ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 3, Issue 2, pp: (115-129), Month: April - June 2015, Available at: www.researchpublish.com

Retinal Blood Vessel Detection and Segmentation for Diabetic Retinopathy

Atul Kumar Pal & Upendra Kumar

1. INTRODUCTION

The effect of diabetes on the eye is called Diabetic Retinopathy (DR) which can lead to partial or even complete loss of vision if left undiagnosed at the initial stage. Diabetic Retinopathy is the leading cause of blindness in the working age population of developed countries. That is the reason for which efforts that has been undertaken in last few years in developing tools to assist diagnosis of diabetic retinopathy. DR is caused by changes in the blood vessels of the retina. In some people with DR, blood vessels may swell and leak fluid or abnormal new blood vessels grow on the surface of the retina. Images of patient with DR, can exhibits red and yellow spots which are problematic areas indicative of hemorrhages and exudates.

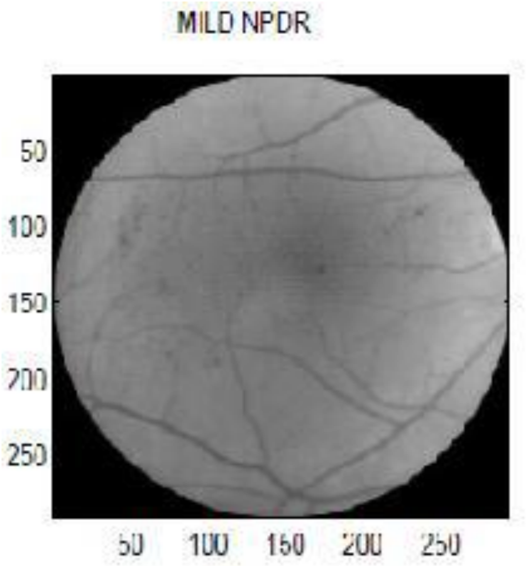
DR has mainly four stages:

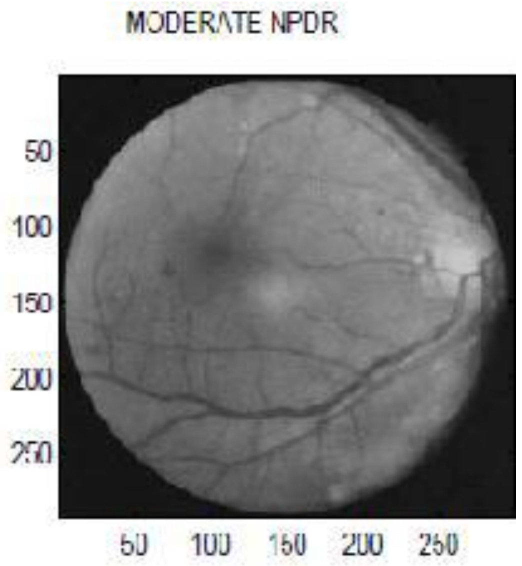
A) Mild Non-Proliferative Retinopathy- At this early stage, micro-aneurysms may occur. These manifestations of the disease are small areas of balloon-like swelling in the retinas tiny blood vessels. Approximately 40 percent of people with diabetes have at least mild signs of DR.

B) Moderate Non-Proliferative Retinopathy- As the disease progresses, some blood vessels that nourish the retina are blocked. Cotton wool spots and limited amount of venous bleeding can be seen. Generally 16 percent of patient with moderate NPDR will develop PDR within one year.

C) Severe Non-Proliferative Retinopathy- Many more blood vessels are blocked, depriving several areas of the retina with their blood supply. These areas of the retina send signals to the body to grow new blood vessels for nourishment.

D) Proliferative Retinopathy-This is the advanced stage, the signals send by the retina for nourishment trigger the growth of new blood vessels. These new blood vessels are abnormal and fragile. They grow along the retina and along the surface of the clear, vitreous gel that fills the inside of the eye. By themselves, these blood vessels do not cause symptoms or vision loss. However, they have thin, fragile walls. If they leak blood, severe vision loss and even blindness can result. About 3 percent of people in this condition may suffer severe visual loss.





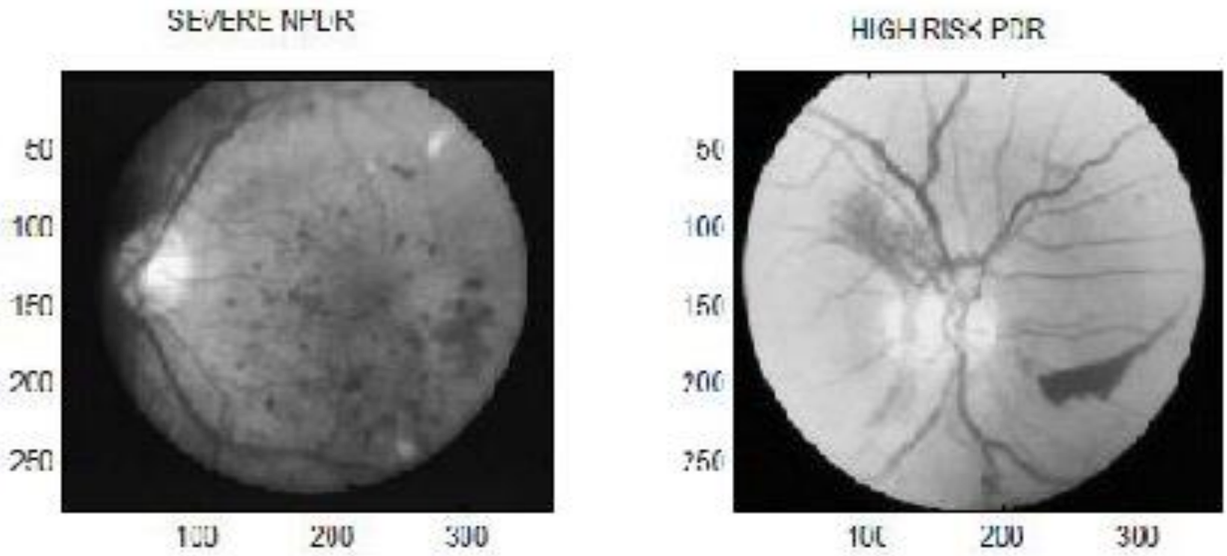


Figure1.1: Different stages of Diabetic Retinopathy

The early stage is further classified as mild NPDR and moderate to severe NPDR. In mild NPDR, signs such as micro-aneurysms, dot and blot hemorrhages and hard or intra retinal exudates are seen in the retinal images. Micro-aneurysms are small, round and dark red dots with sharp margins and are often temporal to macula. Each pixel in the fundus image consists of three values namely red, green and blue, each value being quantized to 256 levels. Diabetic Maculopathy is a stage where fluid leaks out of damaged vessels and accumulates at the center of the retina called macula (which helps in seeing the details of the vision very clearly) causing permanent loss of vision.

Diabetic Retinopathy is one of the most severe and common among the various vision related disorders. It is said to have been caused when the capillaries carrying the oxygenated and deoxygenated blood (nutrient supply) gets damaged of the retinal region. It is so because the retina is one of the primary and complicated part of the human body which gets disrupted by the elevated level of glucose (component of sugar). Retinal photography requires the use of a complex optical system called a fundus camera (specialized low power microscope with an attached camera) capable of simultaneously illuminating and imaging the retina. It is designed to image the interior surface of the eye, which includes the retina, optic disc, macula etc. The location of optic disc is used as a reference length for measuring distances in these images, especially for locating the macula. Optic disc appears as a bright spot of circular or elliptical shape, interrupted by the outgoing vessels. It is seen that optic nerves and blood vessels emerge into the retina through optic disc. Therefore it is also called the blind spot. From patient to patient the size of optic disc varies, but its diameter always lies between 80 and 100 pixels in standard fundus images.

