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Retinal blood vessel localization to expedite PDR diagnosis

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ABSTRACT

Ophthalmologist relies on the retinal fundus image segmentations for accurate diagnosis of Diabetic Retinopathy caused due to prolonged deterioration in retinal blood vessels. Blood vessel and optical disc localization determines the vascular alterations helpful in identifying retinal diseases with accurate identification of pathological symptoms. This work comprises evaluation of proposed Optical Disc Segmentation and blood vessel localization techniques followed by a statistical analysis using SPSS package to examine the statistical significance of the feature set utilized. Fractal dimensions explored are beneficial for Proliferative Diabetic Retinopathy (PDR) diagnosis as its value for vascular structures increases with increasing level of PDR. Two benchmark fundus image databases, DRIVE and STARE were evaluated for performance validation of proposed blood vessel localization approach and average accuracies of 96.79% and 95.68% were achieved for extracted blood vessels using the proposed approach.

Keywords: Blood Vessel Extraction, Diabetic Retinopathy, Fractal Dimension Analysis, Ophthalmic Image Processing, Optical Disc Segmentation

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1. Introduction

Retinal vascular analysis approach is widely being used in the modern era for eye related complexities like cardiovascular strokes [1], glaucoma, hypertension and Diabetic Retinopathy (DR), etc. Regular screening and diagnosis can reduce the chances of vision loss upto a large extent, although it needs precise automated blood vessel localization for Computer-Aided Diagnosis (CAD) systems. According to the statistical analysis done by International Diabetic Federation (IDF), there are 10 million adults suffering from diabetes and most of them are undiagnosed [2]. This prolonged situation of diabetes arises many other severities, out of which DR is the most common complication. DR and Glaucoma have become the leading cause of blindness among the people aged between 20-74 years [3]. PDR is the most severe complication arising in the DR patient and it is indicated by vascular bifurcations in retinal blood vessels. PDR generally occurs due to blood vessel overgrowth and these newly grown vessels are fragile and leaky which leaks out into the retinal area causing the severity. In the diagnosis of ophthalmic pathologies, segmentation and assessment of retinal blood vessel plays a very important role. Blood vessel segmentation proves beneficial for determining the branching pattern of blood vessels, their width, density, retinal vessel variability, etc. Thus there is a need for fast and accurate blood vessel segmentation algorithm for automated screening of DR blood vessel abnormalities. Some techniques reported in the literature for blood vessel segmentation require masking of vascular structures so as to ensure that the blood vessels are not misclassified as red lesions due to similarity in intensity [4, 5]. However some of the retinal vessel segmentation methods like line detector, template matching methods, etc. have achieved 92% of segmentation accuracy [6]. But the attempts to improve the segmentation accuracy above 92% while maintaining the low computational complexity is still a challenge to the researchers. The other important anatomical features in retinal fundus photographs are optical disc (OD) and the position of origin of blood vessels in the OD part. For the effectual diagnosis of retina related abnormalities, especially for the accurate identification of yellow (bright) lesions in the DR infected patients, OD detection and extraction is an important step. When subjected to uneven illumination along with the large

number of pathological abnormalities, it becomes more challenging to extract the OD portion having the shape and size similar to bright lesions (exudates) [7].

Various segmentation algorithms are accessed in [8], out of which the wavelet filter method was proved efficient for distinguishing retinal blood vessels from other retinal structures. Wavelet filters are effective in object identification and segmentation from the noisy background. Performance of classification is improved in [9] by minimizing the large number of features extracted using Principle Component Analysis (PCA) but all these are not useful for classification. Particle Swarm Optimization (PSO) optimization is used to provide the better results in terms of entropy, sensitivity, accuracy, etc. In [10], parameters indicating global quality are evaluated in retinal vessel segmentations for pixel based comparison between automated segmentation and manually labeled images. A new supervised blood vessel detection approach utilizing neural network (NN) [11] scheme was presented in [12] and gray-level and moment invariant features were utilized for effective pixel representation. A combination of fundus registration and multimodal approach was presented in [13] for retinal vascular segmentation in spectral-domain optical coherence tomography (SD-OCT) volumes. The results obtained were considerably improved than the previous approaches obtaining the area under the curve (AUC) of 0.85 and 0.89 for registration and multimodal approaches respectively. A blood vessel segmentation and optic disc localization method was presented in [14] which act as a supporting system for non-intrusive diagnosis to modern ophthalmologists. Graph cut technique was implemented to extract the retinal vascular structures and the two alternative methods (Markov Random Fields (MRF) and compensation factor method) were utilized for optical disc localization. A three stage segmentation algorithm was proposed in [15] to achieve consistent blood vessel segmentation accuracy as compared to the existing supervised segmentation approaches. Blood vessel distribution and directional characteristics are used in [16] to come up with a precise and speedy optic disc detection method. The accuracy of the system lies in the range of 83% to 99% when tested on 4 publically available databases providing a robust and efficient solution. A fully connected discriminatively trained conditional random field model was presented and evaluated in [17] for blood vessel segmentation. Conventional segmentation methods are not useful when applied on very thin or elongated blood vessels. This problem was overcome using conditional random field model and the supervised support vector machine method (SVM) was used for classification. Evaluation done in terms of sensitivity, F1-score, G-mean and correlation coefficient shows that the approach proposed in [18] outperforms the other techniques.

