BRAIN VASCULATURE SEGMENTATION FROM MAGNETIC RESONANCE ANGIOGRAPHIC IMAGE

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This dissertation is dedicated to Masood

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Contents

A	ckno	wledgments	i				
Sı	ımm	ary	iii				
\mathbf{Li}	st of	Figures	vi				
1	Intr	oduction	1				
	1.1	Medical Image Segmentation	1				
	1.2	Applications of Segmentation	2				
	1.3	MRA images	3				
	1.4	Thesis Focus and Main Contributions	4				
	1.5	Organization of the Thesis	5				
2	A F	Review of Segmentation Methods for Medical Images	6				
	2.1	Introduction	6				
	2.2	Region-Oriented Methods	9				
		2.2.1 Thresholding Methods	9				
		2.2.2 Region Growing Methods	10				
		2.2.3 Watershed Methods	10				
	2.3	Edge-Oriented Methods	11				
		2.3.1 Classical Edge Detection Methods	12				
		2.3.2 Active Contours	13				
	2.4	Hybrid methods	23				

3	Compensated Active Contours	26					
	3.1	Background					
	MRA Images and Their Properties	27					
		3.1.2	Review:Vasculature Segmentation	31			
		3.1.3	Geodesic Active Contours & the Speed Functions $\ . \ . \ .$.	34			
	3.2	Gradi	ent Compensated Active Contours	38			
		3.2.1	Thickness vs . Intensity Gradient in MRA Images \ldots .	38			
		3.2.2	Stopping Forces in Active contours	41			
		3.2.3	Gradient Compensator Function	42			
		3.2.4	Implementation	45			
4	Res	sults ar	nd Discussion	49			
	4.1	Result	ts based on synthetic data	49			
	4.1 4.2	Result Segme	ts based on synthetic data	49 52			
	4.1 4.2	Result Segme 4.2.1	entation Results of 3D MRA Images	49 52 53			
	4.1 4.2	Result Segme 4.2.1 4.2.2	entation Results of 3D MRA Images	49 52 53 59			
	4.14.24.3	Result Segme 4.2.1 4.2.2 Summ	ts based on synthetic data	49 52 53 59 64			
5	4.14.24.3Con	Result Segme 4.2.1 4.2.2 Summ	entation Results of 3D MRA Images	 49 52 53 59 64 65 			
5	 4.1 4.2 4.3 Con 5.1 	Result Segme 4.2.1 4.2.2 Summ nclusio Future	extra based on synthetic data	 49 52 53 59 64 65 66 			
5	 4.1 4.2 4.3 Con 5.1 	Result Segme 4.2.1 4.2.2 Summ nclusio Future 5.1.1	<pre>ts based on synthetic data</pre>	 49 52 53 59 64 65 66 66 			
5	 4.1 4.2 4.3 Con 5.1 	Result Segme 4.2.1 4.2.2 Summ nclusio Future 5.1.1 5.1.2	ts based on synthetic data	 49 52 53 59 64 65 66 66 66 			
5	 4.1 4.2 4.3 Con 5.1 	Result Segme 4.2.1 4.2.2 Summ nclusio Future 5.1.1 5.1.2 5.1.3	ts based on synthetic data	 49 52 53 59 64 65 66 66 66 67 			

Bibliogr	aphy
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Summary

Precise segmentation of vasculature from three-dimensional (3D) magnetic resonance angiography (MRA) images plays an important role in image-guided neurosurgery, pre-operation planning and clinical analysis. Level sets based evolution algorithms are being widely applied to MRA data sets. Our objective is to develop an automated segmentation scheme to accurately extract vasculature of the brain, especially the thin vessels. Inspired by the intrinsic properties of MRA, we have proposed a scheme called the *gradient compensated active contour* (GCAC), which compensates for the low gradient near the edge of thin vessels' contour. The GCAC, which is based on level sets, has been tested on both synthetic volumetric images and real 3D MRA images. Our experiments show that the introduced gradient compensation can facilitate more accurate segmentation of thin blood vessels.

List of Figures

1.1	Block diagram of medical image analysis scheme incorporated with visualization.	3
2.1	Classification of segmentation methods	7
2.2	Illustration of Watershed algorithm	11
2.3	Concept of zero set in a level set	19
2.4	The implicit level set curve is the black line superimposed over the image grid. The location of the curve is interpolated by the pixel values of a signed distance map. The grid pixels closest to the implicit curve are shown in gray [23]	20
2.5	Illustration of mumford-shah algorithm, the fitting term is mini- mized when the curve is on the boundary of the object [28]. \ldots .	24
3.1	Volumetric MRA data set	28
3.2	TOF technique: v_i is the velocity of blood flow, THK is the slice or slab thickness and T_R is the repetition time. [31]	29
3.3	Displacement (Intensity) vs. Flow and $T_R 1001[32]$	30
3.4	(a) MIP of a MRA data set and (b) its Gradient magnitude	39
3.5	The boundary gradient vs. the thickness of the vessels for a sample data set	40
3.6	Vessel gradient <i>vs.</i> vessel thickness	41
3.7	M(Th(x)) vs. estimation of thickness at point x	43
3.8	Estimation of the local contour thickness	45

4.1	Illustration of the effects on varying α in Equation (3.11)on (a) a synthetic 3D vessel whose cross section along the axis is shown in (b). (c) Segmented vessel, $\alpha = 0$. (d) Segmented vessel, $\alpha = 1.2$. (e) Segmented vessel, $\alpha=3.2$.	51
4.2	Maximum intensity projections of the two segmented MRA data sets.	52
4.3	Samples of cerebral MRA data set. Bright regions and points are blood vessels	54
4.4	First data set: view 1	55
4.5	First data set: view 2	56
4.6	Second data set: view 1	57
4.7	Second data set: view 2	58
4.8	MIP of the segmented MRA	59
4.9	Region of interest	59
4.10	MRA data set 1	61
4.11	MRA data set 2	62
4.12	MRA data set 3	63

3.9 $\,$ An overview of the Gradient Compensated Active Contour Algorithm $\,46$

Chapter 1

Introduction

1.1 Medical Image Segmentation

An important issue in medical image analysis is the segmentation problem. It can be defined as the process of labeling each voxel in a medical image data set to indicate its tissue type or anatomical structure. The labels that result from this process have a wide variety of applications in medical research and visualization. For instance, in a liver transplant surgery, it is essential to know the available volume of livers before the surgery. It will be possible by collecting the required information through medical imaging. The input to a segmentation procedure is grayscale medical image, for example the result of a CT or MRI scan and the desired output, contains labels that classify the input grayscale voxels. Currently in hospitals, radiologists manually do the segmentation task after getting the images. However, this process can be quite time consuming. In addition, the manually obtained results are not reproducible. With the fast increasing size and number of medical images, the use of computers in facilitating their processing and analysis has become inevitable. The digital revolution and the rapid growing processing power of the modern computer in combination with medical imaging modalities have helped doctors to achieve more accurate diagnosis and surgery. Segmentation techniques have an important role in extracting the necessary boundaries, surfaces, and segmenting volumes of these organs in the spatial and temporal domains. Algorithms for the segmentation of anatomical structures and other regions of interest are becoming a key component in assisting and automating specific radiological tasks. A large number of algorithms have been proposed for biomedical imaging applications. Some application of these algorithms is discussed in the following section.

1.2 Applications of Segmentation

Image segmentation is often the crucial step, when detailed or quantitative information about the appearance, size, or shape of patient anatomy is desired (Figure 1.1). Applications of interest that depend on image segmentation include threedimensional visualization, volumetric measurement, research into shape representation of anatomy, image-guided surgery, and detection of anatomical changes over time and so on. Segmentation of medical imagery allows 3D surface model visualization of patient anatomy. The advantage of a surface model representation is that it gives a three-dimensional view from any angle, which is an improvement over two-dimensional cross section view of the original grayscale data set. Moreover, volume measurements of the anatomical structures cannot be done without segmenting the images since it is not possible to accurately measure anatomical volumes visually. Image-guided surgery is another medical application where segmentation is beneficial as it can help the surgeons to follow complex trajectories and to avoid anatomical hazards such as blood vessels or functional brain areas. Further discussion on application of segmentation can be found in [52].



Figure 1.1: Block diagram of medical image analysis scheme incorporated with visualization.

1.3 MRA images

Magnetic resonance imaging (MRI) is a method of producing extremely detailed pictures of body tissues without the need for x-rays. The electromagnetic energy that is released when exposing a patient to radio frequency waves in a strong magnetic field is measured and analyzed by a computer, which forms three-dimensional images. MR angiography (MRA) is an MRI study of the blood vessels. It utilizes MRI technology to detect, diagnose and aid the treatment of heart disorders, stroke, and blood vessel diseases. MRA may provide detailed images of blood vessels without using any contrast material [33]. Precise segmentation of vasculature from three-dimensional (3D) magnetic resonance angiography (MRA) images plays an important role in image-guided neurosurgery, pre-operation planning and clinical analysis. However, there are many difficulties to do this task. The following are some of the main challenges and difficulties in vasculature segmentation:

• Vasculature complex topology: Vascular tree is intricate, consisting of several tiny vessels with huge amount of branches. Moreover, this network highl

y varies in size and shape from one person to another.

- Noise and Gaps : There might be intensity discontinuities in the images that results in noise and gaps in the vessels.
- Low intensity contrast between small vessels and their background: Due to MRA imaging properties, small vessels are not easily distinguishable from the background. In addition, there are other organs in the brain, such as skull, which has intensity value close to that of the blood vessel.
- Characteristics of scanning modalities and their limitations: Currently MRA imaging machines produce sets of 2D images which can be viewed as the cross section of the 3D volume and the vessels instead of the 3D view of the vasculature itself.
- A variety of artifacts may appear in MR images: Since the artifacts change the appearance of the image, they may also affect the performance of a segmentation algorithm. The most important artifacts in image segmentation are intensity inhomogeneities and partial volume effect.

