Chapter 2

Background

2.1 Introduction

This chapter provides the details related to basics of medical domain, especially ophthalmology. The anatomy of human eye, ocular fundus and its main anatomical components are briefly explained. Then description about the cause of diabetic retinopathy and maculopathy diseases, their symptoms, complications and risks at the individual level is provided. This chapter also presents a detail literature survey of existing methods on the automatic detection of anatomical structures in retina and current scenario of automatic diagnostic systems. Furthermore, the concepts and techniques used for developing the proposed methods have been presented in this chapter.

2.2 Anatomy of Human Eye

Vision is arguably the most used of five senses in the human body. We rely on our eyes to provide most of the information we perceive about the world, so much so, that a significant portion of the brain is devoted entirely for visual processing. The eye is often compared to a camera because of the way it processes light into information understandable by the brain (Khurana 2007). Both have lenses to focus the incoming light. A camera uses the film to create a picture, whereas the eye uses a
specialized layer of cells, called the retina, to produce an image. However the similarity stops here. The eye’s ability to focus on a wide range of objects having different sizes, luminosity and contrast at a high speed is more powerful than those of current cameras. Figure 2.1 illustrates a cross section of the human eye and highlights the main components. Light reaches the eye by first passing through the cornea which filters it, and begins focusing the image. The anterior chamber contains a viscous substance called aqueous humour that keeps the front of the eye firm and slightly curved. Light travels through the pupil, which compensates for changing light conditions by contracting or relaxing. The muscles responsible for these movements are in the iris. Subsequently, the lens squeezes or stretches to focus the rays of light on the retina. Among the various ocular structures, only the anatomical structures of retina are more relevant to the research work.

Fig. 2.1: Anatomy of human eye [Courtesy: http://fractalontology.wordpress.com]

The retina is a thin multi-layered sensory tissue that covers the inside wall at the back of eye called fundus. It is covered by millions of
photoreceptors (rods and cones). These photoreceptors are responsible for receiving light beams, converting them into electrical impulses and then transmitting these to the brain where they are turned into images. Figure 2.2 illustrates a typical normal retinal fundus image with highlighted regions of fovea, optic disc, blood vessels and macula. The outlying parts of the retina are responsible for peripheral vision while the central area, called macula, is in charge of central vision that allows us to see details and perform tasks that require central vision, for example, reading. The macula is a circular area in the central region of the retina measuring about 4 mm to 5 mm in diameter. A small depression in the center of macula measuring about 1.5 mm in diameter is called fovea. The fovea corresponds to the region of retina with highest sensitivity. The optic disc is the entry and exit site of blood vessels and optic nerve fibers responsible for transmitting electrical impulses from the retina to the brain. It is a brighter region than the rest of the ocular fundus and its shape will be usually round. The optic

Fig. 2.2: Anatomical structures of ocular fundus.
disc is approximately 3 mm nasal to the fovea, and it measures about 1.5 mm to 2 mm in diameter. The optic disc contains a central depression called optic cup and its depth varies among different individuals. The retinal blood vessels are derived from the central retinal artery and vein are responsible for nourishing the inner parts of the retina. The following section elucidates the complications of diabetic eye diseases that affect the normal functioning of retina.

2.3 Diabetic Eye Diseases

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both (Sachin et al., 2007). Diabetes has become one of the rapidly increasing health threats both in India and worldwide (Rakhi et al., 2001). One of the most feared complications of diabetes is damage caused to the eye. It is estimated that people with diabetes have a 25 times greater risk of going blind than the non-diabetic population (Fong et al., 2003). Diabetic retinal changes are a major cause of visual impairment and thus understanding of this diabetic complication is imposed as a particular health, social and economic problems (Kanski 1997). The two main complications associated to the retina are diabetic retinopathy and maculopathy. It is estimated that at any time around 10% of patients with diabetes will have diabetic retinopathy (Smith et al., 2007). According to Bone et al., 2004, early and complete photocoagulation of the affected area is the only treatment for delaying or preventing the decrease in visual acuity.
2.3.1 Diabetic Retinopathy

Diabetic retinopathy is a vascular disorder occurring due to the combination of micro-vascular leakage and micro-vascular occlusion within the retina (McGavin 1996). It is primarily classified into Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). Typically there are no salient symptoms in the early stages of diabetic retinopathy, but the number and severity predominantly increase with the time. Non proliferative diabetic retinopathy is the most common and may arise at any point in time after the onset of diabetes. Ophthalmologists detect these changes by examining the patient's retina and look for spots of bleeding, lipid exudation, or areas of retinal swelling. Identification and recording of the following abnormalities (see Figure 2.3) will aid in the accurate assessment of retinopathy severity.

