New Algorithm of Retinal Blood Vessel Segmentation for Early Detection of Diabetic Retinopathy

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Abstract: Retinopathy is one of the diabetic patient's complications. This has no early warning signs. Modern researches in image processing could help in early diagnosing retinopathy and consequently avoid diabetes patient's blindness. This research proposes a new method in handling the matched filter to extract blood vessels with high accuracy. High pass, Laplacian, Soble and Laplacian of Gaussian are four types of matched filters are used and the result performance is calculated by ROC curves. According to the results of proposed methods, Laplacian of Gausian method provides best performance in comparison with previous work.
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1. Introduction

Diabetic retinopathy (DR) is a common complication of diabetes, it is the leading cause of blindness in the working population of western countries [1], however, early detection combined with appropriate treatment and management can prevent the loss of vision in up to 95% of cases [2, 3-5].

Diabetic retinopathy is the manifestation of systemic disease which affects up to 80% of all patients who have had diabetes for 10 years or more [6], this high prevalence of diabetes therefore makes mass screening an expensive and time consuming process. It has been shown that an automated system could greatly reduce the workload by filtering out 50% of the screening population [7], therefore, there has been an increase in the application of digital image processing techniques for automatic detection of DR [8].

Screening for DR with the use of seven-field stereo fundus photography read by a trained reader is the current, non-invasive gold standard. Diabetic retinopathy grading using the fundus images is significantly more sensitive than standard opthalmoscopy, which can miss approximately 50% of subjects with only microaneurysms, resulting in under reporting of DR prevalence rates by approximately 10% [9,10].

A large retrospective analysis of 10,000 consecutive patient visits was performed, but it was concluded that automated detection of DR using published algorithms cannot yet be recommended for clinical practice. In addition, it was also concluded that if the algorithms can be improved, such a system may lead to improved prevention of blindness and vision loss in patients with diabetes [11].

Fundus photography and computer algorithms can be combined to automatically detect and grade DR [12]. Acquisition of digitized retinal images allow for novel image analysis methods and Web-based connectivity to create models of remote, computer-assisted, or even automated diagnosis and management of diabetic retinopathy. Several systems are in development and are currently being clinically validated [13,14].

The algorithms described by many authors involved four features namely; area of blood vessels, exudates, haemorrhages and microaneurysms [15-19].

There have been many approaches to vessel detection in retinal images, Gardner, Sinthanayothin, and Goldbaum investigated different combinations of edge detection or matched filter methods with artificial neural networks [20-22]. Meehan analysed the vessel width and used edge detectors for finding a suitable piece of vessel [23]. Gagnon utilized a recursive dual edge tracking based on Canny algorithm and connectivity recovering starting at the optic disk [24].

The main problems in former studies had been the need for user-interaction, the presence of the optic disk or intensive computations due to pre-processing. Other difficulties were posed by the use of large kernels or by processing each single pixel in the image, poor scaling with the image size or not providing partial results if there was a computational deadline. Additionally, many algorithms need a particular environment and definite image resolution or image size.

The newly developed algorithm for retinal vessel detection overcomes many described problems by Collorec [25]. The handling of the discontinuous regions by depending on local contrast, edge information and noise is much improved. The computational efficiency of the newly developed algorithm makes it highly sensitive for detection of retinal blood vessels.

Methods of blood vessel segmentation generally fall into three categories; first, is the window based method [26-29], which calculate the symmetry of each pixel with the surrounding pixels window for a given model against the pixel`s surrounding window, second, is the classifier based [30,31], and third, is the tracking based [32-34].

Among the various retinal vessel extraction methods, the matched filter (MF) method, one of the widow based method for vessel segmentation, is a representative one and it has advantages of simplicity and effectiveness [35].

This paper makes use of previously four known mathematical filters with an added new modifications for accurate detection of changes to the retinal blood vessels in comparison with the normal exist fundus photographs. These morphological changes could be used as early detectors for DR.

