CHAPTER 1

INTRODUCTION

1.1 MEDICAL IMAGE PROCESSING

Computer vision and image processing techniques play an important role in all fields of medical science and are especially relevant to modern Ophthalmology. Medical imaging has revolutionized the field of medicine by providing cost-effective healthcare and efficient diagnosis in all major disease areas. Medical imaging allows scientists and physicians to understand potential life-saving information using less invasive techniques. Applications that can interpret an image are being developed, which in turn can aid a physician in detecting possible subtle abnormalities. The computer indicates places in the image that require extra attention from the physician because they could be abnormal. These technologies known as Computer Aided Diagnosis (CAD) systems show that CAD can be helpful to improve diagnostic accuracy of physicians and lighten the burden of increasing workload.

The influence and impact of digital images on modern society, science, technology and art are tremendous. Image processing has become such a critical component in contemporary science and technology that many tasks would not be attempted without it. Digital image processing is an interdisciplinary subject that draws from synergistic developments involving many disciplines and is used in medical imaging, microscopy, astronomy, computer vision, geology and many other fields. The rapid and continuing progress in computerized medical imaging, the associated developments in
methods of analysis and computer-aided diagnosis, have propelled medical imaging into one of the most important sub-fields in scientific imaging. Medical image analysis is an area of research that attracts intensive interests of scientists and physicians and covers image processing, pattern recognition and computer visualization. Medical image processing involves the study of digital images with the objective of providing computational tools which will assist the quantification and visualization of interesting pathology and anatomical structures. The progress achieved in this field in recent years has significantly improved the type of medical care that is available to the patients.

The application of digital imaging to ophthalmology has now provided the possibility of processing retinal images to assist clinical diagnosis and treatment. Automated diagnosis of retinal fundus images using digital image analysis offers huge potential benefits. Due to advances in computer technology, medical diagnosis can be benefited from computers which will assist doctors to analyze medical data and images with improved accuracy. Designing and developing computer-aided diagnostic tools or systems for medical images is a fast growing area in recent years. Development of an automated system for analyzing the images of the retina will facilitate computer aided diagnosis of eye diseases. The interest towards automatic detection of glaucoma and diabetic retinopathy has been increasing along with the rapid development of digital imaging and computing power. However, the most important single event that attracted the wider attention of medical research community has been the decision to recognize digital imaging as an accepted modality to document eye fundus. This introductory chapter presents some background information on the anatomy of the eye, ocular diseases like glaucoma, diabetic retinopathy and the need for screening.
1.2 ANATOMY OF THE EYE

In the optical sciences, the human eye is often compared to a camera. Human eye is a complex biological device. The eye is approximately 1 inch (2.54 cm) wide, 1 inch deep and 0.9 inch (2.3 cm) tall. Light reflected from an object is focused on the retina after passing through the cornea, pupil and lens, which is similar to light passing through the camera optics to the film or a sensor. In the retina, the incoming information is received by the photoreceptor cells dedicated for detecting light. From the retina, the information is further transmitted to the brain via the optic nerve, where the sensation of sight is produced. During the transmission, the information is processed in the retinal layers. Guyton and Hall (1996) have described the anatomy of the eye and the structures involved in the image formation. Figure 1.1 illustrates the cross-section of human eye and points out its major components.

Figure 1.1 Cross section of the eye
There are three important features in the camera which can be seen analogous to the function of the eye: aperture, camera lens, and the camera sensor. In the eye behind the transparent cornea, the colored iris regulates the amount of light entering the eye by changing the size of the pupil. In the dark, the pupil is large allowing the maximum amount of light to enter, and in the bright the pupil is small preventing the eye to receive an excess amount of light. In the same way, the camera regulates the amount of light entering the camera with the aperture. In order for the eye to focus on objects at different distances, the ciliary muscle reshapes the elastic lens through the zonular fibers. For objects at short distances, the ciliary muscle contracts, zonular fibers loosen, and the lens thickens which results in high refractive power. When the ciliary muscle is relaxed, the zonular fibers stretch the lens into thin shaped and the distant objects are in focus. If the eye is properly focused, the light passes through the vitreous gel to the camera sensor of the eye that is the retina. The retina is the inner surface of the eye and consists of transparent tissue of several layers of cells designated to absorb and convert the light into neural signals. The order of the retinal layers is peculiar since the conversion is carried out by the light detecting photoreceptor cells on the layer which is in the back of the retina and furthest from the light. Thus, the light has to travel through the retinal layers before it reaches the photoreceptor cells. Once the light is detected, neural signals collected by the optic nerve are finally transmitted to the brain.

During transmission from the photoreceptor cells to the optic nerve, the electric impulses are further processed in the inner layers of the retina. Forrester et al (2001) explained that the detailed central vision formed in the macula is a highly light sensitive area 5 to 6 mm in diameter in the central region of the retina. The spot where the optic nerve and blood vessels exit the retina is called the optic disc. In the centre of the macula is a round shaped area known as fovea, where the cones are almost exclusively found. The
cones are photoreceptor cells selectively sensitive to different wavelengths of light. Next to the macula is the beginning of optic nerve from where the main artery and vein emerge in the retina.

