33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Automatic Retinal Vessel Profiling Using Multi-Step Regression Method

Behzad Aliahmad, Dinesh K Kumar, *Senior Member, IEEE*, Samira Janghorban
Mohd Zulfaezal Che Azemin, Hao HAO, Ryo Kawasaki

Abstract— **Caliber of the retinal blood vessel is widely used for risk assessment of cardiovascular diseases. Accurate and automatic caliber measurement requires a precise model to be made for the vessel profile. In this paper, we present a new approach for retinal vessel profiling in which the background noise, uneven illuminations and specular reflections have all been considered. In this method, regression analysis is performed with a series of second-order Gaussians to filter and up-sample the original vessel profile. This is then segmented to identify and represent the vessel edges by two Generalized Gaussian functions. The technique has been applied to retinal images and the results have been verified and compared with the state of the art automatic techniques.**

Keywords— Retinal image, Vessel profile, Gaussian representation.

I. Introduction

RETINAL blood vessel morphology has been used as an indicator of different disease conditions. The change in retinal vessel caliber is known to be indicative of high blood pressure, proliferative diabetes, arteriosclerosis and other cardiovascular diseases [1]. Therefore, accurate measurement of retinal vessel caliber is crucial for effective assessment of diseases and monitoring the advances of treatment process.

Accurate vessel caliber estimation requires a precise representation of the vessel profile [2]. Therefore, L. Gang, et al. [3] have proposed an amplitude-modified second-order Gaussian function to model the retinal vessel cross-section. The sigma parameter of the Gaussian best fit was used to estimate the vessel diameter. However, this model failed to consider the presence of central light reflex on the vessel center line, also known as “specular reflection” [4]. Improvement to this representation was the introduction of the modified [2] and piecewise Gaussian [5] models. These models consider the existence of specular reflections to provide a better fit. Another improvement was introduced by G. Xiaohong et al. [6] who developed the twin Gaussian model to measure the average diameter over a small vessel segment. In all of these models, the central light reflex is approximated by a single second-order Gaussian function. However, there are number of sources for profile distortion, mainly due to uneven illuminations and background noise that have not been addressed by the above models. These artefacts would cause the profile and the central light reflex to take more complicated shape than to be approximated by only two second-order Gaussians. Ignoring these artefacts can result into a large residual fitting error between the actual and the representative profile [2]. The main reason for this type of error is due to the invalid assumption of vessel profile as a symmetrical structure, while the uneven illumination causes the profile to be asymmetric against the vessel center line. Efforts by [7] to address this problem, demonstrated the use of sixth order polynomial function. This technique allowed the representation of noise and central light reflex however it required to be remodeled by rectangular approach [8] for caliber estimation purpose.

In addition to the above described artefacts, there are also other distortions due to light scattering by the layers behind the vessels which are captured by high resolution fundus cameras [4]. This phenomenon adds more distortions to the central light reflex area and the edges of the vessels. In the presence of these distortions and without applying any direct averaging or smoothing to the vessel profile, caliber estimation by the above models would either fail or become erroneous. Therefore, there is a need for developing a suitable model for improved vessel profile representation and caliber measurement.

In this paper, a multi-step approach is proposed to address the above limitations and provide an accurate estimation of the vessel intensity cross-section profile. In the first step, a series of second-order Gaussians is fitted to the vessel and the background area of the intensity cross-section recorded on a line normal to the vessel centerline. Some critical points that represent the edges are then detected from the series representation and paired up to identify the two regions corresponding to vessel boundaries. Each of these regions is finally remodeled by a generalized-Gaussian function to remove the background noise and periphery fluctuations from the reconstructed profile. Therefore, the final model consists of a series of second-order and generalized Gaussian functions. The accuracy of the proposed method has been tested on a wide range of intensity distributions and the outcome has been compared with the gold standard

Manuscript received April 12, 2011.
B. Aliahmad is with the RMIT University, Victoria 3001, Australia (e-mail: b.aliahmad@gmail.com).
D. K. Kumar is with the RMIT University, Victoria 3001, Australia
S. Janghorban is with the RMIT University, Victoria 3001, Australia.
M. Z. C. Azemin is with the RMIT University, Victoria 3001, Australia, on leave from Biomedical Science Department, Kulliyyah of Science, International Islamic University, Malaysia, Kuantan 25200, Pahang, Malaysia
H. HAO. is with the RMIT University, Victoria 3001, Australia.
R. Kawasaki is with the Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Victoria 3002, Australia.

and generally accepted piecewise Gaussian [5] model.

