



Automatic Identification of Varies Stages of Diabetic Retinopathy Using Retinal Fundus Images

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Abstract—The detection of retinopathy in digital color fundus photographs is a critical first step in automated screening for diabetic retinopathy (DR), a common complication of diabetes. This disease affects slowly the circulatory system including that of the retina. As diabetes progresses, the vision of a patient may start to deteriorate and lead to diabetic retinopathy. In this study on different stages of diabetic retinopathy, 124 retinal photographs were analyzed. As a result, four groups were identified, viz., normal retina, moderate non-proliferative diabetic retinopathy, severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy. Classification of the four eye diseases was achieved using a three-layer feedforward neural network. The features are extracted from the raw images using the image processing techniques and fed to the classifier for classification. We demonstrate a sensitivity of more than 90% for the classifier with the specificity of 100 %.

Keywords: Eye; Normal; Features; Retinopathy; Neural network; Image processing; Feed forward; Classification

I. INTRODUCTION

Diabetic retinopathy (DR) is the most common cause of blindness and vision defects in developed countries. This field involves the study of digital images with the objective of providing computational tools which will assist the quantification and visualization of interesting pathology and anatomical structures. The eye is an organ associated with vision. The eye is housed in a socket of bone called the orbit and is protected from the external air by the eyelids [9]. Physicians have advanced diagnostic tools to evaluate their patients in order to plan different forms of management and monitor the progress more efficiently than before. However, this is a multidisciplinary task and requires comprehensive knowledge in many disciplines such as image processing and computer vision, machine learning, pattern recognition and expert systems.

Diabetic retinopathy (DR) is a complication of diabetes and a leading cause of blindness. Twenty years after the onset of diabetes, almost all patients with type 1 diabetes and over 60% of patients with type 2 diabetes will have some degree of retinopathy [1]. Laser treatment can now prevent blindness in majority of these cases.

Hence, the early screening and identification of patients with retinopathy will help to prevent loss of vision.

Diabetic retinopathy is divided into several stages: mild, moderate, severe and proliferative DR. A brief description of the different stages of DR is given below [8, 25]:

- a) Mild non-proliferative retinopathy: Microaneurysms, i.e., small swellings in the tiny blood vessels of the retina will be formed in this stage.
- b) Moderate non-proliferative retinopathy: As the disease progresses, some blood vessels that nourish the retina are blocked.
- c) Severe non-proliferative retinopathy: Many more blood vessels are blocked, depriving several areas of the retina of their blood supply. The affected areas of the retina begin to show sign of ischemia (lack of oxygen) such as blot hemorrhages, bleeding of the veins and intraretinal microvascular abnormalities.
- d) Proliferative retinopathy: At this advanced stage, the vasoproliferative factors produced by the retina begin to trigger the growth of new blood vessels. These new blood vessels are abnormal and fragile.

II. RELATED WORK

Blood vessel detection in retinal images is a crucial step in the classification of different stages of diabetic retinopathy. Specifically, the number of blood vessels vary with different stages of diabetic retinopathy [8]. Furthermore, feature extraction is difficult to achieve because it involves many branching vessels which are to be distinguished from microaneurysms and hemorrhages.

Kandiraju et al. [15], have proposed a blood vessel detection algorithm for blood vessel detection in retinal images based on the regional recursive hierarchical decomposition using quadrees and post-filtration of edges. This algorithm was able to decrease false dismissals of predominately significant edges and was faster in comparison to the existing approach with reduced storage requirements for the edge map. Grisan et al. [10] proposed a new system for the automatic extraction of the vascular structure in retinal images based on a sparse tracking technique. In this technique, blood vessel points in a given cross section were found using fuzzy C-means classifier.

The ‘matched filter response’ method is a widely used template-based technique that uses a set of 2D Gaussian kernels with a fixed length and orientation to enhance the vessels [13]. A local threshold is then set to differentiate them from the retinal background. The method has some interesting features like handling bifurcations and obtaining fairly robust separation of vessels. However, it is computationally intensive and the threshold selection may be critical. The detection of blood vessels using two-dimensional matched filters has been reported by Chaudhuri et al. [1]. In this method, gray-level profile of the cross section of a blood vessel was approximated by a Gaussian shaped curve. The concept of matched filter detection of signals was then applied to detect piecewise linear segments of blood vessels after the approximation process.

