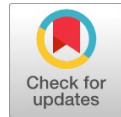# Diabetic Retinopathy Screening using Machine Learning for Hierarchical Classification

Nandana Prabhu, Deepak Bhoir, Nita Shanbhag

Abstract: Diabetic Retinopathy is a consequence of prolonged unaddressed diabetes. It is currently diagnosed by the subjective clinical examination and manual grading of the fundus images by the ophthalmologists. This disease is progressive in nature. Hence early detection and treatment go a long way in helping the patients fight the dire consequences of the disease. Given the fact that number of ophthalmologists is very less as compared to the patients, a cost-effective, computer assisted, automated retina analysis system is highly desirable for the rural health care. This paper proposes an automatic Diabetic Retinopathy detection system based on the presence of bright lesions on the retina which is one of the symptoms of Diabetic Retinopathy. Initially the optic disc is removed from the fundus image as its brightness is similar to that of the bright lesions. Exudates are extracted and its various features are obtained. Later, feature based hierarchical classification is performed for detection of different stages of the disease. This method is based on the same logical steps as followed by the ophthalmologists and hence assures more accurate classification results. Two methodologies, Random Forest algorithm and Artificial Neural Network are explored and accuracy, sensitivity and specificity are evaluated at each stage of classification. The former outperformed the latter. The accuracy obtained using Random Forest are 100%, 85.71% and 87.5% and Artificial Neural network are 100%,78.5% and 66.67% for Stage 1, Stage 2 and Stage 3 respectively.

Index Terms: Artificial Neural Network, Exudates, Non Proliferative, Random Forest, Retinopathy.

I. INTRODUCTION

Diabetes is increasing at an alarming rate particularly in the working age group of 20 to 60 years [1], the reasons being increased mental stress with less physical activity, heredity, age and food habits. Over the years, uncontrolled diabetes affects the vital body parts like eyes, heart, kidneys, nervous system etc. Approximately 40% of the diabetic patients are affected by Diabetic Retinopathy (DR). About 10% of the patients face the risk of completely losing their vision [2]. It is estimated that by 2030, the number of people with diabetes will be around 366 million [3].

Prolonged diabetes leads to several abnormalities in the eye like Glaucoma, DR, Macula Edema etc. All these abnormalities are progressive in nature and can lead to loss of vision if untreated. Hence early detection and treatment are very essential in preventing this extreme consequence.

Retinal abnormalities due to diabetes are diagnosed using Funduscopy which provides accurate and effective information of retinal health [4]. The ophthalmologists use their expertise to visually inspect the fundus images for detection of the disease. They look for symptoms of DR which include an increase in diameter of blood vessels, dark lesions due to microaneurysms and hemorrhages, bright lesions such as exudates and cotton wools. Fig. 1a shows the fundus image of a normal eye and Fig. 1b shows that with symptoms of DR. The manual inspection of fundus images is time-consuming, laborious and demands expertise. Hence an automatic tool for diagnosis is of great help. As the number of patients per ophthalmologist is very high [1], an automatic tool if developed will be of great help in assisting them to quickly diagnose more number of diabetic patients for DR. It can also aid as a tool for preliminary examination, thereby enhancing the performance of health care systems.

The anatomical structure of the retina of the normal eye as shown in Fig. 1(a) consists of Optic Disc (OD), blood vessels
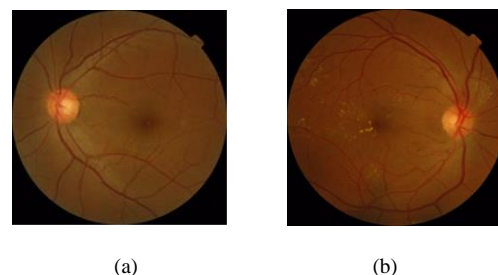

(a)   (b)

Fig 1 Fundus image (a) Normal Fundus image (b) Fundus image with DR [5]

(BVs) and fovea. OD is a very important part of the fundus image. It is a circular, bright yellowish spot. It is of approximately 1.5 mm to 2 mm diameter, occupying about one-seventh of the entire fundus image.

Blood vessels originate from the optic disc. The mean diameter of blood vessels is 100 µm which is about $(1/40)^{th}$ of the diameter of the retina.DR is classified into two types: Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). NPDR is the initial stage of diabetic retinopathy. It is also known as background retinopathy. In this case, the damaged blood vessels in the retina start leaking extra fluid and small amounts of blood into the eye. The basic pathology is in the loss of pericytes of vessel walls altering the pericyte to endothelial cell ratio. Weak wall leads to stasis embolization and leakage distal to it. This leakage manifests in the form of exudates, the centre of which is a leaking microaneurysm. The exudates are of various shapes and sizes. The number of exudates increases with the grade of   NPDR.

