A Combined Preprocessing Method for Retinal Vessel Detection Towards Proliferative Diabetic Retinopathy Screening

Leonarda Carnimeo(✉), Annamaria Roberta Altomare, and Rosamaria Nitti

Department of Electrical and Information Engineering, Technical University of Bari, Bari, Italy
leonarda.carnimeo@poliba.it

Abstract. In this paper, the problem of detecting blood vessels in retinal images with early proliferative retinopathy is faced by highlighting vessels both in retina background and in the optic disc. For this purpose, a Combined Method for preprocessing fundus oculi images is developed. In detail, each retinal vessel image is enhanced via a contrast-limited adaptive histogram equalization after applying a suitable operator for feature extraction. Then, the proposed Combined Preprocessing Method is synthesized to modify each contrast-enhanced retinal image using both a Two-dimensional Matched filtering and a 2D Gabor Wavelet Transformation for vessel highlighting. Combination and segmentation of preprocessed images are subsequently performed and binary maps of retinal vessels are finally derived. The effectiveness of the proposed method is evaluated on obtained outcomes and results are compared to those obtained with available techniques.

Keywords: Retinal Vessel Detection · Preprocessing methods · Medical image classification · Diabetic retinopathy · 2D Gabor wavelets · Matched filters

1 Introduction

In the last years, several improvements have been achieved in medical imaging [1–5]. If ophthalmic advances are considered, at the moment automated diagnostic tools allow clinicians to perform retinal examinations of mass screening for the most common diseases, such as diabetes, hypertension and glaucoma [6–12]. Specific clinical markers help ophthalmologists in diagnosing Diabetic Retinopathy (DR) [7–9]. In this regard the extraction of retinal vessels is essential in the analysis of digital fundus images since it helps in diagnosing several retinal diseases. More in detail, the clinical aim towards the segmentation of blood vessels of retinal images deals with the suppression of the background and the enhancement of all small vessels, so that abnormal neovascularization can become more visually highlighted. Even if the local contrast can be very low in a retinal image, in [10, 11] a segmentation algorithm, which approximates the intensity profile of retinal vessels using a Gaussian curve, was proposed to detect both vessels and other brighter objects, such as lesions, optic disc, etc. Furthermore, among retina diseases, the early diagnosis of proliferative DR, a severe complication of diabetes that damages retina, is crucial to the protection of the vision of diabetic patients [13–16].

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The onset of this disease is signaled by the appearance of neovascular sprouts, which might be identified using some retinal vessel extraction techniques as shown in [13, 14]. In particular, in [14] a procedure of extraction of small retinal vessels is performed, but the main drawback of the approach is that for each considered set of images, all necessary parameters have to be manually set to obtain satisfactory results. In this regard, the use of high values of a particular limiting parameter makes the noise grow in the image, thus increasing the probability of obtaining false detections [14]. Furthermore, beside several edge detection algorithms are available in current literature [1], they do not always lead to acceptable results in extracting various features in a fundus image with proliferative retinopathy. Some drawbacks have not been overcome yet, since every pre-processing procedure provides improvements in certain image areas, but at the same time presents some disadvantages in other retinal zones. As an example, the adoption of the active contour model in the segmentation of wide retinal vessels in [16] involves some disadvantages, as this model can lead to inaccurate segmentations of retinal vessels in some cases of abnormal fundus images.

Since research has shown that the quality of image segmentation depends on the quality of the preprocessing phase, in this paper, the goal of detecting blood vessels in retinal images with DR is reached by developing a Combined Preprocessing Method. The presented technique allows to modify retinal images differently in retinal background and in the optic disc, with the aim of reducing previously mentioned drawbacks towards a screening of proliferative DR. The proposed Combined Preprocessing Method involves more phases as subsequently described in detail. After applying an operator for feature extraction, each retinal vessel image is contrast-enhanced by a contrast-limited adaptive histogram equalization [17, 18]. Then, the suggested Combined Method modifies each contrast-enhanced retinal image both via a two-dimensional matched filtering and via a 2D Gabor wavelet transformation for vessel highlighting. In this way, pairs of modified images containing different vessel informations are obtained, which are properly combined and subsequently segmented. The effectiveness of the proposed method is evaluated on outcomes and results are compared to those obtained with the methods developed in [14] and in [16].

