SEGMENTATION METHODS FOR MEDICAL IMAGE ANALYSIS
Blood vessels, multi-scale filtering and level set methods

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Segmentation Methods for Medical Image Analysis
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Abstract

Image segmentation is the problem of partitioning an image into meaningful parts, often consisting of an object and background. As an important part of many imaging applications, e.g. face recognition, tracking of moving cars and people etc, it is of general interest to design robust and fast segmentation algorithms. However, it is well accepted that there is no general method for solving all segmentation problems. Instead, the algorithms have to be highly adapted to the application in order to achieve good performance. In this thesis, we will study segmentation methods for blood vessels in medical images. The need for accurate segmentation tools in medical applications is driven by the increased capacity of the imaging devices. Common modalities such as CT and MRI generate images which simply cannot be examined manually, due to high resolutions and a large number of image slices. Furthermore, it is very difficult to visualize complex structures in three-dimensional image volumes without cutting away large portions of, perhaps important, data. Tools, such as segmentation, can aid the medical staff in browsing through such large images by highlighting objects of particular importance. In addition, segmentation in particular can output models of organs, tumors, and other structures for further analysis, quantification or simulation.

We have divided the segmentation of blood vessels into two parts. First, we model the vessels as a collection of lines and edges (linear structures) and use filtering techniques to detect such structures in an image. Second, the output from this filtering is used as input for segmentation tools. Our contributions mainly lie in the design of a multi-scale filtering and integration scheme for detecting vessels of varying widths and the modification of optimization schemes for finding better segmentations than traditional methods do. We validate our ideas on synthetical images mimicking typical blood vessel structures, and show proof-of-concept results on real medical images.
ACKNOWLEDGMENTS

The writing of this thesis coincided with a lot of major events in my life: buying the first home, doing major renovations and last but not the least, expecting our second child. Actually, our son showed his sense of humor by arriving on the day before my thesis deadline. Thank you, little Vide. Also, thank you Sara and Mira for constantly reminding me what is important in life and for keeping the balance.

My PhD studies were initiated right after the completion of my MSc. Weighing between industry and academia, I was pulled by my first supervisor Ken Museth to pursue the PhD. I thank him and Hamish Carr for a lot of inspiration and for introducing me to the never-ending problem of image segmentation.

For the last period, I’ve been working closely with my current supervisor and co-supervisor Reiner Lenz and Magnus Borga. Thank you for the numerous discussions and great ideas which have given many new insights.

Thank you also friends and colleagues in the Digital Media and Medical Informatics groups for creating a friendly environment and appreciated coffee breaks during hectic periods. A special thanks to Ola Nilsson for lending me the nice \LaTeX-style for the thesis. Finally, thanks to the members in the “Graphics Group” for sharing all the great software for level set methods and various algorithms.

Gunnar Läthén
Norrköping, Sweden
April 2010
LIST OF PUBLICATIONS

The following papers are included in this thesis:


CONTRIBUTIONS

Paper I

This paper presents a localization of the “active contours without edges” model [Chan and Vese, 2001] to better fit applications where you want to extract particular objects in e.g. medical images. Furthermore, the paper presents a user guided approach to initialize the segmentation near objects of interest, based on topological analysis of the data. My main contribution to this paper was identifying the problem with global behavior of the Chan-Vese model and suggesting a method to localize the computations. Furthermore, I implemented the prototype application for performing the experiments.

Paper II

Here, we present an approach to detect blood vessels using multi-scale filtering and use the filter response for level set segmentation. I was part in brainstorming the basic idea of the multi-scale filtering, taking active part in the implementation of the filtering and implemented the level set methods toolbox. As the main author, I did most of the writing of the paper. This paper received a best scientific paper award at the ICPR conference 2008.

Paper III

This paper presents an alternative optimization method for level set segmentation, which shows faster convergence and the tendency to overstep local optima solutions. The basic idea was presented by my co-supervisor and I adjusted and formalized it to fit the level set framework. The formalization was based upon an energy formulation of the level set propagation used in Paper II. The implementation was built on my level set toolbox and I did the writing of the paper.

Paper IV

This is a variation of Paper III which uses a different optimization method. The implementation is based on the same level set toolbox, but I took on a secondary role in implementing the optimization and the writing of the paper.

Paper V

This is an extension to Paper II which evaluates some parameters of the model and provides a more general presentation of the segmentation part of the method. I implemented most parts of the experiments and produced the article.
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CHAPTER 1
INTRODUCTION

The primary theme of this thesis is image segmentation applied on medical images. This chapter will begin by outlining the basic problem of segmentation and motivate its importance in many applications. Modern medical imaging modalities generate larger and larger images which simply cannot be examined manually. This drives the development of more efficient and robust image analysis methods, tailored to the problems encountered in medical images. The aim and motivation of this thesis in Section 1.3 are directed towards the particular problem of segmenting blood vessels. However, the generality of the problem can lead to potential impacts also in other areas of image analysis.

1.1 Image Segmentation

Image segmentation is the problem of partitioning an image in a semantically meaningful way. This vague definition implies the generality of the problem - segmentation can be found in any image-driven process, e.g. fingerprint/text/face recognition, detection of anomalies in industrial pipelines, tracking of moving people/cars/airplanes, etc. For many applications, segmentation reduces to finding an object in an image. This involves partitioning the image into two class of regions - either object or background. Segmentation is taking place naturally in the human visual system. We are experts on detecting patterns, lines, edges and shapes, and making decisions based upon the visual information. At the same time, we are overwhelmed by the amount of image information that can be captured by today’s technology. It is simply not feasible in practice to manually process all the images (or it would be very expensive, and boring, to do so). Instead, we design algorithms which look for certain patterns and objects of interest and put them to our attention. For example, a recent popular application is to search and match known faces in your photo library which makes it possible to automatically generate photo collections with a certain person. An important part of this application is to segment the image into “face” and “background”. This can be done in a number of ways, and it is well accepted that no general purpose segmentation algorithm exists, or that it ever will be invented. Thus, when designing a segmentation algorithm, the application is always of primary focus: Should we segment the image based on edges, lines, circles, faces, cats or dogs?
1.2 Medical Image Analysis

An interesting source of images is the medical field. Here, imaging modalities such as CT (Computed Tomography), MRI (Magnetic Resonance Imaging), PET (Positron Emission Tomography) etc. generate a huge amount of image information. Not only does the size and resolution of the images grow with improved technology, also the number of dimensions increase. Previously, medical staff studied two-dimensional images produced by X-ray. Now, three-dimensional image volumes are common in everyday practice. Even four-dimensional data (three-dimensional images changing over time, i.e. movies) is often used. This increase in size and dimensionality provides major technical challenges as well as cognitive. How do we store and transmit all this data, and how can we look at it and find relevant information? This is where automatic, or semi-automatic, algorithms are of interest. In the best of worlds, we would like to have algorithms which can automatically detect diseases, lesions and tumors, and highlight their locations in the large pile of images. But another complication arises, we also have to trust the results of the algorithms. This is especially important in medical applications - we don’t want the algorithms to signal false alarms, and we certainly don’t want them to miss fatal diseases. Therefore, developing algorithms for medical image analysis requires thorough validation studies to make the results usable in practice. This adds another dimension to the research process which involves communication between two different worlds - the patient-centered medical world, and the computer-centered technical world. The symbiosis between these worlds are rare to find and it requires significant efforts from both sides to join on a common goal.