Enhanced lipid levels are a contributory factor. The different stages of NPDR are mild, moderate and severe.

PDR, on the other hand, occurs when several blood vessels in the retina close, stopping adequate amount of flow of blood to the retinal tissue, resulting in growth of new blood vessels. These are abnormal and do not ensure the proper flow of blood to the retina thus blocking the vision. Persons with a prolonged history of diabetes have a greater risk of DR.

This paper proposes an automatic system for detection of DR. The automatic process featured here operates on the fundus image of the retina and consists of preprocessing, OD elimination, morphological operations, and thresholding. After these initial operations, definite features of DR are extracted from the fundus image and classification is performed. A hierarchical classification is used with three steps of operation. In the first step, the fundus image is checked whether it is of the normal retina or DR affected retina. In the next step, classification of the affected fundus images is done to determine whether the DR is mild and in the third step, moderate to severe NPDR or PDR.

The exudates are very small in size. It is very difficult to detect them particularly when they are close to the blood vessels. In the process of elimination of blood vessels, there are chances of the exudates getting eliminated. In some of the normal images, bright spots may be seen which do not actually correspond to exudates. Hence identifying the normal images is also a difficult task.

Moreover, the datasets are skewed thereby making the classification challenging.

II. RELATED WORK

A number of techniques have been reported in the literature for the detection and classification of DR. Achieving an improved efficiency in the automatic grading of severity of DR has been an area of active research. The advancement in the field of medical image analysis combined with the tools of artificial intelligence has added refinement to the classification results over the past decade. The techniques used for classification vary from rule-based algorithms to deep learning methods.

Several unsupervised and supervised classification techniques have been explored for classification.

The preprocessing of images itself consists of various techniques depending on the purpose, which could be noise reduction, image contrast enhancement, correction of non-uniform illumination etc. In addition, image color conversion, image normalization, binarization etc. are used to improve the quality of the image thereby improving the accuracy of classification. Mean and median filtering is used for removal of noise. Nonuniform illumination causes a rise in brightness in some areas such as optic disc and less brightness in regions away from the optic disc. Illumination equalization technique is used for overcoming the defects due to non-uniform illumination. The adaptive histogram equalization makes the dark region with blood vessels and microaneurysms dominant. A variation to this technique is Contrast Limited Adaptive Histogram Equalization (CLAHE). Here, histogram equalization operates on sub-images called as tiles. Bilinear Interpolation is then used to eliminate the artificially induced boundaries [6, 7]. Other preprocessing methods are color normalization by performing histogram stretching and clipping for standardization of color range.

Many researchers have proposed methods for individually extracting OD, blood vessels, exudates and microaneurysms. A completely automated system considering all the features has not been reported to the best of our knowledge.

Majority of researchers have used morphological techniques for detection of OD [8]. Intensity based line scanning analysis [9], least square classifier for detecting the OD region and connected component labeling and intensity information for determining the center of OD are also reported [10].On the other hand, Bharkad [11] has used green component extraction and adaptive histogram equalization for preprocessing followed by two-dimensional low pass FIR filter for blood vessel elimination. Position and centre of OD are obtained by performing thresholding in the region around pixel with the brightest intensity. Compactness test is done for assuring circularity. Then OD is segmented using image cropping around the OD, followed by morphological dilation and median filtering. Marin et al., have used iterative opening and closing operations followed by two-step thresholding to obtain the region of interest [12]. Prewitt edge detection followed by Circular Hough transform is used to obtain OD.

The blood vessel is similar in intensity to dark lesions. The removal of the blood vessel is an important task as it can be used further for classification of DR. In case of classification of DR using exudates, blood vessels need to be detected and eliminated to avoid false positives. To detect blood vessels, morphological operations and various transforms are used. Patwari et al., detected blood vessels using morphological operations and binarization [13]. Badshaa et al., have detected the blood vessels using kirsch template for edge enhancement, morphological operations, thresholding and unwanted small objects removal using object classification [14].

