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Diagnosis System for Diabetic Retinopathy to Prevent Vision Loss

Siva Sundhara Raja DHANUSHKODI[1,*], and Vasuki MANIVANNAN[2]

[1] Department of Electronics & Communication, SACS MAVMM Engineering College, Madurai 625301, India.
[2] Department of Electronics & Communication, Velammal College of Engineering & Technology, Madurai 625009, India.
E-mail: ssrrvs@gmail.com (*)

* Author to whom correspondence should be addressed; Tel.: +91-98651 30941

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Abstract
Aim: Diabetic Retinopathy (DR) is one of the major problems of diabetic patients. The diabetic patient is not aware of any symptom until it is too late for effective treatment. It is the leading cause of blindness. Diabetic retinopathy results in retinal disorders that include Microaneurysms (MA), soft exudates, hard exudates and intra-retinal vascular abnormalities. *Methods*: Soft Computing Neural Networks are used to detect and diagnose lesions or abnormalities associated with diabetic retinopathy which facilitate the Ophthalmologists in accurate diagnosis and early treatment to prevent vision loss in diabetic patients. *Results*: The result shows that the methodology used is well suited for the early diagnosis of the diabetic retinopathy disease. *Conclusions*: By evaluating the exudates and fovea region, and analyzing the relation between them, the severity of DR can be easily identified to prevent vision loss in diabetic patients.

Keywords: Diabetic Retinopathy (DR); Microaneursym (MA); Exudates; fovea; diagnosis.

Introduction

Early detection and diagnosis of retinal fundus images for diabetic patients are necessary steps for the Diabetic Retinopathy treatment to prevent vision loss in diabetic patients. Diabetic Retinopathy causes retinal abnormalities in the form of Microaneurysms, hemorrhages and exudates. This paper proposes a new computer aided detection method for the exudates detection and fovea region detection in the retinal images and also describes the linear relationship between exudates and fovea for the diagnosing the Diabetic Retinopathy. Exudates are the blood clot of retinal blood vessels in the form of yellowish color lesion which may be formed in and around the fovea region due to damage in retinal blood vessels [1]. The present methods [1-6] are having high time cost and expansive process. In our proposed method, we present a computer aided approach for automatic exudates and fovea detection and diagnose for early treatment of Diabetic Retinopathy. Screening of diabetic patients for the development of diabetic retinopathy can potentially reduce the risk of blindness in these patients by 50%. This method used entropy theory in detecting the edges in gray level images. Computer based detection method has been proposed in [11]; so that this method can help to improve the diagnostic performance of clinicians in their image interpretations. The thick and thin retinal blood vessels are detected initially and intersection of this is used to find the approximate location of the optic disk and localized using color properties.

The exudates were indentified using fuzzy c-means clustering algorithm [1]. A set of initial features such as color, size, edge strength and texture were extracted to classify segmented regions into exudates and non exudates. A genetic based algorithm is used to rank these features. The selected feature vectors are then classified using a multilayer neural network classifier on 300 manually labeled retinal images which provided 96% sensitivity and 94.6% specificity.

In [2], the exudates present within the macular region of retinal image were found using morphological filtering techniques and watershed transformation. The algorithm was tested on a small image data base and was compared with the performance given by an ophthalmologist. The method achieved a sensitivity of 92.8% and mean predictive value of 92.4%.

Exudates lesions were identified and analyzed by Phillips et al. [3] using a global and local thresholding method. Before applying threshold on the retinal images, the image was enhanced. A set of only 14 images were used and this method achieved a sensitivity of 61% and specificity of 73%. This work did not analyze the exudates lesions detection based on accuracy. This paper mistakenly detected other bright lesions such as cotton wool spots which were similar in color to that of exudate lesions.

Wang et al. [4] applied the minimum distance discriminant classifier to identify and segment the exudates lesions and cotton wool spots in retinal images. The spherical color space model was used to extract the color features. But, these features failed to differentiate the exudates and cotton wool spots in the retinal images. This work accessed 92% sensitivity and 70% specificity based on a set of 150 images.