1.3 Aim and Motivation

The aim of this thesis is to develop segmentation methods for medical imaging applications. In particular, the main project involves the segmentation of blood vessels in the liver. The segmentation generates a computer model of the vessel tree which can be used for simulating blood and heat flow during surgical interventions. The motivation for this work is to increase patient safety by providing better and more precise data for medical decisions. As stated in the previous section, this work involves much multi-disciplinary communication, so an overall goal of the work is to establish links and identify important and relevant medical problems.

1.4 Conventions and Terminology

The examples throughout this thesis will use two-dimensional images since the illustration and visualization of the ideas are much simpler and provide better understanding. Three-dimensional medical images are important, especially when studying blood vessels, but most of the main ideas in this thesis generalize
introduction

to three dimensions without much effort. Such three-dimensional results are presented in the papers, as proofs of concept. Thus, to keep the language simple, many terms used are natural for two dimensional images, i.e. curve and pixel. In most cases however, these terms can be exchanged with higher-dimensional counterparts such as surface and voxel.

1.5 thesis outline

This thesis contains two major parts. The first part in Chapter 2, describes the detection of lines and edges (i.e. blood vessels) by using filtering techniques. The second part is introduced by Chapter 3 which presents common methods and theories on image segmentation. Next, Chapter 4 will describe our contributions to the field of segmentation, and detail how the filtering results in Chapter 2 are used for segmenting blood vessels. Conclusions and presentation of future work are given in Chapter 5 and Chapter 6. Finally, an overview of the contributed papers are presented in Chapter 7.
CHAPTER 2
LINEAR STRUCTURE DETECTION

The focus of this thesis is on the detection and segmentation of blood vessels in medical images. There are numerous ways to model a blood vessel, but we have chosen to think of a vessel as a collection of lines and edges. In a sufficiently small neighborhood, a vessel can even be described by straight lines and edges which simplifies the analysis greatly. In this chapter, we will describe the general problem of detecting linear structures, i.e. lines and edges, by means of filtering. The next section will present some well known techniques for line and edge detection using simple digital filters. Then, Section 2.2 will continue by describing quadrature filters, which form the basis of our algorithms. The remainder of the chapter will explain the output from the quadrature filters and how it is used in a multi-scale setting to determine the location of blood vessel edges.

2.1 BACKGROUND

One of the simplest ways to detect lines, edges and other structures in an image is to design a mask, or filter which resembles this structure [Gonzales and Woods, 2002, Chap. 10.1]. When convolving an image with the mask, the pixels with a neighborhood similar to the mask will give strong output. For example, the mask in Figure 2.1(a) would give a strong output for horizontal lines, while the remaining masks in Figure 2.1 would indicate lines at different orientations. If the convolved result is thresholded, the pixels which fit the given mask can be identified. Note that all the masks in Figure 2.1 sum to zero. This is important since we do not want any output in constant areas of an image. In technical terms, we say that the mask, or filter, should have a zero DC level.

It is possible to construct masks that perform well for simple type of struc-

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(a) Horizontal & (b) \(+45^\circ\) & (c) Vertical & (d) \(-45^\circ\) \\
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\caption{Masks for detecting one pixel thick lines at different orientations.}
\end{figure}
2.1 Background

Figure 2.2: A model of an edge with first and second derivatives.

tures and rather idealistic type of images. If, for example, we want to detect lines of varying width in noisy images, more robust algorithms and general models might be needed. Turning to the problem of detecting edges, a typical model used is a ramp with a linear transition from dark to bright or vice versa as illustrated in Figure 2.2. On the right, we can see a profile of the edge and its first and second derivatives. From this, it can be noted that the first derivative is a candidate for edge detection, since it gives a non-zero output across the entire edge transition. In fact, the magnitude of the first derivative is probably the most common feature used for edge detection. The second derivative can be used to determine whether the edge is a transition from dark to bright or vice versa. But it can also be noted that the zero-crossing of the two peaks in the second derivative can identify the center of the edge.

2.1.1 Gradient operators

Since we are studying images, the first derivative is represented by the gradient, defined by partial derivatives \( \nabla I = (\partial I/\partial x, \partial I/\partial y)^T \), for a two-dimensional image \( I \). Now, edges can be identified by locating pixels with a high gradient magnitude: \( |\nabla I| = \sqrt{(\partial I/\partial x)^2 + (\partial I/\partial y)^2} \). The only thing missing is a discrete formulation of the partial derivatives. Two such common formulations are given in Figure 2.3 which shows the Prewitt and Sobel filter masks.

Figure 2.3: Common masks (filters) for gradient computation.
2.1.2 Laplace operators

Turning to the second derivative, a measure often used for images is given by the Laplace operator:

\[ \nabla^2 I = \frac{\partial^2 I}{\partial x^2} + \frac{\partial^2 I}{\partial y^2} \]  

(2.1)

Two commonly used discrete filter masks are given in Figure 2.4. As previously noted, this filter can be used for identifying the type of edge transition, or to locate an edge by its zero-crossing. However, due to the small size of this filter, it is very susceptible to noise in the image. A popular approach is to first smooth, or low-pass, the image using a Gaussian filter defined by:

\[ G_\sigma = -e^{-(x^2+y^2)/2\sigma^2} \]  

(2.2)

Equivalent to applying the Gaussian followed by the Laplace filter, the Laplace and Gaussian operators can be combined into the Laplacian of a Gaussian (LoG):

\[ \text{LoG}_\sigma = -\left(\frac{x^2+y^2-\sigma^2}{\sigma^4}\right)e^{-(x^2+y^2)/2\sigma^2} \]  

(2.3)

The continuous representation of this filter is shown in Figure 2.5(a) and one possible discretization in Figure 2.5(b). The width of the filter and the size of the mask should be tweaked to suppress the noise in the image, while giving as “distinct” zero-crossings as possible. The idea of using the zero-crossings of the Laplacian as an edge indicator is however not easily implemented in practice (see e.g. Huertas and Medioni [1986]), so gradient based edge detection schemes are most widely used.

2.1.3 Hessian operators

A different second derivative-based measure is given by the Hessian matrix:

\[ H = \begin{pmatrix} \frac{\partial^2 I}{\partial x^2} & \frac{\partial^2 I}{\partial x \partial y} \\ \frac{\partial^2 I}{\partial y \partial x} & \frac{\partial^2 I}{\partial y^2} \end{pmatrix} \]  

(2.4)

The simplest possible filter masks for computing the partial derivatives on a sampled image are shown in Figure 2.6. Much work on blood vessel enhancement and segmentation (see e.g. Sato et al. [1997] and Frangi et al. [1998])
2.1 Background

Figure 2.5: Laplacian of a Gaussian (LoG).

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Figure 2.6: Filters for computing second order partial derivatives.

(a) $\frac{\partial^2}{\partial x^2}$

(b) $\frac{\partial^2}{\partial y^2}$

(c) $\frac{\partial^2}{\partial x\partial y}$

have used the eigenvalues of the Hessian matrix to determine the “vesselsness” (similarity to a line) of a pixel neighborhood. For a 2D image, we have two sorted eigenvalues $\lambda_1 \geq \lambda_2$. If $\lambda_1 \approx \lambda_2$, the neighborhood is isotropic, indicating that the pixel is either noise or in a homogeneous (flat) area of the image. If, on the other hand $\lambda_1 \gg \lambda_2$, the structure in the neighborhood has a clear orientation, implying that we have a line pixel.

