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A HYBRID FILTERING APPROACH TO RETINAL VESSEL SEGMENTATION

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ABSTRACT

We propose a novel vessel enhancement filter for retinal images. The filter can be used as a preprocessing step in applications such as vessel segmentation/visualization, and pathology detection. The proposed filter combines the eigenvalues of the Hessian matrix, the response of matched filters, and edge constraints on multiple scales. The eigenvectors of the Hessian matrix provide the orientation of vessels and so only one matched filter is necessary at each pixel in a given scale. This makes the proposed filter more efficient compared with existing multiscale matched filters. Edge constraints are used to suppress the response of spurious boundary edges. Experimental evaluation on the publicly available DRIVE dataset demonstrate improved performance of the proposed filter compared with known techniques.

***Index Terms*—** vessel enhancement, vessel segmentation, Hessian directions, matched filters, edge constraints, retinal images, medical imaging

1. INTRODUCTION

Optic fundus assessment has been widely used in the medical community for diagnosing vascular and non-vascular pathology. Inspection of the retinal vasculature may reveal hypertension, diabetes, arteriosclerosis, cardiovascular disease and stroke [1]. Due to various imaging conditions retinal images may be degraded. Consequently, the enhancement of such images and vessels in them is an important task with direct clinical applications.

There has been substantial research on vessel segmentation in retinal images. Hoover [2] proposed the segmentation of vessels using matched filters, where the second derivative of Gaussian functions in 12 directions are convolved with the image. To detect vessels of various radii, the Gaussian functions at multiple scales are applied. Many other methods have been proposed, such as adaptive thresholding [3], intensity edges [4], region growing [5], statistical inferencing [6], mathematical morphology [7], principal component separation [8], probabilistic modeling [9, 10], and Hessian measures [11]. Hessian-based multiscale segmentation/enhancement of vessels in retinal images have been extensively studied. By convolving with Gaussian kernels of various sizes, the normalized second order derivatives [12] can indicate the scale and orientation of vessels. The use of eigenvalues of the Hessian on multiple scales is still not sufficient to distinguish false positives at the boundary of retinal images, the optic disc, and various pathologies. Sofka et al. [13] proposed a method to segment vessels based on six features: response of multiscale matched filters, vessel confidence measure, gradient at the boundary of vessels, and the edge strength at the boundary. The features on all pixels are computed and their distributions are evaluated based on training images from the publicly available DRIVE database [14]. Based on the distribution of features of known vessels from 20 training images, the vesselness of each pixel is defined statistically by the the likelihood ratio based on the Neyman-Pearson Lemma [15]. The six features have some redundancy in them. For example, vessel confidence measure is correlated with edge strength.

In this paper, we propose an effective enhancement filter for vessels in retinal images. This filter combines the advantages of Hessian-based filters and matched filters, and incorporates edge constraints of vessels. Since the green channel of retinal images shows the largest contrast between vessels and the background, we first convert retinal color images into grayscale images by only keeping the green channel. Unlike vessels in other imaging modalities, vessels in retinal images appear darker than the background. To be consistent with other modalities, we invert the image intensities so that that the intensity of vessels is higher compared to the background. The following discussion is based on inverted grayscale images.

The paper is organized as follows. Section 2 introduces Hessian-based vessel filters. Section 3 introduces the multi-scale matched filter. A detailed description of the proposed filter is presented in section 4. Experimental results are shown in section 5. Section 6 concludes this paper.

2. HESSIAN-BASED VESSEL ENHANCEMENT

It is widely assumed [16, 13, 2, 17] that the intensity profile of a vessel in the cross section can be modeled by a Gaussian function due to the fact that pixels at the center of vessels are brighter than pixels near the boundary. It is also commonly assumed that the intensity does not change much along vessels. Although some large vessels in retinal images may have a dark line in their center, such lines can be easily removed by smoothing, and so such lines do not invalidate the Gaussian profile assumption. To distinguish vessels from other non-tubular structures such as planes, second order derivative features such as curvatures in Hessian-based enhancement filters are used. Planes have zero curvature in all directions except at the boundary. Vessels have a large curvature in the sectional direction and a small curvature along their center lines. The two principal curvatures can be obtained from the Hessian matrix H which is a second order descriptor. For a 3D image the Hessian is given by:

$$H = \begin{bmatrix} I_{xx} & I_{xy} & I_{xz} \\ I_{yx} & I_{yy} & I_{yz} \\ I_{zx} & I_{zy} & I_{zz} \end{bmatrix} \quad (1)$$

