## Retinal Image Analysis: From Fundus Images to OCT Images

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#### **1** INTRODUCTION

Unlike the 2D fundus images which are now widely available at high-street opticians, the OCT is relatively new, and it is the first technique that offers the possibility of 3D imaging with the additional dimension going deep underneath the retina, and even with reach to the choroid.

Layer segmentation of the retina is one of the early processes of OCT retina image analysis, but it has already played an important role in clinics. For example, the thickness profile of the Retinal Nerve Fiber Layer (RNFL), which can be calculated directly from the segmented layer, has been used in a standard protocol for diagnosis of glaucoma. Also, the structure of retina can change dramatically during disease. An automatic segmentation of the layers can provide the critical information for abnormality detection, e.g. against the population average, or monitoring the disease progression, e.g. against previous scans.

The work included in this report has been published previously in the following journals and conferences: (Dodo et al., 2019d) (Dodo et al., 2019c) (Dodo et al., 2019b) (Dodo et al., 2019a) (Dodo et al., 2018a) (Dodo et al., 2018b) (Eltayef et al., 2017b) (Dodo et al., 2017) (Eltayef et al., 2017a) (Wang et al., 2017) (Eltayef et al., 2016a) (Eltayef et al., 2016b) (Wang et al., 2015b) (Wang et al., 2015c) (Wang et al., 2015a) (Kaba et al., 2015) (Kaba et al., 2014) (Kaba et al., 2013) (Salazar-Gonzalez et al., 2014) (Salazar-Gonzalez et al., 2012a) (Salazar-Gonzalez et al., 2012b) (Salazar-Gonzalez et al., 2011) (Salazar-Gonzalez et al., 2010)

### 2 2D FUNDUS RETINA IMAGES

# 2.1 Segmentation of the blood vessels and optic disk in retinal images

Retinal image analysis is increasingly prominent as a nonintrusive diagnosis method in modern ophthalmology. In this paper, we present a novel method to segment blood vessels and optic disk in the fundus retinal images. The method could be used to support nonintrusive diagnosis in modern ophthalmology since the morphology of the blood vessel and the optic disk is an important indicator for diseases like diabetic retinopathy, glaucoma, and hypertension. Our method takes as first step the extraction of the retina vascular tree using the graph cut technique. The blood vessel information is then used to estimate the location of the optic disk. The optic disk segmentation is performed using two alternative methods. The Markov random field (MRF) image reconstruction method segments the optic disk by removing vessels from the optic disk region, and the compensation factor method segments the optic disk. (Salazar-Gonzalez et al., 2014)

# 2.2 MRF reconstruction of retinal images for the optic disc segmentation

The retinal image analysis has been of great interest because of its efficiency and reliability for optical diagnosis. Different techniques have been designed for the segmentation of the eye structures and lesions. In this paper we present an unsupervised method for the segmentation of the optic disc. Blood vessels represent the main obstruction in the optic disc segmentation process. We made use of our previous work in blood vessel segmentation to perform an image reconstruction using the Markov Random Field formulation (MRF). As a result the optic disc appears as a well defined structure. A traditional graph is then constructed using spatial pixel connections as boundary term and the likelihood of the pixels belonging to the foreground and background seeds as regional term. Our algorithm was implemented and tested on two public data sets, DIARETDB1 and DRIVE. (Salazar-Gonzalez et al., 2012a)

# 2.3 Automatic graph cut based segmentation of retinal optic disc by incorporating blood vessel compensation

Glaucoma is one of the main causes of blindness worldwide. Periodical retinal screening is highly recommended in order to detect any sign of the disease and apply the appropriated treatment. Different systems for the analysis of retinal images have been designed in order to assist this process. The segmentation of the optic disc is an important step in the development of a retinal screening system. In this paper we present an unsupervised method for the segmentation of the optic disc. The main obstruction in the optic disc segmentation process is the presence of blood vessels breaking the continuity of the object. While many other methods have addressed this problem trying to eliminate the vessels, we have incorporated the blood vessel information into our formulation. The blood vessels inside of the optic disc are used to give continuity to the object to segment. Our approach is based on the graph cut technique, where the graph is constructed by considering the relationship between neighbouring pixels and by the likelihood of them belonging to the foreground and background from prior information. Our method was tested on two public datasets, DIARETDB1 and DRIVE. The performance of our method was measured by calculating the overlapping ratio (Oratio), sensitivity and the mean absolute distance (MAD) with respect to the manually labeled images. (Salazar-Gonzalez et al., 2012b)