![Anatomical and pathological features in colour retinal image.](image)

Fig. 2.3: Anatomical and pathological features in colour retinal image.
**Microaneurysms:** These are the earliest clinical abnormality to be noticed in the eye. These are local swelling of retina capillary and usually appear in isolation or in clusters. Their size ranges from 10 to 100 microns and are dark red spots that look like tiny hemorrhages (Kanski 1997). The number of microaneurysms increases as the degree of retinal involvement progresses.

**Hemorrhages:** Intra-retinal hemorrhages appear when capillaries or microaneurysms rupture and some blood leaks out of these vessels. In Figure 2.3 hemorrhages can be seen as red flame shaped regions.

**Hard exudates:** Hard exudates represent leak of fluid that is rich in fat and protein from surrounding capillaries and microaneurysms within the retina. These are one of the main characteristics of diabetic retinopathy and appear as random yellowish patches of varying sizes, and shapes.

**Soft exudates:** These are often called cotton wool spots and are more often seen in advanced retinopathy. These abnormalities usually appear as little fluffy round or oval areas in the retina with a whitish colour, usually adjacent to an area of hemorrhage. Cotton wool spots come about due to the swelling of the surface layer of the retina in the absence of normal blood flow through the retinal vessels. The nerve fibers are injured in a particular location resulting in swelling and appearance of a cotton wool spot.

Proliferative diabetic retinopathy, the advanced stage retinopathy develops in more than 50 percent cases after about 25 years of onset of the disease. Therefore, it is more common in patients with juvenile onset diabetes (Shah et al., 2000). The hallmark of PDR is the
growth of new blood vessels in the areas where normal capillaries have already closed. These new blood vessels are abnormal and fragile. They grow along the retina and along the surface of the clear, vitreous gel that fills the inside of the eye. By themselves, these blood vessels do not cause symptoms or vision loss. However, they have thin, fragile walls that leak blood resulting in severe vision loss and even blindness can be the end result.

2.3.2 Diabetic Maculopathy

Diabetic maculopathy is a common complication of diabetes mellitus, characterized by macular edema and frequently accompanied by lipid exudation (Chowdhury et al., 2002). Diabetic maculopathy, defined as retinopathy within one disc diameter of the center of the macula is the major cause of vision loss (Zander et al., 2000). One of the morphological characteristics of diabetic retinopathy clinical signs is the onset of retinal hard exudates, which are manifested as whitish-yellowish changes. They are most frequently localized in the area of the macular region, surrounding the zones of retinal edema, although they can also be noticed in other localizations at the posterior pole of the eye fundus. They are a dominant feature in both exudative and mixed types of diabetic maculopathy. If they are very apparent and affect the center of macular region called fovea centralis, visual function is significantly and irrevocably damaged as shown in Figure 2.4. Diabetic maculopathy comprises of two aspects: First is the macular edema in which fluid and lipoproteins accumulate within the retina. Second is the macular ischaemia in which there is closure of perifoveal capillaries demonstrable on fundus fluorescein angiography. It is not known to what extent macular ischaemia contributes to the visual loss
attributable to diabetic maculopathy and this work is limited to the automatic detection of macular edema and its severity stages.

Fig. 2.4: Normal vision (left) and same scene viewed by person with diabetic maculopathy (right) [Courtesy: http://www.nei.nih.gov].

### 2.4 Literature Review

Recent advances in technology has led to the development of digital imaging systems offering very high-resolution images that are sufficient for most clinical scenarios (Facey et al., 2002; Fransen et al., 2002). In ophthalmology, retinal digital imaging provides a permanent, high quality record of the appearance of the retina with application for screening program of diabetic retinopathy (Hansen et al., 2004). Digital retinal images can be subjected to image analysis to perform objective quantitative analysis of fundus images and has the potential for automated diagnosis to aid in decision making. Retinal image analysis is a complicated task, particularly because of the variability of the images in terms of the colour, the morphology of the retinal anatomical pathological structures and the existence of particular features in different patients, which may lead to an erroneous interpretation. This has led to the development of many retinal image analysis methods. Retinal images are usually processed in an algorithmic sequence, with
the output of one stage forming the input to the next. Typical sequence may consist of one or more preprocessing procedures followed by image segmentation, feature extraction and classification stages. This literature survey reviews the work related to digital retinal image analysis in the automated diagnosis of diabetic retinopathy with emphasis on detection of normal and abnormal features in the digital colour retinal image.