Let $|\lambda_1| \geq |\lambda_2| \geq |\lambda_3|$ be the three eigenvalues of the Hessian matrix. For a 3D vessel, λ_3 should be close to zero while $|\lambda_1| \approx |\lambda_2| \gg |\lambda_3|$. Therefore, many researchers [18, 19] have proposed using the ratio between the eigenvalues to enhance vessels. Frangi et al. [16, 18] compute the scores $R_B = |\lambda_3|/\sqrt{|\lambda_1||\lambda_2|}$, $R_A = |\lambda_2|/|\lambda_1|$, and $S = \sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}$ and define the response of his filter for 3D vessel as:

$$V_s(x) = \begin{cases} (1-\exp(-\frac{{R_A}^2}{2\alpha^2}))\exp(-\frac{R_B^2}{2\beta^2})(1-\exp(-\frac{S^2}{2\gamma^2})) \\ \quad \text{if } \lambda_1 < 0 \ \wedge \ \lambda_2 < 0 \\ 0 \quad \text{otherwise} \end{cases} \tag{2}$$

where parameter α, β and γ are constants. For 2D images the first exponential is removed, and so this filter is not effective in distinguishing between step edges and vessels. Hence, in 2D images more information is necessary for effective vessel segmentation.

3. THE MULTISCALE MATCHED FILTER

A multiscale matched filter [17, 13] is based on the same vessel profile assumption. It differs from Hessian filters in that it convolves the image with the second order derivative of a Gaussian function over multiple scales and takes the maximum response of the output. Given a input function $f(x)$ and a filter $s(x)$, the output of the filter is:

$$h(x) = \int_{-\infty}^{\infty} s(x-x')f(x')dx' \tag{3}$$

The filter that produces the largest response is the matched filter. Its shape can be obtained by reversing the shape of the signal to be detected [15]. Chaudhuri et al. [20] used a matched filter to detect vessels in retinal images. The filter gives maximum response when its orientation and shape is the same as the intensity profile. Vessels are modeled as piecewise linear segments with Gaussian cross sections. Twelve Gaussian templates at different orientations and a single scale are used. The work in [13, 17] proposed using multiscale matched filters to measure the vesselness of vessels in retinal images based on normalized derivatives [12, 21]. The filtering at each scale is implemented by maximizing the response over a set of kernel orientations. In [13], two one dimensional kernels are applied successively to compute the response of a two-dimensional separable kernel. The kernel in the tangential direction is simply a Gaussian function and the kernel in the normal direction is the second order derivative of the Gaussian function. In a coordinate system rotated to align u with the tangential direction and v with the normal direction, the matched filter response is defined as

$$\begin{aligned} M(R; u, v; t_u, t_v) = -\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} g_{vv}(v-v'; t_v)\cdot \\ g(u-u'; t_u)\cdot f(u', v'; t_0)du'dv' \end{aligned} \tag{4}$$

where t_u and t_v are the variances of the Gaussian kernel in each direction and $f(u', v'; t_0)$ is the image intensity after smoothed by a Gaussian function with kernel size equal to t_0. To detect vessels at a variety of widths, the matched filter is applied at multiple scales and the response on multiple scales are combined.

4. THE PROPOSED HYBRID FILTER

As discussed earlier, a Hessian-based filters can enhance vessels of various size and estimate their directions at the same time. However, Hessian-based filters can not distinguish step edges from vessels effectively. Matched filters can distinguish step edges from vessels more effectively. Matched filters are normally applied at multiple scales, whereas at each scale multiple kernels are used to enhance vessels in different directions. Consequently, the computational cost of matched filters is higher than that of Hessian-based filters. To solve the problem of false detection of edges, Sofka [13] proposed using the edge information at the boundary of vessels. A vessel should have two edges on each side of it which can be used to effectively distinguish between vessels and edges in the image. The proposed enhancement filter combines the advantages of Hessian-based filters, matched filters, and edge information. The proposed filter is parametric and is simple to implement.