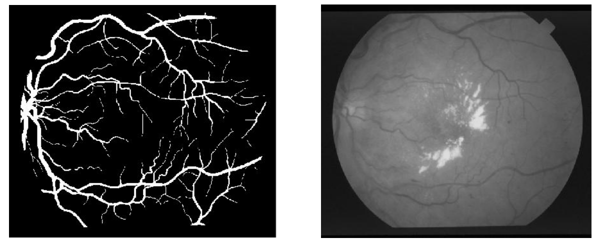
2. Material and Methods

Retinal blood vessel detection through segmentation of the retinal vasculature is very important for many reasons; many information about the patient health could be determined and diagnosed well, as well as it is important for spatial alignment and image registration for vascular change detection process.

Fundus photographs were taken, collected, and stored using STARE database, these images were then processed using four types of filters; High pass filter, Laplacian filter, Soble filter and Laplacian of Gaussian filter with a new modification for these mathematical filters. The results of this new modification on the filters were compared to detect the best filter for detecting retinal blood vessel in fundus images.

2.1 Images database:

There are many images databases like DRIVE database (Digital Retinal Images for Vessel Extraction) as well as STARE database (STructured Analysis of the Retina) are used to evaluate segmentation performance. In this work STARE database was used to evaluate our algorithm performance. Database was twenty retinal fundus images captured by a TopCon TRV-50 fundus camera with 35 degree field of view. Each image with a resolution of 605 x 700 pixels, each pixel is 24-bits. It also contained ground truth image which are an accurate segmented images for blood vessels, they were carefully labelled by specialist hand as shown if Fig. 1 [36].



(a) (b)

Fig.1: One of STARE data base images. (a) Ground truth image. (b) Color image.

2.2 Blood Vessels Segmentation:

Mathematical image filtration is an operation can be used to perform a specific task on the image, it may be used to enhance the image structure like the sharpening appearance of blood vessels, and also it can assist to extract the blood vessels from fundus images.

As shown in fig.1, blood vessels and capillaries appear in the image as non-straight lines, they are with different color from the background. High pass image filtering can be used to extract these lines from fundus images. High Pass, Laplacian, Soble, and Laplacian of Gaussian filters are four types of matched filters had been used severally for vessels exteraction.

Detecting blood vessels using MF method is usually done by thresholding after filtering process, the result of this detection is not only detects vessels but also non-vessels, like the edges of bright blobs and red lesions in the original image.

Blood vessels extraction using mentioned filters is done according to the following algorithm:

Filter is rotated many times depending on the angular steps to cover the 360 degrees, then applying these rotated patterns to the image, this spin is done to obtain white walls to the blood vessels in all possible directions.

Image is processed by each rotated filter kernel "ker" using shift and multiply operation, the kernel is shifted over the image and multiply its values with the corresponding pixels of the input image "InIm", for kernel with MxM dimension, the output image "OutIm" could be calculated according to the following formula:

$$OutIm_1^N(i,j) = \sum_{m=-\frac{M}{2}}^{\frac{M}{2}} \sum_{n=-\frac{M}{2}}^{\frac{M}{2}} Ker_1^N(m,n)\ InIm(i-m, j-n) \quad (1)$$

Choosing the maximum pixel value from the same location of these images, a new image is obtained with white walls to the vessels in all directions.

$$OutIm(i,j) = max\,[OutIm(i,j)_1, OutIm(i,j)_2, \ldots, OutIm(i,j)_N] \quad (2)$$

c) Automatic thresholding stage is finally applied to enhance the image to an adequate level to observe the blood vessels clearly.

$$OutIm(i,j) = OutIm(i,j) \geq Threshold\ Level \quad (3)$$

The used filters are similar in their target, they are used to extract the blood vessels from the retinal image, but they are different in their shape, the difference is common in the filter kernel values and arrangement as the following:

A) High pass filter:

The following matrix is an example of 3 by 3 kernel for high pass filter.

$$H = \begin{matrix} -1 & -1 & -1 \\ -1 & 8 & -1 \\ -1 & -1 & -1 \end{matrix} \quad (4)$$

This filter is not only used to detect, enhance edges and removes low-frequency components such as the background image, but also passes high-frequency components like walls of blood vessels.