2.4.1 Vessel segmentation methods

The segmentation and measurement of the retinal vasculature is of primary interest in the diagnosis and treatment of a number of ophthalmologic conditions (Al-Rawi et al., 2007; Dougherty et al., 2010). The accurate segmentation of the retinal blood vessels is often an essential prerequisite step in the identification of retinal anatomy and pathology. In addition, the segmentation of the vessels is useful for registration of patient images obtained at different times (Laliberté et al., 2003; Ritter et al., 1999; Kubeka et al., 2004). Existing vessel extraction techniques and algorithms can be classified into four main approaches as follows.

**Matched filter approaches:** Matched filtering involves convolution of the image with multiple filters for extraction of objects of interest. In Chaudhuri et al., 1989, a two-dimensional kernel was proposed for segmentation of the vasculature. The profile of the filter is designed to match that of a blood vessel, which typically has a Gaussian or a Gaussian derivative profile. The kernel is typically rotated in 30 to 45 degrees increments to fit into vessels of different orientations. The highest Matched Filter Response (MFR) is selected for each pixel and is typically thresholded to provide a vessel image. As noted by several authors (Patton et al., 2005; Teng et al., 2002; Heneghan et al., 2002) a
MFR method is effective when used in conjunction with additional processing techniques. However, the convolution kernel may be quite large and needs to be applied at several rotations resulting in a computational overhead, which may reduce the performance of the overall segmentation approach. In addition, the kernel responds optimally to vessels that have the same standard deviation of the underlying Gaussian function specified by the kernel. As a consequence, the kernel may not respond to vessels that have a different profile. The retinal background variation and low contrast of the smaller vessels also increases the number of false responses around bright objects such as exudates and reflection artifacts. Several authors have proposed refinements and extensions which address many of these problems (Hoover et al., 2000; Yang et al., 2000; Chanwimaluang et al., 2003). In Hoover et al., 2000, the local and region-based properties are used to segment blood vessels in retinal images. The method examined the matched filter response image using a probing technique. The technique classified pixels in an area of response image as vessels and non-vessels by iteratively decreasing the threshold. In each of the iteration, the probe examined the region-based attributes of the pixels in the tested area and segmented the pixels classified as vessels.

**Vessel tracking approaches:** Vessel tracking algorithms segment a vessel between two points (Wu et al., 2006; Pinz et al., 1998; Kochner et al., 1998; Frame et al., 1996). Unlike the previously described techniques for vasculature segmentation they work at the level of a single vessel rather than the entire vasculature. A vessel tracking approach typically steps along the vessel. Here the center of the longitudinal cross-section of vessel is determined with various properties of the vessel including average width and tortuosity measured during tracking. The main advantage of vessel tracking methods is that they provide highly accurate vessel widths, and can provide information
about individual vessels that is usually unavailable using other methods. Unfortunately, they require the starting point, and usually the end point, of a vessel to be defined by a user and are thus, without additional techniques, of limited use in fully automated analysis. In addition, vessel-tracking techniques may be confused by vessel crossings and bifurcations and often tend to terminate at branch points.

**Classifier based approaches:** Artificial neural networks have been extensively investigated for segmenting retinal features such as the vasculature (Akita et al., 1982). The operation of a neural network is analogous to that of a matched filter. Both take sub windows of the image as input and return a probability measure as output. Two studies, both using the back-propagation algorithm, have detected (Gardner et al., 1996) and segmented (Sinthanayothin et al., 1999; Soares et. al., 2006) the retinal vasculature. Detection involves classifying sub windows as containing vessels or not. Segmentation involves classification of individual vessel and non vessel pixels. In Sinthanayothin et al., 1999 images are preprocessed with principal component analysis to reduce background noise by reducing the dimensionality of the data set and then applied a neural network to identify the pathology. They reported overall sensitivity and specificity of 83.3% and 91%, respectively. The result of the approach was compared with an experienced ophthalmologist manually mapping out the location of the blood vessels in a random sample of seventy three 20×20 pixel windows and requiring an exact match between pixels in both images. The neural networks researched by Gardner et al., 1996 used 20×20 pixel sub windows. Nine thousand of these sub windows were marked for neural learning validation. Generalization assessment over 1200 unseen sub windows resulted in a sensitivity of 91.7%. One of the advantages that make neural networks attractive in medical image segmentation is its ability to use nonlinear classification boundaries
obtained during the training of the network and ability to learn. However, one of the disadvantages of it is that they need to be trained every time whenever a new feature is introduced to the network and another limitation is the necessity for configuring the network with training data or a gold standard. This gold standard data set consists of a number of images whose vascular structure must be precisely marked by an ophthalmologist. However, as noted by Hoover et al., 2000, there is significant disagreement in the identification of vessels even amongst expert observers.

