Retinal Blood Vessels Segmentation for ROP Plus Form Diagnosis

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Abstract. Retinal Conditions can have highly adverse outcomes without an early diagnosis and correct monitoring. Retinopathy of Prematurity (ROP) Plus Form, in particular, is a disease that can lead to childhood blindness, and its diagnosis requires medical experts to examine the retinal condition manually. Although developments in screening equipment have helped, this is still a time-consuming and subjective task. The development of automatic tools for diagnosing such diseases could solve both problems. The first stage of such tools should be an algorithm that identifies relevant objects in retinal images, which can be achieved by performing a segmentation. The ROP Plus Form is characterized by the tortuosity in the main blood vessels, making them the essential objects to be segmented. Retinal Blood Segmentation is a widely explored task with different methodologies that can be followed. However, many studies try to segment all the blood vessels rather than only the most important ones. In this work, we present a segmentation pipeline to segment only the main vessels whose characteristics can be used to assess ROP Plus Form disease. This pipeline uses different operations and filters, including CIELAB Enhancement, Background Normalization, Bell-Shaped Gaussian Matched Filtering, Modified Top-Hat operation, and Frangi Filtering. The final segmentation is done by determining a threshold value using the Triangle Threshold algorithm. The pipeline was tested in the well-known DRIVE Database, achieving an Accuracy of 94.71%, Specificity of 96.01%, and Sensitivity of 76.34%.

Keywords: Retinopathy of Prematurity · Segmentation · Retinal Blood Vessels · Vessel Enhancement · Thresholding.

1 Introduction

Different diseases and conditions can be diagnosed and monitored by analyzing the condition of the patient's retina. Such diseases include Retinopathy of Prematurity (ROP), a well-known condition recognized as one of the leading causes of childhood blindness worldwide. While ROP can be subclassified into different types, the Plus Form, characterized by high tortuosity, even in the main vessels, has been emphasized in recent studies.

Traditional methods for assessing the state of such conditions were based on live diagnoses by ophthalmologists, which came with some issues like being time-consuming, not having the possibility to store retinal images for further evaluation, and having a higher risk of misdiagnosis.

Recent developments in screening methodologies allowed the design of different products to acquire retinal images. This means that images can now be digitally acquired and then sent and analyzed by ophthalmologists or even used for future studies in the area, making retinal imaging a cost-effective and more accurate approach for ROP diagnosis and monitoring. [2] Such products include the RetCam Systems, a global reference for acquiring RGB retinal images in newborns. [9]

Although a huge step has been made in this area with the adoption of such equipment, an expert's manual evaluation of the retinal images is still required, making the diagnosis and monitoring time-consuming and even subjective to a certain degree.

Thus, the next significant step in this area is developing automatic classification methods that could help solve both problems. Since diseases, including ROP, are mainly assessed by studying the conditions of retinal blood vessels, the first step of these methods should be to extract the necessary information from these structures. This can be achieved by an Automatic Segmentation of Blood Vessels in Retinal Images.

2 Related Work

Retinal Blood Vessel Segmentation has been the focus of many recent studies due to its importance in improving healthcare in ophthalmology.

By analyzing the literature, it is clear that different paths can be followed to perform this segmentation task. These paths include Unsupervised Methods, such as region-based deformable models, which include Active Contours algorithms, multi-scale segmentation, tracking approaches, kernel algorithms, and morphologic operations, usually combined with adaptative thresholding operations. These methodologies usually include initial image preprocessing steps that help enhance blood vessels and remove other objects and noise.[3]

In recent years, Machine and Deep Learning have been receiving an increased focus for segmentation tasks. Many authors also explore using such models for retinal blood vessel segmentation. Supervised learning methods usually achieve higher accuracy than unsupervised methods. However, more data and manual annotations are needed to train robust models, which can be an issue in many cases, especially in the area of Biomedical Engineering. Thus, using Unsupervised Methods still has the advantage of not needing training data, although a deeper pre-knowledge is required to develop such algorithms.