1.4 Thesis Focus and Main Contributions

In particular, a new deformable model, gradient compensated geodesic active contour (GCAC), is formulated and developed to extract vasculature from MRA images. Unlike existing MRA segmentation techniques, which have difficulty on extracting tiny vessels, the GCAC is able to segment the whole structures successfully from 3D MRA images with the help of the compensator function. This method is applied on clinical MRA images and compared with other state-of-the-art MRA segmentation methods.

1.5 Organization of the Thesis

The remainder of the thesis can be divided into four parts. First, we provide an overview of medical image segmentation methods in Chapter 2. Next, in Chapter 3, some backgrounds on 3D magnetic resonance angiography (MRA) images and their segmentation methods are provided. Later in this chapter, a new method for MRA image segmentation, called gradient compensator active contour, is presented that is based on geodesic active contours. This method is able to extract vasculature from MRA images of the brain. Experiments which demonstrate the capability of our algorithms are presented and discussed in Chapter 4. Finally, in Chapter 5, we present our conclusions and discuss some possible future works.

Chapter 2

A Review of Segmentation Methods for Medical Images

In this chapter, a brief survey of the various segmentation techniques, for medical images, is presented. First, we begin with a review of medical image segmentation techniques in section 2.1. Then, in section 2.3.2, we provide some background on parametric active contours and the basis of deformable models, which have been successfully used in medical image segmentation. Following that, an introduction to geometric deformable models and geodesic active contours, is provided.

2.1 Introduction

Image segmentation essentially involves, partitioning an image into several constituent regions. In the context of medical imaging, these regions have to be anatomically meaningful. Essentially, there are two aspects of medical imaging that make the segmentation process a difficult problem. First, is the imaging process itself. The imaging modalities, for example MR, CT, or ultrasound, is chosen

so that its interactions with the tissues of interest will provide clinically relevant information about the tissue in the output image. But this does not mean that the anatomical feature of interest will be particularly separable from its surroundings. This means that it will not be a constant gray scale value, and strong edges may not be present around its borders. In fact, the interaction of the imaging process with the tissue of interest will often produce a "grainy" region that is more detectable by the human eye than by even sophisticated computer algorithms. This is due to the noise in the imaging process and inhomogeneity of the tissue itself. Consequently, simple image processing methods, such as thresholding or edge detection, may not be very successful when applied to medical image segmentation. The second aspect, that makes segmentation a difficult problem, is the complexity and variability of the anatomy that is desired to be segmented. It may not be possible to locate or delineate certain structures without detailed anatomical knowledge. Since, a computer does not approach the expert knowledge of a radiologist and it cannot make use of all the information that exists about the image, such as anatomical knowledge. This may lead to a meaningless segmentation results, which means that the segmented regions may not correspond to different tissues. The above facts make general segmentation a difficult problem, as the prior knowledge must either be built into the system or provided by a human operator.



Figure 2.1: Classification of segmentation methods.

Segmentation methods for medical images vary enormously, depending on im-

age type, image modality used, and the properties of the desired objects, since each imaging modality has its own characteristics and produces quite different image for same tissue. There is currently no single segmentation method that produces reasonable results for all medical image types. Although some methods are more general and can be applied to a variety of data sets, but, specialized methods for particular applications can often achieve better performance by taking prior knowledge into account [7], [9].

There are many ways to classify medical images segmentation methods depending on different criteria, such as the user interactivity. Accordingly, the groups are manual methods, that require a high level of user interactivity, computer-aided semiautomatic methods, and completely automatic methods [13]. Currently, manual approach is the most commonly used, as it is conceptually simple. Manual segmentation is done in each two-dimensional slice for the entire "stack" of slices that constitute a three-dimensional image volume. However, due to the huge size of medical images the process is quite time-consuming and subject to human errors. In addition, they often suffer from *interobserver* and *intraobserver* variability [65]. These terms simply mean that, the same or different users can make different choices that affect the segmentation process and it leads to segmentation results that are very much dependent on the user. For these reasons, developing computeraided semi-automatic and automatic methods have received great attention in the medical imaging field.

In another classification, segmentation methods can be broadly divided into three main categories: *edge-oriented*, *region-oriented* and hybrid methods (Figure 2.1). In edge-oriented approaches, edges between different regions are first found, and the resulting regions become the segmented regions. Therefore, the task of image segmentation essentially becomes an edge detection problem, which has been well studied. Focusing only on the boundaries is computationally less complex but also less robust since information inside the region is discarded. On the other

hand, region-oriented methods, start from one point given inside the object and then add other points until the region encompasses the desired object. The main advantage of these methods over the edge-oriented ones is that they make use of the information inside the edges. However, these methods are not robust enough and they are highly sensitive to the noise and they need a high level of user interactivity. Finally, there are hybrid methods, which make use of both approaches to do the segmentation process. In the following sections these three categories will be discussed in more details.

2.2 Region-Oriented Methods

In Region-Oriented approaches, images are segmented into regions of pixels based on certain criteria and similarities and the desired regions are found directly. These methods mainly consist of thresholding, region growing, and watershed methods [4].

2.2.1 Thresholding Methods

Segmentation methods based on thresholding attempt to determine intensity values, called thresholds, which separate the pixels, based on their intensities, into ranges that correspond to the tissue types. The success of segmentation process highly depends on the selection of the proper threshold values. There are several ways for this selection: First, is to obtain this values manually. This selection may lead to a quite reasonable result. However, this method suffers from the problems discussed previously for the manual methods. Another alternative is to obtain the thresholding values in a more automatic manner and image histograms are often used for this mean. These approaches are based on the assumption that different objects in an image have distinct distribution function. But, the difficulty of the these approaches is that this assumption is mostly wrong and the intensity distributions of different objects are overlapped.

2.2.2 Region Growing Methods

Region growing algorithms, the other class of region-oriented algorithms, start with a set of pixels called seeds, that belong to the structure of interest. These seeds can be selected either manually or by an automatic process [64]. In the region growing process, all the pixels neighboring a seed are examined to see if they meet the similarity criteria and if they do, they will be added to the region containing the seed. The procedure continues until all the pixels are checked and there is no new pixels to be added to the region. Region growing algorithms vary depending on the criteria used to decide whether a pixel should be included in the region or not, the type of connectivity used to determine neighbors, and the strategy used to visit neighboring pixels [64]. While the original region-growing algorithm [14] formalism is somewhat crude, interesting extensions have been proposed by Adams *et al.* [67] where some statistical information is derived from the region as it expands. These techniques have been applied to medical image analysis as well [68], [69]. However, there are some limitations to these methods as they are unstable and their performance highly depends on the choice of homogeneity criterion [79]. Furthermore, if partial volume effects (see Section 3.1.1) are present or if there are small connections between objects, it can cause the objects to combine into one larger region. Noise can also affect the segmentation negatively [66].

2.2.3 Watershed Methods

Watershed approach can be best understood, if one can assume an image as a landscape where bright pixels represent heights and dark pixels valleys. Then

flooding will be simulated (Figure 2.2). The water intends to fill the valleys. But dams are built at points where water coming from different valleys would meet. The dams stop the mixing of the water. The process will stop when the water level has reached the highest peak in the landscape. In this way, the landscape is partitioned into regions or valleys separated by dams [80]. These dams are called watersheds. They are the boundaries of objects and segmented valley regions are considered to be distinct objects in the image. In the context of medical imaging, some algorithms have been implemented using this approach, for instance Segonne, *et al.* [15] uses the watershed algorithm to get an approximate boundary of the brain. However, A known drawback of the watershed algorithm is over-segmentation due to noise or local discontinuities in the gradient image [70].



Figure 2.2: Illustration of Watershed algorithm.

2.3 Edge-Oriented Methods

Edge-Oriented segmentation looks for sharp changes in the intensity of the images. An edge can be defined as the boundary between two regions with relatively distinct properties. The assumption of edge-based segmentation is that every subregion in an image is uniform enough so that the change between two sub-regions can be determined on the basis of discontinuities. Therefore, the main weakness of these approaches are dealing with noisy images. Another major difficulty is that extracted edges need to be connected into topologically meaningful region boundaries. To address this problem, Kass *et al.* [10] set the topology of the boundary and then deform this model in a variational framework to finally reside on the edges. It was first implemented in two dimensions, and was named snakes (Section 2.3.2). Improvements of this technique include *Geometric Active Contours* and *Geodesic Active Contours* (Section: 2.3.2) [9].

2.3.1 Classical Edge Detection Methods

Computation of a local derivative operator is the essential idea underlying most edge detection methods. The gradient vector of an image I(x, y, z), given by

$$\nabla \mathbf{I} = \begin{bmatrix} \frac{\partial I}{\partial x} \\ \frac{\partial I}{\partial y} \\ \frac{\partial I}{\partial z} \end{bmatrix}$$
(2.1)

And boundary is known to be in the vicinity of points where the norm of the gradient is large. This is the approach taken in the 60s and 70s by Roberts and Sobel [71], [87], who proposed slightly different discrete convolution masks to approximate the gradient of digital images. Disadvantages with these approaches are that edges are not precisely localized and may be corrupted by noise [9], [14]. Canny [78] proposed adding a smoothing preprocessing step, in order to reduce the influence of the noise as well as a thinning post-processing phase to ensure that the edges are uniquely localized. A slightly different approach was proposed by Marr and Hildreth [72] where edges are defined as the zeros of the Laplacian of a smooth version of the image. The Laplacian of an image function I(x, y, z) is the summation of the second-order derivatives and is defined as:

$$\nabla^2 I = \frac{\partial^2 I}{\partial x^2} + \frac{\partial^2 I}{\partial y^2} + \frac{\partial^2 I}{\partial z^2}$$
(2.2)

Laplacian of an image highlights regions of rapid changes in intensity which corresponds to the location of its zero-crossings [14]. A critical disadvantage of the gradient approaches is that the derivatives enhances the noise. As a second-order derivative, the Laplacian is even more sensitive to noise. However, an alternative could be smoothing the image by convolving it with a Gaussian function [14].