B) Laplacian filter:

This type is another way to detect the blood vessels walls, it used to compute the second derivative of the image, this type can be described as the following kernel.

$$H = \begin{matrix} 0 & -1 & 0 \\ -1 & 4 & -1 \\ 0 & -1 & 0 \end{matrix} \quad (5)$$

C) Soble filter

This filter could be described by two basic edge detection routines like the following kernels;

$$H1 = \begin{matrix} 1 & 0 & -1 \\ 2 & 0 & -2 \\ 1 & 0 & -1 \end{matrix}, \quad H2 = \begin{matrix} 1 & 2 & 1 \\ 0 & 0 & 0 \\ -1 & -2 & -1 \end{matrix} \quad (6)$$

By these two kernels edges are detected by applying these patterns simultaneously to the image, but in this work one of the two patterns is sufficient to detect the blood vessels, while the second is obtained from rotation.

D) Laplacian of Gaussian (LOG) filter:

Gaussian filter is added before Laplacian filter in this type inorder to enhance the filter quality, as Laplacian filter is sensitive to noise. This filter also described as negative Laplacian as the central value is negative. This filter could be described by the following image.

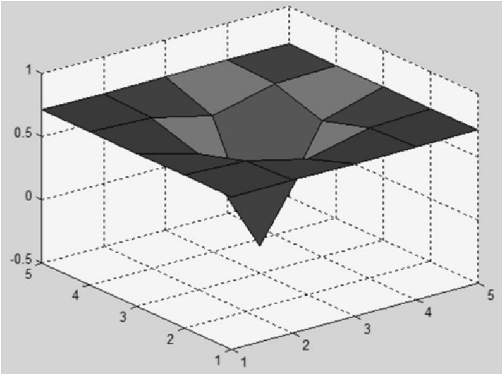


Fig. 2: Surface representation of Laplacian of Gaussian filter.

In this paper we propose a novel method, the central value of The High pass, Laplacian, Soble, and Laplacian of Gaussian filters had been shifted from the centre of the matrix to one side instead. These new irregular filters are able to detect the edges in one side only, and by rotating the filters on angular steps, the walls of the blood vessels are obtained in all possible directions as shown in fig. 3.

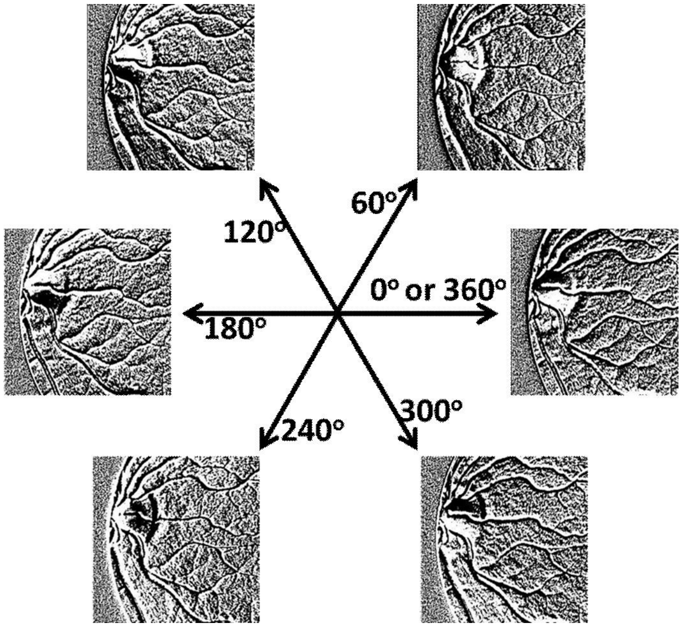
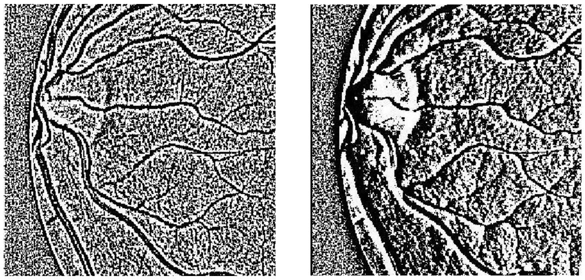


Fig. 3: Six rotations of high pass filter, 60 degree for each rotation.

