An Automatic Grading System for Detection of Diabetic Retinopathy Severity Levels

Thesis submitted in partial fulfillment of the requirements for the award of degree of

Master of Engineering
in
Computer Science and Engineering

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CERTIFICATE

I hereby certify that the work which is being presented in the thesis entitled, "*An automatic Grading System for detection of Diabetic Retinopathy severity levels*", in partial fulfillment of the requirements for the award of degree of Master of Engineering in *Computer Science and Engineering* submitted in Computer Science and Engineering Department of Thapar Institute of Engineering and Technology, Patiala, is an authentic record of my own work carried out under the supervision of *Dr. Avleen Kaur Malhi* and *Dr. Palika Chopra* refers other researcher's work which are duly listed in the reference section.

The matter presented in the thesis has not been submitted for award of any other degree of this or any other University.

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ABSTRACT

Diabetic retinopathy has become one of the most leading and recurrent cases of blindness among children and adults who have been suffering from diabetes for an extremely long period of time. The increase in the level of the glucose in the blood causes lack of oxygen in the veins which further fails to supply nutrition to the retina. The signals are sent to brain for formation of newer blood vessels that are weak and causes their breakdown, hence releasing blood spots and other lesions that hinder the vision capability of retina. Exudates, micro aneurysms, cotton wool spots and hemorrhages are the features of diabetic retinopathy. The existing researches have focused either on the detection of the features of diabetic retinopathy or on the use of image processing for grading in diabetic retinopathy. In our work, grading has been done to know the severity of diabetic retinopathy i.e. whether it is mild, moderate or severe using exudates and micro aneurysms in 1361 fundus images. An automated approach that uses image processing, features extraction and machine learning models to predict accurately the presence of the exudates and micro aneurysms and grade accordingly has been proposed. The research is carried out in two segments; one for exudates and another for micro aneurysms. The grading is done via exudates based upon their distance from macula whereas grading via micro aneurysms is done by calculating their count. For grading using exudates, Support Vector machine and K-Nearest neighbor show the highest accuracy of 92.1% and for grading using micro aneurysms, decision tree shows the highest accuracy of 99.9% in prediction of severity levels of the disease.

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LIST OF ABBREVIATIONS

DR	Diabetic Retinopathy
MA	Micro Aneurysms
GLCM	Gray Level Co-occurrence Matrix
CLAHE	Contrast limited adaptive histogram equalization
SVM	Support Vector Machine
KNN	K-Nearest Neighbor Algorithm
ROC	Receiver Operating curve

CHAPTER 1

INTRODUCTION

Diabetic retinopathy (DR) is a vision threatening medical condition in which the retina of the diabetic patients gets damaged to an enormous amount. It is a secondary disease caused in the people already suffering from Diabetes Mellitus. It has become one of the most leading and recurrent cases of blindness among children and adults who have been suffering from diabetes for an extremely long period of time. Approximately 93 million people have been reported to suffer from DR, 17 million people are targets of proliferative DR, whereas diabetic macular edema is prevalent in 21 million people worldwide [1]. The strong reasons and associations behind DR are longer duration of diabetes, poor blood pressure and glycemic control. These statistics point out the substantial growth of DR and the global health burden caused by it. In Indian urban population, the prevalence of diabetic retinopathy is found to be 18% with men at a higher risk [2]. The figure 1.1 shows normal retina and retina affected with diabetic retinopathy.

(a) (b)

Figure 1.1: Retinal images; (a) Normal Retina, (b) Diabetic Retinopathy affected retina.

Diabetic Retinopathy, also goes by the name of diabetic eye disease caused to the people with high blood sugar level that badly affects the retina's blood vessels by swelling and leaking. In some cases, they might also restrict the blood to pass through. The retina gets badly damaged by diabetes mellitus. The blindness happens due to this prolonged medical condition. Due to high and abnormal levels of glucose in blood, there is restriction of oxygen flow in the blood vessels which results in weakened smaller blood vessels in retina and their destruction which further leads to formation of newer but weaker blood vessels. The condition of diabetic retinopathy can happen to anyone who has been suffering either from diabetes type-1 or diabetes type-2. The consequences of this disease are life threatening but with proper care, medications and treatment, diabetics can have a normal life. If people show no urgency to the treatment of diabetes then it goes uncontrolled which can further cause bad effect on a persons' eyesight, cause damage to nervous system and spread infections on the feet also. The diagnosis of this disease at earliest possible stage is very important so that help in complete elimination and preservation of the vision of the people suffering from diabetic retinopathy is achieved. A lot of people can save themselves from being blind if the treatment to Diabetic Retinopathy is done at early possible stage. It has become very important for the formation of automatic detection of this problem and serve the people where there is lack of good quality infrastructure and experts. Thus, automated grading system for diabetic retinopathy has been proposed in this work that saves a lot of manual labor and with the help of image processing and machine learning, it can predict accurate results for large image dataset in very less time.

1.1 Background

1.1.1 Diabetes

Diabetes is the major reason for development of diabetic retinopathy in patients who have been suffering for long time. It is a condition where appropriate amount of insulin is not being produced by human body which is required as a source of energy to the body or the insulin is being produced properly but the cells are not responding adequately to it. Insulin is important because it causes the movement of glucose, which is basically a simple sugar, from the blood into the body's cells. It also causes many other effects on the metabolism of body. Majorly the glucose is provided to us from the kind of food we eat, and utilized as a source of energy by the human body cells. Without insulin, there is hindrance in glucose movement from the blood into cells resulting in blood full of glucose. The toxicity of high glucose in our blood is very dangerous and as a result, cells lack the fuel they need to function properly if they don't get glucose.

The main Symptoms of diabetes include:

- Increase in thirst and urination
- Hunger pangs increase at unusual rate
- Increase in fatigue
- Blurry vision
- Tingling sensation in feet or hands
- Poorly healing sores
- Extreme weight loss

The major type of diabetes are type 1 and type 2 diabetes:

- **Type 1 diabetes**

  It is a chronic condition in which little or no insulin is produced by the human body. It is also referred by the name juvenile diabetes or insulin-dependent diabetes. Type 1 diabetes is majorly caused by pancreatic - Beta cell. It is accounted for only about 5–10% cases, however, its occurrences are continuing to expand globally thereby causing dangerous implications that can be short-term or long-term. The exact reason behind cause type 1 diabetes is not known. Usually, insulin-producing cells in the pancreas are mistakenly destroyed by the body's own immune system that usually kills harmful bacteria and viruses. Tackling and managing Type 1 diabetes is best under the hands of a health team which has expertise in multiple disciplines and needs to continuously pay attention to many spheres of this disease, that include administration of insulin, monitoring of the glucose level in the blood, planning, scheduling type, amount of meal intake and also screening and searching for any other complications and problems arising due to diabetes.

- **Type 2 diabetes**

  Type 2 diabetes is a condition where insulin is produced but not being properly used by the body i.e. insulin resistance happens. The ever increasing global problem of obesity, lack of physical activity, and sedentary lifestyle or calories dense diet has caused unimaginable rise in the number of patients suffering with type 2 diabetes. There are approximately 415 million people living with diabetes, and an estimated 193 million people are unaware about them being diabetic. Out of all the cases of diabetes, Type 2 diabetes is accounted for about 90% cases resulting in deep psychological and physical distress in the lives of people and their careers. It has also a huge pressure on health-care systems and industries. Despite increasing awareness of the risk factors for type 2 diabetes and proof for successful detection and prevention methodologies, the disease still is rising globally.

1.1.2 Diabetic Retinopathy

DR is an impediment caused by prolonged diabetes and has accounted for one of the major reasons behind loss of vision among huge populations across the globe. The back of human eye is covered by a membrane known as retina which is super light sensitive. The major purpose of retina is conversion of any light which hits the eye into signals which is interpreted by the human brain. This is how sight operates in the human eyes since this procedure leads to production of visual images. Due to diabetic retinopathy, there is lack of oxygen which leads to destruction of the blood vessels that are present within the tissues of the retina, that causes the leak of fluids and distorts the vision of diabetic patients. During the early stages of diabetes, there are usually no symptoms or visible traces of diabetic retinopathy in the patients. It is majorly at an advanced stage that DR symptoms become observable and are noticed due to the problems arising because of vision loss. Diabetic Retinopathy signs and symptoms can be one of the following:

- Blurry vision.
- Damaged colored vision.
- Presence of transparent, colorless spots often called as floaters that disrupt the patient's vision.
- Blocked vision due to patches and streaks.
- Difficulty in viewing objects at night.
- Complete and sudden loss of vision.

The vision of both the eyes are usually affected by DR which is why it is an urgent task to make sure that there is minimum possible vision loss. Eye examinations conducted by doctors should be religiously attended by the diabetic patients so that they can get examined timely. Anybody who is suffering from diabetes is at a very high stake of being victimized by DR. But still, a person is highly likely to be affected by DR if:

- Sugar levels in blood are not properly and carefully maintained
- Blood pressure levels are high
- Cholesterol is high
- Person is pregnant
- Regular habit of smoking
- Diabetic patient for a very long period of time

Damage to the network of blood vessels that nourish the retina is the key cause of diabetic retinopathy. Blood vessels majorly nourish the retina and due to diabetes and above stated reasons, network of blood vessels get highly destroyed which weakens the retina. The blood flow to the retina is restricted due to enormous amounts of glucose present in the bloodstream hence disrupting the vessels. The degree of problems arising within the blood vessels can vary from mild as tiny bumps or bulges in the blood vessels wall that cause leak of blood to breaking of existing vessels and formation of newer, weaker blood vessels which cause lack of oxygen and fluids emission causing loss of vision among the people. Diabetic retinopathy generally starts without any noticeable change in vision. However, an ophthalmologist, or eye specialist, can detect the signs. It is crucial for people with diabetes to have an eye examination at least once or twice annually, or when recommended by a physician. The beginning stage of diabetic retinopathy does not showcase any observable changes in viewing things. However, it is advisable to be regular with an eye specialist who can help with the detection of the problem.

1.1.3 Retinal Imaging Techniques

As discussed above, diabetic retinopathy has adverse effects on the retina and results in vision loss among diabetic patients majorly. Retinal imaging is all about capturing a digital image of the hind side of the human eyes. It helps in display of retina, which contains blood vessels and optic disc that hold together the optic nerves and is useful for sending information of what is perceived by eyes to brain. A large number of eye diseases and also many other diseases like diabetic retinopathy, age related degeneration and glaucoma are undisguised in the retina. Various imaging methodologies exist like Fundus Photography, Optical Coherence Tomography, Angiography, Scanning Laser Ophthalmoscopy, Retinal Function Assessment, Metabolic Imaging, Retinal Oximetry. We make use of fundus images dataset in our approach for grading in diabetic retinopathy.

Fundus imaging - It is a method of capturing retina images by giving a 2-D representation of a naturally 3-D retina which is projected on an imaging plane and reflections of light help for getting 2-D images. Therefore, a process where varying intensities of the light are used for letting us know about how much amount of light is reflected back and thus lead to formation of 2-D images is called as fundus imaging. Fundus imaging also includes the following broad categories of imaging techniques mentioned in table 1.1.

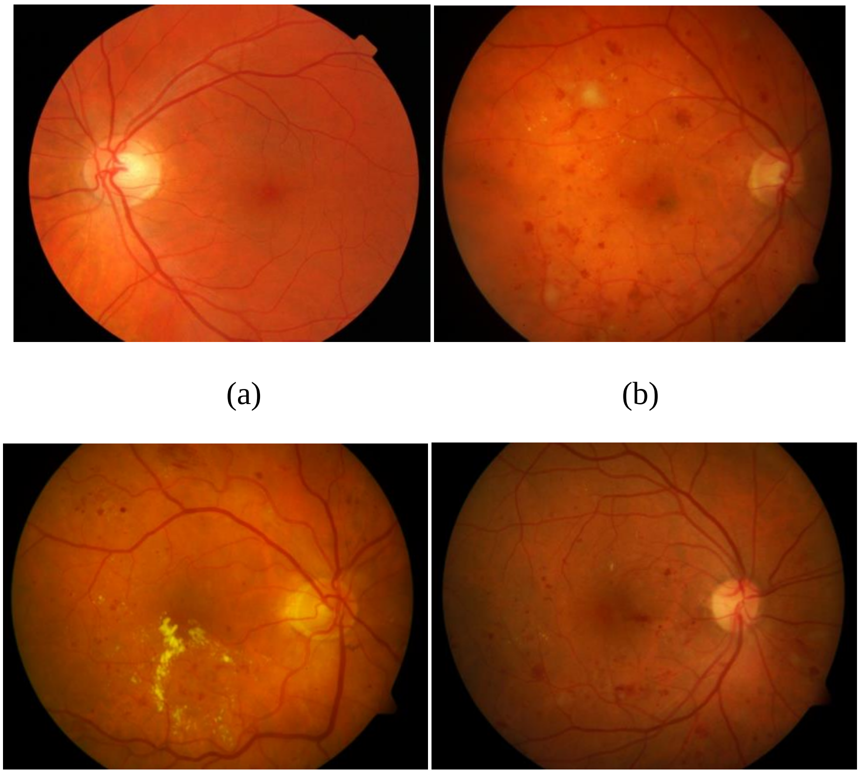
Table 1.1: Categories of fundus imaging technique

Fundus Imaging Category	**Description**
Fundus photography	The proportion and quantity of light reflected of a specific waveband is represented by the varying intensities of the images.
Colored fundus photography	The spectral sensitivity of the sensor determines the proportion and quantity of Red, Green, Blue channels of light reflected as represented by the varying intensities of the images.
Stereo fundus photography	Few different view angles for depth resolution are used to determine the proportion and quantity of light reflected as represented by the intensities of the images.
Hyperspectral imaging	The proportion and quantity of light reflected of various specific wavelength bands is represented by the intensities of the images.
Scanning laser ophthalmoscopy	The proportion and quantity of an individual wavelength laser light reflected is represented by the intensities of image that is acquired via time sequence.

Adaptive optics scanning laser ophthalmoscopy	The proportion and quantity of laser light reflected is optically improved and corrected by shaping the irregularity in the wavefront as represented by the intensities of the images.
Fluorescein angiography(indocyanine angiography)	The proportion and quantity of the fluorescein or indocyanine green fluo-rophore's photons emitted that are injected into circulation of the subject is represented by the intensities of images.

1.2 Lesions in retina due to Diabetic Retinopathy

The features like soft exudates, hard exudates, micro aneurysms and hemorrhages are the major representatives of diabetic retinopathy.



(c) (d)

Figure 1.2 : Typical fundus images; (a) Normal eye, (b) Soft exudates, (c) Hard exudates, (d) Micro aneurysms and hemorrhages.

1.2.1 Soft Exudates

Soft exudates also known by the name Cotton wool spots as this is what they appear like on the surface of retina. The appearance is usually cloud like, grayish-white or yellowish white with fringy borders. They cause swelling in the retina and may not lead to threatening vision loss in the diabetic patients only if they are present away from fovea which is the central portion of the eyes that gives high definition and focused vision. Because of reduction in axonal transport within the blood vessels, swelling happens due to ischemia. Figure 1.2 (b) shows the presence of cotton wool spots or soft exudates in the retina.

1.2.2 Hard Exudates

Due to suffocation caused in the blood vessels because of lack of oxygen due to formation of newer capillaries, this results in pressure and breakage of the blood vessels that result in the formation of white or yellow pots in retina that have sharper boundaries than soft exudates. These can be arranged as patches, dots or sheets in the retina. Around the retinal veins, their depositions can be found too. Hard exudates cause great damage to the retina by posing threat to the vision of the patients. The figure 1.2 (c) shows the yellow exudates.

1.2.3 Micro Aneurysms (MA)

Micro aneurysms are the earliest possible signs in the retina of people suffering from diabetic retinopathy. Their appearance is like small, red and round blots that have sharp boundaries. The swellings in the blood vessels and high pressure built up in the network of vessels results in rupture of blood from them, thus forming micro aneurysms. The treatment can reverse their presence as they are in the early stages of diabetic retinopathy and also by treating the high blood pressure patients. The figure 1.2 (d) shows micro aneurysms in the retina.

1.2.4 Hemorrhages

The pressure built inside the network of blood vessels due to lack of oxygen and high levels of glucose in bloodstream results in formation of new, weak tiny capillaries as the existing blood vessels are not able to carry signal to the brain which causes the brain to react by forming new vessels but that are weaker in nature. Since these are weak, this results in the leakage of capillaries into retina thus forming flame shaped hemorrhages or dot or blot shaped hemorrhages. Dots are usually associated with diabetic retinopathy whereas flames are caused due to breakage of nerve fibers of retina. Their appearances are irregular shaped or distinct edged objects in the retina. The figure 1.2 (d) shows the hemorrhages in the retinal image.

1.3 Stages of Diabetic Retinopathy

For the people suffering from diabetes for an extended period of time, they are highly likely to be affected by diabetic retinopathy. As we know blood vessels are damaged and fluids are leaked into retina causing threat of lifelong vision loss. Timely treatment can reverse the effects of diabetic retinopathy. There are majorly four different stages namely mild, moderate and severe Non Proliferative Retinopathy and Proliferative Retinopathy.

(a) (b)

Figure 1.3: Effects of diabetic retinopathy; (a) scene viewed by normal person, (b) same scene viewed by diabetic retinopathy patient.

1.3.1 Mild Non-Proliferative Retinopathy

Presence of micro aneurysms onsets the mild behavior of diabetic retinopathy. The tiny bulges or the bumps which look like balloons, present in the blood vessels are the signs of mild behavior. It does not pose very immediate threat of vision loss to the patients but with delay in the treatment can cause further lead to higher stage of diabetic retinopathy. As it is known, these tiny red spots or dots are result of leakage of fluids and blood from the vessels.

1.3.2 Moderate Non-Proliferative Retinopathy

There is an increase in the number and quantity of the hemorrhages, fleece spots and micro aneurysms which start posing threat to the loss of vision among people. If delay in treatment is done, it can cause adverse effects on the retina and cause blindness. Since blood vessels that feed the retina and nourish it are breaking down and being destroyed, the transportation of blood through vessels can stop too.

1.3.3 Severe Non-Proliferative Retinopathy

A large number of blood vessels start getting blocked. This is extreme case of non-proliferative retinopathy where the flow of blood does not reach wider areas in retina. These areas which are devoid of blood and oxygen in turn send signals to brain for need of newer vessels to nourish and feed them. Thus, causing more leakage of blood and fluids into the retina and obstructing the vision of people.

1.3.4 Proliferative Retinopathy

This is the most advanced stage of diabetic retinopathy where the triggers are sent by retina for growth of newer blood vessels to the brain that results in formation of newer, weaker vessels and capillaries that are too timid to carry blood and oxygen to retina to nourish them , hence they breakdown causing serious effects on retina's viewing capacity by covering fovea and other regions with liquids and protein leaks. Also there is contraction of scar tissue which accompanies the retina causing detachment of retina from underlying tissue. It is similar to wallpaper being peeled off and removed from the wall. The detachment of retina can cause permanent loss of vision.