Another major limitation of these low-level edge detection methods is that they only consider local information of medical images segmentation as in general, shape, location and orientation of objects is known. They do not make use of the *priori* knowledge like the desired shape, size or location of the objects.

2.3.2 Active Contours

Deformable models or Active contours have overcome many of the problems with the classical edge detection approaches by providing compact and analytical representations of object shape, by incorporating anatomic knowledge, and by providing interactive capabilities [83]. Active contours, are curves (2-D) or surfaces (3-D) defined within an image domain that can move under the influence of internal forces coming from within the curve itself and external forces computed from the image data. The internal and external forces are defined so that the evolving surface will conform to an object boundary or other desired features within an image [61].

They were first introduced by Kass *et al.* [10] for 2-D problems, as *snakes*. Since then, different varieties of these models have been developed and used successfully for medical image segmentation purposes [16]. These approaches are able to segment anatomic structures by exploiting constraints derived from the image data together with a priori knowledge. This knowledge may be incorporated into the deformable model in the form of initial conditions, data constraints, constraints on the model shape parameters, or into the model fitting procedure. The use of

implicit or explicit anatomical knowledge to guide shape recovery is especially important for robust automatic interpretation of medical images. Deformable models are capable of handling the significant variation of anatomical structures. Furthermore, deformable models are highly interactive that allow medical expertise to bear on the model-based image interpretation task when necessary.

There are three main approaches in deformable models based on the their mathematic implementation and representation: Parametric Active Contours, move predefined contours points based on an energy minimization scheme and the anatomical knowledge is represented explicitly as parameterized contours in a Lagrangian frame work [61]. While Geometric Active Contours, move contours implicitly as a particular level of a function. Priori knowledge is represented implicitly as level sets of a higher-dimensional, scalar level set function and it evolves in an Eulerian fashion [19], [18]. A major advantage of geometric deformable models over parametric deformable models is topological flexibility due to their implicit representation. However, in non-interactive applications, both forms of deformable models must be initialized close to the structure of interest to guarantee a good performance. Moreover, they should be used with extreme caution, when dealing with several adjacent objects [16]. Further details about these two approaches will be discussed in section 2.3.2. Finally, the last class of active contours are known as Geodesic Active Contours. This new formulation for active contours was presented by Caselles *et al.* [12]. The model is intrinsic (geometric) and topology independent connection between the energy based active contours (snakes) and the computation of geodesics or minimal distance curves in a Riemannian space derived from the image [12]. These models can also be interpreted as a connection between the two previous, parametric and geometric, active contours that we have talked about. In other words, they can be viewed as a more mathematically sophisticated variant of classical snakes which are an improvement on the previous approaches.

Parametric Active Contours

The first type of parametric deformable model was proposed by Kass *et al.* and named snakes due to the appearance of the contour [10]. The idea is to match deformable models to image data by means of energy minimization. The traditional snake is a curve, that moves through the spatial domain of an image to minimize the energy functional:

$$E(\mathcal{C}) = \int_0^1 \left(\alpha \left| \frac{\partial \mathcal{C}}{\partial s} \right|^2 + \beta \left| \frac{\partial^2 \mathcal{C}}{\partial s^2} \right|^2 - f(\mathcal{C}(s)) \right) ds$$
(2.3)

where $\mathcal{C}(s)$ is an evolving curve, parameterized by $s \in [0, 1]$. The energy function is defined as a weighted sum of internal and external energy terms. The internal energies, also called regularization terms, are the first two terms in the above equation and depend solely on the shape of the curve $\mathcal{C}(s)$. Their role is to control the curves tension and rigidity. The contour interacts with the image through fwhich is the external energy, derived from the image and it takes on its smaller values at the features of interest, such as boundaries. Given a gray-level image , typical external energies designed to lead an active contour toward step edges [61].

$$f(\mathcal{C}(s)) = |\nabla I(s)|^2 \quad \text{or} \tag{2.4}$$

$$f(\mathcal{C}(s)) = |\nabla (G_{\sigma}(s) \cdot I(s))|^2, \qquad (2.5)$$

where $G_{\sigma}(s)$ is a two-dimensional Gaussian function with standard deviation σ and ∇ is the gradient operator. It is easy to see from these definitions that larger σ s will cause the boundaries to become blurry. Such large σ s are often necessary, however, in order to increase the capture range of the active contour. In the above model, the external image force (last term of Equation 2.3) is significant only in the immediate vicinity of the desired object boundaries. Elsewhere, the model's evolution is driven dominantly by the internal forces only (the first two terms of Equation 2.3), which

leads to shrinking and smoothing of the contour. Therefore, an initialization of the model needs to be close enough to the actual object boundaries. α and β are real positive constants, called weighting parameters. The tradeoff between edge proximity and edge smoothness is played by these parameters in the Equation 2.3. A snake that minimizes the above energy function must satisfy the following Euler equation:

$$\frac{\partial}{\partial s} \left(\alpha \frac{\partial \mathcal{C}}{\partial s} \right) - \frac{\partial^2}{\partial s^2} \left(\beta \frac{\partial^2 \mathcal{C}}{\partial^2 s} \right) + \nabla f(\mathcal{C}(s)) = 0$$
(2.6)

This can be viewed as an internal and external energy balance equation.

$$E_{\rm int} + E_{ext} = 0 \tag{2.7}$$

where $E_{\text{int}} = \frac{\partial}{\partial s} \left(\alpha \frac{\partial \mathcal{C}}{\partial s} \right) + \frac{\partial^2}{\partial s^2} \left(\beta \frac{\partial^2 \mathcal{C}}{\partial^2 s} \right)$ and $E_{ext} = \nabla f(\mathcal{C}(s))$. The internal force prevents stretching and bending while the external potential force pulls the snake toward the desired image edges. To find a solution to Equation 2.6, the snake is made dynamic by treating as a function of time as well as s. Then, the partial derivative of C with respect to t is then set equal to the left hand side of Equation 2.6 as follows:

$$\vec{\mathcal{C}}_t = \frac{\partial}{\partial s} \left(\alpha \frac{\partial \mathcal{C}}{\partial s} \right) - \frac{\partial^2}{\partial s^2} \left(\beta \frac{\partial^2 \mathcal{C}}{\partial^2 s} \right) + \nabla f(\mathcal{C}(s)).$$
(2.8)

Adding a time directive term of C is equivalent to applying gradient descent algorithm to find the local minimum of Equation 2.3 [84]. When the solution stabilizes, the term $\vec{C_t}$ vanishes and we achieve a solution of the Equation 2.6. A numerical solution to Equation 2.8 can be found by discretizing the equation and solving the discrete system iteratively [61]. Approaches based on parametric active

contours produce reasonable results and have been used extensively in literatures (See [16] for a survey of snakes in medical image analysis). However, one limitation to these methods, is that the active contour or snake cannot change topology. For example, if it starts out being a topological circle, will always remain a topological circle and will not be able to break up into two or more pieces, even if the image contains two unconnected objects. In addition, the functional in 2.3 is not intrinsic since it depends on the parametrization s that is arbitrary. This is an undesirable property, since parameterizations are not related to the geometry of the curve (or object boundary). Therefore, it is not natural for an object detection problem to depend on the parametrization of the representation [12].

Geometric Active Contours

In order to obtain a better understanding of the geometric active contours, we need to study the Front Evolution Theory and the Level Sets approaches [18].

Front Evolution Theory and Level Sets Solution: Let C(q,t), defined as $\{x(q,t), y(q,t)\}$, a curve in 2D or $\{x(q,t), y(q,t), z(q,t)\}$, a surface in 3D, be a closed front or contour, propagating along its normal direction, starting with an initial contour $C_0(q) = C(q,0)$ (t represents time and q parameterizes the given contour). The basic result from the front evolution theory is that the geometric shape of the contour is determined by the normal component of the evolution velocity, while the tangential component affects only the parameterizations [18]. The evolution equation, according to Level Sets approach, can be written as

$$\vec{\mathcal{C}}_t(q,t) = F(\mathcal{C}(q,t))\vec{\mathcal{N}}(\mathcal{C}(q,t))$$
(2.9)

with

$$\mathcal{C}(q,0) = \mathcal{C}_0(q)$$

where $F(\mathcal{C}(q,t))$ is a scalar function that often depends on the curvature (κ) of the contour, and $\mathcal{N}(\mathcal{C}(q,t))$ is the unit normal vector along the contour $\mathcal{C}(q,t)$. Level set methods have been proposed to solve the front evolution Equation 2.9. Level set methods are numerical techniques for analyzing and computing interface motions([18], [12]). Since implicit representation is used, the level sets methods allows for topological changes to occur without additional computational complexity [7]. Therefore they can be applied when there is no prior assumption about the object topology. When solving problems, the level sets method increases the dimensionality of the problem. For example in front evolution problems, instead of evolving the 2D curves, the method evolves a 3D surface and the 2D objective curve is represented implicitly as the zero level set of a smooth, Lipschitz-continuous scalar function $\Psi(x, t)$, as shown in Figure 2.3. Function $\Psi(x, t)$ is also known as the *level set function*, where $x \in \mathbb{R}^2$ in 2D and $x \in \mathbb{R}^3$ in 3D.

