Novel level set based statistical frameworks for segmentation of MR images

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**Novel Level Set Based Statistical Frameworks for
Segmentation of MR Images**

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Summary

Segmentation is one of the most challenging research areas in medical image analysis. In this context, a tremendous amount of research has been focused on the active contour models based on implicit-based level set methods. In the literature, the non-parametric models have been proposed which are more robust to noise, but they suffer from local minima. On the other hand, the statistical model based methods (i.e. the parametric models) allow object shape variations subject to some shape prior constraints. Although these methods are more robust in dealing with noise and low contrast, they are very restricted to cover large range of shape variability.

In the first major part of this thesis, we address these difficulties by proposing a new joint parametric and non-parametric curve evolution algorithm where the advantages of both the parametric and non-parametric curve evolutions are integrated using a Maximum a Posterior (MAP) framework. Our framework is a unified analytical formulation jointly using two curves to match the object shape in an iterative manner. As a result, our new joint curve evolution algorithm is robust and reliable and at the same time, yields more accurate segmentation results when it is compared to both the parametric and non-parametric methods. We conclude this part of our research work by demonstrating the utility of the proposed joint curve evolution algorithm by applying it to Magnetic Resonance Images (MRIs): the segmentation of the ventricle frontal horns, the putamens and the thalamus structures. In general, comparative results illustrate that our novel framework performs significantly better than the parametric methods and the non-parametric models.

The second major part of our thesis is focused on various contributions for solving very important problems for estimating level set function using a Maximum a

Posterior (MAP) framework. Firstly, we propose a novel Expectation-Maximization (EM)-based shape evolution algorithm. In our framework, the distributions of the incomplete observation data are identified with the help of estimated hidden variables. The hidden variables are presented as underlying local voxel labeling. In the experimental results obtained, the utility of the proposed EM-MAP framework is illustrated by applying it to 2D and 3D MRIs. The segmentation of basal ganglia structures such as the caudate nucleus and the putamens. The comparative results show that the proposed EM-MAP framework outperform compared to the statistical shape model-based techniques in the same framework as well as a current state-of-the-art region competition level set method.

The third contribution of this part of the thesis is the integration of the EM-MAP approach with the new PCA technique from a training set of joint object shape information and image intensity patterns inside the object. Specifically, the utility of the integration is illustrated by applying it to the segmentation of 3D medical images. The comparative results show the reliability and the robustness of the integration in this new framework over the traditional level set based segmentation approaches.

In summary, two automated frameworks for segmentation of medical images are proposed. They are the joint curve evolution and the EM-joint shape based algorithms. In addition, the generalization of our frameworks to 3D models of multiple structures. The resulting implementation is tested on a variety of studies to parceling of anatomical structures. The proposed algorithms can be used for surgery navigation and 3D visualization. They could also be applied to neuroscience studies in finding new diseases related to anatomical characteristics and the increase in reliability in diagnosing of illnesses such as schizophrenia.

Contents

Acknowledgements	i
Summary	iii
List of Figures	x
List of Tables	xvii
List of Symbols	xxi
1 Introduction	1
1.1 Motivation	1
1.2 Related Work	3
1.3 Objectives	5
1.4 Original Contributions of the Thesis	6
1.5 Organization of the Thesis	10
2 A Literature Review on Segmentation of Medical Images	11

2.1	Introduction	11
2.2	Voxel-wise Segmentation Methods	13
2.3	EM Criteria for Voxel-wise Segmentation	14
2.4	Active Contours in Segmentation Approaches	18
2.4.1	Deformable Models	19
2.4.2	Level Set Approach	22
2.4.3	Level Set Methods versus Graph Cut Approach	26
2.5	New Generations of Level Set Active Contours	27
2.5.1	Level Set Geodesic Measures	27
2.5.2	Using of Level Set for Solving Minimum Partition Problems	28
2.6	Coupled Level Set Methods and Statistical Theories	34
2.6.1	Non-parametric Shape Evolution	35
2.6.2	Parametric Shape Evolution	38
2.6.3	Nonlinear Shape Distribution as Shape Priors	40
2.6.4	Couple Hidden Features and the Shape Evolution	42
2.7	Concluding Remarks	45
3	A Novel Joint Parametric and Non-parametric Curve Evolution for Segmentation of Medical Images	46
3.1	Introduction	46
3.2	Construction of Statistical Model	48

3.2.1	Definition of Implicit PCA	49
3.2.2	Application of Implicit PCA Model	50
3.3	A Segmentation Framework within Joint Curve Evolution	53
3.4	Global Registration within the Segmentation Framework	59
3.4.1	Parametric Curve Evolution	60
3.4.2	Non-parametric Curve Evolution	64
3.5	Experimental Results and Discussion	65
3.5.1	Segmentation of Ventricle Frontal Horns	66
3.5.2	Segmentation of Putamen Structures	69
3.5.3	Segmentation of Thalamus Structures	70
3.5.4	On the Robustness Issues	73
3.5.5	Quantitative analysis of segmentation accuracy	78
3.6	Concluding Remarks	81
4	A Novel Expectation-Maximization (EM) Approach to Joint Curve Evolution for Medical Image Segmentation	82
4.1	Introduction	82
4.2	Motivation	84
4.3	Constructing Shape/Appearance based Training Model	87
4.3.1	Detail of Shape/Appearance based Model	88

4.3.2	Applying Registration to Similarity-Invariance	88
4.4	Expectation-Maximization (EM) Approach to Joint Curve Evolution	91
4.4.1	Non-parametric Shape Evolution	93
4.4.2	Parametric Shape Evolution	95
4.4.3	Comparison between EM-Joint Shape Based and Voxel-Wise Labeling Approaches	97
4.5	Experimental Results and Discussion	98
4.5.1	Segmentation of Putamen	100
4.5.2	Segmentation of Caudate Structures	104
4.5.3	Evaluating Joint Shape and Appearance Training Model . . .	109
4.5.4	Extending to 3D Models	110
4.6	Concluding Remarks	117
5	Extension of the EM-MAP Framework for Segmentation of Multi- ple Structures	122
5.1	Introduction	122
5.2	Construction of the Statistical Model	124
5.3	Segmentation Framework	127
5.3.1	Non-parametric Multi Objects Shapes Model	131
5.3.2	Weighted Objective Function	133
5.3.3	Parametric Multi Objects Shapes Model	133

5.4	Avoiding Overlap between Shapes	135
5.5	Experimental Results and Discussion	136
5.5.1	Segmentation of Three-nuclei Subcortical of Brain	137
5.5.2	Segmentation of Close Nuclei Structures	141
5.5.3	Extension to 3D Multiple Structures Segmentation	147
5.6	Concluding Remarks	150
6	Conclusion and Recommendations for Future Work	151
6.1	Conclusion	152
6.2	Recommendations for Future Work	156
6.2.1	Coupled Spatial Prior Probability of Neighboring Configuration	157
6.2.2	Prior Probability of Joint Shape-Intensity	158
6.2.3	Prior Probability of Shape Features	159
	Author's Publications	161
	Bibliography	163

List of Figures

1.1	Motivational example. (a) MR image showing an axial cross section of the brain with in-slice resolution of 256×256 pixels. (b) Neuroanatomic structures of interest whose contours were identified by a neuroanatomist.	3
2.1	The generative intensity model in the mixture model form for a T1-weighted brain MR image (a) and its intensity histogram with mixture normal distributions to white matter, gray matter and CSF (adapted from [1]).	16
2.2	PV segmentation of an axial slice of a T1-weighted image (adapted from [1]). (a) real data; (b) histogram with the initialization superimposed; (c) histogram fit after model estimation; (d) extracting white matter, (e) gray matter, and (f) CSF; (g) estimated probability for partial voluming between white matter-gray matter, (h) white matter-CSF, and (i) gray matter-CSF.	17
2.3	PV segmentation of the same MR slice as in Figure 2.2, but when MRF model was used as a spatial prior instead (adapted from [1]).	18
2.4	(a) intuition idea of the geodesic curve evolution framework that leads to the curve C evolves based on the curvature flow and edge-detector function $g \equiv 1$. (b) The similar idea of the surface evolution, and shows that the tangential velocity has no effect on the geometric shape evolution (adapted from [2]).	21

2.5	Example of mean curvature of shortening flow to final circle shape. The points with high curvature change faster and disappear (adapted from [3]).	22
2.6	Propagating Circle (adapted from [3]).	23
2.7	Left: 2D level set examples. Figure (a) Initial curve and corresponding function in Figure (d). Intermediate curve evolution step and corresponding function in figures (b and e). Final target curve, Figure (c), and its corresponding function in Figure (f), evolution has topological changes by splitting operator. Right: 3D Level set representation leads to change in topology of the initial ellipsoid surface (adapted from [4]).	24
2.8	Regularized dirac and Heaviside function with $\epsilon=1$	29
2.9	Applying Active Contour Without Edge method on the interior brain images. (a) Initial active curve, (b) and (c) distinguish between white matter from the gray matter inside the brain image.	33
2.10	Segmentation results of various anatomical structures using statistical priors. (a-c) Segmentation of two 2D slides of the femur and corpus callosum; in (c) blue curve denotes segmentation without prior shape information. Image data courtesy of Leventon [5]. (d-g) curve evolution for cardiac ventricles with occlusion and noise [6].	38
2.11	The overall demo of Tsai's method including training phase (<i>top</i>) and segmentation phase (<i>down</i>) (adapted from [4]).	39
2.12	Shape evolution for an ultrasound segmentation with uniform shape prior via updating level set function optimized on the linear subspace spanned by the first few eigenmodes computed from a set of training shapes (<i>top</i>). Shape evolution with non-parametric shape prior(<i>down</i>) (adapted from [7]).	42

2.13	The 3D shapes evolution of different structures after 20 iterations based on the segmentation method (adapted from [8]) which is initialized with the mean shape of each structure.	43
2.14	The ability and better performance of Pohl's approach due to estimating and combining the extra spatial shape information (adapted from [8]).	43
2.15	Results (adapted from [9]), shows a coupled 4D segmentation of a cardiac sequences for diastolic, systolic, and midphase for a basal (top row), midslice (middle row), and apical slice (bottom row).	44
3.1	The conceptual representation of our proposed <i>joint parametric and non-parametric curve evolution</i> framework. It shows two major steps including training (Section 3.2) and segmentation phases (Section 3.3 and 3.4).	48
3.2	Outlines of the aligned putamens shapes of 13 training images embedded as the zero level set of a higher dimensional surface, signed distance function, figures (a)-(m).	52
3.3	Putamen shapes by varying the weights for the first and second principal components ($\sigma = \sqrt{\psi_1}$).	53
3.4	Figure (a) shows the 14 aligned training ventricle shapes of the training set. Figure (d) shows the mean shape. Figure (c) and (e) presents $\pm 2\sigma_1$, in the first variation mode of the SDF ventricle. Figure (b) and (f) shows $\pm 0.3\sigma_1$. Figure (g)-(j) shows the corresponding second variation mode. The zero level sets of the shape function is recorded in red curve.	54
3.5	Figure (a) shows the 14 aligned training thalamus shapes of the training set. Figures (b)-(f) show the shape function by varying the weights for the first and second principal components ($\sigma = \sqrt{\psi_1}$).	55

3.6	Figures (a)-(n) 14 segmentation results for the ventricle frontal horns of MR images by using the joint curve evolution algorithm with leave-one-out training strategy.	68
3.7	Comparison results for extracting the shapes of the ventricle frontal horn corresponding to Figure 3.6	69
3.8	Figures (a)-(m) 13 segmentation results of putamens by using our proposed algorithm with leave-one-out training strategy.	71
3.9	Comparison results for extracting the shapes of the putamens corresponding to Figure 3.8.	72
3.10	Figures (a)-(m) 14 segmentation results for the thalamus of MR images by using the joint curve evolution algorithm with leave-one-out training strategy.	74
3.11	Comparative figures of segmentation of the thalamus from one sample in the dataset using applied the joint curve evolution (Figure (a)), Tsai method (Figure (b)) and non-parametric curve evolution (Figure (c)).	75
3.13	Segmentation results of putamen shapes from MR images that are occluded by a horizontal bar.	76
4.1	The proposed <i>EM-joint shape based framework</i>	86
4.2	Diagram illustrating the formation of the column vectors $\{\hat{\Phi}_1, \hat{\Phi}_2, \dots, \hat{\Phi}_n\}$ for building shape/intensity-based PCA model.	89
4.3	Shape/intensity variation of caudate nucleus in the axial (<i>top</i>) and sagittal (<i>down</i>) cuts by varying the weights for the first principal component ($\sigma = \sqrt{\Sigma_1}$).	90
4.4	Putamen shapes by varying the weights for the first principal component ($\sigma = \sqrt{\psi_1}$).	90

- 4.5 The 3D shape variation of the caudate nucleus shape, figure (a) the mean shape with the positive variation of the first and second principle modes, figures (b) and (c), and with the negative variation of them, figures (d) and (e). 92
- 4.6 Automatic segmentation of putamens shapes of MR images by applying the proposed EM-joint shape based method for all the eighteen subjects, the mean error recorded as $1.19mm$. The green curve shows the initial curve and the red curve shows the segmentation result. 102
- 4.7 Comparison results for extracting putamens corresponding to eighteen experimental tests on Figure 4.6 between the EM-joint shape based, solely parametric and non-parametric curve evolution methods (Figure (a), the mean errors are recorded as $1.19mm$, $1.3mm$ and $1.45mm$) and joint curve evolution as non-EM Shape based method (Figure (b), the mean error is recorded as $1.25mm$). 103
- 4.8 Automatic segmentation of caudate shapes of MR images by applying the proposed EM shape based evolution method for all the nine subjects. The initial curve presented by green color. 105
- 4.9 Comparison results for extracting caudate corresponding to nine experimental tests on Figure 4.8 between the EM-joint shape based algorithm and joint curve evolution method as non-EM shape based technique, the mean errors are recorded respectively as $1.26mm$ and $1.85mm$ 106
- 4.10 Automatic segmentation of the caudate shapes in the sagittal cuts of MR images by applying the proposed EM shape based evolution method for all the eighteen subjects in the dataset. 108

4.11	Comparison results for extracting caudate of sagittal cuts corresponding to eighteen experimental tests on Figure 4.10 between the EM-joint shape based algorithm and joint curve evolution method as non-EM shape based technique, the recorded mean errors are $6.8mm$ and $8.12mm$ respectively.	109
4.12	An example of the segmentation results. (a) an input image from nine testing images. (b) the segmenting result after applying traditional PCA analysis. (c) the result after applying new PCA analysis.	110
4.13	Illustrates one example from twenty-three testings (Dataset1) of the segmentation of the caudate nucleus using the EM-joint shape based model. Figure (a) shows the 3D representation of this sample and figures (b) to (l) show 11 contiguous slices in the sagittal cuts from the 3D segmentation result.	112
4.14	Assessing the performance segmentation results of the EM-joint shape based model over twenty-three subjects in the sagittal view (Dataset1) to extracting the caudate nucleus.	113
4.15	One example from Dataset2 of the segmentation of the caudate nucleus using the EM joint shape-based model. Figure (a) shows the 3D representation and figures (b) to (g) show 6 contiguous slices in the axial cuts from the 3D segmentation result. The rest 9 slices are shown in Figure 4.20.	113
4.16	Cont'd, Figures (a)-(i) 9 contiguous slices from Figure 4.15.	114
4.17	Assessing the performance segmentation results of the EM-joint shape based model over twenty-three subjects in the axial view (Dataset2) to extracting the caudate nucleus.	115

4.18	The 3D segmentation result of caudate nucleus from dataset3. The EM-joint shape evolution approach (red color) compared with parametric shape evolution approach [4] (blue color). Figures (b)-(g) show slices 75,77,78,80,83,86. The green curves represent initial curves.	118
4.19	Cont'd, the rest presenting slices from Figure 4.18 ended with slice 103.	119
4.20	Summarized 3D segmentation results of Dataset3 via computing dice coefficients measurement.	119
5.1	The Basal Ganglia and its components inside the cortex in the lateral view and frontal view (adopted from “ http://thebrain.mcgill.ca ”).	123
5.2	The interconnection between the components of basal Ganglia in the human brain actions (adopted from “ http://thebrain.mcgill.ca ”).	123
5.3	Illustration of the shapes variations in the nuclei brain structures, caudate, putamen and thalamus, based on the implicit statistical multi-shape/appearance model. The shape classes are changed by varying the weights for the first, second, third, forth and fifth principal components, ($\sigma_i = \sqrt{\Sigma_i}$).	128
5.4	Illustration of the shapes variations in the close nuclei brain structures, putamen and pallidus, based on the implicit statistical multi-shape/appearance model. The shape classes are changed by varying the weights for the first, second, third and forth principal components.	129
5.5	The 3D shape variation of multiple caudate, putamen and thalami objects: figure (a) is the mean shape with the positive variation of the first and second principle modes (figures (b) and (c)) and with the negative variation of them (figures (d) and (e)).	130

5.6	The recommended initial curves and segmentation results of Chan/Vese approach ([10]) and Vese/Chan method ([11]).	137
5.7	Illustrates two samples from eleven testings and comparison between the generalization of the proposed EM-joint shape evolution for multiple objects segmentation, Tsai method [4] as “Parametric” and Chan/Vese method as “Non-parametric” curve evolution [10]. Figures (1) and (2) show the improvement compared to the Tsai and Chan/Vese approaches with 4.61%, 6.15% and 13.0%, 6.63% respectively. The initial curves are shown in white.	139
5.8	The segmentation results of the caudate, putamen and thalamus from eleven images. For each group, the first figure shows the result of the novel extended EM-joint shape based algorithm, the second figure using Tsai method and the last figure for Chan/Vese.	140
5.9	The 9 segmentation results of the putamen and pallidus structures. For each sample, the first, second and third figures show the results of the extended EM-joint shape based algorithm, Tsai method and Vese/Chan approach respectively. .	144
5.10	One example of the graynuclei segmentation of the caudate nucleus, the putamen and the thalamus from the twenty-five samples using the EM-joint shape based model. Figure (a) shows the 3D representation and figures (b) to (i) represents eight consecutive coronal slices convey three graynuclei structures.	148
5.11	Similarity values with the ground truth for the segmentation of the caudate nuclei, putamen and thalamus from twenty-five experiments.	149

List of Tables

3.1	Implementation Process	61
3.2	The mismatching distance (<i>mm</i>) between the result and the ground truth measured using applied the joint curve evolution, Tsai method and Chan/Vese approach, and with the taken time (<i>sec</i>). The mean mismatching error and standard deviation of the joint curve evolution method (7.75 <i>mm</i> , 0.09) proves the improvement performance than parametric method (11.88 <i>mm</i> , 0.83)and also non-parametric model (8.79 <i>mm</i> , 0.04).	75
3.3	Mismatching errors (<i>mm</i>) of the obtained results in Figure 3.12 of ventricle and Figure 3.13 of putamen shape segmentation from occluded MR images.	77
3.4	Quantitive validation of <i>DC</i> measures on the ventricles segmentation results from Figure 3.6 compared with three different ground truths.	77
3.5	Quantitive validation of the <i>DC</i> measures on the putamens segmentation results from Figure 3.8. The mean and the standard deviation of them are calculated over three different ground truths.	79

3.6	Quantitive validation of the DC measures on the thalamus segmentation results from Figure 3.10. The mean and the standard deviation of them are calculated over three different ground truths.	80
4.1	Implementation Process	99
4.2	Mean and standard deviation of the similarity value H_d for the segmentation of the putamens structures (unit in mm).	104
4.3	Summary over nine subjects of caudate segmentation comparison between results of EM-joint shape based algorithm and Non-EM shape based method with the ground truth, unit in mm	106
4.4	Summary over eighteen subjects of caudate segmentation comparison between results of EM-joint shape based algorithm and Non-EM shape based method with the ground truth, unit in mm	107
4.5	Summary over twenty-three 3D images of the caudate nucleus segmentation, in the sagittal view (Dataset1) and in the axial view (Dataset2), comparison between obtained results of the EM-joint shape based algorithm and associated ground truth, unit in mm	112
4.6	The statistical results of Table 4.20.	117
5.1	Implementation Process	130
5.2	Mismatching errors (units in mm) of the obtained segmentation results in the figures 5.8 and 5.7 using applied Tsai with taken time (unit in sec).	141

5.3	Mismatching errors (units in <i>mm</i>) of the obtained segmentation results in the figures 5.8 and 5.7 using applied Chan/Vese methods with taken time (unit in <i>sec</i>).	142
5.4	Illustrates the obtained mismatching error (units in <i>mm</i> and time in <i>sec</i>) of the figures 5.8 and 5.7 using the extended EM-joint shape based algorithm and how much better the performances are for each sample than Tsai approach (Improvement 1) and Chan/Vese method (Improvement 2).	142
5.5	The comparison mismatching errors of the Figure 5.9 between the extended EM-joint shape based algorithm, Tsai method and Vese/Chan approach using applying dice coefficient measurement.	145
5.6	The summary of Table 5.5.	145
5.7	The obtained mismatching error (units in <i>mm</i>) with taken time (units in <i>sec</i>) of the Figure 5.9 using applied Tsai approach.	146
5.8	The obtained mismatching error (units in <i>mm</i>) of the Figure 5.9 using the extended EM-joint shape based algorithm with taken time (units in <i>sec</i>) and presents the better performance sample by sample than Tsai approach.	146
5.9	Summary over twenty-five subjects of the caudate nucleus, the putamen and the thalamus segmentation comparison between obtained results of the EM-joint shape based algorithm and associated ground truth, unit in <i>mm</i>	147

List of Symbols

$ \cdot $	2-Norm, unless indicated otherwise
∇	The gradient operator
$P(x)$	Probability for the random variable x
δ	Delta function
H	Heaviside function
Δt	Gradient update step size
$\mathbb{R}^n$	The space of n-dimensional vectors
$\vec{C}$	Denotes a family of smooth curves
$\frac{\partial \vec{C}}{\partial t}$	Curve evolution equation
dp	Infinitesimal arc length
κ	Principle curvature of the curve
$\vec{N}$	Outward unit normal of a curve
$\mathbf{p}$	Pose parameter vector
$\mathbf{t}$	Translation matrix
χ	Scaling matrix
R_θ	Rotation matrix
$\mathbf{w}$	Shape parameter
ϕ	Level set function
Φ	Parametric level set function
Ψ	Diagonal matrix of eigenvalues
φ	Diagonal matrix of eigenvectors
S	Object shape

Chapter 1

Introduction

1.1 Motivation

Over the past two decades, medical image analysis has greatly influenced the medical science elevation by providing increased knowledge of human anatomy. In particular, techniques for the delineation of anatomical structures and extracting useful information, known as *image segmentation techniques*, are becoming increasingly important in numerous biomedical-imaging applications, such as the quantification of tissue values [12], diagnosis [13], localization of pathology [14], study of anatomical structure [15], treatment planning [16], and computer-integrated surgery [17]. In the last two decades, the field of medical image segmentation has developed greatly many areas in neuroscience via analysis of Magnetic Resonance (MR) images. Manual image segmentation procedures are often used in medical science by human experts. However, these human-based processes are time consuming and increase the risks related to inter-and-intra-observer reliability [18] in achieving reproducible results for measuring shape and voxel of anatomical structure. Therefore, many image segmentation algorithms have been proposed to overcome and automate these

difficulties. However, the main challenge of automatic brain tissue segmentation stems from combination of multiple factors such as:

1. Most of the anatomical structures have weakly visible boundaries (missing data) that blend in surrounding tissues.
2. Intrinsic anatomical varying through time and between individuals makes designing a segmentation technique difficult.
3. Presence of noise and obscuration in medical images due to low signal-to-noise ratio (SNR) data.
4. Field inhomogeneity that has a shading effect where the pixel or voxel intensities of the same tissue class vary slowly over image domain.
5. Partial volume effect in the extreme slices of MRI volumes, thus each voxel in the images could represent more than one tissue type and leads to blurring edges.

These difficulties lead image segmentation techniques to use object-orientation concept. This ability, exactly in a same way as human brain, comes from the *learning process* to reduce the complexity and unseen of the segmentation process. This thesis focuses on object-oriented segmentation frameworks for MR images utilizing prior shape-based information obtained from learning process and in conjunction with the incomplete observation input data. An example of a difficult segmentation process is provided in Figure 1.1, an axial MR brain image along with is shown and also hand segmented subcortical brain structures are seen. In this thesis, we have focused on extracting the ventricle frontal horns, caudate nucleus, putamen, globus pallidus and thalamus. These structures are depicted in color in Figure 1.1(b). In this MR image, it can be seen that segmenting the caudate nucleus, putamen, pallidus and

Figure 1.1: Motivational example. (a) MR image showing an axial cross section of the brain with in-slice resolution of 256×256 pixels. (b) Neuroanatomic structures of interest whose contours were identified by a neuroanatomist.

thalamus are more challenging than the ventricle frontal horns, because of high contrast-to-noise ratio of the ventricle to its surrounding area and subtle appearances of the caudate nucleus and the putamen. Moreover, the subcortical pallidus and thalamus have more complexity since missing and diffused edges. We will show that our vision system obtains successful results for segmenting these structures in such challenging conditions. We will introduce new prior information of shape variabilities and also the spatial dependencies between the subcortical structures.

1.2 Related Work

In this section, we briefly introduce general categories for image segmentation methods and focus on ones that are most pertinent to our work. These algorithms are known as active contour segmentation models [4, 10, 5, 19, 20, 21, 8].

Image segmentation is a fundamental method in image processing [22, 23] which partitions image $\Omega \in \mathbb{R}^2$ into some disjoint regions $\{R_i \subset \Omega\}_{i=1 \dots m}$. Each region has

some specific and common properties:

$$\Omega = \bigcup_{i=1}^m R_i \quad , \quad R_i \cap R_j = \emptyset \quad \forall i \neq j. \quad (1.1)$$

The criteria for partitioning an image depend on properties of interest object. For example an object can be separated from its background by considering edge information, color, intensity, texture, or motion information. Over the past thirty years, more than a thousand algorithms on image segmentation have been proposed. One of the most famous segmentation methods that has received considerable interest is curve evolution framework. This method is mathematically well defined in *continuous* formulation. This technique, described in [4], [10] and [21], is worth mentioning as it is most closely related to our segmentation frameworks in this thesis. Our models share common aspects with this class of segmentation approaches via integrating template-based meaning to process the global high-level knowledge of object shapes. One important property of the template-based approaches is that the variability of object shapes is formed from training samples as prior information. The shape prior information can be used for both parametric and non-parametric curve evolution.

Parametric Shape Prior Models: these models are a class of active contour models in which the evolution of the active contour depends on a set of parameters of object shape features. Cootes et al. [24, 25] applied the PCA to capture the shape variability as the shape-based prior model. Leventon et al. [5] proposed a technique that is set entirely within level set framework that extended geometric active contour evolution [26] by integrating parametric statistical shape model. This method applied PCA on training level set images to capture shape variations and encode shape prior constraint. Tsai et al. [4, 27] derived a unified level set function parameterized by shape and pose parameters. This approach performed curve evolution parametrically via updating the shape and poses parameters constrained by

the statistical parametric model obtained using PCA.

Non-parametric Shape Prior Models: these models include those active contour models that employ non-parametric curve evolution in the shape-based statistical domain. Chen et al. [28] extended geodesic active contours [26] by using coupled shape prior knowledge. They constructed non-probabilistic prior model from the training set of curves. Rousson and Paragios et al. [6] proposed a variational method in level set framework which constrains the flow of the shape to remain as a distance function of the prior shape knowledge. Cremers et al. [12] assimilated nonlinear statistical shape model derived by performing kernel PCA along level set-based Mumford-Shah segmentation. Cremers et al. [29] and Kim et al. [30] used non-parametric density estimation for shape priors in the level set framework.

1.3 Objectives

The objective of this thesis is the development of statistically robust, computationally efficient and global knowledge-based frameworks that are targeted towards automatically segmenting the major subcortical brain structures in MR images. The design of such a model is guided by the overall philosophy that they should be applicable to a wide variety of large problems with a minimal amount of learning effort. Mainly, this thesis attempts to answer following questions:

- What type of model-based framework should be used to provide a combination of both image information and statistical prior model?
- How should the information be introduced into the framework?
- What type of shape representation should be used for segmentation?

Our answers to these questions are embedded in robust unified and analytical segmentation frameworks and generally are classified into three major directions:

1. **Modeling:** this direction is focused on formulating the knowledge of similar properties within groups of shapes called shape models. In this work, the shape model relied on statistical analysis of training samples which convey both shape and appearance information.
2. **Boundary Extracting:** in this direction, we focus on deriving segmenting curve/shape towards desired boundaries using Bayesian framework.
3. **Shape Representation:** the goal of this direction is to represent segmenting shape which can be applicable in both directions (1) and (2).

The remainder of this chapter explains in further detail the major contributions of this thesis.

