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System for Diagnosis of Diabetic Retinopathy using Neural Network

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Abstract: ***The main cause of blindness for the working age population in western countries is Diabetic Retinopathy - a complication of diabetes mellitus - is a severe and wide- spread eye disease. Digital color fundus images are becoming increasingly important for the diagnosis of Diabetic Retinopathy. In order to facilitate and improve diagnosis in different ways, this fact opens the possibility of applying image processing techniques. An algorithm able to automatically detect the microaneurysms in fundus image captured is a necessary preprocessing step for a correct diagnosis as microaneurysms are earliest sign of DR. The key for low cost widespread screening is a system usable by operators with little training. Some methods that address this problem can be found in the literature but they have some drawbacks like accuracy or speed. The aim of this thesis is to develop and test a new method for detecting the microaneurysms in retina images. To do so preprocessing, gray level 2D feature based vessel extraction is done using neural network by using extra neurons\ which is evaluated on DRIVE database which is superior than rule based methods. Morphological opening and image enhancement are performed to identify microaneurysms in an image. The complete algorithm is developed by using a MATLAB implementation and the diagnosis in an image can be estimated with the better accuracy and in shorter time than previous techniques.***

Index Terms: ***Contra storm aviation, fundus, microaneurysms, retina, pixel classification, retina.***

I. INTRODUCTION

In medical imaging an accurate diagnosis is dependent on two factors. The first factor is the successful acquisition of the image; the second factor is the successful interpretation of the image. Computers have arguably a huge impact on the acquisition of medical images. Most of modern medical imaging would not exist without them. They control imaging hardware, perform reconstruction and postprocessing of the image data and store the scans. In contrast, the role of computers in the interpretation of medical images has so far been limited. Interpretation remains an almost exclusively human domain. In recent years this has started to change. Applications are being developed in which a computer interprets an image to aid a physician in detecting possibly subtle abnormalities.

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The way in which the computer helps the physician is similar to how a spell-checker helps a writer correct a text. A spell-checker indicates words or grammar it suspects to be incorrect.

This may or may not be the case and the human operator, the writer in this case, either accepts or rejects the machine's suggestions. A similar process can be used for medical image analysis. The computer indicates places in the image that require extra attention from the physician because they could be abnormal. These technologies are called Computer Aided Diagnosis (CAD). The most established CAD application is the early detection of breast cancer using automated analysis of mammograms (x-rays of the breast). Several commercial products, approved by regulatory authorities, are available on the market. Other emerging CAD applications are the automatic detection of polyps in the large intestine and automatic lung nodule detection.

II. SCREENING OF DIABETIC RETINOPATHY

Early detection of diabetic retinopathy is critical for successful treatment. Screening can help to enable this early detection. Studies have shown that people who suffer from diabetes benefit from regularly attending a screening session . In this screening session the retinas of both eyes are examined by an ophthalmologist and if diabetic retinopathy is detected the patient can be followed. Regular monitoring continues until the ophthalmologist decides treatment is necessary. In addition to direct examination by an ophthalmologist, the retina can also be indirectly examined using (digital) photographs. The ophthalmoscope used for direct examination is a small and portable instrument comprised of a light source and a set of lenses which allows a person to view the retina. The digital fundus camera is a normal CCD based digital camera with special optics that can be used to make color photographs of the retina. The pupil is narrow and does not allow much light to enter the eye. To facilitate imaging the pupil can be widened by lowering the ambient light intensity, performing mydriasis (administration of pupil widening eye drops) or both these things. With modern fundus cameras, however, mydriasis is not needed in the majority of cases. Fundus photography is the preferred medium for large scale screening. Digital fundus photography specifically has the advantage that is is cheaper than regular photography. It allows instantaneous examination of the retina when necessary, quick storage and access of the images and decoupling of the acquisition and interpretation stages of the screening. The images can be acquired anywhere, but read at a central, specialized institution.