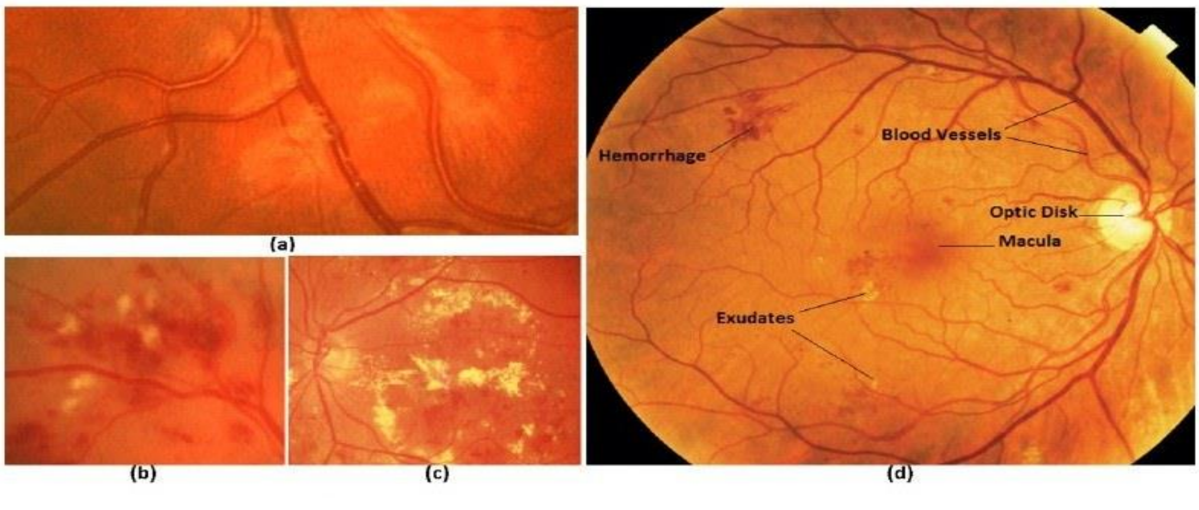


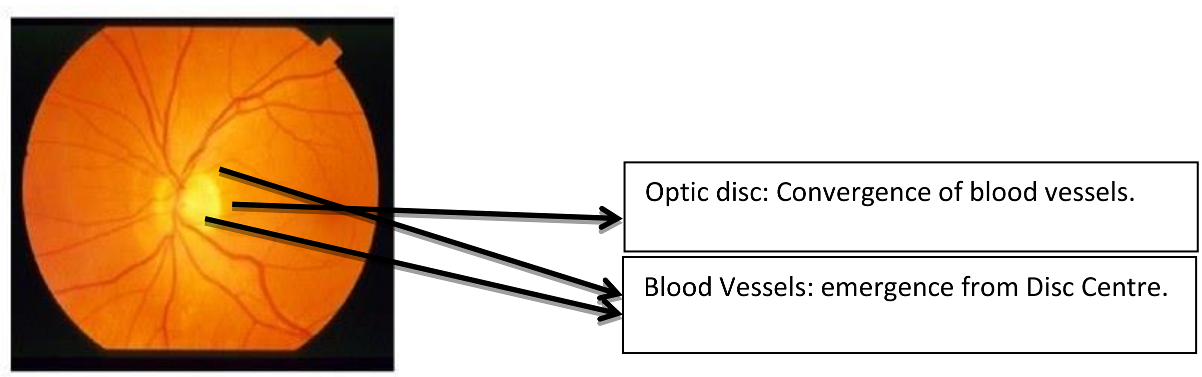
Figure1.2: Different features of Diabetic Retinopathy

1.1 An Introduction to basic terminology involved

Every retinal image has optic disc, blood vessels and fovea. However, an infected or diseased retinal image might notice certain other features like exudates and micro-aneurysms, referred to as hemorrhages. A brief description about them is illustrated below-

1.1.1 Optic Disc

It is characterized by a bright patch in the back of an eye. The blood vessels emerge from its Centre. The first step in the blood vessel segmentation process initiates from the detection of optic disc in retinal fundus images. If there are any variations in texture or appearance then it may serve as an indication of any possible pathology. The image is shown below;



(a)

1.1.2 Blood Vessels

Blood is a connective medium or fluid throughout our body and our somatic cells derive all its nutrients including oxygen from the blood. The blood reaches every part of our body through a network of arteries and veins. Arteries carry the oxygenated blood from outside to the body whereas; veins carry the deoxygenated blood from body back to heart and lungs for exhalation.

1.1.3 Fovea

The term used for the central part of the retina is FOVEA and is the region of highest visual activity. Fovea is located in the center of macula.

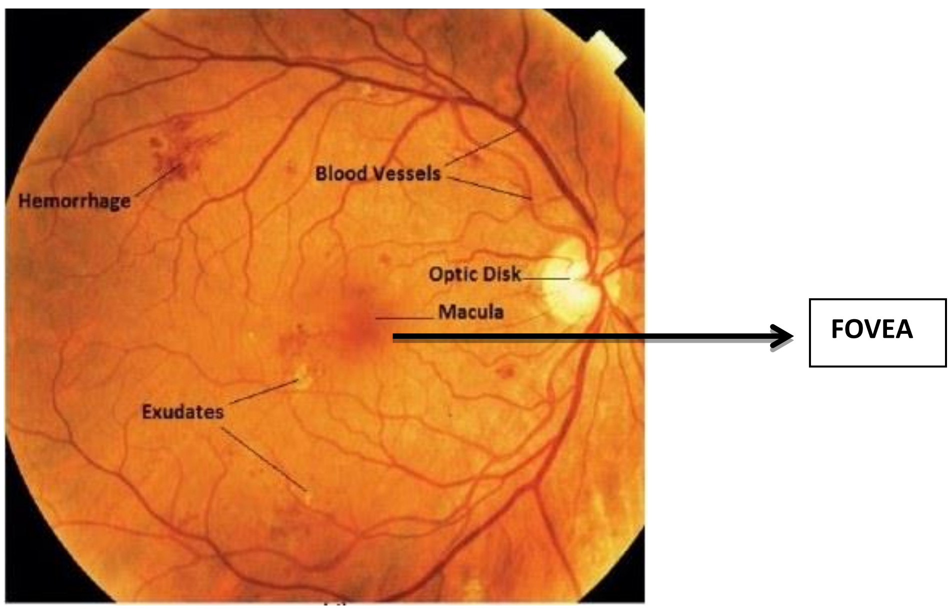


Figure 1.3: Showing fovea

1.2 Abnormal Features of Retina:

1.2.1 Exudates:

Retinal image analysis by detection of exudates and recognizes retina to be normal or abnormal. Exudates are yellowish intra retinal deposits, serum lipoproteins. This is formed when lipid or fat leaks from abnormal blood vessels. Vision loss occurs if exudates extend into macular area. There are various morphological approaches for exudate detection in retinal images and compared with normal retinal images for detection of exudates. The shape and size of the exudates changes as the severity of the disease changes. The figure above clearly supports the text in illustration.

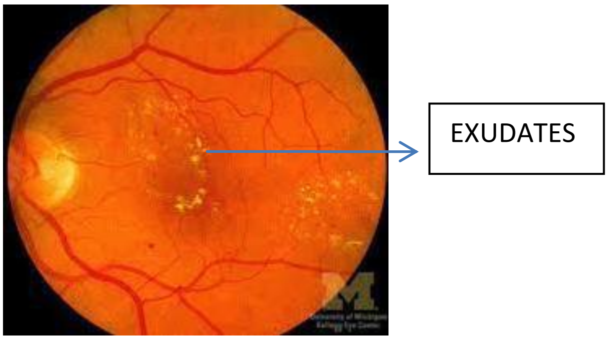


Figure 1.4: Showing exudates

1.2.2 Hemorrhage:

It occurs when blood leaks from the retinal vessels. The blockage of arterial vein by hypertension or by diabetes mellitus. It can cause severe impairment of vision.