1.4 Original Contributions of the Thesis

The original contributions of this thesis can be listed as follows:

1. A novel analytical and robust segmentation framework, called *joint parametric and non-parametric curve evolution*, is presented based on a combination of the directions 1, 2 and 3 of Section 1.3. In this framework, both the nonlinear space of level set function (non-parametric model) and the linear subspace of level set function spanned by the principle components (parametric model) are employed in the evolution procedure. Following direction 1 (modeling), body of the modeling is constructed by parametric and implicit shape-based prior model via applying PCA on an aligned training set of Signed Distance

Functions (SDFs). We interpret direction 2 (boundary extraction) as the major part of the proposed segmentation framework. Integrating the advantages of both parametric and non-parametric level set curve evolution methods, in this work, we formulate the segmentation problem using a maximum a posteriori (MAP) framework such that the overall energy function consists of both the parametric and the non-parametric curve evolution terms. To achieve the direction 3 (shape representation), our algorithm introduces jointly two curves to match the object shape in an iterative manner: one curve is represented by the level set function (non-parametric curve) and another is represented by the statistical model (parametric model), according to the Bayesian framework. They are jointly constrained via a similarity measure between them in each iterative evolution. Finally, the non-parametric level set curve is regarded as the final matching result since it is more accurate as compared to the parametric curve. Experimental results demonstrate the influence of the joint curve evolution framework on the segmentation process. The comparison results show the improvement of the joint curve evolution in terms of the accuracy and robustness compared to the parametric methods [4] and the non-parametric curve evolution such as [10].

2. We develop a novel statistical knowledge-based shape evolution technique for segmentation of MR brain images that deal with answering these questions: 1) what type of model-based framework should be used to provide a combination of both image information and statistical prior knowledge? and 2) how should the information be introduced into the framework? To answer these questions, we propose a novel Expectation-Maximization (EM)-based shape evolution algorithm, called *EM-joint shape based evolution*. In the proposed algorithm, the evolution shape is constrained not only by a shape-based statistical model but also by a hidden variable model from the image observation. As a result,

we deal with incomplete observation data by considering missing or hidden features in the input image domain. The hidden variable model is defined by the local voxel labelling, which is unknown and estimated by the expected likelihood function defined by the image data and the built prior anatomical knowledge. In the M-step, the shapes of the structures are estimated jointly by encoding the hidden variable model and the statistical prior model obtained from the training stage. For the learning process, the traditional PCA technique is applied to encode shape-based prior information from a set of training samples represented by SDFs. The experimental results illustrate the influence of the joint hidden variables model and shape based statistical approach in the segmentation process. The comparison results illustrate the robustness and more accuracy of the EM-joint shape based framework than other related works such as the joint curve evolution [31], the parametric curve evolution [4] and the non-parametric curve evolution such as [10] and multi-phase level set framework [11].

3. A new implicit parametric shape based model is presented that deal with answering this question: what type of training information should be applied to direct a level set based segmentation? A training set includes the shape information of the object represented by SDF and also gray-level information inside object shape. Upon the use of PCA technique, this new statistical shape model is derived using the covariance relation between the shape and appearance of inside object shape. This prior model is then used to help further localize the boundary of an object in the image. We apply this new prior model to the EM-joint shape based evolution segmentation framework. The comparison results show the reliability and robustness of the new model compared to the traditional PCA technique.

4. The generalization of the EM-joint shape based framework is presented from a 2D model to a 3D model. Knowing a prior about the shape in 3D way, the 3D datasets are employed from the Open Access Series of Imaging Studies (OASIS) [32] for single object segmentation. The new implicit parametric shape base model using joint shape and appearance information of the training set is used in 3D version for encoding 3D shape prior model.
5. Finally, we describe the extension of previous parts of our contributions to represent multiple shapes simultaneously in a single segmentation framework. We detail the extensions that we make to adapt our techniques that are capable of handling multiple shape classes simultaneously, exploiting the statistical relationships among all of the shapes (as well as the statistical variability of each shape/appearance individually). Finally, we demonstrate the utility of our multiple shape classes framework by applying it to specific medical application of 2D experiments and the volumetric (3D) segmentation.

It is essential to investigate the minimum-probable bias comparison between the proposed approaches and other pertinent works. In order to implement the parametric curve evolution [4] which is known as Tsai approach in this thesis, the exact implementation was used as the parametric curve evolution part of our novel approaches. Therefore, they carried out same tuning process. The non-parametric curve evolution and multi-phase level set framework are known as Chan/Vese and Vese/Chan approaches in this thesis. These implementations follow the basic concept of the region-based implicit curve evolution. The non-parametric curve evolution part of our approaches utilized the same implementation as Chan/Vese approach. However, our EM-joint shape-based approach added the hidden information of voxel labeling.

1.5 Organization of the Thesis

We have organized the rest of this thesis as follows:

Chapter 2 reviews the background material related to our understanding and development of our work. The chapter begins with introduction of discrete segmentation algorithms, known as voxel-wise approaches. Then, we propose an overview of data-based deformable models and their relation to level set methods. In the final section, we describe template-based deformable models in which prior information has been integrated to regularize and constraint the solution curve.

Chapter 3 includes the first part of our contributions, the proposed segmentation framework called joint parametric and non-parametric curve evolution. We also present the medical application, demonstrating the properties of our method.

Chapter 4 introduces the second part of our contributions known as EM-joint shape based framework or EM-joint shape evolution and explain learning process using new PCA shape/appearance-based model. We also present the medical application, demonstrating the properties of our method.

Chapter 5 presents the extensions of the previous parts of our works to represent multiple shapes simultaneously in a single segmentation framework. This chapter presents our results on different set of 3D training sets.

Chapter 6 provides the conclusion of the thesis and recommendations for future research work in this area.

Finally, the Appendix gives a review of the relevant concepts and establishes the mathematical notations used in this thesis.

Chapter 2

A Literature Review on Segmentation of Medical Images

2.1 Introduction

The rapid development and proliferation of medical imaging technologies is revolutionizing medicine. The medical imaging is playing an increasingly prominent role in the diagnosis and treatment of disease, extracting accurate, repeatable and quantitative data about anatomic structures imaged through CT, MR, PET. Furthermore, the application of medical imaging is extended into radiotherapy and surgery [33, 34, 35, 36]. Segmenting structures from neuro-imaging is a fundamental task to measure the size and the shape of brain structures, to guide spatial normalization of anatomy between individuals and to plan medical intervention. Furthermore, segmentation serves as an essential element in a great number of morphometry studies that tests various hypotheses about the pathology and the pathophysiology of neurological disorders [35, 37, 38].

This chapter surveys the segmentation methods of promising and vigorously re-

searched approaches to computer-assisted medical image analysis. Based on the generative models from observation data, we categorize two different techniques for medical image segmentation. The first technique, investigated in Section 2.2 and Section 2.3, we explain the first category of medical image segmentation which primarily assigns each voxel to the specific tissue type, e.g., white matter, gray matter and cerebrospinal fluid (CSF). Each tissue type is identified by their characteristic signal intensity in T1 or T2 weighted MR images. The typical shortcomings of data, such as sampling artifacts, spatial aliasing, and noise, may cause the voxel-wise approaches to fail to provide accurate and reliable results. Furthermore, segmenting structures from medical images and reconstructing a compact geometric representation of these structures are difficult due complexity of applying statistical models locally and non-rigidity of the anatomic shapes of interests.

In Section 2.4, the second technique in medical image segmentation, known as deformable modeling, is explained. This technique is proposed for use in computer vision by Terzopoulos et al. [35] and plays an increasingly prominent role in medical image segmentation and real-time applications [39, 40]. The promising potency of deformable models stems from their ability to accommodate significant variability in biological structures over time and across different individuals. Consequently, these models provide reliable reconstruction tools that are robust and generic [41]. Furthermore, based on approximation theory in deformable models, anatomic structures can be detected by exploiting (bottom-up) constraints derived from the image data together with (top-down) a prior knowledge about their location, size and shape. Implementation of the deformable models is based on functional minimization. Using different shape representation algorithms, these approaches are divided into explicit and implicit models. In explicit deformable models [42, 43], curves or surfaces are represented in their parameterizations with fixed topology during deformation. Parametric active models are expressed by some control points and

shape information will be explicitly acquired by verifying these points. Each point on the boundary is imposed by the image data and prior forces. These methods can be used in fast real-time application due to their efficient computational costs and a compact mathematical representation. Although the explicit deformable models have an enormous impact in the segmentation application, they suffer from several drawbacks: 1) the implementation of the explicit models requires application of a delicate re-parameterization process to keep control points away from overlapping and self-intersection. 2) Intrinsically, the explicit representation does not cope with topological changes. 3) The respective cost functionals tend to have more local minima due to the use of local gradient information. Consequently, for many realistic images, they may get stuck in undesired local minima. Therefore, these models are quite sensitive to initialization. Reducing sensitivity to initialization has been proposed by [44, 45] which reported successful results. In Section 2.5, we will review recent developments in the segmentation community which aim at solving the mentioned problems of explicit deformable models. The implicit deformable models known as level set methods which allow intrinsic handling of topological changes and achieve free parametrization of the evolving curves and surfaces through geometric flow [46, 47, 48]. Finally, in Section 2.6.1, we discuss numerous efforts to introduce deformable templates or statistical shape knowledge in the level set based image segmentation in order to improve the missing low-level information regarding the intensity, texture, color and motion of objects.

2.2 Voxel-wise Segmentation Methods

The first family of brain segmentation methods is region-labeling which obeys intensity-based classification concepts. The aim is to assign each voxel to a specific tissue type [49, 50]. These methods generate intensity models from the data in order to

segment the image into different tissue types. They also address imaging artifacts explicitly, such as the partial volume effects [51, 52, 53, 54] and the intensity inhomogeneity in MR images [55, 56, 57, 58]. In order to design the generative models from the observation data, one can adopt the probability-based approaches such as maximum-likelihood (ML) estimation based solely on experimental measurement [59, 55, 60] and maximum a posteriori (MAP) by using encoded prior information on the models [61, 62]. The Expectation and Maximization (EM) method can be used to formulate the ML estimation by taking hidden features into consideration from the image [59, 1, 63, 64]. As an extension of this work, the spatial techniques were proposed in which the statistical atlas is used as the prior probability for each voxel to be assigned to the specific tissue type [1, 65, 66]. One can adopt the hidden Markov Random Field (HMRF) to model the neighboring voxels [1, 67, 62, 63]. The incorporation of both EM algorithm and HMRF into one unique statistical framework was introduced [62].

In the next section, we present a detailed description of constructing the voxel-wise intensity models. Then, the use of the EM method is explained to estimate the tissue-specific intensity in the image with its distribution (see Appendix for complementary information).

2.3 EM Criteria for Voxel-wise Segmentation

Let $I = \{I_1, \dots, I_n\}$ be an observation image data with a total of n voxels where I_i indicates the possibly multi-spectral intensity of voxel i . Assuming there are K tissue types in the image area. Let $x = \{x_1, \dots, x_n\}$ as the underlying segmentation such that $x_i = [x_{i,1}, \dots, x_{i,K}]^T$ is a binary unit and indicates to which tissue type voxel i belongs. In the generative model of the observation image data, it is assumed

that a set of parameters $\theta = \{\theta_1, \dots, \theta_K\}$ are used to explain K tissue types. Each tissue type has a typical intensity in the image with the normal distributed intensity variation in the voxels. If a proper estimation of the model parameters is available, then, it will be possible to estimate the underlying segmentation based on the image I . In other words, the voxel-wise intensity model helps to interleave the segmentation with the estimation of the model parameters [20, 68]. Based on the ML framework, the model parameters are estimated as follows:

$$\hat{\theta} = \arg \max_{\theta} \log P(I, x | \theta) \quad (2.1)$$

where $\hat{\theta}$ indicates the estimate of the model parameters set that optimally explains the observation image. One can consider a prior known probability of each voxel and re-write the full observation log likelihood as:

$$\begin{aligned} \hat{\theta} &= \arg \max_{\theta} \log P(I, x | \theta) \\ &= \arg \max_{\theta} \sum_i \sum_k x_{i,k} \log P(I_i, x_{i,k} | \theta_k) \\ &= \arg \max_{\theta} \sum_i \sum_k x_{i,k} \log (P(I_i | x_{i,k}, \theta_k) P(x_{i,k} | \theta_k)) \end{aligned} \quad (2.2)$$

The first probability term, $P(I_i | x_{i,k}, \theta_k)$, presents the probability density of the observation image data. The second term, $P(x_{i,k} | \theta_k)$, shows the prior information about the voxels assignments. Figure 2.1 shows the generative model fitted to a T1-weighted brain MR image as a mixture model. The intensity histogram of the image shows that all the tissues, white matter, gray matter and CSF, have normal distributions.

The EM algorithm simplifies the estimation of the parameters set by maximizing the log likelihood of the complete observations (I, x) . The EM algorithm estimates the parameters by applying expectation of above formulation with respect to the

Figure 2.1: The generative intensity model in the mixture model form for a T1-weighted brain MR image (a) and its intensity histogram with mixture normal distributions to white matter, gray matter and CSF (adapted from [1]).

posterior distribution of $x_{i,k}$. The EM algorithm follows two steps:

- E-step: the posterior of x conditioned on the previous parameters estimations θ^* and the observation derived as:

$$E_{i,k} \equiv P(x_{i,k} | I_i, \theta^*). \quad (2.3)$$

- M-step: the expected log-likelihood maximized as:

$$\hat{\theta}_k = \arg \max \sum_i E_{i,k} \log(P(I_i | x_{i,k}, \theta_k) P(x_{i,k} | \theta_k)). \quad (2.4)$$

It is assumed that the label for each voxel is drawn independently from the labels of the other voxels. In the experiments, building generative models is statistically and spatially dependent on by the image intensity data and biological objects in the medical imaging may have similar intensity distribution with different structural properties. In order to increase the fidelity of fitting, certain spatial dependencies need to be incorporated using MRF theory [62]. In this case, the observation likelihood is computed dependent on the given parameters set $\theta = \{\theta_1, \dots, \theta_k\}$ and the

Figure 2.2: PV segmentation of an axial slice of a T1-weighted image (adapted from [1]). (a) real data; (b) histogram with the initialization superimposed; (c) histogram fit after model estimation; (d) extracting white matter, (e) gray matter, and (f) CSF; (g) estimated probability for partial voluming between white matter-gray matter, (h) white matter-CSF, and (i) gray matter-CSF.

random field x 's neighborhood configuration x_N , see Eq. 2.5.

$$\begin{aligned}
 \hat{\theta} &= \arg \max_{\theta} \log P(I, x | \theta) \\
 &= \arg \max_{\theta} \sum_i \sum_k x_{i,k} \log P(I_i, x_{i,k} | \theta_k) \\
 &= \arg \max_{\theta} \sum_i \sum_k x_{i,k} \log (P(I_i | x_{i,k}, \theta_k) P(x_{i,k} | \theta_k) P(x_{i,k} | x_{N_i})) \quad (2.5)
 \end{aligned}$$

where the probability function $P(x_{i,k} | x_{N_i})$ provides the context-dependent image voxels and x_{N_i} is the set of neighboring voxels i .

As an advanced example of employing the EM algorithm in the voxel-wise segmentation, Leemput et al. [1, 69, 70, 71] proposed a statistical framework that solves partial volume (PV) effects in segmentation and the EM algorithm is used to simultaneously estimate the parameters of the resulting model and perform a partial volume classification. Figure 2.2 illustrates the segmentation results of white matter, gray matter and CSF without considering the spatial correlation and uniform prior.

Figure 2.3: PV segmentation of the same MR slice as in Figure 2.2, but when MRF model was used as a spatial prior instead (adapted from [1]).

In addition, Leemput et al. developed a unified framework for PV segmentation by applying a MRF model for the label image x . Figure 2.3 compares application a MRF model and a spatial prior instead of uniform prior in Figure 2.2. The better performance of PV segmentation is presented in the corresponding figures. In summary, the overall strategy of the voxel-wise segmentation approaches is to generate the observed density model at each voxel that optimally describes the characteristics of the particular tissue type. As a result, the generative models are used to *synthesize* the observation image data and segmenting into specific regions.

2.4 Active Contours in Segmentation Approaches

In image analysis, active contours have gained popularity in medical applications. In the literature, the Kass-Witkin-Terzopoulos model [72], *snake* model, is one of the first efforts in this direction. The mathematical foundations of active contours represent the confluence of geometry, physics, and approximation theory. Geometry

serves to represent object shape, physics imposes constraints on how the shape may vary over space and time, and optimal approximation theory provides the formal underpinnings of mechanism for fitting the models to measured data [45, 73, 74]. The extensions of the snake models were proposed for employing more promising global optimization process [75, 76, 77]. In Section 2.4.1, we explain the physics of these models in the form of deformable models which are presented in *variational* concepts and their applications in the medical image segmentation. In Section 2.4.2, we explain how the geometric properties of object shapes can be extracted in deformable models. One famous method that also have advantages in solving optimization problem is known as *level set approach*.

2.4.1 Deformable Models

Snake, the Kass-Witkin-Terzopoulos model, [72] is an active contour that is defined within an input image domain. It can move under *internal forces* which control the deformation of elastic and rigid contour, and *external forces* whose local minima coincide with edges, and other image features of interest. This leads to the following energy function:

$$E_{Snake}(C) = \int_0^1 \alpha |C'(s)|^2 ds + \int_0^1 \beta |C''(s)|^2 ds - \lambda \int_0^1 g^2(|\nabla I(C(s))|) ds, \quad (2.6)$$

where $I : \Omega \in \mathbb{R}^2 \rightarrow \mathbb{R}^+$ is a given image, $C(s) : [0, 1] \rightarrow \Omega$ is explicit parameterized closed curve, α , β , λ are constants to weight each term. The first two terms are defined by the first and second derivation of the curve, and enforce the smoothness constraint on the curve. The third term stands for external energy to characterize edges. The g function is defined as an edge-detector function which is monotonically

decreasing depending on gradient of the input image where boundaries are located. Upon solving the optimization problem, the snake (deformable model) matches to an image by detecting the desired boundaries. Unfortunately, this approach has significant drawbacks:

- The energy function is non-convex.
- The energy function is not intrinsic, since it depends on how the parametrization is achieved.
- The snake contours cannot move through any significant curvature due to restricted regularity constraints. In other words, this model does not handle changes in topology.
- In practice, formulating the optimization problem of this model can be embedded into a dynamic system by considering time. For discretizing the parameterized evolving curve, some marked points are needed, which should be updated in time according to the estimation in the equations of the motion.

To overcome these problems, next generation of deformable models were proposed known as *geodesic active contour model*, which is intrinsic and formulated as follows [78, 26, 79, 80]:

$$E_{Geodesic}(C) = 2\sqrt{\lambda} \int_0^1 g(|\nabla I(C(s))|) |C'(s)| ds. \quad (2.7)$$

This formulation brings the snake idea, however, reformulated from the snake model without the rigidity term using the *Maupertuis principle*. Now compared to the E_{snake} , $E_{Geodesic}$ is intrinsic and can be translated as a weighted Euclidean length. The solutions of these two minimization problems are equivalent according to explanation in [78, 26] and more accurately in [81]. They show that by considering

Figure 2.4: (a) intuition idea of the geodesic curve evolution framework that leads to the curve C evolves based on the curvature flow and edge-detector function $g \equiv 1$. (b) The similar idea of the surface evolution, and shows that the tangential velocity has no effect on the geometric shape evolution (adapted from [2]).

time in the equation Eq. 2.7, the motion of the curve is formulated in terms of direction of which the energy function Eq. 2.7 decreased as:

$$\frac{\partial C}{\partial t} = \left(\kappa g(\nabla I) - \left(\nabla g \cdot \vec{N} \right) \right) \vec{N}. \quad (2.8)$$

Using the geodesic active contour model, Figure 2.4(a) shows that the motion of the curve is performed based on the mean curvature κ where $g \equiv 1$ and in the normal direction $\vec{N}$. This flow is called shortening flow because it imposes the shrinking force and smoothing force into the initial curve to a point in finite time with circle shape. Figure 2.5 illustrates one example of such shortening flow with changing topology to a final circle shape.

According to the [3], authors show that the optimization problem in the snake model and in the geodesic active contour model are *equivalent* by introducing following definition:

Definition 2.4.1 (equivalence between $\inf_C E_{Snake}$ and $\inf_C E_{Geodesic}$)

The optimization problems of the snake model and the geodesic active contour model are equivalent if for any curve C a neighborhood $V(C)$ of curve exists such that in $V(C)$ the flow that most decrease E_{Snake} is also a decreasing flow for $E_{Geodesic}$ and vice versa.

Figure 2.5: Example of mean curvature of shortening flow to final circle shape. The points with high curvature change faster and disappear (adapted from [3]).

2.4.2 Level Set Approach

Level set methods has been focused on a wide variety of settings such as numerical techniques for understanding, analyzing, and computing complex interface motion. Originally, the time-dependent level set idea was introduced by Osher and Sethian [82] in the community of physics as a mean of propagation interfaces. The challenges associated with the level set methods attracted a lot of attention [83, 84, 85, 86, 87]. The main advantages of this propagation approach is the provision of an efficient and robust numerical scheme on a fixed Cartesian grid. This is permitting topological changes, corner and cusp development, and intrinsically measuring the geometric properties of the front such as curvature and normal direction.

The main idea behind the level set methodology is to implicitly represent the hypersurface (the front) as zero level set of a higher dimension function (the interface). The time-dependent level set methods formulate tracking of the motion of the front propagating along its normal direction with speed F . The speed function depends on the local geometric properties of the front such as curvature κ and normal direction $\vec{N}$ and also the global characteristics which depend on the shape and position of the front. Let a closed $p - 1$ dimensional hypersurface $C : [0, 1] \times \mathbb{R}^+ \rightarrow \mathbb{R}^p$, evolves with time in the Eulerian coordinate system and builds the level set function (in

Figure 2.6: Propagating Circle (adapted from [3]).

higher dimension) $\phi(w(t); t) : \mathbb{R}^p \times \mathbb{R}^+ \rightarrow \mathbb{R}$ such that $C(t) \equiv \phi(w(t); t) = 0$. Notice that $w(t) : \mathbb{R}^+ \rightarrow \mathbb{R}^p$ denotes spatial coordinates in p -dimensional space and $\Omega \in \mathbb{R}^p$ refers to the whole image domain. Figure 2.6 illustrates one example of the time-dependent level set methods, in which the front is shown by the closed and smooth circle curve in $\mathbb{R}^2$ and propagates along its normal direction with the specific speed function. In Figure 2.6, the goal of the level set methods is to produce an equation for the evolving function ϕ which contains the embedded motion of the curve $C(t)$ as the zero level set.

To summarize, *the curve evolution is performed by propagation of the interface along its gradient that is imposed by curvature-dependent speed through normal direction while the front is fixed.*

In order to implement the level set function, Osher and Sethian [82] proposed to use

Figure 2.7: Left: 2D level set examples. Figure (a) Initial curve and corresponding function in Figure (d). Intermediate curve evolution step and corresponding function in figures (b and e). Final target curve, Figure (c), and its corresponding function in Figure (f), evolution has topological changes by splitting operator. Right: 3D Level set representation leads to change in topology of the initial ellipsoid surface (adapted from [4]).

Signed Distance Function (SDF). It is defined as follows:

$$\phi(\mathbf{x}; t) = \begin{cases} 0 & \mathbf{x} \in C(t) \\ -D(\mathbf{x}, C(t)) & \mathbf{x} \in C_{inside}(t) \\ +D(\mathbf{x}, C(t)) & \mathbf{x} \in C_{outside}(t) \end{cases} \quad (2.9)$$

where $D(\mathbf{x}, C(t))$ is minimum Euclidean distance from point $\mathbf{x} \in w(t)$ in $\mathbb{R}^p$ to curve $C(t)$. Let $\mathbf{x}(t)$ be the path of a point on the propagating front $C(t)$. Thus, according to the curve evolution theory and geometric flows, the associated flow equation is as follows: $C_t = F\vec{N}$ and equivalently it takes the following equation form:

$$\frac{\partial \mathbf{x}(t)}{\partial t} = F(\mathbf{x}(t)) \frac{\nabla \phi(\mathbf{x}(t); t)}{|\nabla \phi(\mathbf{x}(t); t)|}, \quad (2.10)$$

such that the speed function F is a function of only local geometric properties of the curve such as curvature. The mean curvature of the curve κ and normal vector

$\vec{N}$ are expressed in terms of level set function defined in [88] as follows:

$$\vec{N} = \frac{\nabla\phi(\mathbf{x}(t);t)}{|\nabla\phi(\mathbf{x}(t);t)|}$$

$$\kappa = \nabla \cdot \frac{\nabla\phi(\mathbf{x}(t);t)}{|\nabla\phi(\mathbf{x}(t);t)|}. \quad (2.11)$$

Using chain rule, first derivation of $\phi(\mathbf{x}(t);t) = 0$ is taken as follows:

$$\frac{\partial\phi(\mathbf{x}(t);t)}{\partial t} + \nabla\phi(\mathbf{x}(t);t) \cdot \frac{\partial\mathbf{x}(t)}{\partial t} = 0. \quad (2.12)$$

After substitution Eq. 2.10 into Eq. 2.12, final evolution equation for the level set function is deduced as follows:

$$\frac{\partial\phi(\mathbf{x}(t);t)}{\partial t} + F |\nabla\phi(\mathbf{x}(t);t)| = 0, \quad (2.13)$$

with initial condition $\phi(\mathbf{x}(t);t=0)$ is given by initial curve $C_0 = C(t=0)$. Another needed boundary condition is defined on $\partial\Omega$, where $\frac{\partial\phi}{\partial N} = 0$. Eq. 2.13 is the main formulation of level set approaches and identified as a Hamilton-Jacobi equation. In summary, we list the main advantages of level set method specifically in medical image segmentation.

The main advantages of the level set method:

- During evolution of the level set function ϕ , although the zero front may change topology, the level set function is well-behaved as long as speed function is smooth. Therefore, topological changing is achieved naturally.
- From a numerical analysis point of view, since a fixed discrete plane is used in the spatial domain (surface domain), we can use choose finite-difference approximation for the spatial and temporal derivatives.

- Level set method has the ability to represent the geometric properties of object shapes intrinsically such as the curvature and the normal vector.
- By choosing p value, the level set formulation can be extended into any dimension.

These advantages are summarized in Figure 2.7, which show an example of the idea of automatic topology adaptation in level set methods. It can be seen that the red front can become very contorted, while the gray level set function is well-behaved.

2.4.3 Level Set Methods versus Graph Cut Approach

Using just a few simple grouping cues, one can now produce rather impressive segmentation on a large set of images. This is major motivation of using graph based technique. Graph cut provides a clean, flexible formulation for image segmentation. It provides a convenient language to encode simple local segmentation cues, and a set of powerful computational mechanisms to extract global segmentation from these simple local(pairwise) pixel similarity. Computationally graph cuts can be very efficient [89, 90]. The level set method and the graph minimal cut approaches have emerged as two powerful paradigms to compute the segmentation of images. Both methods are based on fundamentally different representations of images. Level sets are formulated as infinite-dimensional optimization on a spatially continuous image domain. These method compute gradient flow by estimating speed of counter points. The graph cuts, on the other hand, are defined as minimal cuts of a discrete graph representing the pixels of the image. Thus, discrete or continuous max-flow algorithms directly estimate integral motion of a contour as a whole [91].

2.5 New Generations of Level Set Active Contours

In Section 2.5.1, we focus on the influence of the level set methods for finding solution of a geodesic active contour, which is formulated in an Eulerian design. Despite the mentioned advantages of the variational methods of the geodesic active contours, the curve is attracted by the closest edges in homogenous regions. Therefore, they are generally sensitive to the image noise and often stuck in local minima for extracting the anatomical structures with smeared boundaries and cognitive contours (boundaries of larger objects defined by grouping smaller ones) [189]. To overcome these limitations, more global stopping controls such as regional statistics of the image is incorporated to improve the robustness and stability of deformable models. In Section 2.5.2, we propose a review of the influence of the level set methods for finding solution to the region competition approaches, we specifically focus on *minimum partition problem*, because of its relevance to our contribution.

2.5.1 Level Set Geodesic Measures

The geodesic active contour models [26, 80, 79], see Eq. 2.8, introduced as a solution of the minimization of the curve length that is weighted by edge-detectors, take the level set representation as:

$$\frac{\partial \phi}{\partial t} = g(\nabla I) |\nabla \phi| \left(\operatorname{div} \left(\frac{\nabla \phi}{|\nabla \phi|} \right) + \nu \right) + \nabla g(\nabla I) \cdot \nabla \phi. \quad (2.14)$$

The first term (on the right) permits the evolution of implicit curve to stop at desired object boundaries with respect to the g function. The role of the second term $\nabla g(\cdot) \cdot \nabla \phi$ is much more important and is the only difference between these

models and the geometric active contours [92, 93, 94]. Because, in real situation, the gradient values are different along the curve, it is necessary to restrict g function by using the edge detector ∇g that points toward the middle of the boundaries. Therefore, geodesic active contours increase the attraction of the curve toward the edge, especially the edges that have high variations.