It was also noticeable the use of the DRIVE Database as a gold standard and the use of Accuracy, Specificity, and Sensitivity as preferred metrics to assess the segmentation performance.

3 Materials and Methods

Although many of these studies achieve good segmentation performance and results, they focus on segmenting all the blood vessels in the retinal image. In the ROP Plus Form diagnosis case, the main vessels are sufficient for assessing the disease. On the other hand, retinal images from newborns are more prone to noise than the ones from adults. Thus, methods that try to capture and segment more details could fail in filtering unwanted noise in those images.

In this work, we propose a novel Retinal Blood Vessel Segmentation Pipeline intended to be used for retinal images from newborns, such as the ones acquired with RetCam Systems, and the assessment of ROP Plus Form disease.

3.1 DRIVE Database

It became clear from the literature analysis that the DRIVE Database [7] is the most widely used for developing and testing Retinal Blood Vessel Segmentation algorithms.

This database contains two sets of images, a training and a test set, with 20 images each. Both training and test sets include FOV masks for each image. However, only the training set contains manually annotated blood vessel masks that can be used as Ground Truth (GT).

The age range of the subjects in this database is from 25 to 90 years. The provided images are RGB with 565x584 pixels resolution in the TIFF format and with 45 degrees of FOV. The camera used to acquire them was a Canon CR5 nonmydriatic 3 Charge-Coupled Device (CCD).

To test and compare the proposed pipeline to others in the literature, the training set of this Database was used, and the metrics described at the end of this section were computed using the provided GTs.

Fig. 1 shows an image example from the DRIVE Database.

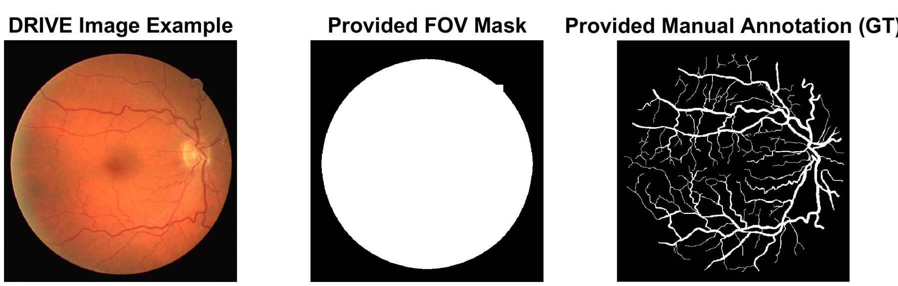

Fig. 1. Image 22 of the training set from DRIVE Database, its FOV Mask and Manual Annotation

3.2 FOV Mask generation

The visual information in retinal images is restrained to the Field of View (FOV), making it essential to have an FOV binary mask that can focus all other segmentation steps in this area. By accounting for the fact that, in every image, the outside of the FOV is always black, the mask can be generated by applying the Otsu Thresholding on the green channel of the raw RGB image. To the resulting binary image, firstly, a fill operation is used to ensure we have a complete disk within the FOV without any holes. Secondly, an erosion with a disk with radii ten as a structure element is also applied. Both these steps are essential since gradient-based operations will be used in the part of the image identified as FOV by the generated mask. If black holes existed or the border between the FOV and the outside were contained, it could lead to errors in the segmentation.

3.3 Image Preprocessing

Like many other approaches found in the literature, the first part of the pipeline should be the preprocess of the retinal images, which should allow the standardization of the image's brightness and contrast and better separate the objects from the background. The preprocessing of the images can be divided into several steps.

