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Chapter 15. AUTOMATIC BLOOD VESSEL SEGMENTATION ALGORITHM IN ULTRAWIDE-FIELD FLUORESCEIN ANGIOGRAPHY

15.1. Introduction

Latest data from the IDF (International Diabetes Federation) published in November 2019 shows that already 463 million people in the world suffer from diabetes. With the current upward trend, the epidemic will increase to 700 million by 2045 [1]. Diabetes is an incurable disease, but its early detection allows extending the patient's life by an average of 5 years and prevent serious complications such as heart attack, stroke or diabetic retinopathy [2].

Diabetic retinopathy is the most frequent cause of blindness among adults aged 20-74 years. During the first two decades of disease, retinopathy occurs in nearly all patients with type 1 diabetes and 60% of patients with type 2 diabetes [3]. In the early stages of development, the disease is asymptomatic. It does not cause any deterioration in vision nor causing pain. The small retinal blood vessels thicken locally to form microaneurysms. The disease can be diagnosed only during a specialist ophthalmological examination with the use of funduscamera. In later stages of retinopathy, high levels of sugar damage the blood vessels in the retina of the eye. Weakened vessels crackle and their contents ooze into the vitreous. This causes a visual disturbance leading to complete blindness.

Given the benefits of rapid diagnosis, it is essential to develop screening tests that cover as much of the population as possible. Such tests, supported by computer programs,

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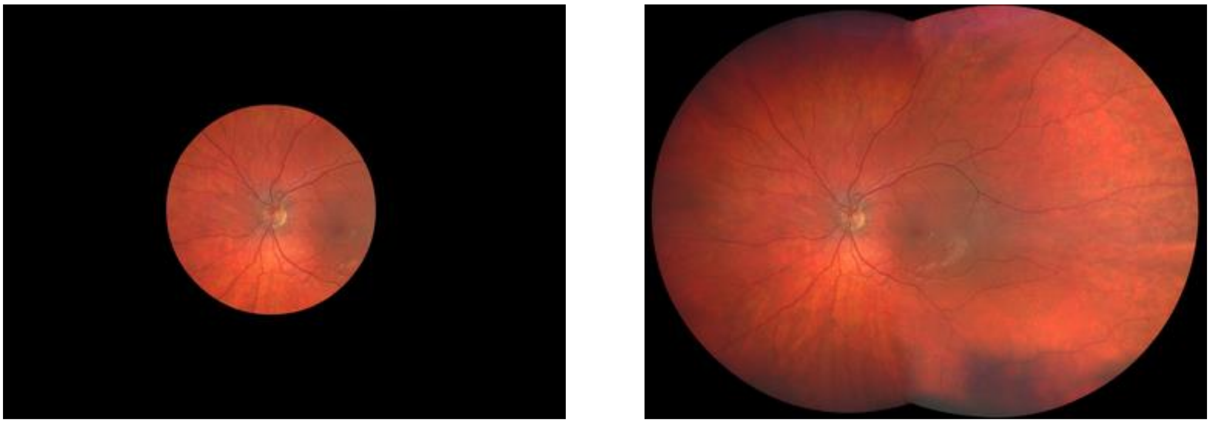
allow for quick reactions and treatment of the disease in its initial stage [4]. Automatic segmentation of blood vessels is one of the tools that helps diagnosing retinopathy [5].

15.2. Materials

Researchers have proposed many algorithms to address the problem of segmentation of blood vessels in the retina of the eye. Unfortunately, all methods were developed for images recorded with standard funduscameras with a range of 45^{o} from the DRIVE [6] and STARE [7] databases. These databases contain original images, hand-segmented blood vessel masks and additional annotations made by experts. Fig. 15.1 presents difference between standard and ultrawide-field fluorescein angiography [8].