Optic Disc (OD) is considered as one of the main features of a retinal fundus image and is located 3 to 4 mm to the nasal side of the fovea. It is vertically oval, with an average dimension of 1.76mm horizontally and 1.92mm vertically. There is a central depression, of variable size, called the optic cup. The optic nerve head is the location where ganglion cell axons exit the eye to form the optic nerve. There are no light sensitive rods or cones to respond to a light stimulus at this point. This causes a break in the visual field called the physiological blind spot. Millions of nerve fibers that run from the retina to the optic nerve meet at the optic disc. As fluid pressure within eye increases, it damages these sensitive nerve fibers and they begin to die. As they die, the disc begins to hollow and pushes the optic nerve into a cupped or curved shape. If the pressure remains too high for too long, the extra pressure can damage the optic nerve and result in loss of vision. The change in the shape, color or depth of OD is an indicator of various ophthalmic pathologies especially for glaucoma and to measure abnormal features.

OD is the brightest feature of the normal fundus, and it has approximately a slightly oval (elliptical) shape vertically and the size varies from one person to another, occupying about one tenth to one fifth of the image. In colored fundus images, the disc appears as a bright yellowish or white region and considered as the exit region of the blood vessels and the optic nerves from the retina. The optic nerve is a bundle of more than one million nerve fibers. As the nerve enters the eye, it is contracted and forms the optic disc or papilla.
The nutritional support to the retina is provided by the choroid, nerve fiber layer network and the connecting neuron layer network. The fovea is dependent on the choroidal blood supply from the vascular layer behind the retina (choroid). The presented anatomical parts (macula, fovea, capillaries, and optic nerve head), highlighted in Figure 1.1, are the relevant structures of the retina in terms of retinal diseases and for this work. A standard way of recording and tracking the extent of cupping as shown in Figure 1.2 is with the Cup to Disc (C/D) ratio or (CDR). The greater this ratio is, the greater is the apparent damage.

1.3 DISEASES CAUSED IN OPTIC NERVES AND OPTIC DISC

The various diseases caused in optic disc and optic nerves are as follows

- Glaucoma
- Diabetic Retinopathy
- Aplasia and Hypoplasia
- Morning glory syndrome
- Optic nerve pit
- Ischaemia and Infarction of the nerve tissue
There are a number of reasons that can cause reduced visual acuity, visual impairment, and blindness. The most common form of glaucoma is very slow to develop and in the early stages does not cause any pain, discomfort or change of vision. Early detection gives the best chance of successful control and hence regular eye examinations are essential. Acute glaucoma which has a sudden onset is not common but causes severe pain, headaches, nausea and foggy vision with halos around lights. In these cases immediate treatment is essential. In diabetic eye diseases, the cause of visual disturbances is related to the vascular changes. Effects of glaucoma and diabetic retinopathy on vision are shown in Figure 1.3.

(a) Normal vision

(b) Glaucoma

(c) Diabetic Retinopathy

Figure 1.3  Effect of glaucoma and retinopathy on vision
1.4 GLAUCOMA

Glaucoma is defined as a multi factorial optic neuropathy which results in damage to optic nerve fibers and consequent impairment of vision leading to blindness. Risk assessment of the disease goes a long way in diagnosis and management of the disease. Glaucoma is called the sneak thief of sight because it is usually symptom-less until significant vision loss has occurred. Worldwide, it is the second leading cause of blindness. Glaucoma affects one in two hundred of the people aged fifty and younger and one in ten over the age of eighty.

Glaucoma is an eye disorder in which the optic nerve suffers damage, permanently impairing vision in the affected eyes and progressing towards complete blindness if untreated. It is often, but not always, associated with increased pressure of the fluid in the eye. The term ocular hypertension is used for cases having constantly raised Intraocular Pressure (IOP) without any associated optic nerve damage. Conversely, the term normal or low tension glaucoma is suggested for the typical visual field defects when associated with a normal or low IOP.