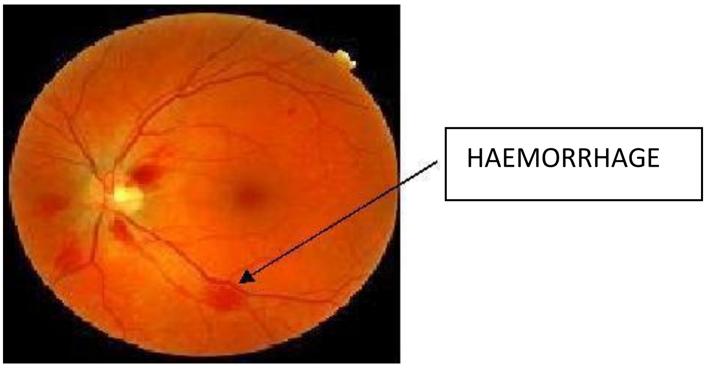


Figure 1.5: Showing haemorrhage

Exudates are one of the prior sign of the diabetic retinopathy and its detection is one of the main important tasks. Hence the detection of exudates must be done prior as optic disc and exudates are of the similar contrast. For automatic assessment of retinal images, segmentation of the vessels and optic disc from the background is considered as a prior requirement. However as the retinal images acquired with a fundus camera often are identified with low grey level contrast and poor illumination, hence the problem can seriously affect the segmentation results.

It is known that fovea is one of the landmarks of retinal fundus images but due to the above discussed regions, the focus here is laid only on blood vessels and optic disc. Several authors have proposed their work on segmentation of optic disc and blood vessels and they are summarized in the form of literature survey given below. Therefore the work related to thesis is to segment the landmarks in the retinal fundus images that are optic disc and blood vessels so that we can diagnose the abnormalities related to disease properly.

Therefore it is very necessary to carry out contrast enhancement as one of the main step required pre-processing particularly for those cases where the original retinal image is considered not good candidate for producing the desired segmentation. Several techniques have been employed for improving the quality in terms of contrast and illumination of the retinal images. Hence in this proposed work we have removed optic disc with the help of thresholding. Firstly morphological operation dilation is applied on the contrast limited equalized image and after getting the proper region of optic disc we applied thresholding.

1.3 Proposed Work:

The objectives of this thesis work are:

1. To study the terms and features associated to the term Diabetic Retinopathy.
2. To study methods proposed for pre-processing, optic disc removal, blood vessel segmentation with illustrations.
3. To draw comparison with the output images to the provided images of standard database (DRIVE) for blood vessel segmentation.

1.4 Organization of Thesis:

The thesis is orchestrated as follows:

Chapter 1 introduces the term Diabetic Retinopathy and brief idea about the factors contributing to Diabetic Retinopathy. The image segmentation problem can be stated as the division of an image into regions that separate different objects from each other, and from the background. This chapter will review many of the existing features and terms, and discuss the particular characteristics of each feature. The purpose of this chapter is to give the reader an overview of the currently studied image, and, together with the review chapter on perceptual grouping, to provide a background against which the contributions of our research can be weighted. However, before undertaking a review of image segmentation techniques, it is important to be more precise about the definition of the problem we are interested in.

Chapter 2 discusses the literature survey of optic disc removal, detection of exudates and blood vessel segmentation.

Chapter 3 discusses the methodology applied or the steps proposed for the removal of optic disc, blood vessel segmentation and the detection of exudates and results and discussion with limitations.

Chapter 4 deals with results and discussions of our project.

Chapter 5 deals with conclusions and future work for our project.

2. METHODOLOGY

The method is divided into four phases: Pre-processing, Optic disc removal, Blood vessel segmentation, and Detection of exudates. In the first step of proposed methodology landmarks are segmented as it was described earlier they are optic disc and blood vessels. Then in the next step exudates are detected taken on a different image. Fig 7 shows a chart of the proposed scheme. First the retinal image is taken from the database and converted into grey scale image. Basically pre-processing steps include contrast enhancement and dilation and it is applied to the grey image. Contrast Limited Adaptive Histogram Equalization (CLAHE) is applied as the original image taken is blurred and the contrast is very low. Hence to improve the contrast of the image is a very necessary step.

According to the proposed work the method is divided into following phases:

1. Pre-processing.
2. Locating Optic disc and its removal.
3. Blood vessel segmentation.
4. Exudates Detection.

2.1 Steps for pre-processing:

Step 1: Original Image

First and foremost step is to acquire an original image. They are originally RGB in nature and hence it is necessary to convert it into the grey scale image.

Step 2: Greyscale image

After taking the original image we are going to convert it into grey scale image. As we know that original image is RGB and only green and grey scale image has to be extracted. Hence greyscale image is used for pre-processing. Greyscale image is considered as the natural basis for many segmentation algorithms.

ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 3, Issue 2, pp: (115-129), Month: April - June 2015, Available at: www.researchpublish.com

Step 3: Contrast Enhancement

Contrast enhancement is one of the main parts of pre-processing. The result of adaptive histogram equalization. Histogram equalization is performed to improve the image quality. Histogram equalization is nothing but a finding of cumulative distribution function for a given probability density function. After the transformation, the image will have an increased dynamic range, high contrast and probability density function of the output will be uniform. Instead of using normal histogram equalization, adaptive histogram equalization is used as it operates on small regions in the image which are called tiles. Adaptive histogram combines neighboring tiles using bilinear interpolation to eliminate artificially induced boundaries. It consequently improves the contrast of every region and thus helps in making the invisible features of the image more visible. The main purpose of using this technique is that the **CLAHE algorithm** partitions the images into different regions and then applies the histogram equalization to each region. Here the CLAHE algorithm has applied on the grey image. Earlier simple histogram equalization was also applied but it showed little improvement in the color balance. That's why CLAHE is applied in this procedure instead of simple histogram equalization.

2.1.1 Importance of Pre-processing:

1. Helps to improve original image data
2. Helps in extracting morphological features.
3. Morphological features of different pathological structures can be obtained.
4. Provides important information essential for clinical diagnosis.

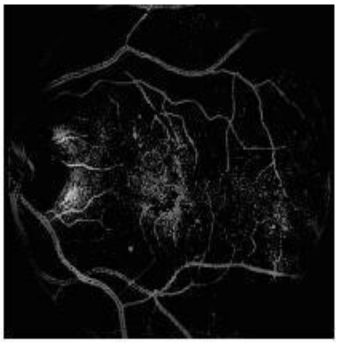
2.2 Location of Optic Disc:

Some of the previous work done by researchers in this domain is as follows: Fengshou Yin proposed the use of edge detection algorithm and applied on the pre-processed image to make it suitable for detection of the optic disc, blood vessel and exudates. For contour detection, canny edge detector is employed. This algorithm is useful in finding the edges where the greyscale intensity of the image changes. It also enhances the blurred edges which are not visible properly. The mask image was created in the region of interest, is the optic disc. The masked image, optic disc is subtracted from the edge detected image.

