Imperial Journal of Interdisciplinary Research (IJIR)
Vol-2, Issue-6, 2016
ISSN: 2454-1362, http://www.onlinejournal.in

A Method of Disease Detection and Segmentation of Retinal Blood Vessels using Fuzzy C-Means and Neutrosophic Approach

Ishmeet Kaur[1] & Lalit Mann Singh[2]
[1]Department of Computer Science & Engineering, SGGSWU, Fatehgarh Sahib
[2]Assistant Professor, Department of Computer Science & Engineering, SGGSWU, Fatehgarh Sahib

***Abstract**: Diabetic Retinopathy is a disease which causes a menace to the eyesight. The detection of this at an early stage can aid the person from vision loss. The examination of retinal blood vessel structure can help to detect the disease, so segmentation of retinal blood vessel vasculature is important and is appreciated by the ophthalmologists. In this paper, we present the approach of blood vessel segmentation using computer intelligence by deploying fuzzy c-means and neutrosophic set. Further, the input image is scrutinized and the result achieved is whether the image is diseased or not. The various diseases detected in this technique are cotton wool spots, exudates and lesions with the help of region growing and neural network classification method. The proposed approach is tested on DRIVE and DIARETDB1 databases and is compared with the other approaches. The segmentation approach achieved the average accuracy of 98.7% whereas the diseased image was detected with 99% accuracy.*

***Keywords**— Diabetic Retinopathy, Retina, Blood vessels, Neutrosophy, Fundus Images, Segmentation*
.

1. Introduction

The retina is anatomical structure which consists of retinal vasculature, optic disk, macula and anomalous structures like cotton wool spots, different types of exudates, micro aneurysms, haemorrhages and many more, if the eye is diseased [24]. Optic disk which is a bright oval structure in retina represents the start of the optic nerve and is the entry point of the major blood vessels to the eye. Macula is the dark region devoid of vessels with fovea at its center is responsible for central and high resolution vision. The blood vasculature is a tree like structure having a high frequency component exhibited more clearly at high contrast spanning across the fundus image. The retinal blood vessels are the most important component of the retina as they provide the blood supply to the retina and also transmit the information signals from retina to the brain [12]. The diseased eye can be detected by examining the changes in the retinal vasculature. The different types of diseases can be detected by examining the retinal structure such as diabetic retinopathy, cardiovascular disease, hypertension and stroke. The retinal diseases, if not detected and diagnosed at early stage can further lead a person to a vision loss. The complete vision loss of a person can be prevented by diagnosing these diseases at initial stage. Further, for detection of these disorders segmentation of blood vessels is necessary.

Diabetic Retinopathy (DR) is a sight threatening disease which causes blindness among the working age people. It involves the identification of abnormalities like cotton wool spots, hard exudates, haemorrhages, red lesions and soft exudates [1]. Hence, for detection of diabetic symptoms, segmentation of blood vessels is important as few morphological changes like diameter, branching angle, length or tortuosity occur in retinal blood vessels. The symptom of diabetic retinopathy which can be noticed in retinal images is the variation in width of retinal vessels [12].

Manual segmentation requires the people with expertise as it is very complex and time consuming and effort prone task. Further, with the help of computer intelligence the blood vessels can be automatically segmented along with the diseased area in the fundus images which would be highly appreciated by the oculists. The ophthalmologists can detect the disease by examining the segmented vessels with the help of the growth of number of extra vessels, their shape and size. Different techniques have been adopted for segmentation. However, the segmentation of blood vessels is very difficult task because the size of the blood vessels is thin and varies from vessel to vessel, presence of the noise, variation of the intensity level between the vessels and presence of the abnormal structure such as exudates, haemorrhages and lesions [27]. The presence of all these components can lead to improper segmentation of blood vessels by ignoring the thin vessels and detecting boundary pixels as vessels. So, to prevent this, proper segmentation algorithm needs to be implemented. Figure 1 represents the structure of retina with signs of diabetic retinopathy.