Proliferative diabetic retinopathy, non-proliferative diabetic retinopathy and macular edema (maculopathy) have been differentiated by using threshold techniques and edge detection (Gaussian filter) [33]. They have obtained correct classification of 79% in macula related diseases using 24 eye images. Vascular abnormalities in diabetic retinopathy have been detected and classified [30]. The original image was filtered (in Fourier domain) through a Gabor filter bank consisting of several filters tuned to specific scales and orientations. The stages of non-proliferative diabetic retinopathy (NPDR) were determined by analyzing the number of maxima in the energy versus orientation plot.

The presence of microaneurysms in retinal fluorescein angiograms was identified by first locating the fovea by sub-sampling image by a factor of four in each dimension [4]. Then the image was subjected to median filtering with a 5 by 5 mask to reduce high-frequency components. The image was then correlated with a two-dimensional circularly symmetric triangular function with modelled gross shading of the macula.

Exudates were detected using their high gray level variation, and its contours were determined by means of morphological reconstruction techniques. The optic disc was detected by means of morphological filtering techniques and the watershed transformation [31]. Morphologic classifications of diabetic retinopathy was performed based on the number, location, and type of discrete microvascular lesions in the fundus of the eye [6]. The performance was evaluated using an automated fundus photographic image-analysis algorithm for sensitivity and/or specificity in patients with diabetes with untreated diabetic retinopathy and those without retinopathy [21]. The automated lesion detection correctly identified 90.1% of patients with retinopathy and 81.3% of patients without retinopathy.

The retinal thickness analyzer (RTA) was found to be suitable for application in tele-screening of diabetic retinopathy. It yielded a mean sensitivity of 93% for proliferative diabetic retinopathy and 100% sensitivity for detecting diabetic macular edema as compared to specificities ranging from 58 to 96% during clinical examination. The topography of the optic disc was found to be highly reproducible and can be used for glaucoma diagnostics [22].

Cree et al. have proposed an integrated automated analyzer of the retinal blood vessels in the vicinity of the optic disc using retinal images. The proposed system showed a mean accuracy of 70% using Bayes rule [5]. The features of the red lesions were extracted and classified using k-nearest neighbor classifier. The automated system showed a sensitivity of 100% and specificity of 87% for all the test images [23]. Web-based screening was conducted in a primary healthcare using uncompressed images and open source technology. The high incidence of suspected diabetic retinopathy was detected in type 1 diabetes patients using this type of screening programs [12]. Top-down and bottom-up strategies were applied to detect the lesions from background diabetic retinopathy images [34]. Hierarchical support vector machine (SVM) classification structure was applied to classify bright non-lesion areas, exudates and cotton wool spots.

The work discussed so far focused mainly on the automatic identification of diabetic retinopathy and normal retinal images. However, in this paper, we have discussed the automatic classification of different stages of the diabetic retinopathy.

The layout of this paper is as follows: Section 2 presents a review of the related work and Section 3 discusses the data acquisition process, preprocessing and extraction of six features, viz., red layer of perimeter (RLP), green layer of perimeter (GLP), blue layer of perimeter (BLP), red layer of area (RLA), green layer of area (GLA) and blue layer of area (BLA). Section 4 of the paper discusses the configuration of a neural network used for the classification process. Section 5 presents the results of the system. Finally, Section 6 presents the conclusion of this paper.

III. COMPUTER METHODS AND THEORY

In this work, 124 retinal photographs of moderate non-proliferative diabetic retinopathy (NPDR), severe NPDR, proliferative diabetic retinopathy and normal cases, have been studied. These data were provided by the National University Hospital, Singapore. The number of subjects and details of photographs in each group is shown in Table 1. These images were taken using Zeiss Visucamlite fundus. Fig. 1 shows a sample of the optical images of normal, moderate, severe and proliferative diabetic retinopathy.