We assume that vessels in retinal images have the following three properties: the profile in the cross section is Gaussian, the intensity changes little along the center line of vessels, and there are two edges at the boundary of vessels. Similar to Hessian-based filters, we compute the Hessian matrix at each pixel of the image on multiple scales by convolving the image with Gaussian kernels of multiple sizes. Let $|\lambda_{1\tau}| > |\lambda_{2\tau}|$ be the eigenvalues of the Hessian matrix at scale τ and let u_τ, v_τ be the eigenvector associated with $\lambda_{1\tau}$, $\lambda_{2\tau}$ respectively. Based on the vessel assumptions above the ratio $\frac{|\lambda_{2\tau}|}{|\lambda_{1\tau}|}$ should be close to zero and u_τ should be in the cross section of the vessel whereas v_τ should be in the direction of the center line. Based on $\lambda_{1\tau}$, $\lambda_{2\tau}$, and τ, we define the following term:

$$V_{h\tau}(x) = \begin{cases} \exp(-\frac{|\lambda_{2\tau}/\lambda_{1\tau}|^2}{2\beta^2})(1-\exp(-\frac{|\lambda_{1\tau}|^2}{2\gamma^2})) & \text{if } \lambda_{1\tau} < 0 \\ 0 & \text{otherwise} \end{cases} \tag{5}$$

where $\gamma = I_{xy}/(\alpha/\tau^{0.5})$, I_{xy} denotes the intensity at point (x, y) of the image, and α is a constant. The filter is not sensitive to the choice of α. In our experiments, it is set to 36. The Hessian matrix is computed on multiple scales. Because retinal images have many wide strip areas with low intensity, the introduction of the width τ in γ can effectively suppress the response of such structures.

As discussed earlier, the ratio of eigenvalues can not distinguish edges from vessels as effectively as matched filters. Therefore, an additional filter response is obtained by convolving the image with a matched filter in the cross direction of the vessels. The matched filter is a second order derivative of a one dimensional Gaussian function as shown in Equation 4. The kernel size of the Gaussian function is τ. For simplicity, this filter can be implemented by convolving the pixels in the cross section with a vector m, where $m_i|_{i=1:\tau} = -1$, $m_i|_{i=\tau+1:3\tau} = 1$, $m_i|_{i=3\tau+1:4\tau} = -1$. Let p represent the intensities of pixels in in the cross section. Obviously, the length of p is 4τ. The response of the matched filter at scale τ is computed as $V_{m\tau} = \frac{p\cdot m}{|p||m|}$. The vesselness of the proposed filter at scale τ is defined by $V_\tau = V_{h\tau}\cdot V_{m\tau}$.

Beside the vesselness measure V_τ, the proposed filter also incorporates the constraint that a vessel has two edges. Given a vessel of radius r, there should be two parallel edges at distance r from the center line. The two edges can be simply modeled as step edges. The response of the two edges is obtained by convolving the pixels with a step edge filter m', where $m'_i|_{i=1:\tau} = 1$ and $m'_i|_{i=\tau+1:2\tau} = -1$. Let p' be a vector that contains the intensity of pixels in the cross direction of the vessel on one side of the center line. The edge response at scale τ is given by: $V_{e\tau} = \frac{p'\cdot m'}{|p'||m'|}$. Since vessels are brighter than the background, the edge response on vessels should be positive. Let $V^1_{e\tau}$ and $V^2_{e\tau}$ be the two edge responses. By applying the constraint that both $V^1_{e\tau}$ and $V^2_{e\tau}$ must be positive, we can effectively distinguish step edges in retinal images from vessels. The final response of the filter on one scale is defined by:

$$F_\tau(x) = \begin{cases} V_{h\tau}\cdot V_{m\tau} & \text{if } V^1_{e\tau} > 0 \ \wedge \ V^2_{e\tau} > 0 \\ 0 & \text{otherwise} \end{cases} \tag{6}$$