Inspecting the resultant image after applying this new pattern; we could easily notice the following changes in the image; first, more details appear as shown in Fig. 4b, second, the details make the image looks like volume in three dimensions.



(a) (b)

Fig. 4: High pass filter result (a) Normal high pass filter result. (b) New high pass filter result

2.3 Automatic thresholding

Thresholding is done using maximum local entropy of the image. The threshold value "S" that would be used in object-background classification is the maximum value of local entropy of the object and the background can be written as:

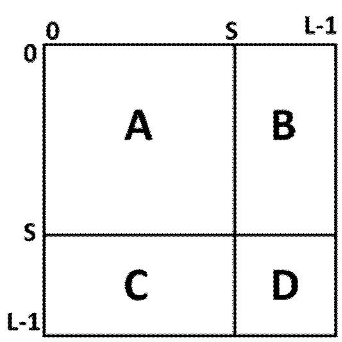
$$Max(H_T(s) = H_A(s) + H_C(s))$$

The entropy H of an image is defined as:

$$H = -\frac{1}{2}\sum_{i}\sum_{j} P_{ij}\, Log_2(P_{ij})$$

Where the quadrants of co-occurrence matrix shown in following figure are calculated using the following relations:

$$P_A = \sum_{i=0}^{s}\sum_{j=0}^{s} P_{ij}, P_D = \sum_{i=s+1}^{L-1}\sum_{j=0}^{s} P_{ij}$$



Threshold value using local entropy could be now calculated using the following programming steps:

Build co-occurrence matrix of given gray scale image → CoOcuMx

Calculate the probability of co-occurrence matrix → prob

From 1 to 255

Calculate PA and PD then their entropy → EntroA & EntroD

Sum EntroA & EntroD → Store in array → EntroSum

End

location of Max of EntroSum → The threshold value

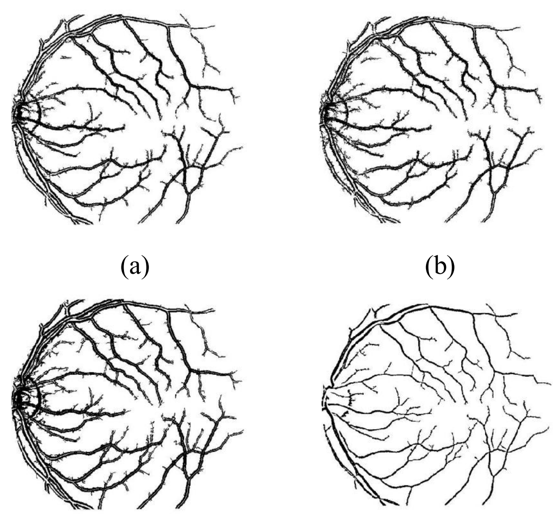
2.4 Statistical analysis

To compare different retinal vessel segmentation algorithms, we used the corresponding TPR (true positive rate), and the FPR (false positive rate). These performance measures were defined and widely used in literature [37-45].

The TPR is defined as the ratio of the number of correctly classified vessel pixels to the number of total vessel pixels in the ground truth. The FPR is defined as the ratio of the number of non-vessel pixels but classified as vessel pixels, to the number of non-vessel pixels in the ground truth. The hand-labelled images by the first human expert were used as ground truth.

3. Results

The four rotating filters with the new modification were applied on selected images from STARE database.



