CHAPTER 1

INTRODUCTION

Detection of retinal anatomical features is crucial to clinically assess the health of the retina. Automated diagnostic system helps in accurately detecting the optic disc (OD). The OD detection procedure further assists in detecting other anatomical features such as retinal blood vessels, macula, optic cup, and lesions (Gagnon.L et al. (2001)). In particular, the OD detection is extremely useful in diagnosing a retinopathy condition called glaucoma, which is the leading cause of blindness next to the cataract (Kingman.S (2004)).

According to Nayak.J et al. (2004), the glaucoma affects one in two hundred individuals around the age of 50, and one in ten above 80 years. Moreover, the detrimental effects of glaucoma surface only at a later stage, and hence it is commonly known as the ‘Sneak thief of sight’. If glaucoma is detected at an early stage, the progression of the disease is retarded (Johnson.C.A (2009)). In other words, the structural change in the OD provides vital clues concerning the prognosis of glaucoma. Fueled by the diagnostic and prognostic significance, automatic OD detection schemes have been attempted by many and their design still remains as a vibrant research area (Tiilikainen.N.P. (2007)).

An accurate OD segmentation with computer-aided techniques faces several challenges due to factors that are common to other medical images, for in-
stance, boundary inefficiencies—missing edges and/or inadequate texture contrast between regions of interest (ROIs) and the background. On the other hand, manually segmenting the OD is not deemed admissible, since it is subject to impediments such as limited perception of the human eye, fatigue, and the availability of voluminous fundus image data. Therefore, developing algorithms that reliably detects accurate OD boundaries with less computational overheads is an imperative research goal. To provide an overview of the research efforts along this direction, a brief survey on the state-of-the-art OD segmentation schemes is carried out.

In view of the inherent advantages of active contour models (ACMs), efforts have been made to make use of ACMs in OD segmentation tasks. In general, ACMs have been used in image segmentation applications (Caselles.V et al. (1997)). They are based on profound mathematical properties and efficient level-set-based numerical schemes. It is possible to achieve a sub-pixel accuracy of object boundaries with the ACMs. They lend themselves to incorporate apriori knowledge, e.g., shape and intensity distribution. Furthermore, they are implemented to exploit several properties, e.g., edges, statistics, and texture, which are normally considered by other segmentation procedures. Besides producing quite regular contours, the segmented regions possess continuous boundaries. In addition, the level set based contour models offers a lot of exibility in their implementation (Shi and Karl (2008)).

Notwithstanding a dedicated research effort in the design of ACM-based image segmentation tools, as far as it is known, a rigorous comparison of a wide range of ACM techniques has not yet been reported in the context of the OD segmentation. In fact, empirical results from an exhaustive study involving popular ACM methods on a large collection of retinal images would be suggestive of the kind of ACM scheme to be advocated in the design of a fully automated OD segmentation system for clinical screening purposes. A methodical comparison of the OD segmentation results from ten theoretically well-established ACM techniques
is substantiated. The ACM models are supplied with 169 diverse retinal fundus images annotated by five domain experts. All the ACM algorithms were initialized with a contour obtained by a morphological process and the Circular Hough Transform (CHT). The initial contour of the CHT is unaltered and kept at 100% for Xu-ACM, Patrick-ACM and Chan-ACM as the segmentation is accurate in these models. For the other models the initial contour is altered to provide better results.

1.1 ANATOMY OF THE EYE

A brief anatomical overview of the human eye and the retina is described in this section. The most used among the five senses of the human body is the vision and the eye perceives most of the information about the world (Wikipedia (2008a)). A considerable portion of the brain is used in visual processing. Each eye is a slightly asymmetric globe of approximately 2.5 cm diameter. The front part of the eye includes:

- The iris (the pigmented part)
- The cornea (a clear dome over the iris)
- The pupil (the black circular opening in the iris that lets light in)
- The sclera (the white part)
- The conjunctiva (a thin layer of tissue covering the front of the eye, except the cornea)