Glaucoma is a disease caused by increased intraocular pressure resulting either from a malformation or malfunction of the eye’s drainage structures which means that the fluid in the eye is at higher pressures than in the normal condition. This increased pressure leads to damage of optic nerve axons at the back of the eye, with eventual deterioration or loss of vision. Raised intraocular pressure is a significant risk factor for developing glaucoma (above 21 mmHg). A person may develop nerve damage at a relatively low pressure, while another person may have high eye pressure for years and yet never develop damage. Patients will sometimes notice patchy loss of peripheral vision or reduced clarity of colors and these people may be benefited from a review by an eye specialist.
Glaucoma is an eye disease that involves an increase in the fluid pressure inside the eye which is associated with damage to the retinal nerve fibres. Once nerve fibers have been damaged the associated loss of vision is permanent and cannot be restored. The nerve damage involves loss of retinal ganglion cells in a characteristic pattern. Glaucoma is a disease of the major nerve of vision, called the optic nerve. The optic nerve receives light-generated nerve impulses from the retina and transmits these to the brain, where the electrical signals are recognized as vision. Glaucoma is characterized by a particular pattern of progressive damage to the optic nerve that generally begins with a subtle loss of side vision known as peripheral vision. A fluid inside the eye called the aqueous is continuously being produced by the eye, circulated through the anterior chamber of the eye, and then drained from the eye. This process produces a pressure gradient inside the eye called the intra-ocular pressure. At the back of the eye, in the retina, are nerve fibers that carry visual nerve impulses through the optic nerve to the brain. These nerve fibers are damaged if the IOP increases above a normal range. Damaged nerve fibers result in blind areas in the field of vision. IOP can rise above the normal level if there is disruption in the normal dynamics of the aqueous circulation, most likely caused by a restriction in the drainage of aqueous fluid from the eye. There are rarely any symptoms in the early stages of the disease. Regular eye checkups by qualified professionals are important.

Glaucoma can be divided into two main categories, open angle glaucoma and closed angle glaucoma. Closed angle glaucoma can appear suddenly and is often painful. Visual loss can progress quickly but the discomfort often leads patients to seek medical attention before permanent damage occurs. Open angle glaucoma tends to progress at a slower rate and the patient may not notice that they have lost vision until the disease has progressed significantly.
1.4.1 Importance of Detecting Optic Disc Changes

The retina is the innermost layer in the eye and the retinal nerve fibers transmit the visual signal from the photoreceptors in the eye to the brain via the optic nerve. The portion of the optic nerve head that is clinically visible by an ophthalmoscope is known as the optic disc. Glaucoma can cause damage to the optic nerve in a variety of ways. It has been proved that irrespective of the type of damage, the development of visual field defects is always preceded by optic nerve damage in glaucoma. Examination of the Optic Nerve Head (ONH) has always been of importance in both diagnosis and detection of progressive damage. The more of the rim present between the disc and the cup is lost, the more likely glaucoma is present.

The appearance of the optic disc is a very important characteristic to determine glaucomatous damage. There are various patterns of optic disc changes in glaucoma and the detection of change is the diagnosis of glaucoma. The concentric enlargement of the optic cup, notching and other similar patterns of glaucomatous damage are the most commonly found. The optic cup to disc ratio is usually taken into consideration while evaluation. Optic disc cupping is the excavation that occurs more in the vertical direction, initially known as the vertical ovalization of the cup. Cupping is the major difference between glaucomatous optic neuropathies and other optic neuropathies. However, the asymmetries of CDR can have other diseases as a cause and are therefore not reliable. Other features taken into account are the size, shape of the rim around the optic disc and the presence of optic disc haemorrhage. Other signs of possible glaucoma include pallor and focal notching of the rim. Accurate and early detection of disc change allows the clinician to make appropriate clinical decisions and monitor the patients. The inter-individual variation in optic disc parameters is considerable and many individuals who are not glaucomatous may be classified as glaucomatous.
Research shows that many eyes with glaucoma have pressures within the normal range, so simply measuring pressure is not a reliable way to detect glaucoma. It is associated with loss of tissue in the neuroretinal rim of the optic disc and a consequent increase in the size of the optic cup as shown in Figure 1.4. More importantly, individuals who are in the statistically normal range may undergo optic disc change over time and still remain within the normal range when analysis of single examinations alone are done. For example, a patient with an initial CDR of 0.5 in a large disc may have a concentric enlargement of the cup such that the CDR is now 0.6. The ability to perform sophisticated analysis with computer aided diagnosis provides the clinician with important information. Optic disc changes usually occur in a non-uniform manner across the disc, that is, the progression may be more rapid in some disc sectors compared to others. Glaucoma risk assessment is based on number of factors such as elevated intraocular pressure, increased cup-to-disc ratio, age, family history and race. As the optic nerve damage progresses, the cup tends to elongate vertically which results in increased vertical cup to disc ratio. Untreated glaucoma leads to permanent damage of the optic nerve and resultant loss of visual field, which can progress to loss of central vision and blindness. If the condition is detected early, it is possible to arrest the development or slow down the progression with medical and surgical means.
1.5 DIABETIC RETINOPATHY

Diabetic retinopathy (DR) is a micro vascular complication of diabetes, causing abnormalities in the retina. There are no salient symptoms in the early stages, but the number and severity predominantly increase with time. If DR is not properly treated it might eventually lead to loss of vision. The diabetic retinopathy typically begins as small changes in the retinal capillaries. The smallest detectable abnormalities, Microaneurysms (MA), appear as small red dots in the retina and are local distensions of the weakened retinal capillary. Due to these damaged capillary walls, the small blood vessels may rupture and cause Haemorrhages (HA) which appear either as small red dots indistinguishable from MA or larger round-shaped blots with irregular outline.