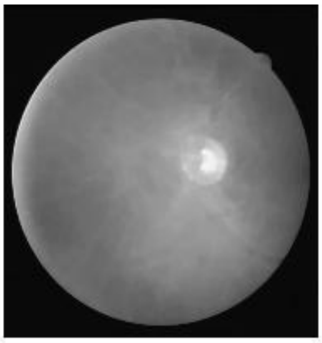
2.2.1 Related Work

Before working on proposed methodology, several already imposed methods have been applied and results are shown below. Mahendran Gandhi proposed the use of edge detection algorithm and applied on the pre-processed image to make it suitable for detection of the optic disc, blood vessel and exudates. For contour detection, canny edge detector is employed. This algorithm is useful in finding the edges where the greyscale intensity of the image changes. It also enhances the blurred edges which are not visible properly. The mask image was created in the region of interest, is the optic disc. The masked image, optic disc is subtracted from the edge detected image.

In second method, Akara Sopharak proposed that the optic disc can be removed by subtracting the image after histogram equalization from the image after applying morphological opening operator. The method has certain limitation, although it is showing blood vessels clearly but the region of optic disc is not clear. **S. Ravishankar** proposed a method by applying morphological closing operator on the grey scale image as it will help in eliminating the vessels and provides a more homogeneous region for optic disc.



(a)



(b)

Fig 2.1: a) subtraction of image after histogram equalization. b) Removal of optic disc after applying closing operator.

2.2.2 Proposed Work:

The method herein presented is described here under the following sub- headings. We have seen that in pre-processed image optic disc region was showing clearly hence for this reason we are using here pre- processed image, the we will apply the dilation function which as its name suggests would dilate the key features thus enhancing the visibility of optic disc. Hence, to make optic disc more clearly we are going to use dilation.

2.2.3 Steps for Optic Disc Removal:

Step 1: Pre-Processed Image:

The first step to this approach is pre-processing. As it has been described earlier that CLAHE is an important part of pre-processing, hence it is necessary to take the pre-processed image for optic disc removal.

Step 2: Dilation

In the second step dilation is applied on the contrast enhanced image. Dilation is a morphological operator and it grows or expands the boundaries of an image. A flat disc shaped structuring element (SE) was used. With the help of dilation it was observed that the region of optic disc has been shown clearly. Certain types of SE elements are available and they are categorized as disc, diamond and square. Structuring element is a matrix consisting of zeros and ones only.

Step 3: Thresholding

The resulting image after applying dilation was binarized by thresholding. Thresholding is useful for removing those components of the image which are not useful. It can also be used to bring out hidden details. Thresholding is useful in that region of the image which is occupied by similar grey levels. In this global thresholding is applied on the dilated image.

2.3 Blood Vessel Segmentation:

The landmark changes in shape, size, diameter and branching pattern of retinal blood vessels is a key indicator of the disorder of the eye. The main focus of this work depends upon the detection of vessel shape and morphological features. The shape and orientation map of retinal vessels is obtained with the help of morphological bit plane slicing on bottom hat image. Bottom hat transform is defined as the difference between the closing image and the input image. Bottom hat transform is applied on the contrast enhancement image.

Figure 3.2: Blood vessels removed after applying bottom hat transform.

2.3.1 Steps for Blood Vessel Segmentation:

Step 1: Contrast Enhancement

Mathematical morphology is a very important tool in image analysis and is used for detection of retinal pathologies in retinal fundus images. The basic morphological operations are opening, closing and dilation with the help of structuring element. The morphological opening operation, which is usually erosion followed by dilation removes objects from the image that are not in the same size than the used structuring element. Therefore enhancement of the objects can be done with the help of subtracting the opened image from the original image. For removal of blood vessels morphological opening operator can be used with a small structuring element.

Step 2: Bottom hat transform

Morphological operator bottom hat transform is used with the help of structuring element. The size of the structuring element can vary from 1 to 8 pixels. For images with different range the size of the structuring element should vary accordingly. Bottom hat transform is used to extract low level grey components such as vessels. In bottom hat transform input image is subtracted from closed image. If a larger structuring element is used then larger vessels can be eliminated and thinner vessels will get blurred. Therefore it would be more preferable to use larger structuring element because in this the blood vessels are showing more clearly.

Step3: Morphological Bit Plane Slicing

Bit plane slicing plays an important role in order to change the total image appearance by specific bits. By separating a digital image into its bit planes, then each bit is helpful in examining the importance of each bit of the image. The image that results from the bottom hat transform is an improved greyscale image in which blood vessels are seen more than the background. The 8 bit gray image can be shown in the form of bit planes and the bit plane 1 is having the least significant bit whereas bit plane 8 is known for its higher significant bit. It can be seen that in bit plane 7 and bit plane 8 more relevant information related to the vessels is present. The other bit plane image is also important but it does not contain any useful information related to vessels and often neglected. Hence the binary image can be obtained by taking the sum of two bit planes and they are bit plane 7 and bit plane 8. Hence the resultant image contains important information related to vessels.

Step 4: Median Filtering:

The final result after combining floor image 7 and floor image 8 although contains relevant information related to vessels but there is also little existence of salt and pepper noise. Hence for proper extraction of blood vessels and to reduce the effect of noise, median filtering plays an important role. Here median filtering is implemented two times due to the presence of noise.

2.4 Exudate Detection:

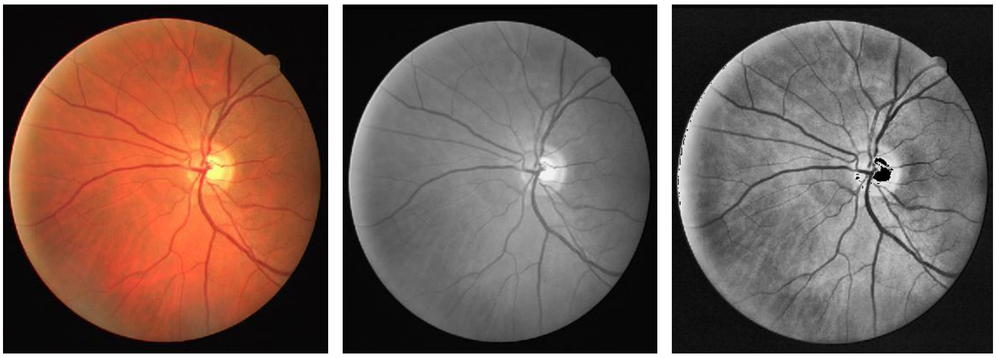
Early detection of DR is necessary for the prevention of visual loss. Hard exudates are one of the main signs of the DR. Due to their high occurrence; their detection would play an important role in the screening purpose, and helps in monitoring and for estimation of the disease. Hence automatic detection of exudates is a very crucial task because normally they have poor contrast, uneven illumination and color variation in retinal fundus images. Exudates become difficult to identify as the stage of diabetic retinopathy changes. Most of the work has been done by the researchers for the detection of exudates.

After removing the optic disc and blood vessels from the retinal fundus images, exudate detection is our main aim. Therefore exudates can be identified with the help of *impixelinfo* operator. *Impixelinfo* tool helps in creating a pixel information tool in the current figure. The pixel information tool displays information related to the pixel in that image where the pointer is positioned over. *Impixelinfo* operator will be performed on the threshold image.

3. RESULTS AND DISCUSSIONS

3.1 Pre-Processing Results:

Pre- processing is done with the help of CLAHE algorithm. The CLAHE algorithm has been applied on the grey scale image.

