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Detection and Grading of Diabetic Retinopathy in Fundus Retinal Images

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Abstract: *Diabetic retinopathy (DR) is the most frequent cause of cases of blindness among adults aged 20–74 years. Since the presence of microaneurysms (MAs) is usually the first sign of DR and occurs due to damage in the retina as a result of long term illness of diabetic mellitus. Early microaneurysm detection can help reduce the incidence of blindness and Microaneurysm detection is the first step in automated screening of diabetic retinopathy. A reliable screening system for the detection of MAs on digital fundus images can provide great assistance to ophthalmologists in difficult diagnoses. This paper presents various pre-processing and candidate extraction techniques to condition or enhance the input image in order to make it suitable for further processing and improve the visibility of Microaneyrysm in color fundus images. Each candidate is then classified based on colour and standard morphological features. Using neural network architecture like Back propagation algorithm, the candidates extracted can be classified as MA's or non MA's. Depending upon number of Microaneurysm(MA) counts obtained by the candidate extraction , average area of MAs spreading & depending upon the progression of the disease, the grading is done which helps to analyse the exact stage of the disease.*

Keywords: *Diabetic retinopathy (DR) grading, fundus image processing, Circular hough Transformation (CHT), classification, microaneurysm (MA) detection.*

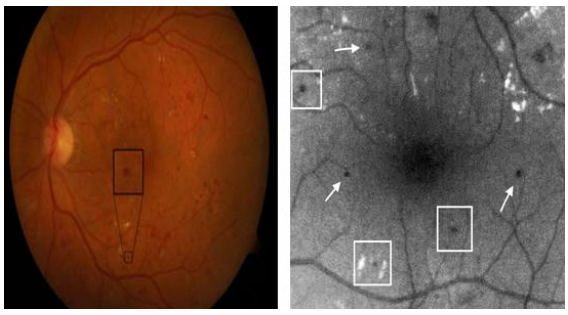
1. INTRODUCTION

Diabetic retinopathy (DR) is a serious eye disease originating from diabetes mellitus and the most common cause of blindness in the developed countries. Early treatment can prevent patients to become affected from this condition or at least the progression of DR can be slowed down. The key to the early detection is to recognize microaneurysms (MAs) in the fundus of the eye in time. Thus, mass screening of diabetic patients is highly desired, but manual grading is slow and resource demanding. Timely detection and treatment for DR prevents severe visual loss in more than 50% of the patients. Therefore, several efforts have been made to establish reliable computer-aided screening systems in this field. Therefore, an automatic or semi-automatic system able to detect various type of retinopathy, is a vital necessity to save many sight-years in the population.

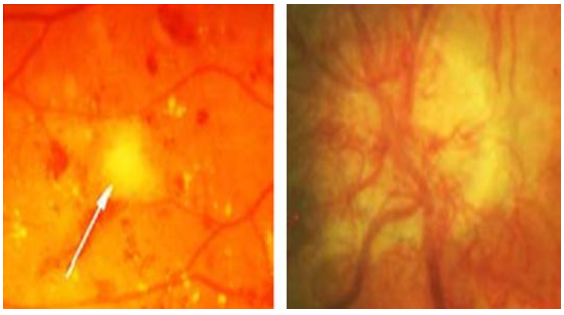
Microaneurysms (MAs) are early signs of DR, so the detection of these lesions is essential in an efficient screening program to meet clinical protocols [2]. MAs appear as small circular dark spots on the surface of the retina. The detection of MAs is still not sufficiently reliable, as it is hard to distinguish them from certain parts of the vascular system. The most common appearance of microaneurysms is near thin vessels, but they cannot actually lie on the vessels. In some cases, microaneurysms are hard to distinguish from parts of the vessel system.