II. Methodology

The aim was to develop a method that does not require extensive manual supervision, and provide the best estimation of vessel profile in the presence of aforementioned distortions while preserving the sigma parameter of the Gaussian models to be used for further analysis, including caliber estimation. For this purpose, multi-step regression has been proposed to obtain a robust and precise retinal vessel profiling method.

The first step in the proposed technique requires localization of a seed point on the vessel boundaries to find and track the edges. This is followed by an estimate of the vessel cross-section profile and representing it by "*n*" additive second-order Gaussian functions. The boundary regions will then be modeled by two generalized Gaussians with different symmetric distribution parameters. These parameters will be determined through regression analysis to provide the best estimation of vessel boundaries. Details of this technique are provided below.

A. Obtaining the blood vessel cross-section profile

In order to obtain the intensity profile of a vessel cross-section, pixel intensities have to be measured and recorded along a normal line made through the vessel centre line. The normal line to the vessel is considered as the shortest Euclidean distance between the points on vessel boundaries. The boundaries are tracked using the eigenvectors of image Hessian matrix as they reflect essential characteristics of the image. Only the green channel is used for this purpose to provide better contrast between the vessels and the background.

At first, a seed point close to a vessel edge is selected manually by a grader. This provides the starting point and specifies the region of interest (ROI) on a vessel segment where the analysis needs to be performed. Then the selected seed point is served as centre of a circle with diameter less than the expected diameter of the vessel, in order the circle not to intersect with the opposite edge. Hessian matrix is then computed for the light intensity on the circumference of this circle and the eigenvectors are obtained. For a point inside the vessel, the eigenvectors corresponding to the largest eigenvalues are normal to the edges and those corresponding to the smallest eigenvalues point to the direction along the vessels. However, for a pixel outside the vessel area this trend is opposite [9]. Therefore direction of the vector sum of the two eigenvectors is used for differentiating vessels from non-vessel pixels and locating the new seed points to initiate the tracking process. The first two consecutive vectors on the circle with maximum change in direction are considered as the pixels reflecting the vessel boundaries. The points on the tracking direction are considered as the centers for the subsequent circles. Repetition of this process gives an estimate of the vessel boundary. The same process is performed for identifying the opposite edge. Once the edges are identified, a point on the tracked segment is taken and paired with another point on the opposite edge based on the minimum Euclidean distance criterion. The line joining these two points is considered as an estimate of the normal to vessel center line. The process is repeated to obtain as many as cross-sectional lines required on the vessel segment. The image intensity is then recorded along these normal lines. An example of a recoded intensity cross-section profile is shown in Fig.1.

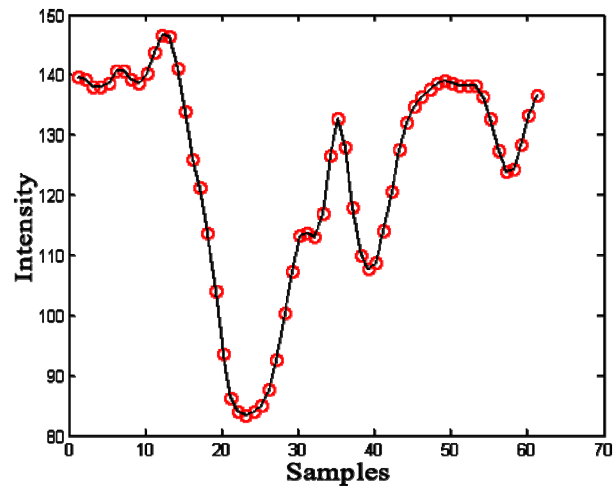

Fig.1 Example of a vessel Cross-section profile with multiple bumps at the centre and periphery fluctuations (red circles). Linearly connected samples for better view and trend estimation (black curve).