**Morphological approaches:** Morphological image processing exploits features of the vasculature shape that are known a priori, such as it being piecewise linear and connected (Zana et al., 1999; Walter et al., 2002; Zana et al., 2001). Algorithms that extract linear shapes can be very useful for vessel segmentation. In Zana et al., 2001 a vessel segmentation algorithm from retinal angiography images based on mathematical morphology and linear processing was presented. A unique feature of the algorithm is that it uses a geometric model of all possible undesirable patterns that could be confused with vessels in order to separate vessels from them. The strength of the algorithm comes from the combination of mathematical morphology and differential operators in the segmentation process. In Jiang et al., 2003, linear bright shapes and basic features are extracted using mathematical morphology operators and vessels are extracted using curvature differentiation and laplacian filter. Gregson et al., 1995 utilized morphological closing to help identify veins in the automated grading of venous beading by filling in any holes in the silhouette of the vein created during the processing procedure. The main disadvantage of exclusively relying upon morphological methods is that they do not exploit the known vessel cross-sectional shape. Also, this approach
works well on normal retinal images with uniform contrast but suffers
from noise due to pathologies within the retina of eye.
In the proposed work, a hybrid method for efficient segmentation of
multiple oriented blood vessels in colour retinal images is presented.
Initially, the appearance of the blood vessels is enhanced and
background noise is suppressed with the set of real component of a
complex Gabor filters. Then the vessel pixels are detected in the vessel
enhanced image using entropic thresholding based on Gray Level Co-
ocurrence Matrix (GLCM) as it takes into account the spatial
distribution of gray levels and preserving the spatial structures. Two
sets of hand labeled images from publicly databases are used to
evaluate performance of the method. The sensitivity and specificity of
86.47% (standard deviation of 3.6) and 96% (standard deviation of 1.01)
respectively is achieved.

2.4.2 Optic disc and Macula detection methods

The location of the optic disc is important in retinal image analysis
(Goldbaum et al., 1996). For example, it is used for vessel tracking
(Gagnon et al., 2001), as a reference length for measuring distances in
retinal images (Li et al., 2001) and for registering changes within the
optic disc region due to disease (Zhang et al., 2002). In case of diabetic
retinopathy lesions identification removing the false positive optic disc
region leads to improved lesion diagnosis performance (Osareh et al.,
2007; Sopharaki et al., 2007). The measurement of varying disc
diameter is used in the detection of glaucoma (Marios et al., 2005).
Existing methods and their drawbacks for the localization and
boundary detection of the optic disc is as follows.

Optic disc localization: There have been few works on locating the
optic disc in retinal images based on the gray level variation in the optic
disc region (Chaudhuri et al., 1989b; Lee et al., 1999; Katz et al., 1988). Here, the optic disc was localized by identifying the largest cluster of bright pixels. These algorithms proved to be simple, fast and reasonably robust for optic disc localization in normal retinal images with negligible variation between images. However, an optic disc obscured by blood vessels or only partially visible will be misidentified using these methods. Also, these methods did not find the center of the optic disc.

In few works (Sinthanayothin et al., 1999; Osareh et al., 2002), characteristics of the optic disc like intensity, morphology and colour were investigated for localizing the disc in the presence of distracters. Sinthanayothin et al., 1999 used an 80×80 pixel sub-image to evaluate the intensity variance of adjacent pixels. The point with the largest variance was assumed to be the center of the optic disk. The assumption was that visible signs of disease such as exudates will have a lower intensity variance than the optic disk. The authors reported a 99.1% sensitivity in localizing the center of the optic disk in images with little or no visible signs of lesions. However, Lowell et al., 2004, reported the misidentification of the optic disc using this algorithm in retinal images with large number of white lesions, light artifacts or strongly visible choroidal vessels. Osareh et al., 2002 proposed a similar technique using a 110×110 pixel template image obtained by averaging the optic disk region in 25 retinal images. They reported of successfully localizing the approximate center of the optic disk in all of 75 images considered. In fact, the authors made an assumption to locate the optic disc from those retinal images with no visible symptoms.