Since the retina is vulnerable to microvascular changes of diabetes and diabetic retinopathy is the most common complication of diabetes, eye fundus imaging is considered a non-invasive and painless route to screen and monitor such diabetic eyes. In pathological sense, microaneurysms are blood-filled dilations of capillary walls. In accordance with the general concept, small circular shaped dark lesions, whose diameter is smaller than 125μm are considered to be microaneurysms. The distinction between MAs and Haemorrhages is quite difficult, and as a matter of fact unnecessary in an actual screening system, since MAs and Hemorrhages are both symptoms of DR. Pigmentations of the retina

also have striking resemblance to true MAs. As a current trend, automatic computer based methods are proposed to assist eye specialists [1].An automated microaneurysm detector can prove to be an effective tool for automated identification of diabetic retinopathy in clinical practice. Automated assessment can save time of the human graders and also provide a history of changes in the fundus using the digital images. A set of techniques being able to quantify vascular changes and detect lesions has been described in [2] [3] [4] [5]. Spencer *et al.* [2] exploited this feature and used the top-hat transform to produce candidate microaneurysms. The true microaneurysms were then pruned by using post-processing based on their earlier work [4] and classification. Baudoin *et al.*[4]put forward the the first automated detection methods for diabetic retinopathy to detect microaneurysms from fluorescein angiograms. The candidate microaneurysm segmentation was conducted using a combination of top-hat transform and matched filtering with region growing. Walter *et al.* [10] attempted to morphologically reconstruct the eye fundus image exclusive of bright lesions. The method was based on the idea that the difference between the reconstructed image and the original image would ultimately express the bright lesion locations. Based on the research in [5, 3], a version of the top-hat transform based method was presented for red-free images by Hipwell *et al.* [11], and for colour eye fundus images by Yang *et al.* [12], and Fleming *et al.* [6]. The top-hat approach was also studied in the detection of haemorrhages by Fleming *et al.* [6].Niemeijer *et al.* [7] proposed a red lesion (microaneurysm and haemorrhage) detection algorithm by introducing a hybrid method to relax the strict candidate object size limitations. Zhang, and Chutatape [9] extracted the characteristic features of haemorrhages from image templates using the principal component analysis (PCA). The extracted features were used with the support vector machine to classify the image patches of previously unseen colour eye fundus imageA color fundus photograph and green plane containing microaneurysms is shown in fig. 1(a) & (b) below and fig. c & d shows next stages of DR.



(a) (b)



(c) (d)

Fig 1. (*a) A color fundus photograph containing microaneurysms (MAs) (b) An enlarged part of the green plane of the image is shown with microaneurysms indicated with arrows, and false positive candidates in squares. (c) Haemorrhages (d) Neovascularisation*

2. METHODOLOGY

In this paper, we present an approach to improve microaneurysm detection in fundus retinal images. Microaneurysm detection is based on the analysis of digital fundus images. The detection process starts with pre-processing of the images, which is followed by a candidate extraction phase. Then the extracted candidates are classified .The flow of the proposed system is as shown in fig 2 below.

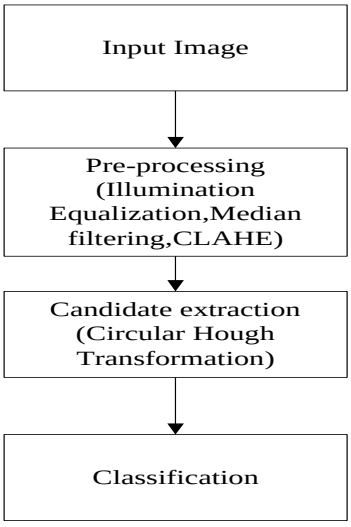


Fig. 2 *Flow of the Proposed System*

2.1. Pre-Processing

Image pre-processing is the pre-requisite step in detecting abnormalities associated with fundus image to improve the visibility of microaneurysms in the input fundus image. The differences in brightness and colors of the retinal fundus images are due to the photographic conditions. Pre-processing of the images commonly involves removing low-frequency background noise, normalizing the intensity of the individual particles images, removing reflections, and masking portions of images. Image pre-processing is the technique of enhancing data images prior to computational processing. In this section, pre-processing methods are considered before executing MA candidate extraction. The algorithms have been selected based on corresponding literature recommendations for medical image processing. The pre-processing methods described below aim to enhance the accuracy of microaneurysm detection but each of them focuses on a different aspect of detection. Thus, methods which are well-known in medical image processing and preserve image characteristics must be selected.