2.5.2 Using of Level Set for Solving Minimum Partition Problems

Using global information based on the region properties criterion, one would like to generate a simplified version of the original image consisting of homogeneous regions separated by sharp edges. This is called *minimum partition problem* [95, 96, 97, 98, 99]. To explain the use of the level set methods in solving the minimum partitioning, first we will explain two primary functions; δ *Dirac delta function* and *Heaviside function* defined from level set function $\phi(\mathbf{x})$. They are used to explain image properties along the curve or area inside/outside region of the object. It is assumed that the interest shape is represented by level set function $\phi(\mathbf{x})$. The Heaviside function is calculated as follows:

$$H(\phi(\mathbf{x})) = \begin{cases} 1 & \text{if } \phi(\mathbf{x}) \leq 0 \\ 0 & \text{if } \phi(\mathbf{x}) > 0 \end{cases}. \quad (2.15)$$

Regularized version of Dirac and Heaviside functions are defined over the entire image domain Ω as follows [83]:

$$H(\phi(\mathbf{x})) = \begin{cases} 0 & \phi(\mathbf{x}) < -\epsilon \\ \frac{1}{2} + \frac{\phi}{2\epsilon} + \frac{1}{2\pi} \sin\left(\frac{\pi\phi(\mathbf{x})}{\epsilon}\right) & -\epsilon \leq \phi(\mathbf{x}) \leq \epsilon \\ 1 & \epsilon < \phi(\mathbf{x}). \end{cases}$$

Figure 2.8: Regularized dirac and Heaviside function with $\epsilon=1$.

$$\delta(\phi(\mathbf{x})) = \begin{cases} 0 & \phi(\mathbf{x}) < -\epsilon \\ \frac{1}{2\epsilon} + \frac{1}{2\epsilon} \cos\left(\frac{\pi\phi(\mathbf{x})}{\epsilon}\right) & -\epsilon \leq \phi(\mathbf{x}) \leq \epsilon \\ 1 & \epsilon < \phi(\mathbf{x}), \end{cases} \quad (2.16)$$

where ϵ is a tunable parameter that determines the size of the bandwidth of numerical smearing. Figure 2.8 shows the diagram of these functions implemented in the Chan/Vese approach [83]. Now let us define the entire domain of the image with a combination of the interior region Ω^- , the exterior region Ω^+ and the boundary $\partial\Omega$ of the object of interest. Therefore, the integral of any function f can be taken over the boundary $\partial\Omega$ using Heaviside and Dirac function, as follows:

$$E_{Curve} = \int_{\Omega} |\nabla H(\phi)| f(\mathbf{x}, C) d\mathbf{x} = \int_{\Omega} \delta(\phi) |\nabla \phi| f(\mathbf{x}, C) d\mathbf{x}, \quad (2.17)$$

and over inside region Ω^- and outside region Ω^+ as:

$$E_{inside} = \int_{\Omega} H(\phi(\mathbf{x})) f(\mathbf{x}, C) d\mathbf{x}, \quad E_{outside} = \int_{\Omega} (1 - H(\phi(\mathbf{x}))) f(\mathbf{x}, C) d\mathbf{x}. \quad (2.18)$$

In order to calculate the curve length, a value should be assigned to f function in energy function Eq. 2.17. The f function in energy function Eq. 2.18 is set equal

to one for inside/outside region area calculation.

The idea to introduce a region-based criterion into the active contours can be explained by the maximum a posteriori partitioning of the image, and obtained by following energy function:

$$E(C, \{\theta_i\}) = - \sum_{i=1}^K \int_{\Omega_i} \log p_{region,i}(I(\mathbf{x})|\theta_i) d\mathbf{x} + \beta|C| \quad (2.19)$$

where p is a Gaussian probability density distribution defined by the set parameters $\{\theta_i\}_{i=1,\dots,K}$ and K is the total number of homogeneous regions.

In [100], Zhu-Yuille proposed a solution for Eq. 2.19 using Bayes and Minimum Description Length criterion. However, using Lagrangian formulation, the model is unable to handle topological changes. In [101, 102, 103], Paragios-Deriche integrated this region-based model into the geodesic/geometric active contours through MAP framework and defined the *geodesic active regions* (GAR) model. Using level set methods, this model designs new speed function that is controlled by global region characteristics and boundary information. The energy function of the GAR model is:

$$E_{GAR}(C) = \sum_{i=1}^K \left\{ (1 - \alpha) \int_0^1 g\left(p_{boundary,i}(I(\partial\Omega(s_i)))\right) |\partial\Omega_{s_i}| ds_i - \alpha \int_{\Omega_i} \log p_{region,i}(I(\mathbf{x})) d\mathbf{x} \right\} \quad (2.20)$$

where $C = \bigcup_{i=1}^K \partial\Omega_i$ are the boundaries between regions. For each region, the first energy term has the boundary information defined by the edge-detector $g()$ and $p_{boundary,i}$ is the boundary probability density function of the region Ω_i . $p_{region,i}$ defines the region probability of the region Ω_i , s_i is the parameterizations of the curve $\partial\Omega_i$ and α is a positive arbitrary parameter. Using following system of level

set updating equations, the entire image is partitioned into K regions:

$$\begin{cases} \forall i \in [1, N] \\ \frac{\partial \phi_i}{\partial t} = |\nabla \phi_i| \left((1 - \alpha)(g() \kappa_i + \nabla g() \cdot \frac{\nabla \phi_i}{|\nabla \phi_i|}) + \alpha \log \frac{p_{\Omega_i}(I)}{p_{\Omega_i} / \Omega_i} \right) \end{cases} \quad (2.21)$$

Active Contour without Edges

Chan and Vese et al. [10] proposed a prominent method to solve Mumford Shah problem: minimum partition problem. From the variational analysis point of view, the basic idea is to find the segmenting curve C that divides the image area into two homogenous regions and each region is approximated by two unknown constants c_1 and c_2 by minimizing the energy function,

$$\begin{aligned} E_{CV}(c_1, c_2, C) = & \int_{\Omega_1} (I(\mathbf{x}) - c_1)^2 d\mathbf{x} + \\ & \int_{\Omega_2} (I(\mathbf{x}) - c_2)^2 d\mathbf{x} + \nu |C| \end{aligned} \quad (2.22)$$

where $\Omega = \Omega_1 \cup \Omega_2 \cup C$ is the entire image domain, and $C = \partial\Omega_1$ shows a set of curves. c_1 represents the average intensity of the image within region Ω_1 , and c_2 is the average intensity of the image within region Ω_2 . Chan and Vese et al. reformulated above energy function with level set function as follows:

$$\begin{aligned} E_{CV}(c_1, c_2, \phi) = & \int_{\Omega} (I(\mathbf{x}) - c_1)^2 H(\phi(\mathbf{x})) d\mathbf{x} + \\ & \int_{\Omega} (I(\mathbf{x}) - c_2)^2 (1 - H(\phi(\mathbf{x}))) d\mathbf{x} + \nu \int_{\Omega} |\nabla H(\phi(\mathbf{x}))|. \end{aligned} \quad (2.23)$$

The optimization process is achieved as follows:

1) Based on the concepts of level set methods, let's assume ϕ is constant and the energy function Eq. 2.23 is minimized with respect to c_1 and c_2 , leading to the

following formulations:

$$\begin{aligned} c_1(\phi) &= \frac{\int_{\Omega} I(\mathbf{x}) H_{\epsilon}(\phi(\mathbf{x})) d\mathbf{x}}{\int_{\Omega} H_{\epsilon}(\phi(\mathbf{x})) d\mathbf{x}} \\ c_2(\phi) &= \frac{\int_{\Omega} I(\mathbf{x})(1 - H_{\epsilon}(\phi(\mathbf{x}))) d\mathbf{x}}{\int_{\Omega} (1 - H_{\epsilon}(\phi(\mathbf{x}))) d\mathbf{x}}, \end{aligned} \quad (2.24)$$

where H_{ϵ} and δ_{ϵ} are regularization of the Heaviside function H and Delta function δ assuming that $\epsilon \rightarrow 0$ and $H'_{\epsilon} = \delta_{\epsilon}$.

2) In the next steps of minimization, c_1 and c_2 are fixed, and E_{CV} is minimized with respect to the function ϕ in the gradient descent approach. Thus, solving the minimum partition problem is equivalent to searching for steady state solution of the evolution $\phi(\mathbf{x}(t); t = 0)$ initial curve:

$$\frac{\partial \phi}{\partial t} = \delta_{\epsilon}(\phi) \left\{ \nu \operatorname{div} \left(\frac{\nabla \phi}{|\nabla \phi|} \right) - (I - c_1)^2 + (I - c_2)^2 \right\} \quad (2.25)$$

Advantages of this method known as Piecewise Constant (PC) include: the initial curve can be located anywhere in the image region, it can segment objects with no clear boundaries compared to the edge-based segmentation methods and the stopping term is independent of the gradient of the image. Figure 2.9 shows the results of our implementation of PC approach in medical image segmentation. The PC approach is able to distinguish white and gray matter of brain with blurring edges and divided the brain image into three homogeneous regions (tissues). However, the limitation of PC approach is that it is unable to provide promising results in the case of input images with inhomogeneous regions which often exist in medical image analysis. Another important limitation is to divide the image into more than two regions at the same time. This limitation was overcome by Vese and Chan et al. [11, 104] with a promising method to segment multiple object simultaneously and objects with triple junctions. Vese and Chan et al. [11] proposed different

Figure 2.9: Applying Active Contour Without Edge method on the interior brain images. (a) Initial active curve, (b) and (c) distinguish between white matter from the gray matter inside the brain image.

multi-phase level set representation so that the distinct phases are disjoint in their constructional model. To represent n regions, it would be needed $\log_2(n)$ level set functions. Each n regions is characterized by the various level set functions. For example for four regions (therefore using two level set functions), the Euler-Lagrange equations obtained by minimizing energy function of CV approach with respect to c and ϕ are obtained as follow:

$$\frac{\partial \phi_1}{\partial t} = \delta_\epsilon(\phi_1) \left\{ \nu \operatorname{div} \left(\frac{\nabla \phi_1}{|\nabla \phi_1|} \right) - [((I - c_{11})^2 - (I - c_{01})^2) H(\phi_2) + ((I - c_{10})^2 - (I - c_{00})^2) (1 - H(\phi_2))] \right\} \quad (2.26)$$

$$\frac{\partial \phi_2}{\partial t} = \delta_\epsilon(\phi_2) \left\{ \nu \operatorname{div} \left(\frac{\nabla \phi_2}{|\nabla \phi_2|} \right) - [((I - c_{11})^2 - (I - c_{10})^2) H(\phi_1) + ((I - c_{01})^2 - (I - c_{00})^2) (1 - H(\phi_1))] \right\} \quad (2.27)$$

where $c = (c_{00}, c_{10}, c_{01}, c_{11})$ is a constant vector indicate the mean intensity of regions $\{\phi_1 < 0, \phi_2 < 0\}$, $\{\phi_1 > 0, \phi_2 < 0\}$, $\{\phi_1 < 0, \phi_2 > 0\}$ and $\{\phi_1 > 0, \phi_2 > 0\}$ respectively.

In summary, the level set methods are used to represent curve evolution in boundary-based techniques (Section 2.5.1) and achieve optimization of associated energy func-

tion in region-based techniques (Section 2.5.2).

In the rest of this literature, we will focus on the deformable shape-based templates, in which the encoded object-oriented models are trained on space of implicit function. The common property of these approaches is that the variability of object shapes is captured from training samples and acts as the shape priors. Two categories of the deformable templates are introduced which shape prior information can be defined on either linear subspace of parametric level set function spanned by principle components or nonlinear space of non-parametric level set function. In Section (2.6.1), a survey of non-parametric curve evolution within probabilistic framework is reviewed, and in Section (2.6.2), parametric curve evolution concept is explained, where curve evolution is performed parametrically by updating the shape and poses parameters constrained by the learned parametric model. Finally, in Section (2.6.3), we survey new family of the curve evolution approaches within level set framework. In these approaches EM algorithm is introduced such that curve evolution brings EM voxel-wised segmentation scheme in geometric and geodesic information.

2.6 Coupled Level Set Methods and Statistical Theories

Several promising and vigorously researched medical image analysis techniques have been offered that involve the need for an automated system to *understand* the images. In this section, we focused on *discrete* and *continuous* image segmentation approaches based solely on low-level image information. However, in real world applications, the low-level properties of the image are insufficient to detect objects. In certain medical images for example, the boundaries of anatomic structures may be smeared, missing and neighbor anatomic structures may have similar intensity

properties. Furthermore, the presence of noise, shading effects and partial volume effects lead to integration of high-level information processing in the segmentation models known as *a priori* knowledge. This prior information such as shape, location and size of the objects information is known and applied into image segmentation in the form of initial conditions, data constraints, constraints on the model shape parameters, or into the model fitting procedures. In this section, we will focus on shape based prior models for solving segmentation problem via building and enforcing a compact representation of the biological structures with the shape complexity and variability [5, 4, 105, 19, 106, 107].

Specifically, we will concentrate on encoding the statistical shape-based models (as a prior knowledge) to enhance the level set method drastically for medical image segmentation. In these approaches, the goal of level set segmentation can be formulated as the estimation problem of the optimal and uncertain level set function ϕ given image $I : \Omega \rightarrow \mathbb{R}$. Using the Bayesian framework, the segmenting results embedded on ϕ are obtained by minimizing following energy function:

$$E_{total}(\phi) = E_{img}(\phi, I) + E_{prior}(\phi). \quad (2.28)$$

2.6.1 Non-parametric Shape Evolution

In [5, 6, 19, 21, 28], the results of researches on integrating the shape prior information into the deformable models were introduced based on the active contour design represented by the level set function. Based on the PCA analysis, the variability of object shapes are captured from a set of training samples via a compact and implicit shape-based model. The training samples are aligned into the standard spatial domain and represented by level set functions sampled on a regular grid. The global registration is applied to perform mapping between the spatial domain and

the image domain or the prior model. *In these methods, the object shape, encoded by its signed distance function, is updated on a nonlinear space of the signed distance function.* Different optimization framework have been achieved to update the embedded functions which present the shape and the pose properties of the anatomical structures. For example, Leventon et al. [5] suggested to represent a set of aligned training object shapes by signed distance function sampled on a regular grid and to apply PCA to this training set to model the distribution of object shapes. Leventon et al. integrated this prior knowledge within the geodesic active contours [26] by adding a term to the curve equation which draws the level set function toward the curvature flow, image data and statistical shape prior model. In the optimization procedure, the shape prior was updated iteratively by estimating the maximum a posteriori probability (MAP) of shape and pose parameters of the shape prior model. The updating equation for level set function embedding the object shapes is given by:

$$\frac{\partial \phi}{\partial t} = \lambda_1 \left[g() |\nabla \phi| \left(\text{div} \left(\frac{\nabla \phi}{|\nabla \phi|} \right) + \nu \right) + \nabla g(). \nabla \phi \right] + \lambda_2 [\phi^* - \phi], \quad (2.29)$$

where λ_1 and λ_2 are the linear coefficients that determine the tradeoff in how much to constrain the updating level set function to the shape prior ϕ^* and the input image I . The evolving shape is performed on the space of the level set function ϕ and formed *non-parametric shape evolution*. Within different optimization process, Rousson et al. [6] proposed a variational method in level set framework to couple the image-specific information and the shape prior model. Rousson et al. proposed a new objective function in the variational concepts as follows:

$$E_{prior}(\phi, A, \mathbf{w}) = \int_{\Omega} \delta_{\epsilon}(\phi) \left(\chi \phi - \underbrace{(\phi_M(A) + \sum_{j=1}^m w_j \varphi_j(A))}_{\phi^*(A)} \right)^2 d\Omega \quad (2.30)$$

Where A is a rigid transformation $A(x) = \chi R_\theta x + \mathbf{t}$, such that χ is scale parameter, R_θ is rotation matrix and $\mathbf{t}$ is the translation vector. Moreover, Rousson et al. consider a similar modeling prior knowledge to [5, 4] through PCA analysis such that φ_j are the eigenvectors and w_j are the corresponding eigenvalues. However, since the average over the training will not be a distance function, Rousson et al. proposed to estimate the distance function ϕ_M that minimizes the following energy function instead of using the mean:

$$E(\phi_M) = \sum_{i=1}^n \int_{\Omega} (\phi_i - \phi_M)^2 d\Omega \quad \text{subject to: } |\nabla \phi_M|^2 = 1. \quad (2.31)$$

In [6], the Geodesic Active Region function [101] in level set representation is used jointly with the shape prior regularization to improve segmentation performance. According to [101], both gradient information of the image and predefined statistical properties of the image regions are used to separate object from background. Let $p_{C_{in}}$ and $p_{\Omega-C_{in}}$ are the densities of $I(x)$ inside the curve C , C_{in} and $\Omega - C_{in}$. Then the image data function is obtained as follows:

$$\begin{aligned} E_{img}(\phi, p_{C_{in}}, p_{\Omega-C_{in}}) &= (1-a) \int_{\Omega} \delta_{\epsilon}(\phi) g(|\nabla I(\mathbf{x})|) |\nabla \phi| d\mathbf{x} \\ &- a \int_{\Omega} [H_{\epsilon}(\phi) \log(p_{C_{in}}(I(\mathbf{x}))) + (1 - H_{\epsilon}(\phi)) \log(p_{\Omega-C_{in}}(I(\mathbf{x})))] d\mathbf{x}. \end{aligned} \quad (2.32)$$

As illustrated in the total energy function, similarity transformation is achieved between evolving implicit representation ϕ and the prior model ϕ^* . The pose parameters are updated by considering gradient descent of E_{prior} as:

$$\begin{cases} \frac{d}{dt} \chi = 2 \int_{\Omega} \delta_{\epsilon}(\phi) (\chi \phi - \phi^*(A)) (-\phi + \nabla \phi^*(A) \cdot \frac{\partial}{\partial \chi} A) d\mathbf{x} \\ \frac{d}{dt} a_i = 2 \int_{\Omega} \delta_{\epsilon}(\phi) (\chi \phi - \phi^*(A)) (\nabla \phi^*(A) \cdot \frac{\partial}{\partial a_i} A) d\mathbf{x} \quad \text{with } a_i = \{R_\theta, \mathbf{t}\}. \end{cases} \quad (2.33)$$

Figure 2.10: Segmentation results of various anatomical structures using statistical priors. (a-c) Segmentation of two 2D slides of the femur and corpus callosum; in (c) blue curve denotes segmentation without prior shape information. Image data courtesy of Leventon [5]. (d-g) curve evolution for cardiac ventricles with occlusion and noise [6].

where χ and a_i determine a rigid transformation. Figure 2.10 shows the results of mentioned methods within curve evolution framework in medical image segmentation where the gradient is not strong enough and illustrates the results with and without global information.

2.6.2 Parametric Shape Evolution

In order to improve robustness, many statistical model-based methods have been proposed to constrain the evolution of level set functions. Tsai et al. [4] integrated parametric statistical shape modeling with the region-based curve evolution to drive the curve by using the statistical shape model as constraints. The shape variability is estimated by performing PCA on the globally aligned level set functions, and the major shape variation is then statistically reflected by the changes along the principal components. Subsequently, a parametric level set function Φ can be described as a function of the feature vector in the PCA space, $\mathbf{w}$, and the pose parameter $\mathbf{p}$, reflecting a global transformation from the shape space onto the image space. Then, the associated energy functions (similar to Eq. 2.22) can be minimized by finding

Figure 2.11: The overall demo of Tsai's method including training phase (*top*) and segmentation phase (*down*) (adapted from [4]).

the optimal parameters $\hat{\mathbf{w}}$ and $\hat{\mathbf{p}}$, where $\hat{\mathbf{w}}$ is constrained by the PCA model. The energy function can be defined as follows,

$$E_{img}(\mathbf{w}, \mathbf{p}, I) = S_u^2/A_u + S_v^2/A_v. \quad (2.34)$$

Notice that the parametric level set function Φ is determined by $\mathbf{w}$ and $\mathbf{p}$, and it divides the image domain into two regions — inside $R^u = \{\mathbf{x} \in \mathbb{R}^2 : \Phi(\mathbf{x}) < 0\}$ and outside $R^v = \{\mathbf{x} \in \mathbb{R}^2 : \Phi(\mathbf{x}) > 0\}$ the zero level set curve, and the areas of these two regions are $A_u = \int_{\Omega} H(-\Phi[\mathbf{w}, \mathbf{p}](\mathbf{x}))d\mathbf{x}$ and $A_v = \int_{\Omega} H(\Phi[\mathbf{w}, \mathbf{p}](\mathbf{x}))d\mathbf{x}$, ($H()$ is the regularized Heaviside function), and $S_u = \int_{\Omega} I \cdot H(-\Phi[\mathbf{w}, \mathbf{p}])d\mathbf{x}$ and $S_v = \int_{\Omega} I \cdot H(\Phi[\mathbf{w}, \mathbf{p}])d\mathbf{x}$ are the total intensities of the two regions. Figure 2.11 illustrates the overall concepts representation of Tsai's algorithm framework.

Although applying statistical shape prior information into the level set methods improves the accuracy and robustness a lot, it has two major drawbacks: First,

the space of embedded function is not a linear space, and the entire statistical processes of this method is based on computing linear operations on these functions. For example, the mean shape and linear combinations of eigenmodes are no longer signed distance functions. Although Gaussian-like shape densities are easily used in this approach, but “multimodal” probability density of shape is unable to be handled. Moreover, the probability density function of anatomical shapes variability is unknown commonly and can be hardly drawn from Gaussian distribution. For the rest, we will focus on finding solutions for these problems with the help of constructing non-parametric shape prior models on the level set space.

2.6.3 Nonlinear Shape Distribution as Shape Priors

The goal of constructing shape prior model or estimating shape prior distribution is to use the prior information of the objects shape in the segmentation. The challenging problem is to define the shape variability distribution from a set of sampling shapes in the space of shapes. To deal with this problem, firstly, the shape dissimilarity measures should be introduced on the space of level set functions. Secondly, based on the proposed shape dissimilarity measures, the probability density of shape is estimated and enforced into the segmentation framework as the shape priors. Cremers et al. [108] proposed an invariance of the shape prior to certain transformation by an intrinsic registration of the evolving level set function. Upon intrinsic registration, the level set function ϕ is evolved in the coordinates relative to its center of gravity μ_ϕ and by its intrinsic scale σ_ϕ . This method removes the global registration which computes the estimation of explicit pose parameters. The proposed shape distance computed as follows:

$$E_{prior}(\phi) = d^2(\phi, \phi_0) = \int_{\Omega} (H(\phi)(\sigma_\phi \mathbf{x} + \mu_\phi) - H(\phi_0(\mathbf{x})))^2 d\mathbf{x}, \quad (2.35)$$

where ϕ_0 represents the given shape priors. The center of gravity and the intrinsic scale of evolving level set function ϕ are defined as:

$$\mu_\phi = \int \mathbf{x}h(\phi)d\mathbf{x}, \quad \text{with } h(\phi) \equiv \frac{H(\phi)}{\int_{\Omega} H(\phi)d\mathbf{x}}. \quad (2.36)$$

$$\sigma_\phi = \left(\int (\mathbf{x} - \mu)^2 h(\phi) dx \right)^{\frac{1}{2}}. \quad (2.37)$$

Cremers et al. [108] shows that this energy function is invariant with respect to translation and scaling of the evolving shape ϕ . Then, he applies this shape dissimilarity to construct a statistical shape prior by introducing the concepts of kernel density estimation on the space of signed distance functions based shape representations. Given a set of training shapes $\{\phi_i\}_{i=1\dots N}$, the kernel density estimator is formulated as:

$$p(\phi) \propto \frac{1}{N} \sum_{i=1}^N \exp \left(-\frac{1}{2\sigma^2} d^2(H(\phi), H(\phi_i)) \right), \quad (2.38)$$

where the kernel width σ is defined as the mean squared nearest-neighbor distance:

$$\sigma^2 = \frac{1}{N} \sum_{i=1}^N \min_{j \neq i} d^2(H(\phi_i), H(\phi_j)). \quad (2.39)$$

In addition to the proposed approaches [109, 110, 111, 112, 113], Cremers et al. and Rousson et al. [7] used a kernel density estimator in the low-dimensional subspace spanned by the training shapes. Figure 2.12 illustrates the comparison results by applying uniform shape prior and non-parametric shape prior adapted from [7]. The level set-based shape representation used for both methods.

Figure 2.12: Shape evolution for an ultrasound segmentation with uniform shape prior via updating level set function optimized on the linear subspace spanned by the first few eigenmodes computed from a set of training shapes (*top*). Shape evolution with non-parametric shape prior(*down*) (adapted from [7]).

2.6.4 Couple Hidden Features and the Shape Evolution

Section 2.3 shows that voxel-wise segmentation techniques can improve the performance of robustness and accuracy by employing the EM algorithm for learning the generative model of the observation. It is straightforward to pose this connection due to direct dependencies between the estimation variables of the generative model and the hidden variables. It is more challenging to make a connection between the hidden variables and the shape model variables in the deformable models based on the shape evaluation framework. Pohl et al. [8] introduced a method to apply hidden variables in the deformable shape variation techniques based on the level set method. The hidden variables act as voxel labelings and defined by an explicit space-conditioned probability model of level set function as follows:

$$p(\mathbf{x}_{i,k}|\phi) = \frac{\wp(\mathbf{x}_i, \phi_k)}{\sum_{j=1}^K \wp(\mathbf{x}_i, \phi_j)}, \quad (2.40)$$

where K is the number of interest structures and $p(\mathbf{x}_{i,k}, \phi)$ explains the spatial dependency between the k th structure and its neighborhoods by computing the likelihood value of the voxel labeling variable which belongs to k th structures. The

Figure 2.13: The 3D shapes evolution of different structures after 20 iterations based on the segmentation method (adapted from [8]) which is initialized with the mean shape of each structure.

Figure 2.14: The ability and better performance of Pohl's approach due to estimating and combining the extra spatial shape information (adapted from [8]).

function $\wp$ is defined as a generic shape function in the logistic mapping:

$$\wp(\mathbf{x}_i, \phi) \equiv \frac{1}{1 + \exp^{-\phi(\mathbf{x}_i)}}. \quad (2.41)$$

In Pohl's approach, this spatial prior information is applied to the traditional MAP-shape based statistical techniques represented by level set function. Figures 2.13 and 2.14 indicate 3D segmentation results by applying Pohl's method for extracting the caudate (green and blue) and thalamus structures (pink and purple). The initial shapes are obtained from the mean shapes evolved after 20 iterations the algorithm converges to a smoother shapes. Figure 2.14 shows the improvement achieved from this method over the traditional shape-based statistical model in segmenting right (red) and left thalamus (purple), right (green) and left caudate (blue), and the right (pink) and left ventricle (turquoise).

Figure 2.15: Results (adapted from [9]), shows a coupled 4D segmentation of a cardiac sequences for diastolic, systolic, and midphase for a basal (top row), midslice (middle row), and apical slice (bottom row).

In the Pohl's approach, the hidden variables are interpreted as the missing data from the image observation. In the active curve models, observation data are defined by both the input image information and the curve. Consequently, the hidden variables can also explain the missing data from the evolving curve. Lynch et al. [9] proposed a new level set speed function which utilizes an adaptive EM algorithm to update and refine encoding prior knowledge about temporal model in segmenting the left ventricle of the heart for 3D+t MRI data. The new force into the level set design is formulated as:

$$\frac{\partial \phi}{\partial t} = g(|\nabla I|)(\kappa + \mathbf{K})|\nabla \phi| + (\nabla I \cdot \nabla \phi) \quad (2.42)$$

where $\mathbf{K}$ represents the normalized difference between the expected value and the evolving level set function ϕ . According to the EM algorithm, expectation step solves fitting problem with the observation data. The model acts as missing data and is a Gaussian model which is inferred from the deformation over the cardiac cycle. The observation data is the evolving level set function ϕ . The maximization step performs the deformation of the level set function ϕ via updating Eq. 2.42,

which is controlled by the parameter $\mathbf{K}$. The process continues and the parameters for the model are assessed at each iteration. Figure 2.15 illustrates the results of applied Eq. 2.42 for different time phases and slice locations.

2.7 Concluding Remarks

In this chapter, we introduced the state-of-the-art in the domain of image segmentation using voxel-wise techniques and deformable models which were focused on the level set methods. We analyzed the most well-known approaches in the generations of the level set methods in order to present our contributions which will improve some existing solutions. In particular, Section 2.6.1 and 2.6.2 emphasized the main drawback of the non-parametric shape evolution and the parametric shape evolution based on the level set methods and Section 2.6.4 focused on finding solution for incomplete and missing observation to get a more satisfactory result. In the following chapters, we propose new curve evolution algorithms for handling these issues using MAP processing.

Chapter 3

A Novel Joint Parametric and Non-parametric Curve Evolution for Segmentation of Medical Images

3.1 Introduction

In this chapter, we will explain a new curve evolution framework for medical image segmentation. The proposed method, a *joint parametric and non-parametric curve evolution framework* is implemented using level set functions.