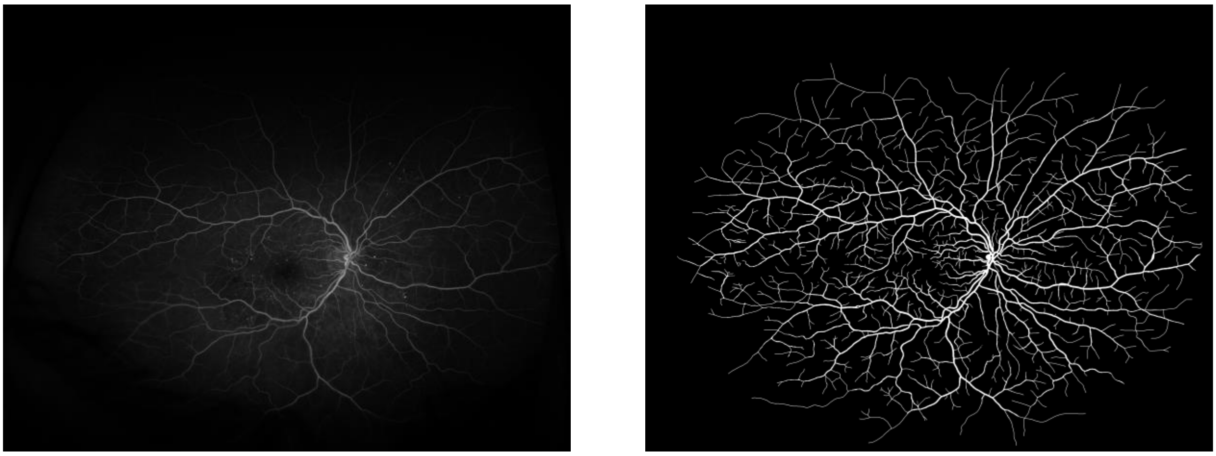
(a) (b)

Fig. 15.1. Funduscamera field of view: (a) 45^{o}, (b) 200^{o} [8]
Rys. 15.1. Zakresy widoczności funduskamer: (a) 45^{o}, (b) 200^{o} [8]

Comparing to standard 45^{o} field of view UWFA allows imaging at 200^{o}. As microaneurysms, which are the most frequent symptoms of retinopathy, occur in the peripheral areas of the image, this technique shows a significant advantage over the standard one. In addition UWFA has high geometrical resolution. A single pixel is a representation of the area that can be approximated with a square with a side reaching several micrometers.

To develop the proposed segmentation algorithm 43 images recorded with ultrawidefield fluoerscein angiography were used. All photos were previously anonymised so as not to infringe the privacy of patients. The images include both physiological and pathological images. Ophthalmologist classified pathologies as: leaks of blood vessels, occurance of ischemic areas, occurance of microaneurysms.

Additionally, 12 photos were outlined by a specialist. The obtained binary masks were used for the numerical evaluation of the quality of the developed algorithm. Fig. 15.2 shows the original image and an exemplary blood vessel mask prepared by an expert.



(a) (b)

Fig. 15.2. Image from funduscamera: (a) original, (b) expert delineation
Rys. 15.2. Obraz dna oka pochodzący z funduskamery: (a) obraz oryginalny, (b) obrys naczyń krwionośnych wykonany przez eksperta

15.3. Method

The blood vessel segmentation algorithm proposed in the current paper is presented in Fig. 15.3.

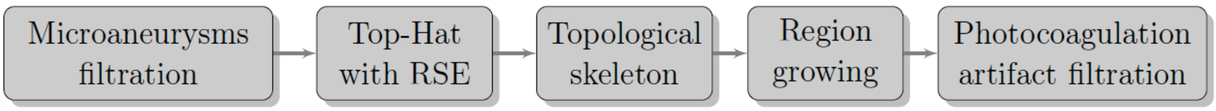


Fig. 15.3. Automatic blood vessel segmentation algorithm in UWFA images
Rys. 15.3. Schemat blokowy proponowanego algorytmu segmentacji

15.3.1. Rotating Structuring Element

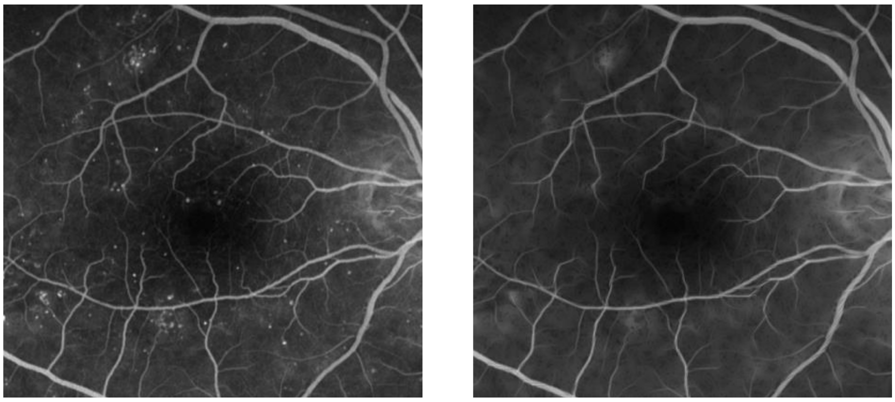
In the chapters that follow, the term "Rotating Structuring Element" (RES) appears twice, so we will cover this approach in detail here. It's used in tandem with mathematical morphology in filtration and signal enhancement.

