Chapter 1

INTRODUCTION

1.1 Medical Imaging

Medical image is a technique and process of creating visual representations of internal part of the body for clinical analysis and medical intervention. Medical imaging has become a major tool in clinical trials since it enables rapid diagnosis with visualization and quantitative assessment. Medical imaging also establishes a database of normal anatomy and physiology to make it possible to identify abnormalities [1]. Many imaging devices are available today to represent internal structures of body visually. X-ray based methods of medical imaging include conventional X-ray, computed tomography (CT) and mammography. To enhance the X-ray image, contrast agents are used e.g. angiography examinations. Molecular imaging is used in nuclear medicine and uses a variety of methods to visualize biological processes taking place in the cells of organisms. Small amounts of radioactive markers, called radiopharmaceuticals, are used for molecular imaging. Other types of medical imaging are magnetic resonance imaging (MRI) and ultrasound imaging. Unlike conventional X-ray, CT and Molecular Imaging, MRI and ultrasound operate without ionizing radiation. MRI uses strong magnetic fields, which produce no known irreversible biological effects in humans [figure 1].
Most of the techniques used in medical imaging use that part of electromagnetic (EM) spectrum that a human eye cannot perceive [figure 2]. Different parts of the spectrum interact in different ways with the body because they have different energies. Medical imaging requires that the energy used to penetrate the body’s tissues also interact with those tissues. The visible light has limited ability to penetrate tissues at depth. Visible light images are used in dermatology, gastroenterology and obstetrics. The most familiar portion of EM spectrum, other than visible part, are x-rays, which are used in mammography and computed tomography (CT); radiofrequency in magnetic resonance imaging (MRI), and gamma rays in nuclear medicine.
1.1.1 Need for Medical Image Processing

Image processing techniques are useful in diagnosis and treatment planning in medicine. These techniques are non-invasive and further they have helped doctors in performing keyhole surgeries for reaching the interior parts without a major surgical opening of the body. Thus helping patients with fast recovery reduced hospitalization time and spend less. Medical imaging also helps us learn more about neurobiology and human behaviors.

Computer Tomography (CT), Magnetic Resonance Imaging (MRI), Ultra Sound (US) and other imaging technique provides information about human anatomy. These tools captures images and may be sent online to a specialist doctor at a remote place for diagnosis and get his advices for patient treatment.

1.1.2 Medical Image Processing

Analysis of diverse types of medical images requires sophisticated computerized quantification and visualization tools. Digital images are composed of individual pixels, to which discrete brightness or color values are assigned. They can be efficiently processed, objectively evaluated, and made available at many places at the same time by means of appropriate communication networks and protocols.

The main goal of medical image processing is to extract clinically relevant information or knowledge from medical images which are stored digitally. Generally, data may be from a microscopic image in the form of X-ray image, the contrast image, the ultrasonic image and the tomographic image. The data can be extracted from these images, for example, detection of tumor, arteriosclerosis, or other harmful changes. Data can also be from organ size, blood flow, and other measuring, etc. Medical image processing focuses on the computational analysis of the images, whereas medical imaging focuses on image acquisition. The methods can be grouped into several broad categories: image segmentation, image registration, image-based physiological modeling, and others. It involves quantitative measurements as well as abstract interpretations of medical images. Prior knowledge on the nature and content of the images must be integrated into the algorithms on a high level of abstraction.

The machine vision-based medical image processing includes following steps
Smoothening- In medical images the imperfections may be inherent to the imaging modality or results of a deliberate delaying during acquisition or due to patient’s movements causing the image to blur. Hence, to reduce these imperfections smoothening is applied to the images that aim to reduce noise by preserving important information and without introducing too much distortion.

Enhancing- Medical imaging deals with more sensitive area- medical science. The images captured by various devices may lead to wrong conclusion and diagnosis. Hence, these images are subjected to a process called image enhancement technique that aims at improving the visual aspects of an image.