CIELAB Enhancement The first preprocessing step of the proposed pipeline is to perform a color enhancement based on the CIELAB color space. Specifically, the RGB image is converted to the CIELAB color space, and then CLAHE is applied to the L* Channel, which translates the perceptual lighting of the image. The image is then converted back to RGB. This allows for better discrimination between vessels and the background, as shown in Fig. 2. [5]

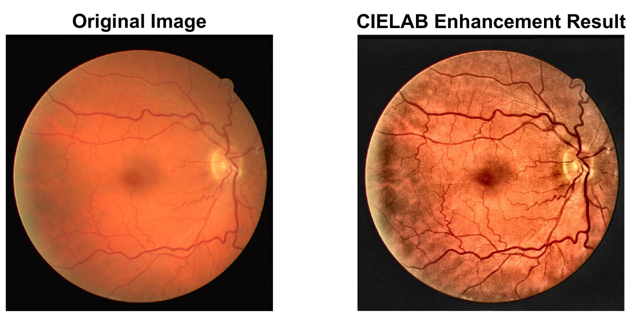

Fig. 2. Result of CIELAB L* Channel Enhancement applied to a Retinal Image

Green Channel Extraction Like many other studies found in the literature, we opt to use the Green Channel of the enhanced image in the remaining steps of the pipeline. This is mainly due to the increased discrimination between blood vessels and other background objects when using this channel rather than the red or blue channels. The difference between the three channels for the enhanced image is present in Fig 3.

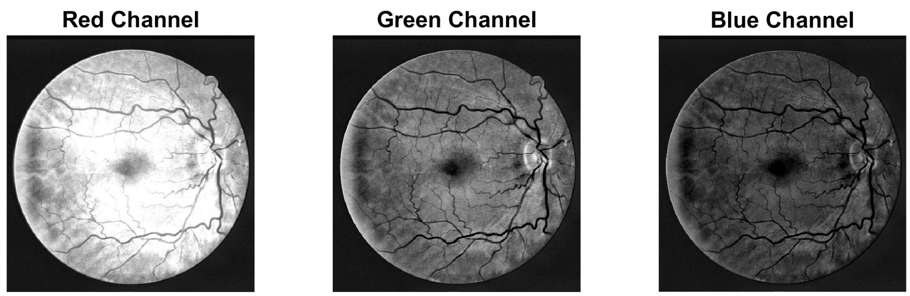

Fig. 3. Difference between the three channels of the enhanced RGB image

Background Normalization A Background Normalization is then applied to the gray image to eliminate the main differences in intensities and overall background noise. The normalized image is obtained by the difference between the gray image and its background estimation, which can be computed by applying a sufficiently large mean kernel to the image. An example of this operation is represented in Fig. 4. [4]

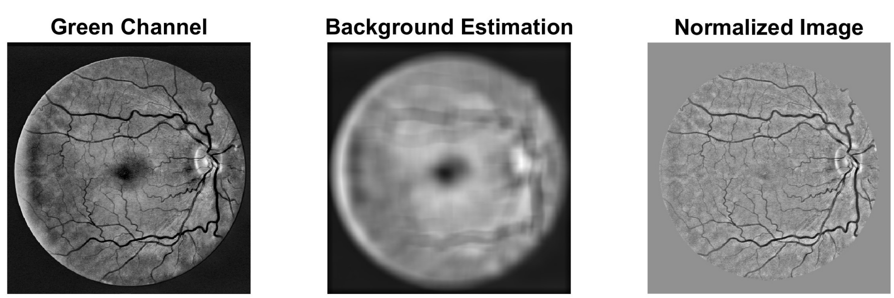

Fig. 4. Image's green channel (left), background estimation (middle), and the result of Background Normalization (right)

3.4 Vessel Enhancement

After preprocessing the image, different successive steps are applied for vessel enhancement. This part of the pipeline should allow us to get an image that is easier to discriminate between the objects we want to segment and the rest of the information inside the FOV.

Bell-Shaped Gaussian Matched Filter The BSGMF has been used before for Retinal Blood Vessel Segmentation [8, 10]. Its effect is enhancing the image's objects, especially the vessel-like structures, and removing other background information.

BSGMF is based on the kernel given by Eq. 1.

$$K(x, y) = \pm exp(-\frac{x^2 + y^2}{2\sigma^2}) \tag{1}$$

And its effect on a gray retinal image is represented in Fig. 5.