3.1. Imaging techniques

Feature extraction is the most important part of the proposed system. The extracted features are used as inputs to the classifiers. Feature extraction is carried out on the pre-processed images after a contrast enhancement process. Our pre-processing step primarily consists of image contrast improvement based on histogram equalization, morphological operators and followed by binarization..

TABLE I RANGE OF AGE, NUMBER OF SUBJECTS IN EACH GROUP

Types	Normal	Moderate DR	Severe DR	Prolific DR
Age (years)	32 ± 8	58 ± 13	45 ± 12	70 ± 10
Number of subjects	29	38	18	39

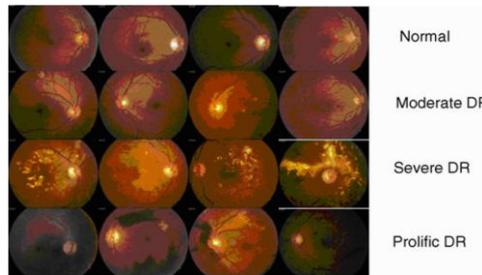


Fig. 1. A sample of normal, moderate, severe and proliferative DR fundus images.

3.1.1. Histogram equalization

Histogram equalization technique increases the dynamic range of the histogram of an image [9]. It assigns the intensity values of pixels in the input image such that the output image contains a uniform distribution of intensities.

3.1.2. Morphological operations

Hemorrhages and microaneurysms contribute to defects in a retina with diabetic retinopathy. All stages of diabetic retinopathy show such defects. Therefore, it is important to distinguish them from the noisy background of the retina image.

The algorithm developed uses a morphological operation to smooth the background and, as a result, veins, hemorrhages and microaneurysms can be seen clearly.

Two types of structuring elements (SE): (i) diamond-shaped, (ii) disk-shaped are used in this work.

- (i) A diamond-shaped structuring element shown in Fig. 2 is used to make veins clearer.
- (ii) A disk-shaped structuring element shown in Fig. 3 is used to remove noise from the background.

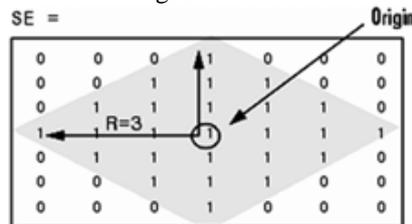


Fig. 2. Diamond structuring element.

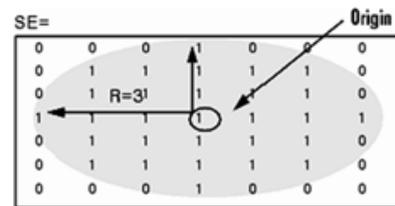


Fig. 3. Disc structuring element.

The structuring elements are determined using prior heuristic knowledge of all the images. The image undergoes several morphological openings using each of the structuring elements. A short explanation of the function used and the mathematics involved is as follows.

The morphological opening operation [11,28], erodes an image and then dilates the eroded image using the same structuring element for both operations with a disc SE where $R = 10$. As a result, the objects completely destroyed by the erosion are not recovered. This behavior is the very basis of the filtering properties of the opening operator. The image structures are selectively filtered out depending on the selection of the shape and size of SE. This means, all foreground image structures that do not contain the structuring element are removed by the opening. The shape and size of SE are set according to image structures to be extracted. The opened set is the union of all SEs fitting the set: where B = structuring element, X = set of pixels that make up the image, cB = opening of set using structuring element B . Alternatively, the opened set can be represented as where $(X \ominus B)$ is the Minkowski sum (dilation of set X by B) and $(X \ominus B)$ is the Minkowski subtraction (erosion of set X by B). Erosion and dilation are equivalent to Minkowski subtraction and addition respectively. All the structuring elements used in the feature extraction are symmetric with respect to its origin.

In addition to the morphological opening, the image is subtracted by the previous morphological opening and its intensity are adjusted such that it spreads pixel intensities more evenly over the intensity range. The image is further processed with a disc SE of $R = 18$, followed by a diamond SE of $R = 3$, each time, and hence the image has its intensity adjusted before the SE morphs the image. The intensity adjustment, maps the values in initial intensity image I to new values in adjusted image J such that 1% of data is saturated at low and high intensities of I . This increases the contrast of the output image J as it spreads pixel intensities more evenly over the intensity range. After the series of openings, the background of the processed image is not as noisy as the original image and the veins, microaneurysms and hemorrhages can be seen clearly (Figs. 4b and 5b). Now, the perimeter and area of the features can be easily extracted from these pre-processed images.