Image Registration - Image registration is the process of bringing two or more images into spatial correspondence (aligning them). In the context of medical imaging, image registration allows for the concurrent use of images taken with different modalities (e.g. MRI and CT), at different times or with different patient positions. In surgery, for example, images are acquired before (pre-operative), as well as during (intra-operative) surgery. Because of time constraints, the real-time intra-operative images have a lower resolution than the pre-operative images obtained before surgery. Moreover, deformations which occur naturally during surgery make it difficult to relate the high-resolution pre-operative image to the lower-resolution intra-operative anatomy of the patient. Image registration attempts to help the surgeon relate the two sets of images.

Segmentation - Segmentation is the process of partitioning an image into different segments. For a medical image, these segments often correspond to different tissue classes, organs, pathologies, or other biologically relevant structures. Medical image segmentation is made difficult by low contrast, noise, and other imaging ambiguities. Although there are many computer vision techniques for image segmentation [1], some have been adapted specifically for medical image computing [1].

Visualization- Visualization is used both for initial exploration and for conveying intermediate and final results of image analyses. The [figure 3] illustrates several types of visualization:

1. The display of cross-sections as gray scale images;
2. Reformatted views of gray scale images (the sagittal view in this example has a different orientation than the original direction of the image acquisition; and
3. A 3D volume rendering of the same data. The nodular lesion is clearly visible in the different presentations and has been annotated with a white line.

![Figure 3: Classification](image)

1.2 The Eye Structure and Abnormalities Associated with Eye

The eye ball is placed close to the brain so that it sends the information captured to brain for analysis. The message is passed through optic nerve. The eye is composed of three layers. The outer most layer is called sclera that protects the soft tissues of the eye. The transparent portion in the front is called cornea that allows the light to pass through and the crystalline lens behind cornea helps focus the light on to retina. The second layer is called choroid. It is classified into three zones. The first zone choroid proper carries nourishment to the tissues of the eye. The next zone is called ciliary body. It is a broad ring shaped band of thin muscle fibers which plays a vital role in vision adjustment of the eye. The third zone is iris which expands and contracts the pupil. The innermost layer of the eye is the retina a very delicate membrane composed of photoreceptors. The retina is part of optic nerve that transmits light pulses to brain. Macula is a small area at the centre of the retina that gives the fine pin point centre of the vision. The area of retina surrounding macula gives the peripheral vision.

![Figure 4: Structure of Human Eye](image)
Most people will have a problem with their eyes at some point in their lives. Most eye problems are not serious and do not require a doctor's care. However, certain eye diseases are serious and can result in blindness if left untreated. Most common eye problems include spots and floaters, pink eye, uveitis, eye herpes, dry eye syndrome, retinal detachment, color blind, and blepharitis. Many eye diseases have no symptoms. These include glaucoma, macular degeneration, diabetic retinopathy, retinous pigmentosa, cataract, and retinoblastoma. Regular comprehensive eye examinations are important for early detection and treatment of eye disease. Many systemic diseases such as diabetes, grave’s disease and Behcet's Disease affect eyes in many different ways. The symptoms of few of the diseases are listed below.

**Cataract**: A cloudy or opaque area in the normally clear lens of the eye.

**Chalazion**: A slowly developing lump that forms due to blockage and swelling of an oil gland in the eyelid.

**Color Vision Deficiency**: The inability to distinguish certain shades of colors or, in more severe cases, sees colors at all.

**Computer Vision Syndrome**: A group of eye and vision-related problems that result from prolonged computer use.

**Conjunctivitis**: An inflammation or infection of the conjunctiva, the thin transparent layer of tissue that lines the inner surface of the eyelid and covers the white part of the eye.

**Diabetic Retinopathy**: A condition occurring in persons with diabetes, which causes progressive damage to the retina, the light sensitive lining at the back of the eye.

**Dry Eye**: A condition in which there are insufficient tears to lubricate and nourish the eye.

**Floaters & Spots**: The shadowy images that are seen moving in your field of vision caused by particles floating in the fluid that fills the inside of the eye.