Although there are many choices of the level set function, in practice, the signed distance function is preferred for its stability in numerical computations [19](see Figure 2.4). The fast marching method proposed in [47] provides an efficient algorithm for constructing the signed distance function from a given initial contour. The initialization can also be as simple as one or several seed points. We use signed distance functions as the representation of function $\Psi(x,t)$ for all of our experiments in this dissertation.

Now, let $\Psi : \Re^2 \to \Re$ be the signed distance function to curve C. If C is evolving according to front evolution Equation 2.9, it can be shown that this contour will be followed by level set approach using the following level set equation:

CHAPTER 2. A REVIEW OF SEGMENTATION METHODS FOR MEDICAL IMAGES



Figure 2.3: Concept of zero set in a level set.

$$\frac{\partial \Psi(x,t)}{\partial t} = F(x,t) |\nabla \Psi(x,t)|$$
(2.10)

where $\Psi(\mathcal{C}_0(p), 0) = 0$, and $|\nabla \Psi|$ denotes the norm of the gradient of Ψ . Note that the function F(x,t) is a *speed function* which is only defined at the contour location originally and, hence, needs to be extended to the whole computational domain (see [19]), in order that (2.10) applies to the whole space. Above equations illustrate that evolving a curve \mathcal{C} is equivalent to updating its signed distance function Ψ according to speed function F. The evolving curve \mathcal{C} is then obtained as the zero level set of Ψ . The formulation is analogous for the case of surface evolving in 3D.

Geometric Deformable Models Caselles *et al.* [20] and Malladi *et al.* [21] applied the above theory to the problem of image segmentation by multiplying the contour velocity by a "stopping" term $g(|\nabla I(x)|)$ that is a monotonically decreasing function of the gradient magnitude of the image I (or its smoothed version). In

Ψ	(x.	t)					8		
	(,	-2.4	-1.3	-0.6	-0.7	-0.8	-1.8		
	-2.4	-1.4	-02	0.4	0.3	7.2	-0.8	-1.8	
-2.4	-1.4	-0A	0.6	1.6	1.3	1.2	0.2	-0.8	-1.8
-1.2	-0.2	0.8	1.8			2.3	1.3	9.3	-0.7
-1.1	-0.	0.9	0.7	1.7		1.2	0.2	- <u>0.8</u>	
-2.5	-1.5	-0.5	-0.8	0.7	2.4	1.4	0.4	-0.6	
	-2.5	-1.5	-1.3	-0.4	1.3	0.3	0.4	-0.6	
			-1.6	-0.6	0.4	-0.7	-0.6	-1.6	
				-1.6	-0.6	-1.7			

Figure 2.4: The implicit level set curve is the black line superimposed over the image grid. The location of the curve is interpolated by the pixel values of a signed distance map. The grid pixels closest to the implicit curve are shown in gray [23].

this way, they arrived at the following evolution equation:

$$\frac{\partial \Psi(x,t)}{\partial t} = g(|\nabla I(x)|)(c + \kappa(x,t))|\nabla \Psi(x,t)|$$
(2.11)

where c is a constant inflation or deflation (depending on its sign) speed term, similar to the function of balloon force in [85], which aims to keep the contour moving in the proper direction, and $\kappa(x,t)$ is the mean curvature of the level set of $\Psi(x,t)$ that passes through the point x, which can be easily computed from the spatial derivatives of $\Psi(\cdot,t)$ (see [19]). We note that, in [20,21], the above formulation is originally derived for planar curves, however, the very same form applies to surfaces as well. In the remainder of this thesis, all of the equations apply to both curves and surfaces unless stated otherwise.

However, the model described in Equation 2.11 does not arise from the minimization of an energy function as in the classical active contour models. Thus, regularization of smoothness and rigidness might not be assured. To address this, Caselles *et al.* [12, 46] and Kichenassamy *et al.* [53] derived another class of deformable models, called the *geodesic active contour* (GCA). The basic idea is to consider the object boundary detection as a problem of geodesic computation in a Riemannian space, according to a metric g(x) induced by the given image *I*. The model has been introduced in the following section.

Geodesic Active Contours

Approaches based on geodesic active contours have been increasingly investigated and developed in medical image segmentation. The derivation of the geodesic active contours are presented as follows. In the original parametric deformable models [10], the energy $E(\mathcal{C})$ is defined as:

$$E(\mathcal{C}) = \int_0^1 \left(\alpha \left| \frac{\partial \mathcal{C}}{\partial s} \right|^2 + \beta \left| \frac{\partial^2 \mathcal{C}}{\partial s^2} \right|^2 - \gamma f(\mathcal{C}(s)) \right) ds$$
(2.12)

where C(s) is a curve and parameterized by $s \in [0, 1]$. Here, α , β and γ are real positive constants, and f is a gradient map of the image. Solving the problem of snakes amounts to finding, for a given set of constants α , β and γ , the curve C that E(C) is minimized. A possible problem of the original deformable models is the need to select the parameters that control the trade-off between smoothness and proximity to the object. Inappropriate parameters make the minimization process difficult, sometimes impossible, to converge. Caselles *et al.* [12] proved that curve smoothing would be obtained even if $\beta=0$. Assuming $\beta=0$, Equation 2.12 reduces to:

$$E(\mathcal{C}) = \alpha \int_0^1 \left| \frac{\partial \mathcal{C}}{\partial s} \right|^2 - \gamma \int_0^1 f(\mathcal{C}(s)) \, ds.$$
(2.13)

The Equation 2.13 can be extended by generalizing the edge detector. Let g: $[0, +\infty[\rightarrow \mathbb{R}^+$ be a strictly decreasing function such that $g(r) \rightarrow 0$ as $r \rightarrow \infty$. Since function f is an edge map of the image $I : [0, a] \times [0, b] \to \mathbb{R}^+$, Equation 2.13 can be extended by replacing f with $g(|\nabla I|)^2$. Then we have a general energy functional:

$$E(\mathcal{C}) = \alpha \int_{\Omega} |\mathcal{C}_s|^2 \, ds + \gamma \int_{\Omega} g \left(|\nabla I(\mathcal{C})| \right)^2 \, ds \tag{2.14}$$

where ∇I is gradient of the image. Equation 2.14 is then further transformed into

$$E(\mathcal{C}) = \int_{\Omega} g\left(|\nabla I(\mathcal{C})| \right) |\mathcal{C}_s| \, ds \tag{2.15}$$

The goal now is to minimize E in Equation 2.13 for C in a certain allowed space of curves [12]. Noting that the Euclidean length of the contour C is: $L(C) = \int_{\Omega} |C_s| ds$ and the object contour is approximated by C when the energy E is minimized. Therefore, the problem of image segmentation is transformed into searching of the global minimal path weighted by $g(|\nabla I(C(s))|)$. In another word, it has been shown that object contours can be delineated through finding out the minimal paths instead of minimizing the energy E directly. It can be shown that in order to minimize Equation 2.15, the initial curve should follow the curve evolution in Equation 2.16.

$$\frac{\partial C(t)}{\partial t} = g(I)\kappa\vec{N} - (\nabla g.\vec{N})\vec{N}$$
(2.16)

where κ is the Euclidean curvature as before and \vec{N} is the unit inward normal vector. This equation can be represented using the level-sets approach as follows:

$$\frac{\partial \Psi}{\partial t} = |\nabla \Psi| div \left(g(I) \frac{\nabla \Psi}{|\nabla \Psi|} \right)$$

$$= g(I) |\nabla \Psi| \kappa + \nabla g(I) \cdot \nabla \Psi$$
(2.17)

where the right hand of the flow is the Euler-Lagrange of Equation 2.15 with C represented by a level-set of Ψ .

The geodesic formulation introduces a new term to the curve evolution models that further attracts the deforming curve to the boundaries, improving the detection of boundaries with large differences in their gradient. This term also partially frees the model from the need to estimate crucial parameters. Therefore, the geodesic formulation improves the previous deformable models [12].

2.4 Hybrid methods

In this approach, the strengths of several segmentation techniques are combined to achieve a better segmentation. Basically theses approaches integrates both edgeoriented and region-oriented methods to amplify their strength and reduce their weakness. Region-based active contours are one of the main classes in this category. These models use the statistical information of image intensity within each subset instead of searching geometrical boundaries. Most region-based active contour models consist of two parts: the regularity part, which determines the smooth shape of contours, and the energy minimization part, which searches for uniformity of a desired feature within a subset. A nice characteristic of region-based active contours is that the initial contours can be located anywhere in the image as region-based segmentation relies on the global energy minimization rather than local energy minimization. Therefore, less prior knowledge is required than edge-based active contours. A region-based active contour derivation, using the Mumford-Shah segmentation model [25], [26] is presented in this section. In this model, the evolving curve C is defines as the boundary of a region Ω . Ω is the area inside the curve C while complement of Ω (Ω^c) outside of the curve C. The method is the minimization of an energy-based segmentation. Assume that image is formed by two regions of approximately piecewise constant intensities of distinct values I^i and I^o and the object to be detected is represented by the region with value I^i and C_o denotes its boundary (Figure 2.5). Now we may define a term,

called fitting term, as in Equation 2.18.

$$E_1(C) = \int_{inside C} |I - M_1|^2 d\vec{x} + \int_{outside C} |I - M_2|^2 d\vec{x}$$
(2.18)



Figure 2.5: Illustration of mumford-shah algorithm, the fitting term is minimized when the curve is on the boundary of the object [28].

where C is any curve and M_1 , M_2 are the averages of I inside C and outside C (See Figure: 2.5) [18]. This was the basic idea underlying the Mumford-Shah segmentation method. In order to apply this method to the active contours, the above energy function has been extended (Equation 2.19).

$$E(M_1, M_2, \Psi) = \mu \int \delta(\Psi) |\nabla \Psi| d\vec{x}$$

+ $\nu \int H(\Psi) d\vec{x}$
+ $\lambda_1 \int |I - M_1|^2 H(\Psi) d\vec{x}$
+ $\lambda_2 \int |I - M_2|^2 (1 - H(\Psi)) d\vec{x}$ (2.19)

It can be seen that the energy function measures the difference between the piecewise-constant and the actual image intensity at every image pixel and moreover it adds some regularizing terms for the boundaries length and the area. The level set equation for a curve evolving according to the energy function in Equation 2.19, is given by:

$$\frac{\partial \Psi}{\partial t} = \delta_{\varepsilon} \left[\mu \nabla \left(\frac{\nabla \Psi}{|\nabla \Psi|} \right) - \nu - \lambda_1 (I - M_1)^2 + \lambda_2 (I - M_2)^2 \right]$$
(2.20)

One important property of this method, compared to other models, is its global nature. All level sets of Ψ have the potential to be important. This means that other isocontours corresponding to nonzero values of Ψ might evolve so they get past $\Psi = 0$ and create new segmented regions. Thus reinitialization to the distance function is not a good idea [18].