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In this project, a large population is screened in family care physician' soffices or family physician laboratories. Images are acquired on site and are sent over the internet to a central server. A trained reader specialized in diabetic retinopathy will log into this server and grade the images. Patients that need to see an ophthalmologist or need to attend the screening more frequently are notified by email.

Such a telemedicine screening program lends itself especially well to the use of CAD technology. A computer could be used to make a selection of the images stored on the central server. Possibly suspect images (patients) could be shown to the ophthalmologist while certainly normal images could be stored immediately. This could potentially lower the total workload of the ophthalmologists. The computer would not have to make a complete diagnosis but just determine whether an image is normal or abnormal. The techniques described in this thesis are aimed at enabling the use of CAD technology for such a pre-selection of retinal images in diabetic retinopathy screening.

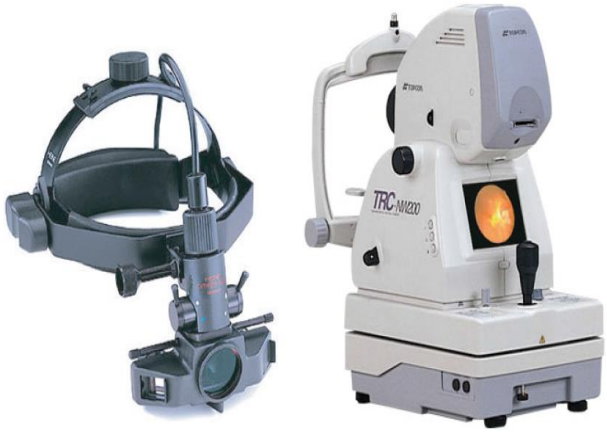

Fig.1. An indirect ophthalmoscope manufactured by Heine OptotechnikGmbH & Co., Herrsching, Germany. (b) A modern digital fundus camera manufactured by Topcon Corporation, Tokyo, Japan.

III. LITERATURE REVIEW

The literature review can be divided in two types based on the segmentation of blood vessel and the detection of the microaneurysms in the fundus image of the retina. First, the blood vessel network, is ubiquitous to all retinal images and can provide a wealth of health and disease information. The second, microaneurysms, is a lesion particularly associated with diabetic retinopathy – a disease of the retina resulting from diabetes. This is polished off with some more recent and sophisticated techniques in wavelet and fractal analysis of the vessel network. First we will consider the literature based on blood vessel segmentation. Many methods for retinal vessel segmentation have been reported. These can be divided into two groups: rule-based methods and supervised methods. In the first group, methods like vessel tracking, mathematical morphology, matched filtering, model-based locally adaptive thresholding or deformable models are used for vessel segmentation. On the other hand, supervised methods are those based on pixel classification (implementing some kind of classifier). Supervised methods are based on pixel classification, which consists on classifying each pixel into two classes, vessel and non-vessel. Classifiers are trained by supervised learning with data from manually-labeled images. Gardner et al. [1] proposed a back propagation multilayer neural network (NN) for vascular tree segmentation. After histogram equalization, smoothing and edge detection, the image was divided into 20 × 20 pixel squares (400 input neurons). The NN was then fed with the values of these pixel windows for classifying each pixel into vessel or not. Each pixel in the image was classified by using the first principal component, and the edge strength values from a 10 × 10 pixel subimage centered on the pixel under evaluation, as input data. Niemeijer et al. [2] implemented a K-nearest neighbor (kNN) classifier. A 31-component pixel feature vector was constructed with the Gaussian and its derivatives up to order 2 at 5 different scales, augmented with the gray-level from the green channel of the original image. The assumption that vessels are elongated structures is the basis for the supervised ridge-based vessel detection method presented by Staal et al. [3]. Ridges were extracted from the image and used as primitives to form line elements. Each pixel was then assigned to its nearest line element, the image thus being partitioned into patches. For every pixel, 27 features were firstly computed and those obtaining the best class separability were finally selected. Feature vectors were classified by using a kNN-classifier and sequential forward feature selection. Soares et al. [4] used a Gaussian mixture model Bayesian classifier. Multiscale analysis was performed on the image by using the Gabor wavelet transform. The gray-level of the inverted green channel and the maximum Gabor transform response over angles at four different scales were considered as pixel features. Finally, Ricci and Pefetti [5] used a support vector machine (SVM) for pixel classification as vessel or nonvessel. They used two orthogonal line detectors along with the gray-level of the target pixel to construct the feature vector.