Diabetic retinopathy also increases the permeability of the capillary walls which results in retinal edema and Hard Exudates (HE). Exudates, the visible sign of diabetic retinopathy are lipid formations leaking from the weakened blood vessels and appear yellowish with well defined borders. If the local capillary circulation fails due to obstructed blood vessels, pale areas with indistinct margins appear in the retina. These areas appear as white, fluffy lesions and are known as Soft Exudates (SE) or nerve fibre layer infarctions. An extensive lack of oxygen and obstructed capillary in the retina lead to the development of new vessels with sudden loss of vision. The growth of these new vessels is called neovascularisation. Symptoms of all these stages are shown in Figure 1.5.
1.5.1 Stages of Diabetic Retinopathy

The severity of diabetic retinopathy is divided into two stages: Non Proliferative Diabetic Retinopathy (NPDR) or background retinopathy and Proliferative Retinopathy (PDR).

A non-proliferative retina is illustrated in Figure 1.6. Mild NPDR is an early stage of the disease in which symptoms will be mild and non-existent. In NPDR the blood vessels in the retina are weakened causing
tiny bulges called microaneurysms to protrude from their walls. In moderate stage, as the disease progresses, some blood vessels that nourish the retina are blocked. In severe cases, many more blood vessels are blocked, depriving several areas of the retina with their blood supply. These areas of the retina send signals to the body to grow new blood vessels for nourishment. If the non-proliferative retinopathy is untreated or undiagnosed, it leads to proliferative retinopathy.

The proliferative diabetic retinopathy shown in Figure 1.7 may cause sudden loss in visual acuity or even a permanent blindness due to vitreous haemorrhage or tractional detachment of the central retina. At this advanced stage, circulation problems cause the retina to become oxygen-deprived and new fragile blood vessels begin to grow in the retina thereby clouding vision.

![Figure 1.7 Proliferative retinopathy](image)

Symptoms of diabetic retinopathy include, seeing spots or floaters in the field of vision, blurred vision, difficulty in seeing well at night and dark or empty spot in the centre of the vision.

1.6 CLINICAL EYE EXAMINATION

Main tools in clinical eye examination are direct, indirect ophthalmoscopes and biomicroscope with indirect lenses. A direct ophthalmoscope is a hand held apparatus through which a medical expert can
observe the patient’s eye. The apparatus consists of the illumination source and corrective lenses, where the light beams are reflected into the patient’s eye using a mirror or prism. In the indirect ophthalmoscopy, the patient’s eye is examined from an arm’s length by focusing high intensity light through a hand-held condensing lens to the patient’s eye and examining the reflected light (stereoscopic image) with the binocular lenses. The illumination source and the binocular lenses are mounted in a medical expert worn headband. The biomicroscope comprises an observation system and illumination system, where the observation system is a biomicroscope capable of wide range of magnifications and the illumination system emits focal light into the patient’s eye that can be controlled with slit mechanism and apertures.

1.6.1 Fundus Imaging

Fundus imaging is defined as the process whereby a 2-D representation of the 3-D retinal semi-transparent tissues projected onto the imaging plane is obtained using reflected light. Thus, any process which results in a 2-D image, where the image intensities represent the amount of a reflected quantity of light, is fundus imaging.

A fundus camera or retinal camera is a specialized low power microscope with an attached camera designed to photograph the interior surface of the eye, including the retina, optic disc, macula, and posterior pole. Fundus cameras are used by optometrists, ophthalmologists and trained medical professionals for monitoring progression of a disease, diagnosis of a disease or in screening programs. Direct ophthalmoscope is one that produces an upright or unreversed image of approximately fifteen times magnification. Indirect ophthalmoscope produces an inverted direct image of two to five times magnification.
Eye fundus photography is considered the preferred diagnostic modality since it is reliable, non-invasive and easy to use. In contrast to traditional ophthalmoscope, it allows to record diagnostic data and enable the expert consultation afterwards. Hutchinson et al (2000) stated that the eye fundus photography results in a better sensitivity rate, that is, a better detection rate of abnormal eye fundus. Due to the rapid development of digital imaging, the eye fundus camera also provide easy-to-file images in portable format that enable automatic diagnosis of diabetic retinopathy using image analysis algorithms. An eye fundus camera is illustrated in Figure 1.8.

![Fundus camera](image)

**Figure 1.8 Fundus camera**

Eye fundus cameras are divided into two groups: mydriatic and non-mydriatic cameras, where the prefix denotes the requirement for dilation of the pupils with eye drops. Non-mydriatic fundus cameras are smaller and suitable for screening purposes, but at the same time the image quality is worse and the Field of View (FOV) is smaller. Thus, mydriatic cameras are used when a more accurate diagnosis is needed. The patient is seated in front of the fundus camera and the head is positioned into the instrument’s head rest. Light produced by a flash lamp is emitted into patient’s eye using optical mirrors and lenses and the reflected light is captured by the camera sensor. The captured images are typically color images, but since the retina is transparent and the penetration depth of the emitted light depends on the wavelength, the desired retinal structures can be emphasized using optical
filters. An alternative for color images for diagnosing diabetic retinopathy are the red-free eye fundus images.