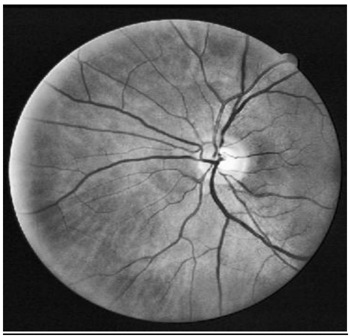


1. **Original image** 2. **Greyscale image.** 3. **Contrast enhanced image**

Figure 3.1: Showing results of the proposed algorithm

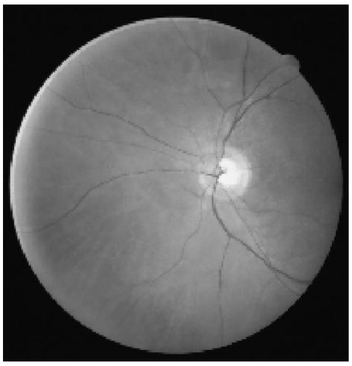
3.2 Results and Discussions of Optic Disc Removal:

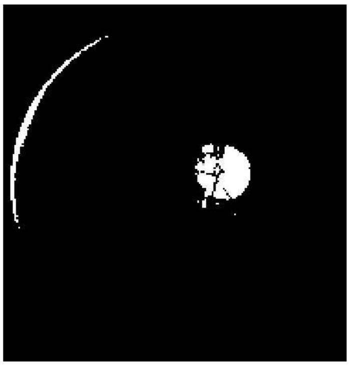
Step 1*:* The result of the pre- processed image is shown in Figure below. Here the pre-processed image is the same as described in the above section



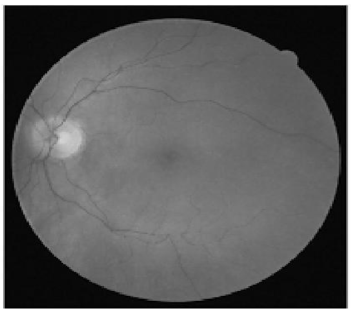
Contrast enhanced image

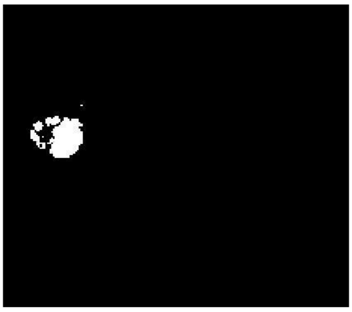
Step 2: The result after applying dilation and thresholding are shown below. After applying dilation proper region of optic disc is shown and after applying thresholding optic disc is removed.



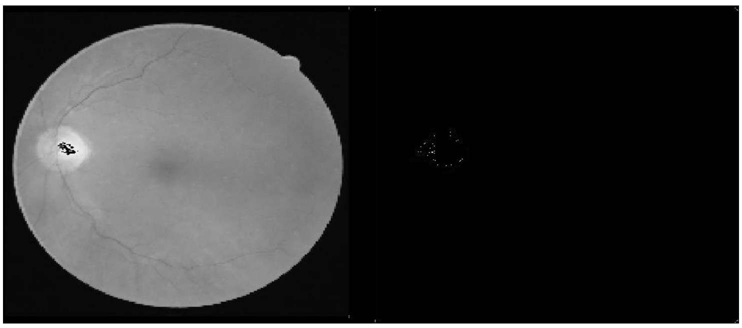


(a) Dilated image **(b) Optic disc removal**





(c) Dilated image; **(d) Optic disc removal**



(g) Dilated image; **(h) Optic disc removal**

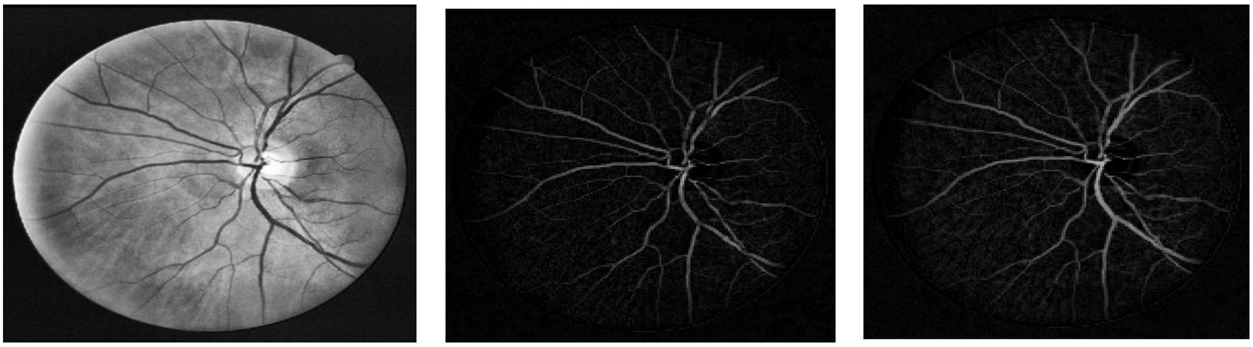
Figure 3.2: Showing comparison of dilated image and after optic disc removal

ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 3, Issue 2, pp: (115-129), Month: April - June 2015, Available at: www.researchpublish.com

The objective of this work is to investigate a method for automatic analysis of retinal images for the detection and recognition of retinopathy diseases. In this work several methods have been investigated and a set of suitable morphological steps for automatic detection of optic disc have been proposed. Despite the existence of pathological reasons, the results of the applied method are satisfactory, and the localization of the centre of the optic disc found to be effective. Images were taken from Drive database. The method was tested on the training set and test set of Drive and it showed remarkable results.

3.3 Results and Discussions on Retinal Blood Vessel Segmentation:

Step 1: The result after applying CLAHE is shown;



Contrast enhanced image a.) Bottom hat transform with smaller structuring element.

b.) Bottom hat transform with larger structuring element.

Figure 3.3: Showing contrast enhanced image comparison

Step 2: Morphological bit plane slicing has been applied for blood vessel segmentation. Fig (a) shows the result of morphological floor bit plane 7. The result of combined morphological floor image 7 and floor image 8.

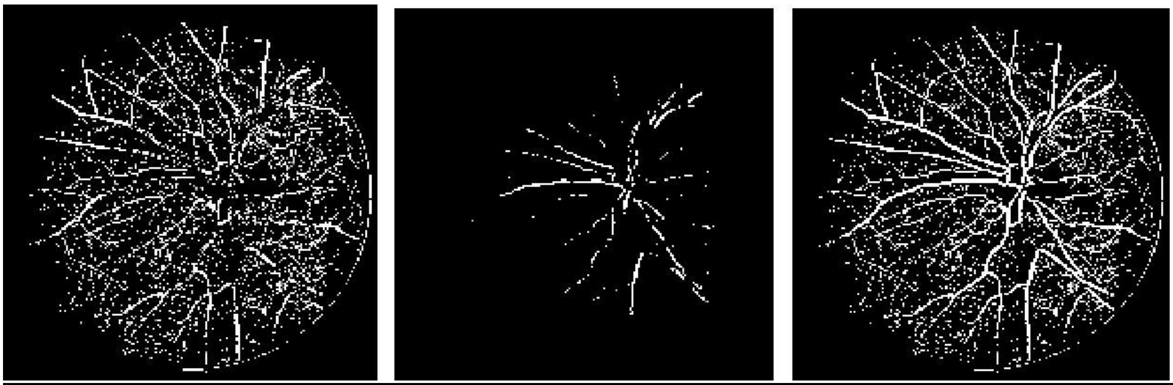


Figure 3.4 (a) Morphological bit plane floor image; (b) Morphological bit plane floor image (c) Combined morphological bit plane slicing 7 and 8.