Figure 1.1 shows the anatomy of the eye. The main function of the eye is to target any object, focus and gather light from the object and transmit a very clear image to the light-sensitive tissues. The image is received and processed initially by these tissues that line the rear part of the eye. The image is then transmitted
by electrical impulses that travels along the optic nerve, which is a nerve that connects the rear part of the eye to the complex brain. The brain connects the optic nerves from both the eyes to produce images that are merged in such a way to give binocular vision. Visual cortex is the part of the brain which receives these visual messages. It lies behind the brain. From the visual cortex, connections reach out to many other parts of the brain. The raw input from the eyes themselves is subjected to very high-level processing of the basic electrical impulses which results in the sight.

**Cornea:** This is the clear front part of the eye. Only clear images enter the inside of the eye as the dense leathery wall present is specialized to make it perfectly clear. Gross abnormalities and dryness of the surface cells are the problems caused due to Vitamin A deficiency (called Nutritional Blindness). It acts as a powerful lens to refract or focus the light from an object. The cornea gets affected by trauma, or by infections such as trachoma, and by nutritional blindness. The major sight-affecting problems in developing parts of the world are the trachoma and nutritional blindness, where many people live in poverty. Impoverished agri-
cultural communities are subjected to trauma more and as a result it is an important cause of vision loss in them.

**Iris:** This controls the amount of light entering the eye and acts as a diaphragm or circular shutter. The beautiful colour of the eye is due to the iris. The amount and type of pigment in the iris creates the eye colour. A person’s eye colour is due to multiple genes inherited from each parent.

**Lens:** This is similar to the camera lens, but it is made up of a clear specialized protein structure which helps focus the images. The eye’s focusing power is adjusted according to whether the object being viewed is close or farther away. All light entering the eye is focused there, hence the lens loses its clarity in light transmission and is affected severely due to this. This clarity loss is called cataract. It is the first major cause of blindness in the world today. Cataract is treatable, but it is not preventable.

**Vitreous Gel:** The main volume of the eye is a clear, firm jelly that helps to support its internal structure.

**Ciliary Body:** The ciliary body allows clear fine focusing of objects. It has a muscle that changes the shape of the lens according to the focus of the eye. It is a gland which produces a watery fluid, the aqueous fluid. The pressure inside the eye is raised due to the balance between the production and the drainage of the aqueous fluid.

**Retina:** The Retina is the nerve tissue which lines the inside of the eye. The inside lining of the eye is covered by special light-sensing cells that are collectively called the retina. The retina, a layered tissue, converts the incoming light signal into a neural signal suitable for it to be processed by the brain. It consists of very finely layered and delicate nerve tissue. When anyone views an object they use the central part of the retina called the macula. The greatest concentration of light-sensitive cells, called photoreceptors is present in this area and hence it is af-
ected by many diseases. Rods and cones in the retina provide sensation of vision to the human eye, which includes colour differentiation and perception of depth.

The retina converts light into electrical impulses. Behind the eye, the optic nerve carries these impulses to the brain. The macula is a small extra-sensitive area within the retina that gives central vision. It is located in the center of the retina and contains the fovea, a small depression or pit at the center of the macula that gives the clearest vision. Due to the ageing change in the central part, the macula, macular degeneration is caused. The effects of diabetes on the retina, causes diabetic retinopathy. Macular degeneration is the main cause of untreatable visual impairment in developed countries and is highly crucial to treat. Early detection of diabetic retinopathy is needed and it is treated with laser before it becomes too advanced. Since diabetes is more common these days it is becoming a rapidly critical problem worldwide.

**Optic Nerve:** The fine nerve fibres which come from all over the retina form the structure called the Optic Nerve. They are gathered into a bundle, where they all join and pass through a fine grid of tiny holes in the wall of the eye. It then extends back, like a fine cable, taking the impulses to the brain. The optic nerve get damaged, if the pressure within an eye is too high at the optic nerve. This condition is called glaucoma. There are many common ways for the pressure to become critically high. People’s vulnerability to this damage is highly variable. Glaucoma is one of the major cause of blindness and visual impairment throughout the world (Kingman.S (2004)). Blindness is caused by all of these conditions. The retina consists of approximately one million nerve fibers, which group together to form the optic nerves.