The optical design of fundus camera is based on the principle of monocular indirect ophthalmoscopy. A fundus camera provides an upright, magnified view of the fundus of the interior surface of the eye. A typical camera views 30° to 50° of retinal area, with a magnification of 2.5x, and allows some modification of this relationship through zoom or auxiliary lenses from 15° which provides 5x magnification to 140° with a wide angle lens which minimize the image by half. The optics of a fundus camera is similar to those of an indirect ophthalmoscope where the observation and illumination systems follow dissimilar paths. The observation light is focused via a series of lenses through a doughnut shaped aperture, which then passes through a central aperture to form an annulus, before passing through the camera objective lens and through the cornea onto the retina.

The light reflected from the retina passes through the unilluminated hole in the doughnut formed by the illumination system. As the light paths of the two systems are independent, there are minimal reflections of the light source captured in the formed image. The image forming rays continue towards the low powered telescopic eyepiece. When the button is pressed to take a picture, a mirror interrupts the path of the illumination system allows the light from the flash bulb to pass into the eye. Simultaneously, a mirror falls in front of the observation telescope, which redirects the light onto the capturing medium, whether it is a film or a digital Charge Coupled Device (CCD). A camera attached to an indirect ophthalmoscope is aimed at photographing the image of the fundus of the eye. A flip mirror within the optical path of the viewing microscope allows the observer to view the image of the fundus and focus it, thus ensuring that the image being photographed is as clear as that being viewed. Fundus cameras
usually require a dilated pupil of about 4 mm and their FOV extend up to 45°. Fundus cameras provide an objective photographic record of any condition in the fundus and can also be used to take photographs of the anterior segment of the eye. The fundus is the inside of the back of the eyeball. Fundus camera uses a specialized digital camera to photograph the inside of the eye. This technology allows detailed color digital images of the pigment layer, major blood vessels, optic nerve head and other structures at the back of the eye to be recorded for immediate assessment and future reference.

Fundus images obtained from Aravind eye hospital, Madurai, were acquired using a Canon CR5 non mydriatic fundus camera with a 45° FOV. Each image was captured using 8 bits per color plane at 768 x 584 pixels. FOV of each image is circular with a diameter of approximately 540 pixels. Fundus images provide immediate information and a benchmark for future reference. This allows normal variations to be identified and recorded and abnormal changes to be identified more easily. This assists in the early diagnosis of disease, in monitoring the outcomes of treatment and in patient education with respect to sight threatening changes caused by general health problems. Photograph can assist in the detection and management of glaucoma, macular degeneration, hypertension, diabetic retinopathy, retinal detachments and other sight-threatening conditions. Currently the preferred way to detect diseases like DR is fundus camera imaging. Additionally when digital photography is used, the image may be enhanced, stored, retrieved more easily than film and images can be transferred electronically to other sites for a trained optical technician or retinal specialist to detect or diagnose disease with the patient at a remote location. A fundus camera is basically a microscope with a bunch of lenses that allows the clinician to see an image of the retina. It has relatively low resolution but this can be good because it allows the clinician to see the entire retina while Optical Coherence Tomography (OCT) can focus only on very small bits of the retina. Also it
does not involve the intense computational requirements of OCT. Consequently, all the following modalities or techniques belong to the category of fundus imaging:

i) Fundus photography (red-free photography)

Image intensities represent the amount of reflected light of a specific waveband.

ii) Color fundus photography

Image intensities represent the amount of reflected R, G, and B wavebands, as determined by the spectral sensitivity of the sensor.

iii) Stereo fundus photography

Image intensities represent the amount of reflected light from two or more different view angles for depth resolution.

iv) Hyperspectral imaging

Image intensities represent the amount of reflected light of multiple specific wavelength bands.

v) Scanning laser ophthalmoscope (SLO)

Image intensities represent the amount of reflected single wavelength laser.

vi) Adaptive optics

Image intensities represent the amount of reflected laser light optically corrected by modeling the aberrations in its wave front.
vii) Fluorescein angiography and indocyanine angiography

Image intensities represent the amounts of emitted photons from the fluorescein that was injected into the subject’s circulation.

1.6.2 Alternate Diagnostic Modalities

In addition to clinical eye examination and eye fundus photography, the fluorescein angiography and OCT play an important role in the diagnosis of diabetic retinopathy. In the fluorescein angiography explained by Margolis and Kaiser (2008), a fluorescent dye is injected in the systemic circulation of a patient by emitting light into patient’s eye in specific wavelength and the fluorescent properties of the dye are activated. The emitted light excites the dye molecules into the higher energy level and as the molecules return to the original state they emit lower energy light that is captured using eye fundus photography. The obtained image is called angiogram. Since the dye circulates in the ocular vasculature, the fluorescein angiography provides valuable information for the diseases pertaining retinal vasculature such as microaneurysms, capillary nonperfusion and vessels leaking exudates in diabetic retinopathy.