**Glaucoma**: A group of disorders leading to progressive damage to the optic nerve, and is characterized by loss of nerve tissue resulting in loss of vision.

**Macular Degeneration**: An eye disease affecting the macula, the center of the light sensitive retina at the back of the eye, causing loss of central vision.

**Retinal Detachment**: A tearing or separation of the retina, the light sensitive lining at the back of the eye, from the underlying tissue.

**Retinitis Pigmentosa**: A group of inherited disorders of the retina, the light sensitive lining at the back of the eye, which cause poor night vision and a progressive loss of side vision.

**Retinoblastoma**: A rare type of eye cancer occurring in young children that develops in the retina, the light sensitive lining at the back of the eye.
1.3 Fundus Image Formation

Fundus photography is performed by an ophthalmic photographer (ophthalmologist) with a fundus camera [figure 5], which basically consists of a specialized low power microscope with an attached camera. Fundus cameras work like digital microscopes that give close-up and personal view of the interior of your eyeballs. The light that passes through the eye is reflected back into the camera, which digitizes an image of the retina at the moment of reflection. Some fundus cameras are integral with, or attached to, the tonometer. This ophthalmic instrument registers the pressure of your inner eye.

![Figure 5: A Fundus Camera](image)

1.4 Diabetic Retinopathy and Diabetic Maculopathy

Diabetes has reached epidemic proportions worldwide. People with diabetes have high blood sugar also known as hyperglycemia. Diabetes is basically a disorder of metabolism. It is classified into two types namely, type-1 and type-2.

Type-2 diabetes is a lifelong condition that can have serious, negative effects on entire body. The majority of diabetes complications results from elevated blood sugar levels. Many parts of the body (brain, kidney, heart and nervous system) pick up the glucose directly from the blood when blood sugar levels are very high, it becomes difficult for capillaries to function and become unable to repair themselves leading to break down of capillary walls and hence prevents nutrient from reaching the cell of the organs and bleeding in those areas.

The most commonly effected organ by diabetes is the eye. The various eye complications due to diabetes are diabetic retinopathy, diabetic maculopathy, glaucoma, etc. A brief description about Diabetic retinopathy is given below.
Diabetic Retinopathy

Prolonged and untreated type-2 diabetes is the cause of diabetic retinopathy among diabetic patients. It is a progressive degenerative retinal disease and is the principal cause of impaired vision in patients between 25 and 74 years of age. The vast majority of patients who develop DR have no symptoms until the very late stages (by which time it may be too late for effective treatment). Because the rate of progression may be rapid, it is important to screen patients with diabetes regularly for the development of retinal disease.

Retinal blood vessels provide nourishment to the retina and its neural fibers. In diabetic retinopathy, these blood vessels leak and cause fluid and blood to enter into the retina, particularly the macula. When this becomes swollen and thickened, the macula (center of vision) cannot properly function. This causes the central vision to become blurred. Sometimes the blood vessels in diabetes become obstructed, and the part of the retina that depends on those vessels for nutrition is no longer able to function. New blood vessels will then become present to try to provide nourishment to the areas that are no longer able to get the proper nourishment from the blocked vessels. This develops neovascularisation, which can cause bleeding and scarring that often leads to severe vision loss and sometimes total blindness. To sum up, diabetic retinopathy is characterized by various pathologies like microaneurysms, hard exudates, soft exudates, hemorrhages, etc.

Microaneurysms: They are always the first clinical sign of the diabetic retinopathy. A microaneurysm is a small swelling that forms in the wall of tiny blood vessels. These small swellings may break and allow blood to leak into nearby tissue. They are red deep spots [figure 6] of 15 to 60 µm in diameter. There is a continuous turnover of microaneurysms. Individual microaneurysms may persist for a longer time before disappearing [figure 7].

