CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

Currently, there is an increasing interest in establishing automatic systems that screen a huge number of people for vision threatening diseases like glaucoma and diabetic retinopathy and to provide an automated detection of the disease. Image processing is now becoming practical and a useful tool for screening. Digital imaging offers a high quality permanent record of the fundus images, which are used by ophthalmologists for the monitoring of progression or response to the therapy. Digital images have the potential to be processed by automated analysis systems. Fundus image analysis is a complicated task, because of the variability of the fundus images in terms of color or gray levels, the morphology of the anatomical structures of the retina and the existence of certain features in different patients that may lead to a wrong interpretation. In the literature, numerous examples of the application of digital imaging techniques used in identification of diabetic retinopathy can be found. There have been few research investigations to identify retinal components like optic disc, optic cup and lesions like hard and soft exudates. The major contributions to detect glaucoma and severity of diabetic retinopathy using fundus images are described in this chapter.

Glaucoma detection algorithms are broadly classified into two categories, which are based on the detection of optic disc and detection of optic cup. Optic disc and optic cup detections are compared based on the
localization, detection and boundary extraction procedure. Techniques to detect diabetic retinopathy are explained with respect to various extractions of features and abnormality detection in fundus images. The shortcomings in the existing algorithms are identified and a method is proposed to detect glaucoma and diabetic retinopathy at an early stage for screening applications.

This chapter is organized as follows. In section 2.2, prevalence of glaucoma, diabetic retinopathy and the need for screening are presented. Section 2.3 reviews the literature related to optic disc localization, detection of optic cup and the major works related to the assessment of glaucoma. Section 2.4 reviews the literature for localization of fovea, segmentation of vasculature, detection of bright and dark lesions for the detection of diabetic retinopathy. Shortcomings of the existing techniques are presented in section 2.5.

2.2 PREVALENCE

Amos et al (1997) pointed out that World Health Organization (WHO) estimates 135 million people have diabetes mellitus worldwide and that the number of people with diabetes will increase to 300 million by the year 2025. An additional 16 million adults between the ages of 40-74 have prediabetes and are at high risk for developing diabetes. Visual disability and blindness have a profound socioeconomic impact upon the diabetic population and diabetic retinopathy is the leading cause of new blindness in working-age adults in the industrialized world. Wild et al (2004) stated that the global prevalence of diabetes for all age groups worldwide was 2.8% in 2000 to 4.4% of the global population by 2030, meaning that the total number of diabetes patients is forecasted to rise from 171 million in 2000 to 366 million in 2030. Quigley and Broman (2006) have suggested optic disc segmentation to be more relevant for automated diagnosis of other ophthalmic pathologies like glaucoma.
Krishnadas and George (2009) have estimated the prevalence of glaucoma based on population based studies in India to be about 11.9 million in India and 60.5 million in the world by the year 2015. Most data on prevalence of glaucoma has been in South India and West Bengal, though one is currently underway in Nagpur, Central India and the data are yet to be made available. There are no data available from North India as of now. There have been four prevalence studies from South India: Andhra Pradesh Eye Disease Study (APEDS), Aravind Comprehensive Eye Survey (ACES), Chennai Glaucoma Study (CGS) and the Vellore Eye Study (VES). Though the methodology employed in each of these population based studies differ widely, all the studies are based on diagnosis of glaucoma on the appearance of optic discs and matching visual field defects on automated perimetry.

Taylor and Keeffe (2001) described diabetic retinopathy as a chronic disease, caused by complications of diabetes mellitus and constitute the primary cause of blindness among people of working age in developed countries. As diabetic retinopathy is not a curable disease, Fong et al (2003) suggested that laser photocoagulation can prevent major vision loss if detected in early stages. As DR patients perceive no symptoms until visual loss develops, diabetic patients need an annual eye-fundus examination.

2.3 DETECTION OF GLAUCOMA

World Health Organization predicted that 79 million people in the world are likely to be affected by the year 2020 due to glaucoma. Glaucoma is asymptomatic in the early stages and the associated vision loss cannot be restored. Michelson et al (2008) pointed out early detection and subsequent treatment is essential to prevent visual damage. With the new advances in digital modalities for retinal imaging, there is a progressive need of image processing tools that provide fast and reliable segmentation of retinal
anatomical structures. Generally, glaucoma detection algorithms are divided into three categories. They are

i) Localization and detection of optic disc

ii) Detection of optic cup

iii) Assessment of glaucoma

2.3.1 Localization and Detection of Optic Disc

Precise localization of the optic disc boundary is an important subproblem of higher level problems in ophthalmic image processing. Location of optic disc is an important issue in retinal image analysis as it is a significant landmark feature to locate anatomical components in retinal images, for vessel tracking and for registering changes within the optic disc region due to disease and sizes. Localizing the disk is often necessary to differentiate the disc from other features of the retina. Correct localization of optic disc may improve the disc boundary extraction. Localizing the optic disc is a prerequisite for computation of some important diagnostic indices for hypertensive or sclerotic retinopathy based on vasculature. OD segmentation is an essential step in developing automated diagnosis expert systems for DR. It is a key preprocessing component in many algorithms designed to identify other features automatically. OD segmentation is fundamental for establishing a frame of reference within the retinal image and is thus important for any image analysis application. Many schemes have been proposed to localize optic disc. Majority of the techniques proposed to detect the optic disc have focused on the localization and have not addressed the problem of contour detection of optic disc. Accurate localization of optic disc is difficult, due to its highly variable appearance and interference of blood vessels. Various techniques used to detect the OD are categorized as shown below.
• Model based method
• Appearance based method
• Template based method
• Vessel based approach
• Deformable model based approach

