machine, an approach to classification that seeks to maximize the margin between two classes.
• **T1-weighted**: An MR image that highlights fat locations.
• **T2-weighted**: An MR image that highlights water locations.
• **Transverse**: A synonym for axial.
• **Voxel**: Volume element, a three-dimensional analog of a picture element (pixel).
Bibliography