The recursive region growing technique based on selective threshold values was used by Sinthanayothin in [5] to detect the exudates lesions in retinal images. But in this work, the researcher failed to consider other bright lesions which were similar to the exudates. The researcher achieved 88.5% sensitivity and 99.7% specificity in detecting the exudates lesions. This work was performed using a small dataset comprising of 21 abnormal and 9 normal fundus images.

The exudate lesions were differentiated from other similar bright lesions such as cotton wool spots and Drusen in fundus images by Niemeijer et al. [6]. In this work, they have used probability map algorithm to classify the pixels as exudates or non exudate lesions. The pixels with highest probability were grouped as a cluster and finally each cluster were classified as either exudate or non exudate lesions. The researchers achieved 70% accuracy, 77% sensitivity and 88% specificity in detecting the exudate lesions against a set of 300 images.

The differentiable concavity algorithm is used to segment the retinal blood vessels by Benson SY Lam [8]. These concavity measures are combined together according to their statistical distributions to detect vessels in general retinal images. It achieved average accuracy of 94% for the detection of blood vessels with respect to ground truth images.

The system is based on extraction of image ridges, which coincide approximately with vessel centerlines by Joes Staal et al. [9]. The ridges are used to compose primitives in the form of line elements. For every pixel, feature vectors are computed that make use of properties of the patches and the line elements. The extracted feature vectors are classified using a KNN-classifier and sequential forward feature selection. The algorithm was tested on a database consisting of 40 manually labeled images.

Li et al. [10] used active shape model to extract the vasculature which was based on the location of the optic disc. The author achieved optimum accuracy for optic disc localization for 89 images. Hoover et al. [11] used fuzzy voting scheme to determine the optic disc location. The thinning methodology was used to segment the vasculature. The accuracy of 89% was achieved over 81 images.

Obviously, all the previous research works for exudate lesion detection were based only on gray level information and they were not applied on a large dataset of retinal images or they failed to provide optimum exudates detection for a huge number of retinal images. Moreover, these works were carried out only for the detection of exudates and merely calculated the values of Sensitivity and Specificity. In our research, we mainly focus not only in detection alone, but also go beyond in diagnosing, which provides a much higher level of accuracy in classification of the exudates to analyze the severity of Diabetic Retinopathy leading to vision loss.

Material and Method

To evaluate the performance of Diabetic Retinopathy, we are using two publicly available databases, DRIVE and STARE. Each database consists of a large number of retinal images under normal and abnormal pathologies. These databases have been widely used by other researchers to test their vessel segmentation methodologies since, apart from being public, they provide manually segmented images for our performance evaluation.

Dataset

We have made use of the publicly available database, DRIVE for our research work. This database consists of a large set of retinal images which includes both normal and abnormal images. Each retinal image was taken with a Canon CR5 non-mydriatic 3 CCD camera with a 45° field-of-view (FOV). All the retinal images in DRIVE were available in LZW compressed TIFF format, which were originally saved in JPEG format. We have accessed retinal images from this open source database and have used the same for training and testing. Each image has 1500×1150 pixels as image size with 24-bit color. Of the 128 images used in our dataset, 90 images are abnormal (contain pathologies such as exudates, cotton wool spots, microaneurysms and hemorrhages) and the rest of the images being normal. We have also used another dataset STARE, which comprises 20 retinal fundus color images captured with a TopCon 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.

Blood Vessel Segmentation

Morphological operations are employed to detect and segment the blood vessels from the retinal images. Initially, the fundus image is converted into three sub-channel bands as red, green and blue. The green color band has high pixel contrast for retinal blood vessels. The separated green band channel is dilated and eroded with the same structuring element of radius 3. Then, an absolute difference mapping image is formed by absolute subtraction of retinal image from the morphologically processed sub-band image as shown in Figure 1(a). The cumulative histogram is formed from this absolute difference mapping image. The new mapping threshold is derived from this estimated cumulative histogram. If the pixel value in absolute difference mapping image exceeds this mapping threshold, it is marked as blood vessel pixel. To confirm and correctly classify the blood vessel pixels, features are extracted, trained and classified using neural network classifier.

Feature Extraction

The Efficient Local Binary Pattern (ELBP), Law's features are extracted from the blood vessel segmented mapped image for better blood vessel classification results. These features are explained in the following sections.