Model based method depends mainly upon extracting and analyzing the structure of the retinal vessels and defining the location of the optic disc as the point where all the retinal vessels originate. Youssif et al (2008) proposed a simple matched filter to roughly match the direction of the vessels at the OD vicinity. Optic disc detection was based on matching the expected directional pattern of retinal blood vessels and segmented vessels were filtered using local intensity to represent OD centre candidates. Vessels direction matched filters have a very high success rate in diseased images but they are computationally very expensive because they require segmentation of the retinal vessels as an initial step of the localization process. Matched filter achieved an accuracy of 98.8% but it took an average computation time of 3.5 minutes per image to correctly locate the OD. Hoover and Goldbaum (2003) described a novel voting type algorithm to determine the origination of retinal vasculature and to localize the OD. Inputs to the fuzzy convergence algorithm were six binary vessel segmentations obtained from the green band image. Each vessel was modeled by a fuzzy segment and OD was detected with the strongest point of vasculature convergence. Method uses brightness as a secondary feature for optic nerve detection. Fisher’s linear discriminant was applied to the regions containing the brightest pixels to detect the OD. Closely related to vasculature fitting on a directional model, Foracchia et al (2004) detected OD in retinal images based on a geometrical parametric model of the direction of main retinal vessels. In this method the main vessels originating
from the OD was modeled using two parabolas with a common vertex. Robustness of the method lies in the prior knowledge provided by this model. The technique achieved a success rate of 97.5% but it took an average time of 2 minutes to localize the OD in a given image. Model based approaches such as geometrical models, convergence of vasculature and vessels direction matched filter have a high success rate in diseased images but they are computationally very expensive. These approaches require segmentation of the retinal vessels as an initial step of the localization process.

Appearance based method identifies the location of the optic disc as the location of the brightest round object within the retinal image. This method includes techniques such as intensity thresholding, highest average variation, matched spatial filter and Principal Component Analysis (PCA). Method of optic disc boundary detection can be divided into optic disc localization and disc boundary extraction. Instead of using the average variance and assuming that the exudates are away from the optic disc, Walter and Klein (2001) approximated the OD centre as the centre of the largest brightest connected object in a fundus image. Binary image was obtained including all the bright regions by thresholding the intensity image. Sinthanayothin et al (1999) used an 80 x 80 pixel sub image to evaluate the intensity variance of pixels. The point with the highest intensity variation was identified as the optic disc with the assumption that visible signs of disease such as exudates will have a low intensity variance adjacent than the optic disc. These methods could obtain satisfactory results only in normal retinal images where optic disc is clear and brightest. Two methods were proposed by (Haar 2005) to detect OD using a vessel branch network constructed from a binary vessel image. In the first method, branch with the most vessels are searched so as to locate the OD. Alternatively in the second method constructed vessel branch network in all paths are searched and since the end point of all paths represents a degree of convergence, OD coincides well with
more path endings. Hough transform (HT) was then applied to these areas to detect the optic disc. Goldbaum et al. (1996) suggested appearance based methods are simple and they have a high success rate in normal images but fail to detect OD correctly in diseased retinal images since the pathologies have similar appearance properties to that of the optic disc.

Lalonde et al. (2001) proposed an algorithm for location of optic disc in low contrast color fundus images. A confidence value was calculated for all the regions having a Hausdorff distance between the edge map and the template less than a threshold value. Optic disc is modeled as a circular or an elliptical object. This matching is performed on an edge map extracted from the image. This approach suffers due to the vessel edges present in and around the optic disc region. A high confidence level is a prerequisite for the reliability of image analysis and the performance of the approach is highly dependent on the thresholded edge map. The template matching approach has a good computation time but the technique relies on various assumptions.

Ahmed E. Mahfouz and Ahmed S. Fahmy (2010) localized the optic disc by reducing the dimensionality of the search space from a Two Dimensional (2D) space to two 1-Dimensional space (1D) Space. Process of dimensionality reduction is achieved through projection of certain image features onto two orthogonal axes. Resulting 1D projection are then searched to determine the location of optic disc. In this technique, a fast technique is presented that requires less than a second to localize the optic disc. Though the technique gives a reduced computation time, the accuracy of the technique is highly dependent upon the accuracy of horizontal localization process.