IV. MATERIALS

To evaluate the vessel segmentation methodology two publicly available retinal databases called DRIVE (Staal et al., 2004) and STARE (Hoover et al., 2000) are used for testing the retinal vessel segmentation method and Messidor standard database is used for testing microaneurysms detection. These databases have been widely used by other researchers to test their vessel segmentation methodologies since, apart from being public, they provide manual segmentations for performance evaluation. The details of these databases are as follows.

A. STARE Database

There are twenty retinal fundus slides and their ground truth images in the STARE (Structured Analysis of Retina) database comprises 20 eye-fundus color images (ten of them contain pathology) captured with a Top Con TRV-50 fundus camera at 35 FOV. The images were digitalized to 700 × 605 pixels, 8 bits per color channel and are available in PPM format. The database contains two sets of manual segmentations made by two different observers. Performance is computed with the segmentations of the first observer as ground truth. Figure 3.1 shows an example of an image from the database.

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B. DRIVE Database

The second image database is referred as the DRIVE (Digital Retinal Images for Vessel Extraction). The DRIVE database comprises 40 eye-fundus color images (seven of which present pathology) taken with a Canon CR5 nonmydriatic 3CCD camera with a 45 field-of-view (FOV). Each image was captured at 768 × 584 pixels, 8 bits per color plane and, in spite of being offered in LZW compressed TIFF format, they were originally saved in JPEG format. The database is divided into two sets: a test set and a training set, each of them containing 20 images. The test set provides the corresponding FOV masks for the images, which are circular (approximated diameter of 540 pixels) and two manual segmentations generated by two different specialists for each image. The selection of the first observer is accepted as ground truth and used for algorithm performance evaluation in literature. The training set also includes the FOV masks for the images and a set of manual segmentations made by the first observer.

C. Messidor Database

The Messidor database has been established to facilitate studies on computer-assisted diagnoses of diabetic retinopathy. The research community is invited to test their algorithm on this database. On this page, you will find instructions on how to download the database. The 1200 eye fundus color numerical images of the posterior pole for the MESSIDOR database were acquired by 3 ophthalmologic departments using a color video 3CCD camera on a Topcon TRC NW6 non-mydriatic retinograph with a 45 degree field of view. The images were captured using 8 bits per color plane at 1440 × 960, 2240 × 1488 or 2304 × 1536 pixels. 800 images were acquired with pupil dilation (one drop of Tropicamide at 0.5%) and 400 without dilation. The 1200 images are packaged in 3 sets, one per ophthalmologic department. Each set is divided into 4 zipped sub sets containing each 100 images in TIFF format and an Excel file with medical diagnoses for each image. Two diagnoses have been provided by the medical experts for each image, Retinopathy grade and Risk of macular edema.

Retinopathy Grade: - 0 (Normal): (μA = 0) AND (H = 0)

- 1 : (0 < μA <= 5) AND (H = 0)

- 2 : ((5 < μA < 15) OR (0 < H < 5)) AND (NV = 0)

- 3 : (μA >= 15) OR (H >=5) OR (NV = 1)

μA: Number of microaneurysms
H: Number of hemorrhages
NV = 1: neovascularization and NV = 0: no neovascularization