2.1.4 Spatial and frequency descriptions

So far we have seen how simple mathematical models (e.g. the edge “ramp”) can be used to derive a set of discrete filter masks which approximate the model for sampled images. All filters described so far are motivated by spatial considerations, i.e. first and second order derivatives of the image. For many applications, it can be useful to apply models in the frequency domain instead. For example, blurring of an image can be viewed as a simple averaging operation in the spatial domain. In the frequency domain on the other hand, blurring is an operation which removes high frequency components of the image. In some cases, the degree of blurring can be specified more precisely in the frequency domain by a cut-off frequency instead of a certain size of averaging filter in the spatial domain. Also, systems in nature, such as the human visual system, are often best described by its frequency properties. This motivates some popular filters in image processing such as Gabor filters [Daugman, 1985, Gabor, 1946].
Figure 2.7: Illustrations of the directional function $D(\hat{n})$. Figure (a) shows this function in 2D with $\hat{n}_k = (\sqrt{2}/2, \sqrt{2}/2)^T$. Figure (b) plots the direction as a function of $\phi$, i.e. the angle between $u$ and $\hat{n}_k$.

2.2 Quadrature Filters

For our work, we use so called quadrature filters for line and edge detection. The schemes presented in the previous section rely on spatial derivatives to determine the location of structures. A major drawback of this approach is the dependence on image contrast. For example, edge detection using the magnitude of the gradient is highly dependent on quick transitions between two regions of distinctly different intensities (i.e. sharp edges). For smooth or low contrast edges, gradient-based approaches often fail. On the other hand, quadrature filters provide a contrast independent means of classifying edges or lines by the local phase, which will be further described in Section 2.3. But first we will introduce the general definition of quadrature filters and their construction in the frequency domain.

Quadrature filters are complex filter pairs where the real and imaginary parts are oriented line- and edge-filters respectively [Granlund and Knutsson, 1995]. They can be defined in the Fourier domain as:

$$F_k(u) = 0, \quad u \cdot n_k \leq 0$$

(2.5)

where $u$ is the frequency coordinate and $n_k$ is the filter direction. This specification says that one half-plane of the Fourier domain is zero, i.e. that the filter does not pick up frequencies on the “negative side” of the filter direction (i.e. the half-plane which has negative projection with $n_k$). Traditionally the filters are designed to be spherically separable into functions of radius ($R$) and direction ($D$):

$$F(u) = R(\rho)D(\hat{u})$$

(2.6)

where $\rho = ||u||$ and $\hat{u} = u/||u||$. To meet certain requirements (invariance and equivariance, see [Granlund and Knutsson, 1995] for a complete description) it
2.2 Quadrature filters

(a) Radial function in 1D
(b) Radial function in 2D

Figure 2.8: Illustrations of the radial function $R(\rho)$.

was shown in Knutsson [1982, 1985] that the directional function can be chosen as:

$$D_k(\hat{\mathbf{u}}) = \begin{cases} (\hat{\mathbf{u}} \cdot \hat{\mathbf{n}}_k)^2 & \text{if } \hat{\mathbf{u}} \cdot \hat{\mathbf{n}}_k > 0 \\ 0 & \text{otherwise} \end{cases}$$  \hspace{1cm} (2.7)

See Figure 2.7(a) for a 2D plot of this function where $\hat{\mathbf{n}}_k = (\sqrt{2}/2, \sqrt{2}/2)^T$. It can be noted that this function varies as $\cos^2(\phi)$ where $\phi$ is the angle between $\hat{\mathbf{u}}$ and $\hat{\mathbf{n}}_k$, see Figure 2.7(b) for a plot of this in 1D. Whereas the directional function determines the angular restriction of the filter to discriminate between different orientation of structures, the radial function decides the radial shape of the filter in the frequency domain. Thus, the radial function is designed to detect structures of particular frequency content, depending on a particular application. A useful class of radial functions is the lognormal functions:

$$R(\rho) = e^{-\frac{1}{\log^2 (\rho/\rho_i)}}$$  \hspace{1cm} (2.8)

where $B$ is the bandwidth and $\rho_i$ is the center frequency. See Figure 2.8 for plots of $R(\rho)$ in 1D and 2D.

However, specifying appropriate radial and directional functions in the frequency domain is not enough to solve the filter design problem. There are also desired properties on the filter in the spatial domain. Especially important is the local support, i.e. a good filter should typically be as small as possible. The requirements on the frequency and spatial designs are often in conflict, so the optimal solution is a balance between the two. In [Knutsson et al., 1999] a general filter optimization framework is presented, which uses weighted ideal functions in the spatial and frequency domains to find an optimal solution in a least-square sense. Examples of filters generated using such a framework are presented in Figure 2.9. Here we have chosen the center frequency $\rho_i = \pi/4$ and bandwidth $B = 2$. The size of the spatial mask is $21 \times 21$. Unless otherwise noted, these filters will be used for all 2D examples in this thesis.
2.3 Local Phase

The output from a quadrature filter is complex valued, where the real and imaginary parts represent the output from the line and edge filter respectively. If the output is purely real, the image contains a line, while a purely imaginary output indicates an edge. More generally, the relationship between the "line"-ness and "edge"-ness of a signal is encoded in the filter output as the argument of the complex value. Representing the filter output by \( q = Ae^{\theta} \), the argument \( \theta \) is referred to as the local phase. The local phase has a number of properties making it robust for detecting lines and edges. Firstly, the local phase is invariant to signal energy, which means that it is not depending on image contrast. In other words, a "weak" line gives exactly the same local phase as a "strong", or distinct sharp, line. Secondly, the phase varies smoothly and monotonically with the position of edges and lines. The magnitude \( A \) of the output gives, on the other hand, an indication of signal strength, or the contrast of the lines and edges.

For illustrations we encode the complex filter output \( q \) using the color mapping of the complex plane shown in Figure 2.10(a).

To illustrate several examples, we use a synthetic image of a spiral displayed in Figure 2.10(b). This is a useful image since it contains lines of varying thickness and orientation. We detail the concept of local phase in Figure 2.11. The cropped filter output from a filter oriented along \( \hat{n} = (1,0)^T \) is shown in Figure 2.11(a). The plots in Figure 2.11(b-d) show the phase \( \theta \) and magnitude \( A \) along the horizontal line of pixels in Figure 2.11(a) where the color of the lines can be used to correlate the position of the filter between the plots. In Figure 2.11(d) we see that the first structure that the filter detects is a line at pixel 22. The line is visualized by a green color in Figure 2.11(a) and characterized by a phase of 0 in Figure 2.11(b,c). The next peak in the magnitude is due to an edge transition from dark (background) to bright (object) around pixel 91. This is represented by an orange color in Figure 2.11(a) and a phase of \(-\pi/2\). Finally, the last structure is an edge transition from bright to dark around pixel 124 which is indicated by a phase of \( \pi/2 \) and a purple color.
2.3 Local phase

Figure 2.10: Filter output mapping and the synthetic spiral image

(a) Cropped view of filter output
(b) Phase transition
(c) Phase plot
(d) Magnitude plot

Figure 2.11: Detailed illustration of the filter response for the pixels along the horizontal colored line in (a). The white curve in (a) gives the true edges of the object. All plots show three different types of structures (line, edge transition dark-to-bright/bright-to-dark) marked by blue circles. It can be seen in (c) and (d) that these structures give maximal magnitude output at phases 0, −π/2 and π/2. The phase transition in the complex plane is shown in (b).
Figure 2.12: Filter results of the spiral image on the second scale.

Figure 2.13: Filter results over different scales.