The Hough transform has been investigated by a number of authors for the localization of the optic disc (Yulong et al., 1990; Pinz et al., 1998; Liu et al., 1997; Kochner et al., 1998; Ege et al., 2000; Lowell et al., 2004; Chrastek et al., 2005). The underlying principle used to
identify the optic disc was to consider that a retinal image is comprised of an infinite number of potential circles which pass through a number of edge points. The edge points are derived from edge information extracted by applying one of several available edge detection algorithms. The Hough transform determines which of these potential circles intersect with the greatest number of circles in the image. Liu et al., 1997 used a circular Hough transform after edge detection to localize the optic disc in the red colour channel. The first stage searched for an optic disc candidate region defined as a 180×180 pixel region that included the brightest 2% of gray level values. A Sobel operator was then applied to detect the edge points of the candidate region and the contours were then detected by means of the circular Hough transform. Kochner et al., 1998, proposed a combination of a Hough transform and steerable filters to automatically detect the location and size of the disk. These kinds of approaches are quite time consuming and rely on conditions regarding the shape of the optic disc that are not always met. Moreover, edge detection algorithms often fail to provide an acceptable solution due to the fuzzy boundaries, inconsistent image contrast or missing edge features.

Principal components analysis has also been used as a means of extracting common features of retinal images including the optic disk and blood vessels (Li et al., 2004; Sanchez et al., 2004; Sinthanayothin et al., 1999). The likelihood of a candidate region being an optic disk was determined by comparing the characteristics of the optic disk extracted from a training image to those derived from an unseen image. Li et al., 2004 reported the correct localization of the optic disc with sensitivity of 99% in 89 images. Few methods have reported a technique for locating the optic disc using a geometrical parametric model. According to Foracchia et al., 2004, the retinal vessels originating from the optic disc follows a similar directional pattern in all images. Hoover
et al., 2003, reported of correctly identifying optic disc with 89% sensitivity using a fuzzy convergence algorithm. Their method finds the strongest vessel network convergence as the primary feature for detection using blood vessel binary segmentation, the disc being located at the point of vessel convergence. In these works, the authors did not address the optic disc boundary localization and also segmentation and tracking of vessels itself is a difficult task. Lalonde et al., 2001 localized the optic disc using a combination of two procedures including a Hausdorff based template matching technique on the edge map, guided by a pyramidal decomposition technique. The edge maps were calculated using Canny edge detection and therefore the low and high hysteresis thresholds must be defined properly. The drawback was that a priori information of the image characteristics and whether the input image is centered on macula or on optic disc had to be provided making it semiautomatic.

**Optic disc boundary segmentation:** Optic disc contour segmentation is usually performed after localizing disc and it is a non-trivial problem. Walter et al., 2001 described an approach using colour space transformation and morphological filtering techniques for disc localization. The optic disc was first localized using the luminance channel of the hue-luminance-saturation colour space and a thresholding operation was applied to determine the approximate locus of the optic disk. The precise contour of the disk was then determined, using watershed transform. The contour of the optic disc was identified in 27 of the 29 images often with slight distortion of the contour due to outgoing vessels or low contrast.

Few works have investigated the parametric active contour model to detect the boundary of optic disc (Mendels et al., 1999; Osareh et al., 2002). Mendels et al., 1999 investigated applying morphological
operator followed by an active contour to segment the disc. Osareh et al., 2002 presented two key extensions in the use of gradient vector flow snakes for optic disc segmentation. Here, the optic disc was first localized using template matching. Secondly, colour morphological processing was used to obtain a more homogeneous inner disk area, which increased the accuracy of the snake initialization. In these methods the parametric active contours depend much on image gradient and less sensitive to location of initial contour resulting in reduced performance weak optic disc boundaries.

**Fovea localization:** Temporal to the optic nerve head is the fovea (or macula), which appears darker in colour and has no blood vessels present in the center. The fovea lies at the center of the macula and is the part of the retina that is used for fine vision. The fovea was detected by looking at the non vessel area and intensity variation (Ibanez et al., 1999). In Sinhanayothin et al., 1999, the location of the fovea was chosen as the position of maximum correlation between a model template and the intensity image, obtained from the intensity-hue-saturation transformation. In these methods, foveal localization was particularly affected if there was poor centration of the fovea in the image. Li et al., 2004 detected the foveal region using model-based methods. They estimated the position of the fovea by extracting the points on the main blood vessels by a modified active model, and fitting a parabola curve with the optic disc as the center. Fovea is then located at 2 disc diameters from the optic disc on the main axis of the parabola.