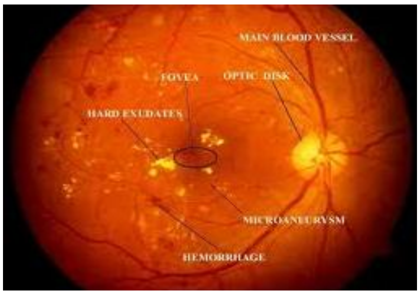


Fig 1 Structure of Retina with signs of DR

Automated image-based disease detection could complement the important role that ophthalmologists and optometrists currently fill in diagnosing diabetic retinopathy as it could reduce the time required of these specialists to interpret medical images, automatically add the results to the patient's record, and overcome possible biases that may skew the clinical assessments.

The main objective of this paper is to perform segmentation of retinal blood vessels and detection of diseases such as exudates, cotton wool spots and lesions from the fundus images. The algorithm which is used for segmentation of blood vessels includes the fuzzy c-means with neutrosophic approach and the disease is detected from the fundus image using the region growing properties and artificial neural network classification technique.

In this paper, we have presented the different types of eye diseases which can be detected with segmentation in section II, the type of publically available databases mostly used for segmentation in section III, the performance measures in section IV, review of various algorithms implemented to extract the blood vessels from two dimensional retinal images in section V and conclusion in section VI.

2. Review of related studies

The segmentation of blood vessels can be acquired through assigning each pixel in the image as a vessel or a non-vessel pixel. According to the study, the blood vessel segmentation can be broadly divided into two categories viz. rule based techniques and pattern recognition based techniques [27]. Rule based techniques involve vessel tracking, matched filtering, mathematical morphology, multi-scale techniques and model-based approaches [19]. On the other hand, pattern recognition based techniques involve supervised and unsupervised techniques which include clustering and classification of data which groups the pixels as vessel or a non-vessel pixel.

An unsupervised method does not require any prior information such as trained data as in the case of supervised methods. These methods include the clustering techniques which groups the data into clusters. Hassanien et al [3] suggested the approach in which artificial bee colony optimization is used simultaneously with fuzzy cluster compactness fitness function with partial belongness in the first level to find coarse vessels. This technique uses two level of clustering. In the first level, artificial bee optimization is applied on the fuzzy c-means objective function to obtain the blood vessels. In the second stage, the cluster centre is further enhanced using local search to retrieve the blood vessels which are thin and small in diameter. The most of the thin vessels are extracted as compared to other methods. The future work can be extended to focus on the extraction of the small diameter and thin vessels more precisely to attain the accurate segmentation results. Emary et al [10] uses possibilistic fuzzy c-means clustering method to overcome the difficulties of conventional fuzzy c-means objective function. To obtain the efficient results with proposed clustering method, a cuckoo search method is used. The cuckoo search method is used for the purpose of optimization of possibilistic fuzzy c-means clustering method. The results are obtained using DRIVE dataset and are able to achieve accurate results and detect the exudates, hemorrhages and pigment epithelium changes.

The supervised methods depend on the pre-classified data. The pixels are classified into the vessel and non- vessel pixel using the trained data obtained from manually- labelled samples. If the image is not prone to any disease, this method is considered appropriate than unsupervised method as training data provided help in achieving the higher performance. However, supervises techniques are sensitive to false edges.

Roychowdhury et al [32] presented a three- stage retinal blood vessel segmentation algorithm. Firstly, a threshold binary image is obtained by high pass filtering and the other binary threshold image is obtained by tophat reconstruction of the red regions in a green plane image. Then the common regions from the two binary images is extracted and combined. Secondly, classification is applied to the image obtained after merging. Finally, all the pixels classified as vessels are combined with major vessels to get the vascular structure. Further, enhancing of image is performed using post-processing techniques. The proposed method segments the major vessels and the fine vessels accurately. It has low dependency on the training data and involves fewer computations. In continuation, the work can be extended to detect neo-vascularisation in the retinal region, and to reduce false positives while detecting red lesions.