Figure 6: Microaneurysms Zoomed Image
Exudates: They are associated with patches of vascular damage with leakage of yellowish lipid. They are classified as hard exudates and soft exudates. Hard exudates [figure 8] are deep yellow in color with sharp margins, often circinate (circular in shape) and are caused by Leakage from pre-capillary arterioles. They appear granular in texture. Whereas, soft exudates, also known as cotton wool spot [figure 9] are fluffy gray-white in color usually appear near optic disc are caused by Micro-infarction. The size and distribution of exudates may vary during the progress of the disease.
Small Hemorrhages: Ruptured microaneurysms and increased capillary permeability give rise to intra-retinal hemorrhages. Small pin point intra-retinal hemorrhages are typically found in diabetic retinopathy. It may be difficult to distinguish between microaneurysms and small hemorrhages and distinguishing between them is of little clinical importance, hence small red lesions can be classified together as ‘hemorrhages and microaneurysms’.
In general, the disease is classified into Non-proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). Non-proliferative Diabetic Retinopathy (NPDR) is further classified into mild NPDR, moderate NPDR and severe NPDR.

**Diabetic Maculopathy**

Diabetic maculopathy [figure 10] also known as Diabetic Macular Oedema (DMO) is the condition that may result from diabetic retinopathy. Maculopathy is damage to the macula which provides the central vision. In this, blood vessels near to the macula leak fluid or protein onto the macula [figure 11]. If the leakages cause the retina to harden and exudates become significantly large and close to the fovea, then the condition is termed as Clinically Significant Macular Oedema (CSMO). Similar to diabetic retinopathy, maculopathy is also classified in stages as mild DMO, moderate DMO and severe DMO.

Figure 10: Diabetic Maculopathy Effected Fundus Images.
1.5 Literature Survey

Digital imaging technology has developed into a versatile non-invasive measurement tool which enables a wealth of applications in medical sciences. Imaging the eye fundus with modern techniques is a current practice in many eye clinics, and it is becoming even more important as the expected lifetime and the costs of health care increase. Normal eye fundus structures, such as blood vessels, vascular arcade, optic disc, macula and fovea, are an essential part in diagnosis of diabetic retinopathy (DR), and fundamental to the subsequent characterization of the disease.

Since the retina is vulnerable to microvascular changes of diabetes and diabetic retinopathy is the most common complication of diabetes, eye fundus imaging is considered a non-invasive and painless route to screen and monitor such diabetic eyes [2]. Observing the state of the optic disc is not only useful in diagnosis of diabetic retinopathy, but also important are glaucoma, diabetic optic neuropathy and other optic nerve related pathologies. Since diagnostic procedures require attention of an ophthalmologist, as well as regular monitoring of the disease, the workload and shortage of personnel will eventually exceed the current screening capabilities. To cope with these challenges, digital imaging of the eye fundus, and automatic or semi-automatic image analysis algorithms based on image processing and computer vision techniques provide a great potential [3,4]. By automating the analysis process, more patients can be screened and referred for further examinations, and the ophthalmologists have more time for patients that require their attention since most of the eye fundus images are not leading to any medical action.
Diabetes mellitus is the growing health problems in developing countries. According to the Diabetes Atlas, India with 40.9 million people with diabetes has already become the 'Diabetes Capital of the World' and this number is set to increase to 69.9 million by 2025 [5]. Twelve million people are affected accounting for 12.8% of the countries blindness. The prevalence of diabetes is growing rapidly in both urban and rural areas in India. In 1972, the prevalence of diabetes in urban areas was 2.1% [6] and this has rapidly climbed to 12-16% representing a 600-800% increase in prevalence rates over a 30 year period. [7,8] Till recently, the prevalence of diabetes was reported to be low in rural areas, but recent studies suggest that the prevalence rate is rapidly increasing even in rural areas [9, 10] similar to the situation seen in developed countries of the world.

In [11], fine blood vessels from color fundus images are extracted using curvature evaluation, entropy filtering and texture mapping followed by morphological operations. In [12], a graph based approach is used for blood vessel boundary detection. The graph is constructed based on the vessels weight. The method fails to differentiate between crossing points and branching points. Retinal blood vessels are segmented using Gabor wavelet and line operator in [13]. In [14], a blood vessel segmentation method is proposed as an initial step to detect fovea by fitting parabola to the main blood vessels. Backtracking the blood vessels to localize optic disc is proposed in [15].