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

Fig. 5: Extracted retinal blood vessels. (a) High pass filter result. (b) Laplacian filter result. (c) Soble filter result. (d) Laplacian of Gaussian filter result.

The first three; High pass, Laplacian and Soble Filters (fig. 6 a, b, and c) gave output blood vessels pictures which are nearly similar, and the resulted image showed additional white pixels connected with the blood vessel walls, which needs further smoothing operation to rectify this defect. It is also clear that the center of the vessels is not white, which needs morphological filling operation to be resolved.

The Laplacian of Gaussian filter output image showed supreme results over the other three filters. It represented smooth blood vessels, moreover this filter extracted and showed tiny blood vessels that couldn't be shown in the other applied filters (fig. 6 d).

The performance comparison of these filters was evaluated by ROC curve for thresholding stage of the four types of filters as shown in fig. 7. Performance of Laplacian of Gaussian has the best performance as it has a breaking point up to 90% true positive rate. True positive rate of Laplacian filter is similar to the that of High pass filter as they have breaking point about 75%, but Soble filter got the lowest performance; it has about 70% true positive rate.

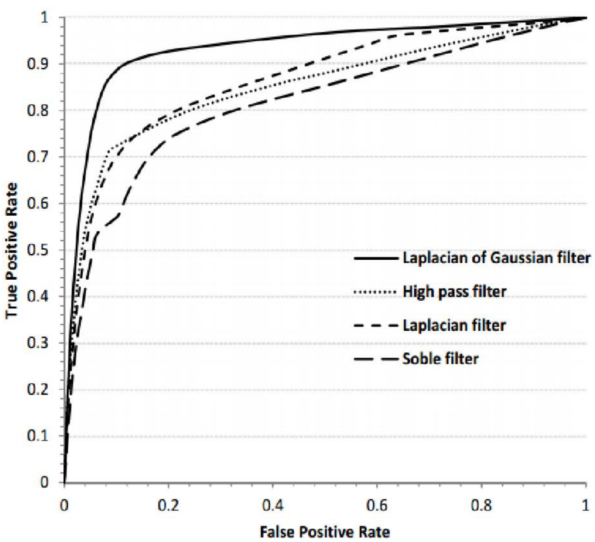


Fig. 6: ROC curves comparison of the four types of filters.

Sensitivity and Specificity were calculated for the four filters, where the Laplacian of Gaussian filter had the maximum values followed by other filters as shown in table 1.

Table 1: Comparison of Sensitivity and Specificity for the four filter types.

Filter type	Sensitivity	Specificity
High pass filter	0.646	0.930
Laplacian filter	0.634	0.940
Soble filter	0.646	0.898
Laplacian of Gaussian filter	0.766	0.985

The following curves are a comparison between the best result of this work –LOG- and some results of previous work.

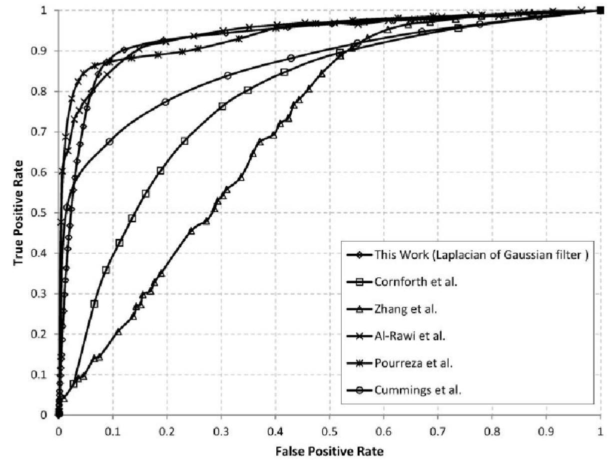


Fig. 7: Comparison of ROC curves between LOG and previous works.

4. Conclusion and Future Work

Segmentation using irregular form of matched filters for detecting retinal blood vessels in fundus images is a very important operation to prevent the danger of blindness of diabetic patients as well as for other purposes like image registration.