Franklin et al [33] proposed a method to identify the retinal blood vessels with the help of multilayer perceptron neural network. In this technique, the input is derived from the three colour components, i.e., red, green and blue. By using this method the sight threatening diseases such as haemorrhages and exudates can be detected. This technique is supervised one so it requires training sets which contains manually segmented images and image features and further the pixel is classified as a vessel and non-vessel. The pixel is considered as a feature vector which belongs to one of the classes and accordingly, the classifier determines the boundary between the classes. It is a simple and easy method for early detection of diabetic retinopathy.

3. Proposed method

This research work provides a solution to disease detection and segmentation of the retinal blood vessels problem. The process of segmentation of blood vessels involves three steps i.e. image pre-processing, unsupervised approach and image post-processing. The image pre-processing step includes the color channel extraction, unsharp masking, contrast enhancement and calculation of image gradient magnitude. The output of image pre-processing is further given as input to unsupervised learning phase where fuzzy c-means clustering technique is applied to the image which is further differentiated by the neutrosophic approach which refines the segmented output by dividing the pixels into vessel, non-vessel and indeterminate sets. The post-processing phase includes mathematical morphological operations and final segmented image is obtained.

The different diseases related to diabetic retinopathy like cotton wool spots or soft exudates, hard exudates and lesions can be detected from the digital retinal image. The database used for disease detection is DIARETDB1. The different phases are followed for disease detection. First is the pre-processing phase in which the image is enhanced using the green channel extraction, unsharp masking and contrast enhancement is done to enhance the quality of the image. The second phase includes the measurement of the image regions using the region properties. The third phase is the classification phase which uses the artificial neural network as a classifier to classify the different diseases related to diabetic retinopathy and the non-diseased image.

3.1. Materials used

The images used for validation of the proposed approach are obtained from publically available DRIVE (Digital Retinal Images for Vessel Extraction) [16, 26] and DIARETDB1 [34] databases. The DRIVE database consists of 40 colour fundus images grouped in two sets: test and training. The photographs were obtained from a diabetic retinopathy screening program in the Netherlands. The screening population consisted of 453 subjects between 31 and 86 years of age. Each image has been JPEG compressed, which is common practice in screening programs. Of the 40 images in the database, 7 contain pathology, namely exudates, haemorrhages and pigment epithelium changes. The images were acquired using a Canon CR5 non-mydriatic 3-CCD camera with a 45◦ field of view (FOV). Each image is captured using 8 bits per color plane at 768 $\times$584 pixels. The FOV of each image is circular with a diameter of approximately 540 pixels. The set of 40 images was divided into a test and training set both containing 20 images. Three observers, the first and second author and a computer science student manually segmented a number of images. All observers were trained by an experienced ophthalmologist (the last author). The first observer segmented 14 images of the training set while the second observer segmented the other 6 images. The test set was segmented twice resulting in a set X and Y. Set X was segmented by both the first and second observer (13 and 7 images, respectively) while set Y was completely segmented by the third observer. The performance of the vessel segmentation algorithms is measured on the test set. In set X the observers marked 577,649 pixels as vessel and 3,960,494 as background (12.7% vessel). In set Y 556,532 pixels are marked as vessel and 3,981,611 as background (12.3% vessel).

DIARETDB1 database is a public database for benchmarking diabetic retinopathy detection from digital images. It contains 89 images out of which 5 images are of a healthy retina while the other 84 have at least some signs of mild proliferative diabetic retinopathy. The images are marked by four experts for the presence of micro-aneurysms, haemorrhages, lesions, hard and soft exudates. The images are acquired with a 50◦ FOV using a fundus camera with unknown settings at a size of 1500$\times$1152 pixels in PNG format.

3.2. Image Preprocessing

The image is pre-processed to enhance the quality of image and to make the further calculations easy and productive. The different steps of image pre-processing include colour channel extraction, unsharp masking, contrast enhancement and calculation of image gradient magnitude. RGB image is taken as input. It is observed that the precision of green channel is much higher than the other two channels. So, green channel is further considered for processing.

The image sharpening technique known as unsharp masking is applied the image to enhance the quality of the image. In this technique, the image is sharpened by subtracting the blurred part of the image from the original image.