Chapter 3

Gradient Compensated Active Contours

MRA is a noninvasive medical imaging modality that produces 3D images of vessels and cavities. Accurate extraction of 3D vascular structures from MRA images has become increasingly important for diagnosis and quantification of vascular diseases. A group of specific methods have been proposed for this particular kind of medical images. In this chapter, we first provide some backgrounds in MRA images (Section: 3.1.1. Then, a brief review of current MRA segmentation techniques is presented in section 3.1.2 and finally, the *Gradient Compensated Active Contours* (GCAC) is proposed and discussed (Section: 3.2).

3.1 Background

While a huge number of different algorithms exist for performing the segmentation task, there is currently no single segmentation method that produces reasonable results for all types of medical images. Proper selection of the segmentation technique depends on the properties of the image being segmented. Different imaging techniques bring out different anatomical structures and may have different properties. For example, CT images which are better at depicting bone, would be useful for detecting fractures. However, a fracture can be very difficult or impossible to detect in an MR image. On the other hand, MR imaging generate images of high contrast between soft tissues in the body.

The following sections aim to give an understanding of MRA image's general properties and the certain characteristics of MR images that have to be taken into consideration when segmenting these images. Also, existing vessel segmentation algorithms are reviewed and discussed briefly.

3.1.1 MRA Images and Their Properties

Magnetic resonance angiography (MRA) is a noninvasive medical imaging technology that produces three-dimensional (3D) images of vessels. The images acquisition process can be done with or without injecting a contrast agent. Both methods can generate two- or three-dimensional data. There are currently four different methods that widely used in non-contrast technique to acquire the MRA images: (1) time-of-flight (TOF-MRA), (2) phase-contrast MR angiography (PC-MRA), (3) black-blood MRA, (4) T_2 -weighted MRA and (5) T_2^* -weighted MRA [31]. In this thesis we limit our discussion to TOF MRA, as this is the most widely used MRA technique which is able to provide robust images for a wide range of clinical issues.

TOF MRA Properties

In the TOF-MRA technique, multiple thin-section images are acquired contiguously, and the images are summed up to make a volume set (Figure 3.1). The only practical way to get a good view of inside the brain is to slice it, so three dimensional anatomical structures are displayed in two-dimensional cross-sections.
The 2D slices can be viewed individually, or they can be stacked to form a 3-D image. It uses the fact that, as blood circulates, even during the acquisition, its magnetization properties differ from the surrounding, non-moving tissues. During data acquisition, the static surrounding tissue produces low signal intensity in the images. While, the flowing spins provide stronger signals that are due to blood flow and thus they are distinguishable from the surrounding background. For optimal imaging conditions, the image plane has to be oriented perpendicular to the main flow. Maximum flow signal is achieved when a totally new column of blood enters the slice every repetition time (T_R) period. Figure 3.2 shows that the intensity of the signal from flowing vessels depends on several factors including the repetition time (T_R) , slice or slab thickness (THK), velocity vector (v) of blood flow (magnitude and directions) [31] and displacement (d). Based on Equation 3.1, it is evident that this technique is highly sensitive to blood flow velocity. Also be noted that the TOF technique provides blood flow images instead of true vessel lumen images.



Figure 3.1: Volumetric MRA data set

$$d = v * T_R \tag{3.1}$$

Equation 3.1 shows that the larger the velocity (v), the larger the displacement. However, In the case when d is greater than a certain value (the slab thickness THK



Figure 3.2: TOF technique: v_i is the velocity of blood flow, THK is the slice or slab thickness and T_R is the repetition time. [31].

), the blood signal intensity will stay constant as indicated by the horizontal curve in Figure 3.2. The major disadvantage of the TOF technique is that it is not robust under complicated flow conditions [31]. Furthermore, the intensities in the MR images are patient dependant. The intensity of the tissues may vary from person to person. However, MR images share some common characteristics and the general appearance of the histogram is similar for different patients.

Artifacts

A variety of artifacts may appear in MR images. Since the artifacts change the appearance of the image they may also affect the performance of a segmentation algorithm. The most important artifacts in image segmentation are intensity inhomogeneities and the partial volume effect.



Figure 3.3: Displacement (Intensity) vs. Flow and T_R [32]

Intensity Inhomogeneities: Intensity inhomogeneities are not always visible to the human eye, but can nonetheless have a negative influence on automatic segmentation. This may manifest itself by for example making intensities as higher or lower in one part of the image than in other parts. It is often caused by the radio frequency (RF) coils. Different methods exist to compensate for the inhomogeneities. The inhomogeneity is often modeled as a field that varies smoothly over the image. The inhomogeneity field is often thought to be a multiplicative field, which means that the true voxel intensity is multiplied by the value of the field in that voxel. There are methods which remove the inhomogeneities during the segmentation process. For example, some approaches, alternate estimation of the inhomogeneity field with classification to obtain inhomogeneity corrections ([74], [75] and [76]).

The Partial Volume Effect: The partial volume effect occurs when a voxel cannot be accurately assigned to one tissue type. This is because the intensity in the voxel originates from more than one tissue. It occurs because one voxel contains many body cells and the signal emitted from these cells make up the detected intensity in this voxel. The partial volume effect is most apparent at edges between

different tissues. It may deteriorate the sharpness of the edges between tissues. The partial volume effect can be a significant problem in brain segmentation since the brain has a complex folded surface. Another concern is the classification of such voxels, i.e., to which of the tissues should it be assigned. One way of dealing with partial volume effects is by using so called soft segmentation. Soft segmentation, as opposed to hard segmentation, means that a voxel may belong to more than one tissue class. Some methods perform soft segmentation by finding the probabilities that a voxel belongs to different tissues ([66]). The partial volume effect is caused by the fact that we have a limited resolution in the images. Smaller voxel sizes reduce the partial volume effect since the probability that more than one tissue type is contained in the same voxel is reduced.

Motion artifacts: Motion can be periodic, as caused by blood flow, heart beat, or respiration, or random, as a consequence of patient movements. The motion of the entire object during the imaging sequence generally results in a blurring of the entire image with ghost images in the phase encoding direction. The nature of the artifact depends on the timing of the motion with respect to the acquisition.

3.1.2 Review:Vasculature Segmentation

Reasonably accurate extraction of 3D vascular structures from MRA images is highly important for detecting and aiding the treatment of heart disorders, stroke, and blood vessel diseases [7]. A variety of methods have been developed for segmenting vessels within MRA data. However, we can broadly divide them into two categories: *Skeleton-based* and *Nonskeleton-based*. Skeleton-based techniques are those indirect methods which segment and reconstruct the vessels by first calculating the centerlines and the cross sections of the vessels from the 2-D slices([30], [3]). Contrary to these methods, nonskeleton-based techniques are those that segment the vessels in 3D directly. Several methods have been developed based on these principles. In the following sections we discuss them briefly.

Skeleton-based Techniques

Several methods have been developed based on this principle and multiscale schemes to allow for the diversity of vessel sizes. In these approaches, the centerline models can be generated explicitly, implicitly or via post processing by vessel modeling [30, 34–38]. They just apply thresholding, and then followed by object connectivity algorithms in many different ways. Next, follow it by a thinning procedure, and a extraction based on graph description. The resulting centerline structure is used for 3D reconstruction of the vasculature [31]. Diversity of vessel sizes can be handled by incorporating multiscale schemes into these Skeleton-based algorithms. Skeleton or indirect-based techniques can broadly be classified into three classes based on the way they estimate the cross section of the vessels: 1) skeleton with vessel cross section estimation using edge-based techniques, 2) skeleton with vessel cross-section estimation using parametric-based models and 3) skeleton with vessel cross section estimation using geometric-based models [3]. Indirect methods have shown to be fast compared to the direct ones. However, direct techniques are more robust and accurate [31], and thus they are preferred for MRA vessel segmentation when a precise extraction of the vessels is needed.