Figure 2.14: Multi-scale integration using different values on the parameter $\beta$. 
2.4 Structures in different orientations

When a quadrature filter is designed, it is optimized to detect signal energy along particular orientations. For most applications, it is important to detect structures in all orientations, so a set of quadrature filters with different orientations is commonly used. To cover the space of all orientations, it has been shown in [Knutsson, 1982, 1985] that at least 3 uniformly distributed orientations are needed in 2D and 6 orientations in 3D. For the examples in this thesis, we use 4 directions in 2D given by:

\[
\begin{align*}
\hat{n}_1 &= (1, 0)^T \\
\hat{n}_2 &= (a, a)^T \\
\hat{n}_3 &= (0, 1)^T \\
\hat{n}_4 &= (-a, a)^T
\end{align*}
\]

(2.9)

where \(a = 1/\sqrt{2}\). In 3D, we use 6 filter directions:

\[
\begin{align*}
\hat{n}_1 &= c(a, 0, b)^T \\
\hat{n}_2 &= c(-a, 0, b)^T \\
\hat{n}_3 &= c(b, a, 0)^T \\
\hat{n}_4 &= c(b, -a, 0)^T \\
\hat{n}_5 &= c(0, b, a)^T \\
\hat{n}_6 &= c(0, b, -a)^T
\end{align*}
\]

(2.10)

where \(a = 2, b = 1 + \sqrt{5}\) and \(c = (10 + 2\sqrt{5})^{-1/2}\). Applying the 2D filter set to the spiral image in Figure 2.10(b) yields the results in Figure 2.12, where the local phase is visualized using the color mapping in Figure 2.10(a).

2.5 Resolving edge ambiguities

As was noted in the illustration of local phase in Figure 2.11, the filter distinguishes between two types of edges: transitions from dark (background) to bright (object) around pixel 91, or vice versa around pixel 124. For our application, it is not important to make this distinction so we want to simplify the filter output by reducing these two cases to only one edge event. This can also be motivated by the fact that two filters with opposing direction will result in edge ambiguities. Consider the last edge around pixel 124 in Figure 2.11. The filter with direction \(\hat{n}_1 = (1, 0)^T\) views this edge as a transition from bright to dark and thus gives a local phase of \(\pi/2\). However, a filter with direction \(\hat{n}_4 = (-1/\sqrt{2}, 1/\sqrt{2})^T\) will approach this edge from the other direction and detects a transition from dark to bright with a local phase of \(-\pi/2\). Direct operations, such as comparisons or summations, on the results of these two filters is not possible due to this ambiguity.

Our solution to this problem is to simply take the absolute value of the imaginary part of the filter response. Then we view all edges as transitions from bright to dark with a local phase of \(\pi/2\). The “rectification” of the filter output makes it possible for direct operations between the results from different filter directions. We use this to produce an orientation invariant output which is the sum of all filter directions. The result after rectification and summation of the filter outputs in Figure 2.12 is shown in Figure 2.13(b).
2.6 MULTI-SCALE INTEGRATION

We perform the filtering on multiple scales to handle vessels of varying width. Figure 2.13 shows the results on multi-scale filtering of the spiral image. We can note that the finest scale in Figure 2.13(a) and Figure 2.13(d) detects the thin parts of the spiral as lines, whereas the thicker parts are detected as edges. As we traverse the scale hierarchy, also the thicker parts are detected as lines as can be seen in Figure 2.13(d) and Figure 2.13(d). In practice, we compute the scale pyramid by subsampling the image and use the same set of filters on each scale.

The final step in the filter processing is to combine all the scales using a multi-scale integration. Our scheme is motivated by the fact that the filter responses carry a certainty measure in the magnitude. We use this magnitude as a weight to favor the scale with largest certainty. For example, if a filter gives strong output indicating an edge at a given pixel on a certain scale, this pixel should with large certainty be an edge pixel. We formalize the multi-scale integration by:

\[
q = \sum_{i=1}^{N} \frac{|q_i|^\beta q_i}{\sum_{i=1}^{N} |q_i|^\beta}
\]  

(2.11)

where \(N\) is the number of scales, \(q_i\) is the filter result for each scale and \(\beta \geq 0\) is a weight parameter. Note that the extreme case \(\beta = 0\) gives the average of all scales, while a very large value of \(\beta\) acts a maximum operation which basically picks out the scale with maximum output. Integrating the results in Figure 2.13 using different values for \(\beta\) is shown in Figure 2.14. Visually, we can argue for choosing \(\beta > 0\) because \(\beta = 0\) results in weaker line detection in the thicker part of the spiral, while the edges are not as crisp. However, a too large value of \(\beta\) gives "ringing" artifacts, also notable in the thicker parts. The choice of \(\beta\) was investigated further in Paper V, in which we concluded that a choice of \(0 < \beta < 5\) generally performs well.

2.7 EDGE LOCALIZATION

The next step is to use the filter results to determine the location of lines and edges in particular. After the multi-scale integration, we have combined the output from quadrature filters with different orientations, applied on a scale pyramid of the image. So the final result is complex valued, where the relation between the real and imaginary parts (the local phase) describes the "line"-ness and "edge"-ness of the structure in each pixel. We can find lines where the real part of the result is locally maximal (or where the phase \(\theta = 0\)) and edges at imaginary maxima (at \(\theta = \pi/2\)). Equivalently, it is possible to locate lines at the zero-crossings of the imaginary part and edges at the zero-crossings of the real part. For our work we use the later formulation, since the detection of zero-crossings can be more robust algorithmically compared to the localization of maxima. Since we are particularly interested in locating the edges of blood vessels, we will mainly study the real part of the filter response and use it for the
2.8 Results

(a) Retinal image.  
(b) Aorta image.

*Figure 2.15: Medical images used as examples.*

segmentation. If we describe the object by bright pixels and the background by dark, we can also note that positive values of the real part indicates that we are inside the object, while negative values indicate outside. In the next chapter, the thesis will continue by describing methods for segmentation in general, and Section 4.2 will use the filter results presented in this chapter for the segmentation of blood vessels in particular.

2.8 RESULTS

To illustrate the behavior of our method, we use two medical images with blood vessels. The first is a retinal image from the DRIVE database [Staal et al., 2004], shown in Figure 2.15(a). The filters used are the same as previously described, i.e. center frequency $\rho_i = \pi/4$, bandwidth $B = 2$ and a spatial size of $21 \times 21$. The filter responses for all filter directions in scale 2 are shown in Figure 2.16. Since there is not much variation in the width of the blood vessels, we only filter on 2 scales. The individual scales and the integrated result using $\beta = 2$ are displayed in Figure 2.17.

A second example is a MIP image of the aorta (data courtesy of CMIV, Linköping University) shown in Figure 2.15(b). This is a challenging image since it contains vessels of very large width variation. The individual filter directions are presented in Figure 2.18 for the third scale. Due to the large width variation, we filter the image on five scales which are integrated with the parameter $\beta = 2$. The results are shown in Figure 2.19.

Both examples show that the filtering method succeeds in capturing most visible blood vessel structures, even for large width variations. Note that the primary purpose of these examples is to illustrate the behavior of the method, quantifying the detection performance would require large efforts and will be the focus of future work. Also note that filter parameters more optimized to these type of images could potentially improve the results even further.
Figure 2.16: Filter results of the retinal image on the second scale.

Figure 2.17: Filter results over different scales.
2.8 Results

Figure 2.18: Filter results of the aorta image on the third scale.

Figure 2.19: Filter results over different scales.
CHAPTER 3
MEDICAL IMAGE SEGMENTATION

This chapter will briefly introduce the most common categories of image segmentation methods used for medical image segmentation. We will start by the most simple techniques typically referred to as thresholding and region growing. Then, we introduce more recent techniques where a segmentation is found by means of optimizing an energy functional. In this context we talk about continuous variational and discrete combinatorial methods.

3.1 THRESHOLDING AND REGION GROWING

Early, and simple, techniques for segmentation mainly used the assumption that relevant objects in an image can be identified based on intensity values. The most simple approach identifies objects using a single threshold value, such that pixels above and below the threshold are object pixels and background pixels respectively. This works fine for high contrast objects with a sharp edge, but the method often fails as soon as the edges are smooth, of varying intensity and influenced by noise. This is most often the case for natural images, which limits the usefulness of this approach.

