CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

Research to discover new techniques to diagnose diseases has been going on worldwide to improve the life of the people as new diseases emerge day after day. The aim of any similar research is to diagnose the disease accurately, quickly and economically. In this present work the development of clinical decision support system to classify and grade the retinal image is focused. Diabetic Retinopathy (DR) is an eye disease that causes problems in vision. This chapter provides the details related to basics of ophthalmology. The anatomy of human eye and its main anatomical components are briefly explained. This chapter also presents DR and types of diabetes. DR has been found to be a leading cause of blindness due to the leakage on blood vessels in the retina. These weakened blood vessels lead to leakage and spreading of blood on the retina which causes visual impairment and is likely to lead to permanent blindness. The increase in number of diabetic victims and the need for developing advanced measurement techniques of various retinal parameters have been focused by many researches in the past few decades. Retinal biometrics involves the scanning of retinal and analyzing the layer of blood vessels at the back of the eye.

Approximately three million are found to suffer from DR in the world. This disease can be prevented from causing blindness if it is treated at an early stage. Digital photography of the retina is widely used for screening of patients suffering from sight threatening diseases such as DR and Glaucoma. Retinal vessels can be extracted by vessel tracking method. The location of the Optic Disc (OD) is important in retinal image analysis, to
locate anatomical components in retinal images, for vessel tracking, as a reference length for measuring distances in retinal images, and for registering changes within the OD region due to disease. OD detection is required as a prerequisite for the subsequent stages in many methods applied for identification of the pathological structures in retinal images. The process of automatically detecting/localizing the OD aims only to correctly detect the centroid (centre point) of the OD.

The structure of retinal vessels is a well-known feature that explains further information on the state of diseases that are reflected in the form of measurable abnormalities. Hence consistent methods of vessel detection that maintain various vessel measurements are needed. Computer Aided Design (CAD) systems have been demonstrated as effective tools for helping ophthalmologist to identify the retinal image as normal or abnormal. In this research, Support Vector Machine (SVM) is used to classify the retinal images effectively. The classification is based on the extensive features set obtained from the images. The features extracted are optical disc, blood vessel thickness, vein diameter measurements, microaneurysms, haemorrhages, hard exudates, cotton wool spots and large plague hard exudates. In this work the features optical disc, blood vessel thickness, vein diameter measurements are used for normal and abnormal classification. The other features microaneurysms, haemorrhages, hard exudates, cotton wool spots and Large Plague Hard Exudates (LPHE) are used for grading the retinal images. Further rule based classifiers have been used to grade the retinal images. The percentages of sensitivity, specificity and accuracy have been found for both bright lesions and dark lesions. It is found that five stages such as Mild non proliferative DR, Moderate non proliferative DR, severe non proliferative DR, very severe non proliferative DR and Proliferative DR can exist. Therefore, regular screening of diabetic patients
retinal is very important. And, automated or computer assisted analysis of diabetic patients retinal can help eye care specialists to screen larger populations of patients.

1.2 ANATOMY OF HUMAN EYE

The eye is nearly a sphere, with an average diameter of approximately 20 mm. The eye consists of three coats, the outer, middle and inner. In addition, the eye contains the refractive media such as the lens, aqueous humour and vitreous body as well as the cornea which forms a segment of the outer coat. The sclera forms the posterior of the eye ball while the transparent cornea forms the anterior of the eye ball. This sclera is pierced posterior by bundles of the optic nerve. The cornea is the transparent anterior part of the eye. It is thicker at the centre than at the periphery. This variation in thickness reduces the spherical berration.

![Anatomy of human eye](image.png)

Figure 1.1 Anatomy of human eye [Courtesy: Picture from Microsoft Encarta 2000]

The middle vascular coat comprises the choroid, ciliary body and iris. The choroid which contains the blood vessels serves as the major source of nutrition to the eye. Even superficial injury to the choroid, often not deemed serious, can lead to severe eye damage as a result of inflammation that restricts
blood flow. The choroid coat is heavily pigmented and hence helps to reduce the amount of extraneous light entering the eye and the backscatter within the optical globe. The ciliary body which is the anterior continuation of the choroid lies in front of the ora serrata and forms the thickest part of the middle coat. The iris forms the contractile diaphragm in front of the lens and can therefore effectively increase or diminish the amount of light entering the eye. The front of the iris contains the visible pigment of the eye, whereas the back contains a black pigment. The lens is made up of concentric layers of fibrous cells and is suspended by fibers that attach to the ciliary body.