In [16, 17], initial segmentation of microaneurysms is achieved by using a bilinear top-hat transformation and matched filtering followed by thresholding. Region-growing algorithm is then used for the analysis of size, shape, and energy characteristics of each candidate results in the final segmentation of microaneurysms. Morphological operations are used to extract microaneurysms in [18]. Morphological opening with linear structuring elements in different directions is applied to the input image and top-hat transformation is then applied to extract details corresponding to microaneurysms candidates. Use of morphological-based operations to identify microaneurysms is also presented in [16, 19]. In [17], mathematical morphology is used to segment microaneurysms within fluorescent angiograms. Gaussian matched filters are used to retain candidate MA from fundus images in [20]. In [21], back propagation neural network is applied to sub-images to extract microaneurysms. In [22], a diameter-closing approach to segment microaneurysms using k-nearest neighbors (kNN) is reported. A detection system based on pixel classification is proposed in [23].
In [24], a k-means clustering algorithm and mathematical morphology is used to detect hard exudates (HEs) in retinal images. They reported a sensitivity of 95.92%, predictive value of 92.28% and accuracy of 99.70%. A method based on dividing the image into 64 sub-images followed by applying a combination of region growing and edge detection to detect exudates is proposed in [25]. In [26], a method based on mixture models to separate exudates from background followed by edge detection technique to distinguish hard exudates from soft exudates is proposed. In [27], a combination of local and global thresholding is used to segment exudates followed by investigating three neural network classifiers to classify exudates. Using back propagation neural network exudates detection method is presented in [28]. A comparative study on machine learning and traditional approaches for exudates detection is presented in [29]. In [30], applied fuzzy C-means clustering techniques to low contrast fundus images with non-dilated pupils is used, and reported exudates detection with 92.18% sensitivity and 91.52% specificity. In [31], HSI color space and morphological techniques are used and achieved 88.1% sensitivity and 99.2 % specificity. In [32], authors worked on green channel and have used various techniques to extract exudates with an average sensitivity of 95%. In [33], authors have presented a review on different techniques used by various authors for exudates detection. Authors in [34], applied normalization and local contrast enhancement on intensity channel of HSI color space. They used fuzzy C means clustering to extract exudates with sensitivity of 88.9%. In [35], work is carried out on green channel and employed global thresholding and binarization technique to extract exudates from fundus images. In [36], a statistical classifiers and edge detectors are used to achieve a sensitivity of 79.62%.

In [37], mathematical morphology and Ostu’s algorithm is used for detecting the optic disc with an accuracy of 97.61%. Adjusted morphological operations to identify the optic disc and exudates proposed in [38] yielded a sensitivity and specificity of 80% and 99.4% respectively. Several methods have been reported in the literature for optic disc detection [39-43].

In [44], a method of classifying the DR stages by computing the area of four features, namely, blood vessels, hemorrhages, microaneurysms and exudates is presented. A neural network in [45] is used to detect diabetic features, namely, vessels, exudates and hemorrhages in fundus images and compared the performance with an ophthalmologist screening method. Blood vessels, exudates, and hemorrhages were detected with accuracy rates of 91.7%, 93.1% and 73.8%, respectively. In [46], the fundus images are classified into normal, NPDR.
and PDR classes with an accuracy of 93%. In [47], SVM classifier is used to categories the fundus images into normal, mild, moderate, severe DDR and PDR. An automated system for detection of diabetic retinopathy using recursive region–growing segmentation (RRGS) is reported in [48].

The following are the observations from the literature survey

1. Blood vessel extraction methods are developed to
   a. Extract the entire blood vessel network from the retina
   b. Find the direction of blood vessels to locate optic disc.
   c. Fitting parabola to main blood vessel to locate fovea.
   d. There is, however, no evidence of extracting only healthy blood vessels, which is required to grade diabetic retinopathy.