B. Modeling the blood vessel profile using additive multiple second-order Gaussians

The aim of this section is to reduce the profile distortions which are mainly due to uneven illumination conditions and background noise. This step also increases the profile resolution and allows for diameter estimation to be performed later, in a fraction of a pixel. Regression analysis is applied to the profile using "*n*" additive Gaussian functions with a DC component defined as:

$$G(x) = \sum_{i=1}^{n} g_i(x) + g_0 \qquad (1)$$

where:

$$g_i(x) = p_{(3i-2)} e^{-0.5\left(\frac{x-p_{(3i-1)}}{p_{3i}}\right)^2} \qquad (2)$$

In the above equations, $p_{(3i-2)}$, $p_{(3i-1)}$ and $p_{(3i)}$ indicate the amplitude, location of the peak and spreading factor of the Gaussian curve respectively. g_0 is a DC component representing the background gray level. All of these parameters are considered as variables and the optimized values are determined by regression analysis using non-linear Levenberg Marquardt method [10]. An example of a second-order Gaussian series, sum of which form the complete vessel profile is illustrated in Fig. 2. As it can be seen in this figure, the profile (Fig.1) is approximated by number of inverse and normal Gaussians.

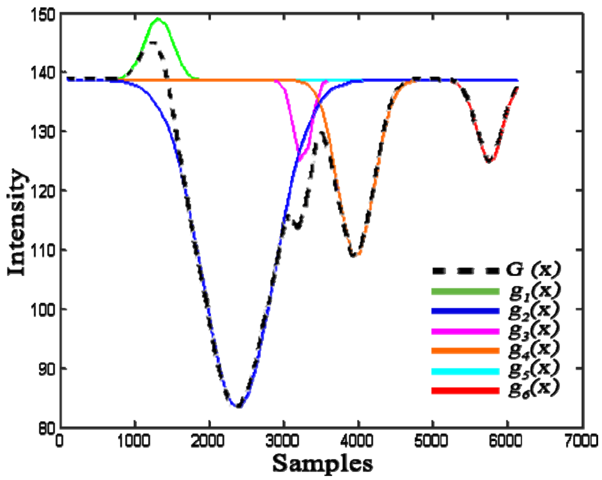

Fig.2 Series of “n” Second-order Gaussians (normal and inverse), sum of which form the complete vessel profile (G(x)).

C. *Fitting Generalized Gaussian functions to the edges*

The next step is the removal of background noise and periphery fluctuations from the reconstructed profile by identifying the critical points representing location of the vessel walls. These points are shown by letters from A to D in Fig.3. To obtain the critical points automatically, the local maxima and minima need to be detected using the first and second derivatives of the modeled profile in section B.

Rules have been established to group these maxima and minima and relate them to the vessel or background regions. The maximums are classified into vessel and non-vessel groups based on their location on the image. In fundus images where the vessels are darker from background, intensity values of the maxima on the vessel are always lower than the minimums corresponding to the background region. In other words, there always exist some maxima with intensity level, less than a number of minimum points. After these maximums are detected, their intensity values are compared to all local minima. Those with values less than the detected maximums are classified as vessel related minima. The ones with largest physical distance on the profile are labeled B and C. Finally, the first and closest maximums before B (left) and after C (right) are considered as critical points A and D respectively.

The next step is the removal of background noise and periphery fluctuations from the modeled profile. The proposed method fits two sets of generalized Gaussian functions to the regions corresponding to the sharp intensity transition areas specified by the critical points, after being mirrored against a vertical line made through the minima points B and C (Fig. 3). This process allows each edge to take a Gaussian-like shape (C_1 and C_2 in Fig. 3), for better regression outcome. After the mirroring process, a generalized Gaussian function is fitted to each curve using the Levenberg-Marquardt method [10]. As the two Gaussian functions are fitted independently they can have different symmetric distributions with different scaling factors which provide a generalized and accurate representation of the vessel boundaries with respect to the background. These functions are defined as:

$$f_i(x) = -a_i e^{-0.5(\frac{|x-\lambda_i|}{\sigma_i})^{\gamma_i}} + b_i \qquad i = 1,2 \qquad (3)$$