Best shape matching blood vessels is line. Vessel network is a complex structure and a single linear structuring element would pick out vessels oriented in only one direction, so more than one structuring element must be utilized [9]. With a compromise in computational complexity and segmentation quality, the structural element is rotated at 18 different angles: from 0° to 170°, rotating 10° per iteration. Final result is a combination of maximum values from the obtained 18 images.

15.3.2. Microaneurysms filtration

Microaneurysms are the protrusions of the walls of the blood vessels of the retina, visible as white, spherical points in the image. They are the earliest symptom of diabetic retinopathy [10]. Filtering them out is crucial in the segmentation of the narrowest blood vessels, which give a much weaker image signal due to the lower blood content.

The proposed method allows segmentation of the mask of microaneurysms, which can be then removed from the original image. It is based on the isolation of contrasting structures which are obtained by subtracting median filter smoothed image from the original image. The effect of this strengthening are microaneurysms and thin fragments of blood vessels network. Morphological opening with linear RSE is then used to remove vascular fragments from the aneurysms mask. Finally, in the original image the places where the microaneurysms are found are then equated with the surrounding background. Fig. 15.4 shows fragment of original image before and after microaneurysms removal.



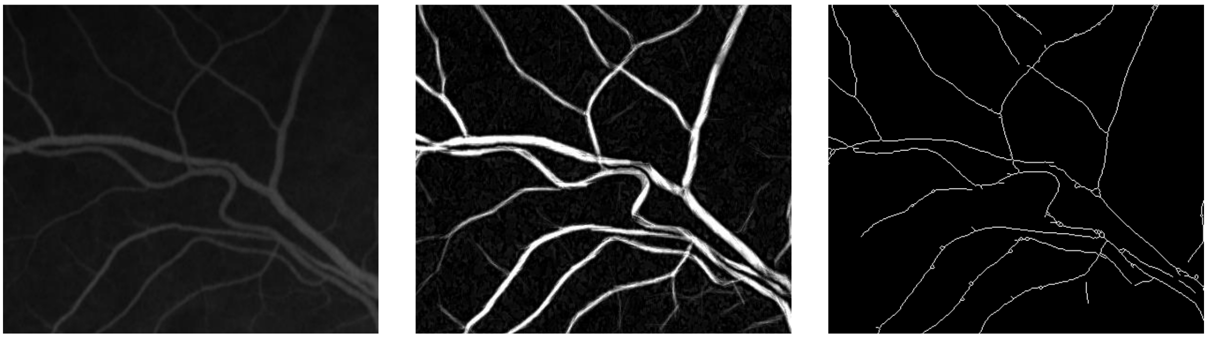
(a) (b)

Fig. 15.4. Microaneurysms filtration: (a) original, (b) result
Rys. 15.4. Filtracja mikrotętniaków: (a) obraz oryginalny, (b) wynik filtracji

15.3.3. Enhancing blood vessel signal

The second step of the algorithm is to apply top-hat transform to image (Fig. 15.5a) obtained in previous step. This operation amplifies the signal coming from the blood vessels against the background (Fig. 15.5b).

Strong contrast between the blood vessels and the background allows binarization with Otsu method to be used. Binarized image is skeletonized (Fig. 15.5c) followed by removal of small elements.



(a) (b) (c)

Fig. 15.5. Enhancing blood vessel signal: (a) original, (b) top-hat transform, (c) skeleton
Rys. 15.5. Wzmocnienie sygnału obrazowego z naczyń krwionośnych: (a) obraz oryginalny, (b) biała transformata cylindryczna, (c) szkieletyzacja