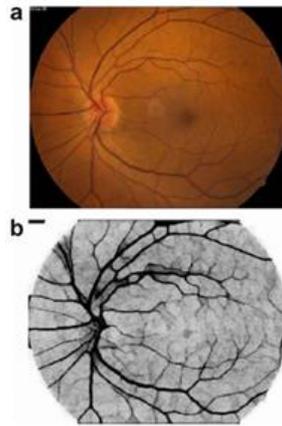


Fig. 4. (a) Normal retina and (b) distinguished veins from background (normal retina) (red layer).

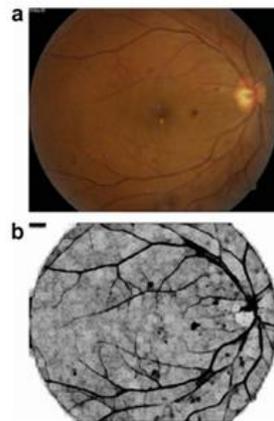


Fig. 5. (a) Moderate DR retina and (b) distinguished veins from background (moderate DR retina) (red layer).

The perimeter pixels of the objects are obtained from a binary image [11]. A pixel is considered a perimeter pixel if it satisfies both of these criteria:

- The pixel is on (non-zero)
- One (or more) of the pixels in its neighborhood is off.

The pixel connectivity used is a 4-connected neighborhood.

The boundary ∂X , the perimeter of the object, of a set X is the set of all points x such that every neighborhood of x has non-empty intersection with both X and its complement X^c :

where X is the X A the opening of X by structuring element A .

Another feature, area is determined by thresholding the image making the background black and the features white. This differs from Otsu's method [24]; which chooses the threshold to convert a grayscale image to binary by minimizing the intraclass variance of the black and white pixels.

3.1.3. Binarization

To binarize the image, a threshold should be carefully chosen. Too small a threshold will produce an image that has edges linked together. However, a big threshold will produce edge segments that form curves. We obtained good results by setting the threshold at 25% of the gray intensities contained into the image (25 % of the lower gray intensities are discarded) and this was set empirically.

3.2. Features

Six features namely, red layer of perimeter (RLP), green layer of perimeter (GLP), blue layer of perimeter (BLP), red layer of area (RLA), green layer of area (GLA) and blue layer of area (BLA) are extracted from the images after preprocessing by the morphological operations. Figs. 6 and 7 are illustrations of the layers extracted for perimeter and area of a normal eye image.



Fig. 6. Perimeter of red, green, blue layers, respectively for a normal eye.



Fig. 7. Area of red, green, blue layers, respectively for a normal eye.

3.2.1. Perimeter of veins, hemorrhages and microaneurysms

The perimeter is determined by the number of pixels present on the periphery of the veins. Figs. 8a–8d are illustrations of these veins; showing the images of normal retina, moderate, severe and proliferative DR retina images respectively.

IV. SYSTEM DESCRIPTION

In this work, we have used backpropagation algorithm for classification of the four stages of eye images. A brief description of the algorithm used for classification is discussed in the following section.

4.1. Backpropagation algorithm for classification

Backpropagation (BPA) algorithm is a supervised learning technique used for training artificial neural networks (ANN). It is most useful for feedforward networks (networks that have no feedback). It requires that the transfer function (Sigmoid) used by the artificial neurons (or “nodes”) be differentiable.

BPA algorithm is an iterative gradient algorithm designed to minimize the mean square error between the actual output and the desired output of a pre-selected neural network. This algorithm is also known as “The generalized delta rule” [32]. The neurons in layers, other than the input and output layers of a neural network, are called hidden units or hidden nodes, as their outputs do not directly interact with the environment. With the BPA, the weights associated with the hidden layers can be adjusted and thus enable the pre-selected neural network to learn. For our above-stated problem we tried with different number of hidden layers; ranging from 1 to 4 layers. Based on the results obtained, a neural network with one hidden layer and eight neurons gave the best classification result. In the present case, a learning constant $g = 0.9$ (which controls the step size), is chosen by trial and error.