An automatic system was presented by Niemeijer et al. (2007) to find the localization of major anatomical structures: optic disc, macula and the vascular arch. The structures are found by fitting a single point distribution model to the image which contains points on each structure.
Tobin et al (2007) used a geometrical model of the vasculature in red free fundus photographs to localize optic nerve and macula. The method relies on the accurate segmentation of the vasculature of the retina followed by the determination of spatial features describing the density, average thickness and average orientation of the vasculature in relation to the position of the optic nerve. These features are used to train and apply a Bayesian classifier to classify the pixels in the original image into the binary category of optic nerve or not optic nerve. Abdel Ghafar and Morris (2007) developed automated techniques to generate quantitative descriptions of the retina to be used in diagnosis and treatment. Only the green channel was processed and OD boundary was detected using edge detector and circular hough transform.

Classical segmentation algorithms like thresholding, edge detection and region growing techniques cannot find the optic disc boundary correctly as they do not incorporate the edge smoothness and continuity properties. In contrast, active contours or the snakes represent the paradigm that the presence of an edge depends not only on the gradient at a specific point but also on the spatial distribution. Deformable models offer a reasonable approach for boundary detection and image segmentation which can be classified into two categories: free form deformable models known as snakes and parametrically deformable models such as Active Shape Models (ASM). In the first stage, described by Mendels et al (1999) images were processed using gray level mathematical morphology to remove blood vessels region. Then a snake was manually placed around the optic disc and allowed to evolve onto its boundary. Xu and Prince (1998) developed an improved version of this snake including gradient vector flow external energy force, calculated as a diffusion of the gradient vectors of a gray level or a binary edge map derived from the image. Accuracy of the method is highly sensitive to initialization together with the sensitivity of the snake to energy minima.
Osareh et al (2002) justified that boundary localization can be improved using color mathematical morphology on the original color image. Boundary of the optic disc was localized using an automatically initialized snake. Template matching is used to find an approximate location of the OD centre which helps to automatically position a snake on a morphologically enhanced image. Thongnuch and Uyyanonvara (2007) segmented optic disc boundary using segmentation by a deformable contour model with Gradient Vector Flow (GVF) as an external force. The first snake is placed closer to the centre of the optic disc approximated by PCA based model. GVF snake followed the external force field until it fitted the boundary of OD. Giri babu kande et al (2009) discussed a technique to localize the disc using the vessel branch with more number of blood vessels in fundus images. Initially color morphology in Lab color space is used to have homogenous optic disc region and then the boundary of the optic disc is estimated by using geometric active contour with new variational formulation. Nova et al (2009) discussed an approach using topological active nets to localize the disc in digital retinal images. This is a deformable model used for image segmentation that integrates features of region and edge based techniques. Active nets incorporate new energy terms for the optic disc localization and their optimization is performed with a genetic algorithm with new genetic parameters. There is no need of any pre-processing of the images which allows a quasi automatic localization of the optic disc. Though the method is robust and solves the initialization problem faced by the deformable models, it needs a tuning of the parameter set which weights the different energy terms.

Li and Chutatape (2004) used PCA to locate the optic disc even for retinal images having bright lesions. Boundary of the optic disc is extracted by a modified active shape model technique, but this technique is very slow. Recently, work in active contours has been focused on region based
approaches which has a lower sensitivity to contour initialization and better ability to capture concavities of objects. In the snake based approach, to fit active contour on to the optic disc, the initial contour must be near to the optic disc boundary, otherwise it leads to wrong convergence. This method captures the range of shape and image variations, but the segmentation accuracy is sensitive to the contour initialization. Gradient based active contour models captures better shape irregularity in the disk region. In these approaches contour is initialized either manually or automatically and deformation in the contour takes place under the influence of energy term defined on the image gradient or as a post processing step. In the case of deformable contours, an approximate contour is placed near the boundary by some mechanism. Using connectivity constraints, energy minimization techniques are used to refine the shape and location of the contour.

Estimating the contour of the optic disc as an ellipse or a circle cannot provide adequate information to the ophthalmologists. Since the contour or boundary of the optic disc is very important to analyze vision threatening diseases like diabetic retinopathy and glaucoma, the accurate contour of the disc has to be determined. A new method based on differential windowing in the polar coordinate domain is presented in this thesis to identify the contour of the optic disc. This method works accurately even though the boundary of optic disc is not continuous or blurred.

2.3.2 Detection of Optic Cup

Optic cup segmentation from the optic disc provides a greater challenge because of the interweavement of cup with the blood vessels. Compared with the disc boundary detection on the 2D fundus image, the variable shapes of cup makes cup detection more difficult to be automatically segmented. Very few methods have been proposed for cup segmentation from fundus image since the depth images are not easily available. Cup
segmentation methods are based on intensity based approach, vessel based approach and deformable model based approach.

Liu et al (2008) identified the optic cup region by deriving a region based on the reference color from a manually selected point. Pixels are selected in the three color channels if their intensity values are all within the range of 25% from selected pixel intensities. Cup boundary is determined by first obtaining an estimate of the cup boundary using threshold techniques and level set method is used to determine the cup contour. Threshold value is selected to segment out the pixels corresponding to the top one third of gray scale intensity. Cup boundary obtained via ellipse fitting yields only coarse cup boundary.