where a_i, λ_i and σ_i have the same definition as $p_{(3i-2)}$, $p_{(3i-1)}$ and $p_{(3i)}$ in (2) respectively. γ_i refers to different symmetric distributions, each having different tail lengths. This time, the symmetric distribution parameter (γ_i) is not kept constant and is determined through regression together with other parameters. For the curves we are dealing with, the best match usually happens for $2 \le \lambda_i < 3$. In this function, b_i is a DC component, representing the background gray level. The proposed function (3) is fitted separately to each Gaussian-like curve and the outcome is demonstrated in Fig. 3 (Blue dashed lines).

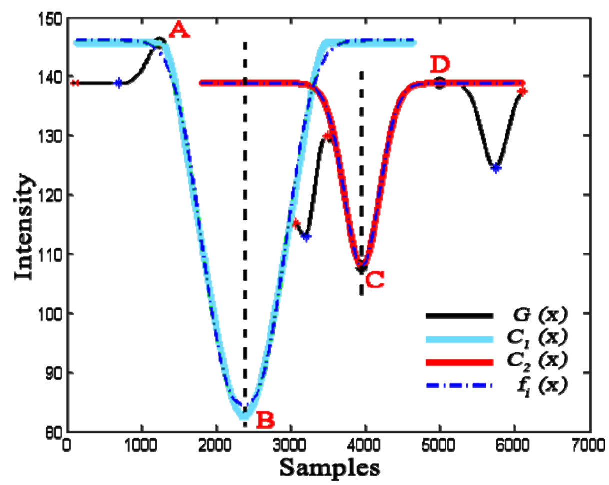

Fig.3 Result of cutting the modeled profile from the critical points and mirroring the segments (C_1 and C_2).The curve fitting outcome using the generalized Gaussians (f_i). Normal lines against which vessel boundaries are mirrored (Black dashed lines)

The complete profile is modeled by a series of second-order Gaussian functions (section B) for the vessel center part and the two generalized Gaussians to represent the edges. Considering the critical points, B, C, (Fig. 3), the proposed model is defined as:

$$f(x) = \begin{cases} -a_1 e^{-0.5(\frac{|x-\lambda_1|}{\sigma_1})^{\gamma_1}} + b_1 & x < B \\ \sum_{i=1}^{n} g_i(x) + g_0 & B \le x \le C \\ -a_2 e^{-0.5(\frac{|x-\lambda_2|}{\sigma_2})^{\gamma_2}} + b_2 & x > C \end{cases} \qquad (4)$$

This function can be used to provide an estimate of the vessel profiles.

III. RESULTS

For quantitative evaluation, 350 different vessels including 175 arteries and 175 veins were selected among 9 fundus images (each 3072×2048 pixels) captured with the Cannon D-60 digital fundus camera provided by the Eye and Ear Hospital, Melbourne-Australia. The cross-section profiles were modeled by (1) with $n=6$ which was obtained heuristically. The mean squared fitting error was calculated for each cross-section using:

$$e=\frac{1}{n}\sum_{i=1}^{n}(y_i-G(x_i))^2 \tag{5}$$

where here n is the number of sample points, y_i is the recorded intensity profile and $G(x_i)$ is the fitted curve using (1). A comparison was made with the state of the art technique and the mean squared error was calculated for the piecewise Gaussian model [2]. Among total number of 350 different cross-section profiles, the proposed second-order Gaussian series resulted in 100% fitting success rate with average squared fitting error of 0.720 (SD=0.584), while the average fitting error for the piecewise model was 6.367 (SD=4.331) with the success rate of 70.85%, demonstrating that the piecewise model was unable to describe some vessel profiles with multiple periphery and central line fluctuations. The outcome is presented in table 1.