1.4 Machine learning in Diabetic retinopathy

Machine learning is a technique for recognizing patterns that can be applied to medical images. Machine learning typically begins with the algorithm system computing the image features that are believed to be of importance in making the prediction or diagnosis of interest. The machine learning algorithm system then identifies the best combination of these image features for classifying the image or computing some metric for the given image region. Computer-aided detection and diagnosis performed by using machine learning algorithms can help ophthalmologists interpret medical imaging findings and reduce interpretation times. These algorithms have been used for several challenging tasks. If a machine learning algorithm is applied to a set of data (in our case, fundus images for detection and grading of diabetic retinopathy) and to some knowledge about these data (in our case, exudates, micro aneurysms extracted using image processing methods and textural features using Gray Level Co-occurrence Matrix (GLCM)), then the algorithm system can learn from the training data and apply what it has learned to make a prediction (in our case, grading the severity of diabetic retinopathy). If the algorithm system optimizes its parameters such that its performance improve that is, more test cases are diagnosed correct then it is considered to be learning that task very well. The figure 1.4 summarizes the role of machine learning algorithms in grading of diabetic retinopathy in terms of the severity of the problem in the diabetic patients.

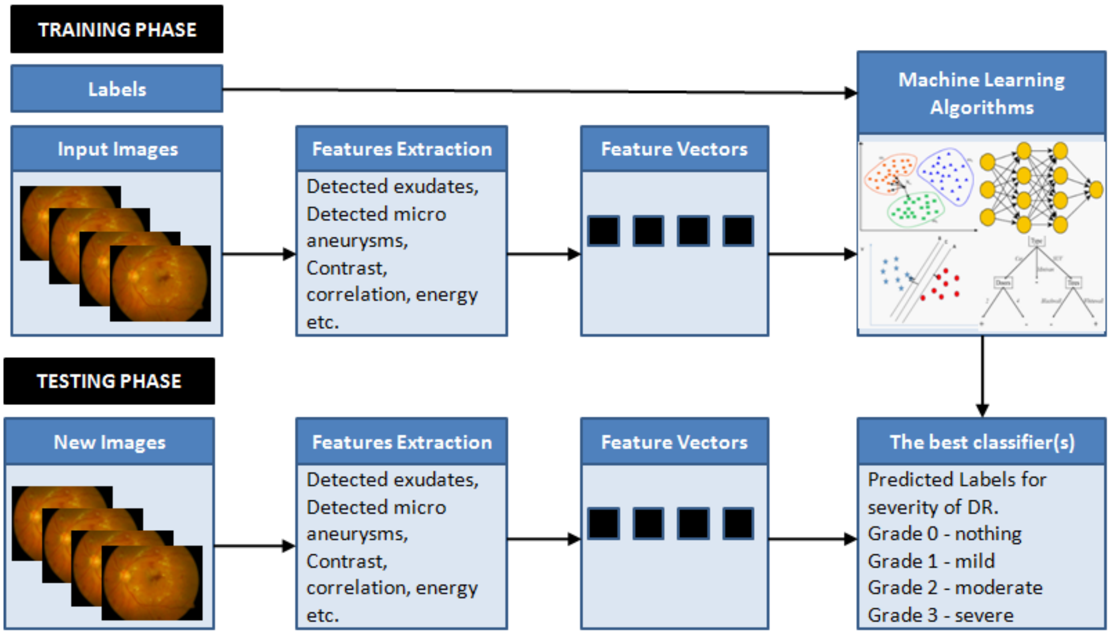


Figure 1.4 : Machine learning in diabetic retinopathy

1.5 Structure of thesis

The thesis is organized into six chapters which include introduction, literature review, problem statement, methodology, results analysis, conclusion and future scope followed by references.

Chapter 1 gives insights into the subject area on which the contribution is done by the research work and enlists the objectives of the thesis.

Chapter 2 includes the literature survey of state-of-the-art techniques that have been previously followed in diabetic retinopathy detection.

Chapter 3 gives the problem statement and research gaps of the recent literature in this field.

Chapter 4 provides steps involved in the proposed methodology in fulfilling the desired objectives which includes image processing, features extraction and machine learning algorithms employed.

Chapter 4 details the results analysis preformed using proposed methodology.

Chapter 6 summarizes the conclusion of the research done and provides future scope.

CHAPTER 2

LITERATURE REVIEW

Diabetic retinopathy is one of the leading causes of vision loss and blindness in people suffering from diabetes for a long time. Its accurate detection is of primary concern for researchers that can help ophthalmologists for lesser manual efforts while dealing with increasing number of patients and data records.

2.1 Review on image processing techniques used in diabetic retinopathy detection

In machine learning approaches, image preprocessing is the fundamental step that has been used widely in detection of diabetic retinopathy recently. Morium Akter et al. [3] have focused primarily over the usage of morphological operations for detection of exudates in the fundus images. Majorly histogram equalization, thresholding to get binary image and watershed transformation has been put to use for pinning out the exudates. Malay Kishore Dutta et al. [4] have worked on Messidor, Drive and local database separately to make use of contrast enhancement, top hat transforms, and intensity thresholds to detect the exudates. For detection of red lesions, vessels detection and adaptive histogram equalization has been worked upon. They have classified into severe, mild, moderate and normal with the help of preprocessing techniques. Srivastava et al. [5] have used two methods of image preprocessing and their strategic combination to finally detect exudates in the fundus images. The first method revolves around vessel detection, intensity threshold and area threshold while the second method involves edge detection and morphological operation. Diptoneel Kayal et al. [6] worked on detecting the hard exudates via image processing methods like median filtering, image subtraction, dynamic thresholding and image addition. P. Ravivarma et al. [7] have worked on detection of micro aneurysms and exudates using various image preprocessing methods like resizing the images, applying contrast limited adaptive histogram equalization and top hat filters for better detection. Removal of blood vessels is done as well for better results in case of micro aneurysm detection.

Sukeerthi. G et al. [8] have used ensemble of image processing methods and candidate extraction methods for grading according to micro aneurysms in retina. After application of several image enhancement methods and candidate extraction methods, CLAHE and circular hough transforms are used for processing the images and giving the final results. P. C. Siddalingaswamy et al. [9] have used image processing methods for grading according to exudates on the basis of their distances from the foveal zone. After detection of optic disc and macula, efforts are placed over hard exudates detection via green channel extraction, intensity difference and overlaying candidates and graded them accordingly. Kranthi Kumar Palavalasa et al. [10] have worked on the detection of yellow lesions detection with the help of image processing in fundus images collected from DiaretDb database. The fundus images have been converted into the green channels due to high contrast and better detection of objects. Contrast limited adaptive histogram equalization has been used for improving the illumination of the fundus images. With the help of morphological operations background removal and subtraction operations have been performed. Region growing algorithm has been applied for detecting the exudates in the images. BüşraYaşar et al. [11] have proposed similar use of image processing mechanisms for hard exudates detection in the fundus images by improving the image quality using median filter and improving illumination of images. Opening and erosion operations have been proposed along with optic disc removal. Edge detection like kirsch algorithm has been used along with these steps for exudates detection. Sinthanayothin et al. [12] made use of image processing methods and a moat operator to detect diabetic retinopathy via exudates and micro aneurysms by working on a very small dataset of 30 retinal images. The colored images have been converted into IHS color format; application of contrast improvement has been done. The optic disc has been extracted also via working on area that has the highest variation in intensity. Blood vessels have been extracted with use of neural networks. With the help of recursive region growing algorithm detection of exudates has been done. To separate and detect the red lesions from the orange background, moat operator has been applied.

2.2 Review on feature extraction methods used in diabetic retinopathy detection.

Shradha Mirajkar et al. [13] focused on diabetic retinopathy detection by processing the images by converting them to grayscale, using adaptive histogram equalization, smoothening them and then extracted particular features like blood vessels network using kirsch's edge detection mechanism upon which application of 2-D gabor wavelet transform is done. Saiprasad Ravishankar et al. [14] worked on detection of exudates and micro aneurysms by working on various features extraction along with the image processing methods. Work is done on detection of optic disc and blood vessels by using blood vessel network color model, also removal of fovea is done. Detection of exudates and micro aneurysms is done using various morphological operations. Harini et al. [15] focused on detection of various features of diabetic retinopathy like exudates, micro aneurysms by using various image processing methods like contrast enhancement, conversion into green channel, morphological operations and extracted blood vessels as well. The textural features are extracted as well using gray level co-occurrence matrix. Ravivarma et al.[16] drove their research towards low quality fundus images and used them for detection of exudates using median filter and segmentation using fuzzy c-means clustering algorithm. After segmentation, various features like color, texture and size were derived and optimized using particle swarm optimization and finally fed to svm classifier.

Mohamed Omar et al. [17] worked on extraction of textural features by first acquiring particular regions of interest through image processing methods and then applying the local binary pattern feature extraction method for detecting the hard exudates from the fundus images. Zhang et al. [18] have worked on extracting features of tongue for detection of diabetic retinopathy that includes color, geometry and texture of the tongue images. Using the 12 color features of the tongue, extracted by taking mean of some 8 color features along with other 9 features of color. Further 13 features are extracted based on certain distances, areas and measurements. With the combination of 34 features, work has been done for detection of diabetic retinopathy by classifying the tongue images into normal and affected ones. Seoud et al. [19] have worked with the detection of red lesions on the basis of their dynamic shape-based features extraction. The contrast and illumination of the images have been improved in this approach, noises have been removed via mean filter and optic disc has been extracted out. Various dynamic features like elongation, relative area, circularity, rectangularity and solidity have been used for hemorrhages and micro aneurysms. Choudhury et al. [20] have proposed detection of exudates from the fundus images with usage of various image preprocessing steps and extracting the exudates with the help of fuzzy c-means clustering that serve as features for their work and also usage of vessel density features. The images have been enhanced with contrast illumination and removal of noises using filters. Li et al. [21] have worked on a relatively smaller datasets that focuses on extraction of certain features like optic disc, blood vessels for exudates detection in diabetic retinopathy. Optic disc has been extracted with the help of sobel edge detection method and blood vessels are extracted with the kirsch's edge detection method. The exudates are extracted by application of kirsch edge detection in green channel of the colored images and the area and count of exudates are maintained.

2.3 Review on machine learning algorithms used in diabetic retinopathy detection system.

Carrera et al. [22] worked on detection and classification of exudates and micro aneurysms. It extracted features like blood vessels by converting RGB into CMY representation and applying various morphological operations to hide the blood vessels. With the usage of hole filling algorithms and edge detection mechanism, thresholding mechanisms exudates and micro aneurysms are extracted and fed into SVM and decision tree classifier. Yu et al. [23] proposed a method of classification of presence of exudates using various morphological operations and image processing steps for detection of optic disc, hiding the blood vessels and used opening operation for finding the exudates and then trained and tested the Convolutional Neural Networks (CNN) model on it. Chandran et al. [24] proposed a technique with am-fm characterization of the images, where amplitude and frequency modulation were used along with demodulation mechanism and gabor filters were used for edge detection among the images. Textural features were acquired along with blood vessel features extraction which were fed into the random forest classifier and rule-based decisions were made regarding classification of diabetic retinopathy. Saravanan et al. [25] worked on the micro aneurysms and used various steps of image processing like thresholding, binarization, blood vessels removal, and various morphological operations to detect the micro aneurysms better and classify using the Gaussian mixture model using the count of red lesions to show the severity of diabetic retinopathy. Yadav et al. [26] proposed a classification mechanism for diabetic retinopathy to classify into normal, dot hemorrhages, exudates using various image processing steps like image addition, subtraction, thresholding and morphological operations, while also extracting certain features like optic disc, blood vessels and trained a feed forward neural network for the same.

Tjandrasa et al. [27] classified the diabetic retinopathy on the basis of exudates and application of soft margin support vector machine. The exudates are segmented using various morphological operations, subtractions and additions of images, intensity thresholding and then features like area, perimeter, standard deviation etc. are extracted from the segmented exudates which are fed into SVM for classification. Yu et al. [28] proposed the usage CNN model for detection of the exudates in the fundus images. A 64x64 patch has been used over the pixels of the green channel and illuminated fundus images. Optic disc has been extracted and removed and opening operation has been used for ultimate extraction of exudates. The method has been applied on e-optha database having 82 images. Yalcin et al. [29] proposed the usage of convolutional neural networks for detection of exudates and classification of presence or absence of diabetic retinopathy in the patients. They worked by pre-treating the fundus images by standardizing the size of the images and converting them to grayscale images before feeding into the model for training and testing Santhakumaz et al.[30] made use of various machine learning algorithms incorporated with image preprocessing for detection of exudates and hemorrhages in the fundus images that includes removal of background details and optic disc as they consume a lot of memory without contributing to detection of diabetic retinopathy. Features like mean, standard deviation etc. have been extracted from all the channels of images and visualized through principal component analysis. Over the extracted features SVM has been used for classification purposes. Gurudath et al. [31] proposed a method of detecting exudates, micro aneurysms and hemorrhages by classifying into no diabetic retinopathy, proliferative retinopathy and non-proliferative retinopathy using extraction of blood vessels with the help of Gaussian filters and automatic mask generation on fundus images from DRIVE and DIARETDB databases and also using their textural features which are fed into artificial neural network and SVM. Pal et al. [32] used machine learning models like Naive Bayesian classifier, SVM, K nearest neighbor algorithm and decision trees for binary classification of diabetic retinopathy on the fundus images collected from Messidor database. The performances of the models used apart from SVM were quite average since no preprocessing on images and features extraction was used.

2.4 Comparative Analysis

The Table 2.1 draws out comparisons between the methodologies discussed in the literature review.

Table 2.1 : Comparative Analysis of related literature

Authors	Lesions	Methodology Used	Results		
			ACC	**SEN**	**SPE**
Morium Akter et al. [3]	Exudates	Image pre processing, morphological operations	99%	N/A	N/A
MalayKishore Dutta et al.[4]	Exudates, micro aneurysms	Image pre processing, contrast enhancement, intensity threshold	>90%	92.16%	83.6%
Kshitij Srivastava et al. [5]	Exudates	Image pre processing, around vessel detection, intensity threshold, area threshold	>85%	N/A	N/A
Diptoneel Kayal et al. [6]	Exudates	Image pre processing, median filtering, image subtraction, dynamic thresholding and image addition	N/A	97.25%	96.85%
P. Ravivarma et al. [7]	Exudates	Image pre processing and features extraction, median filter and segmentation using fuzzy c-means clustering algorithm,	98%	N/A	N/A

		features like color, texture and size optimized using particle swarm optimization	
Sukeerthi.G et al.[8]	Micro aneurysms	Ensemble of image processing methods, CLAHE and circular hough transforms	N/A N/A N/A
P.C. Siddalingaswamy et al.[9]	Exudates	Image pre processing, green channel extraction, intensity difference and overlaying candidates	N/A 97.9% 96.1%
Shradha Mirajkar et al. [13]	Exudates	Image pre processing and features extraction, histogram equalization, smoothening, kirsch's edge detection mechanism, 2-D gabor wavelet transform	86% N/A N/A
Saiprasad Ravishankar et al. [14]	Exudates, micro aneurysms	Image pre processing and features extraction, morphological operations, extraction of optic disc and blood vessels by using blood vessel network color model	N/A 95.1% 90.5%
Harini R et al. [15]	Exudates, micro aneurysms	Image pre processing and features extraction, contrast enhancement, conversion into green channel, morphological operations, textural features using GLCM	96.67% 100% 95.83%
Mohamed Omar et al. [17]	Exudates	Image pre processing and features extraction, local binary pattern	96.7% 98.6% 94.8%

		feature extraction	
Enrique V. Carrera et al.[22]	Exudates, micro aneurysms	Image pre processing, features extraction, SVM, decision tree classifier, morphological operations, hole filling algorithms, edge detection mechanism, thresholding mechanisms	SVM 92.4% 87.3% 97.4% Decision Tree 92% 86.6% 97.4%
Shuang Yu et al. [23]	Exudates	Image pre processing, features extraction and classification using CNN model	91.9% 88.8% 96%
Anaswara Chandran et al. [24]	Micro aneurysms	amplitude and frequency modulation, demodulation mechanism, gabor filters for edge detection, textural features fed into the random forest classifier and rule based decisions	88 % 87.5 % 90%
V. Saravanan et al. [25]	Micro aneurysms	Image pre processing, thresholding, binarization, blood vessels removal, and various morphological operations, classification using the Gaussian mixture model	85% N/A N/A
Jayant Yadav et al. [26]	Dot hemorrhage, exudates	image pre processing, image addition, subtraction, thresholding and morphological operations, optic disc,	75% N/A N/A

		blood vessels extraction classification using feed forward neural network	
Handayani Tjandrasa et al. [27]	Exudates	Image pre processing, morphological operations, subtractions and additions of images, intensity thresholding, extraction of features like area, perimeter, standard deviation etc, SVM for classification.	90.5% N/A N/A
Kranthi Kumar Palavalasa et al.[10]	Exudates	Image processing, green channel extraction, contrast adjustment, morphological operations	N/A 87% 76%
Büşra Yaşar et al. [11]	Exudates	Image processing along with median filter and contrast illumination. Edge detection algorithm.	N/A N/A N/A
C. Sinthanayothin et al. [12]	Micro aneurysms, exudates	Image pre processing, moat operator	For exudates N/A 88.5% 99.7% For micro aneurysms N/A 77.5% 88.7%
Bob Zhang et al. [18]	Tongue lesions	Used feature extraction like color, geometry and texture of the tongue images	80.3% N/A N/A
Lama Seoud et al. [19]	Micro aneurysms, hemorrhage	Used dynamic shape based features extraction with	N/A 93.9% 50%.

	-s	dynamic features like elongation, relative area, circularity, rectangularity and solidity	
S. Choudhury et al. [20]	Exudates	Image pre processing to remove noises and optic disc, extraction of features with the help of fuzzy c-means clustering, vessel density features	97.6% N/A N/A
Huiqi Li et al. [21]	Exudates	Extraction of optic disc, blood vessels using sobel edge detection method, kirsch's edge detection method resp.	N/A N/A N/A
Shuang Yu et al. [28]	Exudates	64x64 patch of CNN model for detection of the exudates in the fundus images, over the pixels of the green channel and illuminated fundus images.	91.9% 88.8% 96%
NurselYalçin et al. [29]	Exudates	Image pre processing, standardizing the images size, usage of convolutional neural network.	98.5% N/A N/A
Santhakumar R et al. [30]	Exudates, hemorrhage	Image pre processing like removal of background, extracted features like mean, standard deviation etc, SVM model for classification	For Exudates 96 % 94% 96% For hemorrhages 85 % 77% 85%

Nikita Gurudath et al. [31]	Exudates, micro aneurysms, hemorrhage	Image pre processing, Gaussian filters and automatic mask generation, textural features fed into artificial neural network and SVM	ANN 97.2% N/A N/A SVM 98.1% N/A N/A
Ridam Pal et al. [32]	N/A	Naive Bayesian classifier, SVM, K nearest neighbor algorithm and decision trees for binary classification of diabetic retinopathy on the fundus images collected from Messidor database	Naive Bayes 65.64% N/A N/A Decision tree 63.51% N/A N/A KNN 60.03% N/A N/A SVM 67.85% N/A N/A

All the recent techniques mentioned above majorly use image processing methods only for grading in diabetic retinopathy using fundus images. A lot of work revolves around detection of diabetic retinopathy using exudates and use of machine learning algorithms. Our research focuses on using two features of diabetic retinopathy i.e. exudates and micro aneurysms and applies image processing methods for grading purposes along with textural features extraction and application of machine learning algorithms for achieving better accuracy.