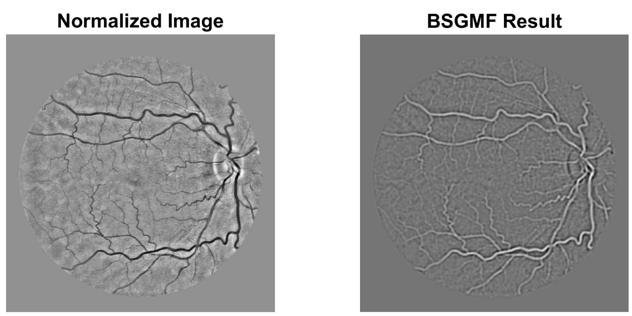

Fig. 5. Normalized Image (left) and the result of applying the BSGMF to it (right)

Modified Top-Hat A Modified Top-Hat Operation has also been proposed for Retinal Blood Vessel Segmentation [4], given by Eq. 2.

$$TopHat = I - min((I \bullet S_c \circ S_o; I) \tag{2}$$

Where $\bullet$ and $\circ$ represent the closing and opening operation, respectively, and S_c and S_o are the correspondent Structural Elements (SE). I is the input gray image.

Using this modified version of the well-known Top-Hat operation allows the enhancement of objects with a specific width, controlled by the size of the opening SE, while reducing the risk of enhancing other background elements. In our case, this operation was applied three times with increasing opening SE (from a disk with radii one through three) and with the closing SE as a disk with radii one. The three resulting images are then combined into one by averaging.

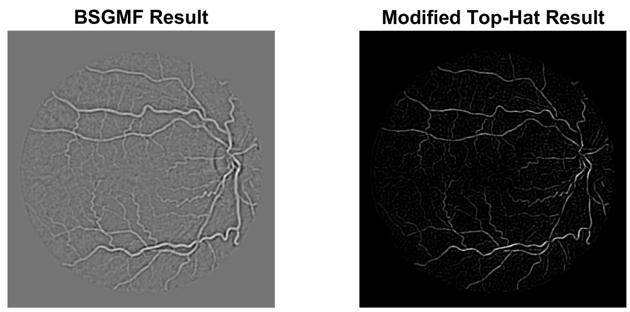

Fig. 6. BSGMF result (left) and the result of applying the Modified Top-Hat operation to it (right)

Frangi Filter This Hessian-based Filter, proposed by Frangi et al. [1], was specially designed to enhance vessel-like structures. It can be mathematically described by:

$$V_{Frangi} = \begin{cases} 0, & \text{if } \lambda_2 > 0. \\ exp(-\frac{(\lambda_1/\lambda_2)^2}{2\beta 1^2})(1 - exp(-\frac{\lambda_1^2+\lambda_2^2}{2\beta 2^2})), & \text{otherwise.} \end{cases} \quad (3)$$

Where λ_1 and λ_2 are the eigenvalues of the image's Hessian Matrix. The computation of this matrix depends on a Gaussian Function used, which in turn depends on its standard deviation (σ). Therefore, σ is a variable that needs to be set for applying this filter. $\beta 1$ and $\beta 2$ are the other two parameters that must be manually set.

The eigenvalues, λ_1 and λ_2, are directly correlated to the vessel properties as they can be used to identify the presence of blood vessels: a λ_1 near zero and a negative λ_2 indicate the existence of bright tubular elements, in this case the blood vessels.

Applying this filter to the result of the modified Top-Hat operation allows almost perfectly to eliminate any object and information that is not a vessel. It also has an essential role in filtering between main vessels and branches, making it possible to control the relative response between both by changing its parameters.

Fig. 7 shows the result of applying the Frangi Filter to the image obtained in the last step. With close attention, it is possible to see that the image on the right still contains some background noise, whereas the image on the left, the result of applying the Frangi Filter, is almost clear of this noise and only includes the body of the blood vessels.