As the optic disc occupies only a small region of the entire retinal image, a region of interest is first extracted via pixel intensity analysis. Variational level-set algorithm is next used to segment the optic disc. Liu et al (2009) described a multi-modal approach consisting of different methods to extract the cup. To obtain a smoother contour, ellipse fitting is applied to the extracted cup and disc. Neural Network (NN) has also been used to fuse the results obtained via the various modes. Automatic Cup to Disc Ratio measurement system for Glaucoma Analysis using Level set image processing (ARGALI) system automatically calculates the cup to disc ratio from non-stereographic retinal fundus photographs, providing a fast, objective and consistent measurement.

Wong et al (2009) applied a level set method to the region within the optic disc for the detection of the optic cup, where accurate segmentation is more difficult due to the denser vascular architecture within the optic disc. An alternate method using histogram based analysis of the color pixel intensity is also employed for optic cup segmentation. Smoothing of the cup contours detected through these methods is similarly performed using direct
ellipse fitting. CDR values calculated are fused with the help of Support Vector Machine (SVM). Zhuo Zhang et al (2009) proposed a fused approach based on multimodalities including level set segmentation, convex hull and ellipse fitting boundary smoothing for optic cup detection. Optimized vertical cup height calculated using intensity and level set based approach is smoothed using convex hull.

Gopal Datt Joshi et al (2010) detected cup boundary based on the color space and the expected cup symmetry. Cup symmetry is used after thresholding to obtain coarse cup segmentation. Fixed thresholding is not adequate to handle intensity variations in the cup region due to the physiological difference across the patients. Energy minimization based deformable models are not appropriate for this problem due to the absence of edge or region based information associated with the cup region to derive energy functional. The cup boundary is interpolated at high curvature points to get a smoother cup boundary. The method gives rise to fewer false positives and high specificity.

In order to address these problems, Wong et al (2009) used additional information such as small vessel bends known as kinks to anatomically mark cup boundary. Bends of small vessels provide a physiological validation from the cup boundary as they traverse from the disc to the cup. Liu et al (2009) extracted image patches around an estimated cup boundary and identified vessel pixels using edge and wavelet transform information. Next, vessel bends, characterized by points of direction change in the vessel pixels are found and used to obtain the cup boundary. This method is highly dependent on the preliminary cup boundary. Further, the statistical rules for selecting vessel pixels are very sensitive to the inter-image variations.
Gopal Datt et al (2011) explained an automatic OD parameterization technique to improve segmentation based on the range of OD instances. The method integrates the local image information around each point of interest in multi-dimensional feature space to provide robustness against variations found in and around the OD region. Segmentation results show consistency in handling various geometric and photometric variations found in the dataset. Deformable models provide high accuracy in boundary tracing but have a large computational complexity. Cup region is segmented using both vessel bends and pallor information. A multi stage strategy is used to derive vessel bends called relevant bends followed by a local interpolating spline to approximate the cup boundary in regions where relevant bends are absent. Segmentation results showed a good consistency in handling geometric and photometric variations. Multiple sources of information namely pallor region which defines the inner limit of relevant bends, bending angle and location in the optic disc region are necessary for the exact cup detection and involves more intensive computations.

Morris and Donnison (1999) proposed an algorithm to identify the boundary using dynamic contours known as snakes. The success of the algorithm is highly dependent on preprocessing of the image to enhance the contrast between the retina and the optic nerve head. Xu et al (2007) introduced a shape model in the energy function to constrain the deformation to be close to a certain predefined shape. Modified deformable model technique is applied to extract the cup boundary by using a different energy function. Disc shape is used as the shape model for cup contour information. CDR achieved in this method showed good consistency and compatibility when compared with the results of Heidelberg Retina Tomograph (HRT). Cup detected by this method depends on the optic disc boundary and the cup boundary is not obvious on the nasal side.
Tan et al (2010) discussed an approach for optic cup segmentation based on Gaussian mixture models. The optic cup is chosen based on the highest probability distribution contributed by the third Gaussian component. The results of the optic cup segmentation via Gaussian Markov Model are able to give a better temporal cup boundary. However, the cup segmentation by ARGALI is capable of getting a good assessment of the cup in the nasal sector. The combination of cup segmentations by Gaussian mixture models and ARGALI results in closer cup-to-clinical cup boundary. Since the 3D images are not available, cup boundary is estimated on 2D fundus images. Finding the optic cup boundary automatically would be useful to perform quantitative shape measurements. However, it is a difficult problem as the boundary of the cup region is ill defined with a decreased visibility and partially obscured by blood vessels. In the proposed approach, pallor is used to estimate the cup boundary on 2D images.

Pallor is defined as the area of maximum color contrast inside the disc area. So a method is proposed to detect cup shape based on color space analysis and to solve the problem of the influence of blood vessels without compromising for accuracy.

2.3.3  Assessment of Glaucoma

Early treatment for glaucoma can decrease the rate of blindness by about 50%. Glaucoma characterized by neurodegeneration of the optic nerve is one of the common causes of blindness. Revitalization of the degenerated nerve fibers of the optic nerve is impossible and so early detection and subsequent treatment is essential to prevent visual damage.

