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Detection of Microaneurysms in Color Fundus Images

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***Abstract*— Diabetic Retinopathy is an eye disease which occurs due to damage in the retina as a result of long term illness of diabetic mellitus. Microaneurysm detection is the first step in automated screening of diabetic retinopathy. To perform this detection, several methods have been proposed in the diagnosis of diabetic retinopathy. In this paper, initially the pre-processing techniques like gamma correction, green channel extraction, location based contrast enhancement process such as Adaptive Histogram Equalization (AHE) are applied to improve the visibility of microaneurysms in the color fundus images. Microaneurysms are segmented using fuzzy c-means clustering algorithm on the pre-processed image. Then features are extracted using Gray Level Co-occurrence Matrix (GLCM), wavelet and first order statistics. All these features constitute the feature set which is used in knn classifier to remove spurious candidates. The remaining candidates can be thresholded further for a binary output which gives the final candidates.**

***Index Terms*— Diabetic Retinopathy, Microaneurysms, color fundus images, Fuzzy C-means clustering, GLCM, DWT, knn classifier.**

I. Introduction

Diabetic retinopathy is retinopathy (damage to the eye) caused due to microvascular complication of diabetes which affects up to 80 percent of all patients who have had diabetes for 10 years or more. This disease causes abnormalities in the retina, and in the worst case, blindness. Depending upon the severity of the disease, Diabetic retinopathy is classified into two types. Non-proliferative and proliferative diabetic retinopathy. In the first stage which is called non-proliferative diabetic retinopathy (NPDR), there are no symptoms and patients will have clear vision. The first detectable abnormalities called microaneurysms (microscopic blood-filled bulges in the artery walls) can be seen in fundus photography which is a way to detect NPDR. That is, the presence of microaneurysms is the first sign of eye damage caused by many years of high blood glucose levels. On the second stage, DR leads to neo vascularization, hemorrhages, macular edema. In later stages, retinal detachment is also caused due to DR progression.

As abnormal new blood vessels (neovascularisation) form at the back of the eye as a part of Proliferative Diabetic Retinopathy (PDR), they can burst and bleed (vitreous hemorrhage) and also blur vision. People with diabetes may get microaneurysms as an early symptom of the disease. Automatic Recognition of DR lesions like microaneurysms, in digital fundus images can contribute to early diagnosis and screening of this disease. An automatic and efficient method for the detection of microaneurysms is proposed in this paper. Damage to endothelial cells leads to dilated capillaries and venules which are called microaneurysms.

(a) (b)

Fig. 1. (a) A Photography of Microaneurysm; (b) A fundus showing Microaneurysms which are zoomed out.

Microaneurysms are small swellings (shown in Fig. 1a) that form on the side of tiny blood vessels. These small swellings may rupture and allow blood to leak into nearby tissue. Microaneurysms appear as tiny round shaped red dots in color fundus images of the human retina which is shown in Fig. 1b. Microaneurysms come from capillaries. As the capillaries are not visible in color fundus images, microaneurysms appear as isolated dots, i.e. separated from the vascular tree. Their diameter normally lies between 10 to 100 micrometer, but it is always smaller than 125 micrometer. That is, they are smaller than the diameter of optic veins. These miniature aneurysms can rupture and leak blood.

From an image processing standpoint, the automatic detection of microaneurysms is a challenging task since their color and size are same as the vessels, they have a variable size and often they are so small that can be easily confused with the image noise (or vice versa). It is also difficult to distinguish whether a red lesion is a microaneurysm or small dot hemorrhage. The only way to be certain is through fluorescein angiography. This is an invasive procedure which involves the injection of a contrast agent in the patient.