#### 2.3.1 Optic disc segmentation by incorporating blood vessel compensation

Glaucoma is one of the main causes of blindness worldwide. Segmentation of vascular system and optic disc is an important step in the development of an automatic retinal screening system. In this paper we present an unsupervised method for the optic disc segmentation. The main obstruction in the optic disc segmentation process is the presence of blood vessels breaking the continuity of the object. While many other methods have addressed this problem trying to eliminate the vessels, we have incorporated the blood vessel information into our formulation. The blood vessel inside of the optic disc are used to give continuity to the object to segment. Our approach is based on the graph cut technique, where the graph is constructed considering the relationship between neighboring pixels and by the likelihood of them belonging to the foreground and background from prior information. (Salazar-Gonzalez et al., 2011)

#### 2.4 Retinal blood vessel segmentation via graph cut

Image analysis is becoming increasingly prominent as a non intrusive diagnosis in modern ophthalmology. Blood vessel morphology is an important indicator for diseases like diabetes, hypertension and retinopathy. This paper presents an automated and unsupervised method for retinal blood vessels segmentation using the graph cut technique. The graph is constructed using a rough segmentation from a pre-processed image together with spatial pixel connection. The proposed method was tested on two public datasets and compared with other methods. Experimental results show that this method outperforms other unsupervised methods and demonstrate the competitiveness with supervised methods. (Salazar-Gonzalez et al., 2010)

#### 2.5 Level set segmentation of optic discs from retinal images

Analysis of retinal images can provide important information for detecting and tracing retinal and vascular diseases. The purpose of this work is to design a method that can automatically segment the optic disc in the digital fundus images. The template matching method is used to approximately locate the optic disc centre, and the blood vessel is extracted to reset the centre. This is followed by applying the Level Set Method, which incorporates edge term, distance-regularization term and shape-prior term, to segment the shape of the optic disc. Seven measures are used to evaluate the performance of the methods. The effectiveness of the proposed method is evaluated against alternative methods on three public data sets DRIVE, DIARETDB1 and DIARETDB0. The results show that our method outperforms the state-of-the-art methods on these datasets. (Wang et al., 2015a)

#### 2.6 Segmentation of retinal blood vessels using gaussian mixture models and expectation maximisation

In this paper, we present an automated method to segment blood vessels in fundus retinal images. The method could be used to support a non-intrusive diagnosis in modern ophthalmology for early detection of retinal diseases, treatment evaluation or clinical study. Our method combines the bias correction to correct the intensity inhomogeneity of the retinal image, and a matched filter to enhance the appearance of the blood vessels. The blood vessels are then extracted from the matched filter response image using the Expectation Maximisation algorithm. The method is tested on fundus retinal images of STARE dataset and the experimental results are compared with some recently published methods of retinal blood vessels segmentation. The experimental results show that our method achieved the best overall performance and it is comparable to the performance of human experts. (Kaba et al., 2013)

#### 2.7 Retinal blood vessels extraction using probabilistic modelling

The analysis of retinal blood vessels plays an important role in detecting and treating retinal diseases. In this review, we present an automated method to segment blood vessels of fundus retinal image. The proposed method could be used to support a non-intrusive diagnosis in modern ophthalmology for early detection of retinal diseases, treatment evaluation or clinical study. This study combines the bias correction and an adaptive histogram equalisation to enhance the appearance of the blood vessels. Then the blood vessels are extracted using probabilistic modelling that is optimised by the expectation maximisation algorithm. The method is evaluated on fundus retinal images of STARE and DRIVE datasets. The experimental results are compared with some recently published methods of retinal blood vessels segmentation. (Kaba et al., 2014)