Existing works related to glaucoma detection in fundus images focus only on the estimation of CDR to detect glaucomatous cases. However, CDR has been found to be inconsistent in explaining the amount of OD
damage caused by glaucoma. For instance, few patients have small CDR but significant visual field loss, whereas some have large CDR with little visual field loss. This is mainly argued to be due to limitations with the CDR parameter which cannot account for various configurations of optic cup, neuroretinal rim and focal notching (local enlargement of cup region). Consequently, an alternate OD evaluation methodology, called the disc damage likelihood scale has been introduced by Spaeth et al (2002) to precisely describe the amount of OD damage caused by glaucoma.

As determination of cup area is difficult, Yuji Hatanaka et al (2010) used vertical profile calculation on the disc to measure the CDR. Blood vessels were first erased from the image and then the edge of optic disc was then detected by use of a canny edge detection filter. Twenty profiles were obtained around the center of the optic disc in the vertical direction on blue channel of the color image, and the profile was smoothed by averaging these profiles. After that, the edge of the cup area on the vertical profile was determined by thresholding technique. Although the proposed method is not error-free, the results indicated that it can be useful for the analysis of the optic disc in glaucoma examinations.

Cup features were selected by (Stapor 2006) using genetic algorithm. Classification of fundus eye images is achieved using Support Vector Machine (SVM) classifier. The method finds clusters of non-linearly separable as well as clusters of varying shapes and sizes and enables automatic classification of digital fundus into normal and glaucomatous ones. This paper presents the improved version of the classification system for supporting glaucoma diagnosis in ophthalmology using support vector machine classifier and achieves 94% sensitivity and 97% specificity. Stapor et al (2004) used morphological features for the quantitative evaluation of cup based on genetic algorithms. The computed features are then used in
classification procedure based on Multi Layer Perceptron (MLP) with Back Propagation (BP) learning rule. Shape of the cup and the numerical characteristics correlate to a certain extent with the progress of glaucoma and achieved 90% sensitivity and 86% specificity.

The high-dimensional preprocessed images are statistically compressed by principal component analysis and different generic feature types are compressed by an appearance-based dimension reduction technique. Bock et al (2010) proposed a probabilistic two-stage classification scheme and combined these features types to extract the novel Glaucoma Risk Index (GRI). GRI can only capture glaucomatous signs that are visible on these images and shows a reasonable glaucoma detection performance. The proposed appearance-based technique does not rely on accurately determined geometric parameters. An accurate segmentation of the cup rim as for automated determination of CDR is omitted. Due to glaucoma specific preprocessing and the appropriate combination of generic features, the generic data-driven approach can be applied for this medical classification task. The proposed two-stage classification scheme helps to combine classifiers of different image inputs.

Mei-Ling Huang et al (2007) used an automated classifier based on adaptive neuro-fuzzy inference to differentiate between normal and glaucomatous eyes from the quantitative assessment of summary data reports of OCT in Taiwan Chinese population. With Stratus OCT parameters used as input, the results from neuro fuzzy showed promising results for discriminating between glaucomatous and normal eyes with 90% accuracy. Rajendra Acharya et al (2011) developed a glaucoma diagnosis system using a combination of texture and higher order spectral features with a random forest classifier and achieved an accuracy of 91%. 
ANFIS was proposed by (Roger Jang 1993) to construct an input-output mapping based on both the human knowledge in the form of fuzzy if-then rules and stipulated input-output data pairs. ANFIS architecture is employed to model nonlinear functions, identify nonlinear components in control systems and predict a chaotic time series. ANFIS approach can be extended to automatic control and signal processing applications. As there are too many fitting parameters, the resultant model is not reliable for certain inputs.

Jang and Sun (1995) selected inputs that have more prediction power instead of using all the inputs or scatter partitioning. Jang et al (2004) assumed a fixed ANFIS structure and solved parameter identification through the hybrid learning rule. Effective partitioning of the input space can decrease the number of rules and thus increase the speed in both learning and application phases. Adaptive capability of ANFIS makes it almost directly applicable to adaptive control and learning control. ANFIS can replace almost any neural network in a control system and can perform the same function. By using adaptive network as a common framework adaptive fuzzy models can be constructed for applications such as data classification and feature extraction. Ubeyli and Guiler (2005) suggested that neural networks, fuzzy systems and the combination of both can be applied to computer aided diagnosis for various applications.

Rami J.Oweis and Muna J.Sunna (2005) classified the image pixels into three sets of pixels: contour, regular and texture. The method is based on the spatial properties of the image features and makes use of multi scaled representations of the image. The method showed high quality classification for images of simple components. The presented pixel classification tool is highly powerful and independent of expert or any prior knowledge and supports intelligent decision at low costs. Method can be extended to
biomedical field due to the vast availability of images. Chin Ming Hong et al (2006) proposed a refined K means algorithm and a gradient based learning rule to logically determine and adaptively tune the fuzzy membership functions. Proposed neuro fuzzy network with feature reduction based on the gray-relational analysis identifies simplified and interpretable fuzzy rules to support medical diagnosis. Elwakdy et al (2008) used subtractive clustering to find the details of the training signals and to put them in a group of clusters. High recognition performance can be achieved through ANFIS. ANFIS systems have been recently used for optimization, modeling, prediction, signal and disease detection.