2. Optic disc extraction methods developed
   a. Works on only intensity values. They do not consider other important features of optic disc.
   b. Do not ensure the detected part is optic disc.

3. Exudates extraction methods
   a. Very few attempts have been made to classify hard and soft exudates.
   b. No attempts are made to use the color information that readily comes with the RGB fundus images.

4. The experiments have been carried out on small dataset.

5. There is no evidence of grading diabetic retinopathy based on the distribution of pathologies throughout retina.

1.6 Research objective

Diabetes has reached epidemic proportions worldwide. As one of the major complications of diabetes, diabetic retinopathy is leading cause of blindness that is typically associated with diabetic macular oedema. According to the World Health Organization, the ratio of ophthalmologist to population in India is 1:100000 [49]. However, effective diagnosis of Diabetic Retinopathy and treatment can prevent blindness. Due to the large number of people that require screening, an automated and accurate screening tool is a useful adjunct in diabetes clinics. An automated detection system would significantly improve the efficiency of ophthalmologists the automated system enables the medical personnel to
immediately and visually demonstrate the existing problem to the patient which makes it easier to convince them of the urgency of their situation. In continuation they can schedule appointments for the patients for continued diagnosis and follow-up visits. An automated system also helps local doctors in rural areas to detect diabetic retinopathy cases without the need for ophthalmology experts. Consequently, in the ideal case, one can perform early detection of diabetic retinopathy cases in rural areas by training health workers.

In order to develop an automated system, digital image processing and pattern recognition algorithms need to be used in pipeline. Several algorithms have been used in efforts to solve the problem of automated diabetic retinopathy. From literature survey, it is evident that, though many techniques have been proposed for detection of DR, the results are demonstrated for either standard database fundus images or few locally acquired fundus images. The methods also do not generalize well when presented with the variety of real data observed by practitioners. Moreover, they typically operate on images with a good amount of contrast, few occlusions of retinal objects and few, if any, manifestations of retinal disease. A study on data set consisting of standard images and a large set of locally acquired images together is absolutely essential to validate the methods for detection of DR. Also, there remain many techniques from recent computer vision literature that have not utilized in pipeline of digital image processing methods. This motivated us to work on large set of fundus images for automatic detection of DR through effective combination of image processing and pattern recognition algorithms.

Hence, objective of the research work is to design and develop efficient algorithms/techniques to aid ophthalmologist with accurate and fast diagnosis and classification of eye abnormalities associated with diabetic retinopathy and also to speed up the process of diagnosis so that number of patients to be treated can be increased.

1.7 Conceptual Framework and Methodology

1.7.1 Data Description

A local data base consisting of fundus images has been created for the research work. The images are collected from Karnataka Institute of Diabetology, Bangalore. The images are captured using NIKON D300 camera. Each image is of dimension 4288X2848. The images from public database, namely, DRIVE database have also been used to perform experiments. Each of these images is of dimension 786X584, captured using Canon CR5 non-mydiatic
3CCD camera. The images collected locally are more susceptible to noise compared to standard database images. The letter of consent for collecting the images is shown in fig. 12. The images collected are solely for purpose of performing experiments and not for any commercial use.

![Letter from Expert](image1.png)

**Figure 12**: Letter from Expert.

### 1.7.2 Methodology

The main aim of the research work is to grade diabetic retinopathy into stages. This task is further subdivided into 4 subtasks.

1. Blood vessel extraction
2. Microaneurysms extraction
3. Optic disc detection and elimination
4. Exudates extraction

In order to grade diabetic retinopathy ophthalmologist uses the following criteria

1. Area occupied by healthy blood vessels. In a healthy eye most of the area is occupied by healthy blood vessels.
2. Area occupied by microaneurysms and their distribution.
3. Area occupied by exudates and their distribution.
Taking into consideration all of the above points the framework (figure 10) of the proposed method is designed.