Law's Texture feature. Laws' texture energy measures are based on convolution kernels and could be used to generate useful features for better training and classification. The blood vessel segmented mapping image is convolved with the Law's texture masks (25×25) in order to extract the energy feature set.

ELBP. The Efficient Local Binary Pattern (ELBP) features are extracted from the morphologically blood vessel segmented image. It can be computed as follows:

$$\mathrm{ELBP} = \sum_{p=1}^{8} 2^{p} \cdot \mathrm{M}(\mathrm{I_N} - \mathrm{I_C}) \tag{1}$$

where, I_N denotes the neighboring pixel in a square window(3×3), I_C is the center pixel in the square window, 'p' denotes number of neighboring pixels around center pixel noted as 8 in 3×3 square window, 'M' denotes specific function and $M(I_N - I_C)$ is marked as the threshold value and it is estimated as,

$$M(I_N - I_C) = \begin{cases} 1, & \text{if } I_N - I_C \geq 0 \\ 0, & \text{if } I_N - I_C < 0 \end{cases} \quad (2)$$

This ELBP should contain at least 2 transitions (0 to 1) and (1 to 0). If it satisfies this condition then we replace the center pixel with its equivalent decimal value else the center pixel is considered as 0.

Neural Network Classification

The extracted features are trained and the given retinal images are classified in accordance with the trained values by feed forward back propagation neural networks. The preferred neural network has two inputs, a single output layer and two hidden layers. The input layer has the neurons which are equal to the length of the derived feature vector. We have 15 neurons in the middle hidden layer. The designed neural network classifies each pixel in the retinal image as blood vessel or non-blood vessel pixels as depicted in Figure 1(b).

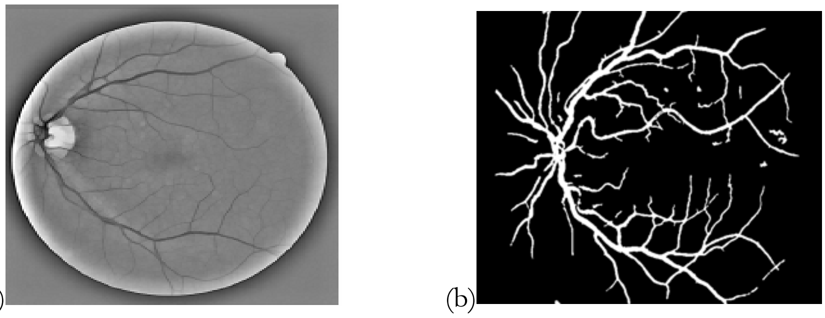


Figure 1. (a) Morphological Mapped Image, (b) Vessel Segmented Image

Optic Disc Segmentation

The detection of the optic disk in fundus images is a significant task because of its similarity in brightness, color and contrast with the exudates. The optic disc segmentation can be used to diagnose other diseases like Glaucoma. In this paper, the optic disc can be segmented in two stages; elimination of blood vessels from the retina image and constructing the optic disc contour. The blood vessels are being removed by means of anisotropic diffusion filter. The contour points are identified using spline interpolation. However, the existence of blood vessels, especially within the optic disc region may cause misdetection of pixels belonging to blood vessels as optic disc contour points. Therefore, to overcome these drawbacks, here, in our proposed technique we have employed anisotropic diffusion filtering for accurate segmentation of the optic disc region. In the anisotropic diffusion filtering, firstly the blood vessel structures are being eliminated from optic disc region, secondly, the optic disc is accurately detected and segmented. The segmented optic disc proves to be accurate when compared with its ground truth image. The filtering method is as follows:

$$F(\nabla I) = \begin{cases} 1, & \text{for within the blood vessel structure} \\ \dfrac{1}{\left(1 + \dfrac{|\nabla I|^2}{K}\right)}, & \text{for outside the blood vessel structure} \end{cases} \quad (3)$$

where, $[\nabla I]$ is the parameter for the evaluation of blood vessel structures and K is the windowing parameter.