2 Retinal Vessel Detection by a Combined Preprocessing Method

In retinal images the preprocessing phase reveals of a main importance to enhance the contrast between background and retinal vessels, besides removing the effects of improper illumination and noise artifacts. For this purpose, in this section, a Retinal Vessel Detection via a Combined Preprocessing Method is reported as shown in the block diagram reported in Fig. 1, where the input variables of each step are indicated.

After the acquisition of every RGB fundus image, a contrast enhancement step is accurately performed on each gray retinal image I_G. Obtained images are then preprocessed and subsequently properly combined [19]. A Segmentation/Post-processing phase is finally carried out to determine the binary map of blood vessels and reduce noise. In this way each resulting image I_{OUT} is obtained. Each phase is detailed in the following subsections.

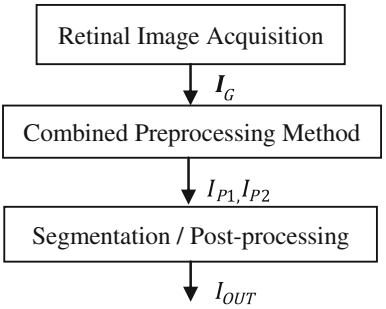

Fig. 1. Block diagram of the proposed Retinal Vessel Detection

2.1 Combined Preprocessing Method

The block diagram of the proposed Combined Preprocessing Method is reported in Fig. 2, where an initial step of Feature Extraction is highlighted. This operation is intended to determine a parameter, called *clip limit* β, which is necessary for the subsequent phase of Contrast Limited Adaptive Histogram Equalization (CLAHE) as in [17, 18].

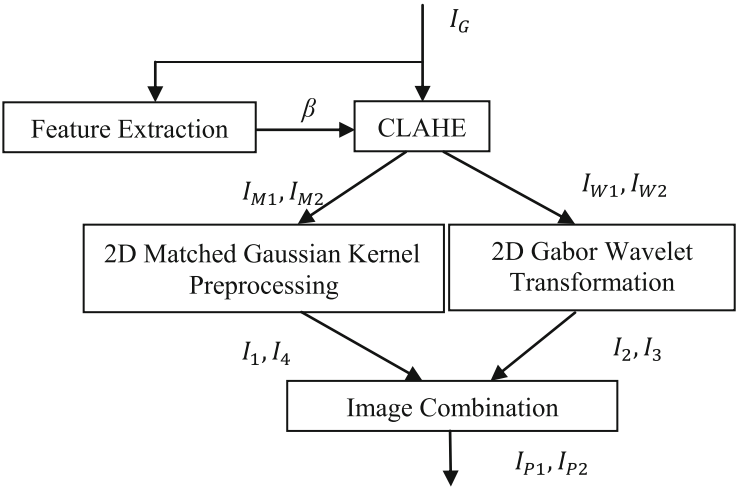

Fig. 2. Block diagram of the combined preprocessing method

Then, an image contrast enhancement step is accurately performed on each gray retinal image I_G to produce two pairs of contrast-enhanced images for every retinal one.

Each couple of obtained contrast-enhanced images I_{M1}, I_{M2} and I_{W1}, I_{W2} is separately preprocessed by a 2D Matched Gaussian Kernel Filtering [10] and a 2D Gabor Wavelet Transformation [16].

Resulting images are finally combined as in [19], determining the preprocessed images I_{P1}, I_{P2} as shown in Fig. 2. The method is subsequently described in detail.

Feature Extraction and Contrast Limited Adaptive Histogram Equalization. The first step of the Combined Preprocessing Method concerns with CLAHE [17, 18, 20, 21]. This technique is a block-based contrast enhancement one, which modifies the dynamic range and the contrast of an image by altering its gray levels, such that its intensity histogram has a desired shape. In detail, it operates on small regions of each retinal image I_G, called *tiles* of size S, to equalize their histograms and control the level of their contrast enhancement by means of the clip limit β, with $0 \leq \beta \leq 1$.