This work contributes in automated OD segmentation and blood vessel localization by achieving better accuracy as well as less complexity. Ten shape features are utilized for OD segmentations and a combination of 14 shape and 3 fractal features are explored for blood vessel extraction. An optimal feature set for blood vessel classification was introduced, utilizing the fractal dimensions of the fundus image. Fractal feature set utilized is beneficial for PDR screening as the increased fractal dimensions are indicative of more bifurcations in the retinal vascular structure. The proposed system provides a robust and flexible solution for effective screening of retinal fundus images having pathological abnormalities and different FOV. The rest of this paper is organized as follows. Section 2 presents the dataset utilized and techniques employed to implement the proposed blood vessel extraction approach. Results of implementation are presented in section 3 and the conclusion of paper is drawn in section 4.

2. Materials and Methods

The materials and methods section should contain sufficient detail so that all procedures can be repeated. It may be divided into headed subsections if several methods are described.

The implementation strategy adopted in this paper is depicted in Figure 1. A detailed discussion of the dataset used and methodology employed is done in the upcoming sections. Fundus image datasets are utilized to obtain fundus images for implementation. Fundus images are pre-processed first and the optical disc localization is performed followed by blood vessel extraction process.

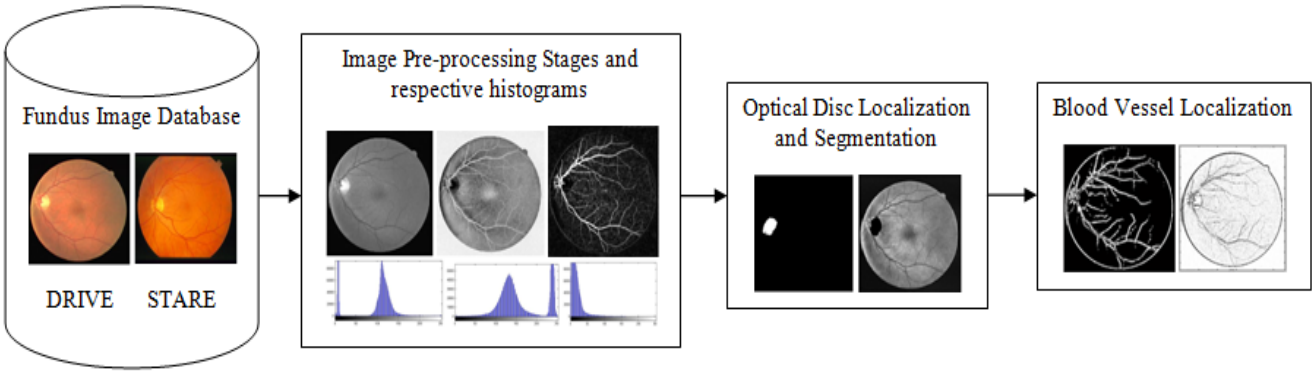

Figure 1. Block diagram of strategy adopted for blood vessel localization

2.1 Dataset

DRIVE [18] and STARE [19] benchmark databases were exploited for validation of blood vessel localization and extraction approaches. These databases are publically and freely available online and are generally used in various blood vessel extraction literatures for comparing the results of the proposed approaches with the expert labeled ground truth images available in the database. For the critical analysis of blood vessel localization approaches these databases are well suited.

2.2 Methodology

Methodology adopted to expedite PDR diagnostic services involves four stage implementation strategy. In the first stage, image pre-processing stages followed by optical disc localization and segmentation in the second stage, third stage comprises two proposed blood vessel extraction approaches and feature description and extraction are done in the fourth stage.

2.2.1 Image Pre-processing Stages: Inter and intra pixel variabilities with respect to the background pigmentation are removed employing pre-processing stages. The steps involed for pre-procssing the fundus image includes image variation attenuation, green channel conversion, denoising and contrast enhancement [20, 21]. Contrast enhancement step employs contrast limited adaptive histogram thresholding (CLAHE) to obtain a contrast improved fundus image without noise amplification. After utilizing pre-processing steps, OD localization and blood vessel extraction approaches are followed.