Nonskeleton-based Techniques

In contrary to above techniques, the vessel reconstruction is done directly and without estimating the vessel cross sections in Non-skeleton based methods. Many different methods have been proposed within this framework like thresholding methods [39], fitting techniques [30, 40], mathematical morphology based methods [41], fuzzy connectedness methods [42], deformable models based methods [43–45, 56], wave propagation based methods [49, 50], and so on. A commonly used technique to evaluate MRA data sets, currently in hospitals, is maximum intensity projection (MIP) [39] (Figure 3.4), which falls in the thresholding category. The MIP is generated by selecting the maximum value along an optical ray that corresponds to each pixel of the 2D MIP image. It is useful because the overall shapes and paths of the vessels become visible. However, it is known that the MIP may lead to underestimation of vessel width and decrease in signal-to-noise ratio (SNR) resulting in poor visualization of blood vessels [57]. Deformable models ¹ based methods are another important category of these techniques .Since their introduction by Kass et al. [10] as active contour model or "snake", numerous models have been proposed and used successfully for medical image segmentation. For instance, Klein et al. [56] proposed to reconstruct 2D vessel boundaries or 3D vessel walls using deformable surface models represented by B-spline surfaces. However, it is not possible to employ parameterized deformable models to effectively deal with whole vessel trees, as the models would be required to change topology during evolution [58]. To address the topology adoption issue, several special strategies have been proposed and incorporated into deformable models [5,6]. For example, Yim et al. [44] proposed a deformable surface model based on triangulated meshes for vessel construction in 3D. Nevertheless, it may be problematic to apply these methods [44,56] for segmentation of vessels from low contrast MRA images.

Another class of deformable models are geometric and geodesic deformable models, which are based on level sets theory and can freely adapt into complex topologies of objects, were then proposed and applied on MRA images ([21], [12]). Geometric deformable models are capable of accommodating the often significant variability of biological structures over time and across different individuals [5]. Therefore, they have become a promising and vigorously researched model-based

 $^{^{1}}$ We will interchangeably use the phrase deformable models and active contour/ surfaces.

approach to computer-assisted medical image analysis. In the following section we will discuss the geodesic deformable models in more detail.

3.1.3 Geodesic Active Contours & the Speed Functions

Geodesic deformable models or geodesic active contours, permit broad shape coverage by employing geometric representations that involve many degrees of freedom. The name "deformable models" stems primarily from the use of elasticity theory at the physical level, generally within a Lagrangian dynamics setting [5]. They can freely adapt into complex topologies of objects. Therefore, they have been proposed and applied widely on MRA images segmentation.

Geodesic deformable models are governed by some curvature dependent speed functions. These speeds govern the evolution of the deforming model and they consists of two terms: a constant (hyperbolic) and a curvature (parabolic) term. In the context of image segmentation the speed function also called "stopping function " as it needs to stop the evolving curve, near the vicinity of the desired object. The accuracy of the segmentation process depends upon when and where this force stops the propagating curve, and how strong this stopping force is [51]. Different types of stopping forces have been proposed for geodesic active contours, such as those based on image gradients [18], edge strength [54], and area minimization [59]. In all of the above stopping forces, the key feature, that attracts the curve to the desired objects, is the intensity gradient of the objective image. Based on the stopping force, we can discuss and review the different geodesic active contours that have been proposed and used for the purpose of segmentation.

In the original model proposed by Caselles and Malladi ([21], [12]), the gov-

erning force is based on the image gradient and the evolution equation is:

$$\frac{\partial \Psi}{\partial t} = \underbrace{g\left(|\nabla I|\right)\left(\kappa + V_0\right)}_{F} |\nabla \Psi| \tag{3.2}$$

where the first term of the speed function, $g(|\nabla I|)$ called *gradient map* of the image, is a monotonically decreasing function of the image gradient, e.g.

$$g(|\nabla I|) = \frac{1}{1 + |\nabla (G_{\sigma}(x) * I(x))|}$$
(3.3)

or

$$g\left(|\nabla I|\right) = e^{|\xi\nabla(G_{\sigma}(x)*I(x))|} \tag{3.4}$$

The local minima of this function are at the image edges. It is the external image dependent force and the main goal of it, is to stop the evolving curve when it arrives to the objects boundaries. κ is the *curvature* of the evolving contour and is expressed as:

$$\kappa = \nabla . \vec{N} = \nabla . \left(\frac{\nabla \Psi}{|\nabla \Psi|}\right) \tag{3.5}$$

The second term of the stopping force, $(\kappa + V_0)$, acts as the internal force in the classical energy based snakes model and it its rule is to smooth out the areas of high curvature, which are assumed to be due to noise. [64]. V_0 is a constant motion term leads to the formation of shocks from which a representation of shape can be derived and it helps the curve to move in the desired direction.

The above approach is topology independent and it is able to detect any number of objects in the image. However, the stopping term is not robust enough and hence it may not stop the "bleeding" or "leaking" of the boundaries. Furthermore, the pulling back feature is also not strong enough. In addition, the pulling back feature is also not strong enough and so the curve can not come back to the goal position once it crosses the boundaries [51]. Kichenassamy *et al.* [53] and Yezzi *et al.* [54] tried to solve the above problems by introducing a new extra stopping term, called the *pull back term*, based on image-dependent Riemannian metrics, as follows:

$$\frac{\partial \Psi}{\partial t} = g\left(|\nabla I|\right)\left(\kappa + V_0\right)|\nabla \Psi| + \left(\nabla\left(g\left(|\nabla I|\right)\right).\nabla\Psi\right)$$
(3.6)

The second term, $(\nabla (g(|\nabla I|)) . \nabla \Psi)$, also called *length minimizing term*, helps the evolving surface, return to its position once it crosses the object boundary and it denotes the projection of an attractive force vector on the normal of the surface. precisely, this technique employs ideas from Euclidean curve shortening evolution which defines the gradient direction in which the Euclidean perimeter is shrinking as fast as possible [54]. Therefore, the new stopping function is obtained by multiplying the Euclidean arc length by the gradient map [18].

The proposed active contour is attracted very quickly and efficiently to the desired feature. In addition, these techniques give reasonable results for rather noisy images [55]. However, they may have difficulty in extracting tiny vessels from 3D images as they suffer from boundary leaking for complex structures [51]. Moreover, the flow can be unacceptably slow to converge in practice [60].

Siddiqi *et al.* ([59], [60], [51]) proposed another extra term, *area minimization term*, that was derived from minimizing a certain weighted area energy functional. More precisely, in analogy to the case of Euclidean arc-length, they have modify the infinitesimal Euclidean area by a conformal factor and compute the gradient flow for the modified area functional [60].

$$\frac{\partial\Psi}{\partial t} = g(x)(\kappa + V_0)|\nabla\Psi| + (\nabla g\nabla\Psi) + \frac{V_0}{2}x\nabla g|\nabla\Psi|$$
(3.7)

where $\frac{V_0}{2}x\nabla g|\nabla \phi|$, area minimizing term, is mathematically equal to the product of the divergence of the gradient map and the gradient of the surface [51]. When applied to shape segmentation, the new flow exhibits a stronger attraction force to features of interest than the constant inflation term previously used, due to the inclusion of a new doublet term. However, this method may not be a robust solution to the segmentation of complex shapes such as in brain segmentation [51].

One of the difficulties in segmentation of MRA images is accurate extraction of small vessels. As, they exhibit much variability in shape and size compare to the thick parts and they often have a low intensity contrast with the surrounding issues. To deal with this problem, Pingkun et al. [7] proposed a new capillary action based active contour, *Capillary Geodesic Active Contours (CGAC)*, which is modeled based on the physical phenomenon of capillary action. The final level sets update equation is represented as:

$$\frac{\partial \Psi}{\partial t} = g(\kappa + V_0) |\nabla \Psi| + \nabla g \cdot \nabla \Psi + (\hat{\kappa}_2 + \lambda) |\nabla \Psi| f(1 - \cos^2 \theta).$$
(3.8)

where parameter λ balances contribution of propagation, advection force and the capillary action. $\cos \theta$ is defined as:

$$\cos\theta = \vec{\mathcal{N}} \cdot \frac{\nabla g}{|\nabla g|}$$

The constant terms V_0 in Equation 3.8 act like balloon force which facilitate evolving surfaces snapping to solid boundaries. Comparing the new speed function with those of the geodesic active contour (Equation 3.6) the third term is new which comes from the capillary action and it is expected to facilitate the evolving surface adapting into thin parts of objects, *e.g.* thin vessels. The incorporated capillary force adapts the evolution surface into thin branches of blood vessels and obtains more accurate segmentation results ([7]). Nevertheless, the capillary active contour does not make use of any priori knowledge of the MRA image properties for the propagation and the speed term is not specialized for MRA images. Thus, it is not surprising that it may exhibit some difficulty in extracting very tiny vessels from 3D MRA images of brain vasculature.

Small vessels and their branches, which exhibit much variability, are very important in planning and performing neurosurgical procedures. More precise navigation and localization information for computer guided procedures can be achieved with greater details. Our work aims to develop an image segmentation algorithm for automatically extracting the whole vasculature from 3D angiography by modifying the speed term of the level set methods. Inspired by the intrinsic properties of MRA and considering the relation between vessels thickness and their intensity in MRA images, a novel variation of level set algorithm has been proposed and tested on both synthetic and real MRA images. Tests shows that our proposed level set algorithm has great potential for segmenting very thin vessels under low contrast conditions.

3.2 Gradient Compensated Active Contours

3.2.1 Thickness vs. Intensity Gradient in MRA Images

Gradient value at each point of an image (I) is obtained as follows:

$$|\nabla I| = \sqrt{\left(\frac{\partial I}{\partial x}\right)^2 + \left(\frac{\partial I}{\partial y}\right)^2 + \left(\frac{\partial I}{\partial z}\right)^2} \tag{3.9}$$

where I is the image intensity. Gradient at each point is the sum of the directional intensity changes. The gradient is likely to be large at the boundaries due to the dramatic changes in voxel intensity values at these points. The higher these changes, the higher will be the value of the gradient.