Step 3: The results after applying median filtering are shown in Fig a); fig. b);

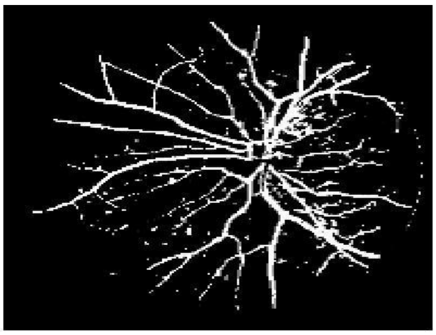


Figure 3.5: (a) Median filtering

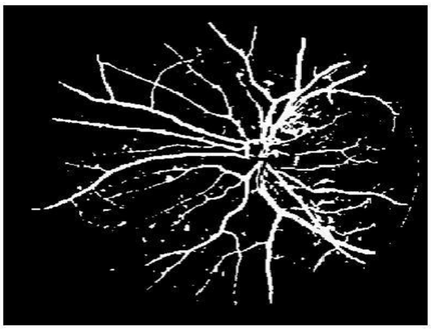


Figure 3.5: (b) Blood vessel segmentation

Step 4: The results of the blood vessel segmentation after removing connected components

The results are compared with the standard database and are shown

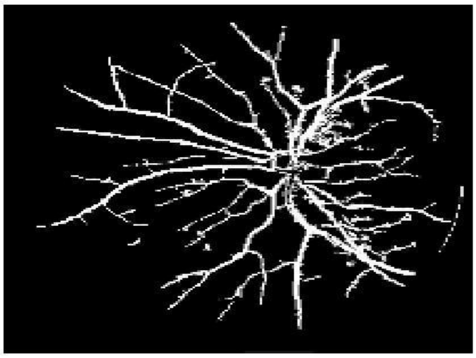


Fig.3.6: (a) BV segmentation.

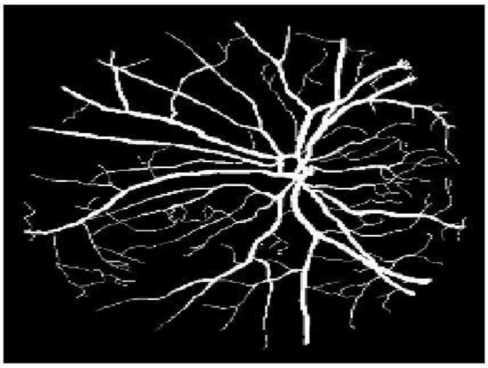


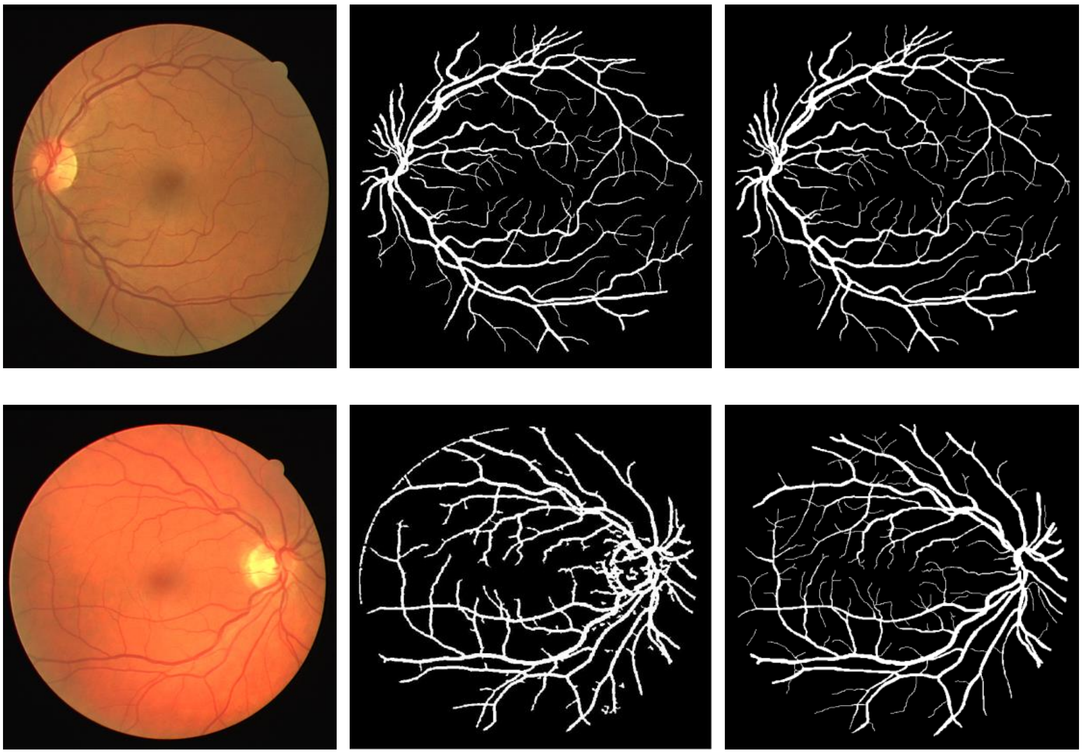
Fig.3.6: (b) standard database.

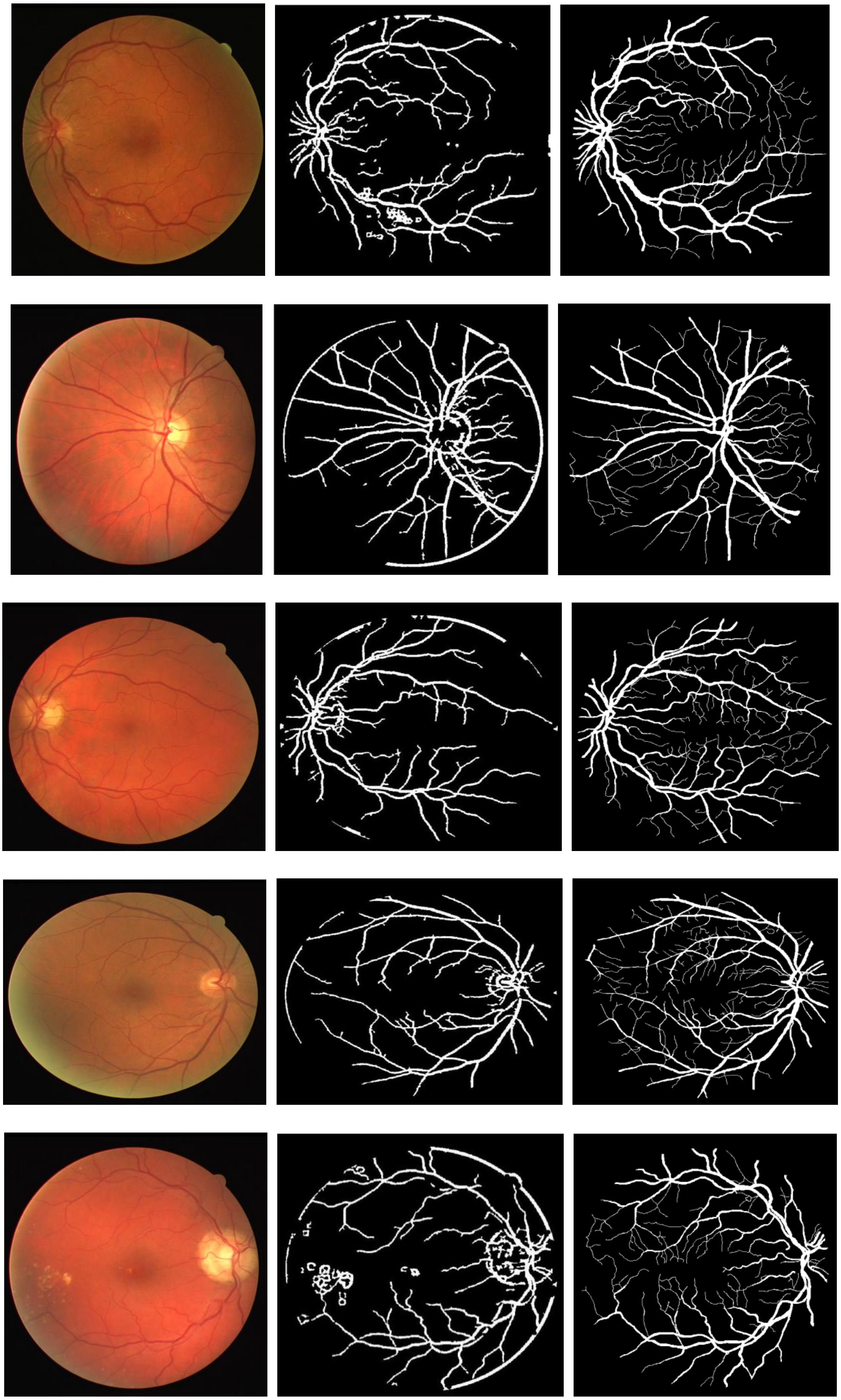
An automated segmentation method has been proposed for identification of blood vessels. Mathematical morphology and bit plane slicing have been used to extract the blood vessels clearly. The shape and orientation maps are generated by the application of a multidirectional bottom hat transform with a linear structuring element which emphasizes the vessels in a particular direction and after that important information is extracted from gray scale with the help of morphological bit plane slicing. The final image containing vessels is obtained with the help of median filtering using two times. The methodology has been tested on Drive database.