Given a set of scales S, the final filter response is given by:

$$F(x) = \max\{F_\tau(x) \mid \tau \in S\} \tag{7}$$

5. EXPERIMENTAL RESULTS

The performance of the proposed hybrid filter is evaluated by comparing it with a multiscale matched filter and the Frangi filter using the publicly available DRIVE database [14]. The three filters were applied to all 40 images in this database. Figure 2 shows an example of obtained results. Figure 1 shows the ROC curves and the 1-Precision Recall curves of the three filters. To cope with potential inaccuracies in the ground truth which was created by manual labeling, true positives are counted as following way. For every pixel in the known vessels, if there is a pixel marked as vessel pixels by the filters within a 3×3 neighborhood, it is counted as a true positive. If a pixel is marked as a vessel pixel but it is not included in any known vessel, it is counted as a false positive. The ROC curve produced by the hybrid filter is better than that of the compared filters. The areas under the ROC curve of the hybrid filter, the multiscale matched filter, and the Frangi filter are 0.97228, 0.96303, and 0.9485, respectively. The difference is not large due to the small area portion of vessels in retinal images, which makes all three ROC curves steep. To demonstrate the effectiveness of the hybrid filter better, we use a 1-Precision Recall curve. The vertical axis of the 1-Precision Recall curve is the same as that of the ROC curve. The horizontal axis is defined as the fraction of false positives and all marked positives. It shows how many detected vessels are false positives. As can be observed, the curve of the hybrid filter is to the left of the curves of the other filters, thus demonstrating that the hybrid filter can distinguish vessels from other structures in retinal images more effectively. Table 1 shows the the sensitivity (SE) and specificity (SP) of the filter on twenty images from the training set of DRIVE database under a single threshold $\tau = 4$, where $SE = TP/(TP + FN)$ and $SP = TN/(FP + TN)$. The mean SP is 0.90234 and the mean SE is 0.95175. This result is better compared to other reported results [22].

6. CONCLUSION

We propose a hybrid filter which combines a Hessian-based filter with a matched filter and incorporates edge constraints. In the hybrid filter, eigenvalues and eigenvectors are computed from the Hessian matrix at multiple scales. The filter response depends in part on the ratio between the smallest and largest eigenvalues. The eigenvectors determine the direction in which the matched filter is applied. Thus, only one matched filter is needed at each scale. This is in contrast to other matched filters which require multiple filters per pixel. The product between the response from eigenvalue filter and the matched filter is computed using an edge constraint which mandates that two edges must exist at the boundary of vessels. The final output of the filter is the maximal response at multiple scales. Experimental evaluation on the DRIVE database show improvement over existing methods. The proposed filter can be used in the preprocessing step of various applications such as vessel segmentation, visualization, and pathology detection.

7. REFERENCES

[1] J. J. Kanski, *Clinical Ophthalmology: A systematic approach*, Butterworth-Heinemann, London, 1989.

[2] A. Hoover, V. Kouznetsova, and M. Goldbaum, “Locating blood vessels in retinal images by piecewise threshold probing of a matched filter response,” *IEEE Transactions on Medical Imaging*, vol. 19, no. 3, pp. 203–210, 2000.