The first computerized approach for the detection of microaneurysms was described by Lay [1] and Baudoin et al. They segmented microaneurysms using morphological approach. T. Spencer et al. [2], M.J. Cree et al. [3] and A. Frame et al. employed a mathematical morphology technique to segment MA with different preprocessing steps and classification methods within fluorescein angiograms. A limitation of the morphological approach [1] is the use of structuring elements. If it is too large, it would result in the detection of tight vessel curvings as possible microaneurysms. However, the use of too small linear structuring element would result in missing of true microaneurysms. Niemeijer et al [8] considered an additional pixelwise classification based candidate extraction method and merged the output. Walter et al [10] aimed at detecting candidates by diameter closing and an automatic threshold scheme. Quellec et al [11] proposed a method in which microaneurysms are detected by locally matching a lesion template in subbands of wavelet transformed images. Mizutani et al [14] proposed a double-ring filter for the initial detection of microaneurysms. Luca Giancardo et al [15] presented their work on the detection of microaneurysms with the help of Radon Cliff operator. Zhang et al [16] proposed a method which constructs a maximal correlation response image from input retinal images for candidate extraction. Antal and A. Hajdu [19] proposed a novel approach that combines several preprocessing methods and candidate extractors before the classification step to improve microaneurysm detection in digital color fundus images.

Lazar et al [21] proposed a method which realizes Microaneurysm detection through the analysis of directional cross-section profiles. Those profiles were obtained from the local maximum pixels of the preprocessed image.

Accurate microaneurysm detection from the background is important for diagnosis of diabetic retinopathy. The standard approach in automatic microaneurysm detection has usually four stages: 1) image pre-processing 2) candidate extraction 3) feature extraction and 4) classification. Due to different shapes and colors of microaneurysms, candidate extraction and feature extracion are the most important stages of all. This paper focuses on segmenting microaneurysms using FCM from the pre-processed image and extracting features using wavelet, GLCM from the segmented image.

II. Proposed Method

The framework of the proposed method is given in Fig. 2. The input retinal images undergo fuzzy C means clustering algorithm to segment microaneurysms. Texture analysis using GLCM, wavelet and first order statistics is done subsequently. Then the features obtained are fed to knn which classifies the images as normal or abnormal based on the presence of microaneurysms.

A. Database

Publically available database DIARETDB1 is used in this study. The database [23] consists of 89 colour fundus images of which 84 contain mild non-proliferative signs of the diabetic retinopathy and 5 are normal which do not contain any signs of diabetic retinopathy. Images were captured using the 50 degree Field-Of-View digital fundus camera with varying imaging settings. The data correspond to a good practical situation where the images are comparable and can be used to evaluate the general performance of diagnostic methods.

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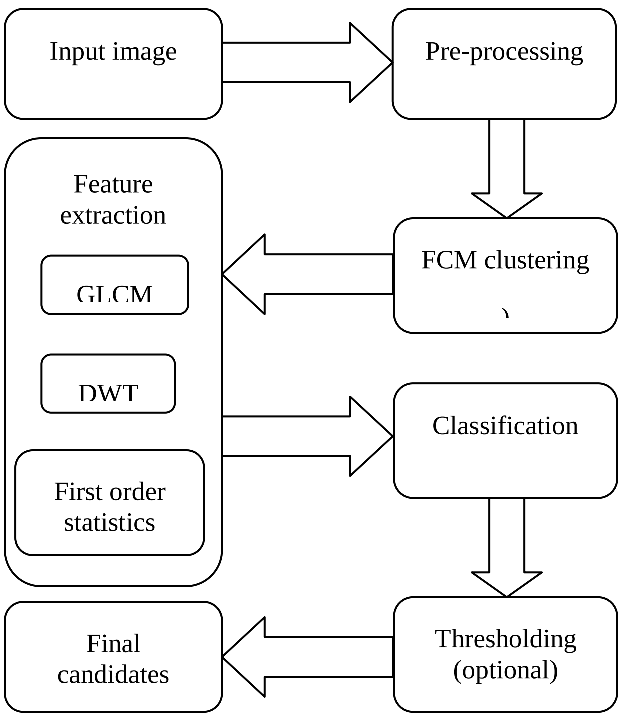


Fig. 2. Workflow of the proposed method.