Contrast enhancement is given by the slope of the transformation function in the neighboring of each pixel P of I_G. This slope is, on its turn, proportional to the slope of the Cumulative Distribution Function (CDF) of the neighborhood of P.

The problem of undesirable visual artifacts and possible over-enhancements is overcome by means of the contrast limiting procedure applied to each tile S. Thus, the parameter β limits both the slope of the CDF and the slope of the transformation function obtained for each tile.

Moreover, the choice of parameters of CLAHE is used to achieve variations of the Standard Deviation r and of the Average Value q of the histogram itself, aiming at expanding its distribution on a more large intensity gray level region.

If an image has a very low gray intensity, a high clip limit β makes its histogram flatter and the image becomes brighter, even if noise can be more highlighted.

Furthermore, the contrast of an image can be further modified for a given β using tiles of different size. In the same way, when the size S grows, the dynamic range becomes larger and the contrast of each image increases [20]. Adjacent contrasted tiles of the same size can be finally combined for each image using a bilinear interpolation [21].

Thus, in the proposed Combined Preprocessing Method retinal image preprocessing are improved by selecting tiles of two sizes with the aim of obtaining two values of contrast enhancement for each retinal image.

In this way, four processed images with various values of contrast enhancement are derived using the same clip limit β, each one containing different informations about retinal vessels.

2D Matched Gaussian Kernel Filtering. Blood vessels in human retinal images are generally darker then the background. If *P(x, y)* indicates any point of the retinal image under exam, the gray intensity profile may be approximated by evaluating the value of a Gaussian curve G in each point P as follows [10]

$$G(P) = a(P)\left\{1 - k\mathrm{e}^{\left(-\frac{d^2}{2\sigma^2}\right)}\right\} \tag{1}$$

where the quantity d is the perpendicular distance between the point P and the straight line that passes through the center of each vessel in the direction of its length, the variable σ defines the spread of the gray intensity profile, the quantity *a(P)* is the gray level intensity of the local background of P and the value k is a measure of reflectance of each blood vessel with reference to its neighborhood.

A 2D-matched Gaussian kernel filtering is herein considered for detecting vessels [10]. This method involves the convolution of a set of Gaussian kernels with the retinal image under investigation, where a generic kernel may be expressed as

$$K(x,y) = -e^{\left(-\frac{x^2}{2\sigma^2}\right)} \quad \text{for } |y| \leq L/2 \tag{2}$$

where L is the length in pixels of the segment for which the vessel is assumed to have a fixed orientation. The negative sign indicates that the vessels are darker than the background. If P' is the generic point in the kernel and φ_i is the orientation of the i-th kernel, with $0 \leq \varphi_i < \pi$ the corresponding point P' (u, v) in the rotated coordinate reference is given by $P'_i = P'\boldsymbol{R}_i^T$ by means of the rotation matrix $\boldsymbol{R}_i$

$$\boldsymbol{R}_i = \begin{bmatrix} \cos\varphi_i & -\sin\varphi_i \\ \sin\varphi_i & \cos\varphi_i \end{bmatrix} \tag{3}$$

By varying the angle φ of an interval of 15°, a set of 12 kernels is given. A neighborhood N is defined as $N = \{(u,v)||u| \leq 3\sigma, |v| \leq L/2\}$. The corresponding weights K_i in the i-th kernel are given by

$$K_i(u,v) = -e^{\left(-\frac{u^2}{2\sigma^2}\right)} \quad \forall P'_i \in N \text{ and } |v| \leq L/2 \tag{4}$$

The mean value m_i of each kernel is given by $m_i = \sum_{P'_i \epsilon N} K_i(u,v)/J$ where J denotes the number of points in N. Then the convolutional mask is

$$K'_i(u,v) = K_i(u,v) - m_i \quad \forall\, P'_i \epsilon N \tag{5}$$

The filter needs to be rotated for all possible angles. Then, the corresponding responses are to be compared and only the maximum one is to be retained for each pixel.