OCT produces a two-dimensional cross-sectional image of ocular tissue structures, where the dimensions are propagation direction of the light and the perpendicular spatial direction. A broadband beam of light (laser) is scanned across the ocular tissue and due to transparent structures of the retina the time of propagation is longer from the deeper tissue layers. Optical coherence tomography image is composed from several axial scans and using several OCT images, a computational three-dimensional reconstruction of the retina can be devised. Other modalities are adaptive optics ophthalmoscopy, color doppler imaging, computed tomography, confocal laser scanning microscope, ophthalmic ultrasound, retinal thickness analyzer and scanning
laser polarimetry. When ophthalmologists use fluorescein with a fundus camera the technique is known as fluorescein angiography.

**1.7 DISEASE DIAGNOSIS**

Testing for glaucoma includes measurements of the intraocular pressure via tonometry, changes in size or shape of the eye, anterior chamber angle examination or gonioscopy, examination of the optic nerve to look for any visible damage to it or change in the cup to disc ratio, rim appearance and vascular change. Diabetic retinopathy is the most common complication of diabetes and the primary cause for visual impairment and blindness in adults. The diagnosis of diabetic retinopathy is based on clinical eye examination and eye fundus photography. The eye fundus photography is the preferred diagnostic modality for the primary health care, and for the cases where retinal fundus photographs are ungradable or unavailable, the clinical eye examination is used. Alternate modalities such as fluorescein angiography and optical coherence tomography are utilized to reinforce the eye examination. If the retina is unreachable and light cannot traverse in the eye, the condition of the retina can be inspected using ophthalmic ultrasound. However, the ultrasound cannot directly detect diabetic retinopathy, but it can detect if retinal detachment is present due to proliferative retinopathy. It is important to note that it is not possible to diagnose diabetic retinopathy using laboratory tests. In the screening of diabetic retinopathy, the primary health care doctor uses either retinal photography or direct ophthalmoscopy to investigate the state of the retina.

**1.8 SCREENING**

In the case of glaucoma, screening can help to identify signs of increased IOP and the early stages of Primary Open-Angle Glaucoma (POAG). The damage to optic nerve fibers can cause blind spots to develop.
These blind spots usually go undetected until the optic nerve is significantly damaged. Since glaucoma progresses with little or no warning signs or symptoms, and vision loss from glaucoma is irreversible, it is important that people at high risk for the disease receive an annual screening.

Early detection of retinopathy based on a proper screening method is highly essential in preventing visual impairment. Detection and grading of DR from retinal images is time consuming and repetitive. It is thus of great interest to develop an automatic DR screening system with capability of differentiating between people with no retinal abnormalities and some kind of abnormalities. Since there are no salient symptoms in the early stages of diabetic retinopathy, and the number of symptoms and severity predominantly increase with time, a cost-effective screening over large populations is required. Screening is a preventative action which aims to find and treat conditions that have already occurred, but which have not reached a stage that require medical attention. Systematic screening for DR should make an important contribution to the preservation of vision for people with diabetes. An automatic approach involving fundus image analysis by a computer could provide an immediate classification of retinopathy without the need for specialist opinions.

1.9 PROBLEM DESCRIPTION

1.9.1 Objectives

New imaging techniques in retinal analysis require skilled personnel and do not provide high sensitivities and specificities to implement a primary population screening tool and are highly expensive. Therefore, an effective approach using a noninvasive, easy to perform, less expensive images are necessary for the detection of eye diseases, to monitor the progression of the disease and for a mass screening to identify the risk patients. Early detection through regular screening and timely intervention
will be highly beneficial in effectively controlling the progress of the disease. The objective of this thesis is to improve the early detection of glaucoma and diabetic retinopathy using monocular fundus images.

Primary open angle glaucoma is a progressive optic neuropathy and its development is associated with the loss of tissue in the neuroretinal rim of the optic disc with a consequent increase in the size of the optic cup. To assess glaucoma in fundus images, optic cup to disc ratio, one of the important physiological characteristics for the diagnosis of the eye disease, is usually taken into consideration during evaluation. However, the asymmetries of cup- to-disc can have other diseases as a cause and subjected to limitations with inter individual variability when two optic nerves have equal cup to disc ratio but with unequal neuroretinal rim width. Further, optic disc size is not measured for the accurate diagnosis of glaucoma. Without this information clinicians may over diagnose the disease in eyes with larger discs and physiological cupping, and they may miss early glaucoma in eyes with small discs and small cups. Interruption of blood vessels is one of the main difficulties to segment the optic cup and disc more reliably and accurately. So an effective, accurate segmentation of optic disc and optic cup is essential to identify the pattern of rim loss, estimate quantitative parameters and to highlight the morphological signs of glaucoma. As glaucoma progresses, optic cup grow larger leading to differences in the respective fundus images.