A slightly more sophisticated version of thresholding are region growing algorithms. The basic idea is to start from a given seed point which is known to be an object pixel. The neighborhood of the pixel is classified as background or object depending on a threshold value. The (connected) object is segmented by a recursive search through the pixels which are classified as object. A typical problem with this type of method is leakage, since it is hard to set a threshold value which confines an actual object.

3.2 VARIATIONAL METHODS

Variational methods are based upon describing an energy functional where the optimum defines a good segmentation. The functional is typically depending on a curve, which defines the partitioning of the image, and a number of image derived terms such as image intensity, image gradients, etc.

3.2.1 Snakes

The first work in this direction was the Snake in Kass et al. [1988] which used an explicit type of curve representation. The energy is defined by:

\[ E[C(s)] = - \int |\nabla I(C(s))|^2 ds + \nu_1 \int |C'(s)|^2 ds + \nu_2 \int |C''(s)|^2 ds \quad (3.1) \]
3.2 Variational Methods

where \( C(s) \) is a parametric curve with parameter \( s \), \( I \) is the image, and \( C' \) and \( C'' \) are the first and second derivatives of \( C \) with respect to its parameter \( s \). The first term is referred to as the external energy and the two last terms are the internal energies of the snake. The external energy is derived from the image, and is used to drive the curve towards points with high gradient magnitude, i.e. strong edges. The first internal energy, weighted by \( \nu_1 \geq 0 \), measures the length of the snake, while the second, weighted by \( \nu_2 \geq 0 \) measures the stiffness. Good segmentations are represented by curves which optimize the energy, i.e. where the first variation of \( E \) vanishes. The first variation can be viewed as a generalization of the first derivative from “ordinary” calculus. Recall that stationary points (maxima, minima, saddles) of a function can be found by searching for points where the first derivative is zero. The first variation in the calculus of variations has exactly the same meaning, but for functionals (a “function of a function” such as Eq. (3.1)) instead of functions. Without going into details, this can be expressed by the Euler-Lagrange equation denoted by \( \delta E / \delta C = 0 \). This equation results in a partial differential equation (PDE) which, in most cases, is hard to solve directly. Instead an energy optimum is found by evolving the curve in the steepest descent direction of the energy, such that \( \partial C / \partial t = -\delta E / \delta C \). This is the basic idea behind the popular variational methods used in image processing. Note however that any solution will be a local optimum, so the result strongly depends on a proper initialization, or a proper starting curve.

The Snakes algorithm was the starting point for image segmentation using variational methods. However, it suffers from a number of drawbacks. The main drawback is the explicit curve representation which does not easily allow topological changes and requires complex reparameterization algorithms. Second, since the nodes of the curve are affected by local image features, i.e. there are no region based information, the solutions tend to be very sensitive to a proper initialization. Also, from a mathematical point of view, the energy function is not intrinsic since it depends on the parameterization of the curve. This means that the energy will change if the parameterization changes, which clearly is an undesirable property.

3.2.2 Level set methods

To address the first issue regarding curve parameterization, approaches using the implicit level set method by Osher and Sethian [1988] were simultaneously proposed by Caselles et al. [1993] and Malladi et al. [1993, 1994]. Using these ideas, a curve is represented implicitly as the zero level set of a time dependent function \( \phi : \Omega \to \mathbb{R} \), such that \( C = \{ x(t) \in \Omega : \phi(x, t) = 0 \} \). By differentiating with respect to time, we can couple the motion of the curve \( dx/dt \) with an evolution of the level set function \( \phi \) using a PDE \( \partial \phi / \partial t = -dx/dt \cdot \nabla \phi \). A special case is when the motion is restricted to the normal direction of the curve, i.e. \( dx/dt = Fn \), where \( n = \nabla \phi / |\nabla \phi| \). In this case, the scalar function \( F \) is usually referred to as the speed function. This representation has the main advantage of allowing arbitrary topological changes, so the initial curve does not need to
have the same topology as the segmented object. Unlike the Snakes algorithm, which was motivated by energy minimization, the work by Caselles et al. and Malladi et al. was motivated by a geometric curve evolution approach. The basic idea was to generate a speed function which "pulled" the curve towards the boundaries of the target object while the curve was regularized with curvature motion. A typical speed function can be based on image gradients, such that it approaches zero when the norm of the image gradient is large (i.e. there is a distinct edge).

The main advantage of this approach is the level set representation, which allows arbitrary topological changes and robust and stable numerical schemes for the curve propagation. However, the motivation is based on geometrical aspects of the image and the curve, so it is hard to validate the solutions and perform "deeper" mathematical analysis.

3.2.3 Geodesic active contours

The next major step in variational methods-based image segmentation was the Geodesic active contour proposed simultaneously by Caselles et al. [1997] and Kichenassamy et al. [1995]. In this work, it is shown that a special case of the Snakes model can be interpreted as finding geodesics (locally shortest paths) in a space with a metric derived by image content. This formalism provides an analogue between segmentation using active contours and minimal distance (geodesic) computations. Formally, the energy to be minimized has the following form:

$$E_{GAC}[C(s)] = \int_0^{L(C)} g(|\nabla I(C(s))|) ds$$ (3.2)

where $L(C)$ is the length of $C$, $g(|\nabla I|)$ is a strictly decreasing inverse edge indicator function, typically $g(|\nabla I|) = 1/(1 + |\nabla I|)$. We can note that choosing $g = 1$ gives the length of the curve $C(s)$, so minimizing Eq. (3.2) gives a minimal curve where the length of the curve is weighted by the function $g(|\nabla I|)$.

Then, if the curve is represented as a level set, it is shown that the geodesic computations reduce to a form similar to the work in Caselles et al. [1993], Malladi et al. [1993, 1994]. The geodesic active contour model provides a coupling between segmentation based on energy minimization and the level set framework. Thus, it is contained in a rigorous mathematical context of optimization while the curve representation is flexible and robust, allowing both thorough analysis and practical implementation.

3.2.4 Active contours without edges

So far, the active contour models have primarily defined the objects by image gradients. This is often problematic due to varying edge contrast and noise. The models will fail completely for objects with too blurred or weak edges, and there are risks of leakage if the edge is not well defined on the complete perimeter of the object. In contrast, the active contours without edges by Chan and Vese [2001] is based on regional measures and do not depend on any edge.
3.3 Combinatorial Methods

Definition. This approach incorporates region information and is a special case of the Mumford-Shah functional for segmentation [Mumford and Shah, 1989]. Basically, it solves the minimal partition problem which aims to find a partitioning of the image which best separates the interior of the curve from the exterior. Formally, it is described as:

$$E_{CV}(C(s)) = \mu \int_0^{L(C)} ds + \iint_{\Omega_C} (I(x, y) - c_1)^2 dxdy$$

$$+ \iint_{\Omega \setminus \Omega_C} (I(x, y) - c_2)^2 dxdy$$

(3.3)

where $$\Omega_C$$ is the interior of the curve $$C$$, $$c_1$$ and $$c_2$$ are the average image intensities in the interior and exterior of $$C$$ respectively and $$\mu \geq 0$$ is a weight parameter. The first term is a regularization which minimizes the length and the second last terms provide the balancing between the interior and exterior. It can be noted that omitting the regularization by $$\mu = 0$$ leads to a solution equivalent to simple thresholding. This model assumes the image to be separable into two regions (phases) which can be reasonably well approximated by constant values $$c_1$$ and $$c_2$$. This is a crude model which was later generalized to multi-phase piecewise-smooth approximations in Vese and Chan [2002].