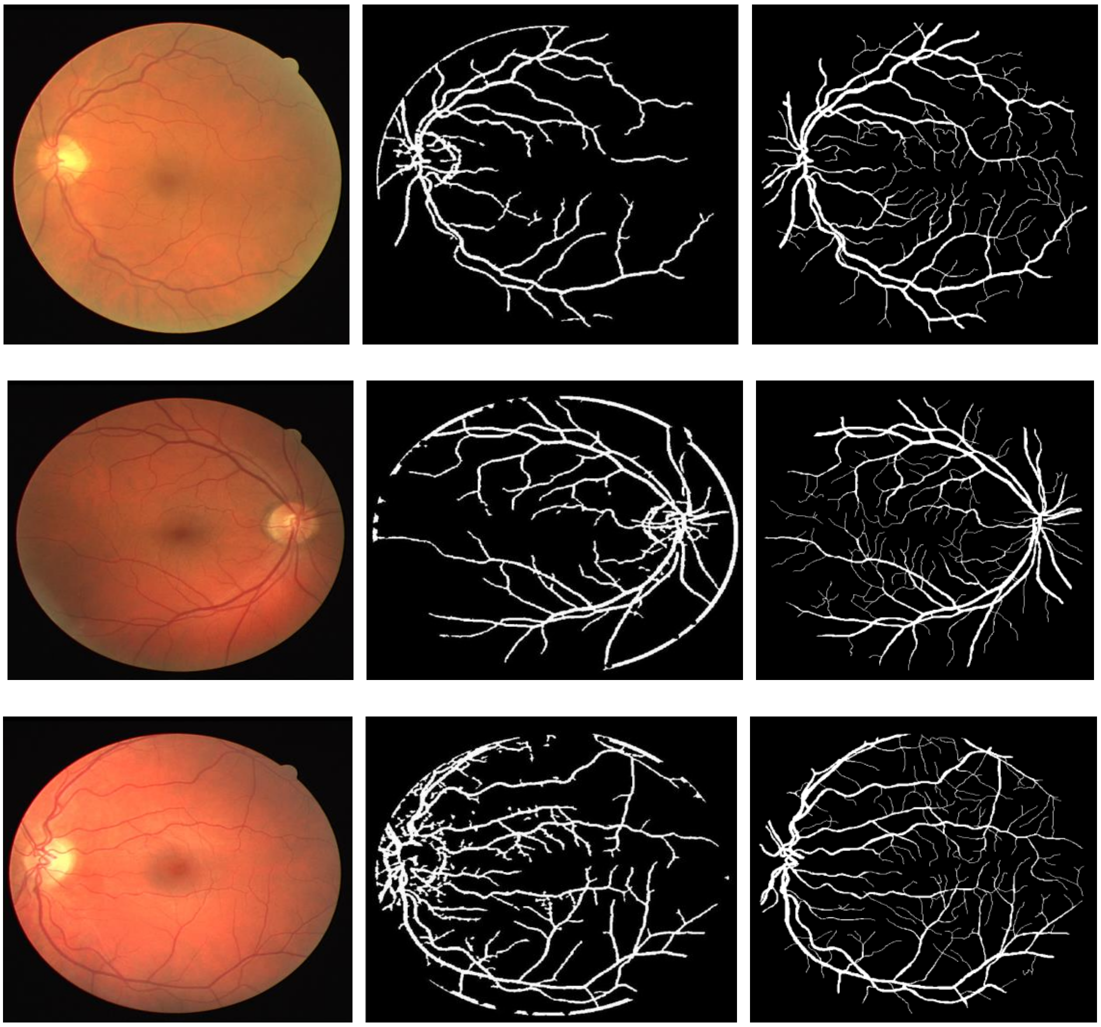
3.4 Limitations:

Blood vessel segmentation plays an important role in the diagnosis of various retinal eye diseases. We are using two methods above; in the first method we are applying median filtering we are observing that some noise is present and if we are using connected components method in that also some of the part of the vessels is eliminating. But these are very little problems and can be overcome in the future.

INPUT IMAGE | **SEGMENTED IMAGE** | **DATABASE IMAGE FOR COMPARISON**







3.5 Results and Comparison:

INPUT IMAGE SEQUENCE	PIXELS IN OUTPUT SEGMENTED IMAGE	PIXELS IN PROVIDED IMAGE	ACCURACY
INPUT IMAGE 1	29440	32611	90 %
INPUT IMAGE 2	33981	33790	99 %
INPUT IMAGE 3	25875	32893	79 %
INPUT IMAGE 4	29841	30354	98 %
INPUT IMAGE 5	23259	30912	75 %
INPUT IMAGE 6	22773	32116	71 %
INPUT IMAGE 7	24861	28389	88 %
INPUT IMAGE 8	19842	26741	74 %
INPUT IMAGE 9	27033	27156	100 %
INPUT IMAGE 10	29539	30987	95 %
Total Accuracy			87 %

The input images in the above figures are followed by the segmented image which is obtained by the methods proposed in the thesis work. This image is then compared to the corresponding image provided in the DRIVE database for each input image. The images are resized and then compared for calculating the overlapping pixels. The output is tabulated above and gave accuracy of 87 %. Based on the results obtained it can be demonstrated that the method will be useful in a wide range of retinal images.

4. CONCLUSION AND FUTURE WORK

The methodology employed a combination of different image processing techniques and the application of morphological bit plane slicing for blood vessel segmentation. The shape and orientation maps can be initiated with the help of morphological operator bottom-hat transform with the help of structuring element which helps in orientation of blood vessels in the particular direction and after that useful information can be selected from the morphological bit plane slicing. The morphology has been tested and compared with two publicly available databases Drive. Experimental results show that the results achieved with the proposed methodology are good and can be compared with the published results and almost equal to the performance of human observers. The vessel tree segmented it depends upon the canter lines of the vessels and the shape and orientation of the vessels. By applying the median filtering and connected components it was found that the vessels are segmented properly although some noise is present but important features are extracted. The vessels which are segmented can be used for the diagnosis of many diseases such as glaucoma and diabetic retinopathy. If a comparison is done between the blood vessels of a diseased person with the normal person the diameter of the blood vessels may change or the occurrence of some new blood vessels. Hence our future work deals with the segmented blood vessels if they belong to normal person or diseased person. In this work a set of morphological steps has been proposed for the detection of optic disc and exudates. If the detection of exudates is required then optic disc must be removed prior to that because they have similar color and contrast with that to exudates. The method developed to detect exudates will help the doctors in screening process of diabetic retinopathy process to detect symptoms faster. The results are encouraging and will be used for further application such as personal identification and are evaluated in terms of sensitivity and specificity and accuracy.

The method has been evaluated and compared with the database images of Drive on both the test and training images both containing 20 images. All the images showed good results either in terms of contrast, optic disc removal and blood vessel segmentation.