2.2.2 Optical Disc Localization and Segmentation Approach: The position of origin of blood vessels and the exact position of optical disc are important for correct diagnosis of yellow lesion (exudates) as OD may be wrong diagnosed as a lesion. The factors hampering OD identification are different FOV of different fundus images, poor illumination and increased number of abnormalities which make it difficult to extract OD portions having size and shape similar to exudates. The approach adopted in this paper for OD localization involves two fold identification strategy. The centroid of optical disc is determined first followed by optical disc boundary localization using morphological operations. Pre-processing steps are applied on ‘V’ plane of HSV model to extract only the intensity values. Morphological closing operation is performed and contours and gaps are filled to find the largest circular region in the intensity plane. The region of maximum area is indicated as the optical disc segment. Flowchart of OD Localization and segmentation approach is given in Figure 2.

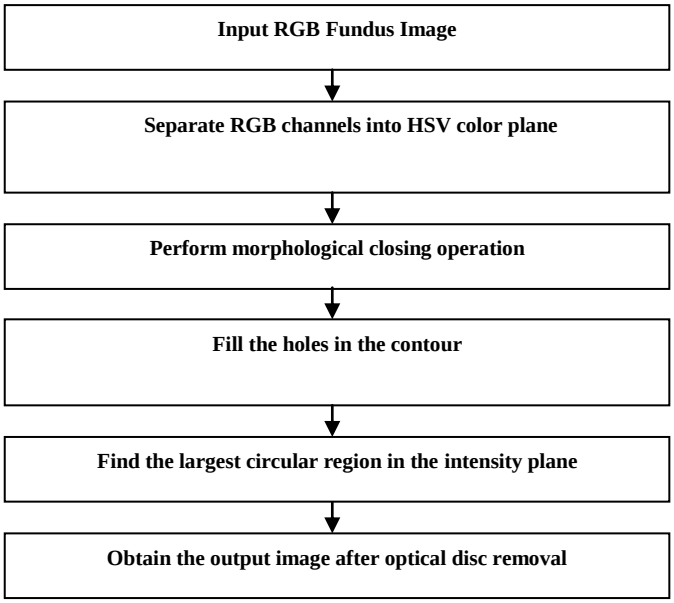

Figure 2. Flowchart of OD Localization and segmentation approach

2.2.3 Blood Vessel Localization Approaches: Later OD segmentation, two blood vessel extraction approaches are proposed; Kirsch's edge detection and fuzzy inference based blood vessel extraction and they are detailed below.

Kirsch's Edge Detection based Approach: Edge detection approaches are used to identify the points of discontinuity in an image by calculating the intensity difference between two neighborhood pixels representing the difference as an edge and else as the background. For Kirsch's edge detection approach, Kirsch template is employed which is rotated in 8 compass directions at angle of 45° each in anticlockwise manner. Image gradients which are indicative of edges or boundaries present in the image are obtained by convolving the eight directional Kirsch's templates with each pixel of the image. The gradients obtained in all the 8 compass directions are then summed up to obtain the blood vessels [22]. A threshold value is selected and if the difference between the pixel and its neighborhood is greater than the threshold value, it is indicated as the edge otherwise it is indicated as background. Flowchart of Kirsch's edge detection based Blood Vessel Localization approach is depicted in Figure 3.

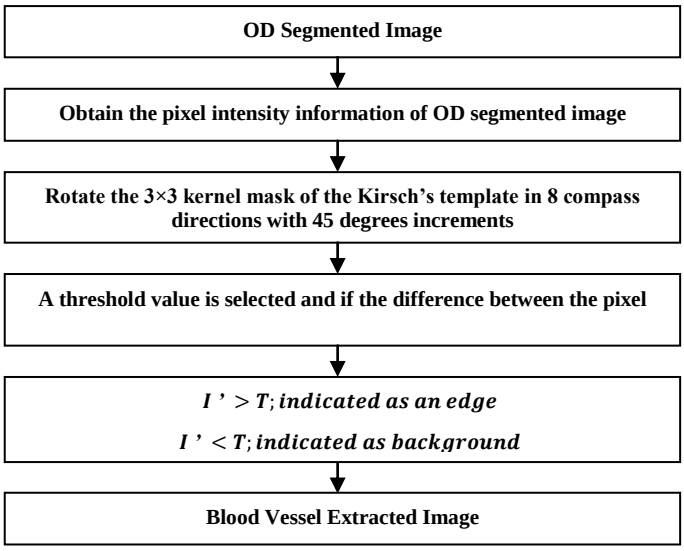

Figure 3. Flowchart of blood vessel localization approach

Fuzzy Inference based Blood Vessel Extraction Approach: Classical edge detection approaches are good for fixed edge thickness applications but it is difficult for them to address the varying thickness of blood vessels. If- Then rule based fuzzy approach may prove beneficial for edge detection purpose unlike the conventional edge detection techniques as the fuzzy approach deals with uncertainty in the information [21]. RGB fundus image is firstly normalized and fuzzy inference in drawn specifying the required membership function. Blood vessels are extracted by comparing the pixels in each row of the image with the corresponding row of image gradients I_x and I_y in x and y directions respectively. Flowchart of fuzzy inference based blood vessel extraction approach is depicted in Figure 4.