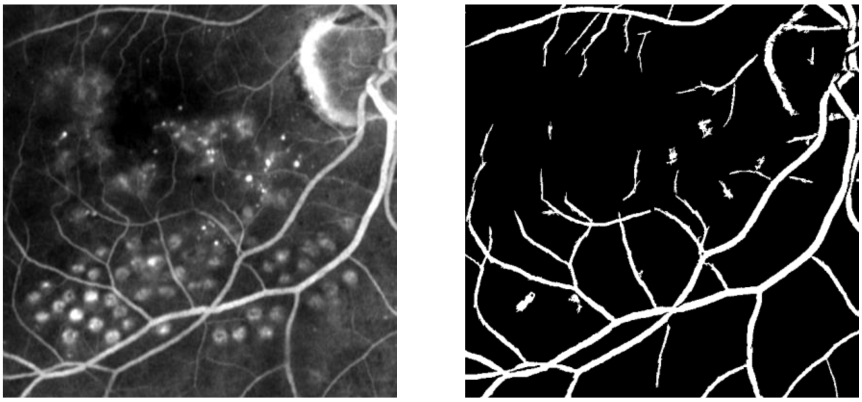
The resulting mask, which reflects the center of the blood vessels is passed as argument (seed points) for region growing function. With each iteration, the vessels widen until they reach their full volume. Region growing algorithm stops when the results of the current iteration do not differ from the previous one.

15.3.4. Filterting photocoagulation artifacts

Last step of proposed algorithm is post-processing filtration of photocoagulation artifacts. Photocoagulation of the retina is a minimally invasive procedure used to treat various diseases of the retina. Unfortunately, the eyes of patients after this procedure have specific changes that negatively affect segmentation. It can be observed as groups of small, white circles in close proximity to blood vessels.

Due to close proximity to blood vessels region growing algorithm often classifies them incorrectly. To decrease the number of false positive pixels in segmentation results post-process filtration is applied.

Photocoagulation filter is based on size and circularity of analysed objects. If an object is big enough and has a shape similar to a circle it is removed from the image (Fig. 15.6). Artifacts that have fused together and have lost their circularity are still challenging.



(a) (b)

Fig. 15.6. Photocoagulation filtration: (a) original, (b) result
Rys. 15.6. Filtracja artefaktów fotokoagulacji: (a) obraz oryginalny, (b) wynik filtracji

15.4. Results

The effectiveness of the segmentation algorithm was assessed by comparing segmentation results with expert contours, expressed as 12 binary masks. Selected numeric indicators determining the degree of similarity of the compared images are summarized in Tab. 15.1. All of them were determined by the values from confusion matrix.

Table 15.1

Parameterized evaluation of segmentation

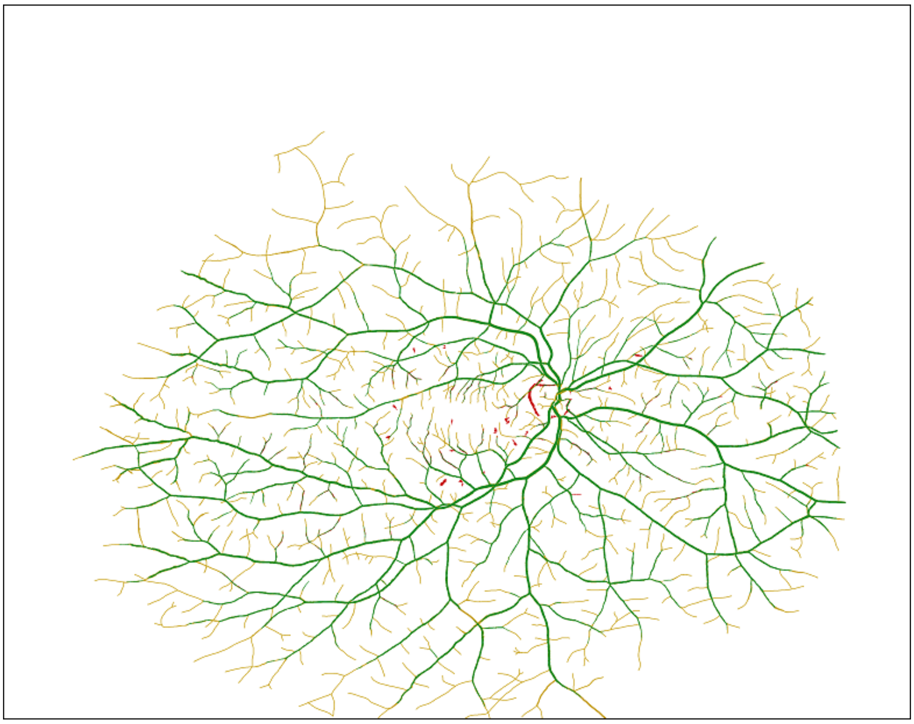
No.	TPR	TNR	PPV	ACC	Dice
1	0.690	0.999	0.981	0.983	0.811
2	0.730	0.999	0.986	0.985	0.839
3	0.823	0.999	0.971	0.989	0.891
4	0.603	0.999	0.955	0.981	0.740
5	0.611	1.000	0.994	0.976	0757
6	0.661	1.000	0.985	0.986	0.791
7	0.665	1.000	0.994	0.978	0.797
8	0.884	0.998	0.954	0.992	0.918
9	0.777	0.999	0.979	0.984	0.866
10	0.648	1.000	0.997	0.985	0.786
11	0.717	1.000	0.994	0.983	0.833
12	0.698	1.000	0.997	0.984	0.821
avg.	0.709	0.999	0.982	0.984	0.820