REFERENCES

[1] AkaraSopharak, B. Uyyanonvarsa, S. Barman, T. H. Williamson, “Automatic Detection of diabetic retinopathy exudates from non-dilated retinal images using mathematical morphology methods”, Computerized Medical Imaging and Graphics on ELSEVIER, vol 32, pp 720 – 727, 2008.

[2] T. Walter, J. C Klein, P. Massin, and A. Erginay, “A contribution of image processing to the diagnosis of diabetic retinopathy – Detection of Exudates in Color Fundus Images of the Human Retina”, IEEE Transactions on Medical Imaging, vol 21, pp 1236 – 1241, 2002.

[3] Mahendran Gandhi, and R. Dhanasekaran, “Diagnosis of diabetic retinopathy using morphological process and svm classifier”, International Conference on communication and signal processing”, pp 873 - 877, 2013.

[4] Eman M. Sahin, Taha E. Taha, W. Al- Nuiamy, S. El Rabaie, Osama F. Zahran, and Fathi E. Abd El- Samie, “ Automated detection of diabetic retinopathy in blurred digital fundus images”, IEEE Transactions on Medical Imaging , pp 20-25, 2012.

[5] S. Ravishankar, A. Jain, and A. Mittal, “Automated feature extraction of early detection of diabetic retinopathy in fundus images”, International Conference in IEEE, pp 210- 220, 2009.

[6] M. G. FakhtarEadgahi, H. Pourreza, “Localization of Hard Exudates in Retinal Fundus Image by Mathematical Morphological Methods”, International Conference on Computer and Knowledge Engineering, pp 185 – 189, 2012.

[7] D. Marin, A. Aquino, M. E. Gegundez –Arias, J.M Bravo, “A new supervised method for blood vessel segmentation in retinal images by using gray level and moment invariants based features”, IEEE Transactions on Medical Imaging, vol 30, pp 146 – 158, 2011.

[8] G. B. Kande, P. V. Subbaih, and T. SatyaSavithri, “Segmentation of exudates and optic disc in retinal images”, 6th Indian Conference on Computer Vision, Graphics and Image Processing”, pp 535 – 540, 2008.

[9] D. Welfer, J. Scharcanski, D. RuschelMarinho, “A coarse to fine stradegy for automatically detecting exudates in colour eye fundus images”, Computerized Medical Imaging and Graphics, vol 34, pp 228 - 235, 2010.

[10] A.W. Reza, C. Eswaran, S. Hati, “Automatic tracing of optic disc and exudates from color fundus images using fixed and variable thresholds”, J. Medical Systems, vol 33, pp 73- 80, 2009.

[11] K. Jeyasri, P. Subathra, and K. Annaram, "Detection of blood vessels for disease diagnosis", International Journal of Advanced Research in Computer Science and Engineering", vol 13, pp 6 – 11, 2013.

[12] A. W. Reza, C. Eswaran, K. Dimyati, "Diagnosis of Diabetic Retinopathy: Automatic Extraction of Optic Disc and Exudates from Retinal Images using Marker-controlled Watershed Transformation", JMedical System, vol 35, pp 1491 – 1501, 2011.

[13] A. M. Mendonca, A. Campilho, "Segmentation of Retinal images".

[14] S. Ravishankar, A. Jain, and A. Mittal, "Automated feature extraction of early detection of diabetic retinopathy in fundus images", International Conference in IEEE, pp 210- 220, 2009.

[15] M. G. FakhtarEadgahi, H. Pourreza, "Localization of Hard Exudates in Retinal Fundus Image by Mathematical Morphological Methods", International Conference on Computer and Knowledge Engineering, pp 185 – 189, 2012.

[16] K. Noronha, J. Nayak, S. N. Bhatt, "Enhancement of retinal fundus image to highlight the features for detection of abnormal eyes", 10th Conference in IEEE, pp 1- 4, 2006.

[17] A. A. H. A. R. Youssif, A. Z. Ghalwash, and A. A. S. A. R. Ghoneim," Optic disc detection from normalized fundus images by means of a vessels direction matched filter", IEEE Transactions on Medical Imaging, vol 27, pp 11 – 18, 2008.

[18] A. S. Gonzalez, D. Kaba, Y. Li and X. Liu, "Segmentation of blood vessels and optic disc in retinal images", DOI 10.1109 / JBHI .2014. 2302749, IEEE Journal of Biomedical and Health Informatics, pp 1-14.

[19] Aquino, M. E. Gegundez-Arias, and D-Marin, "Detecting the optic disc boundary in digital fundus images using morphological, edge detection, and feature extraction techniques", IEEE Transactions on Medical Imaging , vol 29, pp 1860 – 1869, 2010.

[20] J. Lowell, A. Hunter, D. Steel, A. Basu, R. Ryder, E. Fletcher, and L. Kennedy, "Optic nerve head segmentation", IEEE Transactions on Medical Imaging , vol 23, pp 256 – 264, 2004.

[21] M. H. S. P. Kumara, and R. G. N. Meegama, "Active contour based segmentation and removal of optic disk from retinal images", International Conference on Advances in ICT for Emerging Regions, pp 015 – 020, 2003.

[22] M. Foracchia, Grisan, and A. Ruggeri, "Detection of optic disc in retinal images by means of a geometrical model of vessel structure", IEEE Trans. Med. Imaging, vol. 23, pp 1189 – 1195, 2004.

[23] H. Yu, E. S. Barriga, C. Agurto, S. Echegaray, M. S. Pattichis, W. Bauman, and P. Soliz, "Fast localization and segmentation of optic disc in retinal images using directional matched filtering and level sets", IEEE Transactions on Information Technology in Biomedicine, vol 16, pp 644 – 657, 2012.

[24] F. Yin, J. Liu, S. H. Ong, Y. Sun, Damon W. K. Wong, N. M. Tan, C. Cheung, M. Baskaran, T. Aung, T. Y. Wong, "Model based optic nerve head segmentation on retinal fundus images", 33rd Annual International Conference of the IEEE, pp 2626 – 2629, 2011.

[25] M. UsmanAkram, and AasiaKhanum, "Retinal images: Blood vessel segmentation by threshold probing", IEEE Symposium on Industrial Electronics and Applications, pp 493 – 497, 2010.

[26] S. Supot, C. Thanapong, P. Chuchart, and S. Manas, "Automatic segmentation of blood vessels in retinal image based on fuzzy k-median clustering", IEEE International Conference on Integration Technology, pp 584 – 588, 2007.

[27] S. H. Rezatofighi, A. Roodaki, H. AhmadiNoubari, "An enhanced segmentation of blood vessels in retinal images using contourlet", 30th Annual International IEEE Conference, pp 3530 – 3533, 2008.

[28] J. Cheng, J. Liu, D. W. K. Wong, F. Yin, C. Cheung, M. Baskaran, T. Aung, and T. Y. Wong, "Automatic optic disc segmentation with peripapillary atrophy elimination", 33rd International Conference of the IEEE, pp 6224 – 6227, 2011.

[29] S. Huang, Y. Yang, and Y. Xia, "Segmentation of retinal image vessels with a novel automated approach", Sixth International Conference on Intelligent Systems Design and Applications", 2006.

[30] C. I. Sanchez, M. Garcia, A. Mayo, M. I. Lopez, R. Hornero, "Retinal image analysis based on mixture models to detect hard exudates", Medical Image Analysis, vol 13, pp650 – 658, 2009.

[31] S. Chaudhuri, S. Chatterjee, N. Katz, M. Nelson, and M. Goldbaum, "Detection of blood vessels in retinal images using two-dimensional matched filters", IEEE Transactions on Medical Imaging, pp 263 – 269, 1989.