To manifest such physiological changes in the fundus images, features are necessary to quantitatively analyze structural and functional abnormalities in the eye both to observe variability and to quantify the progression of glaucoma. The aim of this thesis is to automatically classify normal and glaucoma eye images based on the structural features and the distribution of texture features in the fundus images. Further prominent features are to be evaluated and selected for enhanced specificity and sensitivity for glaucomatous image classification.
Glaucoma patients when affected by diabetes have more chances of visual disability risk. To reduce the impact of diabetes on vision loss, effective decision support systems are essential for the identification of disease pathology in human eyes. In fundus photographs, retinal blood vessel morphology is an important indicator for disease such as diabetes, arteriosclerosis, cardiovascular disease, hypertension and stroke. Bright lesions representing hard and soft exudates are the earliest signs of diabetic retinopathy and represent a visible sign of retinal damage when these exudates are present in macula. A clinical decision support system have to be designed to extract the landmark features such as the optic disc, fovea, macula, retinal blood vessels, pathological entities such as hard exudates, cotton wool spots and estimate the severity of the disease. The automated method has to reduce subjective variation, detect faint exudates and predict the disease severity with a significant improvement in the specificity and accuracy with a reasonable sensitivity. The system must be able to do it irrespective of variability in illumination levels, color and amount of noise.

An automated clinical support system has to be provided for the diagnosis of glaucoma and diabetic retinopathy that can be applied to efficient, real time population based screening to identify those who are at risk in the early stages of the disease, to monitor the progression of the disease, minimize the examination time and assist the ophthalmologist for a better treatment plan.

1.9.2 Problem Definition

Retinal image analysis relies on computational techniques to make qualitative assessments of the eye more reproducible and objective. As scientists and clinicians, ophthalmologists need to describe both qualitatively and quantitatively their ophthalmoscopic impression of the optic nerves both for diagnosis and to establish a baseline so that change may be detected by
examination. Two sight threatening diseases glaucoma and diabetic retinopathy are assessed in this work to identify the disease progression and prevent further visual loss.

**Glaucoma**

The most commonly used quantitative classification of the optic nerve has been the cup to disc ratio in glaucoma diagnosis. This staging scale describes the optic disc using cup diameter as a percentage of overall disc diameter. The CDR ratio represented a significant advance in quantifying glaucomatous optic neuropathy. Though the advantages, namely, ease of use and lack of magnification artifacts are appealing, the cup to disc ratio has two significant problems that limit its accuracy.

CDR has been found to be inconsistent in explaining the amount of optic disc damage caused by glaucoma. CDR does not take into consideration the diameter of the disc and hence it is prone to give false positive and false negative impressions. CDR focuses on the cup while the actual change occurring in the glaucoma is the loss of neuroretinal rim tissue. For example, some patients have a small CDR, but significant visual field loss, whereas some may have a large CDR with less visual field loss. This is mainly due to the limitations with CDR parameter which cannot account for the various configurations of optic cup, neuroretinal rim and focal notching which refers to the local enlargement of cup region. The two major limitations of the CDR staging system are the fact that the system does not account for disc size and that focal narrowing of the neuroretinal rim is not adequately highlighted. These issues combine to limit the usefulness of the CDR for diagnostic accuracy. It is well known that the size of the optic nerve is widely variable among individuals, while the neuroretinal rim area is similar. If the rim area is roughly constant, the cup area is directly proportional to disc area. If CDR alone is used as a criterion for damage then it is possible that large optic
nerves will incorrectly be called glaucomatous, and small optic nerves incorrectly will be called normal.

The second issue is that focal changes in the neuroretinal rim that are so characteristic of glaucoma are not readily detected by the cup to disc ratio. In Figure 1.9 the two optic nerve drawings contain identically sized cups and discs and the CDR is the same. Even when the vertical CDR is the same, it would not be considered as identical because there is an unequal rim appearance. Ophthalmologists recognize that changes in the rim are often the earliest findings in glaucoma so it stands to reason that a disc interpretation system should highlight the neuroretinal rim, as a unit of measure.

![Figure 1.9: Two optic nerve drawings with equal cup to disc ratio but with unequal rim width](image)

Neuroretinal rim present between the disc and the cup forms the outer boundary of the optic nerve head. Changes in rim shape due to nerve damage result in glaucoma. Its shape can therefore be used in the early diagnosis and assessment of the treatment of this disease. A method is proposed to consider the neuroretinal rim width for a given disc diameter to distinguish between normal or glaucoma suspects as a way to describe the glaucomatous optic nerve. Using a combination of disc size and rim width, a more accurate recording of this information is possible to examine the neuroretinal rim to diagnose glaucoma and understand physiological cupping. As progressive loss of neuroretinal rim tissue is known to occur early in glaucoma, two factors are taken into account (a) the known relation between
optic disc size and neuroretinal rim area (b) rim area calculation in four sectors to detect focal changes. The stages extending from no damage to far advanced damage can be identified based on the width of the neuroretinal rim or the circumferential extent of absence of neuroretinal rim. By categorizing discs as small, medium or large the expectation of rim thickness is adjusted. This reduces the misclassification bias based on the disc size. So an accurate segmentation of optic disc and cup is essential to get better localization of neuroretinal rim to enable new glaucoma evaluation methodologies.