CHAPTER 3

PROBLEM STATEMENT

3.1 Problem Definition

Diabetic retinopathy (DR) is a vision threatening medical condition in which the retina of the diabetic patients gets damaged to an enormous amount. It is a secondary disease caused in the people already suffering from Diabetes Mellitus. It has become one of the most leading and recurrent cases of blindness among children and adults who have been suffering from diabetes for an extremely long period of time. The automation of detection of the lesions and understanding the severity of diabetic retinopathy saves a lot of manual labor and gives more accurate results. Knowing better the severity of this problem is very important to prevent from vision loss. The research work revolves around development of a grading system in diabetic retinopathy. The grading is done using two salient features of diabetic retinopathy i.e. exudates and micro aneurysms. Fundus images are collected from publicly available datasets MESSIDOR[33], E-OPTHA[34] and DIARETDB[35]. Two separate modules are developed for grading using exudates and micro aneurysms respectively. Image processing helps out the application of features extraction and machine learning models by removing the noises, providing necessary grading information and extracting the candidate lesions. With the advancements made in artificial intelligence and machine learning, a lot of time and cost with manual detection can be saved and technological advancements can be put to best use.

3.2 Gap Analysis

- The current diabetic retinopathy systems have used less samples of fundus images.
- The major focus on the diabetic retinopathy researches have been detection of the lesions and their binary classification i.e. whether they are present or absent in the retina.
- Grading to know severity level of diabetic retinopathy have not been explored well.

- Most of the researches for grading in diabetic retinopathy involve usage of image processing methods only.
- Better results and insights can be achieved with help of machine learning models and features extraction that have not been used for grading.

3.3 Research Objectives

The research work revolves around development of a grading system in diabetic retinopathy. The grading is done using two salient features of diabetic retinopathy i.e. exudates and micro aneurysms. Two separate modules are developed for grading using exudates and micro aneurysms respectively. Several steps of image preprocessing are applied so as to highlight the lesions and remove the noises from the images which tend to reduce the accuracy of detection of lesions in the retina. The second step used for more accurate and well performing grading system is features extraction that reduce dimension of the data and focus on more important parameters and characteristics that are more likely to describe the lesions well. Further, the features extracted are used for grading by application of various machine learning models and a comparison is drawn among them on how well they grade for exudates and micro aneurysms. The automation of detection of the lesions and understanding the severity of diabetic retinopathy saves a lot of manual labor and gives more accurate results. Knowing more about the severity of this problem is very important to prevent from vision loss.

The main objectives of the thesis are outlined below:

1. To search, examine and inspect the already existing diabetic retinopathy detection systems and to study their limitations.

2. To propose an automated system for grading the severity levels of diabetic retinopathy in the fundus images by making use of various image preprocessing methods, extracting useful features and employing various machine learning models.

3. To test and validate the proposed technique using various performance parameters.

CHAPTER 4

METHODOLOGY

An automated system for grading in diabetic retinopathy is proposed to understand and learn about the severity levels of the disease and the degree of threat of vision loss. A combined dataset of fundus images of Messidor, DiaretDb and E-optha has been used for the purpose. Initially, to grade with respect to exudates, detection of optic disc and macula are done. The images are fed to image preprocessing mechanism and techniques for better detection of the lesions which are exudates and micro aneurysms in our case. Image processing helps in removal of unwanted entities and bring us closer to better results and detection of regions of interest. Also, to grade according the micro aneurysms, their count helps to grade the severity levels of the disease. The second step involves application of features extraction mechanism which is Gray Level Co-occurrence Matrix (GLCM) in our case, that extracts the textural features of the segmented binary images. After the grading information and features information gets stored in excel sheet, this information is an input to the machine learning algorithms.

4.1 Proposed approach

The proposed approach as shown in figure 4.1 works on two features of diabetic retinopathy i.e. exudates and micro aneurysms.

- Image dataset containing 1361 images is collected and resized.
- Images are processed separately with respect to the detection of interested lesions. Steps are different for yellow and red lesions.
- The grading is done with respect to exudates and micro aneurysms and stored in excel sheet.
- The textural features are extracted using Gray level co-occurrence matrix and stored with grading information.
- The excel sheet information is given as input to various machine learning algorithms.
- The accuracy, sensitivity and specificity of models are computed from confusion matrix and ROC curves are shown.

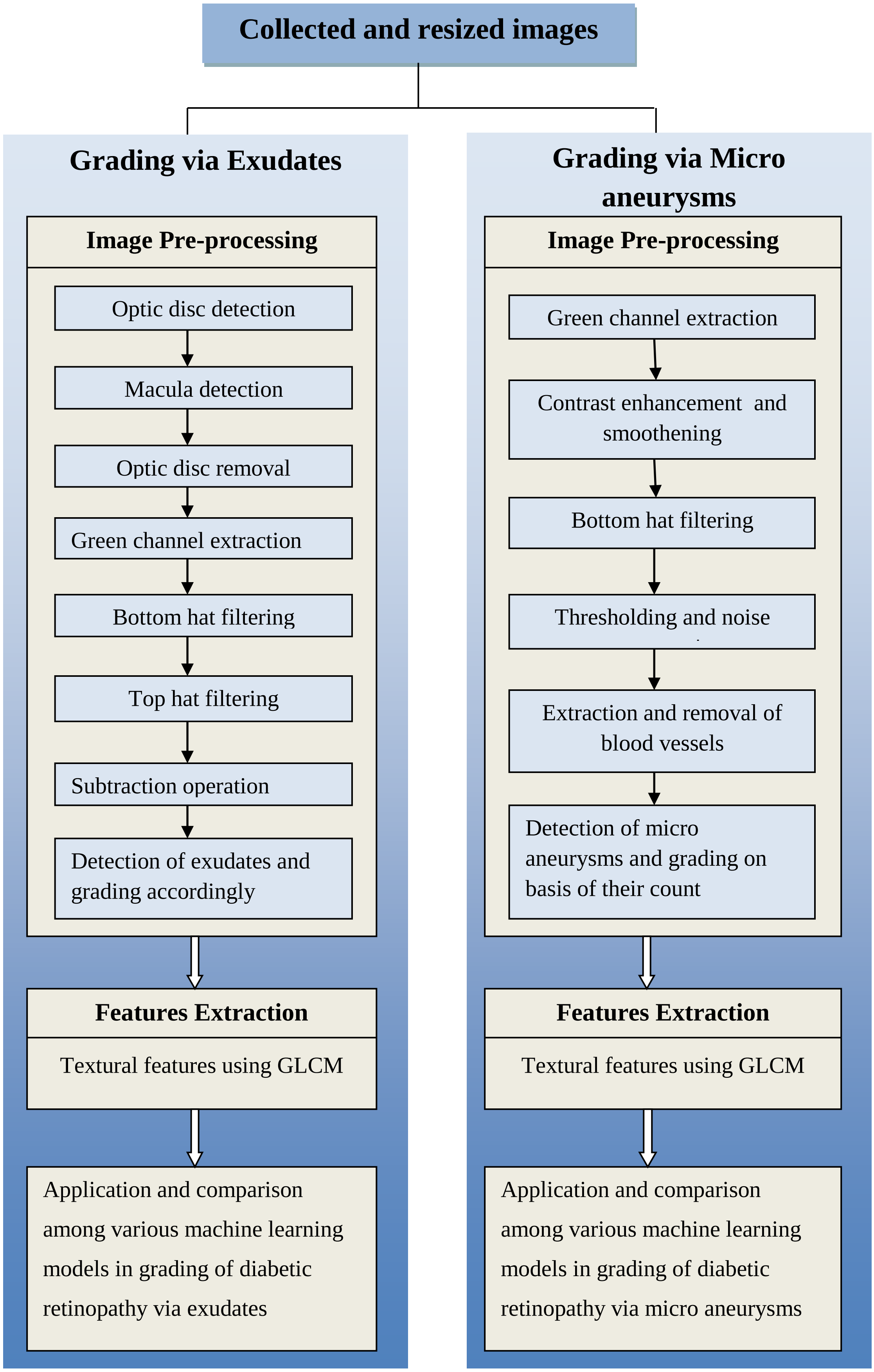


Figure 4.1: Proposed methodology flowchart

4.2 Detection of optic disc and macula

Optic disc has similar intensity value as that of exudates due to which its detection and removal is a very vital step for extraction and detection of exudates. Optic disc's center points are detected by resizing the image, thresholding the image to get bright lesions while ignoring the smaller lesions and vessel map is created to extract bigger vessels since the vessels having highest density are found at the center of optic disc. With help of midline in the image and vessel map, the center of optic disc is detected. The detection of macula is important for the grading purpose as nearer the exudates to the macula, higher is the severity of the disease. The macula has the darkest intensity at the center of retina and is about optic disc diameter away from the optic disc's center. With the help of vessel map least density of vessels is found out since macula is found where vessel density is almost zero, distance from the optic disc and local minima to extract the darkest region macula's center point is detected.

4.3 Image Pre-processing

Image processing helps in improvement of the quality of the image by removing the unnecessary details and noises in the images. The features extraction and grading tasks are done better and give more accurate results if important information is extracted from the images with appropriate processing techniques.

4.3.1 Image processing for Exudates

1. Optic Disc Removal

The optic disc is removed with the help of the known center. The optic disc is masked and hidden by merging it with background so that while detection of exudates, their intensities being similar, are not confused and detection of exudates is done better and error free. This ensures that our detection methods will extract out the exudates and not the optic disc.

2. Resizing the images

The fundus images are resized into a standard size of 512*512 pixels so that the images are of same dimension and the preprocessing steps can yield same effects on all the images as different sized images are prone to some errors and some of the results may not be satisfactory. By not standardizing the image size, the detection of exudates gets tough and inaccurate with the image processing steps that have been used for this work.

3. Green Channel Extraction

The fundus images are originally of RGB pattern and are converted into their respective green channels. Green channel is less saturated as compared to blue and show lesions and other objects distinctly and better as compared to red channel. Green channel is used as this color is sensitive to the human eyes and the proper illuminations and intensity variances are easily visible in green channel which helps us in detection of regions of interest easily. For a particular image I, green channel is extracted from RGB images, using the equation 4.1, where J is a green channel extracted image.

$$J=I(\ ,\ ,2) \tag{4.1}$$

Green channel shows comparatively lesser noises than other channels. As shown in Figure 4.2, light absorption is maximum by green channels which shows objects more clearly and with lesser noise as well.

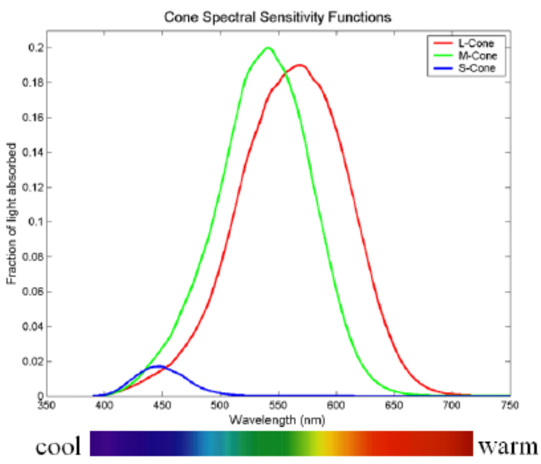


Figure 4.2: Light absorption graph of RGB channels

4. Morphological Operations

These operations are set of handy tools that are useful for extraction of particular components of images that can be used for description and representation of certain shapes of particular regions, boundaries etc. They process the images on the basis of shapes. Structuring element is used in morphological operations that are applied on the input images to deliver output images with same size. Structuring element is used as a template which is an odd matrix of zeros or ones, placed on all the pixels of the input image and then comparison is done with the pixels of image under inspection with the neighborhood of pixels of the structuring element. In some operations, the pixels of image fit with that of neighborhood and intersect or hit in other cases as shown in figure 4.3.

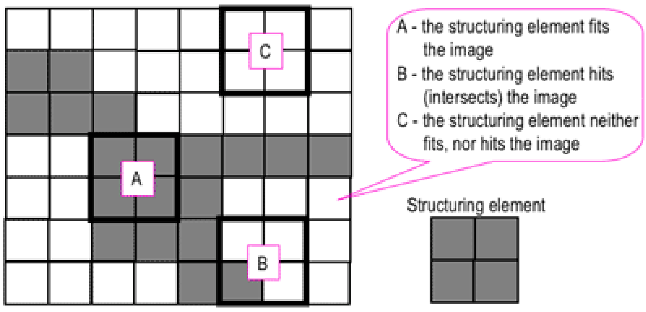


Figure 4.3: Fit and Hit mechanism by structuring element

- **Erosion** - A binary image f's erosion is carried out using a structuring element s (represented as $f \ominus s$) that forms a new binary image g of same size that has 1's in postions (x,y) of element's origin where the element s fits f, i.e. g(x,y)=1 if s fits f else 0, repeating for all (x,y) coordinates. The Figure 4.4 displays use of a 3x3 structuring element that shrinks the input image by removing away a layer of pixels from outer and inner boundaries of image.

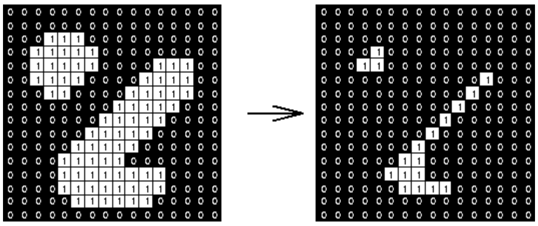


Figure 4.4: Erosion operation with 3x3 structuring element

- **Dilation** - Dilation has an opposite effect to that of erosion. Dilation of input image f using structuring element s (represented $f \oplus s$) gives a new binary image g that has 1's in all the positions (x,y) of element's origin at which s hits the f, i.e. g(x,y)=1 if s hits f else 0, repeating for all (x,y). The holes or gaps between different areas become smaller and the image expands as shown in Figure 4.5.

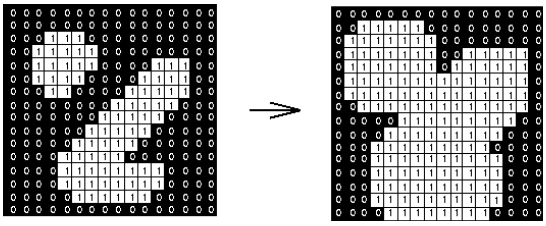


Figure 4.5: Dilation operation with 3x3 structuring element

- **Opening operation** - This operation is erosion followed by dilation using the same structuring element. This helps us to remove the smaller entities in the image and retains the shape and structure of the bigger objects as shown in Figure 4.6.

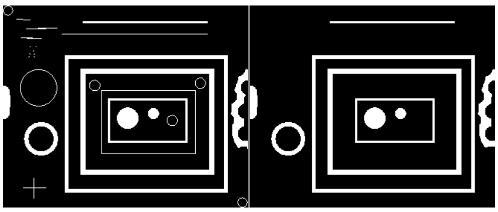


Figure 4.6: Opening operation

- **Closing operation** - This operation is dilation followed by erosion with the same structuring element. It preserves the shape and size of the objects in the image and helps in filling the holes or gaps in between the regions as shown in Figure 4.7.

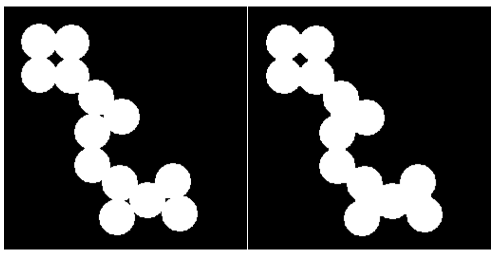


Figure 4.7: Closing operation

- **Bottom Hat Filtering Operation** - Bottom hat filter is applied on the green channel extracted images. A disc structuring element of radius 5 has been used in our case. This morphological filter first closes the image and then subtracts the closed image from the input original image. It helps in finding smaller darker objects in the images by highlighting the intensity troughs of the image as shown in Figure 4.8.

Figure 4.8: Bottom hat filtering operation

- **Top Hat Filtering Operation** - Top hat filter is applied on the green channel extracted images with disc structuring element of radius 8. This filter opens the input image and then subtracts the opened image from the input original image. It isolates and highlights the brighter smaller objects and also improves the contrast of non-uniformly illuminated image as shown in Figure 4.9.

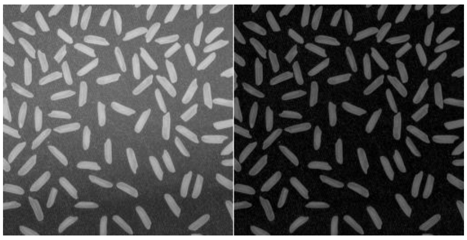


Figure 4.9: Top hat filtering operation

5. Detection of Exudates

The images obtained after the morphological bottom hat and top hat operations are used for extraction of the exudates. Subtraction of the bottom hat filtered images is taken with top hat filtered images that results in the extraction of exudates.

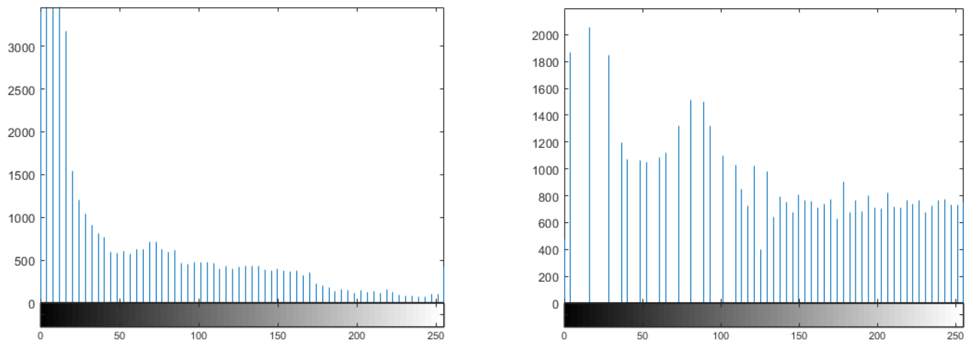
4.3.2 Image processing for Micro aneurysms

1. Green Channel Extraction

Just like for exudates, for micro aneurysms too green channel of the original RGB images is extracted so as to bring out the differences among entities and lesions quite clear.

2. Contrast Enhancement

Contrast enhancement works out well for detection of micro aneurysms since the red lesions and other entities are segmented well from the background. Contrast limited adaptive histogram equalization (CLAHE) is used for improving the contrast of the images. A good contrast image becomes more suitable for further stages of processing of images. The Figure 4.10 below shows the histogram of original image and then contrast enhanced image.