2D-Gabor Wavelet Transformation. The contrast in retinal images is herein enhanced by means of a 2D Gabor wavelet transformation [16]. A continuous wavelet transformation, $T_\psi(\mathbf{b}, \theta, s)$, is determined by the scalar product of a generic image with the transformed wavelet $\psi_{\mathbf{b},\theta,s}$ as

$$T_\psi(\mathbf{b},\theta,s) = \mathrm{C}_\psi^{-1/2}\left\langle \psi_{\boldsymbol{b},\theta,s} | I_W \right\rangle = \mathrm{C}_\psi^{-\frac{1}{2}} s^{-1} \int \psi^*\left(s^{-1} r_{-\theta}(\mathbf{x}-\mathbf{b})\right) I_W(\mathbf{x}) d^2\mathbf{x} \tag{6}$$

where $\mathbf{x} = (x, y)$, ψ^* is the complex conjugate of ψ, and C_ψ is the normalizing constant. The parameters s, $\mathbf{b}$, and θ denote the dilation scale, displacement vector and rotation angle, respectively. The rotation operator r_θ is given by

$$r_\theta(\mathbf{x}) = (x\cos\theta - y\sin\theta,\ x\sin\theta + y\cos\theta) \tag{7}$$

where $0 \leq \theta \leq 2\pi$. The 2D Gabor wavelet may be expressed as

$$\psi(\mathbf{x}) = e^{j\mathbf{kx}} e^{\left(-\frac{1}{2}|B\mathbf{x}|^2\right)} \tag{8}$$

where $\boldsymbol{B} = diag\left[\eta^{-1/2}, 1\right]$ ($\eta \geq 1$) is a (2 × 2)-size diagonal matrix, which defines the anisotropy of the Gabor wavelet filter and **k** is the complex-exponential frequency vector.

The choice of the quantity η, which controls the elongation of the filter in any desired direction, is critical. In fact, a larger value of η generates more extensive widths of the retinal vessels and a smaller value of η has a less effect on the vessel enhancement. Then, the maximum response $M_\psi(\mathbf{b}, s) = \max_\theta \left|T_\psi(\mathbf{b}, \theta, s)\right|$ over all possible orientations is extracted for each pixel, where θ is the angle ranging from 0° to 170°, with a step = 10°.

Image Combination. In the presented Method, a suitable image combination is performed by a (pixel-by-pixel) multiplication between proper couples of preprocessed images [19] both to enhance the gray levels of the bright pixels (generally vessel ones) and darken corresponding pixels of the background.

In detail, this kind of combination enables to reduce wrong detections of vessel pixels coming from previous steps. In detail, the (pixel-by-pixel) multiplication is performed both between the images I_1 and I_2 and between the images I_3 and I_4. The resulting images I_{P1} and I_{P2}, are obtained as

$$I_{P1} = I_1(i,j) \times I_2(i,j) \quad I_{P2} = I_3(i,j) \times I_4(i,j) \tag{9}$$

Images I_{P1} and I_{P2} are then remapped in the range (0, 255) and subsequently segmented.

2.2 Segmentation and Post-processing

The segmentation is performed on each image $I_{Pi,}$ i = 1, 2, by applying twice the following method. An initial point I_{Poi} *(x, y)* is selected for the segmentation of each image $I_{Pi,}$ such that $I_{Poi}(x, y) \geq g_h$-0.05, where g_h is the gray level intensity corresponding to the 99 % of the histogram size of each image I_{Pi} [16]. Every other pixel I_{Pi} *(x, y)* can be related to I_{Poi} *(x, y)* by the relation

$$|I_{Poi}(x,y) - I_{Pi}(x,y)| < e \tag{10}$$

where the value e derives from the gray level distribution of each image $I_{Pi.}$

If (10) is satisfied, the considered pixel $I_{Pi}(x, y)$ belongs to a vessel, otherwise it belongs to background. The segmentation is carried out for all pixels of I_{P1}, I_{P2}. Obtained segmented images are subsequently combined by means a logical OR operation. Proper steps are finally performed to remove falsely detected isolated vessels pixels, providing image I_{OUT}.

3 Experimental Results and Discussion

The proposed Combined Preprocessing Method has been applied to the seven retinal images with DR taken from the publicly available DRIVE database [7], together with the corresponding Ground Truth images.