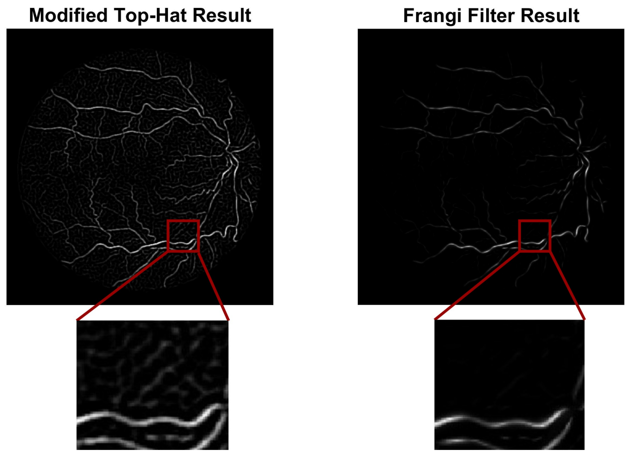

Fig. 7. Result from applying the Modified Top-Hat operation (left) and the result of applying the Frangi Filter to it (right)

3.5 Triangle Thresholding

A robust pipeline for vessel enhancement should allow for better discrimination between the blood vessels and other objects or background noise.

Thus, a thresholding method can perform well in segmenting the retinal blood vessels. The method chosen for our pipeline is the Triangle Thresholding. This method allows to compute a threshold value for images and signals based on a histogram with N bins, where N should be tested and set for each case. The threshold value is computed as follows: a line is drawn between the first non-zero and maximum histogram values. Then, the point of the histogram that distances the most to that line is determined. The abscissa of that point, which translates into a brightness value, is our threshold value. [6]

This method is ideal for images where the background has a well-defined, concentrated range of intensities and is separated from the objects' intensities in the image histogram. Thus, this method should perform well in the segmentation of images, such as the result of applying the Frangi Filter.

Lastly, the binarization result was also filtered to remove the smaller objects.

The complete proposed pipeline is represented in Fig. 8.

3.6 Performance Assessment

Different segmentation metrics were used to assess the proposed methodology's performance.

The three most used metrics for performance assessment of segmentation pipelines are Accuracy (*acc*), Sensitivity (*sen*), and Specificity (*spe*). These metrics can be calculated as follows:

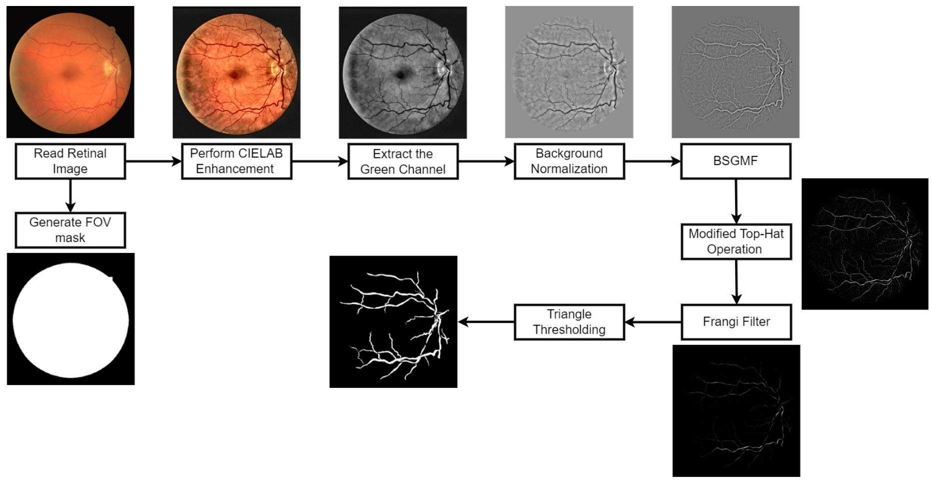

Fig. 8. Proposed Retinal Blood Vessel Segmentation in RetCam3 Images

$$acc = \frac{TP + TN}{TP + TN + FP + FN} \tag{4}$$

$$sen = \frac{TP}{TP + FN} \tag{5}$$

$$spe = \frac{TN}{FP + TN} \tag{6}$$

Where TP and TN are the true positive and negative pixels, and FP and FN are the false positive and negative pixels, correspondingly.