2.1.1. Illumination Equalization

This preprocessing method is used to reduce the vignetting effect caused by uneven illumination of retinal images. Vignetting effect is caused due to the fault settings of camera, which distributes the light unequally. Therefore, MAs appearing near the border of the retina are not properly visualized. Therefore, it becomes mandatory to equally distribute the light, which is said to be the primary step of pre-processing. Each pixel intensity is set according to the following formula:

$$f' = f + \mu d - \mu l \quad (1)$$

Where *f, f'* are the original and the new pixel intensity values, respectively, μd is the desired average intensity, and μl is the local average intensity. MAs appearing on the border of the retina become visible in a proper manner as the light now are equally distributed.

2.1.2. Median filter

In median filtering, the neighboring pixels are ranked according to brightness (intensity) and the median value becomes the new value for the central pixel.
Median filters can do an excellent job of rejecting certain types of noise, in particular, "shot" or impulse noise in which some individual pixels have extreme values. In the median filtering operation, the pixel values in the neighborhood window are ranked according to intensity, and the middle value (the median) becomes the output value for the pixel under evaluation.
The best known order-statistics filter is the median filter, which replaces the value of a pixel by the median of the gray levels in the neighborhood of that pixel.

$$f(x,y) = \underset{(s,t \in \mathrm{Sxy})}{median}\{g(s,t)\} \quad (2)$$

The original value of the pixel is included in the computation of the median.

2.1.3. Contrast Limited Adaptive Histogram Equalization

CLAHE is the refinement of AHE, where the enhancement calculation is modified by imposing a user specified maximum i.e, clip level, to the height of local histogram and thus on the maximum contrast enhancement factor. The enhancement is reduced in very uniform area of the image, which prevents over enhancement of the noise and reduces the edge showing effect of the unlimited area. Contrast limited adaptive histogram equalization (CLAHE) is a technique used in biomedical image processing, since it is very effective in making the interesting prominent parts more visible. For our work the clip limit was set to 0.02 and the distribution was set to "uniform".

(a) *(b)*

Fig. 4 *(a) Original fundus retina image, (b) fundus retina image after pre-processing by CLAHE*

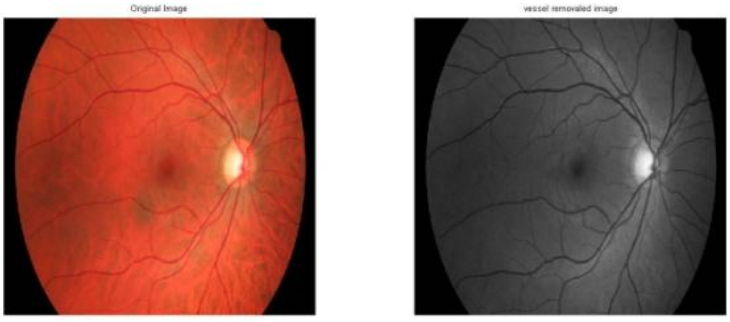
2.1.4. Vessel removal

Many MA candidates are dark spots within a retinal vessel and so false positive MA detection would be reduced by reliable vessel detection in the vicinity of each MA candidate .The method is flexible and allows an MA to occur on a vessel, for example, if it is much darker or wider than the vessel. This section describes how a Boolean valued feature, is vessel, is derived for each MA candidate such that is vessel is true if the MA candidate appears.