The contrast of the image is enhanced with the help of contrast limited adaptive histogram equalization (CLAHE) algorithm which is applied to increase the contrast as a result of which the blood vessels appear more distinguished from the background. The features of the image are more enhanced after the magnitude of the gradient is calculated which helps further in easier segmentation of the blood vessels.

3.3. Unsupervised Learning

Unsupervised Learning is a clustering process in which the output image of pre-processing phase is given as input to the clustering algorithm. Clustering [27] is an unsupervised data mining technique in which the clusters or groups of pixels are formed based on the similarity measure. The algorithm used is fuzzy c-means clustering along with neutrosophic approach which are explained in the following section.

3.3.1 Fuzzy c-means clustering

Fuzzy c-means is an unsupervised clustering algorithm that has been applied to various problems. FCM method was first reported by Joe Dunn [9] in 1974 and further was improved by Bezdek [5] in 1981. This method aims at minimizing the Objective Function JFCM defined in the following equation.

$$J_{FCM} = \sum_{i=1}^{c} \sum_{j=1}^{n} u_{ij}^{m}\, d_{ij}^{2}$$

where uij is the membership function which represents that a particular pixel belongs to a specific cluster or region.dij is the Euclidean distance metric.

3.3.2 Neutrosophic Approach

Neutrosophy is a branch of philosophy which was introduced by Samarandache studies the origin, nature and scope of neutralities, as well as their interactions with different ideational spectra. In this theory, every element has not only a certain degree of the truth, but also a falsity degree and an indeterminacy degree that have to be considered independently from each other [28].

The output from the fuzzy c-means algorithm is divided into neutrosophic domain. A neutrosophic set image PNS is characterized by three membership sets T, I, F. A pixel P in the image is described as P(T,I,F) where t is the true in the set, i is the indeterminate in the set and f is the false in the set, where t varies in T, I varies in I and f varies in F. Further, the pixel P(i,j) in the image domain is transformed to the neutrosophic domain PNS={T(i,j),I(i,j),F(i,j)}. The formulae to derive T(i,j), I(i,j) and F(i,j) are defined as [23] :

$$T(i,j) = \frac{\bar{g}(i,j) - \bar{g}_{min}}{\bar{g}_{max} - \bar{g}_{min}}$$

$$I(i,j) = \frac{\delta(i,j) - \delta_{min}}{\delta_{max} - \delta_{min}}$$

$$\delta(i,j) = abs\left(g(i,j) - \bar{g}(i,j)\right)$$

$$F(i,j) = 1 - T(i,j)$$

where $\bar{g}(i,j)$ is the local mean value of the pixels of the window. $\partial(i,j)$ is the absolute value of difference between intensity g(i, j) and its local mean value $\bar{g}(i,j)$.

3.3.3 Image Post-Processing

The segmented output of the data mining phase is further post-processed using the mathematical morphological techniques [27]. On analyzing the output of the image, it is examined that it contains some isolated pixels and pixels not connected properly. Further, to overcome this, post-processing operations are performed. In this, cleaning is performed to remove the isolated vessel pixels and spurs. In continuation, a majority based procedure is performed where a pixel is set to vessel if 5 or more pixels in its 3 by 3 neighborhood are vessels. The resultant image still consisted of patch like structures occupying very less number of pixels (less than that occupied by the thin vessels). Hence the components which occupy less than 10 pixels are eradicated using connected component analysis. Finally, a bridging operation is done which tries to connect the unconnected vessel pixels by assigning a pixel to vessel if it has two vessel neighbours that are not connected. The final result of the segmentation is the clean and accurate segmentation of retinal blood vessels. The representation of the segmentation result of data mining phase and the final segmented result is shown in figure 2.