A current state-of-art level set algorithm employs non-parametric curve evolution in the nonlinear space of level set function such as [92, 26, 93, 101, 10, 11]. Although matching the boundaries accurately, these approaches are noise-prone, occlusion and low contrast since their objective functions rely on the gradient-based and region-

based information of the image. Moreover, statistical model-based segmentation methods allow parametric object shape variation due to shape prior constraints. They are also more robust in dealing with noise and poor image contrast [4]. However, they suffer from limitation of shape variation range and are not applied in the images different from the statistical model. Using the MAP framework, integrating the advantages of both non-parametric and parametric level set curve evolution methods are employed in the evolution procedure. In our proposed framework, the shape evolution is carried out within nonlinear space of level set function and linear subspace of level set function which is spanned by the principle components. The experimental results demonstrate that our framework is as robust as the parametric statistical model-based curve evolution methods and also yields more accurate and reliable segmentation results than the non-parametric curve evolution methods for images with large noise. The shape priors functions reflect the shape variability from training process. On the other hand, the non-parametric evolution energy term provides infinite degree of curve variations and allows us to achieve better accuracy than the parametric statistical models such as Tsai et al. [4]. Moreover, our framework takes the advantages of the level set methods which are independent of the contour parameterizations, and thus enable handling topological changes. Figure 3.1 shows a block diagram to illustrate how the different components described throughout this chapter fit within the scope of our framework algorithm. As illustrated in this diagram, our framework contains two major phases: a training stage and a segmentation stage. The training stage motivated by Leventon et al. [5] is described in Section 3.2. Given a set of aligned training shapes represented by SDFs, PCA is applied to obtain the mean shape and the eigenshapes particular to the shape dataset. Section 3.3 and 3.4 explain the segmentation phase which uses two curves to match the object shape in an iterative manner: one curve is represented by the non-parametric level set function and the other one is represented by the

Figure 3.1: The conceptual representation of our proposed *joint parametric and non-parametric curve evolution* framework. It shows two major steps including training (Section 3.2) and segmentation phases (Section 3.3 and 3.4).

parametric statistical model, according to the Bayesian framework. They are constrained by a similarity measure between them in each iterative evolution. Finally, the non-parametric level set curve is regarded as the final matching result since it is more accurate compared to the parametric curve. An abstract representation of implementation of Joint Curve Evolution method is given in Table 3.1. Finally, in Section 3.5, we will present some comparative results of the proposed algorithm on segmenting ventricle frontal horns, putamen shapes and thalamus in 2D MR brain images.

3.2 Construction of Statistical Model

As explained in Section 2.5, shape representation has a significant role in the statistical model-based segmentation techniques. In this work, the implicit parametric

shape representation is utilized for building the PCA-based statistical model. This technique attracts a lot of attention because of the following advantages: (1) it is straightforward to extend it into a single framework of multiple object classes representation. (2) It enjoys computational efficiency and accuracy compared to explicit approaches, numerical stability, extract a linear variation of shapes via a simple model and capability to handle topological changes.

3.2.1 Definition of Implicit PCA

Motivated by [24, 25] which introduced the application of the PCA analysis to parametric curves for shape-based segmentation, Leventon et al. [5] proposed a new explanation of the PCA-based statistical model on the level functions of these curves. According to [5], the training shapes from the training dataset are represented implicitly by their corresponding SDFs and aligned rigidly and globally to one coherent coordinate frame (standard shape space). We have used FSL software to do alignments rigidly [114]. As explained in [5], the rigid alignment is acceptable in our work, because the representation is robust to slight misalignment. Let n aligned sample images and the level set functions of these aligned images be $\Phi_{i\{i=1,\dots,n\}}$. It means that the boundary of each object shape in the training set is embedded as the zero level set of a higher dimensional surface, Φ_i , (the signed distance map) with negative distances assigned to the inside and positive distances assigned to the outside of the shape. Each level set function Φ_i is digitalized and re-arranged into a 1D vector, following the PCA analysis, the mean level set function is computed from training shape dataset, $\bar{\Phi} = 1/n(\sum_{i=1}^n \Phi_i)$. To capture shape variability, the mean-offset functions, ψ_i , are obtained by subtracting the mean $\bar{\Phi}$ from each of the n signed distance functions and assemble matrix $\xi = [\tilde{\psi}_1 \ \tilde{\psi}_2 \ \dots \ \tilde{\psi}_n]$. Notice each mean-offset function, ψ_i , is digitized into 1D vector of N ordered samples, $\tilde{\psi}_i$, during

the PCA analysis.

The singular value decomposition of ξ is obtained as

$$\frac{1}{n}\xi\xi^T = \Gamma\Sigma\Gamma^T, \quad (3.1)$$

where Γ is a $N \times n$ matrix whose columns present the n principal variational modes to project an object shape into the eigen-space, and Σ is a diagonal matrix presents the corresponding nonnegative eigenvalues, denoted by $\sigma_1^2, \dots, \sigma_n^2$.

3.2.2 Application of Implicit PCA Model

According to the implicit PCA analysis, an estimation of an object shape is constructed linearly by the first q principle components of Γ matrix after re-sampling as:

$$\Phi[\mathbf{w}, \mathbf{p}](\mathbf{x}) = \bar{\Phi}(\tilde{\mathbf{x}}) + \sum_{k=1}^q w_k \varphi_k(\tilde{\mathbf{x}}), \quad \tilde{\mathbf{x}} = T(\mathbf{p})\mathbf{x}, \quad (3.2)$$

where φ_k presents re-sampled k th eigenvector of the k th variational mode, and weighted by the shape parameter w_k with the variance σ_k^2 and $\bar{\Phi}(\tilde{\mathbf{x}})$ is the mean shape. Choosing the appropriate q is very important, because it should be large enough to extract the main shape variation, but not too large to extract unusefull properties of the shape. Note that $\tilde{\mathbf{x}}$ represents a point in the shape domain, and $\mathbf{x}$ is a point in the image domain. $T(\mathbf{p})$ is a global transformation matrix to map between these two domains. It consists of the translation vector $\mathbf{t}$, the rotation matrix R_θ and the scaling factor χ . Finally, with the assumption that shape probability distribution underlying the training shapes has Gaussian distribution due to the application of

PCA model, the probability to get Φ is as follows:

$$P(\mathbf{w}) = \frac{1}{\sqrt{(2\pi)^q |\Sigma_q|}} \exp \left(-\frac{1}{2} \mathbf{w}^T \Sigma_q^{-1} \mathbf{w} \right), \quad (3.3)$$

where Σ_q contains the first q rows and columns of the eigenvalue matrix Σ and $\mathbf{w} = \{w_1, \dots, w_q\}$ is the shape feature vector.

In this part of experimental work, we consider three training sets of 2D shapes of interest: ventricles, putamens and thalamus. In putamens' case, 13 images are used for training. Figure 3.2 shows these shapes embedded as the zero level set (the red curve) of higher surface (the gray signed distance function). Four principal components are finally chosen which can represent about 97.5% of the total energy of the space spanned by the training set. Figure 3.3 provides some intuition as to how the level set representation of the model in Eq. 3.2 captures shape variability of the putamens by varying the weights for the first principal component of the PCA model. It can be seen that the major shape changes have been captured by the first principal component. For the ventricle and the thalamus, we use 14 2D medical images. Similar with the putamen shapes learning, we extract the ventricle shapes and the thalamus from axial slices of T1-weighted MRI of healthy volunteers to build our shape models. Based on the registration/alignment process in Section 3.2.1, the PCA models are constructed with four principle components that fit at 95.4% for the ventricle shapes and 93.1% for the thalamus structures of the training set. Notice that the major variations of the shapes happen in the first component. Figure 3.4 and Figure 3.5 illustrate the constructed implicit PCA models of the ventricle and the thalamus respectively and correspond to the mean shape and the first eigenmode of variation of the training set.

Figure 3.2: Outlines of the aligned putamens shapes of 13 training images embedded as the zero level set of a higher dimensional surface, signed distance function, figures (a)-(m).

Figure 3.3: Putamen shapes by varying the weights for the first and second principal components ($\sigma = \sqrt{\psi_1}$).

3.3 A Segmentation Framework within Joint Curve Evolution

As mentioned in Chapter 2 (Section 2.5), the active contours in the coupled level set methods and statistical theories evolve in either nonlinear space of the level set function ϕ , known as non-parametric curve evolution, or linear subspace of parametric level set function $\Phi[\mathbf{w}]$, known as parametric curve evolution. Using the implicit curve representation concept, we propose a new joint curve evolution algorithm by integrating the advantages of both parametric and non-parametric level set curve evolution methods. In our method, both local intensity-based features of the object and global properties of the object shape are estimated and optimized to extract the shape of interest. The object shape jointly represented by non-parametric level set function ϕ and its feature vector $\mathbf{w} = \{w_1, \dots, w_q\}$ based on the statistical model

Figure 3.4: Figure (a) shows the 14 aligned training ventricle shapes of the training set. Figure (d) shows the mean shape. Figure (c) and (e) presents $\pm 0.2\sigma_1$, in the first variation mode of the SDF ventricle. Figure (b) and (f) shows $\pm 0.3\sigma_1$. Figure (g)-(j) shows the corresponding second variation mode. The zero level sets of the shape function is recorded in red curve.

Figure 3.5: Figure (a) shows the 14 aligned training thalamus shapes of the training set. Figures (b)-(f) show the shape function by varying the weights for the first and second principal components ($\sigma = \sqrt{\psi_1}$).

are described in Section 3.2. The segmentation task can be formulated by:

$$(\hat{\phi}, \hat{\mathbf{w}}) = \operatorname{argmax}_{\phi, \mathbf{w}} \{p(I|\phi, \mathbf{w})p(\phi|\mathbf{w})p(\mathbf{w})/p(I)\}, \quad (3.4)$$

where $p(I|\phi, \mathbf{w})$ represents the global generative model for the image intensity given $(\phi, \mathbf{w})$, $p(\mathbf{w})$ is the explicit shape prior, and $p(\phi|\mathbf{w})$ is the conditional probability which acts as a bridge between parametric and non-parametric object shape representations. It is worth noting that parametric and non-parametric level set functions, Φ and ϕ , represent different curves in the image domain. This conditional probability measures the similarity between these two shapes to keep them as close as possible during the joint parametric and non-parametric curve evolution. The non-parametric shape ϕ acts as the final result and optimized based on the image intensity modeling and encodes statistical shape model via updating the feature vector $\mathbf{w}$. The joint object shape can be obtained by minimizing the energy function,

$$E_{total}(\phi, \mathbf{w}) = E_{img}(I, \phi, \mathbf{w}) + \lambda_p E_{prior} + \lambda_s E_{similarity}(\phi, \mathbf{w}), \quad (3.5)$$

where λ_p and λ_s are weighting coefficients for the energy terms. The three energy terms are explained in detail as follows.

The first energy term E_{img} explains the statistics of the entire image intensity occupied by object and its background. This term reflects the fidelity of the joint object shape $(\phi, \mathbf{w})$ predictions to the image data in the parametric and the non-parametric form, and it can be decoupled into two terms: $E_{img}(\mathbf{w}, \phi, I) = E_{img}(\phi, I) + E_{img}(\mathbf{w}, I)$. $E_{img}(\phi, I)$ reflects the non-parametric matching degree between the non-parametric curve ϕ and the image data I . $E_{img}(\mathbf{w}, I)$ reflects the parametric matching degree between the curve $\Phi[\mathbf{w}]$ and the image data I in order to divide the image that

occupied by the parametric model. We assume that the domain of the observed image I is formed into two statistically distinguishable regions by regions statistics (e.g., sample mean and variance). In summary, the energy term $E_{img}(\phi, I)$ provides non-parametric curve evolution and performs infinite degrees of shape variation in the image domain, on the other hand, the energy term $E_{img}(\mathbf{w}, I)$ reflects more shape-based restricted evolution of the object shape. This coupling energy functions enables us to estimate the observation likelihood more accurately and flexibly via employing any fitting functions in the parametric and non-parametric implementation. In this work, we employ Chan and Vese energy function [10] as the non-parametric fitting function:

$$E_{CV}(c_1, c_2, \phi) = \int_{\Omega} (I(x) - c_1)^2 H(\phi) dx + \int_{\Omega} (I(x) - c_2)^2 (1 - H(\phi)) dx + \nu \int_{\Omega} |\nabla H(\phi)|, \quad (3.6)$$

where c_1 and c_2 are the regions statistics of the image.

To define the parametric image function, we employ Tsai method [4] as explained in 2.6.2:

$$E_{img}(\mathbf{w}, I) = S_u^2/A_u + S_v^2/A_v, \quad (3.7)$$

where the regions statistics of the image are defined by S_u and S_v that are parameterized by the shape vector $\mathbf{w}$.

The second energy term E_{prior} explicitly constrains the variation of the parametric shape $\Phi[\mathbf{w}]$ subject to the prior distribution learned from training shapes using PCA analysis. Using the statistical model built in Section 3.2 and the probability density

function of the shape, Eq. 3.3, E_{prior} can be defined as,

$$E_{prior} = \mathbf{w}^T \Sigma_q^{-1} \mathbf{w}, \quad (3.8)$$

where Σ_q is the diagonal matrix containing q largest eigenvalues, according to the PCA model.

The third energy term E_{sim} reflects the difference between the parametric and the non-parametric curves. Since the joint object shape includes both the parametric and the non-parametric level set functions, $\Phi[\mathbf{w}]$ and ϕ , it is necessary to constrain them so that they represent similar shapes,

$$E_{sim}(\phi, \mathbf{w}) = \int_{\Omega} (H(\phi(\mathbf{x})) - H(\Phi[\mathbf{w}](\mathbf{x})))^2 d\mathbf{x}, \quad (3.9)$$

where Ω is the image domain, and $H()$ is the regularized Heaviside function. Cremers et al. [108] gave a complete review for computing the dissimilarity of two shapes represented by their embedding functions. In [108], several advantages of this measure to compute the distance between two shapes using Heaviside function are mentioned such as its independence from the image size Ω , its non-negative value, symmetry and most importantly, reliability for SDFs which means that there is no need to constrain the two level set functions to the space of SDFs (more proves are mentioned in [115]). It is explained that this measure is not differentiable and an approximation of the Heaviside function H can be used by a smooth (differentiable) version.

3.4 Global Registration within the Segmentation Framework

In order to build a meaningful statistical model, all the training samples should be globally aligned into the standard shape domain before training the statistical model so that no variations of the position of images have been included. Specifically, the global registration or alignment is critical to compute the optimized pose of object shape as close as possible to the target object shape. In the current state-of-art model-based curve evolution, the corresponding pose parameters can be optimized to align the evolving curve with the prior model [5, 28] or the image data [27, 19]. In this work, global transformation process applies to an entire object shape between the evolving curve and the image data by updating rigid parameter $\mathbf{p}$ consisting of translation vector $\mathbf{t}$, the rotation matrix R_θ and the scaling factor χ . Therefore, we augment the proposed Bayesian formulation in Eq. 3.4 as,

$$(\hat{\phi}, \hat{\mathbf{w}}, \hat{\mathbf{p}}) = \operatorname{argmax}_{\phi, \mathbf{w}, \mathbf{p}} \{p(I|\phi, \mathbf{w}, \mathbf{p})p(\phi|\mathbf{w}, \mathbf{p})p(\mathbf{w})\}. \quad (3.10)$$

By assuming that the distributions of ϕ and $\mathbf{w}$ are independent with that of $\mathbf{p}$, and $\mathbf{p}$ is subject to uniform distribution, the associated energy function is defined as,

$$E_{total}(\phi, \mathbf{w}, \mathbf{p}) = E_{img}(\phi, \mathbf{w}, \mathbf{p}, I) + \lambda_p E_{prior}(\mathbf{w}) + \lambda_s E_{sim}(\phi, \mathbf{w}, \mathbf{p}). \quad (3.11)$$

Notice that the image energy term $E_{img}(\phi, \mathbf{w}, \mathbf{p}, I)$ defines the generative model of the image formulation process, and can be decoupled into two terms,

$$E_{img}(\phi, \mathbf{w}, \mathbf{p}, I) = E_{img}(\phi, I) + E_{img}(\mathbf{w}, \mathbf{p}, I), \quad (3.12)$$

driving the curve toward a homogeneous intensity region by updating the joint parametric and non-parametric object shapes. The parametric fitting is achieved in statistical domain of learning process which is constrained with both the shape and the pose parameters, $\mathbf{w}$ and $\mathbf{p}$, as follows:

$$E_{img}(\mathbf{w}, \mathbf{p}, I) = S_u^2/A_u + S_v^2/A_v, \quad (3.13)$$

such that image regions are defined by both parameters $\mathbf{w}$ and $\mathbf{p}$ (Section 2.6.2).

The similarity energy function $E_{sim}(\phi, \mathbf{w}, \mathbf{p})$ is defined to keep similarity between ϕ and $\Phi[\mathbf{w}, \mathbf{p}]$ as:

$$E_{sim}(\phi, \mathbf{w}, \mathbf{p}) = \int_{\Omega} (H(\phi(\mathbf{x})) - H(\Phi[\mathbf{w}, \mathbf{p}](\mathbf{x})))^2 d\mathbf{x}. \quad (3.14)$$

Given the energy function 3.11, we employ the technique of gradient descent to minimize E_{total} with respect to ϕ , $\mathbf{w}$, and $\mathbf{p}$. Thus, we update the parametric and non-parametric object shapes iteratively. In Section 3.4.1, we achieve the parametric curve evolution via updating $\Phi[\mathbf{w}, \mathbf{p}]$ function, with assuming that ϕ function is fixed. In Section 3.4.2, the non-parametric curve function ϕ is updated while assuming that $\mathbf{w}$ and $\mathbf{p}$ are known.

3.4.1 Parametric Curve Evolution

The parametric vector $\mathbf{w}$ can be updated on the linear subspace of parametric level set function $\Phi[\mathbf{w}, \mathbf{p}]$ by assuming that $\mathbf{p}$ is fixed. The gradient of E_{total} with respect to $\mathbf{w}$ is,

$$\nabla_{\mathbf{w}} E_{total} = \nabla_{\mathbf{w}} E_{img} + \lambda_p \nabla_{\mathbf{w}} E_{prior} + \lambda_s \nabla_{\mathbf{w}} E_{sim}. \quad (3.15)$$

Table 3.1: Implementation Process

Algorithm : Joint Parametric and Non-parametric Curve Evolution:

```

procedure Training ( Training images  $I = \{I_1, I_2, \dots, I_n\}$ )
    define  $B = \{B_1, \dots, B_n\} \leftarrow$  Binary images of desired shapes from  $I$ 
    define align  $B$  into a spatial coordinate
    define  $\Phi = \{\Phi_1, \dots, \Phi_n\} \leftarrow$  construct corresponding level set functions
    define  $\bar{\Phi} \leftarrow$  mean shape of training set  $\Phi$ 
    define  $\varphi \leftarrow$  eigenmodes of shape variation via applying PCA analysis
return  $(\bar{\Phi}, \varphi, \Phi)$ 

procedure Segmentation-Joint-shape (Input image  $I, \bar{\Phi}, \varphi, \Phi$ )
    define Non-parametric curve function  $\phi \leftarrow$  initial curve with mean shape  $\bar{\Phi}$ 
    for some iterations till  $error < \varepsilon$ 
        function Non-parametric-Evolve( $I, \phi, \Phi$ )
            updating non-parametric shape  $\phi$  using Eq. 3.24
        return  $\phi$ 
        define  $\phi \leftarrow$  renew  $\phi$ 
        function Parametric-Evolve( $I, \phi, \Phi$ )
            updating parametric shape  $\Phi$  using Eq. 3.15 and Eq. 3.19
        return  $\Phi$ 
        define  $\Phi \leftarrow$  renew  $\Phi$ 
    end
return  $\phi$  as final result

```


Since the non-parametric curve function ϕ is not related to $\mathbf{w}$, based on Eq. 3.12 only Eq. 3.13 is used to calculate the first term of Eq. 3.15. According to the explicit shape prior function, Eq. 3.8, and the similarity function, Eq. 3.14, Eq. 3.15 can be calculated as,

$$\begin{aligned} \nabla_{\mathbf{w}} E_{total} = & \left[-2 \left(\frac{S_u}{A_u} \nabla_{\mathbf{w}} S_u + \frac{S_v}{A_v} \nabla_{\mathbf{w}} S_v \right) + \left(\frac{S_u}{A_u} \right)^2 \nabla_{\mathbf{w}} A_u + \left(\frac{S_v}{A_v} \right)^2 \nabla_{\mathbf{w}} A_v \right] \\ & + \left[\Sigma_q^{-1} \mathbf{w} \right] + \left[2 \oint_C \left(H(\Phi[\mathbf{w}, \mathbf{p}] - H(\phi)) \nabla_{\mathbf{w}} \Phi[\mathbf{w}, \mathbf{p}] \right) ds \right]. \end{aligned} \quad (3.16)$$

Notice that S_u/A_u is the average intensity in inside region R_u and S_v/A_v is the average intensity in outside region R_v . The last term is an integral along the zero level set curve C defined as,

$$\oint_C ds = \int_{\Omega} \delta(\Phi) d\mathbf{x}, \quad (3.17)$$

where defining the one-dimensional Dirac measure δ concentrated at zero by

$$\delta(z) = \frac{d}{dz} H(z).$$

To obtain the gradients of region statistics A_u , A_v , S_u and S_v with respect to $\mathbf{w}$, it is required to take gradient of Φ in Eq. 3.2 with respect to $\mathbf{w}$, and hence the k th component of these gradients are given by,

$$\nabla_{w_k} \Phi = \varphi_k. \quad (3.18)$$

The pose information $\mathbf{p}$ is updated by assuming that $\mathbf{w}$ and ϕ are known and fixed, and the gradient of E_{total} with respect to $\mathbf{p}$ can be calculated as,

$$\nabla_{\mathbf{p}} E_{total} = \nabla_{\mathbf{p}} E_{img} + \lambda_s \nabla_{\mathbf{p}} E_{similarity}, \quad (3.19)$$

where

$$\nabla_{\mathbf{p}} E_{img} = \left(\frac{S_u}{A_u}\right)^2 \nabla_{\mathbf{p}} A_u + \left(\frac{S_v}{A_v}\right)^2 \nabla_{\mathbf{p}} A_v - 2\frac{S_u}{A_u} \nabla_{\mathbf{p}} S_u - 2\frac{S_v}{A_v} \nabla_{\mathbf{p}} S_v, \quad (3.20)$$

and S_u , S_v , A_v , A_u are described, in Section 2.6.2, as the functions defined by $\Phi[\mathbf{w}, \mathbf{p}]$. The second term of Eq. 3.19 can be calculated as,

$$\nabla_{\mathbf{p}} E_{similarity} = 2 \oint_C \left(H(\Phi[\mathbf{w}, \mathbf{p}] - H(\phi)) \nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}] \right) ds. \quad (3.21)$$

Notice that this line integral is calculated along curve C of Φ . The following formulation enables us to compute the gradient with respect to the $\mathbf{p}$:

$$\begin{aligned} \nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}] &= \nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}](\tilde{\mathbf{x}}) \\ &= \nabla_{\tilde{\mathbf{x}}} \Phi[\mathbf{w}, \mathbf{p}](\tilde{\mathbf{x}}) \cdot \left(\frac{\partial T}{\partial \mathbf{p}} \mathbf{x} \right). \end{aligned} \quad (3.22)$$

where T was explained in Eq. 3.2.

The pose parameter of the evolving curve is taken close to the position of the input image and includes $\mathbf{p} = \{t_1, t_2, \chi, \theta\}$ such that t_1 , t_2 , χ and θ correspond to translation, scale and rotation, respectively. The translation vector $\mathbf{t}(t_1, t_2)$ is defined as,

$$\begin{pmatrix} 1 & 0 & t_1 \\ 0 & 1 & t_2 \\ 0 & 0 & 1 \end{pmatrix}$$

the rotation matrix $R_{\theta}(\theta)$ as,

$$\begin{pmatrix} \cos \theta & -\sin \theta & 0 \\ \sin \theta & \cos \theta & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

and the scaling factor $\mathfrak{S}(\chi)$ as follows,

$$\begin{pmatrix} \chi & 0 & 0 \\ 0 & \chi & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

and therefore, $\frac{\partial T}{\partial \mathbf{p}}$ is calculated as follows,

$$\begin{aligned} \frac{\partial T}{\partial p_1} &= \frac{\partial T}{\partial t_1} = \frac{\partial \mathbf{t}(t_1, t_2)}{\partial t_1} \mathfrak{S}(\chi) R_\theta(\theta) \\ \frac{\partial T}{\partial p_2} &= \frac{\partial T}{\partial t_2} = \frac{\partial \mathbf{t}(t_1, t_2)}{\partial t_2} \mathfrak{S}(\chi) R_\theta(\theta) \\ \frac{\partial T}{\partial p_3} &= \frac{\partial T}{\partial \chi} = \mathbf{t}(t_1, t_2) \frac{\partial \mathfrak{S}(\chi)}{\partial \chi} R_\theta(\theta) \\ \frac{\partial T}{\partial p_4} &= \frac{\partial T}{\partial \theta} = \mathbf{t}(t_1, t_2) \mathfrak{S}(\chi) \frac{\partial R_\theta(\theta)}{\partial \theta}. \end{aligned} \quad (3.23)$$

In summary, *terms $\nabla \mathbf{w} E_{total}$ and $\nabla \mathbf{p} E_{total}$ together are interpreted as the parametric curve evolution in terms of shape and position variations in the linear space spanned by the principle modes.*

3.4.2 Non-parametric Curve Evolution

The non-parametric level set function ϕ is updated by fixing $\mathbf{w}$ and $\mathbf{p}$. The gradient of the total energy with respect to ϕ is,

$$\nabla_\phi E_{total} = \nabla_\phi E_{img} + \lambda_s \nabla_\phi E_{similarity}. \quad (3.24)$$

According to Eq. 3.12, only the energy function $E_{img}(\phi, I)$ as the non-parametric matching term is used to calculate the first term above. Therefore, the gradient of

total energy with respect to ϕ is calculated as

$$\begin{aligned} \nabla_{\phi} E_{total} = & \delta_{\epsilon}(\phi) \left(\nu \operatorname{div} \left(\frac{\nabla \phi}{|\nabla \phi|} \right) - (I(\mathbf{x}) - c_1)^2 + (I(\mathbf{x}) - c_2)^2 \right) \\ & + \lambda_s \left(2 \oint_C (H(\phi) - H(\Phi[\mathbf{w}, \mathbf{p}])) ds \right), \end{aligned} \quad (3.25)$$

where the last term is the integral calculated along the zero level set of Φ , *i.e.*, curve C . c_1 represents the average intensity of the image inside region of the object, and c_2 is the average intensity of the image within outside region of the object. Notice that $\nabla_{\phi} E_{total}$ represents combined parametric and non-parametric curve evolution to find the final segmenting result.

The above three steps are iteratively performed in order to update the parametric curve representation $\Phi[\mathbf{w}, \mathbf{p}]$ as well as the non-parametric curve representation ϕ until convergence. The non-parametric function ϕ acts as the final segmenting result.

3.5 Experimental Results and Discussion

In order to evaluate the performance of the proposed joint evolution algorithm, we apply it to extract the ventricle frontal horns, putamens and thalamus from 2D MR brain images. Knowing *a priori* about the desired organ shape, our segmentation strategy enables us to provide robust and accurate results automatically with no user intervention. To assess the integration between parametric and non-parametric curve evolution, we compare the joint curve evolution with Tsai method [4] as the parametric curve evolution and Chan/Vese approach [10] as the non-parametric curve evolution. The comparative results prove the improvement of performance of the joint curve evolution in the case of noise, low image contrast, diffused boundaries or occluded shapes. Finally, we show several results to assess the robustness of our

proposed method, herein we simulate partially artificial clutter in shape and intensity of the segmenting objects. In practice, some artifacts caused by interventional devices such as probes have similar effects on the MR images.

To assess the obtained 2D results, we compute the mismatching distance between the resultant curve and the ground truth via applying mean Hausdorff measurement. The ground truth is the manual segmentation obtained by an expert in our institute, selecting 300 points on the boundaries of the desired organ. The selected points are assumed to have zero values in the manual segmentation SDF. Based on the obtained absolute values from resultant shape SDF that shows the distance error of each point, we compute the mean error over all selected points. For 2D experimental work, this process provides a promising and an easy way to obtain mean error from the manual segmentation.

3.5.1 Segmentation of Ventricle Frontal Horns

In the first experiment, we used 14 real 2D T1-weighted MR images with the 217×181 dimensions and pixel spacing of $0.9375 \text{ mm} \times 0.9375 \text{ mm}$. The shape-based statistical ventricle model explained in Section 3.2, (see Figure 3.4), is applied in the learning phase. The leave-one-out strategy is used for training and testing the algorithms over all 14 MR samples. In each iteration of this cross validation, the MR brain image of one subject is left out from the training data and used for testing. The average time of constructing the statistical ventricle model took around $3min$. Figure 3.6 illustrates the results for matching the ventricle frontal horns using the joint curve evolution algorithm on the 14 test images. Similarly, in the entire testing images of the dataset, Eq. 3.11 is minimized by tuning coefficients λ_s and λ_p as follows: $\lambda_s = 6$, $\lambda_p = 2000$ and $\Delta t_1 = .0004$ (time step of parametric curve evolution), $\Delta t_2 = .00004$ (time step of non-parametric curve evolution). The average

time of the segmentation phase is achieved in 53.3sec. This makes constrained non-parametric and parametric curves so that they represent similar shapes and furthermore attract the evolving curve towards the shape prior information. To compute the mismatching distance, we use 300 control points for each left and right ventricle and obtain the mean error over all 600 points.