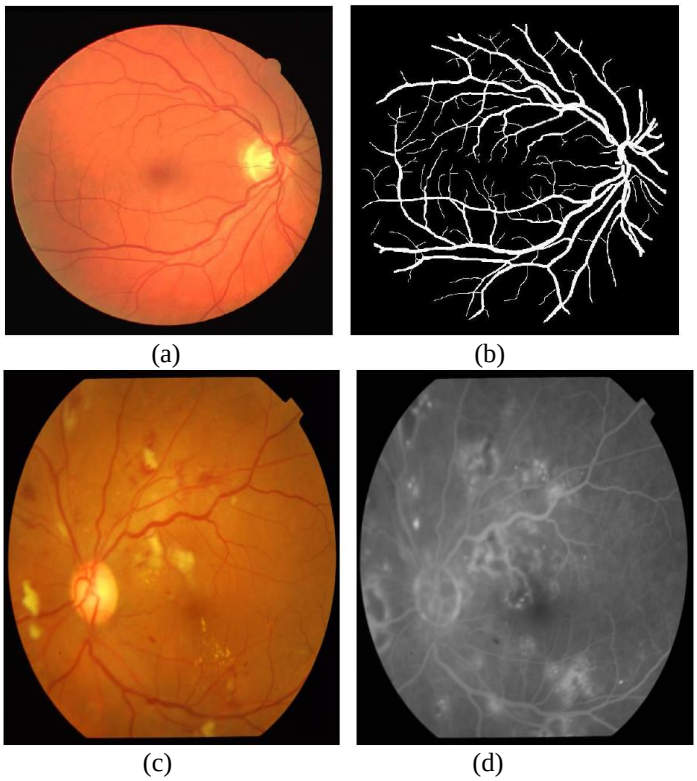

Fig.2. Example of Fundus Image from different Database (a) Retinal image from DRIVE database, (b) hand labeled ground truth vessel segmentation, (c) Retinal image of patient, (d) fundus fluorescence angiography of same patient.

D. Private Database

The private database is collected from the expert ophthalmologist Dr. Ashish Sapkal in which fundus photographs of retina along with fundus fluorescence angiography of the same image of several patients is provided. The color fundus image are having the resolution of 1936 × 1296 pixels, 8 bit per color channel and are available in Tiff format captured with TRC Topcon 50CCD non-mydriatic Camera.

V. FUNDUS MASK DETECTION

The mask is a binary image with the same resolution as that of fundus image whose positive pixels correspond to the foreground area. It is important to separate the fundus from its background so that the further processing is only performed for the fundus and not interfered by pixels belonging to the background. In a fundus mask, pixels belonging to the fundus are marked with ones and the background of the fundus with zeros. The fundus can be easily separated from the background by converting the original fundus image from the RGB to HSI colour system where a separate channel is used to represent the intensity values of the image. The intensity channel image is thresholded by a low threshold value as the background pixels are typically significantly darker than the fundus pixels. A median filter of size 5 × 5 is used to remove any noise from the created fundus mask and the edge pixels are removed by morphological opening with a square structuring element of size 5 × 5.

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After that the mask is obtained by extracting the pixels having the values greater than 0 over the range of 0 – 255 and then FOV is obtained by multiplying the mask image with greatest pixel value i.e. 255. Color fundus images often show important lighting variations, poor contrast and noise. In order to reduce these imperfections and generate images more suitable for extracting the pixel features demanded in the classification step, a preprocessing comprising the following steps is applied: 1) vessel central light reflex removal, 2) background homogenization, and 3) vessel enhancement. Next, a description of the procedure, illustrated through its application to a DRIVE database fundus image is detailed.