In the proposed work a new approach for the automatic localization and accurate boundary detection of the optic disc is presented. Iterative thresholding method followed by connected component analysis is employed to locate the approximate center of the optic disc. Then geometric model based implicit active contour model is
applied to find the exact boundary of the optic disc. The method is evaluated against a carefully selected database of 148 retinal images and compared with the human expert. The center of optic disc is found with an accuracy of 99.3%. The mean sensitivity of 90.67% (standard deviation of ±5) is achieved for correct boundary segmentation. The fovea is located based on its distance from the center of the optic disc. To find the exact center of macula called foveola, a search area is formed to find darkest non vessel region. The method was able to achieve 96.6% sensitivity for locating the center of fovea.

2.4.3 Hard exudates detection methods

Exudates are one of the most commonly occurring lesions in diabetic retinopathy. They are associated with patches of vascular damage with leakage. The size and distribution of exudates may vary during the progress of the disease. The detection and quantification of exudates will significantly contribute to the mass screening and assessment of diabetic retinopathy.

In one of the earliest method by Ward et al., 1989, fundus transparency was imaged, digitized, and then pre-processed, to reduce shade variations in the image background and enhance the contrast between the background and the exudate lesions. Exudates were then separated from the background on a gray level basis. The proposed technique required user intervention for selecting the threshold value. Most exudates show higher gray level values compared to the nearby retinal background, some smaller exudates have about the same intensity as the background of the retinal making it unlikely for simple global thresholding techniques to present a satisfactory result. Therefore, Liu et al., 1997 introduced a dynamic thresholding algorithm, which calculated every pixel's threshold according to its local
histogram. In this way, the images were firstly divided into 64 × 64 pixel patches and then the local threshold of each patch was obtained using its histogram feature. Then, the dynamic threshold of every pixel was found using interpolation of the local thresholds of four neighbouring patches which include that pixel. These methods also detected other type of lesions like cotton wool spots along with exudates.

Classifier based methods were used to separate exudates from other lesions (Wang et al., 2000; Ege et al., 2000; Niemeijer et al., 2005). In Wang et al., 2000, a minimum distance discriminant classifier was used to categorize each pixel into yellow lesion or non-lesion class. This work proposed to differentiate yellow lesions from red lesions, but it involved misclassification of other yellowish lesions at the same time. The image-based diagnostic accuracy of this approach was reported as 100% sensitivity and 70% specificity. Ege et al., 2000 used a combination of template matching, region growing and thresholding techniques for preliminary lesion detection. Then they used Bayesian classifier to classify the yellow lesions into exudates, cotton wool spots and noise. The classification performance for this stage was only 62% for exudates and 52% for the cotton wool spots. Hsu et al., 2001 presented a domain knowledge based approach to detect exudates. Dynamic clustering was used to determine lesion clusters. Then, domain knowledge was applied to identify true exudates. Usher et al., 2004, detected the candidate exudates region by using a combination of region growing and adaptive intensity thresholding. In Goh et al., 2001, the spectrum feature center of exudates and background are computed and then the distance from each pixel to class center is calculated. The pixel is classified as exudate if it falls within the minimum distance.

Neural networks and fuzzy clustering have also been exploited to classify the retinal abnormalities in a few studies (Osareh et al., 2007;
Gardner et al., 1997; Jayakumari et al., 2007). In Gardner et al., 1997, the retinal images were broke down into small squares and are inputted to a back propagation neural network. In Osareh et al., 2007, the image was segmented depending on colour using Fuzzy C-means clustering. Then, 18 different features were inputted to a three layer neural network. They reported detection with 93% sensitivity and 94.1% specificity in terms of lesion based classification. Another neural network based exudate detection research was conducted by Hunter et al., 2000. The network was trained to distinguish exudates from drusen based on 16×16 pixel patches. They introduced a hierarchical feature selection method, based on sensitivity analysis to distinguish the most relevant features. They reported to have achieved 91% in lesion-based classification applied to a relatively small number of images. Sinthanayothin et al., 1999, applied a recursive region growing technique using selected threshold values in gray level images. In this work it was supposed that the processed retinal images are only including exudates, hemorrhages and microaneurysms and other lesions for example cotton wool spots were not considered. The authors have reported an accuracy of 88.5% sensitivity and 99.7% specificity for the detection of exudates.