Let $S^{(W)}$ be a subimage of dimensions 81×81pixels extracted from the contrast normalized subimage, and centered on the candidate MA at q. Consider a transformation $S_{ȧ}{}^{(W)}$ (r,ɵ)= $S^{(W)}$ (r,ɵ') where ɵ'= ɵ + tan^{-}1(ȧ /r) This transformation shifts each point, by a distance , circumferentially on circles centered on .An image which is positive near the centre of approximately radial linear dark features (which are likely to be vessels converging on the candidate MA) can be defined by

$$V=\min(S_{+ȧ}{}^{(W)} - S^{(W)}, S_{-ȧ}{}^{(w)} - S^{(W)}) \quad (3)$$

Extrapolation of the missing parts is carried out using the inpainting algorithm to fill in the holes caused by the removal. MAs appearing near vessels become more easily detectable in this way to be part of a vessel. When the vessels are removed the MAs or the MA like objects are clearly visible.



(a) (b)

Fig. 5 *(a) Original fundus retina image, (b) fundus retina image after pre-processing by Vessel removal and exploration algorithm*

2.2. Candidate Extractors

Candidate extraction is the effort to reduce the number of objects in an image for further analysis by excluding regions which do not have similar characteristics to microaneurysms. Individual approaches

define their own measurements for similarity to extract MA candidates. In this section, we provide a brief overview of the candidate extractors involved in our analysis. The extractor is selected according to current state-of-the-art literature recommendations.

2.2.1. Circular Hough-Transformation

The detection of small circular spots in the image is possible by this method. As MAs are circular objects, so to detect the round features, Circular Hough transformation is used. Candidates are obtained by detecting circles on the images using circular Hough transformation. With this technique, a set of circular objects can be extracted from the image. The radius of the circles is limited based on the observed size of MAs identified in a training set. The equation of a circle is

$$r^2 = (x-a)^2+(y-b)^2 \quad (4)$$

Where, *a* and *b* are the centre of the circle in the x and y direction and *r* is the radius.

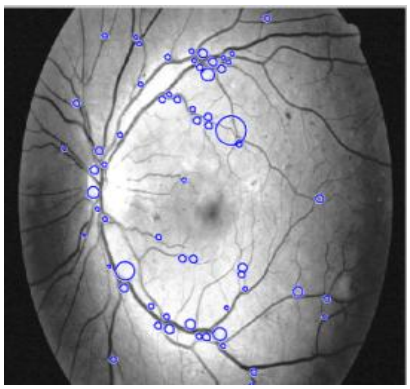


Fig 6. *Sample image from the dataset with Circular Hough transformed method*

The parametric representation of the circle is

$$x = a+ r\cos(\Theta)$$

$$y = b+ r\sin(\Theta) \quad (5)$$

Thus the parameter space for a circle will belong to R^3 whereas the line only belonged to R^2 .In order to simplify the parametric representation of the circle, the radius can be held as a constant. The process of finding circles in an image using CHT is as follows.

- Find all edges in the image by using edge detection method by sobel or canny edge detection methods.
- At each edge point, a circle is drawn with centre in the point with the desired radius
- At the coordinates which belong to the perimeter of the drawn circle, increment the value in accumulator matrix
- The accumulator will now contain numbers corresponding to the number of circles passing through the individual coordinates
- Thus the highest numbers correspond to the centre of the circles in the image.

Here, the setting of radius range is an important and challenging and at the same time an iterative task. As MAs are relatively small objects of 125µm, therefore the radius range should be selected within the 8 pixels, which is the threshold calculated on the basis of Microaneurysm diameter of 125µm.The theory described above of CHT,includes many steps, which may increase the processing time unnecessarily. This can be avoided by using the newest version of MATLAB R2013a, where a new built-in function called, "imfindcircles" can do the job quickly. This function calculates the centre, radii and metric. Also,the function called "viscircles", incorporates centre,radii and metric Here ,on the pre-processed image , the radius range has to be set. The radius range for our proposed work was set as radiusrange[2 ,10],where 2 is called as the minimum radius or R_{min} and 10 is called as the maximum radius or R_{max}. So ,all the circular objects within these radius range will be marked as circles.The same is shown in fig 6.where the The candidates extracted through CHT are, centroid,

area, perimeter, majorlength and minorlength.These features are given to the ANN classifier to train the images. In our proposed work, we trained total 150 images.