B. Image pre-processing

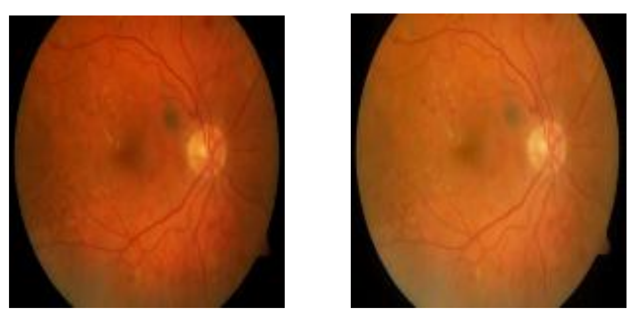
Image pre-processing is the pre-requisite step in detecting abnormalities associated with fundus image to improve the visibility of microaneurysms in the input fundus image. The differences in brightness and colors of the retinal fundus images are due to the photographic conditions. In order to reduce these differences, initially gamma correction is applied to each image as shown in Fig. 3b. Green channel is extracted from the gamma corrected image, since this gives better contrast between microaneurysms /blood vessels /haemorrhages and background as shown in Fig. 3c.

The proposed method further enhances the contrast of the green channel by transforming the values using adaptive histogram equalization (AHE) as shown in Fig. 3d. Adaptive histogram equalization is an image processing technique used to improve local contrast in images.

When compared to ordinary histogram equalization, the adaptive method computes histograms for distinct sections of the image, and uses them to redistribute the lightness values of the image. Hence it is required for improving the local contrast of an image and bringing out more detail.

C. Fuzzy C Means clustering

Clustering is the task of grouping a set of objects in such a way that objects in the same cluster are more similar (in some sense or another) to each other than to those in other clusters . It is an iterative process of finding better and better cluster centers. Fuzzy clustering is an approach operating towards fuzzy logic and it provides the flexible method of assigning the data points to the clusters. According to fuzzy algebra, every element in the universe can belong to any fuzzy set with a degree of membership that varies from 0 to 1 taking real values. In fuzzy clustering, data points are given partial degree of membership in multiple nearby clusters. The strength of association between particular data point and a cluster is indicated by membership levels. By using this membership levels, data points are assigned to more than one cluster. Thus the central point in fuzzy clustering is that the data points are not uniquely partitioned in a collection of clusters. Membership levels are obtained by using distance metric measures which calculate how far away a point is from a cluster center.



(a) **(b)**

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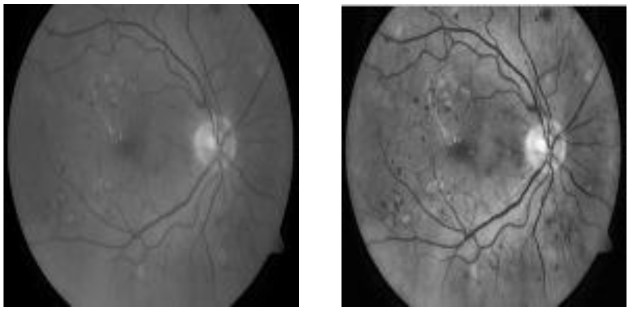


(c) **(d)**

Fig. 3. Image pre-processing. (a)Input image; (b) Gamma corrected image; (c) Green channel output; (d) AHE output.

Fuzzy C means is the most well known fuzzy clustering algorithm which is a modification by Bezdek of an original crisp clustering methodology. Bezdek introduced Fuzzification parameter (m) in the range [1,n] , which was introduced by Bezdek determines the degree of fuzziness in the clusters. In this paper, Fuzzy C means clustering [13] which is an overlapping (clustering) segmentation algorithm is used to extract candidate by excluding regions which do not have similar characteristics to microaneurysms. Thus this step reduces the number of objects in an image for further analysis.

Initially c is fixed where c is (2<=c<n) and then a value for parameter 'm' is selected and there after the partition matrix U(0) is initialized. Each step in this algorithm will be labeled as 'r' where r = 0, 1, 2 …

1)Calculate the c center vector {Vij} for each step.

$$V_{ij} = \frac{\sum_{k=1}^{n} \mu_{ik}{}^{m} x_{kj}}{\sum_{k=1}^{n} \mu_{ij}{}^{m}} \qquad (1)$$

2) Calculate the distance matrix D[c,n].