(a) (b)

Figure 4.10:Contrast Enhancement; (a) Original image histogram, (b) Image histogram after contrast enhancement

3. Smoothening

Smoothening operation is carried out using averaging filter that helps in blurring effect as shown in Figure 4.11 which helps to reduce the presence of unwanted objects and makes sure that they don't get involved in the next image processing steps like binarization.

(a) (b)

Figure 4.11: Smoothening of image; (a) original image, (b) smoothened image

- **Average Filter -** Average or Mean filter helps in smoothing the images by reducing the variations of intensities between pixels with the help of sliding kernel/window. The average is obtained by replacing each pixel of the image with the average of the value of pixels in its window as shown in the Figure 4.12. Here the central value 1 is replaced with value 5 using (5 + 3 + 6 + 2 + 1 + 9 + 8 + 4 + 7 = 45), 45 / 9 = 5.

5	3	6
2	1	9
8	4	7

(a)

*	*	*
*	5	*
*	*	*

(b)

Figure 4.12: Average filter; (a) original matrix, (b)filtered matrix

4. Morphological Operation

Bottom hat filtering operation is used on the smoothened images with a disc structuring element of radius 25. This morphological filter first closes the image and then subtracts the closed image from the input original image. It helps in finding smaller darker objects in the images by highlighting the intensity troughs of the image.

5. Thresholding and noise removal

The images are subjected to binarization for proper segmentation into foreground and background objects that helps to detect the lesions quite effectively. An intensity threshold value is chosen and the images are binarized successfully following which they are filtered using median filter that helps to remove tiny objects of noises that may affect the performance of the system in detection of micro aneurysms. The Figure 4.13 displays the concept of thresholding where the image intensities whose value is greater than a threshold value are partitioned from background as foreground objects.

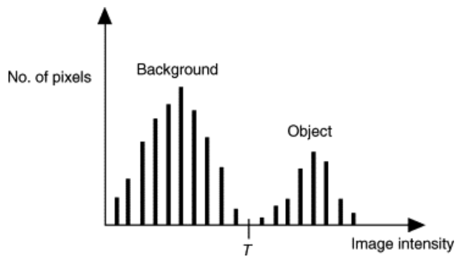
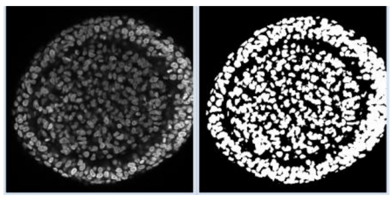


Figure 4.13: Thresholding image with threshold value 'T'

The Figure 4.14 shows the before and after effect on the application of thresholding on the image.



(a) (b)

Figure 4.14:Binarization of image (a) Original image, (b) Binarized image

- **Median Filtering -** Filtering method helps in improving the accuracy of the proposed methodology as it makes sure different entities are not mistaken to be micro aneurysms. Edge preservation is also done by application of median filter. This filter removes small objects and noises with a sliding window where the central value of the window gets replaced with the median of pixel values in the window neighborhood. The Figure 4.15 shows how median filter works with a 3x3 window by ordering the values 0, 2, 3, 3, **4**, 6, 10, 15, 97 and replacing 97 with 4.

6	2	0
3	97	4
19	3	10

(a)

*	*	*
*	4	*
*	*	*

(b)

Figure 4.15: Median filter; (a) Original matrix, (b)Filtered matrix

6. Extraction of blood vessels

The blood vessels have similar intensity to that of micro aneurysms, so their extraction and removal is a vital step so that while features extraction they are not confused with micro aneurysms. Area filtering method is used to extract the large connected blood vessels and remove them. bwareafilt is used in Matlab that extracts connected area of image as per the mentioned range.

7. Detection of micro aneurysms

After removal of blood vessels, focus is shifted on to detection of micro aneurysms which is done via opening operation that is a morphological operation which removes the unwanted objects and noises whose size is smaller than a particular radius. It effectively brings out numerous micro aneurysms.

4.4 Features Extraction

Feature extraction plays a very important role in reduction of dimension of data and giving meaning to the data and extracting useful and non-redundant information from it. It proves to be quite effective and informs about certain patterns that can't be recognized directly. The set of features extracted mostly contain relevant information about the input data and helps in fulfillment of desired tasks using insights provided by the features. Gray Level Co Occurrence Matrix (GLCM) is used in our case which is a statistical mechanism that focuses over the textural properties of the images and represents them. It also goes by the name of Gray Level Spatial Dependence Matrix because the features are extracted by calculating the frequency of certain pairs of pixels that occur together in a particular fashion or specific spatial relationship in the images and draws the information out of them in terms of textural properties. The GLCM is created with the help of graycomatrix function available in Matlab and thus the characteristics are extracted out using graycocrops. The Figure 4.16 displays the usage of graycomatrix.

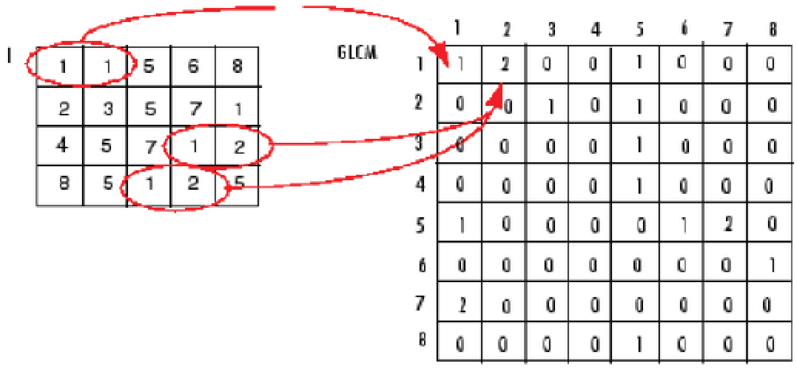


Figure 4.16: Formation of GLCM matrix

In the Figure 4.16, it is shown how the first three values of the GLCM matrix have been computed. The spatial relationship between two pixels say a and b has been taken as how frequently these two pixels are present horizontally adjacent to each other in the input image matrix. The gray levels taken in this example are 8 which is why the size of GLCM is 8x8. Gray levels denote the level of variations in intensities. The first entry of GLCM matrix for pixels (1,1) is 1 since the occurrences of these two-pixel values adjacent to each other is just once in the input image matrix. Similarly, the second entry in the GLCM matrix representing the pixels (1,2) has value 2 as that's how frequently these pixel values occur as per mentioned spatial relationship. The pixel values (1,3) do not occur adjacent to each other in the image, hence their GLCM value is 0.

The properties extracted by GLCM are contrast, correlation, energy and homogeneity. These are second order statistics that give handful information about grey level positions that are present within the image.

- Contrast - Contrast measures the values of intensity of a particular pixel with respect to its neighbor pixel. All the local variations happening in the gray level co-occurrence matrix are captured as contrast.

$$\sum_{m,n=0}^{P-1} R(m,n) * (m-n)^2 \tag{4.2}$$

- Correlation- Correlation measures the correlation between a particular pixel and its neighbor pixel. It computes for particular pair of pixels, their joint probability of occurrence.

$$\sum_{m,n=0}^{P-1} R_{mn} \frac{(m-\mu)(n-\mu)}{\sigma^2} \tag{4.3}$$

- Energy - Energy measures the degree of similarity in image. It measures uniformity. It computes the GLCM elements' squared values' sum.

$$\sum_{m,n=0}^{P-1} (R_{mn})^2 \tag{4.4}$$

- Homogeneity - Homogeneity describes the closeness of pixels in an image. It shows how closely the different elements of GLCM are distributed and arranged with respect to the diagonal of GLCM.

$$\sum_{m,n=0}^{P-1} \frac{R_{mn}}{1+(m-n)^2} \tag{4.5}$$

where following annotations have been used,

m = no of rows in matrix

n = no of columns in matrix

Rmn = Element m, n of normalized symmetric geometry

P = Gray levels used for the image

u = mean of values of GLCM

4.5 Application of machine learning algorithms

Machine learning is a subfield of artificial intelligence that results in a system that intelligently learns from the environment and improves its performance from experience. It revolves around such computations and developing certain algorithms that use data and learns certain patterns from them. Various algorithms are applied on the information collected after image processing and feature extraction stages that are collected in an excel table. The algorithms are applied for both the exudates and micro aneurysms and grading information is fed to the algorithms and different performance parameters are computed as well.

4.5.1 Decision Tree

Decision trees are supervised machine learning algorithms that is they are fed to the classes in the training period and during testing period the outcomes are one of the classes fed depending on the patterns and rules learned by the trees from the data in the training period. Regression-based and classification-based problems can be solved pretty well with the help of decision trees. These algorithms have a tree like representation where the leaf nodes are used for representing the final decision that is the class assigned to the data and the internal nodes are the attributes used to describe the behavior of the data. The decision is taken with respect to the internal nodes according to which the tree branches to different state. This algorithm is very easy to interpret and visualize. It also implicitly performs features selection. Pretty handy as handles both categorical and numeric data. The Figure 4.17 displays the example of decision tree where the values of attributes like outlook, humidity and windy are used for classification where the finally outcome is yes or no.

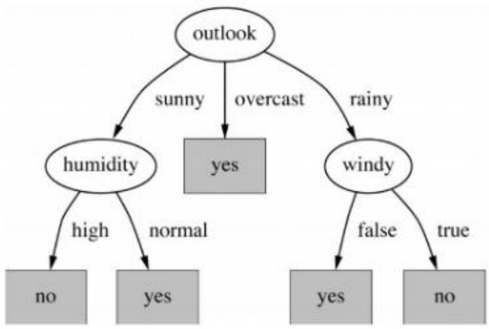


Figure 4.17: Decision tree classification

4.5.2 Support Vector Machine (SVM)

Support Vector Machine is a supervised method of classification where the data that has to be classified, their features and attributes that play important role in classification are plotted in a 2-D space as data points which have to be classified by a hyperplane. Hyperplane acts like a decision boundary as shown in the Figure 4.18. The best hyperplane is the one which has the largest margin that is the plane whose distance from each classes' closest item from plane is maximum is chosen. SVM also makes use of mathematical functions that are the kernels used to resolve the classification problem. The kernels can be linear, cubic, exponential, polynomial etc. Support vectors are the date items which lie on or close to the hyperplane and play a major role in influencing the orientation and location of the hyperplane. With the help of support vectors, the margin of our classifier i.e. the hyperplane can be maximized. If these are deleted, it causes a change in the position of the hyperplane. Basically, support vector are the data points that play a vital role in building up the SVM.

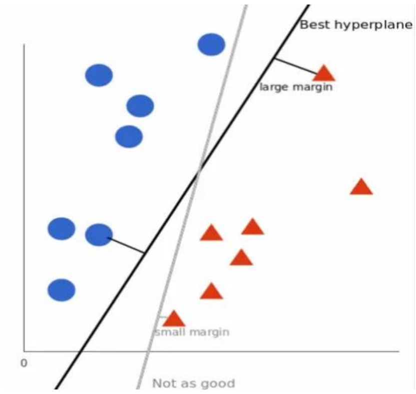


Figure 4.18: Support vector machine classification

4.5.3 K-Nearest Neighbor Algorithm (KNN)

KNN algorithm works well for both regression and classification problems and is easy to calculate, compute and interpret. It is an unsupervised machine learning algorithm that works on assumption that similar things exist at closer proximity. During the training period the input data instances' similarities are computed on the basis of distances and are labeled as particular class. During testing phase, when a new data entry is there, its attributes' values are computed with the data entries belonging to particular classes and the class to which the distance is least, the new data entry belongs to it. K stands for the number of the neighbors chosen for the particular problem for computation. Figure 4.19 shows KNN classification example.

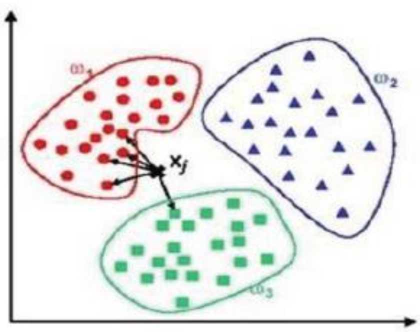


Figure 4.19: K nearest neighbor classification

4.5.4 Ensemble Classifier

Ensemble learning is a method in which various machine learning algorithms are brought together following a particular strategy and their combination is used to compute a particular problem. Functions approximation, regression, classification etc. are improved with the use of ensemble learning. It also aids in improving the overall performance which might be less in case of individual usage of model. The Figure 4.01 shows how different models are combined and used to select the best outcome so as to reduce the error and bias.

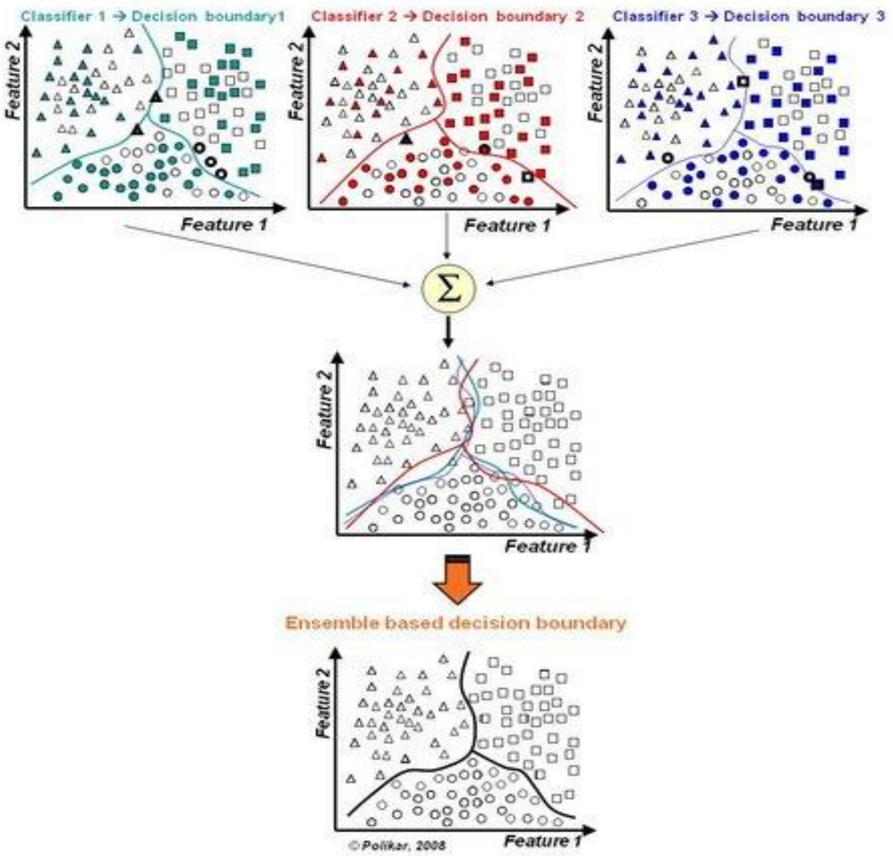


Figure 4.20: Ensemble classification

The types of ensembling methods are listed below:

- Averaging - It is best method to overcome overfitting and work on large sets of data and bigger problems. Prediction probabilities are chosen in this method. The example is shown in Table 4.1.

Table 4.1: Averaging Method

Model 1	Model 2	Average Prediction
40	30	35

- Majority Vote - The classification problem that has the maximum same outcomes i.e. has higher votes is chosen as the final outcome or target class as shown in example in Table 4.2.

Table 4.2: Majority Voting

Model 1	Model 2	Model 3	Voting Prediction
1	1	0	1

- Weighted Average - For giving some more importance to particular models, weights have been introduced which are used along with the predictions of all the participating models followed by the average as shown in example in Table 4.3.

Table 4.3: Weighted Average Method

	Model 1	Model 2	Model 3	Weighted Average
Weight	0.3	0.5	0.2	
Prediction	15	20	10	16.5

The following ensemble models have been implemented in our research work for the ensemble learning:

1. Boosted Trees

Boosting is an ensemble method that tries to boost the performance of the individual weak learners so as to improve the overall performance. It is an iterative process for making the learners stronger in terms of their predictions. In the first iteration, the predictions from all the learners are taken and the classifier giving the worst outcome, is given more importance in next iteration in terms of being given more weight to the outcome of the weak learner so that their predictions get stronger as the classifier learns more with experience and gives more accurate results. With each iteration, it is our aim to reduce the cost. Whatever losses are made at each iteration, the aim of various tree learners is to reduce that loss in the next iteration.

2. Bagged Trees

Bagging is called as Bootstrap aggregation where the weak learners like decision trees are bagged by creating bootstrap replicas of the original dataset and running the weak learners on each of the replicas making them learn from those replicas. These replicas should have data points with replacement. For each decision split, the trees can choose predictors randomly for each of the split. Predict function is used in Matlab to check the predicted responses by each of the weak learners. When trees are used for bagging, individual learner's overfitting are not considered and also the trees grow deep and not pruned due to addition of newer data samples.

3. Random Subspace

Random subspace ensemble methods are also called attribute or features bagging that aims at reducing the correlation and dependency among the predictor variables being used. The classifiers are trained on random samples of features rather than working over the whole feature set.

The following parameters are used in the basic random subspace algorithm:

- m: tells the number of variables or dimensions to be sampled in each of the learners.
- d: tells the data's dimensions, i.e. the number of predictors being used in the input data matrix
- n: tells the total number of classifiers or learners used for ensemble.

The following basic steps are being performed by a random subspace algorithm:

1. From d possible values, a set of m predictors is chosen randomly without replacement.

2. With the m chosen predictors, weak learners are trained.
3. The steps 1 and 2 are repeated till there are n weak learners.
4. The weak learners' predicted scores are averaged ad used for final prediction, thus further classifying into category that has highest average score.

The use of subspace KNN and subspace Discriminant have been used in our approach.

4. RUSBoosted Trees

RUS stands for Random undersampling boosting which helps in classification of data which is highly imbalanced i.e. certain class have fewer number of members in them as compared to others in the training data. The algorithm makes use of N, number of members of the class that has the fewest number of members in it in the input training data. This serves as the basic sampling unit. Thus, the classes that have more member comparatively, have to be under sampled by including n observations of every class. For K classes, all the weak learners used in the ensemble includes subset of data having N observations from all of the K classes. For reweighting and formation of ensemble, the procedure of boosting in Adaptive boosting is followed.