4 Results and Discussion

The pipeline was tested to find the best parameter configuration for the DRIVE Database images. The results presented in this section were obtained with a kernel size of 30x30 pixels for the Background Normalization, a 15x15 kernel with σ set as 2 for the BSGMF, and SE as a square with side 2 for the closing in the modified Top-Hat. The Frangi Filter was performed four times for each image with the σ values ranging from one to seven, with $\beta1 = 0.5$ and $\beta2 = 15$. Finally, the Triangle Threshold was applied with 128 bins.

The segmentation result for the image used as an example in the previous section is represented in Fig. 9.

By visual analysis of the results, the pipeline achieved what was expected: the segmentation of the main vessels, with slight inclusion of smaller vessels and background noise.

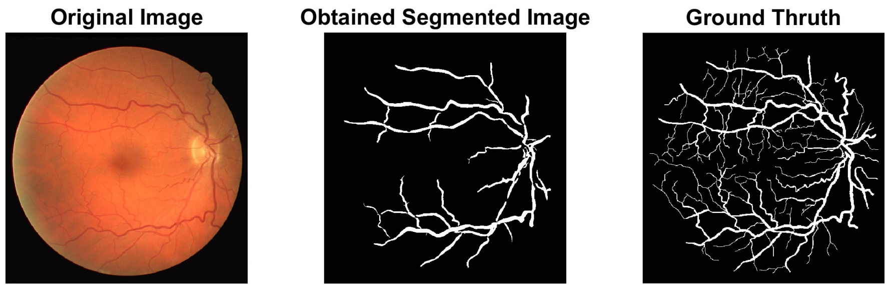

Fig. 9. Original DRIVE Image example(left), segmentation result with the proposed pipeline (middle), and the manual annotation provided in the Database, i.e., the GT (right)

The mean and standard deviation of the metric scores for the 20 images of the training set from the DRIVE Database can be found in Table 1.

Table 1. Segmentation Scores obtained with the proposed pipeline based on the DRIVE dataset

Metric	Acc (%)	Spe (%)	Sen (%)
Scores	94.71 ± 1.00	96.01 ± 1.27	76.34 ± 5.29

Accuracy and Specificity both achieve high mean scores and low standard deviation, which may confirm the effectiveness and robustness of the proposed pipeline. However, Sensitivity did not achieve a high mean score or a low standard deviation. By looking into how this metric is computed (Eq. 5), it is possible to see that it highly depends on the relation between TP and FN pixels. Since we tried to remove secondary vessels from the final segmentation, the amount of FN should be naturally higher, lowering the Sensitivity score. Moreover, the amount of secondary vessels may vary from image to image, which explains the high standard deviation obtained for this metric. The other two metrics are unaffected since the accuracy dependence on FN is low, as it considers the whole set of pixels in the image. Specificity only depends on TN and FP, which are not affected by the non-segmentation of secondary vessels.

5 Conclusion

In this work, we proposed a Pipeline for Automatic Retinal Blood Vessel Segmentation to segment the main vessels of retinal images. The results confirm that this goal was achieved and that the pipeline shows high robustness and good performance.

Further testing should be made to see how this methodology generalizes for different image sources, especially retinal images from newborns, which are known to contain more noise and be less concise regarding brightness, contrast, and other core characteristics.

Particularly with the growing popularity of Deep Learning, the segmented images could be used to build tools for the automatic diagnosis and monitoring of diseases, such as ROP Plus Form. This should significantly impact healthcare, as it could make it less time-consuming and more independent of a medical expert's subjectivity.

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