Exudates were also detected using morphological techniques (Walter et al., 2002; Flemming et al., 2007; Sopharak et al., 2008; Sopharak et al., 2009). In Walter et al., 2002 exudates were identified according to their gray level variation. After initial localization, the exudates contours were subsequently determined by mathematical morphology techniques. The candidate exudate regions are initially found based on the initial threshold value. The second threshold represents the minimum value, by which a candidate must differ from its surrounding background pixels. They have reported an accuracy of 92.8% against a set of 15 abnormal retinal images.
In the proposed work, the hard exudates detection is performed in two successive steps. Initially the possible exudates regions are coarse segmented by \textit{k-means} clustering technique to separate possible exudate regions from the background in the image space. Next morphological reconstruction technique is applied to correctly segment the exudate regions. The method achieved an image based sensitivity of 98\% for exudate detection on set of 148 images and the result is also validated by ophthalmologists.

### 2.4.4 Automatic retinal screening systems

With the ever increasing diabetic population and the availability of fundus images in digital format, there is a need for computer based retinal screening systems. It is assumed that an automatic screening system would save the workload of ophthalmologists and aid in the diagnosis (Sinthanayothin \textit{et al.}, 2002; Lee \textit{et al.}, 2001).

Abràmoff \textit{et al.}, 2008 evaluated the performance of a system for automated detection of retinopathy in fundus images. The system was constructed entirely from published algorithms and it was tested in a large, representative, screening population. They achieved a sensitivity of 84\% and a specificity of 64\%. Philip \textit{et al.}, 2007 assessed the efficacy of automated “disease/no disease” grading for retinopathy within a systematic screening programme. Detection of retinopathy was achieved by automated grading with 90.5\% sensitivity and 67.4\% specificity. The system designed by Estabridis \textit{et al.}, 2007, detected the fovea, blood vessel network, optic disk, as well as bright and dark lesions associated with retinopathy. They reported to have achieved classification accuracy of 90\%.
In Nayak et al., 2008, area of the exudates, blood vessels and texture parameters coupled with neural network are employed to classify the retinal image into normal, NPDR and PDR. They reported a detection accuracy of 90% sensitivity. Again, Nayak et. al., 2009 presented a computer based system for the identification of CSME, Non-CSME and normal fundus eye images. Here, features were extracted from the raw fundus images which are then fed to a neural network classifier to get the result. In Sinthanayothin et al., 2003, an automatic computerized screening system was developed to recognize automatically the main components of the retina. Diseased and normal retina were classified using multilayer perceptron neural network. Their system yielded a sensitivity of 80.21% and 70.66% specificity.

In this work, a computer based system for automatic detection and grading of diabetic maculopathy severity level without manual intervention is presented. The optic disc is detected automatically and its location and diameter is used to detect fovea and to mark the macular region respectively. Next, hard exudates are detected using clustering and mathematical morphological techniques. Based on the location of exudates in marked macular region the severity level of maculopathy is classified into mild, moderate and severe. The method achieves a sensitivity and specificity of 95.6% and 96.15% with 148 retinal images for detecting maculopathy stages in fundus images as comparable to that of human expert. A graphical user interface has also been developed that can be used by clinicians during the mass screening of diabetic related eye diseases.
2.5 Summary

In this Chapter an insight into the domain knowledge, comprising of anatomy of the ocular fundus and the landmark retinal components were discussed. Two complications of diabetes, i.e., diabetic retinopathy and maculopathy were also discussed. This Chapter also provided a detailed literature on automatic detection of retinal anatomical, pathological structures and image analysis systems. From both number and diversity of algorithms used for retinopathy detection it is clear that there is no gold standard which solves the entire problem. Automated diabetic retinopathy detection system must serve patients in clinical practice. If it turns out that the reported approaches do not perform well in practical environments then we have to look for more theory so that we can design systems which cope better with the practical task. The discussion of this Chapter has led to the motivation for the development of fast automatic diabetic retinopathy screening system. The next four chapters propose the methods that lead to the development of this system capable of detecting the normal and abnormal features that aid ophthalmologists in diagnosing the severity stage of diabetic maculopathy.