### **3 3D OCT Retina Images**

#### **3.1 Retinal OCT Segmentation Using Fuzzy Region Competition and Level Set Methods**

Optical coherence tomography (OCT) is a noninvasive imaging modality that provides in-depth images of the retina. Properties of individual layers on OCT have become important markers for diagnosing and tracking medication of various eye diseases in current ophthalmology. Manual segmentation of OCT scans posed many challenges (errors, inconsistency), which can be addressed by automated segmentation methods. Level set method is one of the most popular methods in the literature used for this purpose. Although level set methods have a fundamental way of handling topological changes, the weak boundaries and noise in addition to inhomogeneity in OCT images make it difficult to segment the layers accurately. Inspired by the concept of region competition, we incorporate prior knowledge of the retinal structure to segment nine (9) layers of the retina. (Dodo et al., 2019d)

#### 3.2 Level Set Segmentation of Retinal OCT Images

Optical coherence tomography (OCT) yields high-resolution images of the retina. Reliable identification of the retinal layers is necessary for the extraction of clinically useful information used for tracking the progress of medication and diagnosis of various ocular diseases. Many automatic methods have been proposed to aid with the analysis of retinal layers, mainly, due to the complexity of retinal structures, the cumbersomeness of manual segmentation and variation from one specialist to the other. However, a common drawback suffered by existing methods is the challenge of dealing with image artefacts and inhomogeneity in pathological structures. In this paper, we embed prior knowledge of the retinal architecture derived from the gradient information, into the level set method to segment seven (7) layers of the retina. Mainly, we start by establishing the region of interest (ROI). The gradient edges obtained from the ROI are used to initialise curves for the layers, and the layer topology is used in constraining the evolution process towards the actual layer boundaries based on image forces. Experimental results show our method obtains curves that are close to the manual layers labelled by experts. (Dodo et al., 2019a)

#### **3.3** Automatic Annotation of Retinal Layers in Optical Coherence Tomography Images

Early diagnosis of retinal OCT images has been shown to curtail blindness and visual impairments. However, the advancement of ophthalmic imaging technologies produces an ever-growing scale of retina images, both in volume and variety, which overwhelms the ophthalmologist ability to segment these images. While many automated methods exist, speckle noise and intensity inhomogeneity negatively impacts the performance of these methods. We present a comprehensive and fully automatic method for annotation of retinal layers in OCT images comprising of fuzzy histogram hyperbolisation (FHH) and graph cut methods to segment 7 retinal layers across 8 boundaries. The FHH handles speckle noise and inhomogeneity in the preprocessing step. Then the normalised vertical image gradient, and it's inverse to represent image intensity in calculating two adjacency matrices and then the FHH reassigns the edge-weights to make edges along reti-

nal boundaries have a low cost, and graph cut method identifies the shortest-paths (layer boundaries). The method is evaluated on 150 B-Scan images, 50 each from the temporal, foveal and nasal regions were used in our study. Promising experimental results have been achieved with high tolerance and adaptability to contour variance and pathological inconsistency of the retinal layers in all (temporal, foveal and nasal) regions. The method also achieves high accuracy, sensitivity, and Dice score of 0.98360, 0.9692 and 0.9712, respectively in segmenting the retinal nerve fibre layer. The annotation can facilitate eye examination by providing accurate results. The integration of the vertical gradients into the graph cut framework, which captures the unique characteristics of retinal structures, is particularly useful in finding the actual minimum paths across multiple retinal layer boundaries. Prior knowledge plays an integral role in image segmentation. (Dodo et al., 2019b)