(a)

(b)

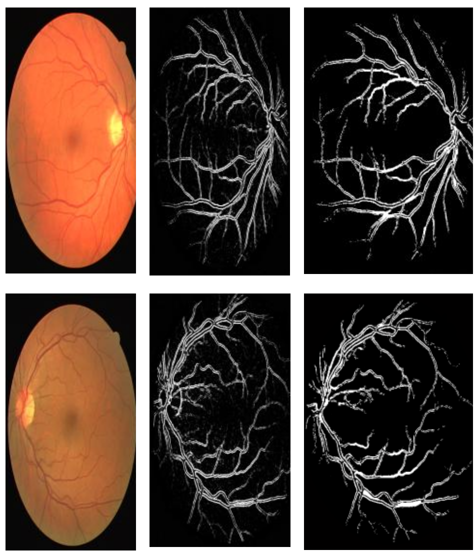
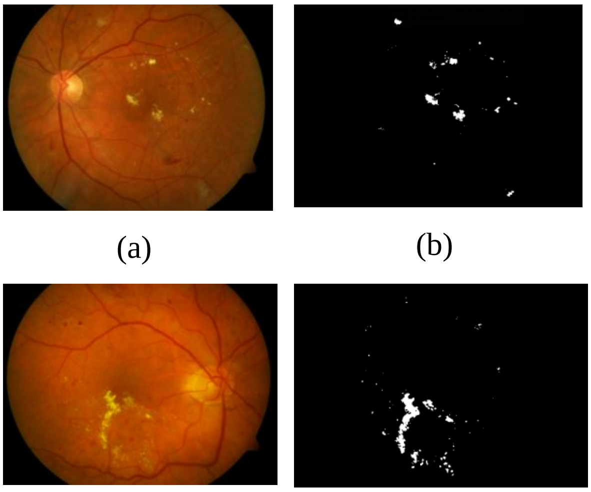


Fig 2 (a) Input Image, Segmented image of data mining phase and post-processing phase image (right eye)(b)) Input Image, Segmented image of data mining phase and post processing phase image (left eye)

3.3.4 Classification algorithm

The neural network is trained using Levenberg-Marquardt backpropagation algorithm. It is a network training function that updates weight (W) and bias (b) values according to Levenberg-Marquardt optimization. It is often the fastest backpropagation algorithm for training moderate-sized feedforward neural networks (up to several hundred weights), although it does require more memory than other algorithms. This algorithm trains, validates and test the input data which is the features of diseased and the non-diseased images.

The results of classification shows that the retinal image was correctly classified as diseased and non-diseased with 97.6% accuracy and only 2.4% of the total images were misclassified. The features which were used to differentiate between the images are entropy, standard deviation, mean, area and variance. The results of disease detection are shown in figure 3.



(a) (b) (c) (d)

Fig 3 (a) Diseased Left Retina (b) Disease detected portion (c) Diseased right eye (d) Disease portion detected

4. Results and discussion

In this research computational approaches are deployed to segment the blood vessels and to identify the diseased part in the image. The accuracy achieved in the proposed approach was found to be better than the existing methodologies. The proposed methodology is imposed on the test images from DRIVE database [16, 26] for the segmentation result comparison and further validated on DIARETDB1 database [34] for disease detection. The proposed technique can help the oculists in better retinal image analysis and disease detection. The segmentation of retinal blood vessels can help in diagnosing the retinal disease at the initial stage and thus aid in better treatment of the patients and if eye is diseased with exudates, microneurysms and lesions, the disease detection helps in identification of the area in which disease is present and ophthalmologists can get to know to which extent it has damaged the retina.

The proposed technique is implemented using Matlab R2013a on a personal computer with i5 processor at 2.50 GHz and 4 GB RAM. The segmentation of blood vessels is achieved through the three phases which are image pre-processing, unsupervised learning technique and image post-processing methods.

The performance of the proposed methodology on segmentation of vessels from fundus image is measured by the performance metrics, namely accuracy, sensitivity, specificity and positive predictive value. This evaluation scheme portrays the efficiency of the proposed framework in segmenting the retinal blood vessels of the fundus image. The different measures needs to be evaluated for the calculation of performance metrics, which are true positive (TP), true negative (TN), false positive (FP) and false negative (FN). TP specifies true positive which depicts that the number of vessels detected are true vessels. TN is the true negative which signifies that the number of non-vessels detected is actually non-vessels. FP signifies false positive which represents the number of non-vessels being wrongly classified as vessels. FN is the false negative which constitute to the number of vessel pixels wrongly classified as non-vessels.