The beginning of the optic nerves in the retina is called the optic nerve head (ONH) or optic disc (OD), which is circular in shape and visibly bright in the fundus images. In one particular area there are no photoreceptors, namely, cones and rods, in the ONH, it cannot respond to the light stimulation, and hence known
as the 'blind spot'. The optic nerves departing from the eye form a natural deep sloping region which is cup shaped, called the neuroretinal rim. The appearance of retina in normal fundus images is transparent and the retinal arterioles and venules run in the nerve fiber layer of the retina and are the only part of the retina readily visible on fundoscopy (Akram and Rubinstein (2005)). The reddish orange glow of the fundus is generated by reflection from the choroids, which is a rich network of blood vessels sandwiched between the retina and the sclera.

The outer wall of the eye is only quite tough as all of these tissues are finely structured and most of them are quite delicate. The eye is placed in a well-protected cavity in the face, which is called the orbit where it is surrounded by bone which is rigid in parts and able to crumple in other parts. The other tissues need to be protected. A good protection system is needed for the eye. The various reflex mechanisms protect the eye. Several diseases affect the retina and a brief overview of the retinal diseases is presented below. Figure 1.2 depicts an image captured through a fundus camera.

![Figure 1.2: A Retinal Fundus Image - Staal.J.J et al. (2004).](image-url)
1.2 GLAUCOMA

Glaucoma is a group of eye diseases that causes a progressive characteristic damage of the eye nerve (called the optic nerve that is responsible for vision). Patients with glaucoma have an associated visual field loss for which elevated intraocular pressure is one of the primary risk factors. The intraocular pressure is the measure of the pressure within the eye ball. In general, patients with glaucoma have high intraocular pressure, but in a few patients the pressure is low. The fundamental mechanisms related to glaucoma are still unknown, which complicates the task of early screening and treatment of specific sub populations.

Early diagnosis of glaucoma is essential to bring awareness among the people. In the event that patients are left untreated, most sorts of glaucoma will result in patients to have a bit by bit intensifying vision loss and results in visual impairment. Visual harm is for the most part irreversible, and this has prompted glaucoma being depicted as the ‘sneak thief of sight’. Nearly half of affected persons in the developed nations are not in any case mindful of having glaucoma. This number raises to 90% in under developed parts of the world which is truly disturbing as persons in these nations have less probable chance of treatment.

As the world population ages, glaucoma has now become an indisputably prominent cause of optical incapacitation. World Health Organization (WHO) statistics show that glaucoma is now the second leading cause of visual impairment globally, after cataracts (Grau et al. (2006), Quigley.H.A and Broman.A.T (2006)). Whilst cataract disease is a curable one, glaucoma, however, represents perhaps an even more preponderant public health challenge than cataracts, because the visual impairment it causes is irreversible. Glaucoma is now accepted globally and by the WHO that it is the number one cause of irreversible visual impairment.

The main reason why glaucoma has now become the second leading cause of optical incapacitation is due to the more immensely colossal aged pop-
ulation in the world. Since 1990, the world population aged over 50 years has increased by 30% (Kingman.S (2004)). In developed countries, the increase in the number of people over 50 was 16%, but in developing countries it was 47%. From 2002, the statistics shows that there are about 37 million people blind worldwide. More than 82% of all blind people are 50 years and older. 12% of all blind persons worldwide are due to glaucoma (approximately 4.5 million) and this is expected to increase approximately by 79 million in 2020. Patients visit to hospitals for a checkup of glaucoma is very expensive. The ophthalmologist visit, surgical procedures related to glaucoma, medications, and various other indirect costs and related services increase the annual cost for the checkup of glaucoma enormously.