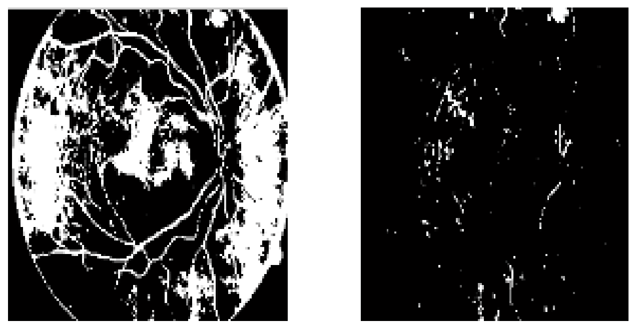
$$\mathrm{D_{ij}} = \left(\sum_{j=1}^{m} (x_{kj} - V_{ij})^2\right)^{1/2} \qquad (2)$$

2) Update the partition matrix for the rth step, U(R) as

$$\mu_{ij}{}^{r-1} = \frac{1}{\sum_{j=1}^{c} \left(d_{ik}{}^{r} - d_{jk}{}^{r}\right)^{\frac{2}{m-1}}} \qquad (3)$$

If ||U(k+1)-U(k)||<δ then the algorithm is stopped otherwise the algorithm returns to step 2 by updating the cluster centers iteratively and also the membership grades for data point.

To be specific introducing the fuzzy logic in K-Means clustering algorithm is the Fuzzy C-Means algorithm in general. Infact, FCM clustering techniques are based on fuzzy behavior and they provide a technique which is natural for producing a clustering where membership weights have a natural interpretation but not probabilistic at all. This algorithm is basically similar in structure to K-Means algorithm and it also behaves in a similar fashion. By applying Fuzzy C means clustering algorithm on the pre-processed image, microaneurysms along with blood vessels are segmented as shown in Fig. 4a. Further blood vessels and other regions, which are larger in size are eliminated to segment the microaneurysms separately which is shown in Fig. 4b.



(a) **(b)**

Fig. 4. (a) Segmentation output using FCM; (b)Image after removal of blood vessel and other regions larger in size.

D. Feature extraction

Feature extraction is useful for solving computer vision problems such as texture classification. When the image sizes are very large to be processed and it is suspected to be notoriously redundant (e.g. the same measurement in both feet and meters) then the input data will be transformed into a reduced representation set of features (also named features vector).

In *feature extraction*, the input data is transformed into the set of features. If the exact features are extracted, it is expected that the feature set will extract relevant information from the input data and perform the desired task using this reduced representation instead of the full size input. Texture features are extracted according to the statistics of GLCM (Gray Level Co-occurrence Matrix) DWT (Discrete Wavelet Transform) and first order statistics.

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1) DWT feature

Many approaches have been suggested for texture based feature extraction. These ranges from using random field models to multiresolution techniques such as wavelet transform. Recent research on texture analysis has shown that algorithms using the multiresolution wavelet transform achieve very good performance.

The 2D discrete wavelet transform [12] is applied to the image. It performs single level two-dimensional wavelet decomposition. Wavelet Transforms enable the decomposition of the image into different frequency sub bands (Low Low (LL), Low High (LH), High Low (HL) and High High (HH) sub bands). This property makes it especially suitable for the segmentation and classification of texture images. For texture classification, absolute features need to be extracted to obtain a representation that is as discriminative as possible in the transform domain. A widely used wavelet feature is the energy of each wavelet sub band.

In this paper, features like energy, homogeneity, contrast are obtained from Low Low component of the wavelet decomposed image.

2) GLCM feature

GLCM method is widely used in many texture analyses. A GLCM is a matrix where the number of rows and columns is equal to the number of gray levels, G, in the image [22]. By using GLCM, second order statistical texture features are extracted from the image. GLCM is a tabulation of how often different combinations of pixel grey levels occur in an image. The matrix element P_{ij} is defined as the relative number of times, gray level pair (i, j) occurs when pixels separated by the distance d within a given neighbourhood along the angle ɵ are compared. Each element is normalized by the total number of occurrences to form GLCM P. The matrix element P (i, j | d, *ɵ*) contains the second order statistical probability values for changes between gray levels 'i' and 'j' at a particular displacement distance d and at a particular angle (*ɵ*). GLCM is sensitive to size of the texture samples on which they are estimated and the number of gray levels can be reduced. The commonly extracted textural features using GLCM are contrast, homogeneity, correlation, entrophy and energy.