Four MF are used in this paper in irregular form, results of these filters were compared using the ROC curve, and the Laplacian of Gaussian filter gave the highest sensitivity (0.766), and specificity (0.985). Also after the comparison with the previous work, it was one of the best rest.

This result could be concluded as; the vessel wall cross-section in a retinal image is LOG shaped, it has the highest spatial frequency at the wall edge then decrease gradually to the vessel center, this feature is repeated for the next wall of the vessel. If this property can be properly used, it is possible to distinguish the symmetric vessel structures from those asymmetrical non-vessel edges in a simple but efficient way, and hence the vessel extraction accuracy can be improved.

In the future work, image registration is an essential step for image comparison in order to easily diagnose DR.

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References

1. Ong, G. L., Ripley, L. G., Newsom, R. S., Cooper, M., and Casswell, A. G.. Screening for sight-threatening diabetic retinop athy: comparison of

fundus photography with automated color contrast threshold test. Am. J. Ophthalmol. 137(3):445–452, 2004.
2. Fong D, Aiello L, Gardner T, King G, Blankenship G, Cavallerano J, Ferris F, and Klein R (2004). Retinopathy in Diabetes. Diabetes Care. 27:584-587.
3. Fong D, Aiello L, Gardner T, King G, Blankenship G, Cavallerano J, Ferris F, and Klein R (2003). Diabetic Retinopathy. Diabetes Care. 26:226-229.
4. Chia D and Yap E. (2004). Comparison of the Effectiveness of Detecting Diabetic Eye Disease: Diabetic Retinal Photography Versus Ophthalmic Consultation. Singapore Medical Journal. 45:276-279.
5. ETDRSRG (Early Treatment Diabetic Retinopathy Study Research Group). (1991). Early Photocoagulation for Diabetic Retinopathy. Ophthalmology, 98:766-785.
6. Kertes PJ and Johnson TM (Eds.). Evidence Based Eye Care. Lippincott Williams & Wilkins 2007.
7. Hipwell J, Strachant F, Olson J, McHardy K, Sharp P, and Forrester J (2000). Automated detection of microaneurysms in digital red free photographs: a diabetic retinopathy screening tool. Diabetic Medicine. 17:588-594.
8. Circulation 100:1134–1146, 1999. 63. Screening for Diabetic Retinopathy in Europe 15 years after the St. Vincent Declaration. The Liverpool Declaration 2005. Retrieved from: http://reseau-ophdiat.aphp.fr/Document/Doc/confliverpool. pdf. Last accessed on 20th December 2007.
9. Kinyoun JL, Martin DC, Fujimoto WY, and Leonetti DL (1992). "Ophthalmoscopy Versus Fundus Photographs for Detecting and Grading Diabetic Retinopathy," Investigative Ophtalmology & Visual Science, 33(6): 1888-1893.
10. Moss SE, Klein R, Kessler SD, and Richie KA (1985). "Comparison between ophthalmoscopy and fundus photography in determining severity of diabetic retinopathy," Ophthalmology, 92:62-67.
11. Abramoff MD, Niemeijer M, Suttorp-Schulten MSA, Viergever MA, Russell SR, and Van Ginneken B (2008). Evaluation of a System for Automatic Detection of Diabetic Retinopathy From Color Fundus Photographs in a Large Population of Patients With Diabetes. Diabetes Care. 31(2):193-198.