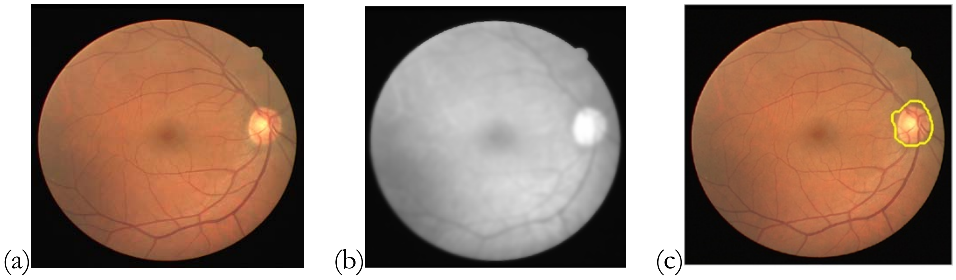


Figure 2. (a) Retinal image showing optic disc, (b) Anisotropic diffused image, and (c) Optic disc segmented image

Fovea Region Detection

The middle of the macula in the retina is known as Fovea. The fovea region detection is important for the analysis of Diabetic Retinopathy by determining the relationship between fovea region and exudates. For the detection of fovea region in the retina, the fundus image is transformed into 'Lab' Color model. This relationship is explained as,

$$L^* = 226 * k(y/b)-16 \tag{4}$$

$$a^* = 300[k(x/a)- k(y/b)] \tag{5}$$

$$b^* = 100[k(x/a)-k(z/c)] \tag{6}$$

where, *a, b* and *c* are the tristimulus values of the reference white point. L channel image is used as an input image. After this transformation, contrast limited adaptive histogram equalization is applied on this transformed image to enhance the contrast of the retinal fundus image. Fovea is the darkest black region in the retina image, hence, the pixel values below the threshold (60) will be marked as fovea region pixel by using morphological operation with a disc shaped structuring element of radius 3. These dark pixels are labeled and the largest value of the darker region is denoted as fovea region . The centroid point (x,y) of the fovea region is then estimated. By using this fovea centroid, a circle is drawn to mark the fovea region in the retinal image with a radius of 60 pixels.

Exudates Detection

The exudates detection is performed by using Kirsch's edge detector. The boundary of exudates' candidates is determined using 8-neighbour pixels only in different directions. This Kirsch's edge detector detects the higher pixel values of the exudates candidate than the existing Sobel and Canny edge detection methods.

Kirsch's Edges. The existing Canny and Sobel edge detectors find the interior edge boundary of the exudates candidate lesions in the retinal images. The detection of outlier edge boundary of exudates lesions by these edge detection methods is unsuccessful. Therefore, the interior and outlier edge boundaries of the exudates lesions are detected and determined by Kirsch's edge detector [7]. This detector works in eight different directions on each pixel in the pre-processed retinal images and the values are tabulated in Table1. The kernel outputs are combined together by selecting the maximum value found on each pixel output. The result is stored in the final 'I_K' image. The average edge outputs of 'I_K' under each lesion cluster are calculated and assigned to the exudates lesion in its entirety.

Classification of Diabetic Retinopathy

The severity of diabetic retinopathy can be analyzed and classified as mild, moderate, and severe. The severity of DR is very useful for proper timely treatment of diabetic patients. For early detection of DR, there is a relation between fovea region and exudates count. If more number of exudates (more than 10% of fovea area) is formed in and around the fovea region, then it leads to

Severe DR which causes blindness. If the exudates cover 5 to 10% of the fovea region, then it leads to Moderate DR which causes starting of blindness. If exudates cover less than 5% of the fovea area, then it leads to Mild DR. Severity estimation of DR is shown in Table 2.