4.6 Grading Mechanism

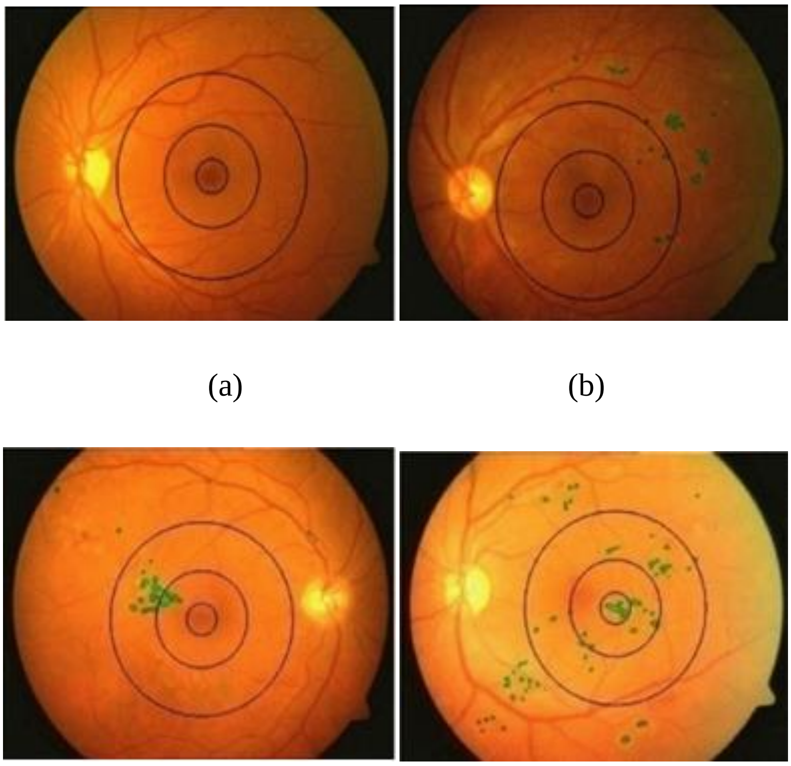
To know the severity of diabetic retinopathy in the fundus images, grading has been done accordingly. The major four grades that have been used to know the degree of damage caused to the retina due to diabetic retinopathy are listed in Table 4.4.

Table 4.4: Severity levels for grading in diabetic retinopathy

Severity Level	Description
Grade 0	No Signs of Diabetic retinopathy.
Grade 1	Mild signs of Diabetic retinopathy.
Grade 2	Moderate signs of Diabetic retinopathy.
Grade 3	Severe signs of Diabetic retinopathy.

4.6.1 Grading via Exudates

The grading via exudates is done depending on the distance and position of exudates with respect to the macula which is the central portion of retina that gives the best color vision. Nearer the exudates, more is the risk of loss of vision as shown in Figure 4.21. The exudates in smaller circular region are closest to macula and show severe level of disease and a drastic threat to vision loss. The exudates present in the second biggest circle show moderate signs of disease and can gradually lead to severity if not treated. The biggest circle show the mild case of diabetic retinopathy.



(a) (b)

(c) (d)

Figure 4.21: Severity levels of diabetic retinopathy; (a) Grade 0, (b) Grade 1, (c) Grade 2, (d) Grade 3

4.6.2 Grading via Micro aneurysms

The grading via micro aneurysms is done using the count of these lesions. More the number of micro aneurysms greater the threat of vision loss as shown in Table 4.5.

Table 4.5: Grading mechanism using micro aneurysms

GRADE	NO. OF MICRO ANEURYSMS (MA)
No Diabetic retinopathy	MA = 0
Mild Diabetic retinopathy	0 < MA <= 5
Moderate Diabetic retinopathy	5 < MA <= 15
Severe Diabetic retinopathy	MA >= 15

4.7 Performance Metrics for Grading

The various performance metrics that have been used for comparison among the machine learning algorithms have been explained below.

4.7.1 Confusion Matrix

The correctness and how accurate a model behave is calculated through confusion matrix which is also termed as error matrix. This helps us in getting a clear view of what correct and incorrect behavior in predictions is being carried out by our model. In our case multi class confusion matrix is created where we have four classes. Class 0 means no DR, class 1 means mild DR, class 2 means moderate DR and class 3 means severe DR. The confusion matrix for the same has been shown in Table 4.6.

Table 4.6: General confusion matrix for our grading purpose

		Predicted			
		0	**1**	**2**	**3**
Actual	**0**	TP_0	E_{01}	E_{02}	E_{03}
	1	E_{10}	TP_1	E_{12}	E_{13}
	2	E_{20}	E_{21}	TP_2	E_{23}
	3	E_{30}	E_{31}	E_{32}	TP_3

The terms associated with the confusion matrix are:

- E_{ij}: This entry depicts that predicted class by the model is j but the actual class is i.
- True Positive (TP): This is the case when the predicted and actual classes are same. For example, in table, TP_0, TP_1, TP_2, $TP_3$is when the model predicted the class as 0, 1, 2, 3 and it in actual is class 0, 1, 2, 3 respectively.
- True Negative (TN): This is the case when the model predicted that a particular instance did not belong to a class which in actual is true. For example in table, TN_0 is $TP_1 + E_{21}+ E_{31}+ E_{12}+TP_2+ E_{32}+ E_{13}+ E_{23}+ TP_3$.
- False Positive (FP): This is the case when model predicts that a particular instance belongs to a class but in actual it does not. For example, in table, FP_0 is$E_{10}+ E_{20}+ E_{30}$.
- False Negative (FN): This is the case when model predicts that a particular instance does not belong to a class but in actual it does. For example in table, FN_0 is $E_{01} + E_{02} + E_{03}$.

4.7.2 Accuracy

Accuracy refers to the total number of correct predictions and classifications done by the model out of the total number of predictions as shown in Table 4.7.

$$\text{Accuracy} = (TP_0 + TP_1 + TP_2 + TP_3) / \text{Total number of observations} \quad (4.6)$$

Table 4.7: Accuracy representation in confusion matrix

		Predicted 0	Predicted 1	Predicted 2	Predicted 3
Actual	0	TP_0	E_{01}	E_{02}	E_{03}
	1	E_{10}	TP_1	E_{12}	E_{13}
	2	E_{20}	E_{21}	TP_2	E_{23}
	3	E_{30}	E_{31}	E_{32}	TP_3

Predicted

4.7.3 Sensitivity

Sensitivity refers to true positive rate of the class under observation in case of multi class confusion matrix. It shows what proportion of values that actually belonged to a particular class are also predicted to belong in that class as shown in Table 4.8. The overall sensitivity is the average of values of sensitivity of all the classes.

$$\text{Sensitivity of class 0} = TP_0/(TP_0 + E_{01} + E_{02} + E_{03}) \qquad (4.7)$$

Table 4.8: Sensitivity representation in confusion matrix

		0	1	2	3
Actual	0	TP_0	E_{01}	E_{02}	E_{03}
	1	E_{10}	TP_1	E_{12}	E_{13}
	2	E_{20}	E_{21}	TP_2	E_{23}
	3	E_{30}	E_{31}	E_{32}	TP_3

Predicted

4.7.4 Specificity

Specificity is referred to as the true negative rate of the class under consideration. It depicts what proportion of values that actually did not belong to a particular class, were predicted to not belong to that particular class as shown in Table 4.9. The overall specificity is the average of values of specificity of all the classes.

$$\text{Specificity for class 0} = TN_0/(TN_0 + E_{10} + E_{20} + E_{30}) \qquad (4.8)$$

Table 4.9: Specificity representation in confusion matrix

		0	1	2	3
Actual	0	TP_0	E_{01}	E_{02}	E_{03}
	1	E_{10}	TP_1	E_{12}	E_{13}
	2	E_{20}	E_{21}	TP_2	E_{23}
	3	E_{30}	E_{31}	E_{32}	TP_3

Predicted

4.7.5 ROC curves

Receiver Operating curve (ROC) is a graphical represenation of how well a model is performing interms of its accuracy in predictions. It is a plot between sensitivity and specificity. The closer the ROC curve is towards the upper left corner the better and higher is the accuracy of the model as shown in Figure 4.22.

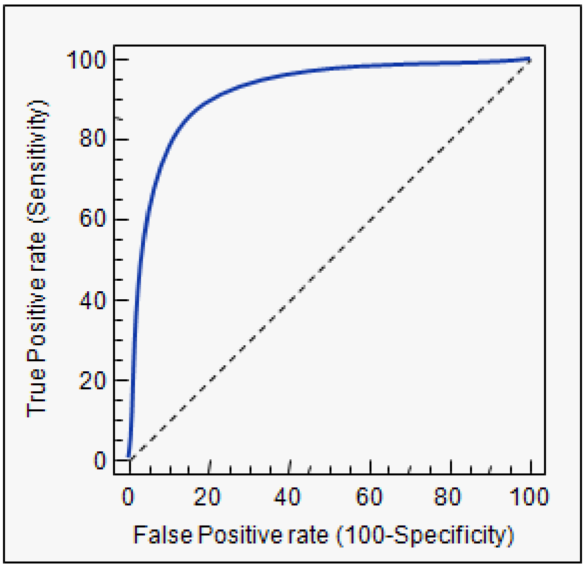


Figure 4.22: ROC curve

As discussed in above sections, the methodology carried out in the thesis focuses on the severity levels of diabetic retinopathy in the fundus images with the help of image processing methods like green channel extraction, removal of noises and extraction of exudates and micro aneurysms, GLCM textural features like energy, correlation, homogeneity and contrast, machine learning algorithms like support vector machine, k nearest neighbor, decision tree etc. that train and test on the information received and stored in excel sheet. A comparison is drawn out on how well the machine learning algorithm grades the severity level of diabetic retinopathy algorithms in terms of accuracy, sensitivity, specificity and ROC curve.

CHAPTER 5

EXPERIMENTAL RESULTS

In our research work, MATLAB 2018a has been used for carrying out the image processing, features extraction and application of various machine learning models on the system having processor Intel Core i5-4210U CPU @1.70 GHz 2.40 GHz with 8 GB RAM and 64-bit operating system. The combined dataset of publicly available datasets Messidor, E-optha and DiaretDb have been used with a total of 1361 colored fundus images.

- **Messidor -** This dataset has 1200 colored fundus images that have been occupied by three departments of ophthalmology with a colored 3CCD camera having a view field of 45^o. Pupil were dilated using Tropicamide and 800 fundus images were taken whereas 400 fundus images are without dilation. 1200 images have been separately stored in 3 sets with one set belonging to each ophthalmology department.
- **E-optha -** This dataset contains 82 colored fundus images with purpose of providing research in the field of diabetic retinopathy. 47 images are found with presence of lesions whereas 35 images have no lesions. A tele-medical network named OPHDIAT© generated these fundus images.
- **DiaretDb -** This dataset includes 89 colored fundus images out of which 84 images show traces of at least mild severity level of diabetic retinopathy and 5 fundus images are normal retinal images with no sign of diabetic retinopathy. 50^o view field was utilized for capturing the fundus images. These images correspond to good usage in practical environment where images being comparable are used to compute and compare performances of the methods used for diabetic retinopathy detection and grading.

The Figure 5.1 shows a snapshot of some of the images having varying illuminations and colors that have been used for our work. A combined dataset of Messidor, e-optha and DiaretDb have been used so that bigger dataset is used in comparison to other works already done in the field of diabetic retinopathy. Also, this helps in better training and testing of the machine learning algorithms.

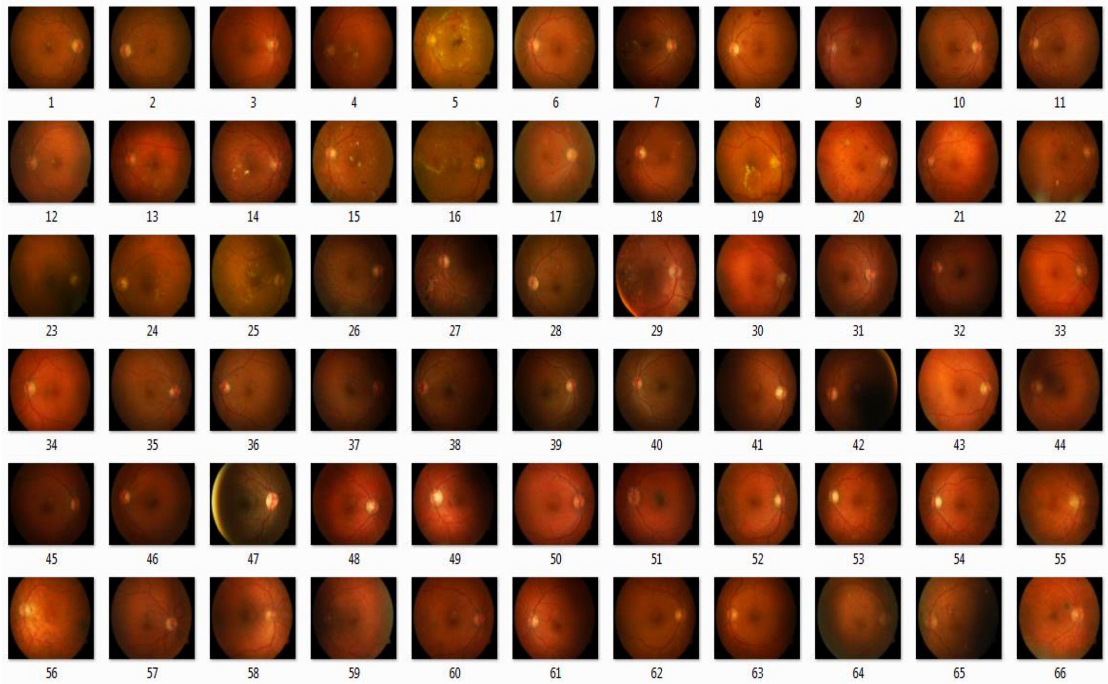


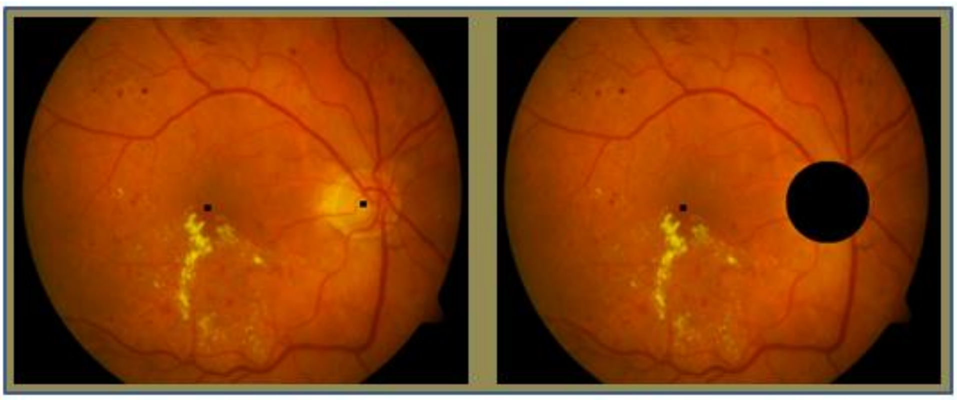
Figure 5.1: Snapshot of the input fundus images

5.1 Grading via Exudates

As discussed earlier, grading of diabetic retinopathy according to exudates is done by computing its location and position from macula.

5.1.1 Detection of Optic disc and macula

The detection of optic disc and macula are very important as they play a vital role in detection of exudates and their grading. The detected centre points and masked optic disc have been shown in Figure 5.2 (a) and (b), respectively.

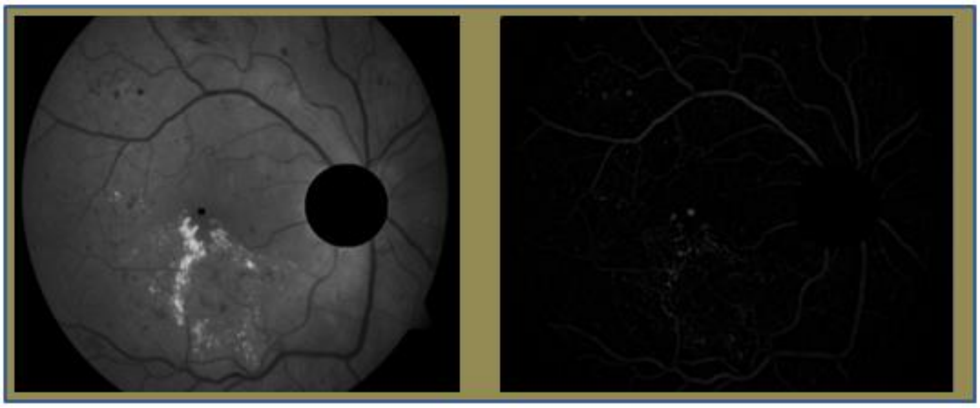


(a) (b)

Figure 5.2: (a) Detection of optic disc and macula, (b) Masking of optic disc

5.1.2 Preprocessing for exudates

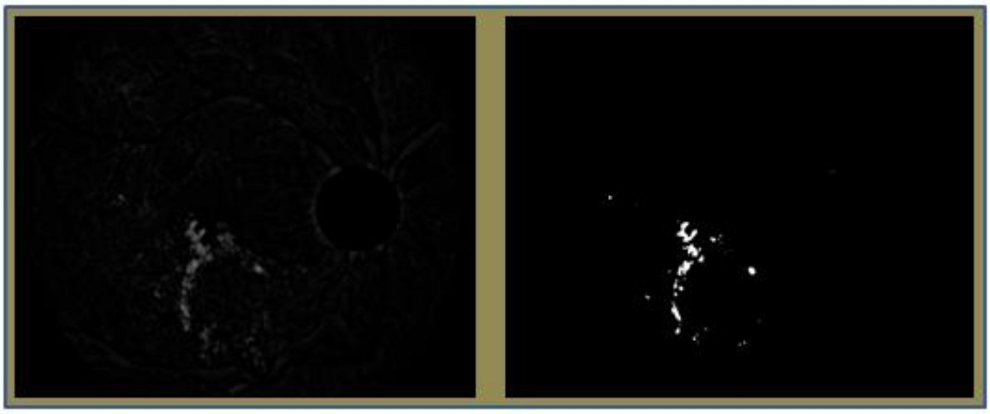
Figure 5.3 (a) and (b) shows the green channel extracted from the original colored image and application of bottom hat filtering that brings out the small dark objects of the image, respectively.



(a) (b)

Figure 5.3: (a) Green channel extracted image, (b) Bottom hat filtered image

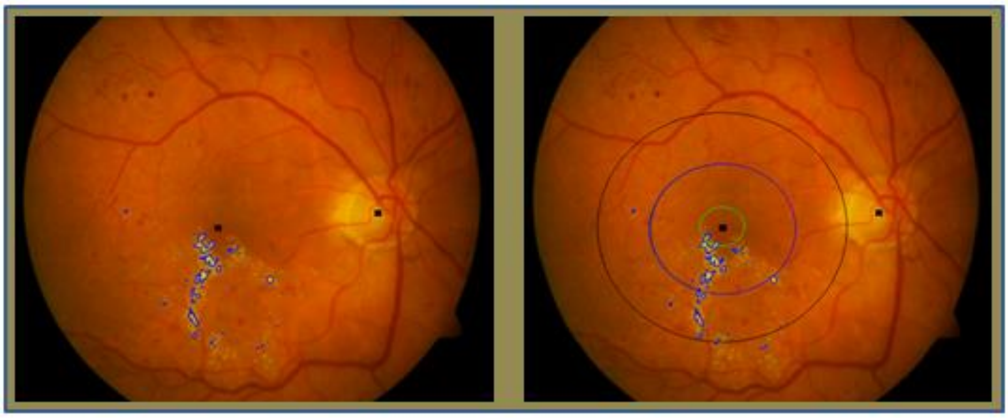
Figure 5.4 (a) and (b) show the result of top hat filtering on the green channel extracted image which brings out the brighter objects and extracted exudates after subtraction operation, respectively.