Accuracy= TP+TN/TP+TN+FP+FN

Sensitivity= TP/TP+FN

Specificity= TN/TN+FP

Positive Predictive Value= TP/ TP+FP

The different performance metrics, accuracy, sensitivity, specificity and positive predictive value [27] are calculated and compared with the existing methodologies as shown in Table 1.

Technique	Accuracy (%)	Sensitivity (%)	Specificity (%)
Proposed technique	98.74	98.38	94.78
Geetha et. al [27]	95.36	70.79	97.78
Franklin et al. [12]	95.03	68.67	98.24

Villalobos-Castaldi et al [13]	97.59	96.48	94.80
Lam et al [16]	94.72	-	-
Soares et al. [29]	94.66	-	-
Miri and Mahloojifar [20]	94.58	73.52	97.95
Mendonca and Campilho [21]	94.52	73.44	97.64
Marin et al [22]	94.52	70.67	98.01
Staal et al [30]	94.41	-	-
You et al. [38]	94.34	74.10	97.51
Fraz et al. [14]	94.30	71.52	97.69
Anzalone et al. [2]	94.19	-	-
Niemeijer et al. [25]	94.16	-	-
Saffarzadeh et al. [31]	93.87	-	-
Zhang et al. [39]	93.82	71.20	97.24
Bankheard et al. [4]	93.71	70.27	97.17
Chakrabortu et al. [7]	93.70	--	-
Espona et al. [11]	93.52	74.36	96.15
Martinez Perez et al. [18]	93.44	72.46	96.55
Xu et al. [36]	93.28	77.60	-
Cinsdikici and Aydin [6]	92.93	-	-
Vlachos and Dermatas [35]	92.90	74.70	95.50
Xiaoyi and Mojon [37]	92.12	-	-
Martinez Perez et al. [17]	91.81	63.89	-
Kande et al. [15]	89.11	-	-
Chauduri et al. [8]	87.73	-	-

Table 1: Comparison of proposed technique with existing methodologies

The average accuracy, sensitivity, specificity and positive predictive value achieved through the proposed approach are 98.74%, 98.38%, 94.78% and 98.61% respectively.

The performance of the proposed methodology on the disease detection from fundus image is measured is measured by the performance metrics, sensitivity. The different measures needs to be evaluated for the calculation of performance metrics, which are true positive (TP), and false negative (FN). TP specifies true positive which depicts the area of diseased portion detected correctly. FN is the false negative constitutes to the diseased area wrongly classified as non-diseased. The proposed technique achieved 99.6% of sensitivity in the area of accurate disease detection.

5. Conclusion and Future Scope

The computer aided automatic disease detection and segmentation system for retinal blood vessels has been proposed in this research. The advantages of the various techniques have been collectively utilized to achieve the better performance. It is seen that the proposed methodology achieves higher accuracy in vessel segmentation when compared with existing techniques. Our methodology achieves an average accuracy, sensitivity and specificity of 98.74%, 98.38% and 94.78% respectively in DRIVE dataset. In addition, the diseased portion is also detected from the image with 99.6% of sensitivity in DIARETDB1 dataset. The signified effectiveness of the proposed methodology can help the oculists in efficient retinal image analysis and thus will provide fruitful treatment to the patient community along with it is a suitable diagnostic tool for the complete prescreening system for early diabetic retinopathy detection.

The future insight includes applying enhanced post-processing techniques to achieve the better results for the segmented image. Neutrosophic technique can also be used to detect different type of tumors efficiently.

6. References

[1] Abràmoff M D , M. K. Garvin, and M. Sonka 2010. “Retinal Imaging and Image Analysis,” IEEE Rev. Biomed. Eng. IEEE Reviews in Biomedical Engineering, vol. 3, pp. 169– 208

[2] Anzalone A, Bizzarri F, Parodi M, Storace M. 2008. A modular supervised algorithm for vessel segmentation in red-free retinal images. Comput Biol Med ;38:913–22.