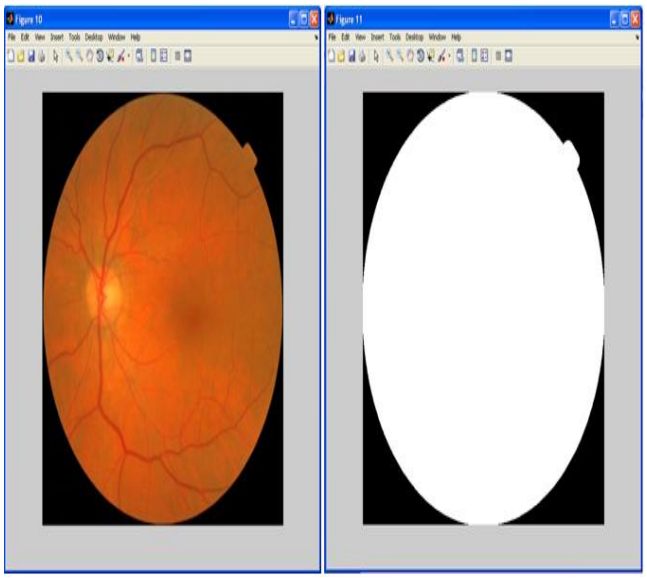

Fig.3.Automatic fundus mask generation. (a) Input image (b) Automatically generated fundus mask.

VI. CLASSIFICATION

In the feature extraction stage, each pixel from a fundus image is characterized by a vector in a 2-D feature space

$$F(x,y) = \{ F1(x,y), F2(x,y)\} \quad (1)$$

Now, a classification procedure assigns one of the classes C1 (vessel) or C2 (nonvessel) to each candidate pixel when its representation is known. In order to select a suitable classifier, the distribution of the training set data (described below) in the feature space was analyzed. The results of this analysis showed that the class linear separability grade was not high enough for the accuracy level required for vasculature segmentation in retinal images. Therefore, the use of a non linear classifier was necessary. The following nonlinear classifiers can be found in the existing literature on this topic: the neural networks [6], kNN method [7], Bayesian classifier [8], or support vector machines [9]. A multilayer feed forward NN was selected in this work. Two classification stages can be distinguished: a design stage, in which the NN configuration is decided and the NN is trained, and an application stage, in which the trained NN is used to classify each pixel as vessel or non vessel to obtain a vessel binary image.

A. Neural Network Design

Multilayer perceptrons are feedforward nets with one or more layers, called hidden layers, of neural cells, called hidden neurons, between the input and output layers. The learning process of MLPs is conducted with the error back-propagation learning algorithm derived from the generalized delta rule (Rumelhart et al., 1986). According to Lippmann (1987), no more than three layers of neurons are required to form arbitrarily complex decision regions in the hyperspace spanned by the input patterns. By using the sigmoidal nonlinearities and the decision rule in selecting the largest output, the decision regions are typically bounded by smooth curves instead of line segments. If training data are sufficiently provided, an MLP can be trained to discriminate input patterns successfully. A discussion on limits of the number of hidden neurons in multilayer perceptrons can be found in Huang and Huang (1991). A multilayer feedforward network, consisting of an input layer, three hidden layers and an output layer, is adopted in this paper. The input layer is composed by a number of neuron equal to the dimension of the feature vector (two neurons). Regarding the hidden layers, several topologies with different numbers of neurons were tested. A number of two hidden layers, each containing 6 and 3 neurons, provided optimal NN configuration. The output layer contains a single neuron and is attached, as the remainder units, to a nonlinear logistic sigmoid activation function, so its output ranges between 0 and 1. This choice was grounded on the fact of interpreting NN output as posterior probabilities. The training set, ST, is composed of a set of N candidates for which the feature vector , and the classification result (C1 or C2 : vessel or nonvessel) are known

$$ST = \{ F(n), Ck(n) \quad n = 1,2\ldots,N; K\epsilon\{1,2\}\} \quad (2)$$

The samples forming were collected from manually labeled non vessel and vessel pixels in the DRIVE training images. Specifically, around 48,000 pixel samples, fairly divided into vessel and non-vessel pixels, were used. Unlike other author [9], who selected their training set by random pixel-sample extraction from available manual segmentations of DRIVE and STARE images, we produced our own training set by hand.1 As discussed in literature, gold-standard images may contain errors due to the considerable difficulty involved by the creation of these handmade images. To reduce the risk of introducing errors in and, therefore, of introducing noise in the NN, we opted for carefully selecting specific training samples covering all possible vessel, background, and noise patterns. Moreover, it should be pointed out that the network trained with the just defined , in spite of taking information from DRIVE images only, was applied to compute method performance with DRIVE databases.Once is established, NN is trained by adjusting the weights of the connections through error interpretation. The back-propagation training algorithm was used with this purpose.