(a) (b)

Figure 5.4: (a) Top hat filtered image, (b) Extracted exudates

Figure 5.5 (a) and (b) outlines the presence of exudates and shows their distance from macula for grading purpose, respectively.



(a) (b)

Figure 5.5: (a) Outlined detected exudates, (b) Grading of exudates

5.1.3 Features extraction in exudates

The textural features like contrast, correlation, energy and homogeneity have been extracted using Gray level co-occurrence matrix shown in Table 5.1. The grades have been shown along with features.

Table 5.1: Features extracted using GLCM for grading via exudates

Images	Contrast	Correlation	Energy	Homogeneity	Grade
1	0.000160531	0.4877246	0.999526	0.999919735	2
2	0.000504525	0.803901715	0.996923	0.999747737	0
3	0.000168175	0.405321306	0.999549	0.999915912	3
4	0.000145242	0.604094032	0.999488	0.999927379	1
5	0.000107021	0.599946483	0.999625	0.99994649	3
6	0.000191108	0.632257362	0.999289	0.999904446	0
7	0.000191108	0.626770093	0.999297	0.999904446	2
8	0.00051217	0.625442064	0.998121	0.999743915	1

5.1.4 Comparison of various machine learning algorithms applied for grading via exudates.

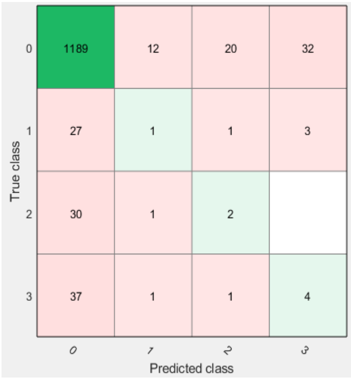
Various machine learning models and their performances have been compared in the Table 5.2. Support Vector Machine (Linear) and K Nearest Neighbor (Medium) show highest accuracy of 92.1%.

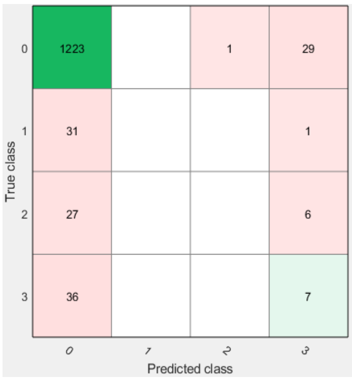
Table 5.2: Comparison of the machine learning models applied for grading via exudates

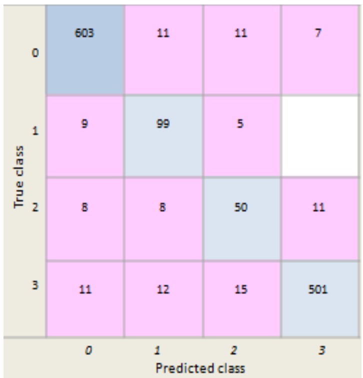
Machine Learning Model	Accuracy	Sensitivity	Specificity
Decision Tree	87.9%	0.78	0.65
Linear Discriminant	90.1%	0.81	0.77
Support Vector Machine (Linear)	92.1%	0.84	0.90
Support Vector Machine (Cubic)	19.3%	0.54	0.76
K Nearest Neighbor (Fine)	85.9%	0.90	0.76
K Nearest Neighbor (Medium)	92.1%	0.83	0.84
K Nearest Neighbor (Coarse)	90.1%	0.89	0.97
K Nearest Neighbor (Cosine)	92%	0.67	0.95
K Nearest Neighbor (Cubic)	90%	0.78	0.96
K Nearest Neighbor (Weighted)	89.9%	0.75	0.75
Boosted Trees Ensemble	91.8%	0.97	0.89
Bagged Trees Ensemble	89.6%	0.78	0.75
Subspace Discriminant Ensemble	91.3%	0.88	0.74
Subspace KNN Ensemble	89.5%	0.81	0.82
RUSBoosted Trees	49.3%	0.39	0.50

5.1.5 Comparison of various machine learning algorithms' confusion matrix for grading via exudates.

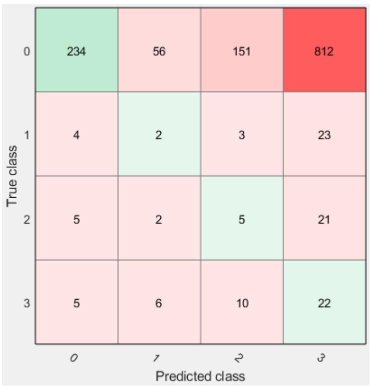
Confusion matrix of all the models that have been applied are shown in Figure 5.6.

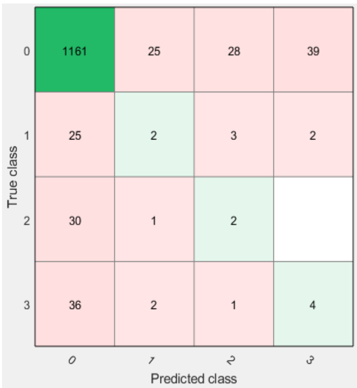


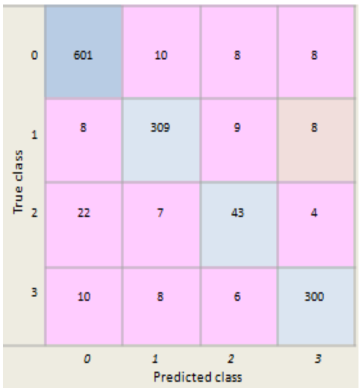




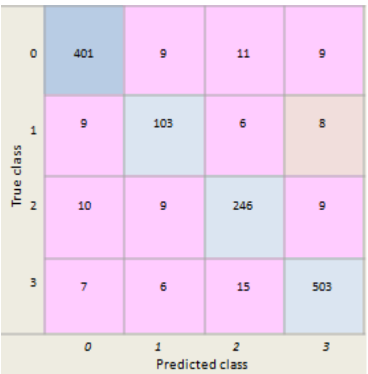
(a) (b) (c)

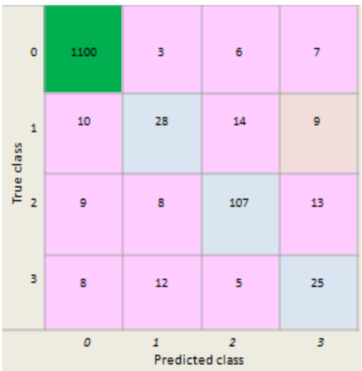


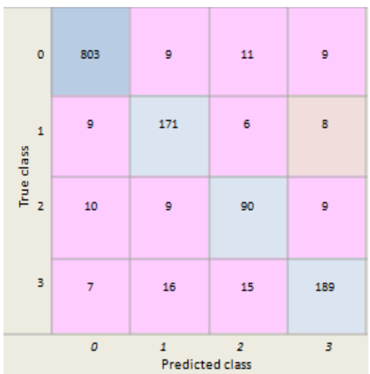




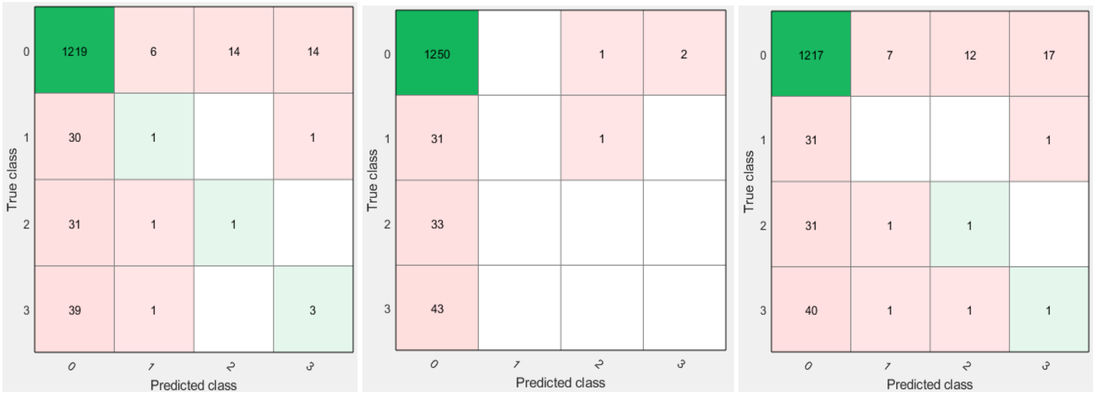
(d) (e) (f)



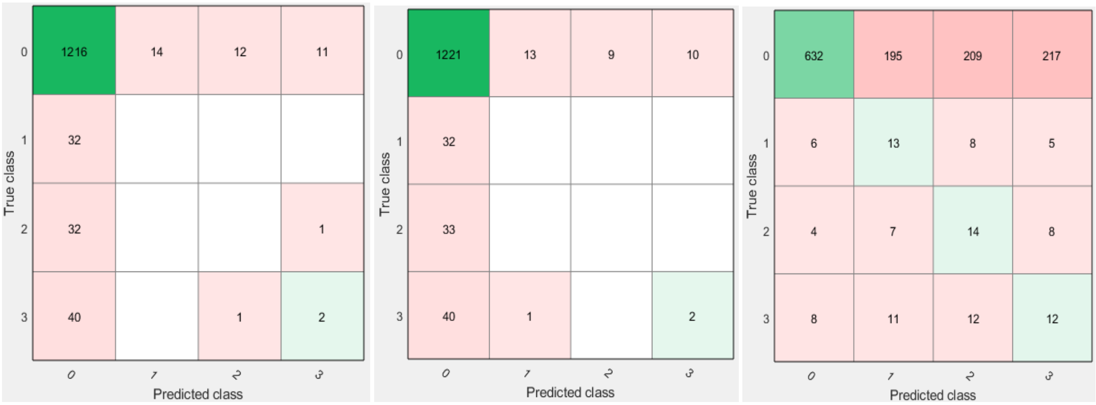




(g) (h) (i)



(j) (k) (l)

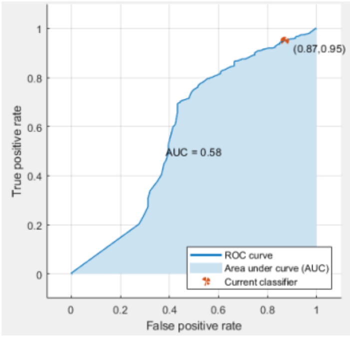


(m) (n) (o)

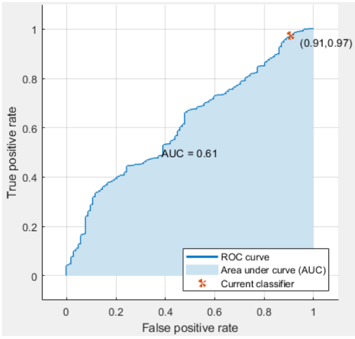
Figure 5.6: Confusion matrix of the applied models for grading via exudates; (a) Decision tree, (b) Linear discriminant, (c) SVM(linear), (d) SVM(cubic), (e) KNN(fine), (f) KNN(medium), (g) KNN(coarse), (h) KNN(cosine), (i)KNN(cubic), (j) KNN(weighted), (k) Boosted tree ensemble, (l) Bagged tree ensemble, (m) Subspace discriminant, (n) Subspace KNN, (o) RUSBoosted tree ensemble.

5.1.6 Comparison of various machine learning algorithms' ROC curves for grading via exudates.

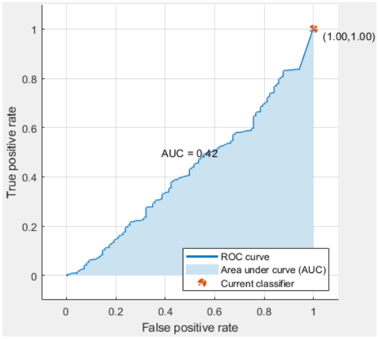
ROC curves depict how well and accurate are the predictions of the models that have been applied for grading via exudates. It is graph between sensitivity and specificity and larger the area under ROC curve (AUC), better and higher is the accuracy of the model. Subspace discriminant displays highest AUC score of 0.75 followed by KNN(coarse) with score 0.72 as shown in Figure 5.7.



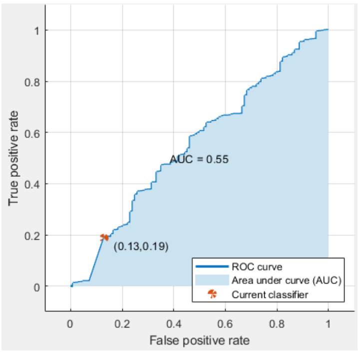
(a)



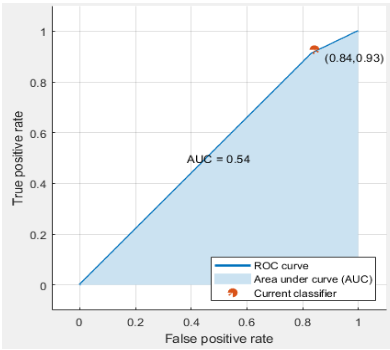
(b)



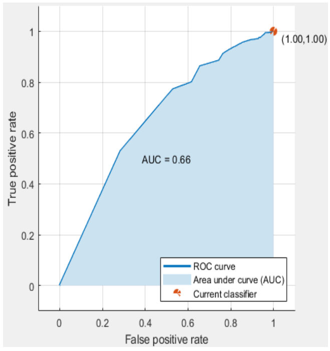
(c)



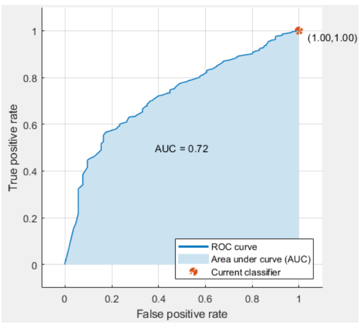
(d)



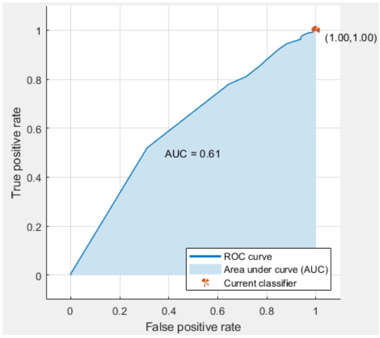
(e)



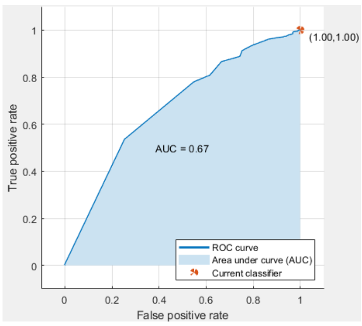
(f)



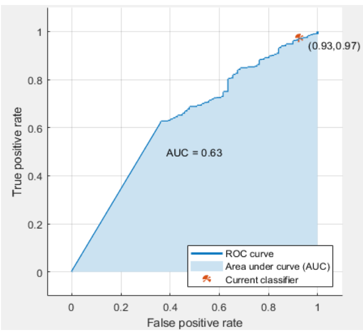
(g)



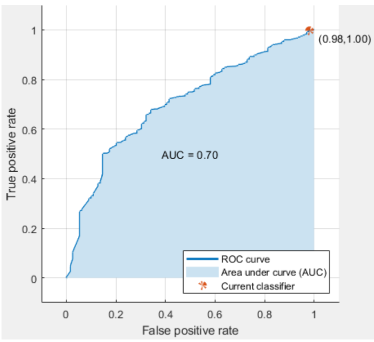
(h)



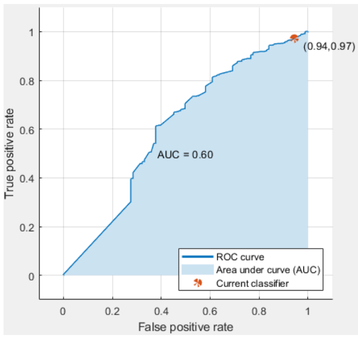
(i)



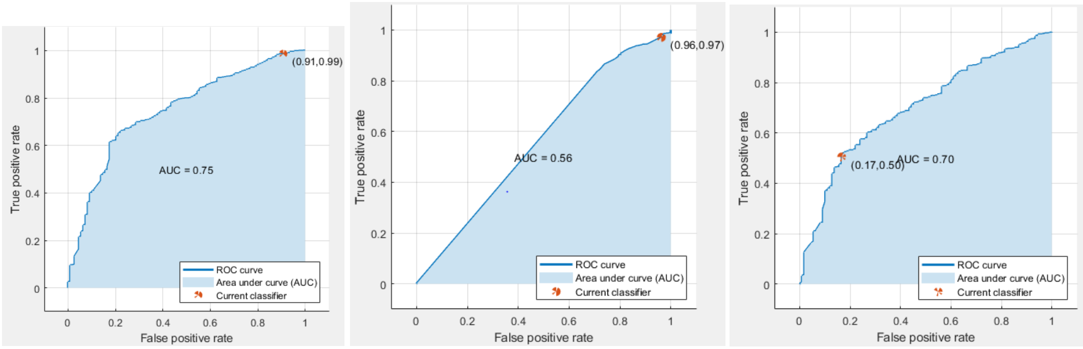
(j)



(k)



(l)



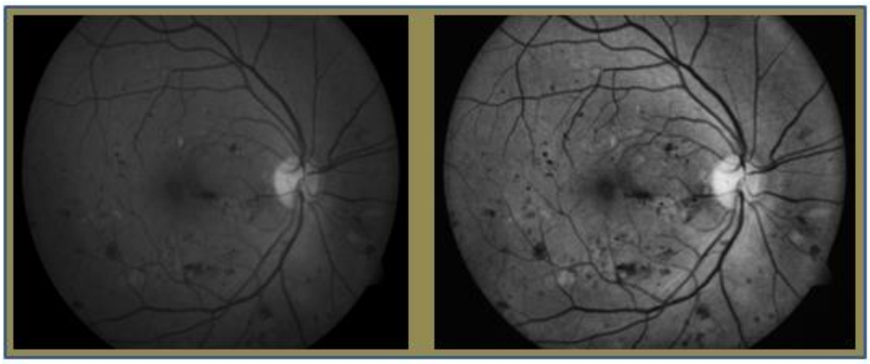
(m) (n) (o)

Figure 5.7: ROC curves of the applied models in grading via exudates; (a) Decision tree, (b) Linear Discriminant, (c) SVM(linear), (d) SVM(cubic), (e) KNN(fine), (f) KNN(medium), (g) KNN(coarse), (h) KNN(cosine), (i)KNN(cubic), (j) KNN(weighted), (k) Boosted tree ensemble, (l) Bagged tree ensemble, (m) Subspace Discriminant, (n) Subspace KNN, (o) RUSBoosted tree ensemble.