#### 3.4 Graph-Cut Segmentation of Retinal Layers from OCT Images

The segmentation of various retinal layers is vital for diagnosing and tracking progress of medication of various ocular diseases. Due to the complexity of retinal structures, the tediousness of manual segmentation and variation from different specialists, many methods have been proposed to aid with this analysis. However image artifacts, in addition to inhomogeneity in pathological structures, remain a challenge, with negative influence on the performance of segmentation algorithms. Previous attempts normally pre-process the images or model the segmentation to handle the obstruction but it still remains an area of active research, especially in relation to the graph based algorithms. In this paper we present an automatic retinal layer segmentation method, which is comprised of fuzzy histogram hyperbolization and graph cut methods to segment 8 boundaries and 7 layers of the retina on 150 OCT B-Sans images, 50 each from the temporal, nasal and centre of foveal region. Our method shows positive results, with additional tolerance and adaptability to contour variance and pathological inconsistency of the retinal structures in all regions. (Dodo et al., 2019c) (Dodo et al., 2018a) (Dodo et al., 2018b)

#### **3.5 Retinal OCT Image Segmentation Using Fuzzy Histogram** Hyperbolization and Continuous Max-Flow

The segmentation of retinal layers is vital for tracking progress of medication and diagnosis of various eye diseases. To date many methods for the analysis exist, however the speckle noise and shadows of retinal blood vessel remains a challenge, with negative influence on the performance of segmentation algorithms. Previous attempts have been focused on image preprocessing or developing sophisticated models for segmentation to address this problem, but it still remains an area of active research. In this paper we propose a simple yet efficient and computationally inexpensive method by using fuzzy histogram hyperbolization for enhancement technique, and continuous max-flow for segmentation of four retinal layers (Inner Limiting membrane, Retinal Nerve Fibre Layer, Outer segment and the Retinal Pigment Epithelium). The results show improvement in segmentation performance. (Dodo et al., 2017)

# **3.6** Automated Layer Segmentation of 3D Macular Images Using Hybrid Methods.

Spectral-Domain Optical Coherence Tomography (SD-OCT) is a non-invasive imaging modality, which provides retinal structures with unprecedented detail in 3D. In this paper, we propose an automated segmentation method to detect intraretinal layers in OCT images acquired from a high resolution SD-OCT Spectralis HRA+OCT (Heidelberg Engineering, Germany). The algorithm starts by removing all the OCT imaging artifects includes the speckle noise and enhancing the contrast between layers using both 3D nonlinear anisotropic and ellipsoid averaging filers. Eight boundaries of the retinal are detected by using a hybrid method which combines hysteresis thresholding method, level set method, multi-region continuous max-flow approaches. The segmentation results show that our method can effectively locate 8 surfaces for varying quality 3D macular images. (Wang et al., 2015b)

#### 3.7 Segmentation of Intra-retinal Layers in 3D Optic Nerve Head Images

Spectral-Domain Optical Coherence Tomography (SD-OCT) is a non-invasive imaging modality, which provides retinal structures with unprecedented detail

in 3D. In this paper, we propose an automated segmentation method to detect intra-retinal layers in SD-OCT images around optic nerve head acquired from a high resolution RTVue-100 SD-OCT (Optovue, Fremont, CA, USA). This method starts by removing all the OCT imaging artifacts including the speckle noise and enhancing the contrast between layers using the 3D nonlinear anisotropic. Afterwards, we combine the level set method, k-means and MRF method to segment three intra-retinal layers around optical nerve head. The segmentation results show that our method can effectively delineate the surfaces of the retinal tissues in the noisy 3D optic nerve head images. (Wang et al., 2015c)

# **3.8 Retina Layer Segmentation Using Kernel Graph Cuts and Continuous Max-Flow.**

Circular scan Spectral-Domain Optic Coherence Tomography imaging (SD-OCT) is one of the best tools for diagnosis of retinal diseases. This technique provides more comprehensive detail of the retinal morphology and layers around the optic disc nerve head (ONH). Since manual labelling of the retinal layers can be tedious and time consuming, accurate and robust automated segmentation methods are needed to provide the thickness evaluation of these layers in retinal disorder assessments such as glaucoma. The proposed method serves this purpose by performing the segmentation of retinal layers boundaries in circular SD-OCT scans acquired around the ONH. The layers are detected by adapting a graph cut segmentation technique that includes a kernel-induced space and a continuous multiplier based max-flow algorithm. (Kaba et al., 2015)