TABLE 1
COMPARISON BETWEEN THE SECOND-ORDER AND THE PIECEWISE GAUSSIAN

	Series of second-order Gaussians	Piecewise Gaussian model
Total No. of profiles	350	350
No. of successful fits	350	248
Success Rate	100 %	70.85 %
Mean squared fitting error	0.720	5.367
SD	0.584	4.331

Further test was performed to assess the agreement between the two generalized Gaussians and the Gaussian-like curves C1 and C2 (Fig 3). For this purpose, the mean squared fitting error was calculated for the same 350 vessel segments. The generalized Gaussian provided a very good fit, with the mean squared error of 0.060 and standard deviation of 0.027 (Table 2).

TABLE 2
MEAN SQUARED FITTING ERROR AND STANDARD DEVIATION FOR THE GENERALIZED GAUSSIAN AND THE GAUSSIAN-LIKE CURVES (C1 AND C2)

	Generalized Gaussian
Total No. of profiles	350
Mean squared fitting error	0.060
SD	0.027

IV. DISCUSSION AND CONCLUSION

In this paper we have proposed and investigated a multi-step approach for accurate and automatic retinal vessel profiling using a combination of second-order and generalized Gaussians. This approach is based on the representation of the vessel edges and the background by two generalized Gaussians, while the vessel surface is represented by sum of second-order Gaussians. It has a distinct advantage over existing approaches in fitting and covering a wider range of vessel profiles by considering the effect of background noise, uneven illumination and specular reflections. Comparison between the fitting success rate of the proposed model and the piecewise Gaussian is a proof for this statement. The proposed technique undertakes multi-step regression analysis, where each step provides a higher resolution. Therefore, as it provides an excellent fitting performance especially at the boundaries, it can be used for accurate automatic caliber measurement without requiring any averaging or smoothing to be applied to the main profile for better fitting outcome. However, averaging may filter out some local maxima or minima that determine the critical points. In this case, caliber estimation will be erroneous. This technique averages the distortions while preserving correct location of the critical points. It does not require any manual supervision and like twin and piecewise Gaussians, it preserves the sigma parameter (vessel width information) for simplicity of caliber calculation. Another significance of this model is in the area of quantifying the image blurriness at vessel boundaries, as σ_i and γ_i in (4) refer to spreading and symmetric distributions at vessel edges.

REFERENCES

[1] Z. Xiaofang, *et al.*, "A method of retinal vessel width measurement," in *The 2nd International Conference on Computer and Automation Engineering (ICCAE),* 2010, pp. 443-446.

[2] H. Li, *et al.*, "A piecewise Gaussian model for profiling and differentiating retinal vessels," in *Proceedings of the International Conference on Image Processing,* 2003, vol.1. pp. I-1069-72

[3] L. Gang, *et al.*, "Detection and measurement of retinal vessels in fundus images using amplitude modified second-order Gaussian filter," *IEEE Transactions on Biomedical Engineering, ,* vol. 49, pp. 168-172, 2002.

[4] M. Hammer, et al., "Light paths in retinal vessel oximetry," *IEEE Transactions on Biomedical Engineering*, vol. 48, pp. 592-598, 2001.

[5] L. Huiqi, *et al.*, "Automatic grading of retinal vessel caliber,", *IEEE Transactions on Biomedical Engineering,* vol. 52, pp. 1352-1355, 2005.

[6] G. Xiaohong, *et al.*, "A method of vessel tracking for vessel diameter measurement on retinal images," in *Proceedings of International Conference on Image Processing,* 2001, pp. 881-884 vol.2.

[7] L. Pedersen, et al., "Quantitative measurement of changes in retinal vessel diameter in ocular fundus images," *Pattern Recognition Letters*, vol. 21, pp. 1215-1223, 2000.

[8] O. Chutatape, Z. Liu, and S. M. Krishnan, "Retinal blood vessel detection and tracking by matched Gaussian and Kalman filters," in *Proc. 20th Annu. Conf. IEEE Eng. Med. Biol. Soc.* ., 1998, pp. 3144–3148.

[9] Z. Xiaofang, et al., "A method of retinal vessel width measurement," in *The 2nd International Conference on Computer and Automation Engineering (ICCAE),* 2010, pp. 443-446.

[10] Press, W.H., Flanney, B.P., Tenkolsky, S.A., Vetterling, W.T., "Numerical Recipes in C --- The art of Scientific Computing", Cambridge University press, Cambridge, England,l990.