Table 1. Kirsch's Eight Directional Templates

Kirsch's edge Detector	Kirsch's Template	Kirsch's edge Detector	Kirsch's Template
H1	[5 -3 -3; 5 0 -3; 5 -3 -3]/15;	H5	[-3 -3 -3; -3 0 -3; 5 5 5]/15;
H2	[-3 -3 5; -3 0 5; -3 -3 5]/15;	H6	[5 5 5; -3 0 -3; -3 -3 -3]/15;
H3	[-3 -3 -3; -3 0 -3; 5 5 5]/15;	H7	[-3 -3 -3; -3 0 5; -3 5 5]/15;
H4	[5 5 5; -3 0 -3; -3 -3 -3]/15;	H8	[5 5 -3; 5 0 -3; -3 -3 -3]/15;

Table 2. Constraints for DR Classification

Classifications of DR	Conditions for DR Analysis
Severe DR	Exudates covered more than 10% of Fovea Area
Moderate DR	Exudates covered between 5% to 10% of Fovea Area
Mild DR	Exudates covered less than 5% of Fovea Area

Results

After the segmentation of fovea region and exudates lesion is done, we analyze the performance of our proposed technique which was exclusively designed for the prevention of vision loss in diabetic patients. This section describes the best and accurate technique to be applied for retinal image diagnosis.

Evaluation details of vessel segmentation

The proposed blood vessel segmentation algorithm have been applied for a set of 128 images available in DRIVE and STARE databases and the segmentation results were compared with their respective ground truth images given by specialized ophthalmologists.

The performance parameters obtained after the segmentation of blood vessel structures for a few set of images are tabulated and is given in Table 3. The same is graphically illustrated in Figure3.

To measure the performance of the proposed method for the detection of blood vessels on the fundus image, the proposed vessel segmentation method is compared to its corresponding ground truth images. The ground truth fundus images used for our experimentation were obtained from the publicly available DRIVE database.

The performance of vessel segmentation is analyzed with the following parameters:

- Sensitivity (Se=TP/(TP+FN))
- Specificity (Sp=TN/(TN+FP))
- Positive predictive value (Ppv=TP/(TP+FP))
- Negative predictive value (Npv=TN/(TN+FN))
- Accuracy (Acc=(TP+TN)/(TP+FN+TN+FP))

These parameters are evaluated and listed in Tables 2 and 6, where, TP denotes true positive, FP denotes false positive, FN is false negative and TN is true negative. True Positive refers to the correctly identified vessel pixels, True Negative refers to the wrongly identified vessel pixels, False Positive refers to the correctly identified background pixels and False Negative refers to the wrongly identified background pixels.

The entire algorithm was run on the DRIVE and STARE database and results for optic disk localization, fovea region detection, exudates detection and blood vessel segmentations were obtained. The MATLAB code takes 10 seconds per image on an average to run on a 2.1 GHz Intel Pentium Dual Core machine with 2GB of RAM.

Table 3. Blood Vessel Segmentation Results using Neural Networks

Images	Se	Sp	Ppv	Npv	Acc
1	0.6817	0.9408	0.4819	0.9734	0.9214
2	0.7482	0.8972	0.4196	0.9729	0.8838
3	0.7400	0.8983	0.3389	0.9800	0.8879
4	0.7074	0.9046	0.4929	0.9593	0.8818
5	0.5504	0.9404	0.4953	0.9517	0.9030
6	0.7672	0.8943	0.3984	0.9768	0.8837
7	0.6764	0.9225	0.4574	0.9672	0.9008
8	0.7658	0.8696	0.3887	0.9717	0.8595
9	0.7199	0.9273	0.4762	0.9730	0.9098
10	0.7291	0.9177	0.4298	0.9755	0.9029
Average	**0.708613**	**0.911275**	**0.437897**	**0.970153**	**0.893454**

Se=Sensitivity; Sp= Specificity; Ppv= Positive Predictive Value; Npv= Negative Predictive Value; Acc=Accuracy.