1.3 RETINOPATHY CONDITIONS

Grau et al. (2006), Quigley.H.A and Broman.A.T (2006) have cited that glaucoma, a chronic disease that affects the optic nerves is the second major cause of blindness in the world leading to losses in the visual field and eventual blindness. Various risk factors associated with glaucoma have been identified, among which the significant one is the raised intra ocular pressure (IOP) that destroys the blood vessels and optic nerves. If glaucoma is left untreated, it leads to permanent damage of the optic nerves and cause blindness. This progressive and irreversible damage to the optic nerves is often accompanied by only subtle signs or even no symptoms, and therefore it is nicknamed as the ‘sneak thief of sight’. Figure 1.3 depicts the different stages of glaucoma as it progresses (Fumero.F et al. (2011)). An early detection of glaucoma is important, which minimizes the damage and the vision loss, and ensure a prompt and adequate treatment.

For an early glaucoma detection, a variety of criteria such as size of the cup, narrowness of the remaining disc rim, vertical ovalness of the cup, and progressive changes in the cup are used (Sommer et al. (1979)). If the position,
Figure 1.3: Retinal Fundus Images of the ONH - Normal and Pathological eyes (a) No Glaucoma. (b) Early Glaucoma. (c) Moderate Glaucoma. (d) Deep Glaucoma.
center, and radius of the OD is detected precisely, it in turn is used as a reference for locating other anatomical regions, for instance, macula and fovea. The patients who complain about a patchy loss of peripheral vision or reduced clarity of colours are to be followed up for early glaucoma diagnosis.

Diabetic Retinopathy (DR) is a progressive pathology and is found in individuals who have diabetes mellitus for several years. It causes a group of lesions in the retina (Abrmoff et al. (2010)). The number and types of lesions present on the retina determine the severity of the disease. It is a disease which is caused due to the insufficient insulin - a hormone that moves sugar from the blood into the cells. Hence the amount of sugar in the blood increases which causes damages throughout the body including blood vessels in the eye. A fundus image with diabetic retinopathy (Kalesnykiene et al. (2006)) is shown in Figure 1.4.

![Figure 1.4: A Fundus Image with Diabetic Retinopathy](image)

In Diabetic Retinopathy, the blood vessels in the retina are affected and vision is lost. If left untreated, it leads to blindness. An over accumulation of glucose and/or fructose damages the tiny blood vessels in the retina. The first lesions which occurs most frequently as a consequence of DR, is the Microaneurisms (MAs) that appears on the side of the blood vessels as small swellings (Quellec et al. (2008)).
During the initial stage, one does not notice any change in vision. A condition called macular edema is developed by some, which occurs when the damaged blood vessels leak fluid and lipids onto the macula (Wikipedia (2008c)) which is the part of the retina that aids in vision. This fluid causes the macula to swell and results in blurred vision. As the disease progresses, blood vessels start to proliferate. Lack of oxygen in the retina causes damage and new blood vessels start to grow in the retina. As a result a clear gel-like vitreous humour fills the inside of the eye. Without timely treatment, these new blood vessels bleeds and lead to cloud vision destroying the retina. The longer a person has mellitus, the higher the risk of developing some ocular problem.

Age-related Macular Degeneration (AMD) (Journals (2012)), is a gradual, progressive, painless deterioration of the macula. It is a leading cause of blindness in people aged 60 and older. The appearance of spots beneath the retina marks the early stage of AMD.

Figure 1.5: Fundus photograph of neovascular Age-related Macular Degeneration

Figure 1.5 shows a fundus photograph (Visionaware (2012)) of an eye with neovascular AMD. These spots are small, round lesions called drusen that cause serious loss of vision. The loss of vision first starts in one eye, since the healthy eye will be compensating for the loss of vision in the damaged eye. It
begins with characteristic yellow deposits (drusen) in the macula with reference to Wikipedia (2008d). Most people with these early changes have good vision. People with drusen develop advanced AMD. The risk is higher when the drusen is large and numerous. Two forms of AMD exist: dry and wet. About 90 percent of those with AMD are affected by the former.