3. CLASSIFICATION

For classification an appropriate number of training images are trained to detect the required MA's and then tested accordingly in order to identify the number of true positives and false positives. For training and testing the images, Artificial neural network models are specified by network topology and learning algorithms [5][6]. Network topology describes the way in which the neurons (basic processing unit) are interconnected and the way in which they receive input and output. Learning algorithms specify an initial set of weights and indicate how to adapt them during learning in order to improve network performance. A neural network can be defined as a "massively parallel distributed processor that has a natural propensity for storing experiential knowledge and making it available for use". A number of simple computational units, called neurons are interconnected to form a network, which perform complex computational tasks. For classification of features the back propagation neural network can be used. Training a network by back propagation involves three stages: The feed-forward of the input training pattern, the back-propagation of the associated error, the adjustment of the weights. The ANN comprises of three layers (one input layer, one hidden layer, and one output layer) trained by back propagation. In proposed method back propagation feed forward neural network with Levenberg-Marquardt algorithm can be used.

***Levenberg-Marquardt Algorithm (LM)*:** For LM algorithm, the performance index to be optimized is defined as

$$F(w) = \sum_{p=1}^{P} \sum_{k=1}^{K} (d_{kp} - o_{kp})^2 \tag{6}$$

where $w = [w_1, w_2 \ldots\ldots w_N]^T$ consists of all weights of the network, d_{kp} is the desired value of the k^{th} output and the p^{th} pattern ,o_{kp} is the actual value of the k^{th} output and p^{th} pattern, N is the number weights, P *is* the number of patterns, and K is the number of the network outputs. N is the number of the weights, P is the number of patterns, and K is the number of network outputs. Equation (7) can be written as,

$$F(W) = E^T E \tag{7}$$

In above equation E is the Cumulative Error Vector (for all patterns)

$E = [e_{11} \ldots e_{k1;} e_{12} \ldots e_{k} \ldots . e_{1p} \ldots e_{kp}]^T$

Where, $e_{kp} = d_{kp} - o_{kp}$, for k=1. .. ..K and p=1…P

When training with the LM method the increment of weights ΔW can be obtained as follows,

$\Delta W_k = - [J^T (W_k) J (Xk) + \mu_k I]^{-1} J^T (W_k) E (W_k)$

Where J is the Jacobin matrix.

$$J(W) = \begin{bmatrix} \frac{\partial e_{11}}{\partial w_1} \frac{\partial e_{11}}{\partial w_2} \ldots\ldots\ldots \frac{\partial e_{11}}{\partial w_N} \\ \frac{\partial e_{21}}{\partial w_1} \ldots\ldots\ldots\ldots\ldots \\ \vdots \\ \frac{\partial e_{kp}}{\partial w_1} \ldots\ldots\ldots\ldots\ldots \frac{\partial e_{kp}}{\partial w_N} \end{bmatrix}$$