The lens is coloured by a slightly yellow pigmentation that increases with age. In extreme cases, excessive clouding of the lens, caused by the affliction commonly referred to as cataracts, can lead to poor color discrimination and loss of clear vision. The retinal is the inner most coat of the eye. The retinal consists of an outer pigmented layer and an internal cerebral layer. The later contains the neural elements concerned with the transformation of light energy into electrical energy whereby the impulses are conducted along the fibres of the optic nerve towards the brain. Pattern vision is afforded by the distribution of discrete light receptors over the surface of the retinal. The retinal contains photoreceptor cells rods and cones and these cells work like the film in a camera by recording light which enters through the pupil. This light information is sent from the retinal, along the optic nerve and into the brain where the image is formed. There are some 120 million rods and only 6 million cones. The rods are generally distributed over the periphery of the retinal and are meant for scotopic (dim light) vision while the cones are more concentrated over an area known as the bright spot. Optic nerve connects the eye to the brain, and brings the retinal its main blood supply. Macula is responsible for fine detail central vision (reading, writing etc) and colour
vision. Fovea—the centre of the macula provides the sharpest point of human vision.

![Figure 1.2 Normal fundus views of right and left eye](image)

The retinal is a multi-layered light sensitive tissue lining the inner surface of the eye. It is approximately 0.5 mm thick and lines the back of the eye. In the centre of the retinal is the optic nerve, a circular to oval white area measuring about 2 x 1.5 mm across. From the center of the optic nerve radiate the major blood vessels of the retinal. Light striking the retinal initiates a cascade of chemical and electrical events that ultimately trigger nerve impulses. These are sent to various visual centers of the brain through the fibres of the optic nerve. The optic nerve of the eye creates an image of the visual world on the retinal, which serves much the same function as the film in camera.

![Figure 1.3 View of retinal image through the ophthalmoscope](image)
1.3 DIABETES AND RETINOPATHY

Diabetes is a disorder of metabolism. The energy required by the body is obtained from glucose which is produced as a result of food digestion. Digested food enters the body stream with the aid of a hormone called insulin which is produced by the pancreas, an organ that lies near the stomach. During eating, the pancreas automatically produces the correct amount of insulin needed for allowing glucose absorption from the blood into the cells. In individuals with diabetes, the pancreas either produces too little or no insulin or the cells do not react properly to the insulin that is produced. The increase of glucose in the blood, overflows into the urine and then passes out of the body. Therefore, the body loses its main source of fuel even though the blood contains large amounts of glucose.

Retinopathy refers to diseases that affect the retinal, the collection of light-sensitive cells lining the back half of each eye. The retinal contains many blood vessels. Abnormalities in these vessels cause several forms of retinopathy. Retinopathy can cause partial loss of vision or complete blindness. It can develop slowly or occur suddenly. Retinopathy can cause permanent damage.

1.4 TYPES OF RETINOPATHY

Retinopathy of Prematurity

Retinopathy of prematurity occurs in some infants who are born prematurely or at a low birth weight. Retinal blood vessels develop at the back of the eye and grow outward to cover the area of the retinal. When a child is born too early, this process doesn't have time to finish. A baby is at risk if the baby is born before the end of the 29th week of pregnancy, or if the baby weighs less than 1,200 grams at birth. Babies who are born before the 35th week of pregnancy or who have a birth weight less than 1,500 grams also may
need an eye examination if they have had other complications from their premature birth. Early stages of this illness involve only subtle changes without obvious symptoms. In more advanced stages, the retinal can become detached, causing blindness. An ophthalmologist should closely monitor infants who are at risk by carefully examining the eyes.

**Diabetic Retinopathy**

DR is a progressive eye disease that affects the retinal microvasculature, resulting in an abnormal change in vascular permeability and proliferation of new, but fragile, blood vessels. If left unmonitored, these pathologies can ultimately result in severe or permanent visual loss. DR is composed of a characteristic group of lesions found in the retinal of individuals having diabetes mellitus for several years. The abnormalities that characterize DR occur in predictable progression with minor variations in the order of their appearance. In the early stages vascular occlusion and dilations occur. It progresses into a Proliferative Retinopathy with the growth of new blood vessels.

DR is the most common diabetic eye disease and a leading cause of blindness in adults. In some people with DR, blood vessels may swell and leak fluid. In other people, abnormal new blood vessels grow on the surface of the retinal. DR is managed at two levels. First, the risk of developing DR is reduced by optimizing diabetes management via strict control of glycaemia levels, blood pressure and serum lipid levels. Second, once DR has developed, laser treatment is clinically effective in delaying the progression of DR and vision loss by sealing permeable blood vessels and destroying proliferative vessels.
Hypertensive Retinopathy

Hypertensive retinopathy occurs in people who have high blood pressure (hypertension). It results from the thickening of the small arteries. Despite the potentially serious nature of high blood pressure, people with this disease frequently have no symptoms. Hypertensive retinopathy sometimes is discovered during a routine eye examination. High blood pressure causes blood vessel abnormalities, including blockages of retinal blood vessels and bleeding from them. These changes may not affect vision in early stages. Sudden, severe high blood pressure may cause swelling of the optic nerve.