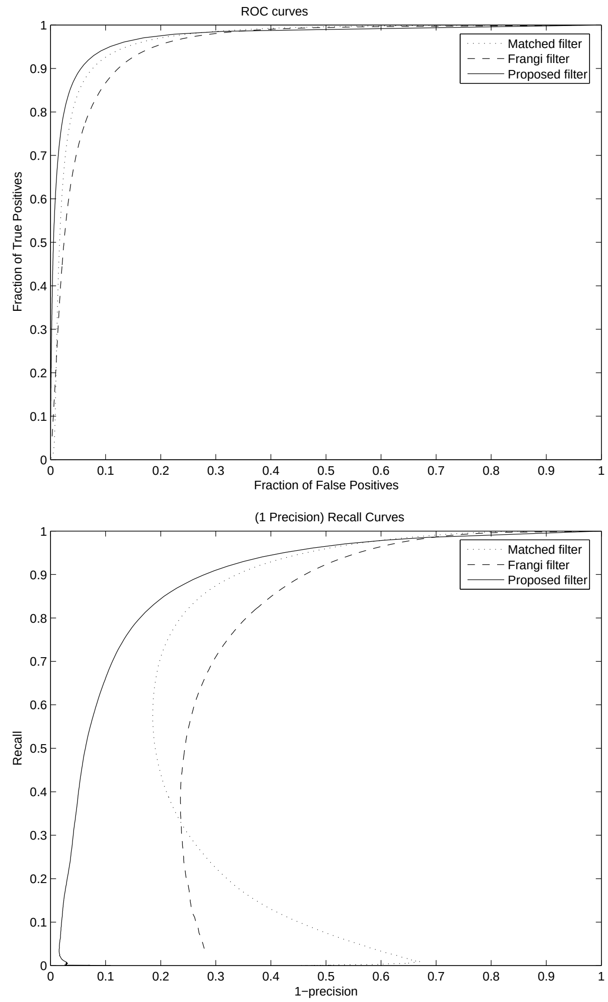

Fig. 1. ROC curves of the matched filter, Hessian-based filter, and the hybrid filter on the DRIVE database (top). 1-Precision Recall curves (bottom).

[3] X. Jiang and D. Mojon, “Adaptive local thresholding by verification -based multthreshold probing with application to vessel detection retinal images,” *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 25, no. 1, pp. 131–137, Jan 2003.

[4] D. Koozekanani, K. L. Boyer, and C. Roberts, “Tracking the optic nervehead in oct video dual eigensapces and an adaptive vascular distribution model,” *IEEE Transactions on Medical Imaging*, vol. 22, no. 12, pp. 1519–1536, 2003.

[5] M. E. Martinez-Perez, A. D. Hughes, A. V. Stanton, S. A. Thom, A. A. Bharath, and K. H. Parker, “Retinal blood vessel segmentation by means of scale-space analysis and region growing,” in *Proceedings of the 2nd International Conference of Medical Imaging Computing and Computer-assisted Intervention (MICCAI)*, 1999, pp. 90–97.

[6] V. Mahadevan, H. Narasimha-Iyer, B. Roysam, and H. Tanenbaum, “Robust model-based vasculature detection in noisy

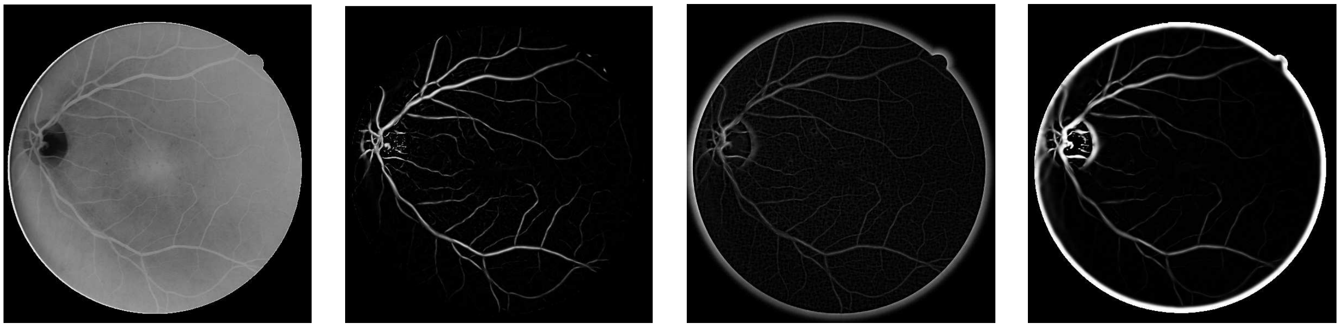

Fig. 2. From left to right: the input image, the enhancement result by proposed filter, the matched filter, and the Frangi-filter respectively.

Table 1. The sensitivity (SE) and specificity (SP) of the filter under a single threshold $\tau = 4$

SP	image 21 to 30	0.8758	0.8728	0.9366	0.9183	0.9486	0.9258	0.8880	0.9400	0.9201	0.9328
	image 31 to 40	0.8571	0.9086	0.8831	0.8789	0.9074	0.8659	0.8639	0.8654	0.9270	0.9307
SE	image 21 to 30	0.9805	0.9734	0.9285	0.9333	0.9167	0.9366	0.9441	0.9088	0.9433	0.9331
	image 31 to 40	0.9491	0.9640	0.9525	0.9739	0.9492	0.9772	0.9675	0.9722	0.9650	0.9660

biomedical imagings," *IEEE Transaction on Information Technology in Biomedicine*, vol. 8, no. 3, pp. 360–376, 2004.