### 4 Choroidal Layer Segmentation

#### 4.1 Automatic choroidal layer segmentation using markov random field and level set method

The choroid is an important vascular layer that supplies oxygen and nourishment to the retina. The changes in thickness of the choroid have been hypothesized to relate to a number of retinal diseases in the pathophysiology. In this paper, an automatic method is proposed for segmenting the choroidal layer from macular images by using the level set framework. The three-dimensional nonlinear anisotropic diffusion filter is used to remove all the optical coherence tomography (OCT) imaging artifacts including the speckle noise and to enhance the contrast. The distance regularization and edge constraint terms are embedded into the level set method to avoid the irregular and small regions and keep information about the boundary between the choroid and sclera. Besides, the Markov random field method models the region term into the framework by correlating the single-pixel likelihood function with neighborhood. (Wang et al., 2017)

### 5 Melanoma Detection from Dermoscopy Images

#### 5.1 Skin Cancer Detection in Dermoscopy Images Using Sub-Region Features

In the medical field, the identification of skin cancer (Malignant Melanoma) in dermoscopy images is still a challenging task for radiologists and researchers. Due to its rapid increase, the need for decision support systems to assist the radiologists to detect it in early stages becomes essential and necessary. Computer Aided Diagnosis (CAD) systems have significant potential to increase the accuracy of its early detection. Typically, CAD systems use various types of features to characterize skin lesions. The features are often concatenated into one vector (early fusion) to represent the image. In this paper, we present a novel method for melanoma detection from images. First the lesions are segmented by combining Particle Swarm Optimization and Markov Random Field methods. Then the K-means is applied on the segmented lesions to separate them into homogeneous clusters. (Eltayef et al., 2017a)

#### 5.2 Lesion Segmentation in Dermoscopy Images Using Particle Swarm Optimization and Markov Random Field

Malignant melanoma is one of the most rapidly increasing cancers globally and it is the most dangerous form of human skin cancer. Dermoscopy is one of the major imaging modalities used in the diagnosis of melanoma. Early detection of melanoma can be helpful and usually curable. Due to the difficulty for dermatologists in the interpretation of dermoscopy images, Computer Aided Diagnosis systems can be very helpful to facilitate the early detection. The automated detection of the lesion borders is one of the most important steps in dermoscopic image analysis. In this paper, we present a fully automated method for melanoma border detection using image processing techniques. The hair and several noises aredetected and removed by applying a bank of directional filters and Image Inpainting method respectively. (Eltayef et al., 2017b)

#### 5.3 Detection of Pigment Networks in Dermoscopy Images

One of the most important structures in dermoscopy images is the pigment network, which is also one of the most challenging and fundamental task for dermatologists in early detection of melanoma. This paper presents an automatic system to detect pigment network from dermoscopy images. The design of the proposed algorithm consists of four stages. First, a pre-processing algorithm is carried out in order to remove the noise and improve the quality of the image. Second, a bank of directional filters and morphological connected component analysis are applied to detect the pigment networks. Third, features are extracted from the detected image, which can be used in the subsequent stage. Fourth, the classification process is performed by applying feed-forward neural network, in order to classify the region as either normal or abnormal skin. (Eltayef et al., 2016a)

#### 5.4 Detection of Melanoma Skin Cancer in Dermoscopy Images.

Malignant melanoma is the most hazardous type of human skin cancer and its incidence has been rapidly increasing. Early detection of malignant melanoma in dermoscopy images is very important and critical, since its detection in the early stage can be helpful to cure it. Computer Aided Diagnosis systems can be very helpful to facilitate the early detection of cancers for dermatologists. In this paper, we present a novel method for the detection of melanoma skin cancer. To detect the hair and several noises from images, pre-processing step is carried out by applying a bank of directional filters. And therefore, Image inpainting method is implemented to fill in the unknown regions. Fuzzy C-Means and Markov Random Field methods are used to delineate the border of the lesion area in the images. (Eltayef et al., 2016b)

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