Glaucoma diagnosis can be considered as a series of steps given below:-

i) Detection of disc boundary to take into account the disc size.

ii) Detection of optic cup to manifest the morphological changes in the fundus images.

iii) Quantification of neuroretinal rim in Inferior Superior Nasal Temporal (ISNT) quadrants and estimate the amount of disc damage in patients with glaucoma.

iv) Extraction of structural features that include disc area, cup area, CDR and rim area.

v) Extraction of textural features to reflect the physiological changes in fundus images due to the increase in cup size.

vi) Evaluation and selection of prominent features for enhanced specificity and sensitivity of glaucomatous image classification.

vii) To automatically classify normal and glaucoma eye images based on the structural features and distribution of textural features using ANFIS.
Diabetic retinopathy

Automated retinal image analysis is an important screening tool for the early detection of certain risks and diseases like diabetic retinopathy, hypertensive retinopathy, age related macular degeneration and glaucoma. Severe progression of diabetes is one of the important challenges to health care. Early diagnosis through regular screening is highly essential to detect abnormalities and prevent visual impairment in patients with retinal complications of diabetes. DR is a sight threatening risk inflicting diabetic patients. Without regular screening, a patient may only become aware of the severity of the condition when the level of retinal lesions has rendered effective treatment nearly impossible. In a large scale screening environment DR can be assessed in an early stage by detecting blood vessels, macula and exudates, a type of early bright lesions in fundus images. Detection of DR is performed using pixel and image based approach with the steps below.

Pixel based approach

i) Detection of hard and soft exudates using color Histogram

ii) Quantification of exudates using color histogram technique

Image based approach

i) Detection of blood vessels using Hessian matrix

ii) Detection of macula using top hat filter

iii) Extraction of second order textural features from the segmented image and anatomical features.

iv) Classification of normal and abnormal DR images using ANFIS.
The system can be integrated with the existing ophthalmologic tests and clinical assessments in addition to other risk factors such as age, race, gender, eye abnormalities and family history, according to a determined clinical procedure. The system proposed in this work is an attempt to improve the fundus image analysis and overcome the subjective variability by making the analysis automated and free of manual intervention.

1.10 APPLICATIONS

Grading the eye fundus images is time consuming and repetitive. It requires attention of an ophthalmologist and makes the diagnosis prone to errors. Automatic image analysis algorithms on fundus image provide a potential solution for the problem. By automating the grading process, more patients could be screened and referred for further examinations, thereby enabling the ophthalmologists to have more time for patients who require their attention. An automated system helps local health workers to detect glaucoma and diabetic retinopathy cases without the need for local ophthalmology experts. One can perform early detection of glaucoma and DR cases in rural areas using automated retinal image analysis by training health workers and conducting mobile health camps without the need for local experts or even internet connectivity.

1.11 ORGANIZATION OF THE THESIS

An introduction to the elements of visual perception, glaucoma and diabetic retinopathy complications with their implications to vision are dealt in chapter one. Further shortcomings of the existing diagnosis system and the benefits of automated eye fundus image analysis are described.

A brief literature review related to existing techniques of optic disc detection, optic cup localization, glaucoma detection, identification of
exudates, traditional and machine learning classifiers are described in chapter two. Shortcomings in the existing algorithms for detection of glaucoma and retinopathy are also discussed.

An algorithm for the segmentation of retinal optic disc in the polar coordinate domain is presented in chapter three. Accuracy of the disc boundary for real time images and datasets are evaluated and compared with few other techniques.

An algorithm for optic cup detection with the experimental results are explained in chapter four with the quantitative analysis for the cup boundary. Diagnostic parameters are evaluated and quantified to diagnose the stages of glaucoma for left and right eye.

An approach is explained in chapter five for the diagnosis of glaucoma using segmented and textural features followed by the ANFIS approach for classification of images. Also a graphical user interface to assist in image analysis is designed.

Automatic detection of hard and soft exudates, quantitative analysis of pixel based approach, extraction of structural and texture features and image classification using ANFIS approach are described in chapter six. Experimental results along with performance measures are presented for pixel and image based approaches.

The role of optic disc segmentation algorithm, color model for optic cup, color histogram thresholding for exudates detection and the performance analysis for glaucoma and diabetic retinopathy using ANFIS are explained in chapter seven. An overview of the achievements of this work, conclusions and future avenues of investigation are presented.
1.12 SUMMARY

This chapter provides an introduction to the elements of visual perception, glaucoma and diabetic complications with their implications to vision, related eye diseases with their symptoms, the diagnostic procedures and modalities, shortcomings of the existing diagnosis system and the benefits of automated eye fundus image analysis. It also deals with the need for automatic diagnosis and screening to detect early stages of the disease. Finally, applications of the automatic detection system to diagnose glaucoma and diabetic retinopathy are discussed.