The database DRIVE consists of 40 fundus images taken from a Dutch screening program for diabetic retinopathy, where 33 images are of healthy retinas and the other 7 show signs of mild early proliferative diabetic retinopathy [14]. All these images were captured in digital form from a Canon CR5 nonmydriatic 3CCD camera at 45 field of view (FOV). They are (565 × 584)-pixel sized, 8 bit per color channel and have a FOV of approximately 540 pixels in diameter.

A mask image is provided for each image to delineate the FOV. All images were manually segmented by three eye doctors. The 40 images are separated into a training set and a test one, each containing 20 images. Retinal images reported in the test set in DRIVE have been segmented twice, resulting in a Ground Truth set A and a Ground Truth set B. In this paper, the segmentation of set A has been considered as the reference Ground Truth set. For each image I_G under investigation, the feature extraction process has provided values of the clip limit β belonging to the range [0.03–0.05], depending on both the values of the standard deviation r and of the average value q obtained from the histogram in the FOV.

In detail, by considering r^* as the average value of the standard deviations r and q^* as the average value among the values q for all considered images, respectively, it follows that

• If $q > q^*$,	then $\beta = \beta'$
• If $q \leq q^*$ and $r \leq r^*$,	then $\beta = \beta^*$
• If $q \leq q^*$ and $r > r^*$,	then $\beta = \beta''$

where the clip limit β^* is the average value in the considered range, β'' and β' are obtained by varying β^* of $\pm$ *25 %,* respectively.

Moreover, tiles of different sizes have been selected for contrast enhancing pathologic retinal images to divide each original image I_G in (8 × 8) tiles and (50 × 50) tiles, respectively. Then, the quantities L and σ have been adopted as in [10] for the 2D Matched Gaussian Kernel Filtering; the variables η, $\mathbf{k}$, s have been considered as in [16], when performing the 2D-Gabor Wavelet Transformation to obtain a reliable comparison with the corresponding methods.

The presented method is herein evaluated quantitatively on all DR images selected from the DRIVE database. Each image of the set is preprocessed according to the above procedure to obtain the corresponding I_{OUT}.

For the sake of a better comprehension, the Combined Preprocessing Method is applied to a selected retinal image I_{G19} and the corresponding images obtained in intermediate phases are reported in Fig. 3.