The main advantage of this model is the global dependence and the tendency to produce globally optimal solutions in practice. However, for many applications in medical image segmentation, the influence of the background intensity can be problematic. This was investigated in Paper I and will be further detailed in Section 4.1.

3.2.5 Active shape models

Many applications can include prior knowledge in the segmentation. For example, shape priors can be used to constrain the topology and general shape of the result. A model for integration shape in medical applications was presented in Rousson et al. [2004]. For a review on approaches to incorporate color, texture, motion and shape, see Cremers et al. [2007].

3.2.6 Direction of descent

As noted in Section 3.2.1, the derivation of level set flows by the Euler-Lagrange equation leads to a gradient descent search for the energy optimum. The use of a gradient implies a notion of inner product in the space of curves. Although a fundamental property of the system, the effect of the choice of inner product has not been studied until recently in parallel work by Charpiat et al. [2005], Solem and Overgaard [2005], Sundaramoorthi et al. [2007], Yezzi and Mennucci [2005].

3.3 COMBINATORIAL METHODS

Whereas the previous section described approaches where the image domain is regarded as continuous and segmentation was posed as an optimization in
a continuous space, there are combinatorial methods formulated as a discrete optimization problem on the pixels of the image. This section will introduce the main directions in this area for completeness, but since this is not the focus of this thesis, the presentation will be brief.

3.3.1 Optimality of solutions

In general, the variational methods previously presented use gradient descent search for optimization which can only be guaranteed to find stationary points. For most cases, it is not known whether the solution found is a local minima, maxima or a saddle point. Furthermore, the solution depends critically on the initial condition (curve). The main benefit of the combinatorial methods is that a global solution can be guaranteed. This has several advantages: First, the solution is not depending on a good initial condition, so the initial curve can be placed arbitrarily in the image. Second, the quality of the solution relates directly to the energy functional and the parameters controlling the functional, rather than the initialization or other numerical implications of the implementation. On the other hand, some applications might benefit from the possibility of inducing a local optima by a controlled initialization, such as extracting a particular branch of a blood vessel tree. But combinatorial methods can in general be considered more robust due to the guaranteed global solution.

3.3.2 Dynamic programming and optimal paths

Like the Snakes algorithm in variational methods, the combinatorial methods for segmentation started with explicit representations of object boundaries. This was first presented by Amini et al. [1990] where dynamic programming was used to find a global optimum of the Snakes energy. Other researchers have proposed similar techniques based on dynamic programming to find optimal paths, see e.g. [Falcão et al., 1998, Geiger et al., 1995, Mortensen and Barrett, 1998]. However, these approaches are limited to 2D images since the properties of 3D geometry require fundamentally different explicit representations.

3.3.3 Graph cuts

An important contribution for segmentation based on graph cuts was presented by Boykov and Jolly [2001] (and extended in [Boykov and Funka-Lea, 2006]). In this work, pixels are classified as being either inside or outside the object, making this a combinatorial method using an implicit-type representation (albeit discrete). Thus, compared to the previously outlined path-based approaches, this method generalizes to higher dimensions more easily. The success of the method relies on an efficient min-cut/max-flow algorithm which computes a globally optimal cut [Boykov and Kolmogorov, 2004].
Level set methods are popular for solving many types of segmentation problems. The popularity is mainly due to the robust deformations and the embedding in a well studied mathematical framework. The previous chapter outlined the history of variational methods, which mostly are implemented using the level set representation. This chapter will continue by describing the contributions in this thesis to this field. Section 4.1 will start by presenting a localized version of the Chan-Vese model in Section 3.2.4 which can target single objects in an image. Then, Section 4.2 will explain how the filter output from Chapter 2 can be used for segmentation in a level set framework. We noted previously how the standard method for computing the segmentations is by a gradient descent search. Inspired by ideas from the machine learning community, Section 4.3 will give two alternative optimization strategies which can be adapted to the level set representation.

4.1 LOCALIZED REGION-BASED SEGMENTATION

In Section 3.2.4 we reviewed the popular Chan-Vese model “active contours without edges”. The main benefit of this method is its ability to segment objects with weak (low contrast) edges. In addition, the global dependence tends to produce globally optimal solutions which do not depend as much on a good initialization as do traditional edge-based methods. However, some applications suffer from this global dependence. For example, a user might want to segment only a single object in a medical image. In this case, the result is also dependent on objects far from the region of interest, which is not natural for the user. The global behavior also implies a background dependence which is not natural. Figure 4.1 illustrates this problem using a segmentation of the gray matter in the brain with the initializing curve in Figure 4.1(a). The background in the bottom row of images is slightly brighter than the top row. Figure 4.1(b) shows the result using the traditional Chan-Vese model. We can note that the segmentations differ purely due to the shift in background intensity. Also, the segmentations are not related in a meaningful way to the initializing curve. One can use a narrow-band level set technique as in [Peng et al., 1999] to localize the curve propagation, but this still leads to different results depending on the background as shown in Figure 4.1(c). By localizing also the computations, i.e. restricting the domain of the Chan-Vese model, we can get meaningful results which are not background sensitive as in Figure 4.1(d). This problem, and a user interface for initializing the segmentation, was presented in Paper I.
4.2 Phase-based level set segmentation

For segmenting linear structures, e.g. blood vessels, the output from the filtering approach in Chapter 2 can be used as input for level set segmentation. The idea of localizing edges by finding zero-crossings in the filter output was outlined in Section 2.7. Recall that edges are located on the zero-crossings of the real part, while positive and negative values indicate inside and outside of the blood vessels respectively. This fact was used a geometric motivation for level set propagation in Paper II. In fact, by directly using the real part of the filter output as a level set speed function and initializing the curve near a blood vessel, the positive and negative forces will drive the curve towards the edges where it will stop. A regularization term was added to increase the smoothness of the curve, which gives:

$$\frac{\partial \phi}{\partial t} = -\text{Re}(q) |\nabla \phi| + \alpha \kappa |\nabla \phi|$$  \hspace{1cm} (4.1)

where $\text{Re}(q)$ is the real part of the filter output $q$, $\kappa$ is the curvature and $\alpha \geq 0$ is a regularization weight parameter. A sequence of iterations on the spiral image described in Chapter 2 using $\alpha = 0.1$ is shown in Figure 4.2. Here the curve is overlaid the real part of the filter output, where positive and negative values are
indicated by bright and dark colors respectively.

In Paper V, it was shown that the geometrically derived speed function in Eq. (4.1) comes from maximizing the energy:

$$E[C(s)] = \iint_{\Omega_C} f(x, y) \ dx \ dy - \alpha \oint_C ds$$

(4.2)

where $f(x, y) = \text{Re}(q)$. This is the so-called weighted region functional [Kimmel, 2003] which aims to maximize the function $f(x, y)$ inside the region $\Omega_C$ (inside of $C$) while at the same time minimizing the length of $C$. Basically, this will find a curve which encloses all points with positive values on $f$ while “small” regions (typically noise) will be removed due to the minimization of length. Thus, Eq. (4.2) can be interpreted as a noise suppressed thresholding on $f > 0$.

This energy interpretation of Eq. (4.1) allows us to embed the phase-based segmentation ideas in a mathematical framework for constructing alternative optimization strategies. This will be further elaborated in the next section.

### 4.3 Optimization aspects of segmentation

As was described in Section 3.2, image segmentation can be formulated as an optimization problem, where the goal is to find a particular segmentation which maximizes/minimizes a given energy functional. Here we will present two optimization strategies commonly used in the machine learning community, and show how these can be adapted to level-set based segmentation.