2.1 Entropy

The entropy of a retinal image can be defined as a measure of the uncertainty associated with a random variable. Entropy quantifies, in the sense of an expected value, the information contained in an image. Entropy shows the amount of information of the image that is needed for image compression. Entropy measures the loss of information or message in a transmitted signal and also measures the image information. It is given by

$$Entrophy = \sum_{i=0}^{N-1} \sum_{j=0}^{N-1} C_{ij} log\, C_{ij} \qquad (4)$$

2.2 Energy

Angular second moment is also known as Uniformity or Energy. It is the sum of squares of entries in the GLCM. Angular second moment measures the image homogeneity. Angular second moment is high when image has very good homogeneity or when pixels are very similar. It can be formulated as

$$Energy = \sum_{i=0}^{N-1} \sum_{j=0}^{N-1} {C_{ij}}^2 \qquad (5)$$

2.3 Homogenity

Homogenity can measure the closeness of the distribution of elements in the GLCM to the GLCM diagonal. It is mathematically represented as

$$Homogeneity = \sum_{i=0}^{N-1} \sum_{j=0}^{N-1} \frac{C_{ij}}{1+|i-j|} \qquad (6)$$

2.4 Correlation

Correlation calculates the linear dependency of the gray level values in the co-occurrence matrix. It is represented as

$$Correlation = \sum_{i=0}^{N-1} \sum_{j=0}^{N-1} \frac{(1-\mu_i)(1-\mu_j)C_{ij}}{\sigma_i \sigma_j} \qquad (7)$$

2.5 Contrast

Contrast is a measure of the local intensity level variation which gives higher value for high contrast image.It is given by

$$Contrast = \sum_{i=0}^{N-1} \sum_{j=0}^{N-1} (i-j)^2 C_{ij} \qquad (8)$$

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3) First order statistics

A fundamental task in many statistical analyses is to characterize the location and variability of a data set. A further characterization of the data includes skewness and kurtosis. First order statistical features such as mean, standard deviation, skewness and kurtosis are extracted in this proposed method.

3.1 Mean

It is the average value of all the elements in the matrix. It can be formulated as

$$\mu = \frac{1}{N}\sum_{i=1}^{m}\sum_{j=1}^{n} P_{ij} \qquad (9)$$

Where,
N is the number of pixels in the image,
i and j are the values of corresponding row and column of the image respectively,
m and n are the final values of the row and column of the image respectively,
P_{ij} is a matrix of the image.

3.2 Standard deviation

Variance is a measure of deviation of gray levels in an image from the mean. Standard deviation is the square root of the variance of elements in the matrix. It is given by

$$\sigma = \sqrt{\frac{1}{N-1}\sum_{i=1}^{m}\sum_{j=1}^{n}\left(P_{ij} - \mu\right)^2} \qquad (10)$$

Totally 12 features are extracted from the segmented image shown in Fig. 4. (b) using DWT and GLCM. Features are extracted from each pixel in the segmented image and those features together constitute the feature set which is then used in classification to determine microaneurysm and non-microaneurysm pixels. Table 1 shows the features and their values of microaneurysm and non-microaneurysm pixels.

Table 1.
Feature extraction of MA and Non-MA pixels

Features		MA	Non-MA
First Order Statistics	Mean	8.681581685744	0
	Standard deviation	16.87217672930	0
DWT features	Correlation	54.60021259005	0
	Homogeneity	0.283049068761	0
	Energy	0.028173308586	0
	Contrast	36.47431203495	0
	Sumvariance	178.4930017104	0
GLCM features	Homogeneity	0.918145161290	1
	Entrophy	0.503924752770	-2.2204e-16
	Contrast	4.583870967741	0
	Energy	0.775088449531	1

E. Classification

After feature extraction, knn classifier [22] is used for classification. A trained knn classifier is set up in a "calibrated" feature space with a set of discriminative features and a set of labeled instances. The knn classifier assigns soft class labels to query pixels based on the labels of their k nearest neighbors in the feature space. When n neighbors are labeled as being a microaneurysm pixel, the posterior probability that the query pixel is a microaneurysm pixel itself, p is determined by p=n/k. For finding the nearest neighbours, the distance is measured with Euclidean metric in the optimized feature space. At the testing stage, features are extracted from the unknown image and given as an input to classifier to see whether the image consists of microaneurysms or not.