2.4 DETECTION OF DIABETIC RETINOPATHY

In recent years, the steadily growing numbers of diabetic patients have largely motivated the research works in developing tools and methodologies to facilitate the screening and evaluation procedures for diabetic retinopathy. Algorithms described in the literature for the detection of diabetic retinopathy can be classified in terms of steps below.

i) Preprocessing

ii) Automatic detection and masking of the optic disc

iii) Segmentation of the retinal vasculature.

iv) Localization of the macula and fovea.

v) Localization and segmentation of lesions
   a) Automatic detection of red lesions–microaneurysms, haemorrhages or vascular abnormalities.
   b) Automatic detection of bright lesions-exudates, cotton wool spots, drusen.
Early diagnosis and accurate staging are essential prerequisites for effective treatment of diabetic retinopathy and reduction of visual disability risk. In the medical imaging field, the accurate and automated delineation of anatomic structures from image data sequences is a lasting issue and there is a growing interest in the research community to explore further in this domain. It progresses around the study of digital images with the main aim of supplying computational tools which aid in quantification and visualization of interesting pathologies and anatomical structures. Patients identified with diabetes are likely to develop eye disorders namely cataracts and glaucoma and its effects on the retina may lead to vision loss. Ege et al (2000) suggested that the existing methods of detection and assessment of DR is expensive and require trained ophthalmologists. The screening of diabetic patients to identify the progression of diabetic retinopathy can lessen the risk of blindness by around 50%.

2.4.1 Database

Digital Retinal Images for Vessel Extraction (DRIVE) dataset consists of 40 color fundus images out of which 33 photographs do not show any sign of diabetic retinopathy and seven images shows signs of mild early diabetic retinopathy. The images were acquired using a Canon CR5 non mydriatic 3CCD camera with a 45° FOV. Each image was captured using 8 bits per plane at 768 x 584 pixels. FOV of each image is circular with a diameter of approximately 540 pixels. Structured Analysis of the Retina (STARE) database consists of 81 fundus images. 31 images represent normal retinas and 50 images represent various diseased retinas. The images were captured using a Topcon TRV-50 fundus camera at 35° FOV and were digitized at 700 x 605 pixels, 8 bits per color channel. Standard Diabetic Retinopathy Database Calibration level 0 (DIARETDB0) dataset consists of 130 color fundus images of which 20 images are normal and 110 images
contain signs of diabetic retinopathy. Images are of size 1500 x 1152 pixels and were captured with a 50° FOV. A data set taken with several fundus cameras containing different amounts of imaging noise and optical aberrations is referred to as calibration level 0 fundus images. Standard Diabetic Retinopathy Database Calibration level 1 (DIARETDB1) dataset consists of 89 color retinal images of size 1500 x 1152 pixels, of which 84 images contain at least mild nonproliferative signs of diabetic retinopathy and 5 images are considered as normal which do not contain any signs of the diabetic retinopathy. Images were captured with the same 50° field of view digital fundus camera with varying imaging settings like flash intensity, shutter speed, aperture and gain controlled by the system. The data can be used to evaluate the general performance of diagnostic methods.

2.4.2 Detection of Fovea

The position of an abnormality relative to the location of fovea is useful for effective diagnosis of diabetic retinopathy and other retinal diseases. Fovea is the centre of macula and is at present approximately 2.5 times the optic disc diameter. Sinthanayothin et al (1999) used template matching approach to detect macula and fovea. Li and Chutatape (2004) used a model based approach to detect fovea. Niemeijer et al (2007) derived information from an active shape model to identify fovea. A single point distribution model was utilized to detect fovea. Jeetinder Singh et al (2008) used a cost function that depends on grouping of global and local cues to locate the exact position of the model points. An appearance-based localization method using different image channels was applied to detect fovea. A novel approach to detect fovea is developed in this thesis based on the information regarding optic disc and the darkest cluster of pixels away from the optic disc.
2.4.3 Bright Lesion Detection

Walter et al (2002) and Wang et al (2000) used correction of nonuniform illumination in retinal images as a preprocessing technique, Sinthanayothin et al (1999) and Usher et al (2004) used contrast enhancement to distinguish objects and the background. Among the abnormalities caused by diabetic retinopathy, bright lesions one of the most usually occurring lesions, are due to the damaged blood vessels which leak proteins and lipids. During the progression of diabetic retinopathy, the size and distribution of bright lesions may be changed. The detection and quantification of bright lesions will considerably contribute to the mass screening and estimation of background diabetic retinopathy. Here, the major bright lesion identification methods in the literature are reviewed.