#### 4.3.1 Gradient descent with momentum

The simplest numerical optimization method is gradient descent, where only the gradient of the cost function is used to guide the search towards an optimal solution. However, common drawbacks of this scheme is the sensitivity to local optima and the poor rate of convergence for many practical problems. More sophisticated methods have been proposed which utilizes higher order information to mainly improve the convergence rate, see [Nocedal and Wright, 2006] for a complete reference.

However, to avoid the added complexity of these more sophisticated meth-
4.3 Optimization aspects of segmentation

(a) Sequence of iterations

(b) Convergence rate

Figure 4.3: Gradient descent with momentum on a simple cost function.

ods, a simple and intuitive approach is to extend traditional gradient descent by adding momentum. This idea was initially proposed in the machine learning community [Rumelhart et al., 1986], where the training of an artificial neural network is formulated as an optimization problem. The basic idea is to add a fraction of the previous step to the current step, which adds a physical "inertia" to the motion in the search space. The practical benefits of this strategy are that local optima can be overstepped while the search accelerates in favorable directions, thereby increasing the rate of convergence. Formally, gradient descent can be described by:

\[ s_k = -\alpha_k \nabla f_k \]  \hspace{1cm} (4.3)

where \( s_k \) is the step in iteration \( k \), \( \alpha_k \) is the step length and \( \nabla f_k \) is the gradient of the cost function \( f \). Gradient descent with momentum can be described by:

\[ s_k = -\eta(1-\omega) \nabla f_k + \omega s_{k-1} \]  \hspace{1cm} (4.4)

where \( \eta > 0 \) is the so called learning rate and \( \omega \in [0,1] \) is the momentum, to adopt some terminology from the machine learning community. We can note that \( \omega = 0 \) gives the traditional gradient descent, while \( \omega = 1 \) gives "infinite inertia" \( s_k = s_{k-1} \). A simple example illustrating traditional gradient descent and gradient descent with momentum on an elliptic cost function is shown in Figure 4.3. Here we see that traditional gradient descent with \( \eta = 0.04 \) and \( \omega = 0 \) gives slow convergence. Increasing the step length to \( \eta = 0.4 \) gives faster convergence but an oscillating motion in search space. Adding the momentum by \( \omega = 0.1 \) stabilizes the motion and accelerates more quickly towards the optimum. However, oscillation is still possible for a large momentum of \( \omega = 0.4 \).

4.3.2 Resilient back-propagation

Both traditional gradient descent and gradient descent with momentum include the problem of finding an appropriate step length \( \alpha_k \) or learning rate \( \eta \). This is very much depending on application and the shape of the cost function in a
neighborhood around the current solution. For simplicity, the step length is commonly set to an ad-hoc constant value which "seems to work", but which could result in either poor convergence or oscillatory motion. To address this issue, the resilient back-propagation algorithm (Rprop) was proposed in Riedmiller and Braun [1993]. This is another technique invented in the machine learning community, which uses adaptive steps based on the behavior of the cost function. The basic idea is to look only at the sign of the gradient along the coordinate axes, according to:

$$ s_k = -\Delta_k \ast \text{sign} (\nabla f_k) $$  \hspace{1cm} (4.5)

where $\Delta_k$ is a vector of step sizes (one for each coordinate axis), $\text{sign} (\cdot)$ is the sign function and $\ast$ denotes element-wise multiplication. The step sizes are updated such that the motion is accelerated if the sign of the gradient is the same for consecutive iterations, while the motion is decelerated if the gradient changes sign. Formally, this update rule is specified as:

$$ \Delta_k = \begin{cases} 
\min (\Delta_{k-1} \cdot \eta^+ \cdot \Delta_{\text{max}}) & \text{if } \nabla^i f_k \cdot \nabla^i f_{k-1} > 0 \\
\max (\Delta_{k-1} \cdot \eta^- \cdot \Delta_{\text{min}}) & \text{if } \nabla^i f_k \cdot \nabla^i f_{k-1} < 0 \\
\Delta_{k-1} & \text{else}
\end{cases} $$  \hspace{1cm} (4.6)

where $\eta^+$ and $\eta^-$ are acceleration and deceleration factors, $\Delta_{\text{max}}$ and $\Delta_{\text{min}}$ are upper and lower limits on the step sizes and $\nabla^i f_k$ denotes the $i$th partial derivative of the cost function. An illustration of Rprop on a simple cost function is shown in Figure 4.4, together with conventional gradient descent. Here we use the parameters $\eta^+ = 1.2$, $\eta^- = 0.7$, $\Delta_{\text{max}} = 1$, $\Delta_{\text{min}} = 0.01$ with initial conditions $\Delta_0 = (0.1, 0.05)^T$. The gradient descent uses a constant step length of $\alpha = 0.04$. This plot shows the typical "zig-zag" behavior of Rprop while approaching the optimum.

Figure 4.4: Rprop on a simple cost function.
4.4 Level-set based segmentation and optimization

4.4 LEVEL-SET BASED SEGMENTATION AND OPTIMIZATION

We proceed with a discussion on how to utilize the alternative optimization methods presented in Section 4.3.1 and Section 4.3.2 in a level set framework. In Section 3.2 we presented the idea of deriving a level set flow by Euler-Lagrange equations which optimizes an energy functional. It was noted that this level set flow describes a gradient descent search in the solution space which, in this context, is the space of all possible curves. The structure, and dimensionality, will depend on the parameterization of a curve. For example, an explicit representation of a curve sampled using \( m \) number of nodes, embedded in \( n \) dimensions can be represented by one point in an \( n \times m \)-dimensional space. For the implicit level set representation, the level set function itself can be interpreted as a parameterization of the embedded curve. This will result in a solution space of \( N \) dimensions, where \( N \) is the number of samples of the level set function.

Returning to the level set flow derived by Euler-Lagrange equations, which resulted in a gradient descent motion in solution space. In light of the previous discussion, we can approximate the gradient by taking the finite difference between two subsequent time instances of the level set function (points in solution space):

\[
\nabla f(t_n) \approx \frac{\phi(t_n) - \phi(t_{n-1})}{\Delta t} \tag{4.7}
\]

where \( \phi(t_n) \) is the level set function at time \( t_n \). This approximation is of first order, depending on the time step \( \Delta t \). The gradient can be directly used to compute a new step \( s(t_n) \) using gradient descent with momentum in Eq. (4.4) or Rprop in Eq. (4.5) and evolve the level set function according to:

\[
\phi(t_n) = \phi(t_{n-1}) + \Delta t s(t_n) \tag{4.8}
\]

**Procedure UpdateLevelset**

1. Given the level set function \( \phi(t_{n-1}) \), compute the next (intermediate) time step \( \tilde{\phi}(t_n) \). This is performed by evolving \( \phi \) according to a PDE using standard techniques (e.g. Euler integration).

2. Compute the approximate gradient by Eq. (4.7).

3. Compute a step \( s(t_n) \) according to Eq. (4.4) or Eq. (4.5). This step effectively modifies the gradient direction by the momentum or Rprop schemes.

4. Compute the next time step \( \phi(t_n) \) by Eq. (4.8). Note that this replaces the intermediate level set function computed in Step 1.

To illustrate the behavior of the alternative optimization schemes, we use an “L”-shaped object consisting of two disconnected regions as shown in Figure 4.5(a). We apply the filtering techniques presented in Chapter 2 which gives the target function \( f(x, y) = \text{Re}(q) \), i.e. the real part of the filter response \( q \). This is shown in Figure 4.5(b) where bright and dark colors indicate positive and
negative values respectively. Applying traditional segmentation level set techniques using the initial curve in Figure 4.6(a) gives the result in Figure 4.6(c) which clearly is a local optimum (the global optimum would contain both regions of the object). Applying the idea of momentum gives the sequence of iterations in Figure 4.7 which succeeds in capturing both regions. The values of the energy functional (Eq. (4.2)) is shown in Figure 4.8 for traditional gradient descent and gradient descent with momentum. We can see that gradient descent with momentum oversteps a number of local maxima during the search while showing a more rapid increase in the energy.