Kavitha et al., applied Curvelet transform for blood vessel extraction as it can handle curve discontinuities using a small number of coefficients compared to Fourier and wavelet transforms [15]. Barkana et al., performed an analysis using Classifier fusion [16]. The statistical features such as mean and median in the four directions are used as inputs to the classifier. The three classifiers used are Support Vector Machines (SVM), Artificial Neural Network (ANN) and Fuzzy logic.

Some researchers have worked on both OD and BV. Salazar-Gonzalez et al., first determined the vessel tree using graph technique [17]. To detect the OD they have used two methods. Markov Random field method determined OD by first eliminating BV inside OD. In the second method called Compensation factor method they used the knowledge of BV to detect OD. On the other hand, Rodrigues et al., have performed wavelet transform and used morphological properties for OD detection [18]. To detect BV, a genetic algorithm, Dijkstra's shortest path algorithm is used to explore its tubular characteristic, along with statistical Student t method. With the emergence of artificial intelligence, convolutional neural networks have become popular. Tan et al., have developed CNN for simultaneous detection of OD, BV, and Fovea [19]. Once the blood vessel and OD are eliminated, the next step is the extraction of exudates, microaneurysms, and haemorrhages.

Sopharak et al. used HSI color model and pixel-based classification whereas Franklin & Rajan used Lab color model and multilayer perceptron neural network for detection of exudates [6, 7]. To extract the exudates, Jaya et al, first performed morphological operations and applied Hough transform for removal of OD [20]. Color and texture features are used as representatives of exudates. Five Law texture features measure features by calculating average grey level, wave, spot, ripple, and edges. For better perception of color, opponent color space is considered. Finally, classification is done using Fuzzy Support vector machine based expert systems. Srivastava et al., detected the microaneurysms and hemorrhages in the presence of blood vessels using filters to differentiate them based the structural characteristics [21].

A variety of classification of DR is done using different databases. Some of the classifications are the presence or absence of DR [22-24].Some classifications are only on NPDR. Some are on three class classification such as Normal, NPDR and PDR. Other variations are individually using blood vessels, exudates, microaneurysms and haemorrhages. Some have used even the entire image.

Ning et al extracted the exudates and performed classification using SVM for classification into normal, NPDR and PDR [25]. Tjandrasa et al., also extracted exudates and performed classification of DR as moderate and Severe DR [26]. Sarni et al., proposed a decision support system for microaneurysms for DR screening [27]. The performance of classifiers such as KNN, RB SVM and polynomial SVM are determined. It is observed that the Radial Basis Function SVM outperformed the others. Antel et al. also extracted microaneurysms but performed classification using ensemble learning [28]. Morales et al., have performed classification using local binary patterns to distinguish between Normal, DR and Age-related Macular degeneration (AMD) [29]. DR also causes changes in the diameter of blood vessels. Hence it is also a feature used for classification of DR. Nikita et al., performed blood vessel segmentation using a Gaussian filter, extracted texture and structural features and performed classification using SVM and ANN [30].

Recently the number of researchers using deep learning for medical image analysis is rising. Pixels, sub-images and entire images are used as inputs to the network for performing classification of DR [31].

III. MATERIALS AND METHODS

This paper proposes an automatic system for the detection of DR. RGB image is initially pre-processed to extract the green component. Blood vessels and OD are then eliminated. The resultant image predominately consists of exudates. Features of these exudates are further extracted and fed to a classification algorithm. In the hierarchical classification, the DR features are extracted and the severity of DR is determined through several levels of classification where each level does a binary classification using Random Forest (RF) and Artificial Neural Network (ANN). Grade 0 is considered as normal, Grade1 as Mild, Grade 2 as moderate to severe, and Grade 3 as PDR. The digital images used for classification are taken from MESSIDOR dataset [5]. The camera used is color video 3CCD camera on a Topcon TRC NW6 non-mydriatic retinograph. The field of view is 45◦. The images are of three sizes: 1440 x 960, 2240 x 1488 and 2304 x 1536 pixels with 8 bits per color plane having TIFF

format. These are graded by an ophthalmologist based on presence of only exudates. The images are divided into different classes: normal, mild, moderate, severe and PDR. To identify each class, they have been given a Grade. Accordingly Grade0 corresponds to Normal, Grade 1 to Mild, Grade 2 to Mod to Severe and Grade 3 for PDR images.