Central Serous Retinopathy

This retinopathy begins for reasons that are not well understood. In this condition, fluid accumulates in the membrane behind the retinal, called the choroid. This fluid seeps in between tissue layers in the retinal and causes them to separate, resulting in blurred vision or poor night vision. This condition usually affects males between the ages of 20 and 50, but women also can get this condition. Certain medical treatments or problems are suspected to be possible triggers. Suspected triggers include steroid medicines, pregnancy, antihistamines, antibiotics, alcohol abuse, nasal allergies, asthma, autoimmune problems and untreated high blood pressure.

1.5  GRADING OF DIABETIC RETINOPATHY

There are five stages of Diabetic retinopathy; they are Mild NPDR, Moderate NPDR, Severe NPDR, Very severe NPDR and Prolific DR.

Mild Non Proliferative Diabetic Retinopathy

This is the mildest form of non-proliferative DR and is characterized by the presence of at least one microaneurysm. Microaneurysms are the early sign of DR that are ophthalmoscopically visible. These appear as red dots and
are difficult to distinguish from small dot haemorrhages. The rupture of these microaneurysms results in haemorrhages. The haemorrhages in the deeper layers of retinal appear as blot haemorrhages. Superficial haemorrhages may appear as flame shaped haemorrhages as those seen in hypertensive retinopathy.

**Moderate Non Proliferative Diabetic Retinopathy:**

This is characterized by intra retinal microaneurysms and dot and blot haemorrhages of greater severity. Cotton wool spots, venous calibre changes including venous beading and intra retinal micro vascular abnormalities are present but mild.

**Severe Non Proliferative Diabetic Retinopathy**

In severe non proliferative DR at least any one of the following is present; Haemorrhages and microaneurysms in all four quadrants of the fundus; Venous beading in at least two quadrants; Intra retinal micro vascular abnormalities in at least one quadrant. Many more blood vessels are blocked, depriving several areas of the retinal with their blood supply. These areas of the retinal send signals to the body to grow new blood vessels for nourishment.

**Very Severe Non Proliferative Diabetic Retinopathy**

Patients are diagnosed with very severe nonproliferative DR when the eye examination shows two or more of the above findings.

**Proliferative Diabetic Retinopathy**

Proliferative DR is characterized by new vessels arising from retinal vasculature. Severity of Proliferative DR is determined by the area covered with new vessels in comparison with the area of the disc. When they are located at or within one disc diameter of the optical disc they are called Neo Vascularisation of the Disc (NVD). When they are further than one disc
diameter from the optic disc they are called Neo Vascularisation Elsewhere (NVE). The characteristics are any new blood vessels on the OD or new vessels elsewhere in the fundus.

![Figure 1.4 Pathological features of retinal image](image)

### 1.6 EARLY TREATMENT DIABETIC RETINOPATHY STUDY

Early Treatment Diabetic Retinopathy Study (ETDRS) classification is now unanimously accepted and is detailed below. The ETDRS acuity test is developed to aid in evaluating the changes in vision following pan-retinal photocoagulation in patients with DR. This grading system has been used extensively used in clinical and epidemiological studies of DR, including the Diabetic Control and Complications Trail (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS), to assess baseline status of retinopathy and progression of disease.
Table 1.1 Classification of Diabetic Retinopathy

<table>
<thead>
<tr>
<th>Early Treatment DR Study Levels of DR [ETDRS]</th>
<th>Nonproliferative Diabetic Retinopathy (NPDR)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>A. Mild NPDR</td>
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<tr>
<td></td>
<td>● At least one microaneurysms</td>
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<tr>
<td></td>
<td>B. Moderate NPDR</td>
</tr>
<tr>
<td></td>
<td>● Haemorrhages or microaneurysms</td>
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<tr>
<td></td>
<td>● Soft exudates, Venous beading and</td>
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<td></td>
<td>Intraretinal Microvascular Abnormalities</td>
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<td></td>
<td>(IMRAs) definitely present.</td>
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<td></td>
<td>C. Severe NPDR (4:2:1 rule)</td>
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<td></td>
<td>● Haemorrhages or microaneurysms in all 4</td>
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<tr>
<td></td>
<td>quadrants</td>
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<tr>
<td></td>
<td>● Venous beading in 2 or more quadrants</td>
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<td></td>
<td>● Intraretinal microvascular abnormalities</td>
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<td></td>
<td>in at least 1 quadrant</td>
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<td></td>
<td>D. Very Severe NPDR</td>
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<td></td>
<td>Any two or more conditions of Severe NPDR</td>
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<tr>
<td>Proliferative DR</td>
<td>One or both of the following</td>
</tr>
<tr>
<td></td>
<td>● Neovascularisation</td>
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<td></td>
<td>● Vitreous/ Pre retinal haemorrhage</td>
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1.7 MOTIVATION