[7] J.J.G. Leandro, RM Cesar, Jr., and H.F. Jelinek, "Blood vessels segmentation in retina: preliminary assessment of the mathematical morphology and of the wavelet transform techniques," in *Proceedings of XIV Brazilian Symposium on Computer Graphics and Image Processing,*, Oct. 15-18 2001, pp. 84–90.

[8] G. Agam, S. G. Armato III, and C. Wu, "Vessel tree reconstruction in thoracic CT scans with application to nodule detection," *IEEE Trans. Medical Imaging*, vol. 24, no. 4, pp. 486–499, 2005.

[9] Changhua Wu and Gady Agam, "Expectation maximization approach to vessel enhancement in thoracic CT scans," in *Proc. of SPIE Medical Imaging: Image Processing*, San Diego, California, Feb. 2005, vol. 5747, pp. 1703–1712.

[10] Changhua Wu and Gady Agam, "Probabilistic nodule filtering in thoracic CT scans," in *Proc. of SPIE Medical Imaging: Image Processing*, San Diego, California, March 2006, vol. 6144.

[11] Joes Staal, Michael D. Abr moff, Meindert Niemeijer, Max A. Viergever, and Bram van Ginneken, "Ridge-based vessel segmentation in color images of the retina," *IEEE Transactions on Medical Imaging*, vol. 23, no. 4, pp. 501–509, April 2004.

[12] T. Lindeberg, "Feature detection with automatic scale selection," *International Journal of Computer Vision*, vol. 30, no. 2, pp. 77–116, 1998.

[13] Michal Sofka and Charles V. Stewar, "Retinal vessel extraction using multiscale matched filters confidence and edge measures," Tech. Rep. 05-20, the Department of Computer Science, Rensselaer Polytechnic Institute, August 16 2005.

[14] M. Niemeijer, J. Staal, B. van Ginneken, M. Loog, and M.D. Abrmoff, "Comparative study of retinal vessel segmentation methods on a new publicly available database," in *Proceedings of SPIE Medical Imaging*, J. Michael Fitzpatrick and M. Sonka, Eds., 2004, vol. 5370, pp. 648–656.

[15] S. M. Kay, *Fundamentals of Statistical Signal Processing: Detection Theory*, Prentice Hall, 1998.

[16] A.F. Frangi, *Three-dimensional Model-based Analysis of Vascular and Cardiac Images*, Ph.D. thesis, Utrecht University, The Netherlands, 2001.

[17] Luo Gang, Opas Chutatape, and Shankar M. Krishnan, "Detection and measurement of retinal vessels in fundus images using amplitude modified second-order gaussian," *IEEE Transactions on Biomedical Engineering*, vol. 49, no. 2, pp. 168–172, February 2002.

[18] Alejandro F. Frangi, Wiro J. Niessen, Koen L. Vincken, and Max A. Viergever, "Multiscale vessel enhancement filtering," *Lecture Notes in Computer Science*, vol. 1496, pp. 130–138, 1998.

[19] Q. Li, "Selective enhancement filters for vessels and airway walls in two- and three-dimensional CT scans," *Medical Physics*, vol. 30, no. 8, pp. 2040–2051, 2003.

[20] Subhasis Chaudhuri, Shankar Chatterjee, Norman Katz, Mark Nelson, and Michael Goldbaum, "Detection of blood vessels in retinal images using two-dimensional matched filters," *IEEE Transactions on Medical Imaging*, vol. 8, no. 3, pp. 263–269, September 1989.

[21] Tony Lindeberg, "Edge detection and ridge detection with automatic scale selection," *International Journal of Computer Vision*, vol. 30, no. 2, pp. 117–154, 1998.

[22] L. Wang and A. Bhalerao, "Model based segmentation for retinal fundus images," in *Proceedings of Scandinavian Conference on Image Analysis*, Gotenberg, Sweden, June 2003.