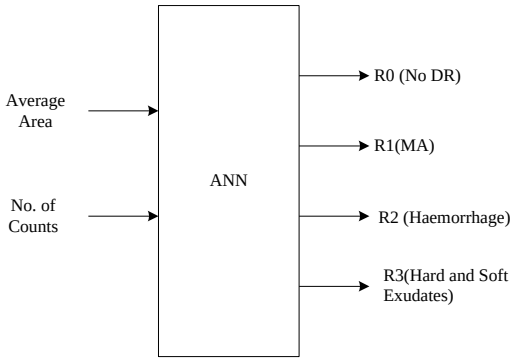
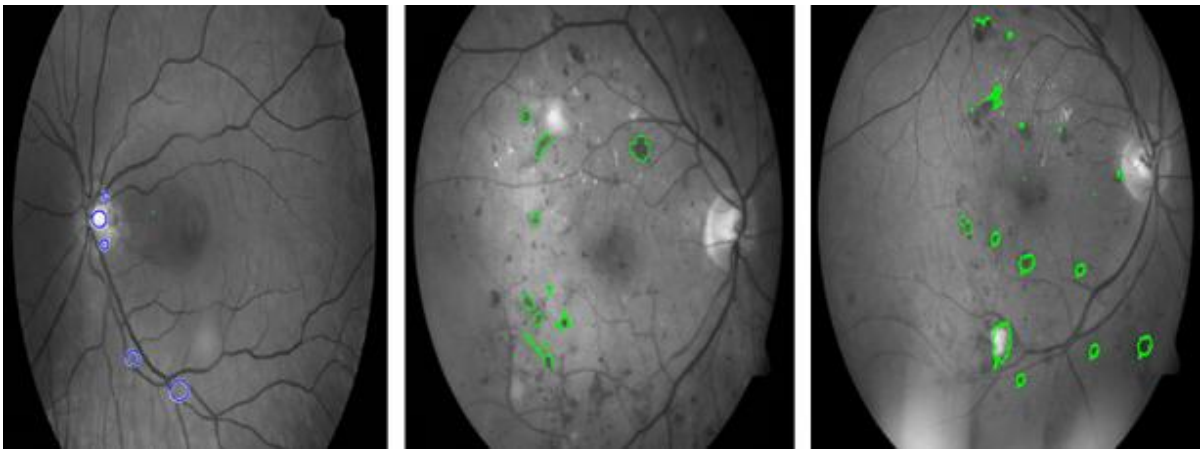


Fig 7. *Classification*

Depending upon number of Microaneurysm (MA) counts obtained by the candidate extraction and the average area of MAs spreading, depending upon the progression of the disease, the classification and the grading can be done as shown in fig. 7. For each image, a grading score ranging from R0 to R3 can be provided. These grades can be corresponded to the following clinical conditions: a patient with R0 grade may have no DR. R1 grade may have MA (first and mild stage of DR) , R2 may have Haemorrhages which is the next progressive stage of DR and R3 may have Hard or Soft Exudates which is considered to be the severe stage of DR. in These features are given to the LM classifier to train the images. In our proposed work, we trained total 150 images. While testing, 200 images ehere considered, out of which 98 images showed true positives and rest of the showed false positives. These images where also cross checked by the ophthalmologists to indicate the correctivity, where the tested images 88% correct as compared to the dilated or Fundus Fluroscein Angiographic images.

4. RESULTS

The proposed framework increases sensitivity using Circular Hough transformation method. After performing the testing task, we have obtained the grading of Diabetic Retinopathy .For testing, input images were taken from the database, and the detection of Microaneurysm was marked as R1,which was the grading status for the first or mild stage of Diabetic Retinopathy which is shown in fig. 9(a),(b) and (c) shows the grading status of R2(Haemorrhages) which is the moderate stage.Fig. 11 shows the grading as R3(Hard exudates) ,the severe stage of DR respectively.



(a) (b) (c)

Fig 8. *(a) R1 (MA), (b) R2 (Haemorrhages), (c) R3 (Hard Exudates)*

5. CONCLUSIVE DISCUSSION

In this paper, we have introduced an approach which improves microaneurysm candidate extraction using circular hough transformation. In Circular Hough Transformation, the central point of Microaneurysm is identified. Levenberg-Marquardt Algorithm used for classification helps us to obtain the severity of the disease, which may help us to analyse the proper recognition of Microaneurysm and grading of DR depending on the severity of the disease.

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