Fig. 10 shows the configuration of the neural network classifier used for this work. The output layer has 4 neurons, giving rise to an output domain of 16 possible classes. However, the network is trained to identify only four classes (normal, moderate DR, severe DR and proliferative DR) given by decoded binary outputs [0001,0010,0100,1000], respectively. Values of the area and perimeter of the red, green and blue layers of the image are computed and fed as input to the classifier.

V. STATISTICS OF SYSTEM

The range of perimeter and area values of veins, hemorrhages and microaneurysms for each stage of DR with the different RGB layers are shown in Tables 2 and 3. The p-value (significance level) shown were

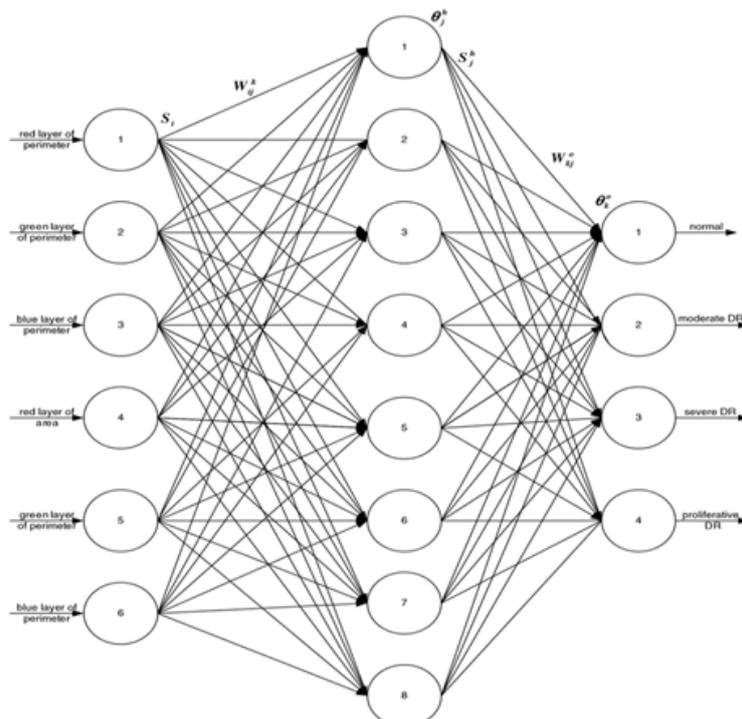


Fig.8. Architecture of the neural network classifier used.

TABLE II RANGE OF INPUT FEATURES TO ANN CLASSIFICATION MODEL

Type	Perimeter of red layer	Perimeter of green layer	Perimeter of blue layer
Normal	13443 ± 1547.2	13240 ± 1618.1	31267 ± 11420
moderate DR	14077 ± 2183.3	13887 ± 2326.4	40346 ± 7811.6
Severe DR	23834 ± 6360.3	29047 ± 12435	37524 ± 6206.3
Proliferative DR	30268 ± 9810.2	30076 ± 11847	38053 ± 7069.8
p-Value	<0.0001	<0.0001	0.0003

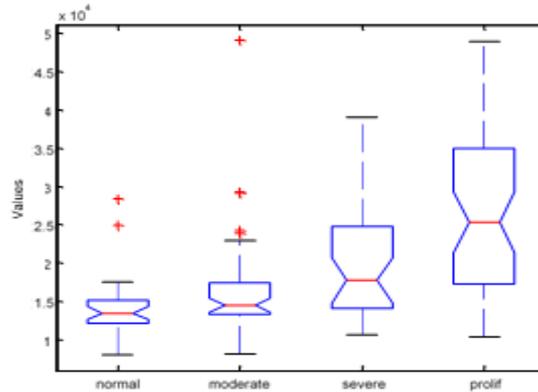


Fig.9. Green layer of perimeter ranges from ANOVA analysis.