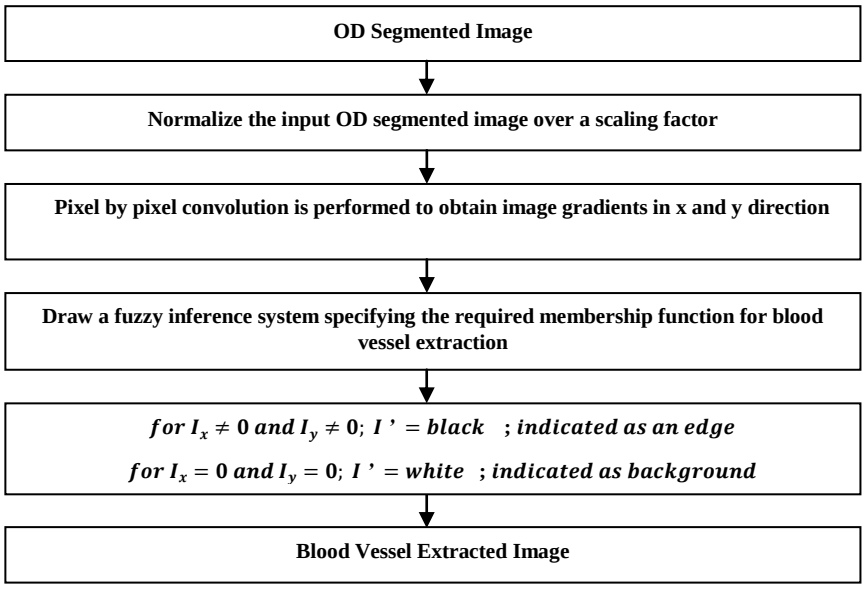

Figure 4. Flowchart of fuzzy inference based blood vessel extraction segmentation approach

2.3 Feature Description: Shape features utilized in this work exploits the region properties for each connected component of the segmentations obtained [23-25]. The feature vector is obtained by finding the geometrical properties of extracted image. Ten geometrical properties are utilized including area, perimeter, major axis length, minor axis length, eccentricity, convex area, equivalent diameter, solidity, extent and compactness. The other set of features used in this work is fractal dimensional characteristics; box counting, information and correlation dimensions [26]. Patients suffering from PDR have increased fractal dimensions due to increased bifurcated vascular patterns thus this set of features is also considered significant for DR screening.

2.3.1 Box counting dimensions: It is defined as the number of boxes of side length '*l*' required for covering the desired object that grows following $\left(\frac{1}{l}\right)^{D_{BC}}$ as *l* tends to 0.

$$D_{BC} = \lim_{l \to 0} \frac{\log N(l)}{\log \frac{1}{l}} \quad (1)$$

where $N(l)$ represents the number of boxed required to cover the binary object under analysis.

2.3.2 Information dimensions: This provides the information content indicated by Shannon entropy for each of the box count which canbe expressed as,

$$D_{Inf} = \lim_{l \to 0} \frac{H(l)}{\log \frac{1}{l}} \quad (2)$$

here $H(l)$ denotes the sum of Shannon entropy for each of the cell in the box count.

2.3.3 Correlation dimensions: This dimension is approximated by the probability density function denoted by,

$$C_l = \frac{1}{n^{l^2}} \sum_{i=1,j=1}^{n_l} \theta(l - \|p_i - p_j\|) \cong \sum_{i=1}^{n_r} p_{i^2}(l) \quad (3)$$

here $\theta(x)$ Heaviside step function, pi position of i^{th} pixel in the object and $pi(r)$ probability of finding the desired object in i^{th} box.

Therefore correlation dimension of an object under analysis is given by,

$$D_{corr} = \lim_{l \to 0} \frac{\log C(l)}{\log \frac{1}{l}} \quad (4)$$

For the visual representation of the features, box plots are used as they are suitable in representing the statistical data as a rectangular box of quartiles. Vertical lines extending from the box plot indicates the variability outside the bounds of upper and lower quartiles. Outliers are indicated as individual points outside the box plot and a vertical line inside the box indicates the median value of data being visualized. Box plots are used for representation as they allow quick graphical comparison of one or more datasets.