5.2 Grading via Micro aneurysms

5.2.1 Image pre processing

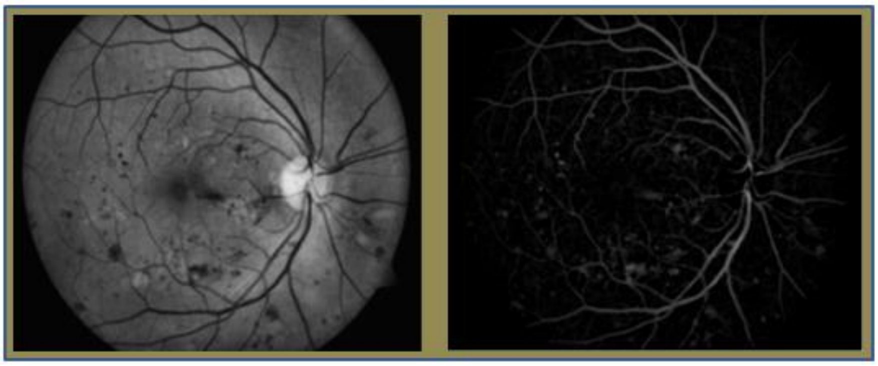
Green channel is extracted from the original colored images and the contrast is enhanced as shown in Figure 5.8 (a) and (b) respectively. Green channel is less saturated as compared to blue and show lesions and other objects distinctly and better as compared to red channel. Contrast enhancement works out well for detection of micro aneurysms since the red lesions and other entities are segmented well from the background.



(a) (b)

Figure 5.8: (a) Green channel extracted image, (b) Contrast enhanced image

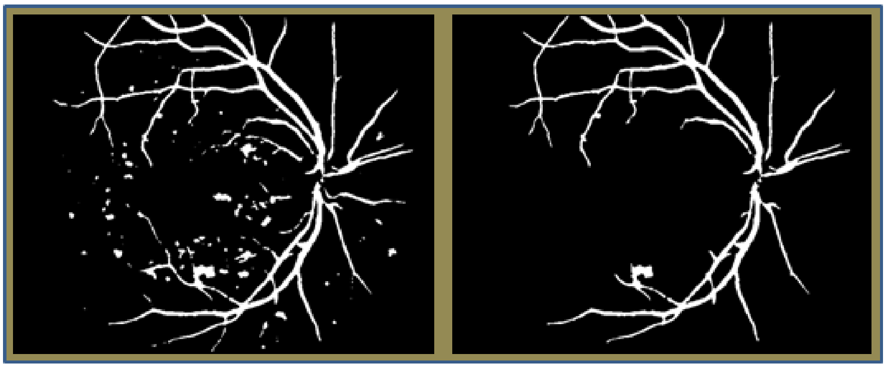
The images are then smoothened and bottom hat filtered as shown in Figure 5.9 (a) and (b), respectively. Smoothening operation is carried out using averaging filter that helps in blurring effect that helps to reduce the presence of unwanted objects.



(a) (b)

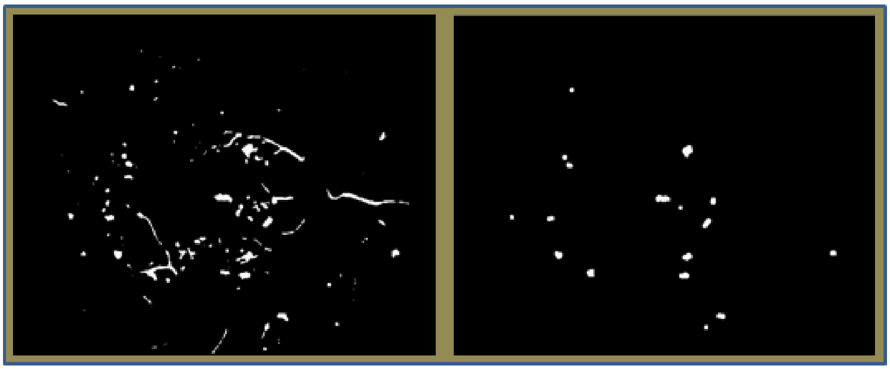
Figure 5.9: (a) Smoothened image, (b) Bottom filtered image

Binarization of the images bring out the lesions well segmented from the background and blood vessels are extracted from images so that they are not confused with the micro aneurysms as shown in Figure 5.10 (a) and (b), respectively. The blood vessels are removed and the micro aneurysms are extracted with the help of morphological opening operation as shown in Figure 5.11(a) and (b), respectively. The count of micro aneurysms helps in grading.



(a) (b)

Figure 5.10: (a) Binarized and median filtered image, (b) Blood vessels extracted image



(a) (b)

Figure 5.11: (a) Blood vessels removed image, (b) Detected micro aneurysms

5.2.2 Features extraction of micro aneurysms

The textural features like contrast, correlation, energy and homogeneity have been extracted using Gray level co-occurrence matrix shown in Table 5.3. The count of micro aneurysms and grades have been shown along with features.

Table 5.3: Features extracted using GLCM for grading via micro aneurysms

Image	Contrast	Correlation	Energy	Homogeneity	Count of MAs	Grade
1	0.000144155	0.941533673	0.99739	0.999927923	4	1
2	0.001063373	0.953057043	0.976285	0.999468313	44	3
3	0.00058563	0.939520568	0.989732	0.999707185	12	2
4	0	0	1	1	0	0
5	0.000609655	0.95209649	0.986664	0.999695172	10	2
6	0.000422736	0.953626031	0.990462	0.999788632	18	3
7	0.000111119	0.939585498	0.99805	0.99994444	3	1

5.2.3 Comparison of various machine learning algorithms applied for grading via micro aneurysms.

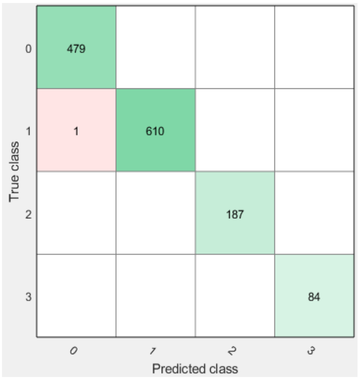
Various machine learning models and their performances have been compared in the Table 5.4.The decision tree and bagged trees ensemble outperform every other model with accuracy as high as 99.9%.

Table 5.4: Comparison of the machine learning models applied for grading via micro aneurysms

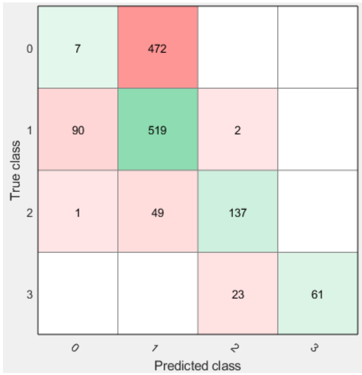
Machine Learning Model	Accuracy	Sensitivity	Specificity
Decision Tree	99.9%	0.99	0.99
Linear Discriminant	53.2%	0.57	0.81
Support Vector Machine (Linear)	96.5%	0.95	0.98
Support Vector Machine (Cubic)	96.8%	0.94	0.98
K Nearest Neighbor (Fine)	63.4%	0.71	0.83
K Nearest Neighbor (Medium)	62.3%	0.69	0.82
K Nearest Neighbor (Coarse)	56.9%	0.53	0.80
K Nearest Neighbor (Cosine)	60.2%	0.63	0.82
K Nearest Neighbor (Cubic)	62.3%	0.69	0.81
K Nearest Neighbor (Weighted)	63.6%	0.71	0.82
Boosted Trees Ensemble	89.0%	0.84	0.95
Bagged Trees Ensemble	99.9%	0.99	0.99
Subspace Discriminant Ensemble	83.0%	0.77	0.92
Subspace KNN Ensemble	99.0%	0.99	0.99
RUSBoosted Trees	89.0%	0.84	0.95

5.2.4 Comparison of various machine learning algorithms' confusion matrix for grading via micro aneurysms.

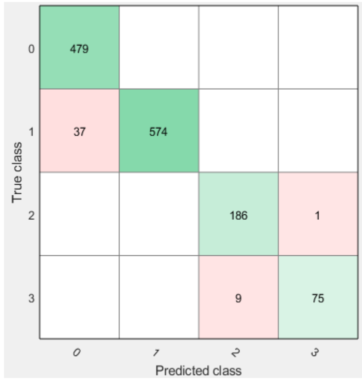
Confusion matrix of all the models that have been applied are shown in Figure 5.12.



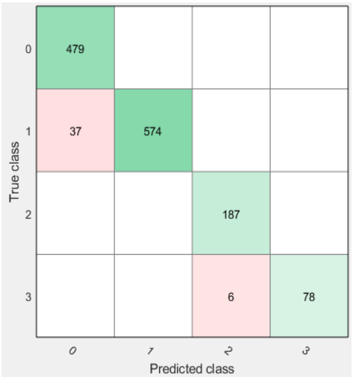
(a)



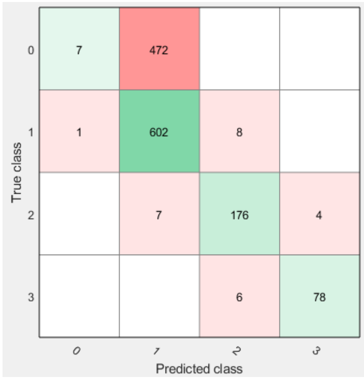
(b)



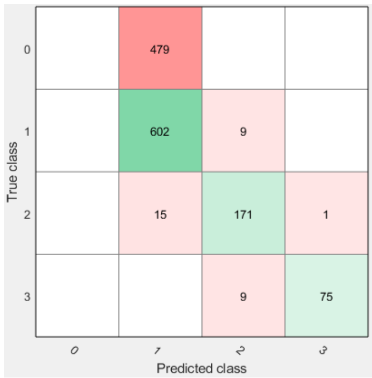
(c)



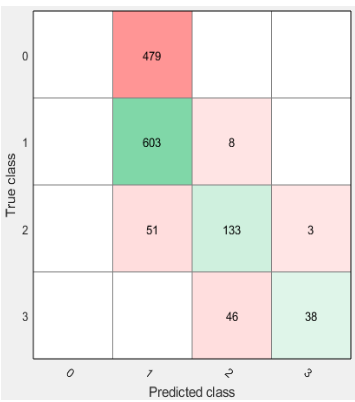
(d)



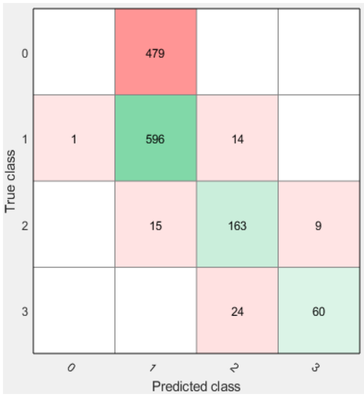
(e)



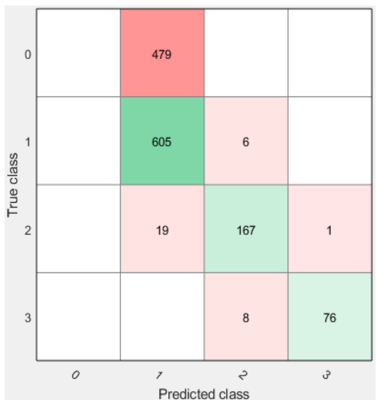
(f)



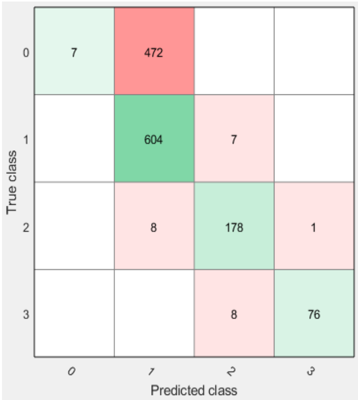
(g)

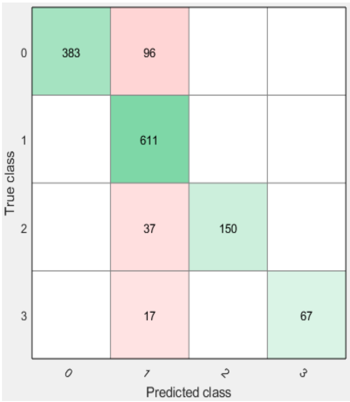


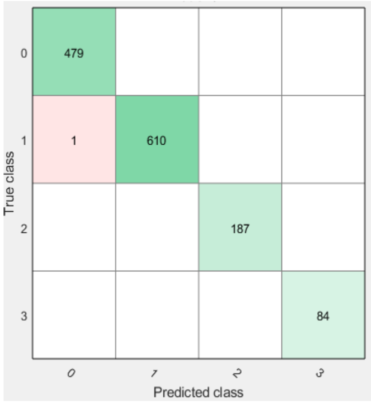
(h)



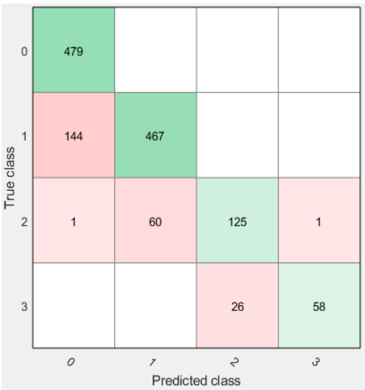
(i)

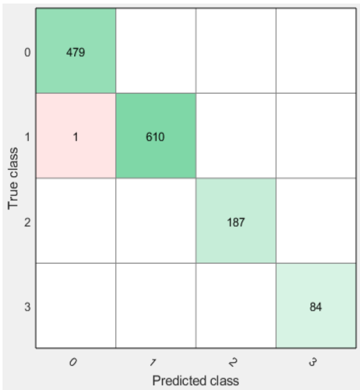


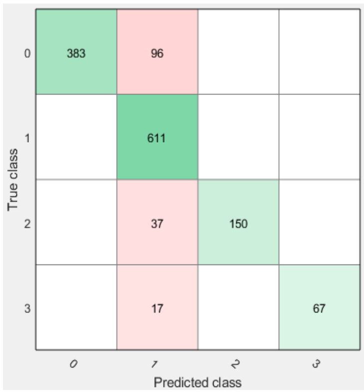




(j) (k) (l)





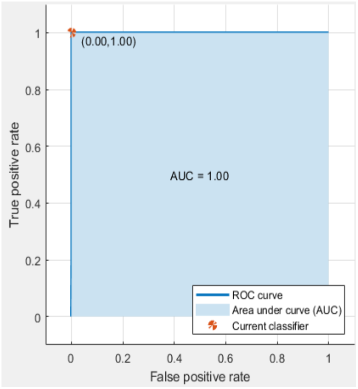


(m) (n) (o)

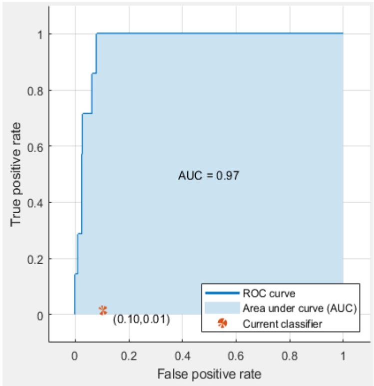
Figure 5.12: Confusion matrix of the applied models for grading via micro aneurysms; (a) Decision tree, (b) Linear discriminant, (c) SVM(linear), (d) SVM(cubic), (e) KNN(fine), (f) KNN(medium), (g) KNN(coarse), (h) KNN(cosine), (i)KNN(cubic), (j) KNN(weighted), (k) Boosted tree ensemble, (l) Bagged tree ensemble, (m) Subspace discriminant, (n) Subspace KNN, (o) RUSBoosted tree ensemble.

5.2.5 Comparison of various machine learning algorithms' ROC curves for grading via micro aneurysms.

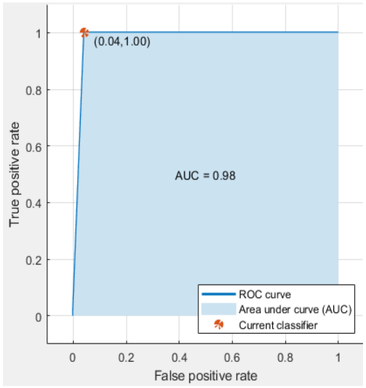
ROC curves depict how well and accurate are the predictions of the models that have been applied for grading via micro aneurysms. It is graph between sensitivity and specificity and larger the area under ROC curve (AUC), better and higher is the accuracy of the model. As shown in Figure 5.13 various models like decision tree, KNN(fine), bagged trees, boosted trees, Subspace KNN ensembles models have high AUC score of 1.00.