Ward et al (1989) proposed a semiautomatic exudate detection system based on shade correction and thresholding, where the user involvement was required in the thresholding. By introducing a dynamic thresholding procedure Philips et al (1993) provided a considerable improvement to the previous system by detecting high intensity areas from red-free eye fundus images using global and local threshold values. The method was able to produce relatively good results in detecting the exudate pixels, but at the same time an unacceptable number of false positives were generated. To counter the false positives, Zheng et al (1997) introduced the use of local neighbourhood in the dynamic block-wise local thresholding procedure. A prototype was presented by Goldbaum et al (1996) on automated diagnosis based on template matching and edge detection to segment bright lesions. This method detected bright objects with an accuracy of 89%. From template matching and thresholding, there was an improvement towards supervised statistical pixel-based lesion classification. A minimum distance discriminant classifier was used by Wang et al (2000) to classify each pixel into bright lesions or non-lesions. The true hard exudate pixels were then pruned using the contrast information of the local neighborhood.
For image based evaluation, this approach achieved 100% sensitivity and 70% specificity. Sanchez et al (2004) detected hard exudates using two features of lesions namely color using statistical classification and its sharp edges using edge detector. The techniques used are highly sensitive to image contrast. Clara I. Sanchez et al (2008) presented an approach based on Fishers Linear Discriminator (FLD) analysis and makes use of color information to perform the classification of retinal exudates. It uses the isolated exudates color to characterize yellow regions, but it cannot represent the color of all exudates found in images. Variations in brightness and size of exudates make it difficult for the algorithm to detect all the exudates.

In addition to the discussed techniques above, neural networks were also exploited to classify the retinal abnormalities in a few studies. Meindert Niemeijer et al (2007) proposed a pixel classification scheme based on K-nearest neighbor classification to detect and differentiate hard and soft exudates and drusen. The system searched for candidate bright lesion pixels according to the features selected in the training stage. By using the density of classified lesion pixels among the neighboring pixels in the feature space, a lesion probability was assigned for each pixel in the test image to find the true bright lesions.

Pixel and block based clustering methods are then provided for segmentation of hard exudates. Hsu et al (2001) demonstrated that the role of domain knowledge improves appreciably the accuracy and robustness of detection of hard exudates in retinal images. Their approach of incorporating domain knowledge enhanced the ability to differentiate from other bright lesions and existing artifacts based on the contrast difference between the bright lesion and non-lesion classes.

The method proposed by Osareh et al (2003) first normalized the fundus image using histogram specification. Local contrast enhancement was
performed to improve both the contrast of lesions against the background and the overall color saturation. This was followed by Fuzzy C-Means (FCM) clustering to segment probable exudate candidates. Multilayer Perceptron neural network with ten inputs was used to classify the exudate candidates from non-exudates. This method attained a sensitivity of 92% and specificity of 82%. Osareh et al (2002) used SVMs to classify the exudate candidates from non-exudates and yielded a sensitivity and specificity of 87.5% and 92% respectively. Osareh et al (2009) identified hard exudate regions from the non-hard exudates regions and image features were extracted from the clustered regions and then classified using a neural network approach.

Akara Sopharak et al (2008) used FCM clustering to segment exudates for non-dilated retinal images. Four dominant features hue, standard deviation, intensity and adaptive edge by FCM were used to get coarse segmentation followed by fine segmentation using morphological reconstruction. Sensitivity and specificity achieved for exudates detection was 80% and 99.5% respectively. The method works effectively even on a poor computing system but failed to localize faint exudates. Akara Sopharak et al (2009) compared naive Bayes and SVM classifiers to a baseline nearest neighbor (NN) classifier employing the best feature sets from both classifiers and proved that the naive Bayes and SVM classifiers executed better than the NN classifier. Zhang and Chutatape (2004) presented a three stage approach to detect bright lesions and classify them into exudates and cottonwool spots. First, a local contrast enhancement was applied as a preprocessing stage. An improved fuzzy C-means was applied in Luminescence, Saturation, Hue angle (LUV) colour space to extract all the candidate bright lesions. A hierarchical SVM classification was used to classify bright lesions from non-lesions. The authors also classified exudates and cottonwool spots using a polynomial kernel in the SVM classification. This method classified bright lesions and bright non-lesions with a sensitivity
and specificity of 97% and 96% respectively. In classifying exudates and cottonwool spots, this method achieved a sensitivity of 88% and specificity of 84%.

Region growing is another clustering technique applied in detection of hard and soft exudates. The widely cited research of Sinthanayothin et al (2002) used a recursive region growing algorithm to segment exudates in fundus images. A sensitivity of 88.5% and specificity of 99.7% were reported. However, these performances were measured based on 10 x 10 patches. A more recent region-growing approach was presented by Eswaran et al (2008), where the bright lesions were detected from edge magnitude image using a marker driven watershed transform. To emphasize the regions of interest, an average filtering and contrast stretching preprocessing steps were performed.

In addition to classification and clustering techniques, morphological techniques were attempted by Walter et al (2002) to morphologically reconstruct the eye fundus image exclusive of bright lesions. Initially, the bright candidate lesions were coarsely located based on their local contrast variation after morphologically suppressing the blood vessels. Secondly, the candidate bright lesion areas were removed and morphologically reconstructed to correspond the appearance of the retinal background. By thresholding the difference of the original image and the reconstructed image, the final lesion areas were obtained.