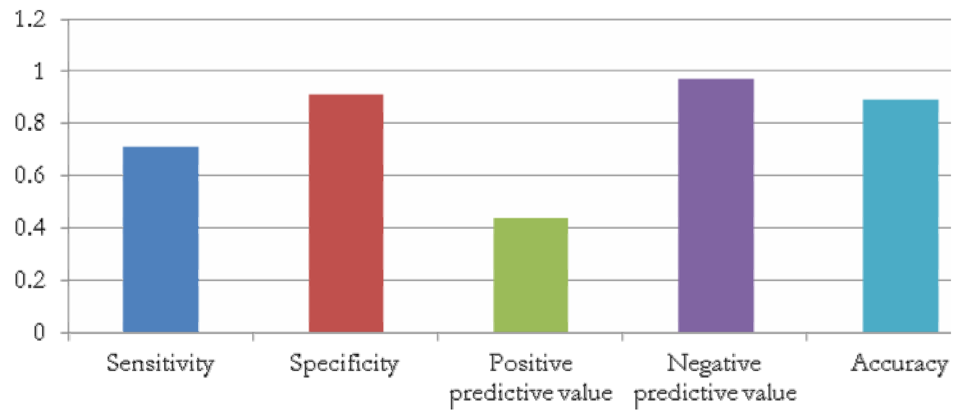


Figure 3. Graphical Representation of Performance Parameters of Blood Vessel Segmentation

Evaluation details of Fovea and Exudates detection

The proposed fovea region detection algorithm is applied for a set of 128 fundus images available in DRIVE and STARE databases. These images exhibit lesions or abnormalities caused by hyper tension, damaged blood vessels, etc. The Fovea detection method calculates the fovea pixels count in the retinal region and the proposed exudates detection method gives an estimation of the exudates pixels present in the retina.

Consequently, the retinal image is being segregated into four equal quarter regions. Next, the exudates pixel count in each of the divided region is computed and tabulated. Based on the exudates count present in the fovea region, the severity of DR is assessed which helps the ophthalmologists for the early treatment for the prevention of vision loss. These computed values are summarized in Tables 4-6 and the corresponding exudates lesion identified images (based on severity) are illustrated in Figure 5.

The parameters, Se and Sp define the ratio of well-classified vessel and non-vessel pixels, respectively. Ppv is the ratio of pixels classified as vessel pixels that are correctly classified. Npv is the ratio of pixels classified as background pixels that are correctly classified. Lastly, Acc is the ratio of total well-classified pixels. All these parameters help in defining the performance of our proposed technique as explained in the previous sections and are tabulated in Table 6. The same is illustrated graphically in Figure 4.

Table 4. Classifications of Diabetic Retinopathy

Image	No. of Fovea Pixels	Total No. of Exudates in Retina	Total no. of Exudates in Fovea Region	DR Classification
1	12187	3739	231	Mild DR
2	12187	553	0	No DR
3	12187	1123	293	Mild DR
4	12187	3345	771	Moderate DR
5	12187	3646	1708	Severe DR
6	12187	657	0	No DR
7	12187	44	0	No DR

Table 5. Hard and Soft Exudates Counts in four quarter regions

Image Sequences	Quarter Region I		Quarter Region II		Quarter Region III		Quarter Region IV	
	Hard	Soft	Hard	Soft	Hard	Soft	Hard	Soft
1	9	1	21	3	6	2	11	1
2	5	5	2	0	9	4	0	0
3	7	3	2	1	13	1	0	2
4	5	0	21	12	0	0	6	6
5	0	3	6	1	0	1	0	1

*Quarter region is formed by splitting the entire image in to 4 sub regions ($0-90^0$, 90^0-180^0, 180^0-270^0, 270^0-360^0).

Table 6. Performance of Exudates Detection on DRIVE and STARE Database

Database	Se	Sp	Ppv	Npv	Acc	SuccessRate
DRIVE	0.9871	0.9956	0.8891	0.9765	0.9867	0.9670
STARE	0.8897	0.8756	0.9978	0.9567	0.9712	0.9382

Se=Sensitivity; Sp= Specificity; Ppv= Positive Predictive Value; Npv= Negative Predictive Value; Acc=Accuracy.