Among results based on confusion matrices the largest number of pixels was classified as true negative. This is due to a relatively small number of blood vessel pixels compared to the background pixels. Value specifying a number of true positive pixels is also high. On average 98% of the all pixels have been correctly segmented.

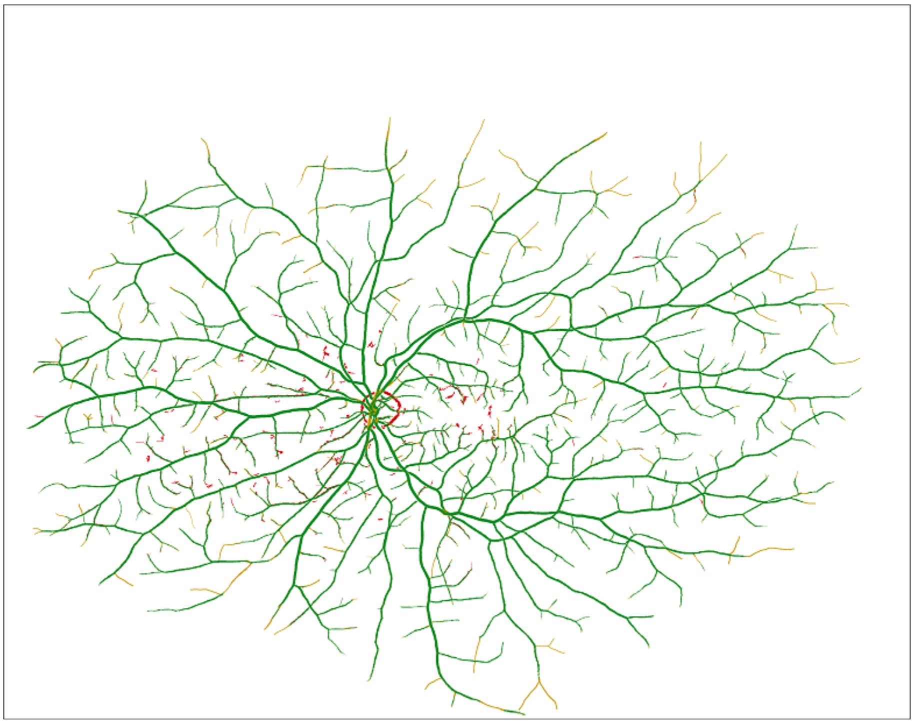
The average number of incorrectly classified pixels is less than 2%. Values of false positive and false negative pixels demonstrate that the developed algorithm is more prone to undersegmentation than oversegmentation. This problem is related to the relatively low contrast of the peripheral areas of the image.

The algorithm correctly segments large blood vessels, located in the central part of the image. On the contrary, thinnest blood vessels in the periphery are usually not detected due to uneven contrast. That causes increase of false negatives. False positive pixels are a result of clustering adjacent microaneurysms or merging bright optic nerve disc with blood vessels.

In addition to numerical results, segmentation results are also presented graphically. Fig. 15.7a shows the worst and Fig. 15.7b shows best result. The effectiveness of segmentation was assessed by comparing the values of the Dice coefficient. For the presented images, they were equal to 0.743 and 0.919, respectively. On both images, the same conventions were adopted: true negative marked as white, true positive as green, false negative as yellow, false positive as red.



(a)



(b)

Fig. 15.7. Graphical comparison of segmentation results with the expert delineations: (a) worst, (b) best case

Rys. 15.7. Graficzna reprezentacja tablicy pomyłek: (a) najgorszy rezultat segmentacji, (b) najlepszy rezultat segmentacji

15.5. Conclusions

Main purpose of the work was to develop and implement an algorithm for automatic segmentation of blood vessels in fundus images, which would be a useful tool for ophthalmologists in the diagnosis of diabetic retinopathy. The proposed approach is based on filtration of image structures that are not blood vessels, top-hat transform that strengthens the vessels, region growing and post-processing transformations reducing artifacts.