![Diagram of the proposed method for grading diabetic retinopathy.](image)

Figure 13: Framework of the Proposed Method for Grading Diabetic Retinopathy.
Retinal Features used

The important attributes of pathologies, which discriminates it from the rest of the retinal structure, are termed as features. Various features used are

- Area and distribution
- Intensity
- Texture
- Edge energy

1.8 Thesis Organization

The thesis is organized into seven chapters.

In chapter 1, a brief introduction of Digital Image Processing and its applications is given. Importance of Medical Image Processing in this contest followed by the description of Diabetes and health hazards caused by it is described. A detailed description of human eye anatomy is given. The various pathologies associated with DR are discussed in detail. Various image processing techniques such as denoising, segmentation, morphological operations used to extract the pathologies associated with DR are defined. Classification techniques such as nearest neighbor, SVM, three-sigma are presented. A literature survey of the state of art methods used for extracting pathologies from fundus images and grading DR is presented.

In chapter 2, we have presented a detailed description of retinal blood vessel network and its functions. A Literature survey of the methods used for extracting retinal blood vessels is presented. The procedure for extracting retinal blood vessel network based on morphological operations and morphological reconstruction is described. Morphological operations are applied to the preprocessed fundus image to first eliminate the retinal structures other than blood vessels such as Optic Disc (OD), Microaneurysms (MA), and exudates. Morphological reconstruction is employed to regain the blood vessels that were lost during OD removal. Experimental results obtained by our proposed method are discussed. Finally, in conclusion the contribution of the procedure is explained briefly.

Chapter 3 deals with detection of Microaneurysms (MA). A Literature survey of the methods used for extracting MA is presented. An efficient method for detection of MA based on morphological operations and segmentation is presented. Morphological operations are
applied to the preprocessed fundus image to first eliminate the retinal structures such as Optic Disc (OD), blood vessels, exudates. Segmentation stage involves edge detection of microaneurysms and blood vessels. Thresholding is applied for removal of exudates and noise. The results obtained by our proposed method are discussed. Finally, in conclusion the contribution of the procedure is explained briefly.

In chapter 4, a detailed description of Optic Disc (OD) and necessity of eliminating OD has been discussed. A survey of the methods available in the literature used for extraction of OD is presented. A method based on connected component analysis is presented to find the largest cluster bright exudative pixels and Hough transform is used for circle fitting to detect OD. The results obtained by our proposed method are discussed.

Chapter 5 deals with exudates detection. A Literature survey of the methods used for extraction and classification of exudates as hard and soft exudates is presented. We have developed three procedures for extracting exudates. First method works in green channel image and uses morphological operations and segmentation, second method is based on k-mean clustering works in CIELAB color space and the third one uses three-sigma and works in RGB color space. Classification of exudates as hard and soft exudates is done based on the edge energy and thresholding techniques. The results obtained by our proposed method are discussed. Finally, in conclusion the contribution of the procedure is summarized.

In chapter 6, combining the method developed for extracting the DR pathologies and the grading strategy, we present a method to grade diabetic retinopathy. Further, a method for grading of stages of Diabetic Maculopathy (DM) is also presented. The experiment results show that the features extracted to grade DR also works well with grading of DM.

In chapter 7, the conclusion and future direction of the research work carried out are discussed. The work can be extended to extract other pathologies like venues bleeding, hemorrhages essential to grade proliferative DR.

The outcome of the research work presented in this thesis is significantly useful for detection of stages of DR.
Summary

One important application of digital image processing is medical imaging. It is an important tool in medicine. Various digital image processing methods can be applied to medical images to obtain essential features of images that help in diagnosis and treatment planning. Generally, medical images are complex in nature (diverse image content, cluttered objects, occlusion non-uniform object texture) and noisy, hence, making it difficult for extracting relevant information. One such application area in medical image analysis is automatic detection of Diabetic Retinopathy. Objective of the research work is to design and develop efficient algorithms/techniques to aid ophthalmologist with accurate information associated with diabetic retinopathy. This chapter presented a brief overview of medical image processing in particular DR, and summary of the organization of the thesis.