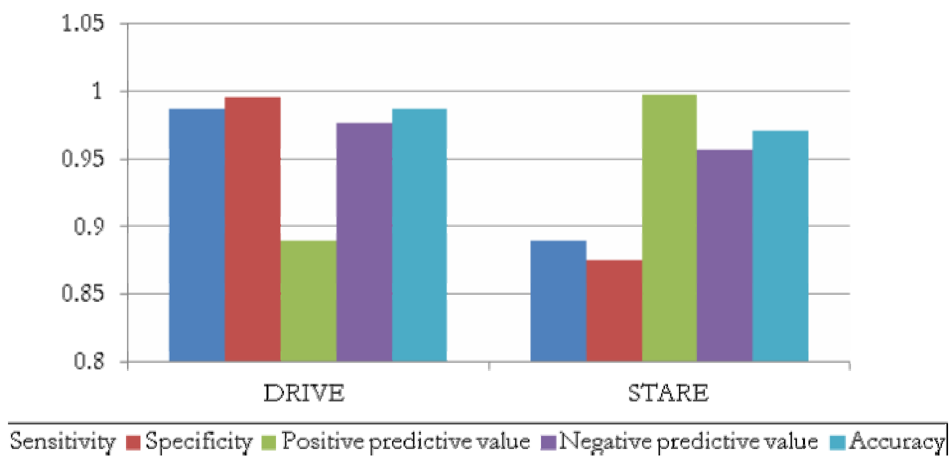
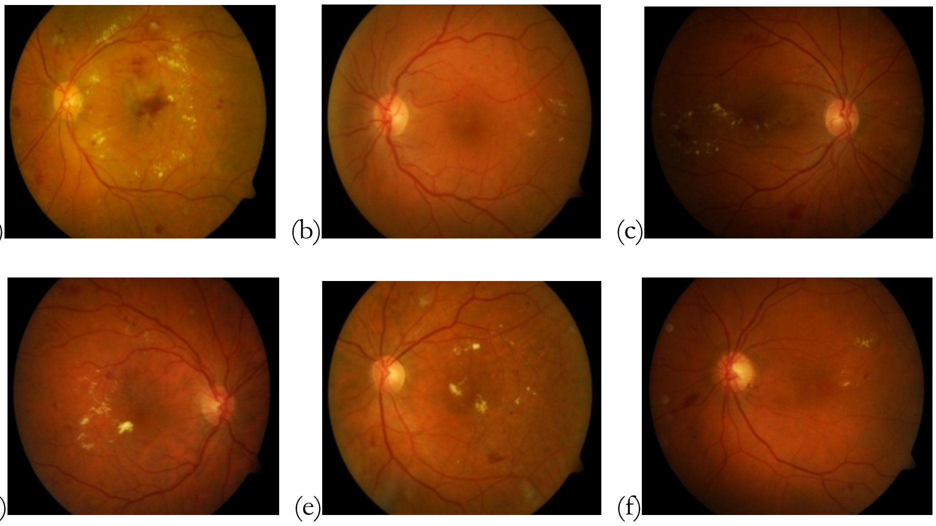


Figure 4. Graphical Representation of Performance Comparison of Exudates Detection



(a) (b) (c) (d) (e) (f)

Figure 5. Classifications of Diabetic Retinopathy. (a) Mild DR. (b) No DR. (c) Mild DR. (d) Moderate DR. (e) Severe DR. (f) No DR

Discussions

The conventional methods presently followed for blood vessel detection in retinal images are unsupervised learning and classification methodologies. This research proposes a method purely based on supervised learning and classification. This method is based on Anisotropic diffusion for detection and Neural Network for classification, with the feature vector representing each pixel composed of Effective Local Binary Pattern and Law's texture based features. Even though Law's texture features have been broadly applied for all the applications of detecting lesions and abnormalities in medical field, these features have never been applied for this type of framework.

The experiment mainly focuses to help ophthalmologists to study the severity of DR from the retinal conditions of the patients. This method provides a clear-cut decision making in selecting the type of treatment to be followed for every individual patient, thereby, reducing the time of decision making for initial treatment.

The reason for proposing a neural network based Diabetic Retinopathy severity detection and further diagnosis is to help ophthalmologists and physicians for effective clinical treatment. This also reduces the time for decision making in diagnosis and treatment. The experimental results prove that, neural network based blood vessel segmentation achieves a performance appraisal of 70% sensitivity, 91%specificity, 43% positive predictive value, 97% negative predictive value and 89% accuracy, which is clearly shown in Table 3. It is also found that, neural network based exudates detection achieves 98% sensitivity, 99% specificity, 88% positive predictive value, 97% negative predictive value and 98% accuracy for a set of retinal images available in DRIVE database with a success rate of 96.7%.