For comparing the joint curve evolution with Tsai method [4] reliably and faithfully, the same shape-based statistical model is applied. Furthermore, the same initialization process is applied for the joint curve evolution approach, Tsai method and Chan/Vese approach [10] as follows: We manually indicate the location of the objects (*i.e.*, the visual estimate of the object center), and then rigidly shift the mean shape to that location, acting as the initial curve. We performed more than 3 random initializations for each image, and the object center is randomly picked within the range of $[-7 \text{ mm}, 7 \text{ mm}]$ with respect to the center. The comparative segmentation results of ventricle with Tsai method and Chan/Vese method are shown in Figure 3.7. Figure 3.7 plots the matching errors of the corresponding images from Figure 3.6. They are ordered according to the slice location of the human brain (inferior-to-superior). This explains the lowest errors in the middle, because of their close proximity to the initial curve. It can be seen from Figure 3.7 plots that the matching errors of the proposed joint evolution algorithm are much lower than those of Tsai method and Chan/Vese method. In the case of ventricle, the average error and standard deviation of our algorithm, Tsai method and Chan/Vese method are 0.89 mm/0.37 mm, 1.59 mm/0.76 mm and 0.98 mm/0.31 mm. Because the parametric approach (Tsai's method) is limited to the linear space of shape and pose variation, the difference between the best and the worst case is above 6 times. The best case has close proximity to the initial curve and the worst case is farthest apart.

Figure 3.6: Figures (a)-(n) 14 segmentation results for the ventricle frontal horns of MR images by using the joint curve evolution algorithm with leave-one-out training strategy.

Figure 3.7: Comparison results for extracting the shapes of the ventricle frontal horn corresponding to Figure 3.6 .

3.5.2 Segmentation of Putamen Structures

In the second experiment, we apply the joint curve evolution for putamen objects segmentation on the dataset including 13 real 2D MR T1-weighted images (with the 217×181 dimensions and $0.9375 \text{ mm} \times 0.9375 \text{ mm}$ spacing). The statistical shape-based model for putamen objects constructed in Section 3.2, (Figure 3.3), is applied which takes around 2.8 min in average. Figure 3.8 illustrates the results for matching the putamen using the joint curve evolution approach on the whole 13 testing images. The same leave-one-out strategy is used for the whole 13 testing and training experiments. In the segmentation phase, we take the associated coefficients of the dissimilarity between parametric and non-parametric curve $\lambda_s = 3$ and the explicit shape prior information $\lambda_p = 2000$. ($\Delta t_1 = .007$ as time step of parametric curve evolution and $\Delta t_2 = .00004$ as time step of non-parametric curve evolution). The average time of the segmentation phase is achieved in 43.76 sec . The average distance between the resultant curve and the ground truth is computed by using

mean Hausdorff measure over all 600 control points on the boundaries of testing putamens shape.

Figure 3.9 plots the evaluation of the proposed joint curve evolution comparing with parametric (Tsai method [4]) and non-parametric curve evolution method (Chan/Vese method [10]). The results are ordered according to the slice location of the human brain (inferior-to-superior), corresponding to Figure 3.8. Notice that the same statistical shape-based putamen model described in Section 3.2 applied for the Tsai method. We use the same initialization process for all three methods to find proper shifted mean shape as the initial active contour. It can be seen that the matching errors of the proposed joint evolution algorithm are much lower than those of Tsai method and Chan/Vese method. For putamen, the average and standard deviation of our algorithm, Tsai method and Chan/Vese method are 0.95 mm/0.24 mm, 3.06 mm/0.81 mm and 1.91 mm/0.40 mm. Since the initial curve for all of the results is the mean shape of the dataset, minimum errors are produced in slices from the middle. The Hausdorff distance errors have a wider spread for parametric shape evolution approach because the results of this method strongly depend on the shape prior model. On the other hand the non-parametric shape approach has a relatively better performance because this method employs mean shape of the dataset as initial curve.

3.5.3 Segmentation of Thalamus Structures

In order to evaluate the joint curve evolution in terms of robustness and reliability, we apply the method on a real 2D dataset of T1-weighted MR images for segmenting thalamus structures. Thalamus is another important component like the basal ganglia (BG) structures and acts as the relay center for nerve impulses in the brain. Thus, the analysis of chemicals of thalamus plays an important role for diagnosing

Figure 3.8: Figures (a)-(m) 13 segmentation results of putamens by using our proposed algorithm with leave-one-out training strategy.

Figure 3.9: Comparison results for extracting the shapes of the putamens corresponding to Figure 3.8.

a large number of diseases, such as schizophrenia [12], Parkinsons disease and multiple sclerosis, etc. The segmentation of thalamus is very challenging because of the low contrast and discontinuous edges in the MR images. In our work, the dataset includes 14 MR images (with the 217×181 dimensions and $0.9375 \text{ mm} \times 0.9375 \text{ mm}$ spacing). We follow the same experimental procedures as applied for the previous datasets to obtaining the training and testing results. We utilize the statistical shape model mentioned in Section 3.2, see Figure 3.5, and it takes around 2.5 min . The Tsai and Chan/Vese approaches took 2 min and 1 min respectively. Figure 3.10 illustrates the entire dataset segmentation results for extracting thalamus using the applied joint curve evolution. The necessary coefficients and time steps of the parametric and non-parametric curve evolution are same as the putamens experiments. Table 3.2 summarizes the comparison results between the joint curve evolution algorithm, Tsai method as the parametric model and Chan/Vese method as the non-parametric curve evolution in terms of the accuracy and taken time over 14 MR images. In this experiment, we use different measurement to find the dis-

tance between the resultant curve and the ground truth. The maximum Hausdorff measure is calculated using following formulation:

Hausdorff Distance =

$$\max \left\{ \sup_{\mathbf{x} \in \Omega} ((1 - H(\phi(\mathbf{x})))\phi(\mathbf{x})(H(\phi_0(\mathbf{x})))), \sup_{\mathbf{x} \in \Omega} ((H(\phi(\mathbf{x})))\phi(\mathbf{x})(1 - H(\phi_0(\mathbf{x})))) \right\} \quad (3.26)$$

This is the reason why the expected segmentation errors using Eq. 3.26 are bigger than previous experiments (ventricle and putamen results). We introduce this measure because of its ability to calculate errors for three dimensional experimental work, explained in Chapter 6. It can be seen that the joint curve evolution provides more accurate results with the mean error $7.75mm$ while the mean errors of Tsai method and Chan/Vese are 11.88 and 8.79 respectively. As a typical example to illustrate the ability of our method, we show the segmentation results in the Figure 3.11 which conveys Tsai method and Chan/Vese approach and provide relatively reasonable results over 14 images in the dataset as well. The mismatching error of the segmentation results of the joint curve evolution (left), Tsai method (middle) and Chan/Vese model are $8.06 mm$, $12.04 mm$ and $8.54 mm$ respectively.

3.5.4 On the Robustness Issues

Segmentation results of three partially cluttering ventricle and putamen images, where they are occluded with horizontal bars, are shown in Figure 3.12 and Figure 3.13 respectively. We have tuned the coefficients of the energy terms as follows: kept the coefficient of the similarity term unchanged, $\lambda_s = 6$ for ventricle and $\lambda_s = 3$ for putamens, and changed the coefficient of the prior term two times larger, $\lambda_p = 4000$, in order to impose the shape-based forces more. The corresponding mismatching

Figure 3.10: Figures (a)-(m) 14 segmentation results for the thalamus of MR images by using the joint curve evolution algorithm with leave-one-out training strategy.

Table 3.2: The mismatching distance (mm) between the result and the ground truth measured using applied the joint curve evolution, Tsai method and Chan/Vese approach, and with the taken time (sec). The mean mismatching error and standard deviation of the joint curve evolution method (7.75 mm , 0.09) proves the improvement performance than parametric method (11.88 mm , 0.83) and also non-parametric model (8.79 mm , 0.04).

Method	Joint (mm, sec)	Parametric (mm, sec)	Non-parametric (mm, sec)
1	7.00, 12.77	10.29, 8.00	8.50, 3
2	7.609, 6.08	11.04, 8.00	8.48, 3.06
3	7.611, 6.00	13.03, 7.04	8.94, 3.12
4	7.608, 5.80	12.04, 6.84	8.94, 3.33
5	8.07, 5.80	12.80, 8.43	8.94, 3.28
6	8.06, 6.12	12.04, 8.43	8.94, 3.08
7	7.613, 5.90	12.64, 6.97	8.54, 3.07
8	8.058, 6.20	13.15, 7.05	8.54, 3.37
9	7.612, 6.44	12.04, 6.89	8.94, 3.25
10	7.607, 5.89	12.16, 6.64	8.94, 3.29
11	8.06, 6.11	12.04, 7.32	8.54, 3.16
12	8, 5.99	11.40, 6.99	8.94, 3.15
13	8.1, 6.21	10.29, 7.75	8.94, 3.09
14	7.611, 6.42	11.00, 7.07	8.94, 3.25

Figure 3.11: Comparative figures of segmentation of the thalamus from one sample in the dataset using applied the joint curve evolution (Figure (a)), Tsai method (Figure (b)) and non-parametric curve evolution (Figure (c)).

Figure 3.12: Segmentation results of ventricle shapes from MR images that are occluded by a horizontal bar. The initial curve is green curve.

Figure 3.13: Segmentation results of putamen shapes from MR images that are occluded by a horizontal bar.

errors are indicated in Table 3.3. The distance between the result and the ground truth curve are presented by d_T via using the mean Hausdorff measure. Comparing to the ventricles, evaluating of robustness of the proposed joint curve evolution on putamen images is much more challenging since the white matter/gray matter contrast of putamen boundaries is lower than other anatomical structures of the brain, especially the ventricles.

In summary, the obtained results verified that our novel framework, joint curve evolution, has better performance in accuracy compared with not only parametric curve evolution methods but also non-parametric active contours. While obtaining more accurate results, our approach is robust to the presence of clutter in the shape and the intensity of the object.

Table 3.3: Mismatching errors (mm) of the obtained results in Figure 3.12 of ventricle and Figure 3.13 of putamen shape segmentation from occluded MR images.

Image	a	b	c
$d_T(in \text{ Figure 3.12})$	1.03	0.88	0.98
$d_T(without \text{ occlusion})$	1.02	0.45	0.557
$d_T(in \text{ Figure 3.13})$	1.19	1.16	1.30
$d_T(without \text{ occlusion})$	0.659	0.881	1.162

Table 3.4: Quantitive validation of DC measures on the ventricles segmentation results from Figure 3.6 compared with three different ground truths.

Subject	Experiment1	Experiment2	Experiment3	Mean	Stdev
1	0.99354	0.99348	0.99344	0.99349	$4.84974E - 05$
2	0.99353	0.99363	0.99351	0.99356	$6.4291E - 05$
3	0.99340	0.99355	0.99358	0.99351	$9.64365E - 05$
4	0.99332	0.99330	0.99331	0.99331	$1E - 05$
5	0.99311	0.99326	0.99320	0.99319	$7.54983E - 05$
6	0.99301	0.99304	0.99310	0.99305	$4.58258E - 05$
7	0.99294	0.99293	0.99291	0.99293	$1.52753E - 05$
8	0.99280	0.99296	0.99291	0.99289	$8.18535E - 05$
9	0.99266	0.99280	0.99279	0.99275	$7.81025E - 05$
10	0.99279	0.99277	0.99278	0.99278	$1E - 05$
11	0.99275	0.99281	0.99268	0.99275	$6.50641E - 05$
12	0.99271	0.99292	0.99290	0.99284	0.000115902
13	0.99289	0.99297	0.99270	0.99285	0.000138684
14	0.99291	0.99284	0.99293	0.99289	$4.72582E - 05$

3.5.5 Quantitative analysis of segmentation accuracy

In this section, we explained how to assess the segmentation results accuracy by applying two different Hausdorff-based measurements: the average surface distance and the maximum surface distance (Eq. 3.26). In this part, we include dice coefficient measurement to further quantify the segmentation results accuracy: The dice coefficient is defined as:

$$DC = \frac{2|S_0 \cap S|}{|S_0| + |S|} \quad (3.27)$$

where S_0 and S are the volumes of ground truth and automatic segmentations, and $|S_0 \cap S|$ is the volume of their intersection. This coefficient can be expressed directly with the level set representations:

$$DC = \frac{2 \int_{\Omega} H(\phi_0) H(\phi) dx}{\int_{\Omega} H(\phi_0) dx + \int_{\Omega} H(\phi) dx} \quad (3.28)$$

In general, a value of DC superior to 0.7 is considered a good agreement [116]. We have applied the DC measurement on the ventricles segmentation results from Figure 3.6. Table 3.4 gives values of the DC as errors of distance between the segmentation results and three ground truths which were obtained from three different experts in our lab. The obtained values of DC fall in range of [0.99266-0.99363] and approve promising and acceptable accuracy for ventricles segmentation. Furthermore, we have added two more manual segmentations as ground truths for each subjects which were obtained by two different experts in our lab. Table 3.4 gives the mean and standard deviation of each subject over three different ground truths using applying DC measurement and indicates the capability of our approach in obtaining robustness and reliable results.

Table 3.5: Quantitive validation of the *DC* measures on the putamens segmentation results from Figure 3.8. The mean and the standard deviation of them are calculated over three different ground truths.

Subject	Mean	Stdev
1	0.98927	$6.35E - 05$
2	0.98997	$7.02E - 05$
3	0.99019	$8.91E - 05$
4	0.99032	$2.10E - 04$
5	0.99064	$6.05E - 05$
6	0.99043	$4.55E - 05$
7	0.99042	$1.53E - 05$
8	0.99067	$7.77E - 05$
9	0.99088	$8.12E - 05$
10	0.99094	$1.00E - 05$
11	0.99133	$6.44E - 05$
12	0.99160	0.000086002
13	0.99175	0.000142684

Table 3.6: Quantitive validation of the DC measures on the thalamus segmentation results from Figure 3.10. The mean and the standard deviation of them are calculated over three different ground truths.

Subject	Mean	Stdev
1	0.990720	$5.44E - 05$
2	0.990200	$6.22E - 05$
3	0.990320	$7.65E - 05$
4	0.989140	$3.21E - 03$
5	0.990920	$4.07E - 05$
6	0.989960	$1.55E - 05$
7	0.989500	$2.33E - 05$
8	0.989600	$6.54E - 05$
9	0.989540	$4.32E - 05$
10	0.989010	$2.10E - 04$
11	0.990930	$7.64E - 05$
12	0.989550	$2.10E - 04$
13	0.989760	0.000224122
14	0.989940	$1.28E - 05$

In addition, we have applied the DC measurement on putamens and thalamus segmentation results from Figure 3.8 and Figure 3.10 . Table 3.5 and Table 3.6 show the obtained DC measures respectively. For each subject the mean and the standard deviation of the obtained DC measures are calculated over three different ground truths. Similar to the ventricles segmentation results, we have obtained promising accuracy for the putamens and thalamus segmentation and approved the ability of our approach in subcortical structures segmentation.

3.6 Concluding Remarks

This chapter explains our novel joint curve evolution framework for medical image segmentation. In this algorithm, both parametric and non-parametric curve evolution methods are employed based on the Bayesian framework to extract object shapes using level set functions. As a result, the algorithm has the advantages of both parametric and non-parametric curve evolution. Our framework is as robust as the statistical model-based parametric curve evolution algorithm and at the same time, yields more accurate segmentation results. There are also recent works by Rousson et al. [19] and Bresson et al. [21], which obey the same parametric and statistical model in level set method. However, one important difference is that these methods directly apply a PCA model to constrain the level set function while matching it with the image features. Thus, the level set function is more constrained by the prior distribution. Furthermore, our algorithm is more flexible for segmenting complicated shapes by using joint parametric and non-parametric curve evolution idea.

Chapter 4

A Novel

Expectation-Maximization (EM)

Approach to Joint Curve

Evolution for Medical Image

Segmentation

4.1 Introduction

In Chapter 2, we proposed two alternative groups for MR brain segmentation techniques. The first group is called region-based labeling or voxel-wise technique which obeys the intensity-based classification to assign each voxel to a specific tissue type. In these algorithms, applying local statistical methods is straightforward to model tissue intensity and spatial information. Since these methods utilize low level pixel information of images, they tend to fail in the case of noise, low image contrast,

diffused boundaries and occluded shapes. Therefore, the second group is suggested as the model-based statistical method that utilizes Bayesian inference for solving the uncertainties in medical segmentation problem via integrating prior knowledge and generative image model. This group of segmentation methods is defined in the family of deformable shape matching or curve evolution. The objective is to find the optimal partition of the image domain in terms of a closed curve which is evolved using the image data and prior constraints on the variation of shape, size and spatial positions. Compared to the first group approaches, statistical deformable models can provide more reliable and accurate segmentation of objects in images in the case of noise and incomplete observation data, due to utilization of relatively global information about objects [5, 4, 19, 21, 31].

The important advantage of the first group compared to the second group is that hidden features known as underlying local voxel labeling could be applied. However, an important disadvantage of the voxel-wise segmentation techniques is lack of provision to integrate statistical shape-based models. In this chapter, we introduce our approach to integrate the advantages of both groups. Our method can be categorized as implicit deformable shape matching. In our proposed algorithm, the evolution curve is constrained not only by a shape-based statistical model but also by a hidden variable model from the image observation. The hidden variable model is unknown and estimated by the expected likelihood function defined by the image data and the built prior anatomical knowledge. Consequently, our segmentation framework takes the advantage of traditional EM-based segmentation and also deformable shape models.

4.2 Motivation

The motivation of this chapter is to solve major problems associated with voxel-wise approaches and deformable models. In these techniques, maximizing the posterior distribution of the desired parameters corresponding to the statistical models is not tractable due to:

- The limitation of the observation data as missing values in the image domain.
- Applying an infinite-dimensional optimization in the deformable models.

To simplify these segmentation problems, the additional features can be considered for modeling the missing (hidden) information and integrated into the basic segmentation framework. In this context, the EM algorithm is a well-known technique in which distributions of the incomplete observation data are identified with help of estimation of hidden variables. The missing data in segmentation methodologies is introduced by underlying local voxel labeling. In our work, the hidden variables are unknown and associated with missing data and defined by SDF of probability of allocated labeling for each voxel. In the literature, it has been illustrated that voxel-wise segmentation techniques can utilize the EM algorithm for learning generative models due to the direct dependencies between estimation variables of the models and the hidden variables. However, in the shape evolution techniques, it is more challenging to find the relation between the hidden variables and the shape model variables. In [8], dependencies between the learning data from the EM algorithm and the shape model parameters is defined by an explicit space-conditioned probability model, where the shape model parameters are represented by level set functions. In [28], the evolving boundary is constrained by the normalized difference (least squares fitting) between the expected value and the actual value from current boundary using an adaptive EM model.

In this chapter, we introduce our contributions as a new shape evolution approach in the concept of active contours deformation where the data features are “incomplete”. In our contributions, the EM algorithm is employed for maximum-a posterior estimation of shape-based model parameters which poses in the infinite-dimensional optimization. The additional features are used as the hidden variables for compensating the incomplete observation data. The hidden variables are unknown and associated with missing data and presented as underlying local voxel labeling. We employ the joint shape evolution method [31] for the shapes representation and the shapes are deformed in two different domains: the image domain, which adopts the non-parametric shape evolution, and the statistical shape domain, which adopts the parametric shape evolution using the PCA concept. The difference is that herein the shapes are estimated using the EM algorithm. Building upon the EM-joint shape based framework, our scheme can be carried out tractably and analytically by integrating the shape-based statistical techniques and the hidden variable model. In the E-step, the expected likelihood of the complete data is computed, which includes two terms: the observation likelihood and the prior distribution of the hidden variables given current shape-based model and the image information. In the M-step, the parametric and non-parametric level set functions are updated by maximizing their posterior distributions, weighted by the results of the E-step. In order to build a reliable EM-joint shape based framework, some assumptions are made as follows:

- 1) The non-parametric shape estimation, denoted by ϕ , is related to the local voxel labels (missing data) and the image data. The non-parametric shape evolution utilizes the computed weights from the expected likelihood of the complete data and is constrained by the similarity measure with the parametric shape.
- 2) The parametric curve evolution, denoted by Φ , is independent of the observation data and the local voxel labels (missing data) and is constrained by the similarity with the non-parametric shape representation as well as the explicit shape priors defined by

Figure 4.1: The proposed *EM-joint shape based framework*.

the new PCA model.

Our framework, called *EM-joint shape based method*, is depicted in the Figure 4.1. In the training stage, we employ new PCA algorithm such that the covariance matrix is defined by not only the shapes information but also the image intensity patterns inside the object. The details of the new PCA algorithm are explained in the next section.

The remainder of this chapter is organized as follows. In the Section 4.3, the new PCA algorithm is introduced. In the Section 4.4, we describe the combination of hidden variable model and statistical shape-based model via introducing the new level set speed function. In sections 4.4 and 4.4.1, the proposed EM-joint shape based framework is explained. A consolidated representation of implementation of our novel EM-joint shape based framework is given in Table 4.1. We demonstrate several segmentation applications for 2D and 3D medical imaging. Finally, the discussion and conclusion is presented in Section 4.6.

4.3 Constructing Shape/Appearance based Training Model

In the joint curve evolution approach (Chapter 3), we applied traditional PCA analysis to build the shape-based model from a training dataset of aligned images. The corresponding level set functions of these images are defined as the training set of shapes. Consequently, the covariance matrix of data (shapes) is used to find the encoded shape based prior knowledge. Furthermore, we observe that gray level variation in the image is related to the shape prior information consistently. The new research area in explicit curve evolution have been begun by proposing Active Shape Model (ASM) [24] and Active Appearance Model (AAM) for medical images segmentation. Yang et.al. [117] and Fritscher et al. [118] proposed 3D implicit deformable shape matching and used joint probability distribution over the variations of the shape and appearance. Considering non-linear variations, Cremer et al. [119] proposed kernel PCA to update level set function in non-linear space. Similar to the relationship between Active Shape Model (ASM) [24] and Active Appearance Model (AAM) [25], we employ new PCA analysis in the training stage, herein the covariance matrix is defined by not only the shapes information but also the image intensity patterns inside the object. Since we have applied joint shape and intensity information in one covariance matrix and then applied them to the segmentation framework, optimization process looks for the best solution of shape-intensity fitting. The correlation information between shape and intensity of the object would be implemented easily by applying one level set function as a function of curvature and intensity. Then, a PCA model is constructed from a training set of aligned subject defining the statistics of both shape and intensity/appearance information. The new PCA model enables us to provide more robust and reliable results compared to the traditional shape-based PCA model which utilizes only

training information of the shapes. Validation results prove that the new PCA analysis is more accurate and reliable compared to the traditional PCA.

4.3.1 Detail of Shape/Appearance based Model

The diagram of the new PCA model is illustrated in Figure 4.2, we form n column vectors, $\hat{\Phi}_i$, consisting of $2N$ samples of each training example (using identical sample locations for each). The $2N$ samples convey the shape information defined by Signed Distance (SD) values and also the intensity information inside the shape. The mean function and then the mean-offset matrix ($2N \times n$) are obtained from the set $\{\hat{\Phi}_1, \hat{\Phi}_2, \dots, \hat{\Phi}_n\}$. The singular value decomposition of the mean-offset matrix is applied to extract the n principal variational modes to project a shape/intensity into the eigenspace and corresponding eigenvalues matrix.

4.3.2 Applying Registration to Similarity-Invariance

In order to achieve similarity invariance between the constructed shape/intensity model and the current shape evolution, the global registration is applied via using the observation image data. Using the registration process, our segmentation framework enforces the evolving shape to extract the desired shape in the image that has the same geometric properties as the constructed shape/intensity prior model. In order to handle the geometric variations, pose parameter $\mathbf{p}$ is added to the shape-based PCA model. Then, the statistical model is obtained as follows,

$$\Phi[\mathbf{w}, \mathbf{p}](\mathbf{x}) = \bar{\Phi}(\tilde{\mathbf{x}}) + \sum_{k=1}^K w_k \varphi_k(\tilde{\mathbf{x}}), \quad \tilde{\mathbf{x}} = T(\mathbf{p})\mathbf{x}, \quad (4.1)$$

where $\mathbf{w}$ defines the feature vector of shape and φ_k presents re-sampled k th eigenvector of the k th variational mode, and weighted by the shape parameter w_k with

Figure 4.2: Diagram illustrating the formation of the column vectors $\{\hat{\Phi}_1, \hat{\Phi}_2, \dots, \hat{\Phi}_n\}$ for building shape/intensity-based PCA model.

the variance σ_k^2 . The corresponding eigenvalue is denoted by matrix Σ ($n \times n$). Notice that the shape-based statistical model explained in Section 3.2 does not take advantage of the gray-level information available inside the shapes as the new PCA algorithm does. In the experimental results, we apply the new PCA algorithm for training stage to obtain the 2D and 3D segmentation results of the putamen and the caudate nucleus in the sagittal and axial views of the MR images. Furthermore, in order to show ability and robustness of the new PCA, we compare the obtained segmentation result of caudate object with the one using traditional PCA algorithm.

Figure 4.3 provides some intuition as to how the new level set representation of the model Eq. 4.1 captures shape/intensity variability of the caudate nucleus by varying

Figure 4.3: Shape/intensity variation of caudate nucleus in the axial (*top*) and sagittal (*down*) cuts by varying the weights for the first principal component ($\sigma = \sqrt{\Sigma_1}$).

Figure 4.4: Putamen shapes by varying the weights for the first principal component ($\sigma = \sqrt{\psi_1}$).

the weights for the first principal component of the new PCA model. In order to construct the statistical model of the caudate nucleus in the axial view (Figure 4.3(top)), we used nine training images as the training data, and four principal components that fit 97.3% of the total energy. The second example of statistical model (Figure 4.3(bottom)) is built from eighteen MR images in the sagittal view. Also four major components are used that fit 96.96% of the total energy. It can be seen that for these two models the major shape changes have been captured by the first principal component. Knowing *a priori* about the shape of putamen, we employ the 2D dataset of eighteen MR images to obtain the mean shape and the eigenshapes of our implicit shape/intensity model. Four principal components are finally chosen, which can represent about 97.5% of the total energy of the space spanned by the the training dataset, see Figure 4.4. For 3D experimental works,

Figure 4.5 shows the demonstration of 3D statistical and implicit model from twenty-three patients. In this example, four major principle components are chosen which involve 87% of the total energy of the space spanned by the training set. We employ the mean shape as the initial active surface, shown in Figure 4.5a.

4.4 Expectation-Maximization (EM) Approach to Joint Curve Evolution

In Section 2.4.2, the general idea and formulation of image segmentation techniques based on the shape evolution system was explained such that the shape is represented implicitly using level set method. According to Eq.2.10, the propagating shape is represented via updating the zero level set of a higher dimensional function $\phi(\omega(t); t)$ where $\phi_t = \frac{\partial \phi}{\partial t}$ as follows,

$$\begin{aligned} \phi_t + F(\omega(t); t) |\nabla \phi| &= 0 \\ \text{given an initial condition } \phi(\omega(t); t=0) &= 0 \end{aligned} \quad (4.2)$$

where $\omega(t)$ denotes the coordinates and $F(\cdot)$ is the speed propagation function that controls the evaluation of the level set. The speed function employs the mean curvature motion and can be further decoupled into several terms as $F(\cdot) = F_1 F_2 F_3$. F_1 indicates the internal geometric properties of the shape which helps evolve the shape to be smooth and regularized. F_2 allows the image information to be expressed in terms of level set framework to evolve the shape towards desired boundaries and the regions in the input image. Simply put, this term is represented by the log likelihood of the observation data. The third term F_3 encodes spatial prior knowledge and allows the evolution of the shape subject to the prior constraints. In

Figure 4.5: The 3D shape variation of the caudate nucleus shape, figure (a) the mean shape with the positive variation of the first and second principle modes, figures (b) and (c), and with the negative variation of them, figures (d) and (e).

this study, our contribution can be interpreted as the design of new speed function as follows,

$$F(\omega(t); t) = \kappa(\omega(t); t)p(I|\phi)\eta(\phi), \quad (4.3)$$

where the first term shows the intrinsic geometric shape properties, the second term is defined as the observation likelihood which explains the matching degree between the evolving shape and the input image. Finally, the last term shows the new defined shape prior constraint on the evolving shape. In order to normalize the dynamic range of the shape prior information, the sigmoid map function is used: $\eta(\phi) = \frac{1}{(1+\exp(-\frac{\phi-\beta}{\alpha}))}$. In our method, the non-parametric shape ϕ is calculated by maximizing its posterior distribution, weighted by the estimated hidden variables and constrained by the parametric shape in order to make formal link the level set scheme into EM criterion.