CHAPTER 3. GRADIENT COMPENSATED ACTIVE CONTOURS

In MRA images, vessels appear brighter than the background. However, the range of the intensity values of blood vessels in MRA images are not restricted to a small interval but are spread out widely. Figure 3.4 (a) shows the MIP of a MRA data set. It can be observed that thick vessels appear much brighter than the thinner ones. Thus, thick vessels are easily distinguishable while thin vessels appear to not differ much from the surrounding tissues. Therefore, the prominent boundaries of the thicker vessels lead to higher gradient values compared to small vessels. This can be seen in the Figure 3.4 (b), which is the gradient of an MIP image.



(a)



Figure 3.4: (a) MIP of a MRA data set and (b) its Gradient magnitude.

As discussed in Section 3.1.1, within the blood vessels, the intensity depends very much on the blood flow (see Figure 3.3). The velocity of blood flow in thick vessels is higher than in thin vessels. Therefore, the thicker the vessel, the more will be the flow and hence the higher the intensity and gradient values. Also, thin vessels are affected by the partial volume effect, which further reduces their intensity. [4].

The boundary gradient *vs.* the thickness of vessels is plotted for a sample data set in Figure 3.5. Clearly, there is an almost exponential relationship between

vessel thickness and the gradient on their boundaries which is approximated in Equation 3.10.



Figure 3.5: The boundary gradient vs. the thickness of the vessels for a sample data set

$$|\nabla I(x)| \cong MaxGrad * (1 - e^{(-\lambda * Th(x))})$$
(3.10)

where x is any point on the vessel boundaries, $\nabla I(x)$ is the gradient at x, MaxGrad is the maximum of the image gradient values which is usually 255 for MRA images, Th(x) is the thickness of the vessel at point x and λ is a small constant depending on the image properties.

It can be seen from Figure 3.6 that the intensity gradient initially increases sharply with the thickness and levels off beyond a certain thickness. The reason is that in MRA images, for a fixed repetition time (T_R) , if the velocity exceeds a certain value, the intensity due to blood flow will remain constant [31].



Figure 3.6: Vessel gradient vs. vessel thickness

3.2.2 Stopping Forces in Active contours

A crucial factor in the success of level set methods, is the speed function that evolves the surface to the desired boundaries. The accuracy of the segmentation highly depends on when and where the propagating contour needs to stop [51]. The stopping forces can be divided into two classes: static and dynamic [61]. Static forces are those that are pre-computed and do not change as the contour progresses. On the other hand, Dynamic forces are those that change as the contour deforms. Considering the special case of a contour expanding with a speed V > 0. Let T be the time at which the contour crosses a given point. The function T then satisfies $|\nabla T| V = 1$. This equation simply says that the gradient of the arrival time is inversely proportional to the speed of the evolving contour. If the propagating surface needs to stop close to the vicinity of the segmenting topological shape, then the speed of the surface should approximate closely to zero near the final segmenting shape. All the geodesic active contours referred to in section 3.1.3, use the gradient map of the image as an external image-dependent speed term which its main goal is to stop the evolving curve when it arrives at the object boundaries. The gradient map of the image is obtained through the use of a monotonically decreasing function of image gradients (Equations 3.3 and 3.4). Therefore, this external speed decreases with the increase of the gradient values and has its minima when the contour is located in the image regions with high gradient values, i.e., edges. It should be noted that the speed at the boundaries needs to be zero (to make the contour reside there). This means the higher the gradient value, the faster the propagation of the surface is, which results in a robust and accurate segmentation [51]. In the context of MRA segmentation, the accuracy of the segmentation process highly depends on how high the gradient values are at the vessel boundaries. However, as discussed in section 3.2.1, image gradients are not high enough at the thin vessel boundaries and therefore the segmentation process may fail at these vasculature. Considering the variation of blood vessel thickness versus the gradient of the boundaries in MRA images, we have modified stopping forces of the capillary geodesic active contours in order to perform better in the vicinity of the small vessels.

3.2.3 Gradient Compensator Function

As discussed in Section 3.1.3, the gradient map $(g(|\nabla I|))$ of the image is the only image-dependant component of the stopping forces and its role is to stop the contour's evolution near the boundaries of the desired objects. The gradient map is a static function of the image gradient (Equation 3.3, 3.4) i.e., that its values do not change in time, as the contour deforms. However, it can be seen from Figure 3.4(b), that the gradient values are much lower for the thin vessels compared to the thick ones, thus making it difficult to place the contours on the boundaries of thin vessels. To address this problem, we propose a dynamic gradient map that is not only a function of the image gradient but also a function of time and contour location. As the evolving contour gets smaller, it is very likely that it is approaching the smaller vessels whose gradient values may not be high enough to attract the contour. Therefore, it is desirable to make the evolving contour more sensitive to the image gradients as it shrinks. To achieve this, a novel gradient map function is defined such that it produces reasonable values even if the image gradient is not high enough, provided that the contour thickness is also small. To reach this goal, an equalizer function is defined (Equation 3.11), which is a function of the contour's thickness and its role is to strengthen the image gradient values when the contour's thickness is small (i.e., when the contour is most probably in the vicinity of the small vessels). This equalizer function is called *gradient compensator function*, M(x, t), and is defined as follows:



$$M(x,t) = \alpha * (e^{(-\lambda *Th(x,t))})$$

$$(3.11)$$

Figure 3.7: M(Th(x)) vs. estimation of thickness at point x

where x is any point on the contour, Th(x) is the estimated thickness of the surface at that point, λ is the same parameter as in Equation 3.10 and α is a constant, to be set by the user. From Figure 3.7 it can be seen that the value of this function varies between 0 to α for very thick and extremely thin contours, respectively. The same λ as Equation 3.10 has been chosen so that the rate of the change of M(x,t) vs. Th(x) is the same as $\nabla I(x)$ vs. the Th(x) in Equation 3.10. This ensures that M(x,t) increases as the gradient values decrease at the small vessel boundaries. Function M(x, t) is incorporated into the gradient map equation by replacing the term $\nabla I(x)$ in Equation 3.4, with $(1 + M(x, t))\nabla I(x)$, as follows:

$$g(x,t) = e^{|\xi * \nabla (G_{\sigma}(x) * (1+M(x,t)) \nabla I(x))|}$$

= $e^{|\xi * \nabla (G_{\sigma}(x) * (1+\alpha * e^{(-\lambda * Th(x,t))}) \nabla I(x))|}$ (3.12)

Gradient compensator function compensates for the insufficient amount of ∇I on the thin vessels' boundaries. M(x,t) is nearly zero for thick vessels, hence, $(1+M(x,t))*\nabla I \simeq \nabla I$. However, for small vessels, M(x,t) > 0 and is proportional to the gradient difference of that vessel and a thick one. Thus, $(1+M(x,t))*\nabla I >$ ∇I . α , in Equation 3.11, is a constant which is specific to our approach which functions as a trade-off between this compensator term and other forces in the evolution process. Its value can be chosen in the range of 0 and $\frac{Max(|\nabla I|)}{Min(|\nabla I|)} - 1$, where the upper limit is chosen in a way as to strike a balance between the gradients of thin and thick vessels. Choosing a large α , the effect of makeup function will be more prominent and more thin vessels will be extracted (Figure 4.1). However, the approach may become more sensitive to noise. Thus, as in any other segmentation approach, there is a need to keep a balance between these two issues.

In our approach, we need to estimate the thickness of the evolving contour. For this purpose the normal vector at each point x is first obtained as follows:

$$\overrightarrow{N} = \frac{\nabla\phi}{|\nabla\phi|} \tag{3.13}$$

Since blood vessels in MRA images appear brighter than the background, the directions of normals in the image could be known. Assuming that the contour is almost tubular at each point, the thickness of point x, Th(x), could be estimated as the number of voxels along the normal direction within the contour, as shown



Figure 3.8: Estimation of the local contour thickness

in Figure 3.8. This computation is not costly, since the normal of the surface has been calculated in other parts of the level set algorithm.

The evolution equations for the Gradient Compensated geodesic Active Contour (GCAC) is obtained by replacing the g(x) with g(x,t) (Equation 3.12) in CGAC speed terms (Equation 3.8) as follows:

$$\frac{\partial\Psi}{\partial t} = g(\kappa + V_0, t) |\nabla\Psi| + \nabla g(t) \cdot \nabla\Psi + (\hat{\kappa}_2 + \lambda) |\nabla\Psi| f(1 - \cos^2\theta).$$
(3.14)

3.2.4 Implementation

The GCAC described in previous section has been coded for 3D segmentation, based on the *insight segmentation and registration toolKit* (ITK) [64], an open source software developed as an initiative of the United States National Library of Medicine and freely available at www.itk.org. A large number of leading edge segmentation and registration algorithms have been implemented inside this toolkit



Figure 3.9: An overview of the Gradient Compensated Active Contour Algorithm

[64].

The results of the algorithm have been visualized using the visualization toolKit (VTK) [62], which is also an open source software for 3D computer graphics, image processing, and visualization. VTK supports a wide variety of visualization algorithms including scalar, vector, tensor, texture, and volumetric methods, as well as advanced modeling techniques such as implicit modeling, polygon reduction, mesh smoothing, cutting, contouring, and Delaunay triangulation. In addition, dozens of imaging algorithms have been directly integrated to allow the user to mix 2D imaging/3D graphics algorithms and data. It is freely available at www.vtk.org.