True positive rate
False positive rate
(0.00,1.00)
AUC = 1.00
ROC curve
Area under curve (AUC)
Current classifier

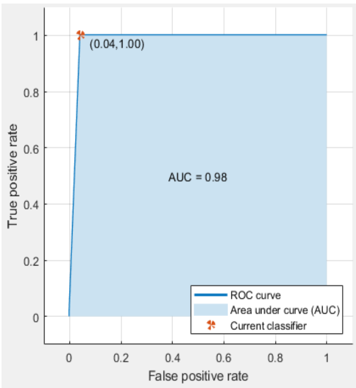
(a)


True positive rate
False positive rate
(0.10,0.01)
AUC = 0.97
ROC curve
Area under curve (AUC)
Current classifier

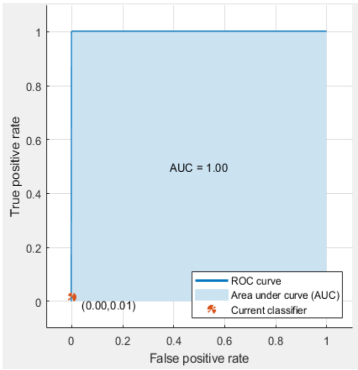
(b)


True positive rate
False positive rate
(0.04,1.00)
AUC = 0.98
ROC curve
Area under curve (AUC)
Current classifier

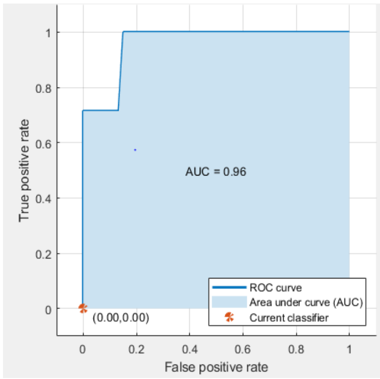
(c)


True positive rate
False positive rate
(0.04,1.00)
AUC = 0.98
ROC curve
Area under curve (AUC)
Current classifier

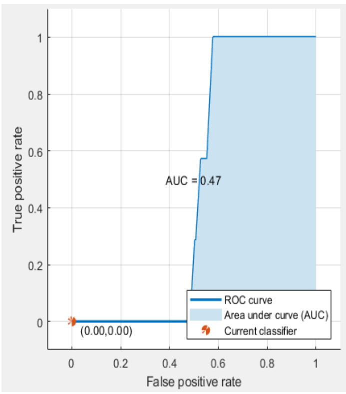
(d)


True positive rate
False positive rate
(0.00,0.01)
AUC = 1.00
ROC curve
Area under curve (AUC)
Current classifier

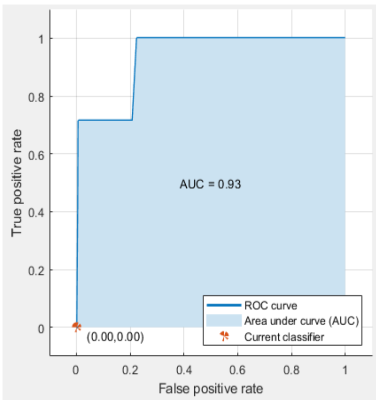
(e)


True positive rate
False positive rate
(0.00,0.00)
AUC = 0.96
ROC curve
Area under curve (AUC)
Current classifier

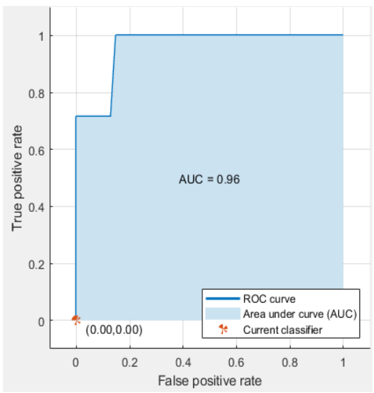
(f)


True positive rate
False positive rate
(0.00,0.00)
AUC = 0.47
ROC curve
Area under curve (AUC)
Current classifier

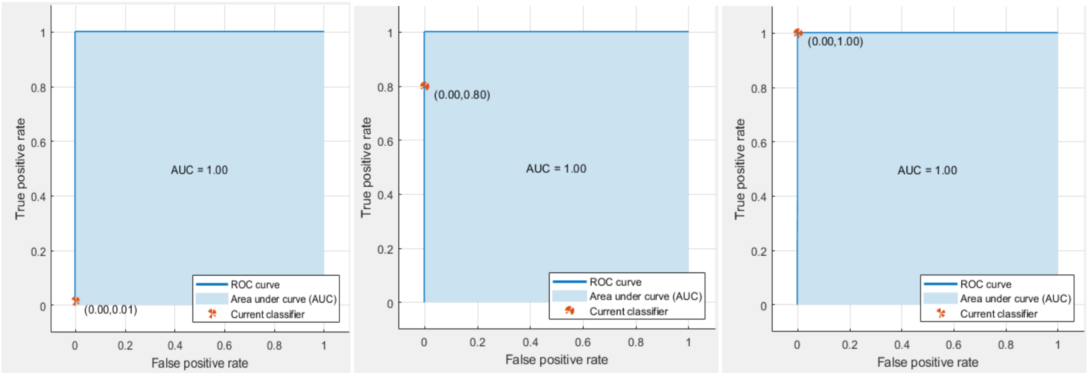
(g)


True positive rate
False positive rate
(0.00,0.00)
AUC = 0.93
ROC curve
Area under curve (AUC)
Current classifier

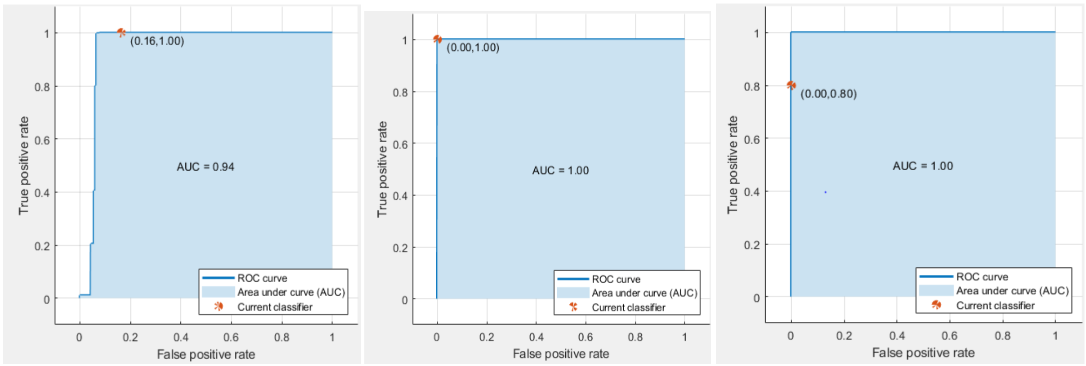
(h)


True positive rate
False positive rate
(0.00,0.00)
AUC = 0.96
ROC curve
Area under curve (AUC)
Current classifier

(i)



(j) (k) (l)



(m) (n) (o)

Figure 5.13: ROC curves of the applied models for grading via micro aneurysms; (a) Decision tree, (b) Linear discriminant, (c) SVM(linear), (d) SVM(cubic), (e) KNN(fine), (f) KNN(medium), (g) KNN(coarse), (h) KNN(cosine), (i)KNN(cubic), (j) KNN(weighted), (k) Boosted tree ensemble, (l) Bagged tree ensemble, (m) Subspace discriminant, (n) Subspace KNN, (o) RUSBoosted tree ensemble.

5.3 Comparisons of the models used for grading via exudates v/s grading via micro aneurysms

A comparison is drawn out between grading via exudates v/s grading via micro aneurysms in terms of the accuracy of the similar machine learning algorithms that have been used in our research work. Figure 5.14 (a) shows that decision tree gives more accuracy of 99.9% for grading via micro aneurysms as compared to grading via exudates. Figure 5.14 (b) shows that linear discriminant gives more accuracy of 90.1% in grading via exudates as compared to grading via micro aneurysms. Figure 5.15 depicts that in grading via exudates SVM linear gives more accuracy of 92.1% and SVM cubic gives higher accuracy of 96.8% in grading via micro aneurysms.

Figure 5.16 shows that all the variants of KNN show higher accuracy for grading via exudates except KNN weighted that shows accuracy of 63.6% in grading via micro aneurysms. Figure 5.17 shows that the ensemble classifiers show higher accuracy for grading via micro aneurysms except for boosted trees that shows accuracy of 91.8% in grading via exudates.

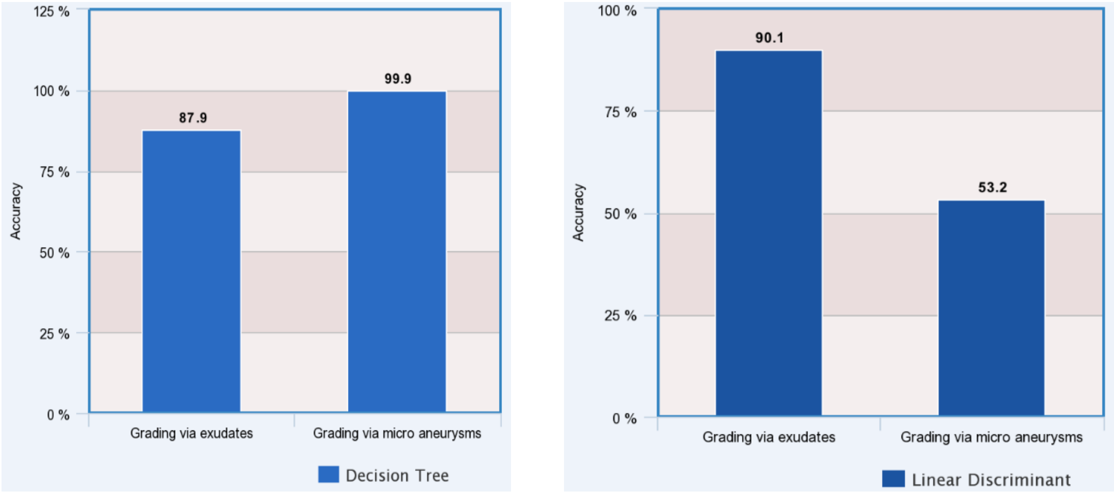


Figure 5.14: (a) Decision Tree's performance for exudates and micro aneurysms, (b) Linear Discriminant's performance for exudates and micro aneurysms

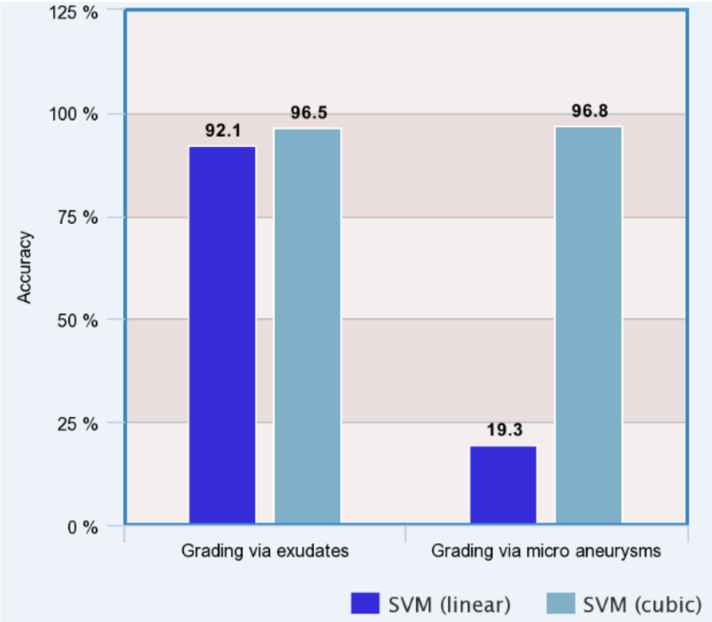


Figure 5.15: SVM variants' performance for exudates and micro aneurysms

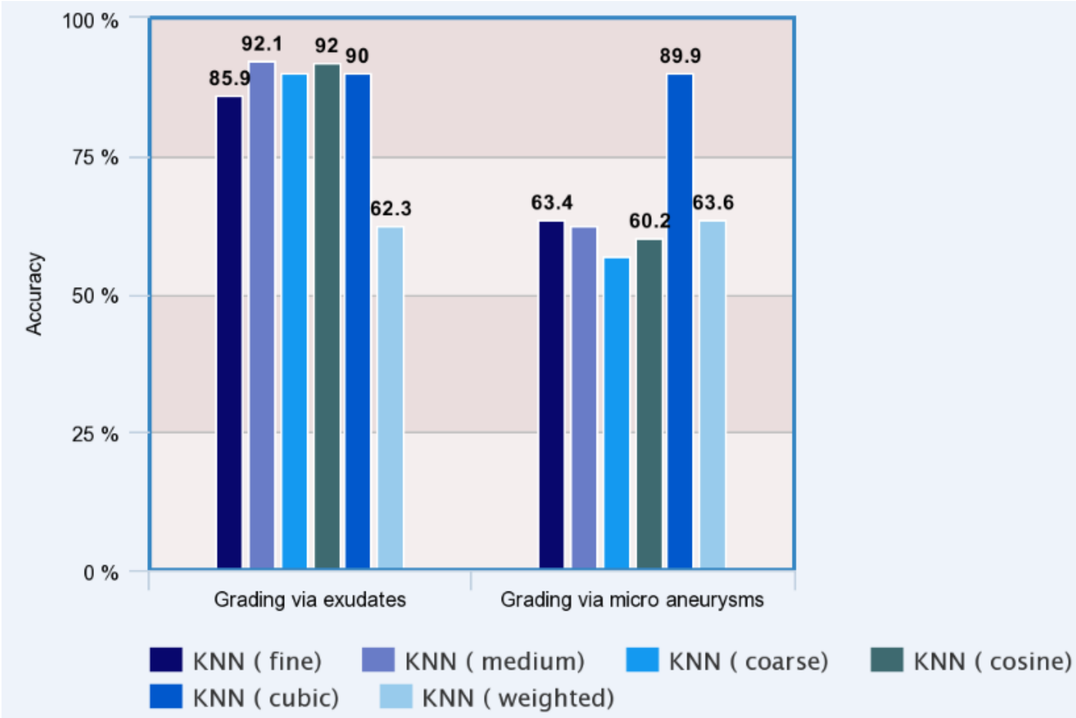


Figure 5.16: KNN variants' performance for exudates and micro aneurysms

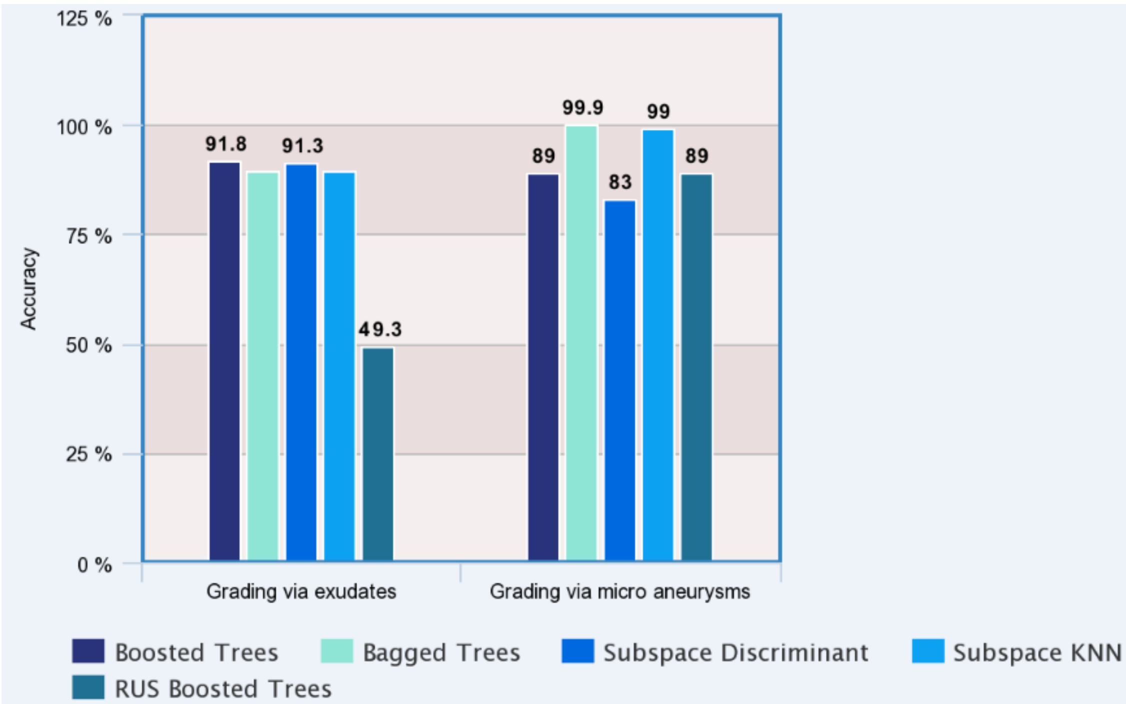


Figure 5.17: Various ensemble classifiers' performance for exudates and micro-aneurysms

Hence, variety of machine learning algorithms have been used in the research work for both exudates and micro aneurysms. The fundus images are processed with different image processing techniques along with textural features extraction and finally trained and tested using machine learning algorithms whose comparisons have been detailed above. Decision tree performs well for grading via micro aneurysms with an accuracy of 99.9% whereas support vector machine and k nearest neighbor predicts the severity levels with an accuracy of 92.1% which is higher than the other models. Thus, with the help of these machine learning algorithms the procedure of grading in diabetic retinopathy to know the severity levels can be automated helping the ophthalmologists in better decision making, time saving and aid in costs reduction for the patients.

CHAPTER 6

CONCLUSIONS

6.1 Conclusions

Diabetic retinopathy has become one of the most leading and recurrent cases of blindness among children and adults who have been suffering from diabetes for an extremely long period of time. The substantial growth of DR and the global health burden caused by it is increasing on an alarming rate. Inspection and detection of the features of diabetic retinopathy like exudates, micro aneurysms, hemorrhages and cotton wool spots is very challenging, time consuming and highly prone to errors especially if it has to be done for a huge population and larger data sets. With the help of image processing methods and machine learning algorithms used in our research work, huge support and help can be provided to the doctors to work on diabetic retinopathy cases in an automated fashion and prone to lesser errors. The existing works on diabetic retinopathy that use the machine learning algorithms focused majorly on detection and presence of the features of diabetic retinopathy without indicating the severity of the damage that can be caused to the patient of diabetic retinopathy. The recent research done on grading in diabetic retinopathy have used image processing methods for knowing the severity of the disease and did not focus on usage of machine learning algorithms. The major segments of the research done are concluded below:

- For our research, fundus images have been combined from Messidor, e-optha and DiaretDb and grading for knowing the severity levels of diabetic retinopathy is done in two modules, once using exudates and then micro aneurysms.
- Image processing has been used separately for the features of the diabetic retinopathy i.e. exudates and micro aneurysms and textural features have been extracted that are given as input to the machine learning models.
- Various machine learning models like Decision tree, SVM, KNN and ensemble classifiers have been used for training and testing the fundus images and predicting the grade of severity level of diabetic retinopathy.

- A comparison has been drawn between the performances of the machine learning models used for grading in diabetic retinopathy.

6.2 Summary of Contributions

The research work carried out is different from the existing works in the field of diabetic retinopathy as image processing, features extraction and machine learning algorithms combined have been put forward for grading in diabetic retinopathy and has been trained and tested for two salient features of diabetic retinopathy that are exudates and micro aneurysms. Exudates are the yellow lesions whereas micro aneurysm are the red lesions. For grading in diabetic retinopathy, machine learning algorithms have not been explored well in the existing pieces of work.

The major contributions of the thesis include:

- A combined dataset of Messidor, e-optha and DiaretDb have been used for better results.

- Grading in diabetic retinopathy has been done using two salient features i.e. exudates and micro aneurysms, separately. Ensemble algorithms have been used as well for grading purpose.

- For grading using exudates, SVM and KNN show the highest accuracy of 92.1% in prediction of the severity level of diabetic retinopathy. Among the ensemble classifiers, boosted trees show highest accuracy of 91.8%.

- For grading using micro aneurysms, decision tree shows the highest accuracy of 99.9% in prediction of the severity level of diabetic retinopathy. Among the ensemble classifiers, bagged trees show highest accuracy of 99.9%.

- Separate, well performing image processing steps have been implemented for extracting the exudates and micro aneurysms. The textural features have been extracted out of the processed images that are fed into the machine learning algorithms.

- The features extracted along with the grading information are trained and tested with the help of various machine learning algorithms. A comparison has been drawn on the performances of the models on how accurate the same models predict in the case of exudates and micro aneurysms, respectively.

6.3 Future Research

Diabetic retinopathy is a vision threatening medical condition in which the retina of the diabetic patients gets damaged to an enormous amount and is a secondary disease caused in the people already suffering from Diabetes Mellitus. An automated process for detection and grading of diabetic retinopathy can be of huge help to the doctors and the patients as it gives more accurate results in lesser time. In future, the following research can be done:

- Grade using the combination of both exudates and micro aneurysms for knowing the severity levels of diabetic retinopathy.
- Detection and grading of diabetic retinopathy should be carried out with the help of other features like cotton wool spots, hemorrhages as they are difficult to detect manually.
- Include bigger data sets so that the models are trained and tested on more images for better results in prediction.

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1. Reaya Grewal, Dr. Avleen Kaur Malhi, Dr. Palika Chopra, "Translating Artificial Intelligence into Healthcare: Diabetic Retinopathy Detection", *IEEE International Conference on Communication and Electronics Systems (ICCES), 2019* [Accepted].

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