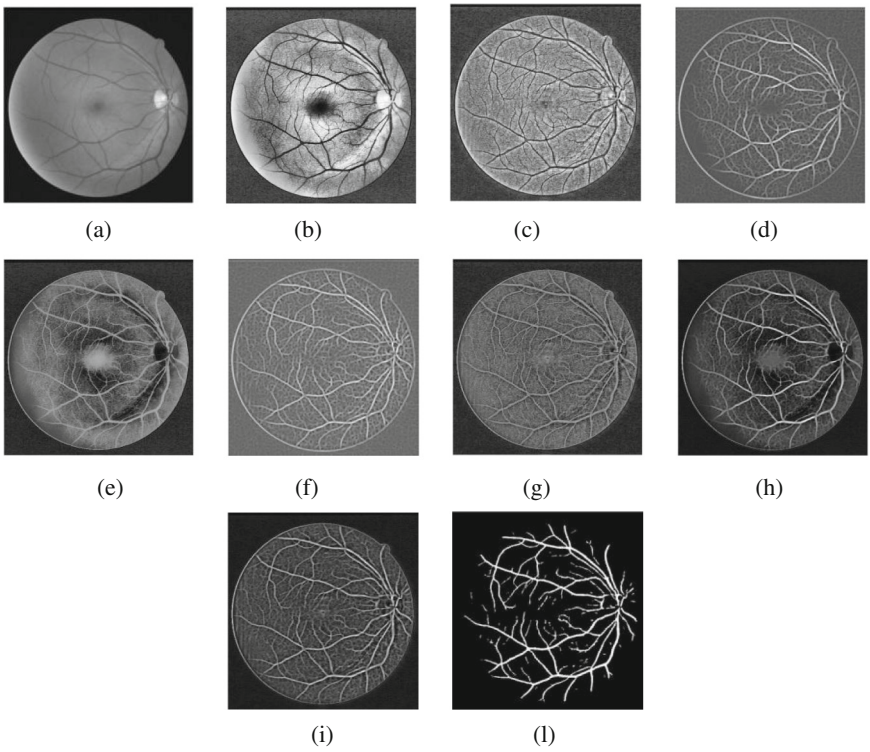

Fig. 3. Outcomes of the Retinal Vessel Detection applied to the retinal image I_{G19}: (a) I_{G19}; (b) I_{M1}; (c) I_{M2}; (d) I_1; (e) I_2; (f) I_4; (g) I_3; (h) I_{P1}; (i) I_{P2}; (l) I_{OUT}

The performances of the presented method have been then investigated by considering the variable Accuracy, which is strongly related to the segmentation quality and it is often used to evaluate and compare different methods.

In detail, the quantity Accuracy is defined as the ratio of correctly classified vessel pixels and non-vessel ones to the total number of pixels in FOV. This quantity represents the most commonly adopted index for performance evaluation, since it is strongly related to the segmentation quality of images.

Moreover, other statistical quantities, such as Precision, Sensitivity and Specificity, which indicate features regarding with binary segmented outcomes, have been computed to characterize the proposed method.

In detail, Precision is given by the ratio of the pixels correctly classified as vessel pixels to the total number of pixels classified as vessel ones; Sensitivity is defined as the number of pixels correctly classified as vessel pixels divided by the number of vessel ones in the corresponding Ground Truth image, whereas Specificity is determined by the ratio of the number of pixels correctly classified as background ones to the number of background pixels in the corresponding Ground Truth one.

Performances obtained for the proposed Retinal Combined Preprocessing Method have been expressed in terms of Accuracy, Precision, Sensitivity, Specificity as shown in Table 1, together with the values of clip limit β.

Table 1. Performance of the proposed method on retinal images with PDR

Image	β	Accuracy	Precision	Sensitivity	Specificity
01	0.03	0.9593	0.7729	0.7701	0.9778
02	0.03	0.9575	0.8787	0.6784	0.9893
10	0.04	0.9597	0.8352	0.6357	0.9888
14	0.03	0.9563	0.7264	0.7367	0.9756
18	0.03	0.9610	0.7548	0.7514	0.9790
19	0.05	0.9688	0.8378	0.7744	0.9864
20	0.04	0.9615	0.7258	0.7650	0.9771
Average value	0.04	0.9606	0.7902	0.7302	0.9820

It can be noted that the Retinal Combined Preprocessing Method presents an Average Value of Accuracy equal to 96,06 %. A comparison of Accuracy values obtained by preprocessing retinal images with the herein proposed method and following both the method proposed in [14] and the one in [16] is reported in Table 2.

Table 2. Comparison of the values of accuracy for retinal vessel detection on the same images with different methods

Method	Image						
	1	2	10	14	18	19	20
[14]	0.9384	0.9373	0.9372	0.9406	0.9373	0.9489	0.9400
[16]	0.9500	0.9498	0.9457	0.9517	0.9501	0.9618	0.9550
Proposed	0.9593	0.9575	0.9597	0.9563	0.9610	0.9688	0.9615

It can be noted that better values of Accuracy are obtained with the proposed method, when compared with the methods developed in [14] and in [16], and lower values of clip limit β for all the retinal images under investigation have been used.

4 Conclusions

In this paper a new Combined preprocessing method for retinal vessel detection towards a proliferative DR screening has been presented and developed. The effectiveness of the proposed method has been evaluated by considering diseased retinal images available in a publicly database for scientific analysis of DR. Obtained outcomes and results have been compared to those obtained with two significant methods. Experimental results show that better values of Accuracy have been obtained with the presented method with respect to the others. Future work could be devoted to perform a dynamic selection of the values of clip limit and size of tiles for preprocessing each damaged retinal image. Finally, the innovative method herein proposed for retinal vessel detection towards a

proliferative DR screening could enable the identification of previously unrecognized novel markers of disease threat.

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