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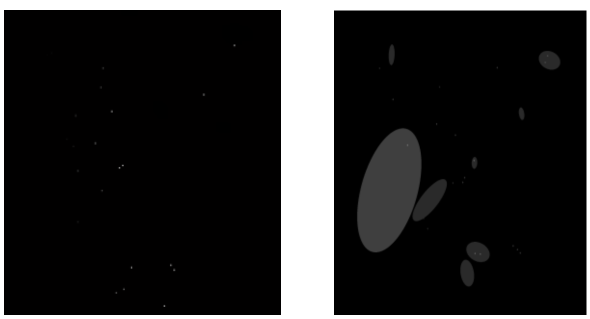
The nearest neighbor rule attempts to estimate the *posterior* probabilities from labeled training samples. A large value of k is desirable to obtain reliable estimates. But only when all of the k nearest neighbors are close enough to the query sample, its *posteriori* probability can be approximated by the majority labels of its neighbors. Therefore, a compromise has to be made so that the value of k accounts for only a small fraction of the training samples. Fig. 5. (a) shows knn classifier output in which white dots represent microaneurysm location. Fig. 5. (b) shows the ground truth in which white/gray dots and ovals represent microaneurysm location



(a) **(b)**

Fig. 5. (a) Classifier output; (b) Ground truth.

III. CONCLUSION

A method for the detection of microaneurysms on retinal images has been presented here, which is based on the principle of analyzing texture features on the segmented results of the pre-processed image. The number of pixels to be processed is significantly reduced by only considering the segmented results for feature extraction and classification. There are two major modules in this work, one that performs image segmentation which is considered as the candidate extraction step and other one that performs knn classification on feature set obtained using GLCM, wavelet and first order statistics. Segmentation of microaneurysm is done by using Fuzzy C-Means (FCM) clustering algorithm. Different pre-processing techniques like gamma correction, green channel extraction and AHE has been applied to improve the contrast of the input image which reduces the missing out of true microaneurysms thereby increasing the true positive rate. Removal of blood vessels and other regions which are larger in size reduces the false positives that come from those regions.

The proposed method achieved a sensitivity of 83% at 5 false positives per image.

IV. FURTHER WORK

The method could probably be extended for the detection of other abnormalities like hemorrhage, exudates etc. The method could also be used for the detection of optic disc and blood vessels. Other classifiers would be used to increase the sensitivity of the method.

REFERENCES

[1] C. E. Baudoin, B. J. Lay, and J. C. Klein, "Automatic detection of MicroAneurysms in diabetic fluorescein angiographies" , Rev. Epidemiol Sante Publique, vol. 32, pp. 254–261, 1984.

[2] T. Spencer, J.A. Olson, K.C.McHardy, P.F.Sharp, and J. V.Forrester, "An image processing strategy for the segmentation and quantification of MicroAneurysms in fluorescein angiograms of the ocular fundus " ,Computer Biomedical Research, vol. 29, pp. 284–302, May 1996.

[3] M. Cree, J. Olson, K. McHardy, P. Sharp and J. Forrester, " A fully automated comparative microaneurysm digital detection system," *Eye*, vol.11, pp. 622–628, 1997.

[4] J. Hipwell, F. Strachant, J. Olson, K. McHardy, P. Sharp, and J. Forrester, "Automated detection of microaneurysms in digital red-free photographs : a diabetic retinopathy screening tool, " Diabetic Medicine, vol. 17, pp. 588–594, 2000.

[5] D. Usher, M. Dumskyj and M. Himaga "Automated Detection of Diabetic Retinopathy in Digital Retinal Images: A Tool for Diabetic Retinopathy Screening" Diabetic Medicine. 21 (2002) 84–90.

[6] C.Sinthanayothin , J.Boycen and T.H.Williamson "Automated Detection of Diabetic Retinopathy on Digital Fundus Image" Diabetic Medicine. 19 (2002) 105–112.