Although irreversible, many patients with dry AMD experience no symptoms, but experience only gradual and minimal changes in their vision clarity. In wet macular degeneration, fine blood vessels at the back of the eye proliferate and leak fluid and blood. Wet macular degeneration develops suddenly in patients with dry macular degeneration. Both forms of macular degeneration are painless and the condition typically affects both eyes. The Figure 1.6 shows the range of vision under normal and pathological conditions for the same picture under different retinopathic conditions. But these vision patterns occur only at a latter stage, when these visions occur, and hence early diagnosis is very important in the case of ocular diseases. Hence an automated diagnosis is essential for retinal diseases.

A new system, known as Retinal Image Vessel Extraction and Registration System (RIVERS), is used by retinal clinicians, researchers, and study directors as an integrated service for retinal image analysis to be used web based and online (Tsai et al. (2008)). The research work illustrates the computer-aided techniques developed for the detection of glaucoma, a disease that occurs in the retina causing deformation of the ONH. The ONH segmentation, the techniques used in determining the progression of the glaucoma is carried out in this research work.

1.4 MOTIVATION OF THE RESEARCH

The data in large scale screening programs usually comes from various operators at multiple locations with different equipment; hence there will be a large variability
Figure 1.6: Signs and Symptoms of Glaucoma, DR and AMD (a) A normal range of vision. (b) The same view with advanced vision loss from Glaucoma - Wikipedia (2008b). (c) The same view with advanced vision loss from DR - Wikipedia (2008c). (d) The same view with advanced vision loss from AMD - Wikipedia (2008d).
in the image acquisition process especially the illumination. The illumination in a fundus image is uneven primarily due to the imbalance of an optical aberration called vignetting, which is caused by improper focusing of light through an optical system. The brightness of the image, gradually decreases radially outward from the center part of the image. The capturing of the retinal image takes place from the inner rear surface of the eye ball through the pupil.

The exact properties of vignetting changes from image to image, since the position of the eye relative to the camera varies from image to image. The uneven illumination obstructs the absolute interpretations of the image. There is a natural variation in the appearance of the retina, which poses different problems like whether they are from the right or the left eye. The positioning of the lens is centered at various parts of the retina, which poses irregularities. Hence an accurate segmentation with computer-aided techniques faces several challenges due to factors that are common to other medical images, for instance, boundary insufficiencies/missing edges and/or inadequate texture contrast between regions of interest (ROIs) and the background.

On the other hand, manually segmenting the anatomical structures is not deemed admissible, since it is subject to impediments such as limited perception of the human eye, fatigue, and the availability of voluminous fundus image data. Therefore, developing algorithms that reliably detects accurate anatomical boundaries with less computational overheads is an imperative research goal. The normal and abnormal structures in retinal fundus images is extracted automatically and robustly with definite efforts. The automated system should be able to select images that have abnormalities in them. Computer colour image processing techniques have been applied to the analysis of retinal images as early as 1974. Many researchers are attracted in developing such automatic retinal image analyzing and diagnostic system since then. The difficulties faced by the researchers are mainly due to the noises, uneven illumination, and variation between different individuals.
The OD detection is extremely useful in diagnosing a retinopathy conditions called glaucoma, which is the leading cause of blindness next to the cataract. According to WHO, the glaucoma affects one in two hundred individuals around the age of 50, and one in ten above 80 years. Moreover, the detrimental effects of glaucoma surface only at a later stage, and hence the person will lose his sight and it is irreversible. Interestingly the detection of this disease at an early stage will help to retard its progression. In other words, the structural change in the OD provides vital clues concerning the prognosis of glaucoma. The diagnostic and prognostic significance makes automatic OD detection schemes to be attempted by many and their design still remains as a vibrant research area.