12. Abramoff MD, Niemeijer M, Suttorp-Schulten MSA, Viergever MA, Russell SR, and Van Ginneken B (2008). "Evaluation of a System for Automatic Detection of Diabetic Retinopathy From Color Fundus Photographs in a Large Population of Patients With Diabetes," Diabetes Care, 31(2):193-198.
13. Rudnisky CJ, Tennant MT, Weis E, Ting A, Hinz BJ, Greve MD: Web-based grading of compressed stereoscopic digital photography versus standard slide film photography for the diagnosis of diabetic retinopathy. Ophthalmology 114:1748-1745, 2007.
14. Chaum E, Karnowski TP, Govindasamy VP, Abdelrahman M, Tobin KW: Automated diagnosis of retinopathy by content-based image retrieval. Retina 28:1463-1477, 2008.
15. Acharya, U. R., Lim, C. M., Ng, E. Y. K., Chee, C., and Tamura, T., Computer based detection of diabetes retinopathy stages using digital fundus images. J. Eng. Med. 223(H5):545–553, 2009.
16. Banumathi A, Karthika, R., Kumar.A, (2003), Performance analysis of matched filter techniques for automated detection of blood vessels in retinal images, Conference on Convergent Technologies for Asia-Pacific Region, 2, pp 543–546.
17. M. Lopez, C. Sanchez, and R. Hornero, "Retinal image analysis to detect and quantify lesions associated with diabetic retinopathy," Ioba, University of Valladolid, Valladolid, Spain, May 2003.
18. Walter T, Massin P, Erginay A, Ordonez R, Jeulin, C, and Klein J (2007). "Automatic Detection of Microaneurysms in Colour Fundus Images," Medical Image Analysis, 11:555-566.
19. Sanchez C, Hornero R, Lopez M, Aboy M, Poza J, and Abasolo P (2007). "A Novel Automatic Image Processing Algorithm for Detection of Hard Exudates based on Retinal Image Analysis" Medical Engineering and Physics, Vol. 30:350-357.
20. Gardner GG, Keating D, Williamson TH, Elliott AT. Au- tomatic detection of diabetic retinopathy using an artifi- cial neural network: A screening tool. Brit J Ophthalmol 1996; 80: 940-944.
21. Sinthanayothin C, Boyce JF, Cook HL, Williamson TH. Automated localization of the optic disc, fovea, and reti- nal blood vessels from digital colour fundus images, Br J Ophthmol 1999; 83: 902-910.
22. Goldbaum MH, Katz NP, Chaudhuri S, Nelson M. Image understanding for automated retinal diagnosis. Proceed- ings of the 13th Annual Symp. on Comp. Appl. in Med- ical Care, IEEE Computer Society Press 1989, pp 756-760.
23. Meehan RT, Taylor GR, Rock P, Mader TH, Hunter N, Cymerman A. An automated method of quantifying reti- nal vascular responses during exposure to novel environ- mental conditions. Ophthalmology 1990; 97(7): 875-881.
24. Gagnon L, Lalonde M, Beaulieu M, Bouchert M-C. Pro- cedure to detect anatomical structures in optical fundus images. Proceedings of the Conference Medical Imaging 2001; SPIE Proc 4322: 1218-1225.
25. Collorec R, Coatrieux JL. Vectorial tracking and directed contour finder for vascular network in digital subtraction angiography. Pattern Recog Lett 1988; 8(5): 353-358.
A. Hoover, G. Jean-Baptise, X. Jiang, P. J. Flynn, D. Goldgof, K. Bowyer, D. Eggert, A. Fitzgibbon and