In the following section, we explain the details of our segmentation scheme as an EM-joint framework which is summarized in a flowchart in Figure 4.1.

4.4.1 Non-parametric Shape Evolution

Our proposed EM shape based algorithm utilizes the joint curve evolution framework (Chapter 3) to achieving the evolution process. The first step is to estimate the non-parametric shape by assuming that the parametric shape is known. Using the complete and full observation dataset with the hidden variables (I, x) , we rewrite the non-parametric optimization part of the joint curve evolution approach as,

$$\phi \leftarrow \operatorname{argmax}_{\phi} \{ \log p(I|x, \mathbf{w}, \mathbf{p}, \phi) + \log p(x|\phi, \mathbf{w}, \mathbf{p}) + \log p(\phi, \mathbf{w}, \mathbf{p}) \}, \quad (4.4)$$

where joint ϕ and $(\mathbf{w}, \mathbf{p})$ explain the shape representation and x is the hidden variable which acts as the underlying voxel labeling. According to our proposed EM-joint shape based algorithm, the hidden variable identifies the distribution used to generate observation data (first term) and is governed by underlying its distribution given the joint shape representation model (second term). In our scheme, we assume that estimation of the non-parametric shape representation ϕ is related to the hidden variable (the local voxel labels) x and the image data I . Using the computed weights, in the E-step, from the expected likelihood of the complete data, the non-parametric shape evolution is estimated optimally while constrained by the similarity measure with the parametric shape. On the other hand, the parametric shape representation $\Phi(\mathbf{w}, \mathbf{p})$ is independent of the hidden variable (the local voxel labels) x and the image data I , it is also constrained by making similarity with the non-parametric shape representation as well as encoded explicit shape/appearance prior model, explained in Section 4.3.

As a result, the M-step can be simplified as follows to estimate the non-parametric

shape,

$$\begin{aligned} \phi &\leftarrow \arg \max_{\phi} E_{x|I,\phi} \{ \log p(I|x, \phi) + \log p(x|\phi) + \log p(\phi|\mathbf{w}, \mathbf{p}) \} \\ \phi &\leftarrow \arg \max_{\phi} \sum_i \sum_{k=1,2} E_{x_{i,k}|I_i,\phi} \{ \log p(I_i|x_{i,k}, \phi) + \log p(x_{i,k}|\phi) \} \\ &\quad + \log p(\phi|\mathbf{w}, \mathbf{p}), \end{aligned} \quad (4.5)$$

where $x_{i,k}$ means the local label of voxel i assigned to region k . In this formulation, we assume that the entire image area is divided into two homogenous regions by the object boundaries, e.g. $k = 1$ refers to all voxels in the inside region of the object, and $k = 2$ means the image region is outside the object. The first energy term of Eq. 4.5 explains the observation likelihood governed by the set of parameters associated with the inside and the outside region of the shape ϕ . For example, the mean and the variance of the inside region can be defined by: $\mu_1 = \sum_i I_i \cdot H(\phi_i) / \sum_i H(\phi_i)$ and $\sigma_1^2 = \sum_i I_i^2 \cdot H(\phi_i) / \sum_i H(\phi_i) - \mu_1^2$. Using the Gaussian emission distribution:

$$\log p(I_i|x_{i,k}, \phi) = \frac{-1}{2} \log \sigma_k^2 - \frac{(I_i - \mu_k)^2}{2\sigma_k^2}. \quad (4.6)$$

The second term of Eq. 4.5, $\log p(x_{i,k}|\phi)$, equals the spatial prior probability of $x_{i,k}$ under the current shape model ϕ which defines the probability of the voxel i assigned to the region k . This term is formulated using the following simple sigmoid map function as:

$$p(x_i|\phi_i) = \frac{1}{1 + \exp^{0.5\phi_i}}, \quad (4.7)$$

which maps the distance map to the range of $[0, 1]$. If voxel i is located inside the object, ϕ_i is negative and $p(x_i|\phi_i) \in (0.5, 1]$. Otherwise, ϕ_i is positive and $p(x_i|\phi_i) \in [0, 0.5]$. This additional prior knowledge ensures that the shape-based model captures larger range of shape variability than solely linear PCA shape-based

model. The idea of sigmoid map function of the distance transform is employed in [8] to provide an explicit space-conditioned probability shape model. Finally, the last term of Eq. 4.5, $\log p(\phi|\mathbf{w}, \mathbf{p})$, defines the difference between the parametric and the non-parametric shapes so that they represent similar shapes.

$$\log p(\phi|\mathbf{w}, \mathbf{p}) = - \int_{\Omega} (H(\phi(\mathbf{x})) - H(\Phi[\mathbf{w}, \mathbf{p}](\mathbf{x})))^2 d\mathbf{x}. \quad (4.8)$$

In Eq. 4.5, the expectation is taken with respect that the computed conditional distribution of the hidden variables given the current non-parametric shape descriptor and the observation (incomplete) data. The computed values are used to form the expected value of the log-likelihood under the probability mass function, i.e., $\log p(I_i|x_{i,k}, \phi) + \log p(x_{i,k}|\phi)$ in the Eq. 4.5. The E-step can be defined as follows:

$$E_{x_{i,k}|I_i, \phi} \equiv p(x_{i,k}|I_i, \phi) = \frac{p(I_i|x_{i,k}, \phi)p(x_{i,k}|\phi)}{p(I_i|\phi)}, \quad (4.9)$$

Therefore, in the non-parametric curve evolution, the minimization of the energy objective function is straightforward when the gradient descent algorithm with respect to the level set function ϕ is used.

4.4.2 Parametric Shape Evolution

In our proposed EM-joint shape based framework, the concept of the parametric shape evaluation known as joint curve evolution approach is similar to the explained in Chapter 3. The parametric shape evolution is constrained by the prior distribution trained from samples of shape and appearance described in Section 4.3. Furthermore, we assume that estimations of $\mathbf{w}$ and $\mathbf{p}$ are not directly related to the observation data I and the hidden variable x , since they are updated in the statistical shape domain. In order to make interaction between parametric shape

and the complete observation data (I and x), the conditional probability between parametric and non-parametric shapes is used to make sure that these two shapes are close enough. Then, the parametric active contour is computed by updating the shape and the pose parameters $\mathbf{w}$ and $\mathbf{p}$ as follows:

$$\frac{\delta \mathbf{w}}{\delta t} = - \left(\Sigma_q^{-1} \mathbf{w} + 2 \int \int_{\mathbf{C}} \left((H(\Phi[\mathbf{w}, \mathbf{p}]) - H(\phi)) \nabla_{\mathbf{w}} \Phi[\mathbf{w}, \mathbf{p}] \right) ds \right), \quad (4.10)$$

$$\frac{\delta \mathbf{p}}{\delta t} = -2 \int \int_{\mathbf{C}} \left(\left(H(\Phi[\mathbf{w}, \mathbf{p}]) - H(\phi) \right) \nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}] \right) ds, \quad (4.11)$$

where Σ_q is the diagonal matrix containing q largest eigenvalues according to the new PCA analysis supposing that in the Eq. 4.10 and Eq. 4.11, the line integral is calculated along the curve $\mathbf{C}$ of zero level set of the function $\Phi[\mathbf{w}, \mathbf{p}]$. The $\nabla_{\mathbf{w}} \Phi[\mathbf{w}, \mathbf{p}]$ describes the gradient of the parametric shapes model Eq. 4.1 with respect to the $\mathbf{w}$. The k th component of this gradients are given by,

$$\nabla_{w_k} \Phi = \varphi_k \quad (4.12)$$

To compute $\nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}]$, we follow these equations:

$$\begin{aligned} \nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}] &= \nabla_{\mathbf{p}} \Phi[\mathbf{w}, \mathbf{p}](\tilde{\mathbf{x}}) \\ &= \nabla_{\tilde{\mathbf{x}}} \Phi[\mathbf{w}, \mathbf{p}](\tilde{\mathbf{x}}) \cdot \left(\frac{\partial T}{\partial \mathbf{p}} \mathbf{x} \right), \end{aligned} \quad (4.13)$$

such that the pose parameter of the evolving shape is taken close to the position of the input image and includes $\mathbf{p} = \{t_1, t_2, \chi, \theta\}$ such that t_1 , t_2 , χ and θ correspond

to translation, scale and rotation, respectively and $\frac{\partial T}{\partial \mathbf{p}}$ is calculated as follows,

$$\begin{aligned}
\frac{\partial T}{\partial p_1} &= \frac{\partial T}{\partial t_1} = \frac{\partial \mathbf{t}(t_1, t_2)}{\partial t_1} \mathfrak{S}(\chi) R_\theta(\theta) \\
\frac{\partial T}{\partial p_2} &= \frac{\partial T}{\partial t_2} = \frac{\partial \mathbf{t}(t_1, t_2)}{\partial t_2} \mathfrak{S}(\chi) R_\theta(\theta) \\
\frac{\partial T}{\partial p_3} &= \frac{\partial T}{\partial \chi} = \mathbf{t}(t_1, t_2) \frac{\partial \mathfrak{S}(\chi)}{\partial \chi} R_\theta(\theta) \\
\frac{\partial T}{\partial p_4} &= \frac{\partial T}{\partial \theta} = \mathbf{t}(t_1, t_2) \mathfrak{S}(\chi) \frac{\partial R_\theta(\theta)}{\partial \theta}.
\end{aligned} \tag{4.14}$$

4.4.3 Comparison between EM-Joint Shape Based and Voxel-Wise Labeling Approaches

Technically, the EM-joint shape-based curve evolution approach employs automated labeling methodology. Since our approach is categorized in the deformable curve evolution, it would be interesting to highlight major differences between the EM-joint shape-based curve evolution and automated labeling approaches. Two strong tools about automated labeling are FreeSurfer [120] developed by Harvard University and Atals Based Classification (ABC) [121] developed by University of North Carolina Chapel Hill. The idea behind these tools is to match image volumes to the atlas image intensity histogram by doing intensity normalization. Using traditional deformable curve evolution approaches, clinician is able to extract the regions of interest by choosing proper initial curve. This is important for studies, which need to investigate some regions of brain. For example, in the study of Huntington disease, atrophy of the caudate nucleus and putamen has been described before clinical manifestation. Although, Freesurfer will be able to do fully segmentation of anatomical structures, however, the segmentation process is very time consuming (around 15 hours running on main server in our lab). This running time increased by doing training process which is totally estimated around 24 hours. On other

hand, using our approach, segmentation process takes around 20 min and training process with same number of training samples takes around 15 min. Moreover, voxel-wise labeling tools such as FreeSurfer and ABC prone to non-smooth subcortical segmentations and may cause difficulties in shape analysis algorithms [122] due to shape-noise. However, the generated segmentation results of our approach are inherently smooth and can be applied directly in shape analysis algorithms. Note that our approach can improve by developing an automated labeling process using MRF models, similar to segmentation method of FreeSurfer.

4.5 Experimental Results and Discussion

In this section, we demonstrate the performance of the proposed EM-joint shape based segmentation framework using real clinical 2D and 3D MR brain images to extract caudate nucleus and putamens, and the results are evaluated by comparing them with the manual segmentations of caudates and putamens structures. The obtained results are trained by the new PCA explained in Section 4.3 and compared with three different methods. 1) Joint curve evolution approach which uses the same joint parametric and non-parametric shape representation [31]. 2) Tsai method as the parametric shape evolution [4]. 3) Chan/Vese algorithm as the non-parametric shape evolution [10].

Notice that to assess the obtained 2D results, we compute the mismatching distance between the resultant shape and the ground truth by applying mean Hausdorff measurement. The ground truth is the manual segmentation obtained by the expert in our institute, selecting 300 points on the boundary of the desired organ. These selected points are assumed to have values of zero in the manual segmentation SDF. Based on the obtained absolute values of these points from resultant shape SDF

Table 4.1: Implementation Process

Algorithm : Expectation-Maximization-Maximum-a-Posterior Joint Shape Evolution:

procedure Training-JointShapeAppearance(Training images $I = \{I_1, I_2, \dots, I_n\}$)

 define $B = \{B_1, \dots, B_n\} \leftarrow$ binary images of desired shapes from I

 define $\Phi = \{\Phi_1, \dots, \Phi_n\} \leftarrow$ construct corresponding level set functions

 define $A = \{A_1, \dots, A_n\} \leftarrow$ appearance information about inside the objects
 corresponding to the set B

 define rigidly align set A into a spatial coordinate and employ the same
 similarity transformation on the set Φ

 define $\hat{\Phi} = \{\hat{\Phi}_1, \dots, \hat{\Phi}_n\} \leftarrow$ merging sets A and Φ sample by sample

 define $\bar{\Phi} \leftarrow$ mean shape/intensity of training set $\hat{\Phi}$

 define $\varphi \leftarrow$ eigenmodes of shape/intensity variation via applying PCA analysis

return $(\bar{\Phi}, \varphi, \Phi)$
procedure Segmentation-EM-joint shape based(Input image $I, \bar{\Phi}, \varphi, \Phi$)

 define $\phi \leftarrow$ initial curve with mean shape $\bar{\Phi}$

 for some iterations till $error < \varepsilon$

 function Non-parametric-Evolve-EM(I, ϕ, Φ)

 E-step: calculate the underlying local segmentation x , given current ϕ and the
 image I using Eq.4.9

 M-step: calculate optimal ϕ by maximizing its posterior distribution and
 make similarity with the parametric shape Φ using Eq. 4.5

 return ϕ

 define $\phi \leftarrow$ renew ϕ

 function Parametric-Evolve(ϕ, Φ)

 updating parametric shape Φ using Equ. 3.15 and Equ. 3.19

 return Φ

 define $\Phi \leftarrow$ renew Φ

 end
return ϕ as final result

that shows the distance error of each point, we compute the mean error over all selected points. For 2D experimental works, this process provides a promising and convenient way to obtain mean error from the manual segmentation.

To assess the advantages of 3D EM-joint shape based algorithm, we compute the maximum mismatching distance between the obtained result and the corresponding ground truth via the Hausdorff measurement as follows:

Hausdorff Distance =

$$\max \left\{ \sup_{\mathbf{x} \in \Omega} ((1 - H(\phi(\mathbf{x})))\phi(\mathbf{x})(H(\phi_0(\mathbf{x})))), \sup_{\mathbf{x} \in \Omega} ((H(\phi(\mathbf{x})))\phi(\mathbf{x})(1 - H(\phi_0(\mathbf{x})))) \right\} \quad (4.15)$$

where ϕ is the segmented result and ϕ_0 corresponds to the shape of the ground truth which is represented by SDF. We will show that the Eq. 4.15 is also capable of measuring distance error for 2D experimental results.

4.5.1 Segmentation of Putamen

We evaluate the performance of the algorithm for segmenting putamen structures from a dataset with a large range of shape variability. The dataset includes eighteen T1-weighted images with 217×181 dimensions, $0.9375 \times 0.9375 mm^2$ spacing and is applied for training and testing using the leave-one-out strategy. Based on the new PCA model, the constructed shape based model of putamen, explained in Section 4.3 and Figure 4.4, is applied for training stage. Figure 4.6 illustrates segmentation of eighteen MR axial slices of putamen structures using applied the EM-joint shape based framework. For each image, the corresponding manual segmentation is used as the ground truth which is obtained by one radiologist from our institute. An

overall 600 points are selected randomly on the desired boundaries as the manual segmentation and used for computing the mean Hausdorff distance of the resultant shapes. The obtained mean error over the dataset is recorded as $1.19mm$.

In order to show reliability and accuracy of the proposed method, we compare the EM-joint shape based framework to three different methods with the manual ground truth: joint curve evolution approach as the non-EM shape based curve evolution [31], Tsai method as the parametric curve evolution [4] and Chan/Vese algorithm as the non-parametric curve evolution [10]. In order to achieve a fair and reliable comparison system, the same training process is performed for the EM-joint shape based algorithm, joint curve evolution and Tsai method. Furthermore, the same initialization process is performed to define a proper location for the initial shape for all four algorithms. We manually estimate the desired object center as the proper location of the object, and then rigidly shifted the mean shape to that location, acting as the initial shape.

Figure 4.7 shows the comparative results of putamen structures segmentation from these eighteen tests. It can be seen that the performance of the proposed EM-joint shape based algorithm is noticeably better than other three algorithms. Table 5.2 summarizes the improvement of the joint parametric and non-parametric curve evolution algorithm [31] (the mean error is $1.25mm$) over the solely parametric curve evolution method [4] and non-parametric curve evolution technique [10] (with the mean errors $1.3mm$ and $1.45mm$) respectively. The advantages of integrating parametric and non-parametric curve evolution. Table 5.2 illustrates the improvement of the proposed EM-joint shape based algorithm (with the matching error $1.19mm$) over the joint curve evolution approach and highlights the advantages of using combination of the hidden variable model and joint curve evolution concept.

Figure 4.6: Automatic segmentation of putamens shapes of MR images by applying the proposed EM-joint shape based method for all the eighteen subjects, the mean error recorded as $1.19mm$. The green curve shows the initial curve and the red curve shows the segmentation result.

(a)

(b)

Figure 4.7: Comparison results for extracting putamens corresponding to eighteen experimental tests on Figure 4.6 between the EM-joint shape based, solely parametric and non-parametric curve evolution methods (Figure (a), the mean errors are recorded as $1.19mm$, $1.3mm$ and $1.45mm$) and joint curve evolution as non-EM Shape based method (Figure (b), the mean error is recorded as $1.25mm$).

Table 4.2: Mean and standard deviation of the similarity value H_d for the segmentation of the putamens structures (unit in mm).

Method	EMjoint	NonEM	Parametric	Non-parametric
Mean	1.19	1.25	1.3	1.45
Std. Dev.	0.12	0.09	0.14	0.08

4.5.2 Segmentation of Caudate Structures

The segmentation of the caudate nucleus is challenging, because difference in intensity values of the caudate nucleus and the cortical gray matter is not high. Furthermore, the caudate nuclei is closely related to the lateral ventricle with high intensity values. The experimental results illustrate that although the EM-joint shape based algorithm is assigned to the region-based active contour family and may suffer from local minima. It achieves a more reliable and accurate approach by integrating hidden variable model and shape-based model in the unique framework.

We apply the proposed EM-joint shape based algorithm trained by the new PCA on two different sets of real clinical MR brain images to extract the caudate nucleus structures. The first dataset contains nine 2D real MR images with the axial cuts and the second set includes eighteen samples in the sagittal view. In the previous section, we showed the promising results of our proposed work, called joint parametric and non-parametric curve evolution approach, compared to the parametric method [4] and non-parametric curve evolution method [10]. Next, we demonstrate the issue of improvement of the EM-joint shape based framework over the non-EM shape based algorithm implemented by the joint curve evolution approach [31].

The first dataset includes nine T1-weighted images (with 256×256 dimension and $0.945 \times 0.945 mm^2$ spacing) of different normal adult subjects. Figure 4.8 illustrates nine MR axial slices of the head caudate nucleus segmentation using applied the EM-

Figure 4.8: Automatic segmentation of caudate shapes of MR images by applying the proposed EM shape based evolution method for all the nine subjects. The initial curve presented by green color.

joint shape based algorithm. The average Hausdorff distance between the results and the ground truth images were then recorded to give the error measurement. For each testing image, 600 points were selected on the desired boundaries of the caudate structures as manual segmentations by one radiologist from our institute. The mismatch errors were then obtained by following the SD values of these manual points of the resultant level set function. Figure 4.9 highlights the improvement of the EM-joint shape based algorithm compared to the joint curve evolution approach with 31.89% over nine subjects in the dataset. Table 5.4 summarizes the reliability and ability of the EM-joint shape based algorithm. The improvements over the joint curve evolution method are as follows: mean error, 31.89%, the standard deviation value, 52.3%, the best and the worst segmenting results, 46.7% and 35.9%. The

Figure 4.9: Comparison results for extracting caudate corresponding to nine experimental tests on Figure 4.8 between the EM-joint shape based algorithm and joint curve evolution method as non-EM shape based technique, the mean errors are recorded respectively as $1.26mm$ and $1.85mm$.

same training process explained in Section 4.3 and Figure 4.3(*top*) was performed for both the EM-joint shape based algorithm and the joint curve evolution.

The second dataset presents experimental results of the caudate nucleus extraction in the sagittal view demonstrating the EM-joint shape based algorithm. It includes eighteen different T1-weighted MR brain slices (with 256×256 dimension and $0.945 \times 0.945mm^2$ spacing). Figure 4.10 illustrates eighteen MR sagittal slices of the head

Table 4.3: Summary over nine subjects of caudate segmentation comparison between results of EM-joint shape based algorithm and Non-EM shape based method with the ground truth, unit in mm .

Method	Mean	Variance	Minimum	Maximum
EM-joint framework	1.26	0.20	0.57	1.85
Joint curve evolution Method	1.85	0.42	1.07	2.89
Improvement in percentage	31.89%	52.3%	46.7%	35.9%

Table 4.4: Summary over eighteen subjects of caudate segmentation comparison between results of EM-joint shape based algorithm and Non-EM shape based method with the ground truth, unit in *mm*.

Method	Mean	Variance	Minimum	Maximum
EM-joint framework	6.800	0.828	5.38	8.892
Joint curve evolution Method	8.121	3.67	5.123	10.92
Improvement in percentage	19.42%	34.32%	-4%	22.83%

caudate nucleus segmentation using the EM-joint shape based algorithm. It could be seen that reasonable segmentation is achieved although this dataset contains a huge range of shape variation of the caudate nucleus. In order to assess the performance of the EM-joint shape based algorithm quantitatively, the maximum mismatching distance between the result and the ground truth shapes is measured using Eq. 4.15 as the Hausdorff measurement. Another comparison demonstration from this dataset between the EM-joint shape based algorithm and the joint curve evolution is also presented. All needed training process has been achieved similar to the one explained in Section 4.3 and shown in Figure 4.3. Figure 4.11 and Table 4.4 show the improvements of the EM-joint shape based algorithm in terms of accuracy criteria. Technically, the main reason for improvement is the application of extra shape-based prior information which is computed by estimating the hidden variable model. The improvements of the EM-joint shape based algorithm are as follows: the mean error, 19.42%, the standard deviation value, 34.32%, the best and the worst segmenting results, -4% and 22.83%. The large difference between the smallest and the largest error values of the joint curve evolution approach can be seen in Figure 4.11 (blue curve). In the following section, we show the performance of the new PCA algorithm (described in Section 4.3) and comparative result with the traditional PCA analysis.

Figure 4.10: Automatic segmentation of the caudate shapes in the sagittal cuts of MR images by applying the proposed EM shape based evolution method for all the eighteen subjects in the dataset.

Figure 4.11: Comparison results for extracting caudate of sagittal cuts corresponding to eighteen experimental tests on Figure 4.10 between the EM-joint shape based algorithm and joint curve evolution method as non-EM shape based technique, the recorded mean errors are $6.8mm$ and $8.12mm$ respectively.

4.5.3 Evaluating Joint Shape and Appearance Training Model

As the last experimental test, we evaluate the EM-joint shape based algorithm when it is trained based on the new PCA algorithm which adopts not only shape information but also inside intensity of the object in training stage and show the comparison result with the one using the traditional PCA technique. Figure 4.12 presents the segmentation results of the caudate object by applied the EM-joint shape based framework. Figure 4.12(b) is obtained with using the traditional PCA technique and Figure 4.12(c) is based on using the new PCA algorithm, and the mismatch error of each figures are recorded as: $0.66mm$ and $0.64mm$ respectively. The difference of the mismatch errors are not very high, and the reason is that the shape information and inside intensity of the object is trained jointly and construct the shape based PCA model. However, it can be seen that if separate appearance

Figure 4.12: An example of the segmentation results. (a) an input image from nine testing images. (b) the segmenting result after applying traditional PCA analysis. (c) the result after applying new PCA analysis.

model is constructed in the EM-joint shape based framework, more promising and accurate results will be obtained.

4.5.4 Extending to 3D Models

In this section, the 3D segmentation results of the extension of our novel EM-joint shape based approach are illustrated to exploit single structure. According to the EM-joint shape based framework, we apply a 3D version of statistical and implicit model for training (Section 4.3) and moreover, extend basic segmentation process to utilize the full 3D spatial information. The comparison system was carried out between our framework and parametric shape evolution extended in 3D [4]. It approves much better performance of our framework in terms of accuracy and running time.

The extension of the EM-joint shape based algorithm into 3D model is applied in the training stage. Here, n binary meshes are aligned into the spatial standard coordinate by using FMRIB Software Library software [114]. Then, proximities of volumetric mesh points to the bounding surface are measured with negative values inside of 3D object. The 3D statistical and is implicit shape and appearance based model are derived in a similar fashion as described in Section 4.3 for 2D training model. Note that the evolving surface is introduced instead of the evolving curve and implicitly described by the 3D joint non-parametric and parametric level set

functions. Now, the EM-joint shape based algorithm provides the 3D segmentation results using an entire volumetric observation data.

Dataset1

Knowing *a priori* that the desired object in the image is the caudate nucleus, we employ a twenty-three set of images with $256 \times 256 \times 160$ dimension and the pixel spacing $1.0mm \times 1.0mm \times 1.25mm$, twelve images are used for training and testing via the leave-one-out strategy and the other eleven images are used for testing. The details of the training stage are presented in Section 4.3, Figure 4.5. Figure 4.13 illustrates one example of these twenty-three experiment tests to extract the caudate nucleus in the sagittal view by showing 11 contiguous slices.

According to Eq. 4.15, the mismatch distances from these twenty-three images are computed and recorded in Figure 4.14. For example the mismatch error of the example shown in Figure 4.13 is recorded as $3.74mm$. The computed mean value and the standard deviation from these twenty-three images are: $3.91mm$ and $0.99mm$. Also the best and the worst results in the entire dataset are: $2.89mm$ and $6.48mm$, see Table 4.5. From the experimental results (shown in Figure 4.14), it could be seen that, based on our formulation (Eq. 4.15), using the joint volumetric hidden information and the entire volumetric observation data enable us to achieve an acceptable segmentation results for 3D segmentation. Furthermore, we demonstrated that, even with a very limited dataset (twelve images), our framework performed very well in segmenting the anatomical structures of interest. With larger dataset available for training, our framework should be able to perform better.

Dataset2

Having another piece of prior information about the caudate nucleus shape in axial view, we employ twenty-three dataset taken from similar patients with the previous dataset. The same learning process is applied as Dataset1. Figure 4.15 and Figure

Figure 4.13: Illustrates one example from twenty-three testings (Dataset1) of the segmentation of the caudate nucleus using the EM-joint shape based model. Figure (a) shows the 3D representation of this sample and figures (b) to (l) show 11 contiguous slices in the sagittal cuts from the 3D segmentation result.

Table 4.5: Summary over twenty-three 3D images of the caudate nucleus segmentation, in the sagittal view (Dataset1) and in the axial view (Dataset2), comparison between obtained results of the EM-joint shape based algorithm and associated ground truth, unit in *mm*.

EM-joint shape based	Mean	Std. Dev.	Minimum	Maximum
Dataset1	3.91	0.99	2.89	6.48
Dataset2	7.14	6.08	3.31	9.80

Figure 4.14: Assessing the performance segmentation results of the EM-joint shape based model over twenty-three subjects in the sagittal view (Dataset1) to extracting the caudate nucleus.

Figure 4.15: One example from Dataset2 of the segmentation of the caudate nucleus using the EM joint shape-based model. Figure (a) shows the 3D representation and figures (b) to (g) show 6 contiguous slices in the axial cuts from the 3D segmentation result. The rest 9 slices are shown in Figure 4.20.

Figure 4.16: Cont'd, Figures (a)-(i) 9 contiguous slices from Figure 4.15.

Figure 4.17: Assessing the performance segmentation results of the EM-joint shape based model over twenty-three subjects in the axial view (Dataset2) to extracting the caudate nucleus.

4.20 illustrate one example of these twenty-three experiment tests with 15 contiguous slices to extract the caudate nucleus in the axial view. Similarly, we apply Eq. 4.15 to evaluate our framework on this dataset. Figure 4.17 shows the result of these twenty-three images. Table 4.5 summarizes the mean, standard deviation values. It can be seen that the results of Dataset1 outperform those of Dataset2, because the surface variation in the 3D version of our framework is slow, using same iteration number the segmenting surface as Dataset2, the desired boundaries could not be captured properly. Using larger iteration numbers, we can obtain more accurate results for Dataset2.

Dataset3

The increased sample size ensures the integrity and usability of our framework compared to other proposed shape evolution approaches. We have selected an approach proposed by Tsai et.al [4] as the parametric shape evolution. The data set provided by Open Access Series of Imaging Studies (OASIS) [123] consists of a cross-sectional collection of 60 subjects without dementia across the adult life span aged 18 to 60

years. According to [123], all images were carefully processed by performing quality control pipeline. The datasets have different quality and this variability provides tool builders with realistic target images. The QC pipeline includes: skull-stripping, correction in terms of motion and gain field inhomogeneity and resampling to 1mm isotropic voxels. After applying QC pipeline, the datasets were registered to the atlas of Talairach and Tournoux (1988) [124].