Changes in the structural appearance of the ONH and retinal nerve fiber layer (RNFL) often precede the development of visual field loss in glaucoma in 3-D analysis (Medeiros et al. (2004)). So far, such evaluation has predominantly been subjective and obtained with high intra and interobserver variability (Naithani et al. (2007), Ventura et al. (2006)). With the emergence of newer optical imaging techniques, assessment of optic disc morphology has become more objective and quantitative. In recent studies the morphology of the ONH has been utilized (Jonas et al. (1995)), as the large optic disc size is a risk factor for a glaucoma. The ONH is a circular area where the optic nerve fibers converge, hence as the glaucoma progresses, it causes the nerve fibers to atrophy and results in apparent changes in the shape of the ONH. Often, variability in the appearance of the ONH caused by the image contrast and obscurity by blood vessels warrants a subjective manual screening and analysis. A quantitative relationship exists in between ganglion cell density and visual sensitivity for the detection of human clinical glaucoma (Harwerth and Quigley (2006)).

In order to prevent people from getting blind due to glaucoma, a proper
medical treatment is necessary at an early stage. If a person is diagnosed with glaucoma at an early stage, the population of blindness due to glaucoma is considerably reduced. Hence automatic diagnosis is a necessary factor for mass screening programmes in aiding the doctors to identify people who are prone to glaucoma. This problem has been chosen as the research area to analyze the glaucoma and its various stages.

1.6 DISSERTATION OUTLINE

This thesis is organized as follows: Chapter 2 deals with literature survey and related works. Chapter 3 presents the pre-processing method with the experiments carried out on other available pre-processing algorithms. The experiments carried out to demonstrate the ONH segmentation using various Active Contour Models are explained in chapter 4. Chapter 5 talks about the results of the research and the database, which has been used for ONH segmentation for this thesis work. Chapter 6 discusses the experimental results carried out in this research. Finally chapter 7 concludes the research work.

Chapter 1 gives the overall introduction to the thesis. It describes the basics of retinal fundus images and the usefulness in optic disorders specifically on glaucoma diagnosis. Details on the eye anatomy and various other optical disorders is given. In addition to this summary of the research issues, motivation of the research and overview of this thesis are outlined.

Chapter 2 gives the literature survey on the different approaches taken to study the usefulness of retinal fundus images in diagnosing optic disorders using computer aided techniques. This chapter discusses about the pre-processing methods, ONH localization methods and ONH segmentation methods and their challenges. This chapter focuses on the human eye dynamics which gives an un-
derstanding on the origin of electrical signals which helps to understand the source localization problems.

Chapter 3 discusses the proposed pre-processing method that reduces the image variation by normalizing the original image with a reference model. Equalization of the irregular illuminations as noise present in the fundus image associated with retinal images are eradicated. Reducing the intra image as well as inter image variability is done. Pure glaucomatous changes are emphasized in the pre-processing step which excludes disease independent variations from the input images. These include variations due to image acquisition, such as inhomogeneous illumination or different ONH localizations and retinal structures not directly related to glaucoma, e.g., the blood vessel tree. Localization of the ONH is investigated in this chapter here.

Chapter 4 describes the methodology of the accurate selection of the OD region, the active contours that have to be drawn for the accurate detection of the OD boundary, as an accurate detection helps in assessing the progression of eye diseases. Data classification of normal and pathological eyes by an expert ophthalmologist is carried out and a comparison of various algorithms is presented.

Chapter 5 deals with the selection of specific algorithms for pre-processing, based on performance measures is elaborated. Assessment of ONH segmentation based on various ACM algorithms by the expert ophthalmologist was carried out and a comparison of various algorithms is presented.

Chapter 6 deals with statistical analysis and subjective assessment carried as part of the work for this research. Discussions on the experimental results is elaborated.

Chapter 7 concludes the research work. It explains how the proposed contrast limited adaptive histogram equalization combined with morphological processing is superior in identifying the localized OD using the Circular Hough
Transform. It summarizes about the various active contour models. Other contributions of this work is summarized with a mention of future areas of research that might be investigated to build up on the methods and findings proposed in this thesis.