R. Fisher,. An Experimental Copmarison of Range Image Segmentation Alogarithms. IEEE Transactions on Pattern and Machine Intelligence, July 1996, pp. 673-689.

26. R. Nekovei, Y. Sun. Back-Propagation and its Configuration for Blood Vessel Detection in Angiograms. In IEEE Trans. On Neural Networks. Vol.6, no.1, Jan. 1995, pp.64-72.
27. T. Pappas and J. Lim. A New Method for Estmation of Coronary Artery Dimentions in Angiograms. In IEEE Trans. On Acaustics, Speech, and Signal Processing. Vol. 36, no. 9. Sep. 1988, pp. 1501-1513.
28. Pinz, S. Benogger, P. Datlinger and A. Kruger. Mapping the Human Retina. In IEEE Trans. On Medical Imaging. Vol. 17, August 1998, pp. 606-619.
29. S. Tamura, K. Tanaka, S. Ohmori, K. Okazaki, A. Okada and M. Hoshi. Semiautomatic Leakage Analyzing System for Time Series Fluorescein Ocular Fundus Angiography. In Pattern Recognetion. Vol. 16, no. 2, pp. 149-162.
30. B. Cote, W. Hart, M. Goldbaum, P. Kube and Nelson. Classification of Blood Vessels in Ocular Fundus Images, technical report, Computer Science and Engineering Dept., University of California, san Diego, 1994.
31. Y. Sun. Automated Indication of Vessel Contours in Coronary Arteriograms by an Adaptive Tracking Alogarism. In IEEE Trans. On Medical Imaging. Vol. 8, no. 1, March 1989, pp. 78-88.
32. S. Tamura, Y. Okamota and K. Yanashima. Zero-Crossing Interval Correction in Tracking Eye-Fundus Blood Vessels. In Patten Recognition. Vol. 21, no. 3, 1988, pp. 227-233.
33. Y. Tolias and S. Panas. Afuzzy Vessel Tracking Alogarism for Retinal Images Based on Fuzzy Clustering. In IEEE Trans. On Medical Imaging. Vol. 17, no. 2, April 1998, pp. 263-273.
34. S. Chaudhuri, S. Chatterjee, N. Katz, M. Nelson, and M. Goldbaum, “Detection of blood vessels in retinal images using two-dimensional matched filters,” IEEE Trans. Med. Imaging, pp. 263–269, 1989.
35. STARE project website (2003, July). [Online]. Available: http://www.ces.clemson.edu/~ahoover/stare
36. J.J. Staal, M.D. Abramoff, M. Niemeijer, M.A. Viergever, and B. van Ginneken, “Ridge based vessel segmentation in color images of the retina,” IEEE Transactions on Medical Imaging, pp. 501–509, 2004.
37. J.V.B. Soares, J.J.G. Leandro, R.M. Cesar-Jr., H.F. Jelinek, and M.J. Cree, “Retinal vessel segmentation using the 2-d gabor wavelet and supervised classification,” IEEE Trans. on Medical Imaging, vol. 25, pp. 1214–1222, 2006.
38. M. Niemeijer, J.J. Staal, B. van Ginneken, M. Loog, and M.D. Abramoff, “Comparative study of retinal vessel segmentation methods on a new publicly available database”, SPIE Medical Imaging, vol. 5370, pp. 648-656, 2004.
39. M. Martínez-Pérez, A. Hughes, A. Stanton, S. Thom, A. Bharath, and K. Parker, “Scale-space analysis for the characterisation of retinal blood vessels,” Medical Image Computing and Computer-Assisted Intervention, pp. 90–97, 1999.
40. Hoover, V. Kouznetsova, and M. Goldbaum, “Locating blood vessels in retinal images by piecewise threshold probing of a matched filter response,” IEEE Trans. Med. Imag., vol. 19, no. 3, pp. 203–210, 2000.
41. X. Jiang and D. Mojon, “Adaptive local thresholding by verification based multithreshold probing with application to vessel detection in retinal images,” IEEE Trans. Pattern Anal. Mach. Intell., vol. 25, no. 1, pp. 131–137, 2003.
42. A.M. Mendonca and A. Campilho, “Segmentation of retinal blood vessels by combining the detection of centerlines and morphological reconstruction”, IEEE Transactions on Medical Imaging, vol. 25, no. 9, pp.1200–1213, 2006.
43. M.E. Martinez-Perez, A.D. Hughes, S.A. Thom, A. A. Bharath, and K.H. Parker, “Segmentation of blood vessels from red-free and fluorescein retinal images”, Medical Image Analysis, vol. 11, no. 1, pp. 47–61, 2007.
44. C. Sinthanayothin, J. Boyce, and C.T. Williamson, “Automated Localisation of the Optic Disk, Fovea, and Retinal Blood Vessels from Digital Colour Fundus Images,” British Journal of Ophthalmology, pp. 902–910, 1999.

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