In order to extend the parametric shape evolution approach into 3D system properly, the 3D computation of the curvature was applied as follows:

$$\kappa = \nabla \cdot \left(\frac{\nabla \phi}{|\nabla \phi|} \right) \quad (4.16)$$

so that we can write the curvature as :

$$\begin{aligned} \kappa = & (\phi_x^2 \phi_{yy} - 2\phi_x \phi_y \phi_{xy} + \phi_y^2 \phi_{xx} + \phi_x^2 \phi_{zz} - 2\phi_x \phi_z \phi_{xz} + \phi_z^2 \phi_{xx} \\ & + \phi_y^2 \phi_{zz} - 2\phi_y \phi_z \phi_{yz} + \phi_z^2 \phi_{yy}) / |\nabla \phi|^3. \end{aligned} \quad (4.17)$$

The same statistical shape-based model was applied for the EM-joint shape evolution and the parametric approach. The time-step for parametric and non-parametric steps of the EM-joint approach were set as follows: .05 and .05. The iteration number was selected as 80 for the whole dataset. The average running time for the EM-joint approach was computed as 20min and 60min for the parametric approach using 2.7 GHz Intel Corei7. Figure 4.18 and Figure 4.19 illustrate the segmentation results of the caudate nucleus. The red shape corresponds to the result of the EM-joint shape-based approach and the blue one belongs to the parametric approach. As seen the results of the EM-joint approach are significantly more accurate. Figure

Table 4.6: The statistical results of Table 4.20.

	EM-Joint Shape Evolution	Parametric Shape Evolution
Mean	0.8256	0.6722
Std. Dev.	0.0522	0.1101
Maximum	0.8952	0.8199
Minimum	0.6536	0.2658

4.20 presents the evaluation step for each datasets. Based on the dice coefficient measurement, the errors between the results and gold standard segmentations were recorded and summarized in Table 4.6. The gold standard segmentations were obtained by three different experts in our lab and the results were evaluated with their average.

4.6 Concluding Remarks

In the literature, medical images segmentation techniques have been categorized into two main groups. First group, voxel-wise labeling technique which obeys the intensity-based classification to assign each voxel to a specific tissue type. A good review of this group can be found in [20, 68]. The second group is defined in a family of deformable shape matching and categorized into explicit [42, 43] and implicit [46, 47, 48] techniques. The important capability of the first group compared to the second group is to apply hidden features known as underlying local voxel labeling. However, a disadvantage of the voxel-wise segmentation techniques is lack of the provision to integrate statistical shape-based models. In this chapter, we introduced our approach to integrate the advantages of both groups. Our method can be categorized as implicit deformable shape matching. Based on EM scheme, the parameters of the statistical shape-based model and the hidden features of image

Figure 4.18: The 3D segmentation result of caudate nucleus from dataset3. The EM-joint shape evolution approach (red color) compared with parametric shape evolution approach [4] (blue color). Figures (b)-(g) show slices 75,77,78,80,83,86. The green curves represent initial curves.

Figure 4.19: Cont'd, the rest presenting slices from Figure 4.18 ended with slice 103.

Figure 4.20: Summarized 3D segmentation results of Dataset3 via computing dice coefficients measurement.

are updated recursively. The differences between our approach and the explicit segmentation techniques are known as using the level set methods.

Our proposed algorithm has the potential to apply extra information about the correlated features of image. This application is important for real medical images, since pixels intensity are spatially depended on intensity of neighboring pixels and different structures have relatively same intensity distribution. This term augments the observation likelihood of each pixel by applying MRF theory incorporated into the active contour model. Moreover, as seen in the results of 2D images, our method is flexible in segmenting shapes with large range of variations, because of employing extra prior probability of the local voxel labeling under the non-parametric model. As a result, while adopting a PCA shape-based model, the final estimate is not limited to linear parametrization of the shapes. In the experiment, the segmentation results are robust to noise because global statistical shape prior information are applied. At the same time, the results yields more accurate by modeling the hidden variables (missing data) with the help of EM algorithm. The important point is that for all test samples, there is no need to tune the effects of shape based and image based energy terms. In summary, we presented an EM-based image segmentation framework using the hidden variables as a connection between the observed image data and the shape parameters. Both parametric and non-parametric shape models are used in the algorithm for more robust and accurate image segmentation. Comparative results showed that the proposed algorithm outperforms the traditional algorithms, proving it to be more suitable for solving medical image segmentation, which often suffers from low-contrast between objects, low-signal-to-noise ratio (SNR) and the limitation of available a prior knowledge.

The 3D segmentation of anatomical structures has an important role in visualization and clinical diagnosis purposes. We have outlined the generalization of the EM-

joint shape based algorithm to a three dimension model. According to the EM-joint shape based framework, we applied a 3D version of mentioned statistical and implicit shape-based model for training. The obtained performance of the EM-joint shape based algorithm shows that the generalization of our novel algorithm in three dimensions enables us to obtain acceptable segmentation results for both single and multiple 3D segmentation in MR images.

In Dataset 2, section 4.7.4, 20% of subjects were over the age of 60 and clinically diagnosed with very mild to moderate Alzheimers disease (AD) for example samples #13, #16, #18 and #19 in Figure 4.17. These samples are all females with ages 69, 83, 90 and 70 years. The results of the caudate structure segmentation for these subjects were satisfactory. Similar to other methods, our approach is capable of segmenting diseased brain structures to some degree. The threshold level may also be improved by enhancing the segmentation method. Furthermore, precise characterization of normal structures obtained by our method could also be used to define and categorize various kinds of abnormalities.

Chapter 5

Extension of the EM-MAP Framework for Segmentation of Multiple Structures

5.1 Introduction

In chapter 1, we explained the comprehensive information about the intrinsic function of a neural network. We mentioned the important role of segmenting a group of nuclei in the brain of vertebrates, called basal ganglia (BG) in a number of neurological conditions including several movements disorders. The important subcortical structures of basal ganglia are the caudate nucleus, the putamen, and the globus pallidus, which are buried deep inside the cortex (see Figure. 5.1). Generally, different anatomical structures in the human brain exhibit strong spatial dependency among each other. This dependency has an important role in the action of basal ganglia structures. Figure. 5.2 shows the interconnection between these nerve cells. They receive information from several different regions of the cerebral cortex. Once

Figure 5.1: The Basal Ganglia and its components inside the cortex in the lateral view and frontal view (adopted from “<http://thebrain.mcgill.ca>”).

Figure 5.2: The interconnection between the components of basal Ganglia in the human brain actions (adopted from “<http://thebrain.mcgill.ca>”).

the basal ganglia have processed this information, they return it to the motor cortex via the thalamus. As shown in Figure 5.2, the spatial interconnection among the structures is present in a hierarchical manner, and can be called as *ordered spatial dependency* [125]. In this chapter, we introduce the extended EM-joint shape based algorithm, which extracts this dependency from the structures via applying new parametric multi-shape/appearance model statistically. Other closely related works are [125, 126, 127, 128], which assume a statistical correlation among the structures. In [125], Rousson et. al. introduced the spatial dependency of the structures of interest by registering to a common reference coordinate system based on the neighboring structures. Tsai et. al. [126] proposed to capture the co-variations among the structures by constructing the implicit multi-shape parametric model via applying PCA analysis. Another research work to extract the co-dependency

was suggested by Uzunbas [127], where jointly multivariate density estimation of multiple shapes is used as the non-parametric shape prior of multiple structures. In this chapter, we introduce a new statistical deformable model for segmenting multi-structures in unified shape evolution framework. The goal of this study is to extend the EM-joint shape based framework to segment multi-nuclei structures at the same time such as caudate, putamen, pallidus in the basal ganglia structures and thalamus. In Section 5.2, we explain the new statistical multi shape/appearance based model as a training phase. In Section 5.3, the extension of the EM-joint shape based framework is explained for exploiting multiple objects at the same time. Using level set functions for representing several objects, it is important to highlight how probable overlap between the level set functions is addressed. Section 5.4 specifically explains how these problems are addressed in our framework. In sections 5.5 and 5.5.3, we demonstrate segmentation results using an extension of the proposed framework for 2D imaging and from a 2D model to a 3D model. Finally, the discussion and conclusion is presented in Section 5.6.

5.2 Construction of the Statistical Model

In this section, we explain the new statistical multi-shape/appearance model that defines the unified training system introduced by Tsai [27]. Our statistical model is an extension of the single object shape/appearance-based model explained in Chapter 4. The PCA analysis is applied on a set of level set functions such that each sample in the set presents implicit multi-shape/appearance classes. This multi-shape/appearance based model defined in the unified system enjoys many advantages such as 1) building simultaneous representation of any number of shape classes, 2) capturing co-dependencies between neighboring and coupling structures which could be very important in segmentation, 3) capturing the spatial dependency be-

tween the inside intensity of the shape classes and 4) obtaining the correlation between the shape and the intensity information within and cross classes.

Based on constructing single shape/appearance model in Chapter 4, the signed distance function Φ is employed as the representation of a particular shape. Let K be the number of shape classes that we would like to represent simultaneously. The boundaries of each of the K shapes are embedded as the zero level sets of K separate signed distance functions $\{\Phi^1, \dots, \Phi^K\}$ with negative distances values allocated to the inside and positive values assigned to the outside of the shape. Let n be aligned images, each conveys K shapes and the intensity inside them, in the collection. The Table 5.1 gives the algorithm of our statistical multiple shape/appearance. Let Φ_i^k denotes the signed distance function associated with the k th shape from i th sample of the training set. Then, we obtain the intensity inside the shape classes for each training sample and make set $A = \{A_1^k, \dots, A_n^k\}_{\{k=1, \dots, K\}}$. We merge set Φ and set A into set $\hat{\Phi}$ and then follow the PCA process. According to the PCA analysis, we obtain K mean level set functions $\{\bar{\Phi}^1, \dots, \bar{\Phi}^K\}$ by taking average n aligned signed distance function for each shape class as follows: $\bar{\Phi}^k = \frac{1}{n} \sum_{i=1}^n \Phi_i^k$. The shapes and appearance variabilities are captured within and across the K shape classes using computing singular value decomposition of matrix $\xi = [\tilde{\psi}_1 \ \tilde{\psi}_2 \ \dots \ \tilde{\psi}_n]$. $\tilde{\psi}_i$ includes K mean-offset functions which are obtained by subtracting the mean level set function of each shape class from $\hat{\Phi}_i$ function belonging to that shape class. Notice each mean-offset function is digitized into 1D vector of N ordered samples, $\tilde{\psi}_i$, during the PCA analysis.

The eigenvalue decomposition is employed to factor the covariance of ξ as

$$\frac{1}{n} \xi \xi^T = \Gamma \Sigma \Gamma^T \quad (5.1)$$

where Γ is a $KN \times n$ matrix whose columns present the n principal variational

modes to project an K object shape/appearance into the eigen-space, and Σ is a diagonal $n \times n$ matrix whose diagonal elements present the corresponding nonnegative eigenvalues, denoted by $\sigma_1^2, \dots, \sigma_n^2$. Note that to derive the i th principal modes or eigen-shapes for all K shape classes, the KN elements of the i th column of Γ are re-sampled into K rectangular structures of the image dimensions, and denoted by $\{\varphi_i^1, \dots, \varphi_i^K\}$. As it can be seen the shape/appearance variations matrix ξ includes information of all K shape/appearance classes and, thus, the eigenshapes projection for each shape class have been affected by co-dependencies between different shape/appearance classes. This is important in the multi-object segmentation when each object shape is individually represented by one level set function and the shapes evolution may suffer overlapping.

An estimation of the K object shape classes are constructed linearly by the first $q \leq n$ eigenshapes for each shape as:

$$\begin{aligned} \Phi^1[\mathbf{w}, \mathbf{p}](\omega(t); t) &= \bar{\Phi}^1(\hat{\omega}(t); t) + \sum_{k=1}^q w_k \varphi_k^1(\hat{\omega}(t); t), \\ &\vdots \\ \Phi^K[\mathbf{w}, \mathbf{p}](\omega(t); t) &= \bar{\Phi}^K(\hat{\omega}(t); t) + \sum_{k=1}^q w_k \varphi_k^K(\hat{\omega}(t); t), \end{aligned} \quad (5.2)$$

where $\hat{\omega}$ denotes the coordinate in the statistical shape-based model, and ω presents the input image coordinate. According to this model, the level set function Φ^j can be defined by $\mathbf{w}$ as the shape parameters and $\mathbf{p}$ as the rigid pose parameters belonging to j th shape class. The pose parameters are updated based on the best match between the built statistical model and the input image data. φ_j presents the j th eigen-shapes of all K shape classes, and Σ is the corresponding eigenvalue which gives the variances of the shape parameter $\mathbf{w}$, $\{\sigma_1^2, \dots, \sigma_q^2\}$.

As an example, we apply our implicit multi-shape/appearance parametric model on a training set including 11 real MR images to construct multi-object model of three

subcortical nuclei structures of brain (caudate, putamen and thalamus). We choose five principal components that fit 93% of the total energy. Figure 5.3 illustrates the shape variations of all three shape classes simultaneously using the applied implicit multi-shape/appearance parametric model Eq. 5.2.

Another experimental work is shown in Figure 5.4 which presents the application of our statistical and implicit multi-shape/appearance model on a training set including 9 real MR images to define the variations of multi-shape/appearance of putamen and pallidus simultaneously. We choose four major variations that fit 95.3% of the total energy.

Finally, we apply the statistical and implicit multi-shape/appearance based model in a 3D presentation of the caudate, putamen and thalamus. The dataset with the volumetric real MR images ($256 \times 256 \times 124$ dimensions and the pixel spacing $0.94mm \times 0.94mm \times 1.70mm$) that includes twenty-five patients is employed. Twenty-five hand segmented 3D models of the caudate nucleus, putamen and thalamus are used for training stage. Simultaneously, we aligned all twenty-five samples into standard space for all three shape classes by using FSL software [114]. Figure 5.5 illustrates the demonstration of this model in which three shape classes are color coded as follows: caudate nucleus (blue), putamen (red) and thalamus (green).

5.3 Segmentation Framework

In the previous section, we proposed new implicit statistical shape/appearance model for multiple structures in the unified system. The important advantages of this model are as follows: 1) capturing the co-variations between the shape/appearance classes which is motivated by the observation that the neighboring structures in medical images generate configurations about the shape and the appearance and they

Figure 5.3: Illustration of the shapes variations in the nuclei brain structures, caudate, putamen and thalamus, based on the implicit statistical multi-shape/appearance model. The shape classes are changed by varying the weights for the first, second, third, forth and fifth principal components, ($\sigma_i = \sqrt{\Sigma_i}$).

Figure 5.4: Illustration of the shapes variations in the close nuclei brain structures, putamen and pallidus, based on the implicit statistical multi-shape/appearance model. The shape classes are changed by varying the weights for the first, second, third and fourth principal components.

Table 5.1: Implementation Process**Algorithm :** Statistical Multiple Shape/Appearance-based Model

```

procedure Training-MultiShapeAppearance( Training images  $I = \{I_1, I_2, \dots, I_n\}$ )
  define  $B = \{B_1^k, \dots, B_n^k\}_{\{k=1, \dots, K\}} \leftarrow$  binary images of desired shapes from  $I$ 
  define  $\Phi = \{\Phi_1^k, \dots, \Phi_n^k\}_{\{k=1, \dots, K\}} \leftarrow$  construct corresponding level set functions
  define  $A = \{A_1^k, \dots, A_n^k\}_{\{k=1, \dots, K\}} \leftarrow$  appearance information about inside
    the objects corresponding to the set  $B$ 
  define rigidly align set  $A$  into a spatial coordinate and employ the same
    similarity transformation on the set  $\Phi$ 
  define  $\hat{\Phi} = \{\hat{\Phi}_1^k, \dots, \hat{\Phi}_n^k\}_{\{k=1, \dots, K\}} \leftarrow$  merging sets  $A$  and  $\Phi$  sample by sample
  define  $\bar{\Phi} \leftarrow$  mean shape/intensity of training set  $\hat{\Phi}$ 
  define  $\varphi_{i\{i=1, \dots, n\}}^{k\{k=1, \dots, K\}} \leftarrow$  eigenmodes of shape/intensity variation via
    applying PCA analysis
return  $(\bar{\Phi}, \varphi, \Phi)$ 

```

Figure 5.5: The 3D shape variation of multiple caudate, putamen and thalami objects: figure (a) is the mean shape with the positive variation of the first and second principle modes (figures (b) and (c)) and with the negative variation of them (figures (d) and (e)).

could yield more reliable results, 2) handling topological changes of the shapes and 3) extending to 3D framework (which will be explained in Chapter 7) in a straightforward manner. In this section, we focus on the segmentation phase based on the EM-joint shape based framework, explained in the Chapter 4, and show the utility of this framework by incorporating it within the statistical shape/appearance multiple structures model for segmenting various (BG) structures.

5.3.1 Non-parametric Multi Objects Shapes Model

The probabilistic framework of the EM-joint shape based approach could be rewritten as a general *region-based partitioning* energy function as follows:

$$E_{total} = E_{img} + E_{prior} + E_{similarity} + E_{regularization}. \quad (5.3)$$

The first energy term, E_{img} , generates a penalty function to each pixel/voxel of region Ω_k based on the statistical properties of that region such as the mean intensity and the variance, and hence the observation matching function, E_{img} , over the entire image area Ω is formulated as:

$$E_{img}(\{\Omega_k, k = 1, \dots, K\}) = \sum_{k=1}^K \sum_{i, \mathbf{x}_i \in \Omega_k} \left(\frac{1}{2} \log \sigma_k^2 + \frac{(I(\mathbf{x}_i) - \mu_k)^2}{2\sigma_k^2} \right) \Delta \mathbf{x}_i, \quad (5.4)$$

where $\mathbf{x}$ is a pixel/voxel in the image and K is the total number of partitioning regions such that $\bigcup_{k=1}^K \Omega_k = \Omega$ and for all $i \neq j$, $\Omega_i \cap \Omega_j = \emptyset$. Simply, in this work, we assume that the likelihood functions are independent among different pixel/voxels. Using the level set representation, a set of $K-1$ level set functions $\{\phi_1, \dots, \phi_{K-1}\}$ are used to express the K regions. As an example, we consider the combination of three level set functions for extracting three objects in the image. The corresponding

characteristic function is defined for each region as $H(\phi_i)$, and $(1 - H(\phi_1))(1 - H(\phi_2))(1 - H(\phi_3))$ for the background region.

The second energy term, E_{prior} , could potentially aid to assign each pixel/voxel to the proper specific region as the prior information and defined as:

$$\begin{aligned} E_{prior} &= - \sum_i \sum_{k=1}^{K-1} \log p(x_{i,k} | \phi_k(\mathbf{x}_i)) \\ &= \sum_i \sum_{k=1}^{K-1} \log(1 + \exp(0.5\phi_k(\mathbf{x}_i))), \end{aligned} \quad (5.5)$$

where $x_{i,k}$ presents the local label of pixel/voxel i assigned into region k and $\mathbf{x}_i$ is the pixel/voxel i in the image domain. This term acts as the spatial prior probability of voxel $x_{i,k}$ under the k th non-parametric shape class model, ϕ_k . We assume that each of non-parametric shape class model is independent on the other non-parametric shape classes model. Notice that the co-variations between the shapes are captured in the parametric shape evolution, see Section 5.3.3. In Eq. 5.5, using the sigmoid map function, the signed distance values map to the range of $[0,1]$, in other words, the energy function is minimized when the voxel is located inside the desired shape class.

The third energy term, $E_{similarity}$, defines the mismatching error between the non-parametric and the parametric objects shapes so that they represent similar shapes. The penalty for the k th shape class is:

$$E_{similarity} = \sum_i (H(\phi_k(\mathbf{x}_i)) - H(\Phi_k[\mathbf{w}, \mathbf{p}](\mathbf{x}_i)))^2. \quad (5.6)$$

The last term, $E_{regularization}$, could help to maintain the objects shapes evolution to

be smooth via posing the energy of the lengths of the objects and their areas.

$$\begin{aligned}\text{Length} &= \sum_i \delta(\phi_k(\mathbf{x}_i)) |\nabla \phi_k(\mathbf{x}_i)| \\ \text{Area} &= \sum_i H(\phi_k(\mathbf{x}_i)).\end{aligned}\tag{5.7}$$

5.3.2 Weighted Objective Function

The Expectation-Maximization algorithm could be applied to the total energy function 5.3. It integrates the hidden variables and the statistical multi-shapes/appearance models into a unique segmentation framework. In our model, the hidden variable, denoted by $x_{i,k}$, is defined as the local voxel labeling and is estimated by taking the expectation of equation 5.3 with respect to its posterior distribution given the image data and the non-parametric multi shape classes model.

$$\begin{aligned}E_{total}(\phi) &= \sum_i \sum_k E_{x_{i,k}|I,\phi} \{E_{img} + E_{prior} + E_{similarity} + E_{regularization}\}, \\ E_{x_{i,k}|I,\phi} &\equiv p(x_{i,k}|I, \phi).\end{aligned}\tag{5.8}$$

where ϕ includes K non-parametric level set functions as $\phi = \{\phi_1, \dots, \phi_K\}$.

5.3.3 Parametric Multi Objects Shapes Model

In previous sections, we explained that extending level set methods into simultaneous segmentation of multiple objects. Each object shape is represented by one separate level set function. Furthermore, in our “EM joint curve evolution approach”, the new spatial shape-based prior model is applied for each shape class which results in better multiple objects segmentation, because the similarity between the hidden variables and the non-parametric shape models. However, different anatomical structures

often have spatial dependencies among each other which could potentially be useful in segmentation of several structures in the brain MR images. In order to capture the co-variations among the structures of the brain structures, the EM-joint shape based framework applies the multi-level set parametric and shape/appearance-based models explained in the section 5.2. As a result, the parametric shape evolution is performed for i th shape class formulated by $\Phi_i(\mathbf{w}, \mathbf{p})$ through updating the shape vector and the pose parameters $\mathbf{w}$ and $\mathbf{p}$. Note that according to the statistical multi shapes model, explained in the Section 5.2, as variations of each shape class and the co-variations between that shape class and other structures are captured by separate q-eigenshapes. However, all the K q-eigenshapes have weights as the shape vector parameter $\mathbf{w}$. The associated energy function of K parametric shape classes evolution is:

$$E_{total}(\mathbf{w}, \mathbf{p}) = E_{similarity}(\phi, \mathbf{w}, \mathbf{p}) + E_{prior}(\mathbf{w}), \quad (5.9)$$

where the first term measures the penalty between the parametric and non-parametric shapes and the second term helps to improve the robustness of the multiple structures segmentation. Notice that ϕ and $\Phi(\mathbf{w}, \mathbf{p})$ present the combination of all K level set functions in the non-parametric and parametric format. The second energy term follows the Gaussian distribution of the shape variability of each structure as:

$$E_{prior}(\mathbf{w}) = \mathbf{w}^T \Sigma_q^{-1} \mathbf{w}, \quad (5.10)$$

where Σ_q contains the first q rows and columns of the eigenvalue matrix Σ .

5.4 Avoiding Overlap between Shapes

The overlap between neighboring level set functions is the common problem when more than one level set function is applied during the implementation of multiple shapes. Several studies in the literature solved the overlap problem between neighboring level set functions [129] by adding new energy term to keep the constraint $\sum_i H(\phi_i) = 1$. Vese and Chan et al. [11] proposed different multi-phase level set representation so that the distinct phases are disjoint in their constructional model. In our approach, the shape of each class is individually represented by one level set function. Therefore, the level set functions might overlap during non-parametric or parametric curve evolution. The overlap during the parametric curve evolution happens because no restrictions have been considered in the range of the statistical variable $\mathbf{w} = \{w_1, \dots, w_q\}$ in each of shapes. This phenomenon can be seen in Figure 5.4 that putamen and pallidus shapes have overlap in each mode with an increase in the shape variable $\mathbf{w}$. In our approach, without applying additional energy terms, we avoid the overlap during the non-parametric and parametric curve evolution. One possible way is to constrain the range of $\mathbf{w}$ so that the neighboring shapes never overlap. However, it is possible that the different shapes overlap during the non-parametric curve evolution step. Therefore, we apply a heuristic approach to perform a check at each non-parametric and parametric optimization steps prior to updating $\mathbf{w}$ and ϕ to determine whether updating $\mathbf{w}$ and ϕ cause any overlap. If updating ϕ or $\mathbf{w}$ causes an overlap, the new updating value is not considered and the algorithm skips forward to update pose parameters $\mathbf{p}$.

5.5 Experimental Results and Discussion

We validated the novel extended EMjoint-shape based framework on several subcortical structures of the brain in the MR images: the head of caudate nucleus, putamen, pallidus and thalamus. Two sets of experiments were conducted with the 2D brain MR images (T1-weighted, 217×181 dimensions and the pixel spacing $0.9375mm \times 0.9375mm$) and one set is considered for the 3D experimental works ($256 \times 256 \times 124$ dimensions and the pixel spacing $0.94mm \times 0.94mm \times 1.70mm$). We performed a manual segmentation of each subcortical structure and computed distance error using the Hausdorff distance measure and the dice coefficient measurement. In order to apply Hausdorff distance measure, we used Hausdorff measurement (similar to Section 4.5.4) as follows:

Hausdorff Distance =

$$\max \left\{ \sup_{\mathbf{x} \in \Omega} ((1 - H(\phi(\mathbf{x})))\phi(\mathbf{x})(H(\phi_0(\mathbf{x})))), \sup_{\mathbf{x} \in \Omega} ((H(\phi(\mathbf{x})))\phi(\mathbf{x})(1 - H(\phi_0(\mathbf{x})))) \right\} \quad (5.11)$$

where ϕ is the segmented result and ϕ_0 corresponds to the shape of ground truth represented by SDF.

Moreover, we compared the results with the segmentation results obtained via performing the parametric shapes evolution with Tsai method [4], the non-parametric shapes deformation with Chan/Vese approach [10] and non-parametric multi-phase shapes evolution adopted by Vese/Chan approach [11].

The Vese/Chan approach, similar to the Chan/Vese approach, uses concepts of region-based active contours. Therefore, the inside intensities of each objects are modeled parametrically and varies in the *piece-wise smooth*. As explained clearly in Chan et. al [10] and Vese et. al [11], the proposed energy functions are not convex

Figure 5.6: The recommended initial curves and segmentation results of Chan/Vese approach ([10]) and Vese/Chan method ([11]).

and there is no uniqueness for minimization results (such as global minimizer). Consequently, the results depend on the initial conditions such as initial curve. In our experiments, we used two different initial curves to show the results of Chan/Vese approach and Vese/Chan method. This type of initial condition is also related to the regional growing algorithm in Koepfler et al. [130]. Figure 5.6(a) shows the first initial curve which is recommended by the authors as having the best chance of converging to global minimum. The segmentation results of Chan/Vese approach and Vese/Chan are seen in Figure 5.6 with that initial curves, iteration = 350 and time step = 10.

5.5.1 Segmentation of Three-nuclei Subcortical of Brain

In the first set of experiments, we tested the novel extended EM-joint shape based algorithm on the 11 real MR images for segmenting three-nuclei structures: caudate, putamen and thalamus. The first step is the training and building statistical multi-shapes/appearance model explained in Section 5.2 and shown in Figure. 5.3. After obtaining the mean shape and the eigenshape for each structure, the next step is achieved by updating the non-parametric and the parametric shapes evolution

considering the co-dependency among all three structures. Figure 5.7 illustrates two sample tests in this dataset which highlight the ability of the extended EM-joint shape based algorithm compared to the Tsai method and Chan/Vese approach. In the first sample, the improvement of the proposed extended EM-joint shape based framework is recorded as 4.61% and 6.15%, and for second sample, the improvement is recorded as 13.0% and 6.63%. Figure 5.8 illustrates the segmentation results over the rest of samples in the dataset. For each sample, the first subfigure refers to the extended EM-joint shape based framework, the second one refers to the Tsai method and the last subfigure shows the result of the Chan/Vese method. From these figures, it could be seen the segmentation results of the extended EM-joint shape based algorithm are much more accurate and robust than Tsai method and Chan/Vese approach. In order to achieve a reliable and fair comparison system, the same training process was performed for the extended EM-joint shape based algorithm and Tsai method. Furthermore, the same initialization process was performed as previous experimental results to define a proper location for the initial shape for all three algorithms. We manually estimated the desired object center as the proper location of the object, and then rigidly shifted the mean shape to that location, acting as the initial shape. We performed three initializations for each test image. The errors (average distance among the surface of each ROI) for manual estimation of the object center are within the range of [7mm, 7mm].