A. reprocessing

In computational processing, preprocessing deals with the enhancement of the images. It is the foremost step in any image processing system. The fundus images are large in size. Moreover, different datasets have different number of images. To speed up computation and bring about uniformity, resizing is performed. In RGB images the microaneurysms and hemorrhages appear as dark red spots and exudates appear as bright spots. The blood vessels have a lower reflectance compared to the retinal background. In RGB images, the green component exhibits the best contrast between the foreground and background. Moreover, it is less sensitive to non-uniform illumination. Hence green channel is used for further processing [13]. Subtle, non- uniform illumination may not be noticeable by naked eyes. However, its effect is seen during feature extraction and classification. The adaptive histogram equalization is used to overcome this.

B. OD Detection

The OD localization is performed by using template matching with normalized cross-correlation [32]. Circle mask of 5 pixels is used to eliminate the noise along the borders of the image.

C. Removal of Blood vessels

This is a challenging task particularly when the exudates are very close to the blood vessels. Adaptive histogram equalization using CLAHE is initially performed. Then morphological operations of dilation followed by erosion are done. The histogram equalized image is subtracted from the resultant image. A binary image is obtained by using a threshold value. The corresponding region in the main image is filled with intensity values from neighboring pixels to reduce the variation of intensities around the blood vessel.

D. Extraction of Exudates

In order to extract exudates of different sizes, patches of multiple sizes are used. The following operations are performed for each patch. The morphological opening operation is performed and the resultant is subtracted from the patch image followed by adaptive histogram equalization and image adjustment as suggested by Patwari et al.,[13]. Multiple binary patches are obtained using a range of thresholds. An average of these binary patches is obtained. A final threshold is now used to eliminate pixels with low probability. In some of the images, spots are still seen on OD. In such cases, a circle with a radius of OD is taken and a circle mask is used to eliminate them.

E. Feature Extraction

A total of eight selected significant features are extracted. These features are extracted in accordance with the approach of Early Treatment of Diabetic Retinopathy Study (ETDRS). It is based on 4:2:1 rule, where 4, 2 and 1 correspond to the quadrants in which the symptoms exist. The image is divided into four quadrants through the detected center of OD.

The count of exudates in each quadrant along with the total number of quadrants where the exudates exist are calculated and used as features. In addition, the total area occupied by the exudates, total perimeter, edge strength, and compactness are also determined.

F. Classification

Once the features are extracted, two classifiers, namely RF and ANN are used for classification. Random forest is an ensemble learning method which combines results from various learners. During the training phase, it grows multiple trees randomly. The results of each tree are combined using the voting method. The Forest uses the highest voted class for prediction. Binary classification is used to perform hierarchical classification.

The artificial neural network is the second method used for classification. It consists of input layer, hidden layers and output layers with neurons interconnected through weights and transfer function. The classification is done based on values at the output layer. The outputs obtained for various stages are shown in Fig 2.

IV. RESULTS

In this research work, the system used is 8 core CPU, with 60 GB SSD and Tesla K80 GPU. Matlab 2016b is used for
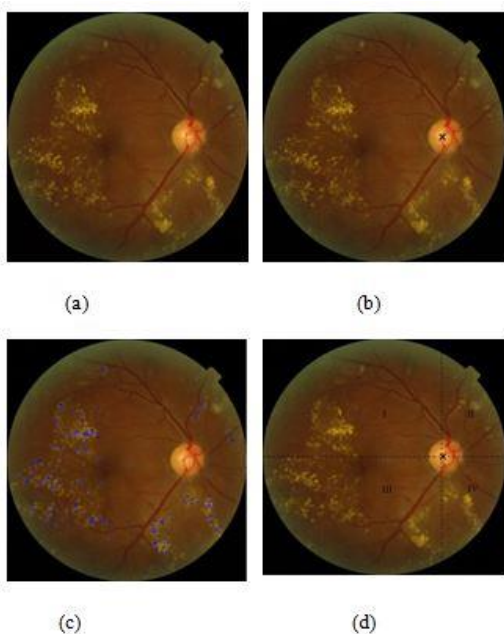

Fig. 2. Outputs obtained for various stages (a) Input image (b) Image with OD center marked (c) Image with exudates extracted (d) Image with Quadrant marked.

image processing operations on fundus images and extraction of features.

In the hierarchical classification, the first classification is done to separate Normal and affected images which is indicated as (0_123) in Table1. Then second level of classification is performed as mild versus remaining grades of images which is indicated as (1_23). Finally, a third classification is done between Mod/severe versus PDR which is (2_3). The performance of the system is evaluated using the performance metrics, accuracy, sensitivity and specificity.