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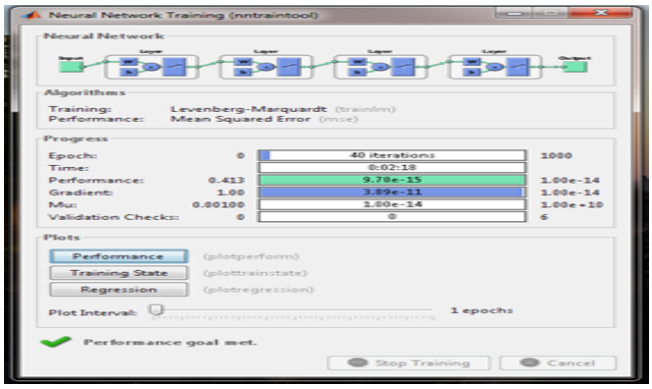

Fig.4. Training of Nueral Network

B. Neural Network Application

At this stage, the trained NN is applied to an "unseen" fundus image to generate a binary image in which blood vessels are identified from retinal background: pixels' mathematical descriptions are individually passed through the NN. In our case, the NN input units receive the set of features provided. Since a logistic sigmoidal activation function was selected for the single neuron of the output layer, the NN decision determines a classification value between 0 and 1. Thus, a vessel probability map indicating the probability for the pixel to be part of a vessel is produced. Illustratively, the resultant probability map corresponding to a DRIVE database fundus image. The bright pixels in this image indicate higher probability of being vessel pixel. In order to obtain a vessel binary segmentation, a thresholding scheme on the probability map is used to decide whether a particular pixel is part of a vessel or not. Therefore, the classification procedure assigns one of the classes C1 (vessel) or C2 (nonvessel) to each candidate pixel, depending on if its associated probability is greater than a threshold Th. Thus, a classification output image ICO, is obtained by associating classes C1 and C2 to the gray level values 255 and 0, respectively. Mathematically

$$ICO = \begin{cases} 255\ (= C1), & \text{if } p(C1|F(x,y)) \geq Th \\ 0\ (= C2), & \text{otherwise} \end{cases} \quad (3)$$

where $p(C1|F(x,y))$ denotes the probability of a pixel (x,y) described by feature vector $F(x,y)$ to belong to class C1. The optimum value of *Th* is selected as 80.