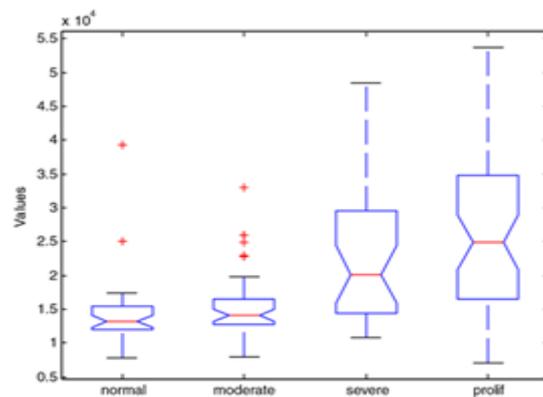


Fig.10 Blue layer of perimeter ranges from ANOVA analysis

The performance of neural networks in recognition and classification is usually evaluated by means of the following four performance indices [20]:

Classification accuracy.

Sensitivity: the probability that test is positive in the unhealthy population.

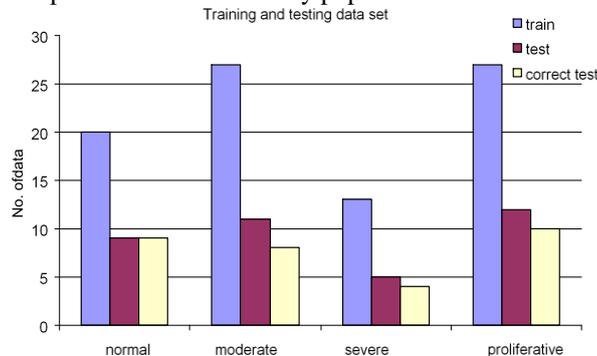


Fig.11 Graphical representation of training and testing data set.

The vessel tracker algorithm was developed to determine the retinal vascular network captured using digital camera [7]. These tracker algorithms were developed to detect the optic disk, bright lesions such as cotton wools spots, and dark lesions such as hemorrhages. This algorithm identifies arteries and veins with an accuracy of 78.4% and 66.5% correctly. The fundus images were subjected to the segmentation to extract the lesions and later subjected to the neural network for the classification [29]. The system showed a sensitivity of 95.1% and a specificity of 46.3 %.

Larsen et al., have used image processing algorithm for the detection of hemorrhages and microaneurysms to diagnose diabetes retinopathy [16]. Their algorithm demonstrated a specificity of 71.4% and a resulting sensitivity of 96.7% in detecting diabetic retinopathy when applied at a tentative threshold setting for use in diabetic retinopathy screening.

A computer system was developed using image processing and pattern recognition techniques to detect early lesions of diabetic retinopathy (hemorrhages and microaneurysms, hard exudates, and cotton-wool spots) [17]. This system was able to diagnose the diabetes retinopathy with an accuracy of more than 90 % of the cases. Classification of non-proliferative diabetic retinopathy (NPDR) based on the 3 types of lesions, viz., hemorrhages and microaneurysms, hard exudates, and cotton-wool spots was proposed [18]. This method was accurate in classifying the different stages to the tune of 82.6%, 82.6%, and 88.3 %.

Our system is more comprehensive as compared to the other works discussed so far. It involves different stages of the non-proliferative DR and proliferative DR class too. In our present work, we are able to identify normal, moderate, severe and proliferative cases of the DR correctly with an accuracy of more than 80% and a sensitivity of more than 90%. However, we can improve the efficiency of the correct classification by extracting better features and by increasing the number of data in each class.

VI. CONCLUSIONS

Diabetic retinopathy is a complication of diabetes and a leading cause of blindness. It occurs when diabetes damages the tiny blood vessels inside the retina, the light-sensitive tissue at the back of the eye. Four different kinds of retinal conditions, viz., normal retina, moderate diabetic retinopathy, severe diabetic retinopathy and proliferative diabetic retinopathy are considered for classification using a neural network. The features are extracted from the raw images using image processing techniques and fed to the feedforward neural network for classification. We demonstrated an accuracy of more than 80% of correct classification, a sensitivity of more than 90% and a specificity of 100% for the classifier. The accuracy of the system can be further enhanced by using proper input features and increasing the size of the training data set.

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