The RF classification is done using R tool. The classification is done after visualizing the importance of different variables at each stage. The ANN is built using the framework Karas package with the Tensor flow at the backend. This helps in

speeding up the network. The variables used are visualized to know their importance, which affect the performance. The network is trained with different values of learning rate, the number of first stage neurons, number of hidden layers, batch size, epochs, drop out, optimizers and type of classifiers to arrive at the optimized configurations. Once training is completed based on training accuracy, validation loss and validation accuracy, testing is performed to get the best output. Proper selection of the above mentioned parameters is a vital task. It decides the performance of the system. It is observed that reducing the batch size, increasing the hidden layers and using a large number of epochs makes the network extremely slow. The results obtained using RF method for classification, are shown in Table 1. Table 2 shows hierarchical classification using ANN. As explained earlier, the RF method is simpler than the ANN method. The accuracy obtained using Random Forest are 100%, 85.71% and 87.5% and ANN are 100%, 78.5% and 66.67% for Stage 1, 2 and 3 respectively

TABLE I HIERARCHIAL CLASSIFICATION USING RANDOM FOREST METHOD

Stages	Level of classification	Number of images	Acc[1].	Sen[2]	Spec[3]
1	0_123	167	100	100	100
2	1_23	69	85.71	88.89	83.33
3	2-3	26	87.5	100	85.71

[1] Accuracy, [2] Sensitivity, [3] Specificity

TABLE II HIERARCHIAL CLASSIFICATION USING ARTIFICIAL NEURAL NETWORK

Stages	Level of classification	Number of images	Acc[1].	Sen[2]	Spec[3]
1	0_123	167	100	100	100
2	1_23	69	85.71	88.89	83.33
3	2-3	26	87.5	100	85.71

[1] Accuracy, [2] Sensitivity, [3] Specificity

It is difficult to directly compare the performance of our system with other methods as hierarchical classification is used in the proposed work. Moreover different researchers have performed classification of different lesions, with different databases and also different number of grades. Sinthanayothin et al. [22] extracted all the lesions and classified the images into normal and abnormal with sensitivity of 80.21% and specificity 70.66%. Prasanna et al. [23], extracted the blood vessels as features and achieved sensitivity of 86%. Pratt et al., used CNN and performed the five class classification [31]. They achieved accuracy of 75%, specificity of 95% and sensitivity of 30%. Some researchers performed multiclass classification after extracting exudates.

V. CONCLUSION

Considering the drastic rise in cases of diabetes and non-availability of the expert ophthalmologists, there is a strong need for an automated tool for the detection of DR which can aid as an assistant to the ophthalmologist or act as a preliminary screening tool, thereby saving time and promoting the health care. In the proposed work, an automated system for determining the severity of DR is explored. In the preprocessing stage, the fundus image is resized and a circular mask is used to extract the retinal region which is region of interest. This reduces the computational cost. Green channel is extracted as it has better reflectance against the background. Median filtering and adaptive histogram equalization are used for noise removal and enhancement of the salient features. Template matching and normalized cross-correlation are used for OD localization. The extraction of exudates is a challenging task, particularly with the reflectance of blood vessels emerging from the OD. A separate iterative procedure is applied to handle this problem. Features of exudates are then extracted to suit the requirement of classification. The severity is graded as normal, mild, mod/severe and PDR. The random forest algorithm and ANN are used for classification. Choice of important features is a critical task in RF. Choosing the parameters of the network is a critical task in classification based on ANN. These parameters decide how the network performs. Too many hidden layers slow down the training. It is observed that the RF method performs better in classification. The proposed system has achieved an accuracy of 100%, 85.71% and 87.5% sensitivity of 100%, 88.89% and 100% and specificity of 100%, 83.33 % and 85.71% at level 0, 1 and 2 respectively.

Limitations of the proposed algorithm are some of OD region not being masked, critical choice of threshold while performing binarization during blood vessel extraction, artefacts in the image, artefacts near the blood vessel and misclassification of faint exudates. The method can further be improved with database having more samples with clear distinction between severe NPDR and PDR images. The proposed algorithms can be further fine-tuned to detect even finer exudates and eliminate blood vessels of higher intensity. To improve the performance of the system in terms of grading, we need to determine the classification for the dark lesions and use larger databases.

According to British Diabetic Association, if a system has sensitivity of 80 % and specificity 95% or above, it can be used for screening of DR [5, 6]. The results demonstrate the effectiveness of the system. The hierarchical classification helps for better demarcation in classification. It can be of great help to the community for screening of Diabetic patients for treatment.

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