4.5 RESULTS

To illustrate the alternative optimization schemes we use the previously introduced retinal image shown in Figure 4.9(a). The target function \( f(x, y) = \text{Re}(q) \) used for the segmentation is displayed in Figure 4.9(b). First, results using conventional gradient descent is shown in Figure 4.10 when initializing manually with the seeds in Figure 4.10(a). Comparing with the results for gradient descent with momentum in Figure 4.11, we see that the momentum approach captures more of the visible vessels. The energy functions are shown in Figure 4.12 which indicate that gradient descent with momentum indeed finds a stronger optimum.
4.5 Results

(a) time = 0  (b) time = 40  (c) time = 70

(d) time = 180  (e) time = 240  (f) time = 485

Figure 4.7: Iterations using momentum.

(a) Without momentum  (b) With momentum

Figure 4.8: Plots of energy functionals for synthetic test image in Figure 4.5(a).
Figure 4.9: Retinal image.

Figure 4.10: Iterations on the retinal image using conventional gradient descent.
4.5 Results

Figure 4.11: Iterations on the retinal image using gradient descent with momentum.

Figure 4.12: Plots of energy functionals for the retinal image.
CHAPTER 5

SUMMARY AND CONCLUSIONS

The primary focus of this thesis is on two different methods - linear structure detection by multi-scale filtering, and the segmentation of these structures using level set methods. We have proposed new schemes in both fields, and have combined them by using the output of the filtering as input to the segmentation. This chapter gives a summary of the work and restates the main conclusions of the results.

5.1 LINEAR STRUCTURE DETECTION

The overall goal of the thesis is to segment blood vessels which can be used for later simulation and processing. We model the vessels as linear structures, i.e. as lines and edges. We detect the lines and edges of the vessels by using quadrature filters, which are complex pairs of line and edge filters. The local phase (the argument of the complex filter output), can be used to classify the "line"-ness and "edge"-ness of a pixel neighborhood. Also, we can study the zero-crossings of the real part and the imaginary part to identify the positions of edges and lines respectively.

A fundamental problem is that blood vessels typically vary significantly in width over an image. We approach this by applying the filtering scheme over multiple scales and integrate the scales by weighting the scales based on the magnitude of the filter output. This is motivated by the fact the magnitude measures the certainty of the structure indication at a given pixel.

We illustrated the filtering results using two medical images of the retina and aorta. Especially the aorta image, with vessel widths spanning five scales, shows the success in detecting both thin and thick blood vessels. By filtering for both edges and lines, the results contains precise measures for both the edges as well as the inside region of the vessels.

5.2 LEVEL-SET BASED SEGMENTATION

The second part of this thesis described the contributions to the field of level-set based segmentation. First, the general problem of "globalness" with the Chan-Vese model [Chan and Vese, 2001] was presented, and a solution for localizing the behavior was suggested. This can be practical for applications where generally a local solution is needed.

Next, we presented the idea on how to use the zero-crossings of the quadrature filter results for segmenting linear structures, and blood vessels in particular.
5.2 Level-set based segmentation

This was motivated geometrically by the positive and negative values of the filter result which acted as "forces", pushing a curve towards the edges of vessels. The idea was natural for implementation using level set methods.

Later, we showed how the geometrically motivated level set speed function can be formulated as the solution of an energy optimization. This provided the formalization of alternative optimization schemes, which can be used to overstep local minima solutions and improve the rate of convergence. Apart from the varying width, another fundamental problem in the segmentation of blood vessels is that the contrast changes over the image. This is mainly due to technical constructions in the imaging modality and varying contrast agent concentrations. In addition, plaques and stenoses can produce visible "gaps" along a vessel structure, making it hard to extract a completely connected vessel tree. These problems, naturally occurring in the imaging of blood vessels, lead to that typical level set segmentation techniques often produce local solutions, where disconnected parts of the vessel tree are missed. The goal of the alternative optimization schemes is to overstep such "gaps" in the vessels, thereby converging to a better solution or segmentation. Using the retinal image, the results showed improvements over traditional methods. It is, however, future work to study the validity of the solutions, i.e. that the vessels are segmented correctly.
CHAPTER 6

FUTURE WORK

Ideas for future work can, like the rest of this thesis, be divided into filtering and segmentation. In addition, an important part of the future work is to design robust and fair methods for evaluating the actual segmentation results. This is very important for the clinical application and usability of these algorithms.

6.1 Filtering

A problem with traditional designs of quadrature filters is “ringing” effects in the filter output, caused by a wrap-around of the local phase in the filter output (wrap-around from $\pi$ to $-\pi$ can be seen in Figure 2.11(c)). This can produce false structure detection when identifying edges and lines by the zero-crossings of the real and imaginary parts. In practice, this would result in repeated “rings” around the true structure. The effects of this is currently under investigation.

A problem with the current filter output is that linear structures also include planes in three dimensions. So currently, there is no distinction between a blood vessel or other sufficiently flat structures, such as the skull, in volumetric medical images. This is why our results for such data only include proof-of-concept results. However, the output from quadrature filters can also be used to construct a tensor representation of the local structure in a point. We plan to use this in future work to mask out plane-like objects which can be detected by the tensor. The major challenge with this idea is using the tensor information across multiple scales.

6.2 Segmentation

The major problem with the current level set approach for segmentation is the long execution time, especially for volumetric images. Because of this, tweaking the parameters, e.g. for regularization, can be cumbersome. This is typical for level set methods and can be improved somewhat with optimized implementations. However, since the segmentation model is basically formulated as a “soft threshold” on the zero-crossing of the filter output, applying the full level set framework is likely overkill. Thus, future work includes investigating alternative, probably simpler, methods for segmentation based on the filter output.
CHAPTER 7

OVERVIEW OF PAPERS

PAPER I

The “active contours without edges” by Chan and Vese [2001] is a segmentation model with two major benefits: it can detect objects with very fuzzy edges and it tends to produce global solutions, independent of the initialization. However, for applications where a user wants to target a specific object in an image, the global behavior can also be the major weakness of the method. This paper identifies this problem and suggests a modification by restricting the computational dependence to a region-of-interest selected in a user interface based on topological analysis of the data.

PAPER II

This paper presents a method for segmenting blood vessels in medical images. It is based on two different components. First, we assume that blood vessels can be described as lines and edges and use filter techniques for detecting such structures. To handle vessels of varying width, the filtering is applied in a scale pyramid and the scales are integrated. Then, the filter output is used as input to a standard level set model for segmentation.

PAPER III

Level set models for segmentation can be derived by optimizing an energy functional depending on a curve and image terms. This derivation includes a gradient descent search in the space of curves. It is well known that gradient descent search suffers from sensitivity to local optima and poor convergence compared to other, more sophisticated, optimization schemes. In this paper we suggest the application of so called gradient descent with momentum for level-set based segmentation to relieve some of these drawbacks.

PAPER IV

The motivation for this paper is the same as for Paper III. In this paper, we study the effect of using the resilient back-propagation (Rprop) optimization scheme in the context of level set segmentation.
This is an extended journal version of Paper II which further investigates parameters of the method (mainly the multi-scale integration) and describes an energy formulation of the level set model for segmentation.


BIBLIOGRAPHY