Figure 3.9 shows the major components involved in the application of the Gradient Compensated Geodesic Active Contours for a segmentation task. An initial segmentation estimate is generated by simply thresholding the 3D MRA image with thin tubular structures. Before applying the algorithm, the image is smoothened by using a small isotropic Gaussian filter, since the level sets algorithm inherently requires some smoothness of gradients. The result is used to generate an initial signed distance function Ψ_0 , which has negative values inside objects and positive values on the outside. As thick vessels appear quite bright in MRA images, we are able to extract the thick parts of the vasculature in the early stage of the algorithm. A 3-D array keeps track of the evolving contour thickness right from the initial contour and is used in the gradient compensator function. The level sets function Ψ is then iteratively updated according to:

$$\Psi^{n+1} = \Psi^n + \nabla \Psi^n \nabla t, \qquad (3.15)$$

where $\nabla \Psi$ is calculated using Equations 3.14. The 3-D thickness array will be updated for the points that have been moved in any iteration. Convergence is achieved when volumetric change is very small over some iterations. Before applying the algorithm, the image is smoothed by using a small isotropic Gaussian since the level sets algorithm inherently requires some smoothness of gradients [19]. The Narrow band level set method [27] has been used for the implementation, in order to restrict most computations to a thin band of active voxels immediately surrounding the interface. Furthermore, the level sets map Ψ is periodically reinitialized to be a signed distance function. It means that, the zero level set C is extracted from Ψ , and then the value at each point is set to be its distance to C. This is needed because Ψ is defined as the signed distance map of C, which, however, cannot be ensured during the evolving process.

Chapter 4

Results and Discussion

he proposed algorithm has been applied on both synthetic data and MRA data sets. First, the effectiveness of the GCAC is studied using a vessel-like computer generated synthetic data. Secondly, the vasculature tree from three different sets of real MRA data is extracted, using the algorithm described in Section 3.2.4 and the results are compared with both that ones of the *Capillary Geodesic Active Contours (CGAC)* algorithm and the reference manual segmentations performed by medical radiologists.

4.1 Results based on synthetic data

Figure 4.1 shows the application of the our proposed approach on a computer generated vessel to illustrate the effects of the gradient compensator function. As seen from Figures 4.1(a, b), which is a generated vessel, the intensity of the voxels in the model decreases as the thickness of the vessel decreases. Starting from the initialization, evolution is done according to the proposed level set equation in 3.14. In our experiment, all the parameters are fixed except that α (in the compensator function) varies between 0 and $\frac{Max(|\nabla I|)}{Min(|\nabla I|)} - 1$. The evolution results with different parameter settings after a number of iterations are visualized in Figures 4.1 (c,d,e). When α is set to zero, our algorithm in fact evolves exactly like the CGAC and is not able to extract the thin and darker portions of the vessel. Other extracted results with different values of (α) in Figure 4.1 shows that the compensator function can facilitate the evolution of the free surface in very thin portions of vessels.



Figure 4.1: Illustration of the effects on varying α in Equation (3.11)on (a) a synthetic 3D vessel whose cross section along the axis is shown in (b). (c) Segmented vessel, $\alpha = 0$. (d) Segmented vessel, $\alpha = 1.2$. (e) Segmented vessel, $\alpha=3.2$.



Figure 4.2: Maximum intensity projections of the two segmented MRA data sets.

4.2 Segmentation Results of 3D MRA Images

The algorithm was applied to different sets of real 3D time of flight MRA (TOF-MRA) images. These images and their manual segmentations by clinicians were provided by the Department of Diagnostic Radiology at the National University Hospital. Each of the these data sets contains approximately 120 slices, with the size of 512×512 , spacing of $0.43 \times 0.43 \times 1.2$ and 16 bits level of gray tone resolution. Some samples of 2D slices of these MRA data sets are shown in Figure 4.3 were bright regions and points are the desired blood vessels to be segmented. The raw images were originally in *Digital Imaging and Communications in Medicine* (DICOM) [24] format, which is the most common standard for storing and transmitting the medical images in hospitals. A single DICOM file contains both a header (which stores the patient's information, the type of scan, image dimensions, etc.), as well as all of the image data (in three dimensions). However, to keep

the personal information of the patients safe, we convert the data sets from DI-COM format to ANALYZE ,which stores the image data in one file (*.img) and the header data in another file (*.hdr). The conversion have been done using MATLAB Image Processing Toolbox. An Intel, Pentium IV with 1.9 GHz CPU speed and 768 MB of RAM, running on Windows XP platform, computer was used in our experiments.

In order to illustrate the effectiveness of the proposed method, we have done some comparisons between our proposed method and other method. The details and the results of these comparisons are presented in the following sections.

4.2.1 Comparison with Manually segmented results

Two sets of real MRA data are segmented, using our proposed algorithm and the extracted vessels are compared with manual segmentation results obtained by clinicians. The MIP (Maximum Intensity Projection) of these two data sets are shown in Figure 4.2. These noisy images are further smoothed, using a small isotropic Gaussian filter. The initial segmentation is obtained by thresholding the raw data set and the evolution is carried out according to Equation 3.14.

Figures 4.4- 4.7 show clinically (manual) segmented and the corresponding GCAC segmentation results in two different points of view.

The proposed algorithm is able to extract much of the vascular tree that appears in the clinically segmented images. In addition, it can be seen that a fair amount of thin vessels have been successfully segmented using our proposed algorithm.



Figure 4.3: Samples of cerebral MRA data set. Bright regions and points are blood vessels.



(a) The proposed algorithm results



(b) Manually segmented results

Figure 4.4: First data set: view 1



(a) The proposed algorithm results



(b) Manually segmented results

Figure 4.5: First data set: view 2



(a) The proposed algorithm results



(b) Manually segmented results

Figure 4.6: Second data set: view 1



(a) The proposed algorithm results



(b) Manually segmented results

Figure 4.7: Second data set: view 2

4.2.2 Comparison with CGAC

In this section, three MRA data sets have been segmented using our proposed method. Figure 4.8 shows the MIP (Maximum intensity projection) of one of these MRA data sets where vessels within the region of interest (Figure 4.9) are enhanced for better visualization.



Figure 4.8: MIP of the segmented MRA



Figure 4.9: Region of interest

We have compared the segmentation results of our proposed method with the

state-of-the-art "Capillary Geodesics Active Contours" algorithm [7]. Identical parameter settings in the evolution equations are used for both methods except for the gradient compensator term, α , which is specific to the our proposed method and determines the contribution of this proposed force. The segmentation results of CGAC and our method are visualized in Figures 4.2.2, 4.2.2 and 4.2.2 from different points of view. From these results, it can be seen that both segmentation algorithms can successfully extract much of the vasculature. However, CGAC does not make use of any priori knowledge of the MRA image properties for the propagation. Small gradient values of the thin vessels make it difficult for CGAC to distinguish them from the background. On the other hand, our proposed gradient compensator function, could strengthens the active contours algorithms and assists them to identify more thin parts of blood vessels without imposing much additional complexity to the geodesic active contours model.



Figure 4.10: MRA data set 1



Figure 4.11: MRA data set 2



Figure 4.12: MRA data set 3
4.3 Summary

In this chapter, we applied the gradient compensated active contour to both 3D synthetic and cerebral MRA images. The incorporated gradient compensator term seems to adapt the evolution surface into very thin branches of blood vessels and obtains more accurate segmentation as demonstrated in our experiments. We have also tested the accuracy of the proposed method by comparing our results with the manually segmented ones.

Chapter 5

Conclusions and Future Work

A novel gradient compensated active contour has been proposed and developed to extract vasculature from MRA images. Considering that, different imaging techniques bring out different anatomical structures and they have their own image properties, we may conclude that specialized methods for a particular applications can often achieve better performance compare to general ones by taking some prior knowledge into account. The prior knowledge acts like regularizers inside the segmentation algorithms. The underlying idea of our approach is also to incorporate the priori knowledge of the MRA images, into the active contours in order to improve their performance.

The performance of this algorithm has been validated by experimental results on both synthetic images and medical MRA images and better results have been obtained compared with other state-of-the-art MRA segmentation algorithm.

5.1 Future Work

This dissertation opens up some interesting directions for further investigation. We describe some of them in the following sections.

5.1.1 Further study of GCAC

The most immediate area of future work would be to ascertain the advantages of the proposed method using more MRA data sets and also to study its limitations. Furthermore, there would be considerable interest in developing an automatic parameter setting program through some learning algorithm.

5.1.2 Clinical application

Extracting organs from medical images is an important problem in many medical applications ranging from collecting clinical diagnosing information to surgery planning and navigating. Although the application of geometric techniques such as active contours have gone well in this field, still there is a far away from achieving stable three-dimensional volumes and a standard segmentation in real-time. Currently, it appears that clinicians prefer the manual approaches to the automatic ones and the adoption of a new automatic system is difficult unless it can perform for all intents and purposes exactly like a manual segmenter. This is not an easy task, and more tweaking of the system would be necessary to achieve this.

Using our algorithm for MRA image segmentation, nearly the whole vasculature can be successfully extracted from 3D MRA images. However, the segmentation process is only the first step to provide diagnostic information to achieve *computer aided diagnosis* (CAD). An important information to be obtained from cerebral MRA is the possibility of stroke or aneurysm. These possibilities are measured through checking the degree of stenosis or dilation along blood vessels. Since the whole vasculature has been extracted out, this could not be a difficult problem. The degree of stenosis or dilation can be measured by computing the diameter of the blood vessels at each point. Nevertheless, efforts need to be make on working out a robust and precise numerical measurement.

5.1.3 Medical Image Segmentation with Priori Knowledge

In this thesis, we present an active contour method that takes the properties of MRA images into consideration. This idea can be extended to other imaging modalities, such as CT images, as well. In addition, brain vascular networks have many other important properties (e.g. concerning density, size, orientation, and adjacency with other structures) which enable the creation of vascular models of brain vasculature that can be incorporated into active contours to further improve the precision and robustness of the segmentation. There is similar work on this [11], but how to efficiently employ such information and incorporated into active contours, still needs to be studied. Development of methods that can incorporate the local object size in defining the connectedness, object material inhomogeneity, noise, blurring, and background variations may also be appealing.

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