[3] A. E. Hassanien, E. Emary, and H. M. Zawbaa, 2015. “Retinal blood vessel localization approach based on bee colony swarm optimization, fuzzy c-means and pattern search,” Journal of Visual Communication and Image Representation, vol. 31, pp. 186–196.

[4] Bankhead P, Scholfield CN, McGeown JG, Curtis TM. 2012. Fast retinal vessel detection and measurement using wavelets and edge location refinement. PLoS ONE ;7(3):e32435.

[5] Bezdek J C 1981. “Pattern Recognition with Fuzzy Objective Function Algorithms”, New York: Plenum Press.

[6] Cinsdikici MG, Aydin D. 2009. Detection of blood vessels in ophthalmoscope images using MF/ant (matched filter/ant colony) algorithm. Comput Methods Programs Biomed ;96:85–95.

[7] Chakraborti T, Chowdry AS. 2014. A Self-Adaptive Matched Filter for Retinal Blood Vessel Detection. Machine Vision and Applications. Berlin HeidelBerg: Springer Verlag.

[8] Chaudhuri S, Chatterjee S, Katz N, et al. Detection of blood vessels in retinal images using two-dimensional matched filters. IEEE Trans Med Imaging 1989;8:263–9.

[9] Dunn J C, J.Cybernet 1973. “A fuzzy relative of the ISODTATA process and its use in detecting compact well separated clusters”, pp 32-57, March.

[10] E. Emary, H. M. Zawbaa, A. E. Hassanien, G. Schaefer, and A. T. Azar, 2014. “Retinal vessel segmentation based on possibilistic fuzzy c-means clustering optimised with cuckoo search,” 2014 International Joint Conference on Neural Networks (IJCNN).

[11] Espona L, Carreira MJ, Penedo MG, Ortega M. 2008.Retinal vessel tree segmentation using a deformable contour model. ICPR, 19th International Conference on Pattern Recognition. pp. 1–4.

[12] Franklin SW, Rajan SE.2014. Computerized screening of diabetic retinopathy employing blood vessel segmentation in retinal images. Biocybern Biomed Eng ;34:117–24.

[13] F. Villalobos-Castaldi, E. Felipe-Riverón, L. Sánchez-Fernández, 2010. A fast, efficient and automated method to extract vessels from fundus images, Journal of Visualization 13 263–270.

[14] Fraz MM, Barman SA, Remagnino P, et al. 2012. An approach to localize the retinal blood vessels using bit planes and centerline detection. Comput Methods Programs Biomed;108(2):600–16.

[15] Kande GB, Subbaiah PV, Savithri TS. 2009. Unsupervised fuzzy based vessel segmentation in pathological digital fundus images. J Med Syst;34:849–58.

[16] Lam BSY, Yongsheng G, Liew AWC. 2010. General retinal vessel segmentation using regularization-based multiconcavity modeling. IEEE Trans Med Imaging ;29:1369–81.

[17] Martinez-Perez ME, Hughes AD, Stanton AV, et al. 1999. Retinal blood vessel segmentation by means of scale-space analysis and region growing. The Second International Conference on Medical Image Computing and Computer-Assisted Intervention. London, UK: Springer-Verlag;. p. 90–7.

[18] Martinez-Perez ME, Hughes AD, Thom SA, et al. 2007. Segmentation of blood vessels from red-free and fluorescein retinal images. Med Image Anal;11:47–61.

[19] M. Fraz, P. Remagnino, A. Hoppe, B. Uyyanonvara, A. Rudnicka, C. Owen, and S. Barman, 2012. “Blood vessel segmentation methodologies in retinal images – A survey,” Computer Methods and Programs in Biomedicine, vol. 108, no. 1, pp. 407–433.

[20] Miri MS, Mahloojifar A. 2011. Retinal image analysis using curvelet transform and multistructural elements morphology by reconstruction. IEEE Trans Biomed Eng ;58:1183–92.

[21] Mendonca AM, Campilho A. 2006. Segmentation of retinal blood vessels by combining the detection of centerlines and morphological reconstruction. IEEE Trans Med Imaging ;25:1200–13.