3. Results and Discussion

The results of proposed blood vessel localization algorithms implemented using MATLAB software are depicted below. Two databases exploited for this study are Digital Fundus Images for Vessel Extraction (DRIVE) and Structured Analysis of Retina (STARE) databases. There are 40 images of size 565×584 and 24 bits resolution per pixel in DRIVE database which are captured using Cannon CR5 3CCD camera considering 45 degrees FOV [18]. STARE database consist of a total of 400 raw fundus images of 605×700 pixel with 24 bits per pixel resolution digitized using TopCon TRV-50 fundus camera at 35 degrees of FOV. Out of these 400 images, 40 ground truth vessel images are segmented and labeled by professional expert ophthalmologists for actual identification and validation of blood vessels [19].

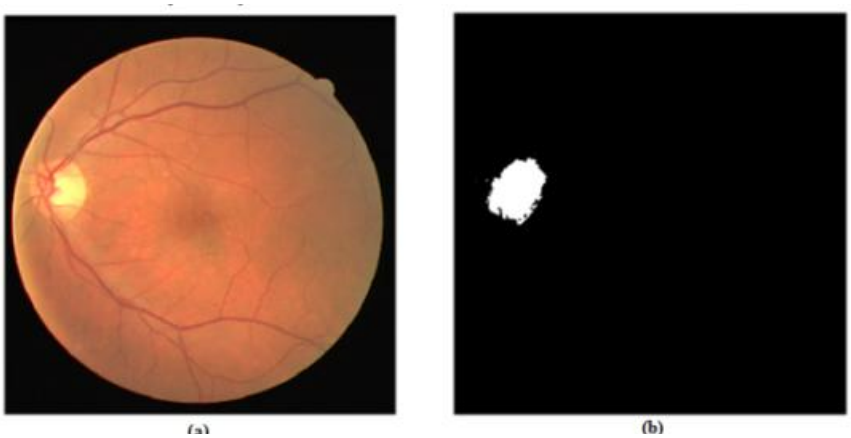

Figure 5. (a) Original Fundus Image from DRIVE database (b) Optical Disc segmented part from the fundus image

Figure 5 depicts the original fundus image taken for analysis from DRIVE database and the optical disc part segmented from the fundus image. Morphology based approach is proposed for optical disc segmentation exploiting intensity value of HSV color model. As OD have the maximum intensity in the whole retinal fundus image, morphological closing operation is followed by filling the holes in the contour and largest circular region in the intensity plane is identified as optical disc segment.

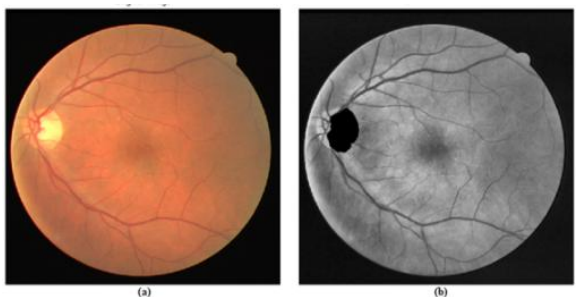

Figure 6. (a) Original fundus image (b) Fundus image after OD removal

The result depicted in Figure 6 indicates the original image of retina and the fundus image after OD extraction. For analysis of OD segmentations obtained, 14 shape features were extracted and box plots of some significant features are depicted in Figure 7.

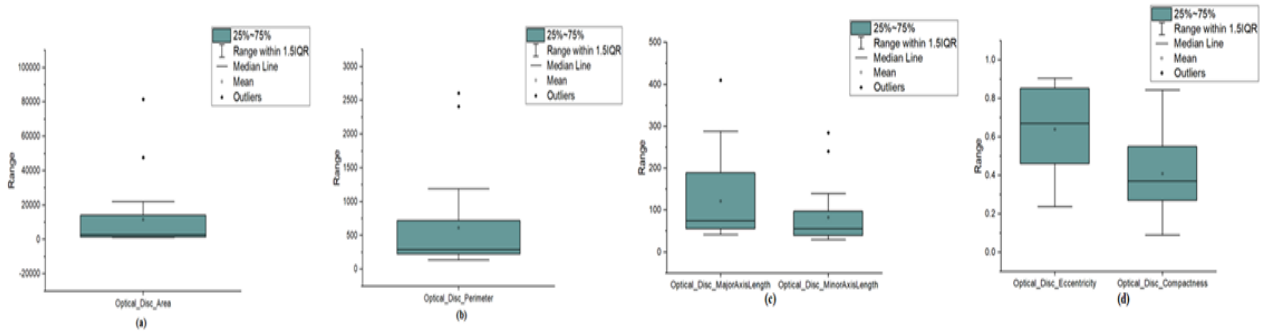

Figure 7. Box plot of (a) OD Area (b) OD Perimeter (c) OD major and minor axis lengths (d) OD eccentricity and compactness

OD segmentation is followed by the implementation of blood vessel segmentation approaches [27, 28]. The extracted blood vessel outputs are compared with the ground truth image obtained from the database. The outputs of blood vessel extraction approaches employing two proposed approaches, Kirsch's Edge detection approach and Fuzzy Inference based approach along with the ground truth blood vessel image are depicted in Figure 8.