To segment the blood vessels in a retinal image, mathematical morphology can be used since the vessels were the patterns that exhibit morphological properties such as connectivity, linearity and curvature of vessels varying smoothly along the crest line. But background patterns also fit such a morphological description. In order to discriminate blood vessels from other similar structures, cross curvature evolution and linear filtering were employed by Zana et al (2001).
A sorting system was developed by Gary G.Yen and Wen -Fung Leong (2008) for fundus images to enhance the efficiency of the graders. The sorting system is based on the idea of hierarchical grading approach and the human inference system with multilevel knowledge representation. Lesions are well classified according to their severity levels and the method helps to assist the working of graders. Hierarchical approach significantly reduces the computational complexity by categorizing the lesions into several groups.

2.4.4 Detection of Dark and Bright Lesions

In the classification of different stages of diabetic retinopathy (Frank 1995) specified that blood vessel detection in retinal images is a crucial step and specifically the number of blood vessels vary with different stages of DR. Saiprasad Ravishankar et al (2009) detected features such as blood vessels, exudates, microaneurysms and haemorrhages using different morphological operations for early detection of DR. The algorithm evaluated on a database of 516 images provided 95.7% sensitivity and 94.2% specificity for exudates detection and 95.1% sensitivity and 90.5% specificity for microaneurysms and haemorrhages detection. Wong Li Yun et al (2008) extracted features from the raw images using image processing techniques and classified eye diseases in DR using a three layer feed forward neural network with a sensitivity of 90% and 100% specificity.

2.5 SHORTCOMINGS OF PREVIOUS TECHNIQUES

Techniques described in the literature are related to the detection of two ocular diseases viz glaucoma and diabetic retinopathy. OD localization is aimed at identifying the approximate centre of the optic disc or placing the disc within a specific region. In either case, optic disc localization is complicated by the presence of significant distracters. Blood vessels may cross the optic disc boundary obscuring the rim of the disc with the edges of
the vessels acting as distracters. Natural variation in the characteristics of OD including the differences in pigmentation and myelineation of the nerve fiber layer are significant problems in defining the contour of the disc. General purpose edge detection algorithms often fail to segment the optic disc due to fuzzy boundaries, inconsistent image contrast or missing edge features. Algorithms which rely on intensity variation proved simple and robust for OD localization in normal retinal images. However, an OD obscured by blood vessels or only partially visible may be misidentified using the methods based on identifying the brightest regions. Such methods are highly sensitive to distracters such as yellow or white lesions or bright features. Optic cup detected using thresholding and level set method requires manual initialization. Bending of small blood vessels at the cup edge is used as a clue to measure the cup boundary. There is a high density of vascular architecture traversing the cup boundary. This method can only provide several points of cup boundary in the area where there are small blood vessels. For the area without small blood vessels, the cup boundary is not easy to be estimated.

Even though many techniques have been proposed in this field, the methods are limited by at least one of the following drawbacks. User involvement is needed to select region of interest and the method is not completely automatic. Segmentation process requires more computational efforts. In the detection of DR, simple thresholding techniques used for the detection of lesions are highly undesirable as the variation in background intensities makes it difficult to find a proper threshold. Region growing methods are straightforward but selecting seed points are difficult. Attempts based on specialized features and morphological reconstruction techniques are highly sensitive to image contrast. Existing methods of exudates detection based on size and orientation are not sufficient for lesion detection. While the results are encouraging, existing techniques are limited by suboptimal feature selection and pixel classification techniques.
2.6 SUMMARY

A survey of techniques for the automatic detection of glaucoma and diabetic retinopathy has been presented in this chapter. The proposed method involves two phases (i) detection of glaucoma and (ii) detection of diabetic retinopathy.

For the detection of glaucoma, a novel approach is proposed initially for optic disc boundary detection to solve the problem of blood vessel occlusion and detect the optic disc even when the boundary of the disc is not continuous or blurred. As the color intensity of the optic cup cannot be fixed, a method for optic cup detection is proposed using the difference in pallor to estimate the cup-disc boundary. Currently, the CDR evaluation is manually performed and it is subjected to individual evaluation by ophthalmologists. Further dependence on manual grading limits its potential use for use in the mass screening of populations for early glaucoma detection. Also, CDR does not take into account the disc size and stages of the disease cannot be identified. Further, the blood collects along the individual nerve fiber that radiate outwards from the nerve. Such physiological changes are manifested in the fundus images and the texture features are used to quantify such difference in eye physiology. Therefore, structural features and textural features are to be combined for better analysis of the images as normal or abnormal. So a method is proposed to detect the early stage of glaucoma using structural and textural features. The approach used can help clinicians in several eye care applications such as diagnosis, screening and monitoring.

An integrated system is to be developed in the second phase for the detection of diabetic retinopathy, to enhance the performance of the system by i) improving the results of other tasks such as the detection of blood vessels, optic disc, localization of faint and small exudates using color and textural features and ii) proper selection of features to improve the performance of
classification techniques. An effective tool should therefore be developed to analyze fundus images to detect features such as exudates comparable to that of an ophthalmologist in order to provide decision support and reduce ophthalmologist's work load.