Similarly, the exudates detection applied for the retinal images in STARE database produced the following results: 88% sensitivity, 87% specificity, 99% positive predictive value, 95% negative predictive value and 97% accuracy with an average success rate of 93.8%.

These results have been clearly shown in Table 6 and Figure 4 for images in both the databases. The severity analysis of DR for various test images are shown in Figure 5. This proposed technique using neural networks helps in reducing the manual work time and reduces the risk of committing classification problems. This also helps in further diagnosis, clinical treatment and quicker remedy in surgical planning. Thus, this discussion helps in the classification of Diabetic Retinopathy-severity, proving that neural networks based segmentation performs well on retinal images.

Conclusions

In this paper, we have studied the abnormality for Diabetic Retinopathy. This proposed method can help the ophthalmologists to eliminate the blood vessels and optic disc, and to detect MAs and Exudates in Diabetic Retinopathy screening process. All of the results are evaluated with ground truth images obtained from expert ophthalmologists. The proposed method detected exudates with an average accuracy of 99.6% in the retinal fundus images. The result shows that, the methodology used is well suited for the early diagnosis of the Diabetic Retinopathy disease. By evaluating the exudates and fovea region, the severity of DR can be easily identified to prevent vision loss in the diabetic patients.

List of abbreviations

Diabetic Retinopathy (DR)
Efficient Local Binary Pattern (ELBP)
Microaneursym (MA)
Sensitivity (Se)
Specificity (Sp)
Positive Predictive Value (Ppv)
Negative Predictive Value (Npv)
Accuracy (Acc)
True Positive (TP)
False Positive (FP)
True Negative (TN)
False Negative (FN)
Field-of-view (FOV)
K (KNN)
L (LZW)
T (TIFF)
Joint Photographic Experts Group (JPEG)
P (PPM)
C Devices (CCD)

Conflict of Interest

The authors declare that they have no conflict of interest.

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References

1. Alireza O, Bita S, Richard M. A computational-intelligence-based approach for detection of exudates in diabetic retinopathy images. IEEE Trans Infor Tech Biomedicine 2009;13:535-45.
2. Thomas W, Jean-Claude K, Pascale M, Ali E. A contribution of image processing to the diagnosis of diabetic retinopathy-detection of exudates in color fundus images of the human retina. IEEE Trans Med Imag 2002;21:1236-41.

3. Phillips R, Forrester J, Sharp P. Automated detection and quantification of retinal exudates. Graefe's Arch Clin Exp Ophthalmol 1993;231:90-4.
4. Wang H, Hsu H, Goh K, Lee M. An effective approach to detect lesions in retinal images. IEEE Conf Comput Vis Pattern Recogn Proc. 2000:181-7.
5. Sinthanayothin C. Image Analysis for Automatic Diagnosis of Diabetic Retinopathy [PhD thesis]. King's College of London; 1999. [cited 2011 March 20] Available from: URL: http://ima.ac.uk/papers/al-hammadi_thesis.pdf, 2010.
6. Niemeijer M, Ginneken BV, Russell SR, Suttorp M, Abramoff MD. Automated detection and differentiation of drusen, exudates and cotton-wool spots in digital color fundus photographs for diabetic retinopathy diagnosis. Invest Ophthalmol Vis Sci 2007;48:2260-7.
7. Kirsch RA. Computer determination of the constituent structure of biological images. Computers and Biomedical Research 1971;4:315-28.
8. Lam BSY, Yongsheng G. General retinal vessel segmentation using regularization-based multiconcavity modeling. IEEE Trans Med Imag 2010;29:1369-80.
9. Staal J ,Abramoff MD, Niemeijer M, Viergever MA. Ridge-based vessel segmentation in color images of the retina. IEEE Trans Med Imag 2004;23:501-9.
10. Li H, Chutatape O. Automated feature extraction in color retinal images by a model based approach. IEEE Trans Biomed Eng 2004;51:246-54.
11. Hoover A, Goldbaum M. Locating the optic nerve in a retinal image using the fuzzy convergence of the blood vessels. IEEE Trans Med Imag 2003;22:951-8.