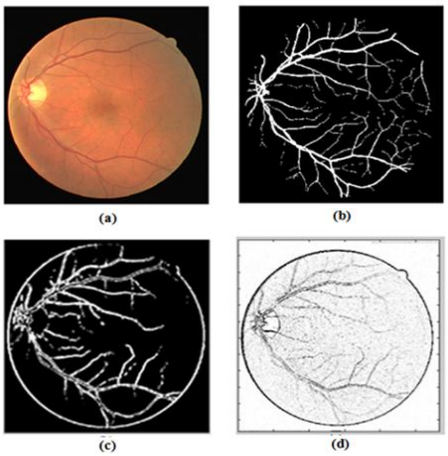

Figure 8. (a) Original fundus image taken from DRIVE database (b) Ground truth blood vessels labelled by experts. Extracted blood vessel output using (c) Kirsch's Edge detection approach (d) Fuzzy Inference based approach

Proposed blood vessel extraction algorithms are applied and obtained results are visualized and compared in Figure 8 with the ground truth blood vessels available in the database. Kirsch's edge detection approach output depicted in Figure 8(c) shows that some holes and empty areas are still visible in the output blood vessel image extracted due to matching of Kirsch's template. This method highlights the edges or blood vessels but unwanted noise is also enhanced using this technique which is indicated as small dots in the output image. Figure 8(d) shows the output of fuzzy based blood vessel extraction technique and the blood vessels are more clearly visualized in this approach but a small drawback of fuzzy based approach lies in somewhat poor visualization of thin blood vessels in the retinal area. However, comparing the visual results of both the methods, fuzzy based approach overcomes the disadvantages of Kirsch's edge detection techniques. Blood vessel feature extraction is also done for performance validation of proposed technique. Ten shape features were extracted and box plots of some of them are shown in Figure 9 for better visualization. Fractal dimension analysis is also done to quantify the self similarity of branching patterns depending upon the box counting method. Fractal dimensions are used in fundus image analysis for vascular structure characterization to compare the Extracted (Ext.) blood vessels to those of ground Truth (GT) blood vessels. In this work three fractal dimensions are calculated (box counting dimensions, information dimensions and correlation dimensions) for both ground truth and extracted vascular structures [29, 30]. The box plots for are shown in Figure 10.

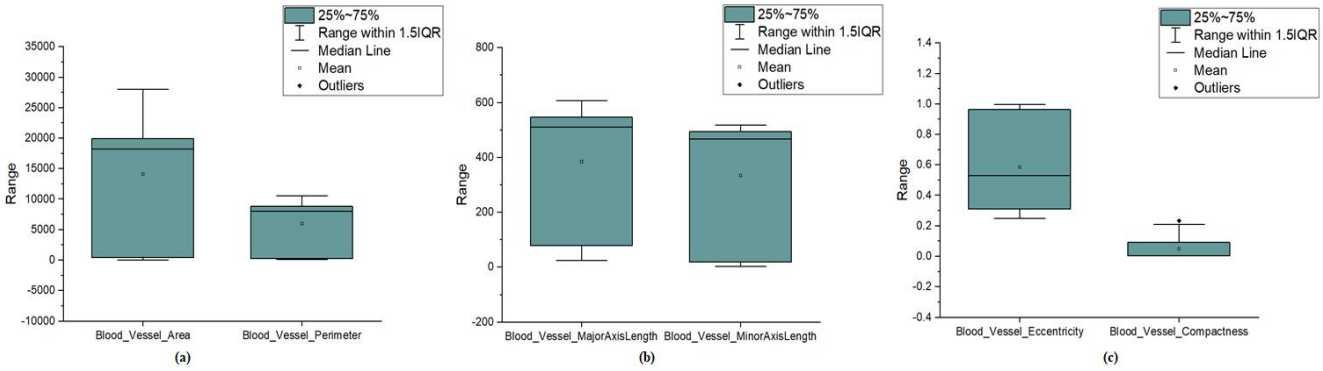

Figure 9. Box plots of Shape Features obtained for Blood Vessel Extraction Approach