[22] Marin D, Aquino A, Gegundez-Arias ME, Bravo JM 2011. A new supervised method for blood vessel segmentation in retinal images by using gray-level and moments invariants-based features. IEEE Trans Med Imaging;30(1):146–58.

[23] Mohan, J, Krishnaveni, V and Guo Y, 2013. MRI denoising using non local neutrosophic set approach of Wiener filtering, Elsevier - Biomedical Signal Processing and Control, 8(6):779-791.

[24] N. Patton, T. Aslam, T. Macgillivray, I. Deary, B. Dhillon, R. Eikelboom, K. Yogesan, and I. Constable, 2006. “Retinal image analysis: concepts, applications and potential,” American Journal of Ophthalmology, vol. 141, no. 3, p. 603.

[25] Niemeijer MJJ, Staal B, van Ginneken. et al. 2004.Comparative study on retinal vessel segmentation methods on a new publicly available database. SPIE ;648–56.

[26] Niemeijer M, Staal JJ, Ginneken Bv, Loog M, Abramoff MD. 2004 DRIVE: Digital Retinal Images for Vessel Extraction, http://www.isi.uu.nl/Research/Databases/DRIVE.

[27] R. GeethaRamani and L. Balasubramanian, 2016. "Retinal blood vessel segmentation employing image processing and data mining techniques for computerized retinal image analysis", Biocybernetics and Biomedical Engineering, vol. 36, no. 1, pp. 102-118.

[28] Samarandache F. 2003. A unifying field in logics Neutrosophic logic, in Neutrosophy. Neutrosophic Set, Neutrosophic Probability. third ed, American Research Press.

[29] Soares JVB, Leandro.J.J.G., Cesar RM, et al. 2006. Retinal vessel segmentation using the 2-D Gabor wavelet and supervised classification. IEEE Trans Med Imaging;25:1214–22.

[30] Staal J, Abramoff MD, Niemeijer M, et al. 2004. Ridge-based vessel segmentation in color images of the retina. IEEE Trans Med Imaging;23:501–9.

[31] Saffarzadeh VM, Osareh A, Shadgar B. 2014. Vessel segmentation in retinal images using multi-scale line operator and K-means clustering. J Med Signals Sens;4(2):122–9.

[32] S. Roychowdhury, D. Koozekanani, and K. Parhi, 2014. “Blood Vessel Segmentation of Fundus Images by Major Vessel Extraction and Sub-Image Classification,” IEEE Journal of Biomedical and Health Informatics IEEE J. Biomed. Health Inform., pp. 1–1.

[33] S. W. Franklin and S. E. Rajan, 2014. “Computerized screening of diabetic retinopathy employing blood vessel segmentation in retinal images,” Biocybernetics and Biomedical Engineering, vol. 34, no. 2, pp. 117–124.

[34] T. Kauppi, V. Kalesnykiene, J.-K. Kamarainen, L. Lensu, I. Sorri, A. Raninen, R. Voutilainen, J. Pietilä, H. Kälviäinen, H. Uusitalo, 2007. DIARETDB1 diabetic retinopathy database and evaluation protocol, in: Medical Image Understanding and Analysis (MIUA2007), Aberystwyth, Wales, UK, pp. 61–65.

[35] Vlachos M, Dermatas E. 2009.”Multi-scale retinal vessel segmentation using line tracking”. Comput Med Imaging Graph ;34:213–27.

[36] Xu L, Luo S. 2010 “A novel method for blood vessel detection from retinal images”. BioMed Eng Online ;9(14).

[37] Xiaoyi J, Mojon D 2003. “Adaptive local thresholding by verification-based multithreshold probing with application to vessel detection in retinal images”. IEEE Trans Pattern Anal Mach Intell ;25:131–7.

[38] You X, Peng Q, Yuan Y, et al. 2011. “Segmentation of retinal blood vessels using the radial projection and semi-supervised approach”. Pattern Recognit;44:2314–24.

[39] Zhang B, Zhang L, Zhang L, Karray F. 2010. “Retinal vessel extraction by matched filter with first-order derivative of Gaussian”. Comput Biol Med ;40:438–45.