[7] Lee Streeter et al, "MicroAneurysm Detection in Colour Fundus Images", Image and Vision Computing NZ. Palmerston North, November 2003.

[8] Niemeijer et al, " Automatic Detection of Red Lesions in Digital Color Fundus Photographs ", IEEE transactions on medical imaging, vol. 24, no. 5, may 2005.

[9] A. D. Fleming, S. Philip, and K. A. Goatman, "Automated MicroAneurysm detection using local contrast normalization and local vessel detection," IEEE Transactions Medical Imaging, vol. 25, no. 9, pp. 1223–1232, Sep. 2006.

[10] T. Walter, P. Massin, A. Arginay, R. Ordonez, C. Jeulin, and J. C. Klein, "Automatic detection of microaneurysms in color fundus images," Med. Image Anal., vol. 11, pp. 555–566, 2007.

[11] G. Quellec, M. Lamard, P. Josselin, G. Cazuguel, B. Cochener, and C. Roux,"Optimal wavelet transform for the detection of MicroAneurysms in retina photographs," IEEE Transactions Medical Imaging, vol. 27, no. 9, pp. 1230–1241, Sep. 2008.

[12] Ke Huang and Selin Aviyente, Member,IEEE,Wavelet Feature Selection for Image Classification. IEEE Transactions On Image Processing, Vol. 17, No. 9, September 2008.

[13] Akara Sopharak , Bunyarit Uyyanonvara and Sarah Barman "Automatic Exudate Detection from Non-dilated Diabetic Retinopathy Retinal Images Using Fuzzy C-means Clustering. Journal of Sensors / 2009. ISSN 1424 - 8220. www.mdpi.com/journal/sensors.

[14] A. Mizutani, C. Muramatsu, Y. Hatanaka, S. Suemori, T. Hara, and H. Fujita, "Automated MicroAneurysm detection method based on double ring filter in retinal fundus images," in Proc. SPIE Medical Imaging 2009. Computer.-Aided Diagnosis, 2009, vol. 72601N.

[15] Luca Giancardo, Fabrice Meriaudeau, Thomas P. Karnowski, Kenneth W. Tobin, Yaqin Li and Edward Chaum, M.D "MicroAneurysms Detection with the Radon Cliff Operator in Retinal Fundus Images", in Proc. of SPIE Medical Imaging 2010 ,Image processing , 2010,Vol. 7623, 76230U.

[16] B. Zhang, X. Wu, J. You, Q. Li, and F. Karray, "Detection of MicroAneurysms using multi scale correlation coefficients," Pattern Recognition, vol. 43, no. 6, pp. 2237–2248, 2010.

[17] K. Ram, G. D. Joshi, and J. Sivaswamy, "A successive clutter-rejection- based approach for early detection of Diabetic Retinopathy," IEEE transactions on Biomedical Engineering, vol. 58, no. 3, pp. 664–673, Mar. 2011.

[18] Sopharak et al, "Automatic MicroAneurysm Detection from Non-dilated Diabetic Retinopathy Retinal Images Using Mathematical Morphology Methods", IAENG International Journal of Computer Science, 38:3, IJCS_38_3_15, Aug.2011.

[19] Antal and A. Hajdu, "An ensemble-based system for MicroAneurysm detection and Diabetic Retinopathy grading," IEEE transactions on Biomedical Engineering, vol. 59, no.6, pp. 1720–1726, Jun. 2012.

[20] Adal et al ," Automated Detection of Microaneurysms Using Robust Blob Descriptors" SPIE Medical Imaging – Computer-Aided Diagnosis, Feb 2013.

[21] Istvan Lazar and Andras Hajdu, "Retinal MicroAneurysm Detection Through Local Rotating Cross-Section Profile Analysis" IEEE transactions on medical imaging, vol.32, no. 2, February 2013.

[22] Li Tang et al, "Splat Feature Classification With Application to Retinal Hemorrhage Detection in Fundus Images" IEEE transactions on medical imaging, vol. 32, no. 2, February 2013

[23] DIARETDB1 Database, http://www2.it.lut.fi/project/imageret/diaretdb1/