Tables 5.2, 5.3 and 5.4 summarize the mismatching errors of all 11 segmentation results of the caudate, putamen and thalamus nuclei structures using performed Tsai method, Chan/Vese approach and the extended EM-joint shape based framework. The obtained results illustrate the superior performance of the extended EM-joint shape based framework. The improvements of the novel extended EM-joint shape based algorithm were recorded compared to the Tsai method as the parametric shapes evolution (see Table 5.4, Improvement 1) and the Chan/Vese approach as

Figure 5.7: Illustrates two samples from eleven testings and comparison between the generalization of the proposed EM-joint shape evolution for multiple objects segmentation, Tsai method [4] as “Parametric” and Chan/Vese method as “Non-parametric” curve evolution [10]. Figures (1) and (2) show the improvement compared to the Tsai and Chan/Vese approaches with 4.61%, 6.15% and 13.0%, 6.63% respectively. The initial curves are shown in white.

Figure 5.8: The segmentation results of the caudate, putamen and thalamus from eleven images. For each group, the first figure shows the result of the novel extended EM-joint shape based algorithm, the second figure using Tsai method and the last figure for Chan/Vese.

Table 5.2: Mismatching errors (units in mm) of the obtained segmentation results in the figures 5.8 and 5.7 using applied Tsai with taken time (unit in sec).

Samples	Caudate (mm)	Putamen (mm)	Thalami (mm)	Time (sec)
1	5.00	6.71	9.84	28.01
2	7.28	7.21	7.61	28.76
3	6.21	7.21	7.07	26.89
4	6.08	7.07	8.94	25.11
5	6.00	6.90	7.31	25.00
6	6.08	6.08	8.06	25.62
7	5.32	7.21	7.07	24.81
8	6.40	6.70	8.54	25.60
9	5.81	7.07	9.20	25.09
10	5.90	7.20	9.04	25.22
11	6.00	7.30	9.00	25.22

the non-parametric shapes evolution (see Table 5.4, Improvement 2).

5.5.2 Segmentation of Close Nuclei Structures

In the second experiment, we validate the novel extended EM-joint shape based algorithm on the nine real clinical MR images to extracting the putamen and pallidus structures. The segmentation of the putamen and pallidus is very challenging, because their boundaries are tightly close and have a low intensity contrast. Furthermore, their corresponding level set functions may suffer overlapping. Figure 5.9 illustrates the segmentation results of all 9 sample images, where subfigures are the result of applying extended EM-joint shape based algorithm, Tsai approach and Vese/Chan approach respectively. The same statistical multi-shapes/appearance model, explained in Section 5.2 (see Figure 5.4) were utilized and thus the obtained mean shapes were used as initial curves. Table 5.5 shows the mismatching errors of

Table 5.3: Mismatching errors (units in mm) of the obtained segmentation results in the figures 5.8 and 5.7 using applied Chan/Vese methods with taken time (unit in sec).

Samples	Caudate (mm)	Putamen (mm)	Thalami (mm)	Time (sec)
1	5.00	5.83	8.98	3.42
2	5.44	6.10	9.00	3.61
3	5.40	6.20	9.10	3.52
4	5.38	5.93	9.00	3.65
5	5.72	5.90	9.01	3.53
6	5.75	5.71	9.00	3.41
7	5.69	5.87	8.99	3.58
8	5.65	5.83	8.94	3.47
9	5.64	5.83	9.00	3.83
10	5.65	5.30	9.00	3.55
11	5.65	5.80	8.98	3.55

Table 5.4: Illustrates the obtained mismatching error (units in mm and time in sec) of the figures 5.8 and 5.7 using the extended EM-joint shape based algorithm and how much better the performances are for each sample than Tsai approach (**Improvement 1**) and Chan/Vese method (**Improvement 2**).

Samples	Caudate	Putamen	Thalami	Time	Improvement1	Improvement2
1	5.65	6.56	6.00	59.15	18.64 %	8.78%
2	5.66	6.54	5.83	52.15	22.57%	13.92%
3	5.83	6.60	7.07	55.53	4.61%	6.15%
4	5.65	6.84	6.70	53.23	15.11%	5.83%
5	5.83	6.70	6.67	58.49	5.20%	7.44%
6	5.84	6.74	7.00	55.38	3.2%	4.49%
7	5.73	6.52	7.07	55.63	1.45%	6.36%
8	5.83	6.43	6.89	58.40	13.00%	6.63%
9	5.68	6.73	6.70	53.99	15.54%	7.11%
10	5.55	6.69	6.65	59.11	17.20%	5.61%
11	5.80	6.74	6.54	59.15	16.87%	12.31%

Figure 5.9 using dice coefficient measurement. Tsai method delivers poor results for putamen and palladis structures. The main reason is that the intensity-based models of putamen and palladis follow the same distributions. Also, the intensity-based models are parameterized with the same set of shape parameters ($\mathbf{w}$). Consequently, the shapes evolution of these structures depended on each other. Using Vese/Chan approach, the segmentation results depends on the initial curves. In Figure 5.6, two circle curves were used as the initial curves which according to the authors tend to converge to global minimum. As shown the results are completely unacceptable. In Figure 5.9, the mean curves were used as the initial curves obtained from the training process. Although, the prior knowledge has been given to Vese/Chan approach, putamen and palladis have not been extracted correctly. The overlapping between the two level set functions still exist. Using two level set functions, four regions are obtained and one intensity-based model is assigned to each region. The intensity distribution of each region is similar. Thus, after 350 iterations, Vese/Chan was not able to extract correct boundaries and overlapping areas were not disappeared. It can be seen that the performance of the novel extended EM-joint shape based algorithm is noticeably better than Tsai method and Vese/Chan approach. Tables 5.5 explains superior performance of the extended EM-joint shape based algorithm compared to the Tsai approach and Vese/Chan approach. The summarized results are shown in Table 5.6. It is important to show the mismatch errors using both dice coefficient measures and maximum mismatching errors measured by Hausdorff function. For example, sample seven from Figure 5.9 emphasizes unacceptable segmentation results of Tsai approach which can be more clearly detected, through Hausdorff measurement compared to dice coefficient. Tables 5.7 and 5.8 express the significance of using hausdorff measurement and acceptable performance of the extended EM-joint shape based algorithm compared to the Tsai approach.

Figure 5.9: The 9 segmentation results of the putamen and pallidus structures. For each sample, the first, second and third figures show the results of the extended EM-joint shape based algorithm, Tsai method and Vese/Chan approach respectively.

Table 5.5: The comparison mismatching errors of the Figure 5.9 between the extended EM-joint shape based algorithm, Tsai method and Vese/Chan approach using applying dice coefficient measurement.

Sample	EM-Joint Putamen	Palladi	Parametric Putamen	Palladi	Multi-phase Putamen	Palladi
1	0.97300	0.98400	0.96600	0.97600	0.96600	0.98900
2	0.97700	0.98200	0.96800	0.97500	0.96800	0.98700
3	0.98700	0.97500	0.96900	0.96700	0.96600	0.99300
4	0.98600	0.98900	0.97600	0.97800	0.97100	0.98800
5	0.98400	0.98800	0.97500	0.97800	0.97400	0.98700
6	0.98700	0.99400	0.97600	0.98500	0.96800	0.98300
7	0.98600	0.99500	0.97000	0.98100	0.96800	0.98100
8	0.98600	0.99100	0.97300	0.98600	0.97100	0.97700
9	0.98500	0.98900	0.97800	0.99100	0.97700	0.97100

Table 5.6: The summary of Table 5.5.

Putamen	EM-Joint Shape-based	Parametric	Multi-phase
<i>Mean</i>	0.983	0.972	0.961
<i>Std</i>	0.004	0.004	0.004
Palladi	EM-Joint Shape-based	Parametric	Multi-phase
<i>Mean</i>	0.987	0.961	0.98
<i>Std</i>	0.006	0.007	0.007

Table 5.7: The obtained mismatching error (units in mm) with taken time (units in sec) of the Figure 5.9 using applied Tsai approach.

Samples	Putamen (mm)	Pallidums (mm)	Time (sec)
1	6.95	5	30.23
2	6.98	4.98	32.54
3	7.04	4.97	32.35
4	7.32	4.89	31.35
5	6.96	5.38	32.84
6	6.90	5.35	31.35
7	7.15	5.23	31.65
8	7.32	5.24	32.36
9	6.89	4.98	31.15

Table 5.8: The obtained mismatching error (units in mm) of the Figure 5.9 using the extended EM-joint shape based algorithm with taken time (units in sec) and presents the better performance sample by sample than Tsai approach.

Samples	Putamen (mm)	Pallidums (mm)	Time (sec)	Improvement
1	6.80	4.24	40.17	8.24%
2	6.12	4.03	41.25	17.83%
3	6.90	4.62	40.22	4.25%
4	6.12	4.32	42.00	16.95%
5	6.36	5.09	40.50	7.77%
6	6.40	4.25	40.99	15.02%
7	6.85	4.32	40.65	10.83%
8	6.54	4.22	42.23	16.72%
9	6.40	4.28	41.56	11.14%

Table 5.9: Summary over twenty-five subjects of the caudate nucleus, the putamen and the thalamus segmentation comparison between obtained results of the EM-joint shape based algorithm and associated ground truth, unit in *mm*.

	Caudate nucleus (<i>mm</i>)	Putamen (<i>mm</i>)	Thalamus (<i>mm</i>)
Mean	5.70	3.60	5.22
Std. Dev.	1.51	0.63	2.16

5.5.3 Extension to 3D Multiple Structures Segmentation

According to the recent research about characteristic degenerative pathology in Alzheimer’s disease, neuroscientists confirm the presence of the reduced global gray matter volumes. In addition, they have investigated reduced volumes of both left and right putamen and thalamus in patients who diagnosed with probable Alzheimer’s disease [131]. They found this degeneration of the smaller the volumes of putamen and thalamus is also associated with cognitive deterioration. Consequently, 3D segmentation of the basal nuclei and the thalamus have received more attention. In this section, we assess the use of the 3D extended EM-joint shape based algorithm in multiple shapes segmentation for exploiting the deep gray nucleus (the head of caudate nucleus and putamen) and the thalamus simultaneously.

The dataset with the volumetric real MR images ($256 \times 256 \times 124$ dimensions and the pixel spacing $0.94mm \times 0.94mm \times 1.70mm$) including twenty-five patients. Twenty-five hand segmented 3D models of the caudate nucleus, putamen and thalamus are used for training stage. Simultaneously, we aligned all twenty-five samples into standard space for all three shape classes by using FSL software [114]. We follow the constructed model as the training stage Figure 5.5 and then, the 3D EM-joint shape based algorithm is applied as the segmentation phase. The leave-one-out strategy is used to achieve the training and the testing process on this dataset.

Figure 5.10: One example of the graynuclei segmentation of the caudate nucleus, the putamen and the thalamus from the twenty-five samples using the EM-joint shape based model. Figure (a) shows the 3D representation and figures (b) to (i) represents eight consecutive coronal slices convey three graynuclei structures.

Figure 5.11: Similarity values with the ground truth for the segmentation of the caudate nuclei, putamen and thalamus from twenty-five experiments.

Figure 5.10 shows one example from this dataset after applying our framework by presenting 8 consecutive coronal slices of the basal nuclei and the thalamus MR volumetric and the 3D representation of the segmentation result. Similarly, Eq. 5.11 is used to evaluate the performance of our algorithm on this dataset. In this example, the mismatching distances for the caudate nucleus, putamen and thalamus are $3.4mm$, $2.44mm$ and $5mm$. The segmentation evaluation of EM-joint shape based algorithm on twenty-five subjects is shown for caudate nucleus, putamen and thalamus in figure 5.11. The average time of the training process was 6 min and the segmentation phase was achieved in 20 min on average in a workstation: 2.67GHz PC station. For the entire dataset, the tuning of the coefficients for each energy term in the core formulation are same which shows the ability and reliability of the algorithm for different input data. Table 5.9 summarizes the mean errors and standard deviation for each of three shapes as follows: caudate nucleus ($5.70mm$, $1.51mm$), putamen ($3.60mm$, $0.63mm$) and thalamus ($5.22mm$, $2.16mm$). It can

be seen that the results obtained from putamen are more accurate than caudate nucleus and thalamus. Firstly, caudate nucleus in the coronal view has very tiny shapes and is near the ventricle objects with high intensity. Since our framework utilizes a local optimization process, the segmenting surface may be fall in local minima. Secondly, thalamus suffers ambiguity information near boundaries. Segmenting putamen would be more reliable because of the above reasons.

In summary, the obtained performance of the extended EM-joint shape based algorithm shows that (Eq. 5.11) the generalization of our novel algorithm in three dimensions can enable us to obtain acceptable segmentation results for multiple 3D segmentation in MR images.

5.6 Concluding Remarks

This chapter presents unified analytical framework that extends our contributions explained in Chapter 4, EM-joint shape based framework, to multiple shapes. In particular, we describe a new multiple shape modeling algorithm with some important advantages such as: 1) capturing main co-dependencies of both shape and appearance information shared among the different shape classes, 2) eliminating the need for point-based parameterizations, 3) handling topological changes, 4) employing hidden variable model as extra shape-based prior information, 5) easily extending from a 2D to a 3D framework.

It is also important to mention that our statistical multiple shape/appearance model that is extended from Tsai's method [27] and our previous work [132] is flexible in the sense that it can be combined into other segmentation methods. An algorithmic representation of our statistical multiple shape/appearance model is given in Table 5.1.

Chapter 6

Conclusion and Recommendations for Future Work

In this thesis, we have proposed the various proposed segmentation frameworks that seamlessly extend previous works of level set curve evolution to more accurate, statistically robust and globally knowledge-based system. The segmentation algorithms provide plenty of important applications in the field of medical image analysis that can help to apply better treatments for patients. For example surgical navigation and surgical simulation use 3D visualization of anatomical structures which require segmentation methods of extracting these structures from the internal scans. We have presented empirical results which demonstrates the effectiveness of our segmentation frameworks for clinical applications. To perform a satisfactory analysis of the image, we have combined voxel-wise information and statistical models to address the segmentation problems in medical applications. This connection provides a potential capability to extend our frameworks into either voxel-wise based techniques or statistical models. We have explained each of our frameworks as a unified analytical formulation and the extensions of it into three dimensional multiple shapes.

The datasets used include normal older brains or mild or moderate Alzheimers disease (AD). There were no obvious pathological findings in the MRI images, such as lesions or tumors. Similar to other methods, our approach is capable of segmenting diseased brain structures to some degree. The threshold level where this method could perform satisfactorily has not been the focus of this work. It is obviously an interesting topic for future research. The threshold level may also be improved by enhancing the segmentation method. Furthermore, precise characterization of normal structures obtained by our method could also be used to define and categorize various kinds of abnormalities. This chapter summarizes the contents of this thesis and outlines its contributions followed by a discuss of various open research problems which are motivated by this thesis.

6.1 Conclusion

In the first part of this thesis, we introduce a new active contour model implemented by the level set methods as an analytical and robust segmentation framework, called *joint parametric and non-parametric curve evolution*. The model is constructed by parametric and implicit shape-based prior model via applying PCA on an aligned training set of SDFs. Integrating the advantages of both parametric and non-parametric level set curve evolution methods, in this work, we formulate the segmentation problem using a maximum a posteriori (MAP) framework such that the overall energy function consists of both the parametric and the non-parametric curve evolution terms. By employing level set based representation, our framework is set in an Eulerian shell. It does not need control points during building statistical model and thus, can be applied to handle topological changes of the segmenting curve. Relying on the stage of parametric curve evolution, our framework is capable of segmenting images contaminated by large noise and structures with diffuse

or missing edges information. In addition, relying on integrating parametric and non-parametric curve evolution, our framework is flexible in handle more complex shapes segmentation than the one which only uses the PCA shape-based prior into the curve evolution. Furthermore, employing a region-based information for estimating the input image likelihood, makes our framework more global and robust to noise and less sensitive to the initial curve. The comparative results of our joint curve evolution illustrated significantly better performance compared to parametric and non-parametric approaches in terms of accuracy, robustness and reliability. In the experimental results, we applied the joint curve evolution on three sets of 2D samples to segment ventricles, putamens and thalamus structures. In each set, there was plenty of variability among the shapes. The segmentation results were compared with one example of parametric curve evolution approach (Tsai et al.[4]) and one example as non-parametric curve evolution approach (Chan/Vese et al. [10]). The results were evaluated using three different ground truths obtained by three different experts. Using mean Hausdorff distance measurement for ventricle, the average error and standard deviation resulted from our algorithm, Tsai method and Chan/Vese method were 0.89mm/0.37mm, 1.59mm/0.76mm and 0.98mm/0.31mm. For putamen, the average and standard deviation were 0.95mm/0.24mm , 3.06mm/0.81mm and 1.91mm/0.40mm. Using maximum Hausdorff distance measurement for thalamus, the mismatch error of the segmentation results of the joint curve evolution, Tsai method and Chan/Vese model were 8.06mm, 12.04mm and 8.54mm respectively. It could be seen that, the results of ventricles were satisfactory because of the intensity-based energy term. However, in the case of putamen structures, the errors were mostly observed in the areas not covered by the training set. One way to tweak the algorithm for better results is to employ non-linear shape-based prior model. Furthermore, we used dice coefficient measurement for evaluating the joint curve evolution. In order to show consistency of our results, three manual segmen-

tation results were used as the ground truth. The errors of ventricles, putamens and thalamus segmentations resulted in means of $0.993mm$, $0.991mm$ and $0.9899mm$ and standard deviations of 0.0003, 0.0007 and 0.0008 respectively. Sufficient sampling size is important for achieving a reliable statistical model. It is seen that segmentation of the subcortical structures such as putamens is very challenging using non-parametric methods as they pose less-constrained forces. Therefore, our approach has advantages of balancing constrained and non-constrained forces over parametric and non-parametric approaches. However, since medical structures variations are not formed in linear space, applying linear statistical model can remove much useful information about shapes.

In the second part of our contributions, we developed a novel statistical level set based shape evolution technique for segmentation of MR brain images. We have proposed a novel EM-based shape evolution algorithm, called *EM-joint shape based evolution* that the evolution shape is constrained not only by a shape-based statistical model but also by a hidden variable model from the image observation. The hidden variable model is defined by the local voxel labeling and is estimated by the expected likelihood function defined by the image data and the built shape based prior anatomical model. In the M-step, the shapes of the structures are estimated jointly by encoding the hidden variable model and the statistical prior model obtained from the training stage. For modeling, we introduce new parametric and statistical shape-based model to encode shape-based prior information from a set of training samples with the shape and appearance data. By using the PCA technique, our new statistical approach employs the covariance relation between the object shape and appearance of inside object shape to make our model more robust and reliable. The comparative results shows that novel EM-joint shape based framework outperformed statistical shape-based techniques in terms of robustness and accuracy in the same framework and a current state-of-the-art region competition

level set method. We applied the EM-joint approach on real clinical 2D and 3D sets to extract putamens and caudate nucleus. For 2D segmentation of putamens, using mean Hausdorff distance measurement, the resulted error of the EM-joint shape based approach was obtained as follows: mean = $1.19mm$ std = 0.12 . The corresponding errors of the joint curve evolution (explained in Chapter 3), parametric approach (Tsai et al.[4]) and non-parametric method (Chan and Vese et al.[10]) were obtained as follows: (mean = $1.25mm$, std = $0.09mm$), (mean = $1.3mm$, std = $0.14mm$) and (mean = $1.45mm$ std = $0.08mm$). For 2D caudate segmentation, we obtained 19.42% and 34.32% improvements in mean and standard deviation between the EM-joint shape based approach and the joint curve evolution method. For 3D sets, using maximum Hausdorff measurement, the errors were obtained for set1 and set2 as: (mean = $3.91mm$ and 7.14), (standard deviation = 0.99 and 6.08), (max error = $6.48mm$ and $9.8mm$) and (min error = $2.89mm$ and $3.31mm$). For 3D segmentation results, we increased the sample size into 60 samples and compared our results with the parametric approach in 3D. The performance of the EM-joint shape based evolution was significantly higher. The errors of our method and the parametric approach resulted in means of 0.8256 and 0.6722 and standard deviations of 0.0522 and 0.1101 respectively using dice coefficient measurement. Similarly with the joint curve evolution approach, enough sampling size is very vital to utilize from the EM-joint approach. Although there is still the problem of modeling shape variations linearly, the obtained results were improved due to hidden features in segmentation.

In the third part of our contributions, we have extended the previous parts of our contributions to represent multiple shapes simultaneously in a single segmentation framework and also from a 2D to 3D model. We have provided the extensions that we have made to adapt our techniques that are capable of handling multiple shape classes simultaneously, exploiting the statistical relationships among all of the

shapes (as well as the statistical variability of each individual shape). Finally, we demonstrated the strength of our multiple shape classes framework by applying it to volumetric segmentation of medical images. Based on using maximum Hausdorff distance measurement, for 2D segmentation of three-nuclei subcortical (caudate, putamens and thalamus) the improvements of the novel extended EM-joint shape based algorithm were recorded compared to the Tsai's method [4] as the parametric shapes evolution (12.13% improvement) and the Chan/Vese's approach [10] as the non- parametric shapes evolution (7.69% improvement). Similarly using the maximum Hausdorff distance measurement, 3D segmentation results of caudate nucleus, putamens and thalamus were recorded as: $5.7mm$, $3.6mm$ and $5.22mm$ as mean values and 1.51, 0.63 and 2.16 as their corresponding standard deviations. It is important to note that if the variations of different shapes change non-harmoniously, it will not be suitable for use our approach because different shapes would evolve by same parameters of the statistical shape-based model.

6.2 Recommendations for Future Work

In this section, we will focus on limitations of our research work and motivating research areas that are worth pursuing for future works. The statistical shape-based models (including our approaches) result in successfully segmentation of brain structures from normal subjects. The performance of the statistical shape-based models highly depends on a training set that covers modeled variation of shape. These approaches are also suitable for segmentation of brain structures from elderly subjects, if training set expresses enough information about shape variation. However, the disadvantage of these approaches is that they cannot be applied to abnormal subjects in the absence of prior shape-based knowledge in diseased brain anatomies. Therefore we do not expect that our approaches to be able to segment structures

suffering deformations from diseases.

In the following sections, we will explain our researches avenues as our future work and focus on their importances in medical image segmentation application.

6.2.1 Coupled Spatial Prior Probability of Neighboring Configuration

The Bayesian formulation for image segmentation is simplified assuming that pixel intensities are independent realizations of the corresponding random process. However, in practice, pixels intensity have spatially dependency. Since medical images with same intensity distribution may have different structural properties, in order to fit the actual image better, the spatial dependency should be modeled using the Markov Random Field (MRF) theory. MRF theory provides a convenient way to model context-dependent image pixels and correlated features referred to as neighborhood system. Applying this spatial dependency into total energy function which is defined by curve evolution is very challenging. In this thesis, we introduced new curve evolution formulation (see Chapter 4) to which this spatial dependency can be applied in a convenient way. In Chapter 4, we explained our proposed EM-joint shape based framework mainly formulated by:

$$\begin{aligned} \phi &\leftarrow \operatorname{argmax}_{\phi} E_{x|I,\phi} \{ \log p(I|x, \phi) + \log p(x|\phi) + \log p(\phi|\mathbf{w}, \mathbf{p}) \} \\ \phi &\leftarrow \operatorname{argmax}_{\phi} \sum_i \sum_{k=1,2} E_{x_{i,k}|I_i,\phi} \{ \log p(I_i|x_{i,k}, \phi) + \log p(x_{i,k}|\phi) \} \\ &\quad + \log p(\phi|\mathbf{w}, \mathbf{p}). \end{aligned} \quad (6.1)$$

Let the sites S be related to one another via a *neighborhood system*, which is defined as $N = \{N_i, i \in S\}$, where N_i is the set of sites neighboring i , $i \notin N_i$ and $i \in N_j \Leftrightarrow j \in N_i$. In Chapter 4, we introduced a random field X as the underlying local voxel

labeling and is said to be an MRF of S with respect to a neighborhood system N if and only if

$$\begin{aligned} p(x) &> 0, \\ p(x_i|x_{S-\{i\}}) &= p(x_i|x_{N_i}). \end{aligned} \quad (6.2)$$

The augmented formulation Eq. 6.1 based on the MRF model can be shown as:

$$\begin{aligned} \phi \leftarrow \operatorname{argmax}_{\phi} \sum_i \sum_{k=1,2} E_{x_{i,k}|I_i,\phi} \{ \log p(I_i|x_{i,k}, \phi) + \log p(x_{i,k}|\phi) + \log p(x_{i,k}|x_{N_{i,k}}) \} \\ + \log p(\phi|\mathbf{w}, \mathbf{p}). \end{aligned} \quad (6.3)$$

As a future work, some demonstrations can be provided in medical imaging to show the effectiveness of this term in the curve evolution techniques.

6.2.2 Prior Probability of Joint Shape-Intensity

In this thesis, we explained different aspects of active shape evolution which is constraint subject to the statistical shape-based prior model. Based on the level set representation, the speed function of shape evolution depends on various elements, e.g. the geometric properties, the data-driven information and shape-based prior knowledge,

$$F(\omega(t); t) = \kappa(\omega(t); t) \cdot p(I|\phi) \cdot \eta(\phi). \quad (6.4)$$

It might be more promising to be able to capture the gray level variation in an image and encode a unified shape-intensity prior model as $\eta(\phi)$. As a future work, we will propose a modification of the level set speed function to add an appearance prior knowledge. Consequently, the new level set speed function allows to encoding

statistical models of both shape and texture (intensity model). It is achieving optimizing process by minimizing the difference between the synthesized model image and the target image. These parameters are related to the shape features such as shape-based PCA parameters as well as appearance model such as appearance-based PCA parameters. The non-rigid transformation can then be applied as a free-form deformation to the updating level set function which is obtained from the synthesized model. Finally, level set shape function is updated using this deformation and the statistical shape prior models.

The estimation parameters of the shape and the appearance models can be achieved by applying EM algorithm. Based on the EM-MAP approach, the formulation Eq. 6.4 can be changed as follows:

$$\phi, \tau \leftarrow \operatorname{argmax}_{\phi, \tau} \eta(\phi) \cdot \eta(\tau) \cdot \{ \log p(I|\phi, \tau) \}, \quad (6.5)$$

where ϕ and τ correspond to the shape and the appearance parameters. $\eta(\phi)$ reflects the shape prior constraint and $\eta(\tau)$ applies the appearance knowledge subject to the constructed appearance model. According to the EM algorithm, in the M-step, ϕ and τ are estimated by maximizing the fitting data-driven term $\log p(I|\phi, \tau)$ such that weighted by the shape and appearance prior models. The prior models acted as weighted terms ($\eta(\phi)$ and $\eta(\tau)$) are calculated in the E-step.

6.2.3 Prior Probability of Shape Features

As mentioned before, the construction of appropriate shape dissimilarity measures amounts to a problem of density estimation of the object shape. We have provided a review of some methods that address this problem by modeling the space of familiar shapes by linear subspaces (PCA). Furthermore, for level set based shape

representations, in [6, 4, 5], it is suggested to fit a linear sub-space to the sampled signed distance functions. Yet, they have two limitations: Firstly, they rely on the assumption of a Gaussian distribution which is not well suited to approximate shape distributions encoding more complex shape variation. Secondly, they work under the assumption that shapes are represented by signed distance functions. Yet, the space of signed distance functions is not a linear space. Therefore, in general, neither the mean nor the linear combination of a set of signed distance functions will correspond to a signed distance function. Cremers et al. [7] and Kim et al. [30] proposed a statistical shape prior by introducing the concept of kernel density estimation to the domain of level set based shape representation. In contrast to existing approaches of shape priors in level set segmentation (which are based on the assumption of a Gaussian distribution), this prior allows to obtain well approximate arbitrary distributions of shapes.

Author's Publications

Journal Papers:

1. M. Farzinfar , Z. Xue and E. K. Teoh, “A novel approach for curve evolution in segmentation of medical images”, *Computerized Medical Imaging and Graphics*, vol. 34, pp. 354-361, July 2010.
2. M. Farzinfar , E. K. Teoh and Z. Xue, “A Joint Shape Evolution Approach for Medical Image Segmentation Using Expectation-Maximization Algorithm”, *Magnetic Resonance Imaging*, vol. 29, no. 9, pp. 1255-1266, Nov 2011.

Conference Papers:

3. M. Farzinfar , Z. Xue and E. K. Teoh, “Joint Parametric and Non-parametric Curve Evolution for Medical Image Segmentation”, *10th European Conference on Computer Vision (ECCV(1) 2008)*: 167-178, France, 12-18 Oct 2008.
4. M. Farzinfar , E. K. Teoh and Z. Xue, “A Coupled Implicit Shape-Based Deformable Model for Segmentation of MR Images”, *10th International Conference on Control, Automation, Robotic and Vision (ICARCV 2008)*: 651-656, Vietnam, 17-20 Dec 2008.
5. M. Farzinfar , E. K. Teoh and Z. Xue, “An expectation-maximization approach to joint curve evolution for medical image segmentation”, *SPIE Medical Imaging*, vol. 7623, p. 76231M, SPIE 2010, 2010 USA, 12-19 Feb 2010.

6. M. Farzinfar , E. K. Teoh and Z. Xue, “Applying Training Hidden Features to Joint Curve Evolution for Brain MRI Segmentation”, Accepted for oral presentation in the *11th International Conference on Control, Automation, Robotic and Vision* (ICARCV 2010), Singapore, 7-10 Dec 2010.

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