Segmentation results were verified on the basis of physiological and pathological images. The observed pathologies were classified by the ophthalmologist as: leaks of blood vessels, the presence of ischemic areas and microaneurysms. The database consists of 43 images, 12 of which have the expert contour of the blood vessel network. Medical annotations allow numerical determination of the quality level of segmentation. The obtained results allowed to state that on average 98% of segmented pixels are

consistent with the outlines prepared by a specialist. Moreover, the average value of Dice coefficient has relatively high value, equals to 0.82.
The proposed algorithm can be used by ophthalmologists to develop a screening strategy to minimize the incidence of diabetic retinopathy. However, the disease also manifests itself through the presence of microaneurysms or macular deformities. Therefore, the best solution would be to create a modular system that checks for more symptoms of the disease. The blood vessel segmentation algorithm would be an integral part of such a system. Information from other modules could be used to eliminate structures that negatively affect the result of segmentation of blood vessels. For example, a method of optic disc filtration would be useful, thus reducing the number of false positives.

The two-dimensional image obtained from wide-angle fluoerscein angiography is in fact a reflection of the spherical plane, therefore it is characterized by a strongly uneven distribution of brightness. The central part of the image is best lit, while the peripheral areas are less lit. The contrast is also deteriorating: the blood vessels differ only by a few levels of gray from the background. By using a transform that would enhance the brightness of the pixels located in the peripheral parts of the image without changing the central pixels, the algorithm would probably be able to segment the narrowest blood vessels as well.

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Bibliography

1. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: International Diabetes Federation, 2019.
2. Konstantinos Papatheodorou, Maciej Banach, Eleni Bekiari, Manfredi Rizzo, Michael Edmonds, Complications of Diabetes 2017, Journal of Diabetes Research, vol. 2018, Article ID 3086167, 4 pages, 2018. https://doi.org/10.1155/2018/3086167

3. D.S. Fong, L. Aiello, T. W. Gardner, G.L. King, G. Blankenship, J.D. Cavallerano, F.L. Ferris, R. Klei,. Retinopathy in diabetes.Diabetes Care 27, Supplement 1 (Dec. 2003), S84-S87.
4. P. Scanlon, The english national screening programme for diabetic retinopathy 2003-2016. Acta diabetologica 54 (02 2017).
5. H. Jelinek, M. Cree, J. Leandro, J. Soares, R. Cesar Junior, A. Luckie, Automated segmentation of retinal blood vessels and identification of proliferative diabetic retinopathy. Journal of the Optical Society of America. A, Optics, image science, and vision 24 (06 2007), 1448-56.
6. DRIVE, Digital Retinal Images for Vessel Extraction: https://drive.grandchallenge. org, accessed: 10 March, 2021.
7. STARE, STructured Analysis of the Retina: https://cecas.clemson.edu/ ahoover/stare, accessed: 10 March, 2021.
8. Zeiss Clarus 500, product website: https://www.zeiss.com/meditec/us/products/ ophthalmology-optometry/retina/diagnostics/fundus-imaging/clarus-500.html, accessed: 10 March, 2021.
9. B.D. Thackray, A.C. Nelson, (1993), Semi-automatic segmentation of vascular network images using a rotating structuring element (ROSE) with mathematical morphology and dual feature thresholding. IEEE Transactions on Medical Imaging, 12(3), 385-392. doi:10.1109/42.241865
10. T. Spencer, J. Olson, K. McHardy, P. Sharp, J. Forrester, An image-processing strategy for the segmentation and quantification of microaneurysms in fluorescein angiograms of the ocular fundus. Computers and biomedical research, an international journal 29, 4 (August 1996), 284-302.

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Abstract

Extraction of blood vessels in retinal images is an important step for computer-aided diagnosis of ophthalmic pathologies such as diabetic retinopathy. So far, methods have been developed to work on narrow-angle images – the most popular DRIVE and STARE datasets. This paper presents a segmentation algorithm for ultrawide-field images based on mathematical morphology with the use of rotating structuring element. Along with the segmentation, filters have been developed to remove non-blood vessel structures from the images. The proposed method successfully segments most of the blood vessel network. Experimental results on prepared dataset, show that the segmentation results reach an average Dice coefficient of 0.82%. Segmentation errors are mostly false negative pixels due to uneven contrast on peripheral image areas.

Keywords: ultrawide-field fluorescein angiography, rotating structuring element, blood vessels, segmentation.