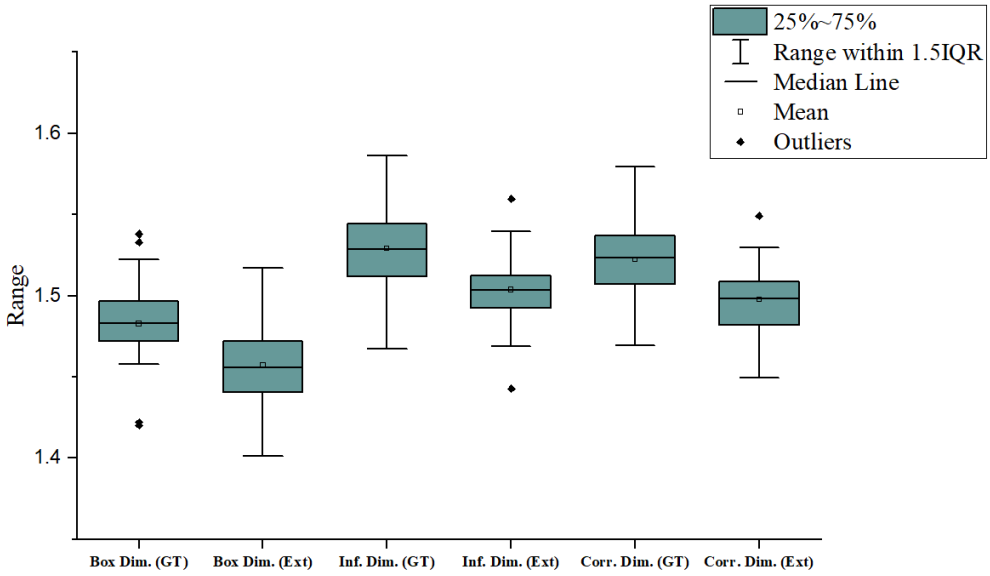

Figure 10. Fractal Dimension Analysis of Retinal Blood Vessels

Analysis and interpretation of feature set is done using Design of Experiments (DOE[32]) SPSS tool package. Statistical analysis of fractal dimensions and feature selection is done using pair-wise linear correlation, Levene's test and *t*-test [31, 32, 33, 34]. Comparison was made for ground truth and extracted vascular structures. Pearson and Spearman correlation coefficients were used to quantify the relationship between fractal variables and they are tabulated in Table 1 and Table 2 respectively.

Table 1. Pearson Correlation analysis of fractal features obtained for Ground Truth (GT) and Extracted (Ex) vessels using SPSS package

Fractal Features	**Pearson Coeff.**					
	Box dim. (GT)	**Box dim. (Ext.)**	**Inf. Dim. (GT)**	**Inf. Dim. (Ext)**	**Corr. Dim. (GT)**	**Corr. Dim. (Ext)**
Box dim. (GT)	1.000	0.966**	0.970**	0.920**	0.971**	0.960**
Box dim. (Ext.)	0.966**	1.000	0.932**	0.894**	0.932**	0.957**
Inf. Dim. (GT)	0.970**	0.932**	1.000	0.957**	0.990**	0.966**
Inf. Dim. (Ext.)	0.920**	0.894**	0.957**	1.000	0.939**	0.941**
Corr. Dim. (GT)	0.971**	0.932**	0.990**	0.939**	1.000	0.958**
Corr. Dim. (Ext.)	0.960**	0.957**	0.966**	0.941**	0.958**	1.000

Table 2. Spearsman's Correlation analysis of fractal features obtained for Ground Truth (GT) and Extracted (Ex) vessels using SPSS package

Fractal Features	**Spearsman's Coeff.**					
	Box dim. (GT)	**Box dim. (Ext.)**	**Inf. Dim. (GT)**	**Inf. Dim. (Ext)**	**Corr. Dim. (GT)**	**Corr. Dim. (Ext)**
Box dim. (GT)	1.000	0.910*	0.955**	0.869	0.965*	0.923**
Box dim. (Ext.)	0.910**	1.000	0.871**	0.853**	0.880**	0.948**
Inf. Dim. (GT)	0.955**	0.871**	1.000	0.934**	0.991**	0.917**
Inf. Dim. (Ext.)	0.869**	0.853**	0.934**	1.000	0.911**	0.906**
Corr. Dim. (GT)	0.965**	0.880**	0.991**	0.911**	1.000	0.912**
Corr. Dim. (Ext.)	0.923**	0.948**	0.917**	0.906**	0.912**	1.000

Table 1 and Table 2 compares fractal dimensions of the ground truth blood vessels with the extracted blood vessels and also computes the relation of these fractal dimensions with each other. From Table 1 and Table 2 it is revealed that information dimensions and correlation dimensions are highly correlated to each other having correlation coefficient of 0.993 while lower correlation was found between box counting dimensions and correlation dimensions yet higher enough (>0.5) considering the features in strong association to each other.