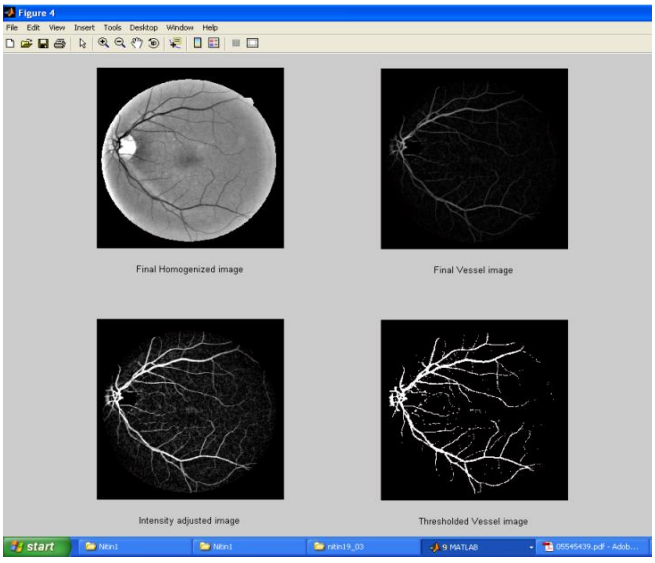

Fig.5. Output of Vessel Segmentation Method

C. Methodology for Microaneurysms Detection

Diabetic retinopathy (DR) is a progressive disease that results in eye-sight loss or even blindness if not treated. Pre-proliferative diabetic retinopathy (loosely DR that is not immediately threatening eye-sight loss) is characterized by a number of clinical symptoms, including microaneurysms (small round outgrowths from capillaries that appear as small round red dots less than 125 µm in diameter in color retinal images), dot-haemorrhages (which are often indistinguishable from microaneurysms), exudate (fatty lipid deposits that appear as yellow irregular patches with sharp edges often organized in clusters) and haemorrhage (clotting of leaked blood into the retinal tissue). These symptoms are more serious if located near the centre of the macula. For microaneurysms detection we consider the output of vessel segmentation process i.e. IVE and after that the intensity of the image is adjusted such that intensity values in grayscale image IVE to new values in intensity adjusted image, IAI such that 1% of data is saturated at low and high intensities of Ive. This increases the contrast of the output image IAI. In addition to this it will also enhance microaneurysms structure which were difficult to identify in the vessel enhance image, IVE. In order to identify microaneurysms the morphological opening of the intensity adjusted image is done. For that the disk type structuring element with radius of 2 and the 4-neighbor hood connectivity is selected. Since microaneurysms are basically small round dots. So that they can fit into the structuring element but vessel and other retinal artifacts have irregular shape hence they cannot fit into the structuring element. Since morphological opening removes the structures which are smaller than the structuring element. Hence the microaneurysms get removed from the intensity adjusted image leaving only vessels and other retinal artifacts. After that the morphological opened intensity adjusted image, IMO is substracted from the original image IAI. So that major vessel and retinal artifacts gets removed from the intensity adjusted image leaving only microaneurysms and tiny retinal vessels as shown in fig 4.10.

$$IMD = IAI - IMO \quad (4)$$

So from the observation of the morphological opened intensity adjusted image, IMO and the difference image IMD , microaneurysms get visible.

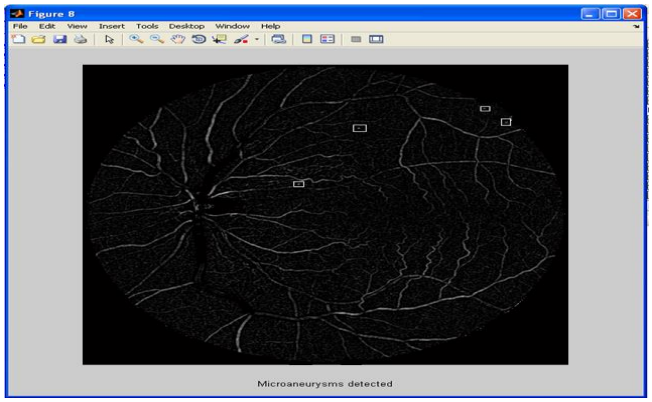

Fig.5. Difference Image I_{MD}

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VII. CONCLUSION

Automated analysis of retinal images is an ongoing active field of research. Since there are large number of diabetic patients yet not screened are under the danger of vision degradation or loss. In this research work some of the simpler and some of the more recent analytical tools bought to analyse retinal images have been discussed. We have seen that standard image processing techniques that may be found in any good text on general image processing can go a long way to detecting certain features/lesions in retinal images and produce seemingly good results. The proposed algorithm is able to detect the microaneurysms from the fundus image without the need of doing fundus flourescene angiography and it is simple, flexible and robust. Vessel segmentation has been done using two pixel feature, still an appreciable accuracy is attained. The advantage of the proposed method is less computation time, so that an ophthalmologist can concentrate on more severe patients rather than testing every patient. With such a screening system a person with little training can able to do testing of patient so it is not necessary to have expert ophthalmologist. Since this system is able to detect microaneurysms at earliest stage there will be remarkable cost saving in treatment.

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