The World Health Organization (WHO) estimates that 135 million people have diabetes mellitus worldwide and that the number of people with diabetes will increase to 300 million by the year 2025. Medical image analysis is one of the research areas that are currently attracting intensive interests of scientists and physicians. It consists of the study of digital images with the objective of providing computational tools that assist quantification and visualisation of interesting pathology and anatomical structures. The progress, which has been achieved in this area over recent years, has significantly improved the type of medical care that is available to patients. The severe progression of diabetes is one of the greatest immediate challenges to current
health care. The number of people affected continues to grow at an alarming rate. According to recent survey, 4% of the country’s population has been diagnosed of diabetes disease alone and it has been recognized and accepted as one of the main cause of blindness in the country, if not properly treated and managed. Early detection and diagnosis is identified as one of the ways to achieve a reduction in the percentage of visual impairment caused by diabetes, with more emphasis on routine medical check up with the use of special facilities for detection and monitoring of the said disease. The use of medical image processing for diagnosis of diabetes related disease like DR using images of the retinal is suggested.

1.8 METHODOLOGY

1.8.1 Classification of Normal / Abnormal Retinal Images

The retinal image is taken with dedicated fundus camera and digitized with a laser film scanner [ZEISS STRATUS OCT, Modern 3000]. Gabor filtering is used for preprocessing and applied to a retinal image to obtain the maximum output at the edges. Adaptive Histogram Equalization is used to enhance the image to highlight the image features. RGB based thresholding method is used for segmentation and features are extracted from the segmented anatomical structures. Three features namely optic disc parameters, retinal blood vessel thickness and vein diameter are focused and estimated. SVM classifier is used for classifying the retinal image as normal or abnormal, based on the features extracted.
1.8.2 Grading of Retinal Images

If the image is abnormal then it is graded by Mild NPDR, Moderate NPDR, Severe NPDR, Very severe NPDR, and Proliferative DR based on the features of bright lesions and dark lesions present. The features considered for bright lesions are Hard Exudates, Cotton Wool Spot and Large Plaque Hard Exudates. The dark lesion features are Microaneurosyms and Haemorrhages. Rule based classifier is used to grading the abnormality of retinal images. The performance of the proposed method is evaluated on the basis of four measures, namely True Positive (TP), True Negative (TN), False Positive (FP) and False Negative (FN). From these quantities, the sensitivity, specificity and accuracy values are computed using equations. TP represents a number of pixels of both bright and dark lesion correctly represented. This measure is also known as sensitivity. TN represents pixels of both bright and dark lesions correctly represented. This is also known as specificity. FP represents a number of non-bright lesion and dark lesion pixels which are detected wrongly as bright and dark lesion pixel. FN represents a number of bright lesion and dark lesion pixels that are not detected. The performance measurements of TP, TN, FP and FN, sensitivity, specificity and accuracy values are obtained using the proposed method on different data base images.
Figure 1.5 Developed clinical decision support system for grading of diabetic retinopathy
1.9 OBJECTIVES

- To extract shape and texture features from retinal images after preprocessing.
- To implement a CAD system for analyzing and classifying the retinal images.
- To identify the grade of retinal images.
- To estimate the performance of the classification algorithm.
- To validate the developed algorithm and compare with the existing algorithms.
- To perform a clinical study to validate the results obtained.

1.10 ORGANIZATION OF THE THESIS

The thesis has been organized as follows:

Chapter 1: The introduction to the research problem, importance of the study, and the objectives of the study are presented.

Chapter 2: The extensive literature review and the advantages and disadvantages of existing study are presented.

Chapter 3: The automatic clinical decision support system to classify the DR as normal or abnormal has been developed and presented.

Chapter 4: Provides the automatic clinical decision support system to grade the bright lesions of DR images.

Chapter 5: The clinical decision support system to grade the dark lesions of DR images are presented.

Chapter 6: The conclusion, drawn along with the future scope of the work to carry out and improve the performance is presented. This is followed by the list of papers referred for the research and the peer reviewed papers published in Journals and conferences.