Further, feature selection is done on the basis of Levene's F test and t-test. Equality of variance is determined using Levene's test commonly known as F- test and eqality of means is inferred from *t*-test. Levene's test provides the statistical evidence of whether the variances of the two samples are approximately equal or not. The assumption of homogeneity of variance for Levene's test starts with the null hypothesis (H_0) stated in Eq. 5.

$$H_0: \sigma_0 = \sigma_1 \tag{5}$$

Null hypothesis rejection (H_1) states that there exist no homogeneity between the variances of the feature set and this is expressed in Eq. 6.

$$H_1: \sigma_0 \neq \sigma_1 \tag{6}$$

The null hypothesis is accepted if significance value for the test is greater than 0.05 otherwise the hypothesis is rejected.

t-test is a statistical hypothesis test which is based on the null hypothesis (H_0`) that there is no significant difference between the mean values of the feature set and it is stated in Eq. 7. Null hypothesis rejection states that there is significant difference between the means and it is expressed in Eq. 8.

$$H_0': \mu_0 = \mu_1 \tag{7}$$

$$H_1': \mu_0 \neq \mu_1 \tag{8}$$

The DOE experiemental results for Levene's test and *t*-test for fractal feature set are summarized in Table 3.

Table 3. Levene's Test and t-test results for the feature set

Shape features				
Features	**Levene's Test**		***t*-test**	
	F	**Sign.**	**t**	**Sign. (2-tailed)**
Area	24.975	0.002	3.544	0.001
Perimeter	22.995	0.000	5.846	0.000
Major_Axis_Length	39.471	0.000	4.684	0.000
Minor_Axis_Length	11.255	0.001	4.871	0.000
Eccentricity	0.008	0.928	0.673	0.505
Convex_Area	15.163	0.000	5.770	0.007
Equiv_dia	23.716	0.000	5.897	0.000
Solidity	9.362	0.004	6.720	0.000
Extent	13.619	0.001	13.797	0.001
Compactness	12.440	0.001	7.822	0.000
Fractal features				
Features	**Levene's Test**		***t*-test**	
	F	**Sign.**	**t**	**Sign. (2-tailed)**
Box Dim.	24.975	0.000	2.730	0.010
Inf. Dim.	15.545	0.000	2.991	0.005
Corr. Dim.	23.674	0.000	2.938	0.006

From the tabular representation it is revealed that the experimental results for both Levene's test and 2-tailed *t*-test for the feature set are significant as the significance value is less than 0.05. Therefore, rejecting the null hypothesis, it shows that there is no significant difference between the mean and variance values. However, eccentricity feature among shape features shows relatively less significance as compared to the other features and therefore this feature is not selected after selection process. Thus all the fractal features and shape features except eccentricity feature are selected for analysis after evaluating their contribution for the detection of vascular structures. This feature set can be further used for classification of blood vessels so as to diagnose Proliferative Diabetic Retinopathy (PDR) symptoms at the early stage by estimating the bifurcated vascular patterns at the early stage.

The proposed fuzzy inference based retinal blood vessel localization technique provides 96.79% average accuracy rate over ground truth blood vessels for DRIVE database and 95.68% average accuracy for STARE database. The comparison of proposed method with the other methods reported in the literature is provided in Table 4.

Table 4. Tabular comparison of Proposed Technique with other techniques reported in the literature

Technique used	Accuracy for DRIVE Database (%)	Accuracy for STARE Database (%)
Staal, et al. [16]	94.41%	94.70%
Goa, et al. [35]	92.12%	90.09%
Martinez-Perez, et al. [36]	93.44%	94.10%
Fraz, et al. [37]	94.30%	94.42%
Ana Salazar-Gonzalez et al. [38]	94.12%	94.41%
Proposed Method	**96.79%**	**95.68%**

4. Conclusions

This paper provides an exhaustive research and implementation of proposed OD segmentation and blood vessel extraction approaches validated on DRIVE and STARE database images. Shape and fractal features are utilized for the quantitative analysis of the proposed approaches. The proposed OD segmentation approach is effective in identifying optical disc for effective blood vessel extraction near the OD area. Fuzzy inference based blood vessel localization approach outperforms existing blood vessel extraction methods providing 96.79% and 95.68% of average accuracies for DRIVE and STARE databases evaluated. An exhaustive study of reliability of proposed blood vessel extraction technique is carried out so as to identify and diagnose PDR patients at the earliest. Shape and fractal features were exploited for the study and their statistical significance is evalulated using DOE tool. Thus this visual and statistical analysis provides a robust solution for early stage detection of DR. Other features like textural, intensity features, etc. will also be explored further in the imminent part of this research. The future scope in this work is optimal feature selection and classification of fundus images for effective DR diagnosis.

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