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DIABETIC RETHINOPATHY SCREENING BY BRIGHT LESIONS EXTRACTION FROM FUNDUS IMAGES

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Retinal images are nowadays widely used to diagnose many diseases, for example diabetic retinopathy. In our work, we propose the algorithm for the screening application, which identifies the patients with such severe diabetic complication as diabetic retinopathy is, in early phase. In the application we use the patient's fundus photography without any additional examination by an ophtalmologist. After this screening identification, other examination methods should be considered and the patient's follow-up by a doctor is necessary. Our application is composed of three principal modules including fundus image preprocessing, feature extraction and feature classification. Image preprocessing module has the role of luminance normalization, contrast enhancement and optical disk masking. Feature extraction module includes two stages: bright lesions candidates localization and candidates feature extraction. We selected 16 statistical and structural features. For feature classification, we use multilayer perceptron (MLP) with one hidden layer. We classify images into two classes. Feature classification efficiency is about 93 percent.

K e y w o r d s: diabetic retinopathy, fundus images, automatic diagnostic and screening, machine learning, neural networks

1 INTRODUCTION

Diabetes mellitus is one of the most widespread diseases in the world, it is characterized by impaired glucose metabolism and it causes complications, which lead to chronic dysfunctions and failures of some organs [1]. One of these complications is diabetic retinopathy (DR), causing worsening of the vision and finally the blindness. For diagnostic and screening purposes of DR, patient-friendly method - digital retinal fundus photography can be used. Retinal fundus images reflect the interior surface of the eye, visible through the ophthalmoscope. They are taken with special microscope, digital fundus-camera. Fundus camera can take color high-resolution images. Typical image of the healthy human eye fundus can be seen in the Fig. 1. This figure contains yellow and red color shades.

Main visible components are macula, blood vessels and optic disc (OD). Optic disc is usually the brightest part of the image and it is round-shaped. Macula and its central part fovea are also round- shaped with darker part in the center. Retinal blood vessels radiate from the center of the optic disc in two major directions, up and down. The OD can be located right or left, subjected to the photography of the left or of the right eye. As you can see in the Fig. 1(a), peripheral parts of the fundus photography are lighter, because of the globe-shape of retina. On closer parts of the eye-ball to the camera, there falls more flash light than on the more distant ones.

1.1 Diabetic retinopathy and eye fundus

Diabetic retinopathy (DR) is the major cause of the blindness in western countries [2]. DR is progressive disease. Patient with diabetes mellitus firstly does not have any signs of DR. Later non-proliferative DR (NPDR) is developed and in the last phase proliferative DR (PDR) and its complications occur. Some authors still describe preproliferative DR (PPDR), which might be the stage between NPDR and PDR.

NPDR is characterized by creation of microaneurysms, dilatations of the retinal veins and hard exudates Fig. 1(b) [3]. Microaneurysms are dilated parts of small blood vessels. On the fundus we can see them as small red dots. Their red color is almost the same as blood vessels red color. Hard exudates are composed of lipoprotein and cells and are caused by chronic localized retinal edema. We can see them on the fundus as yellow spots, which are sharply demarked and can have different shapes. They are mostly well visible, but the intensity of image pixels in hard exudates is similar to intensity of pixels in the optic disc. Venous dilatation can be seen as a change of the continuance of the veins, the dilated part of the vein is thicker than the other parts. In advanced disease we can find cotton wool spots (older name is soft exudates), which are whitish fluffy not so sharply demarked lesions caused by leakage from the blood vessels. Hard and soft exudates together with drusen can be called "bright lesions" due to their bright color.

In the case of proliferative diabetic retinopathy (PDR), Fig. 1(c), we can find all findings as in NPDR and neovascularisation and/or hemorrhage can be observed. Neovascularisation means creation of new blood vessels, which are deficient and therefore they can bleed easily. They can be located on the optic disc or elsewhere on the fundus and we can find them also on the iris. Bleeding in or on the retina is severe and we can see it as a huge red colored fields, especially near to the blood vessels.

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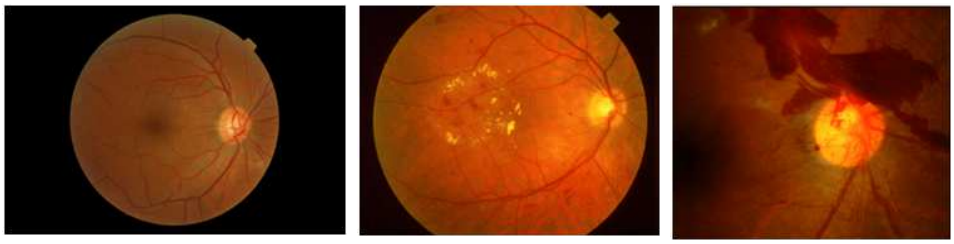


(a) (b) (c)

Fig. 1. Healthy fundus of the human eye (a), examples of NPDR (b) and PDR (c)

1.2 Fundus Images Automatic Diagnostic

In general, there are two types of fundus images automatic diagnostic. The first one is the global diagnostic, which means we want to know whether the patient suffers from specified diagnosis or not. The second one, more sophisticated, is to find specific findings right in images. We are focused on the first type of automatic diagnostic. We developed algorithm as a part of a screening tool of diabetic retinopathy. In this work, we aimed our effort to detection and localization of areas in the image which we can call "bright lesions". As bright lesions we can mark whitish or yellowish colored findings which are not found on retinal fundus of a healthy person. Their size, shape, sharpness and intensity could differ. We can mark drusen, soft and hard exudates as "bright lesions", but we are interested only in soft and hard exudates as possible signs of diabetic retinopathy. We can assume several different diagnoses upon the bright lesions findings.

In the preprocessing step, it is necessary to unmask several segments in fundus images for simpler bright lesions detection. The brightest spot of fundus image is optic disc (OD). This yellow ring area is undesired in this diagnostic process because of its brightness value which is very close to the bright lesions brightness. Optic disc localization can be done by different approaches and methods. In [4], authors used Gabor filters and phasing images to localize OD. The other approach was chosen by T. Kauppi [1], whose method is based on color de-correlation templates with PCA. Morphological operations can be also used to localize OD. In [5], authors used morphological operations to find center of OD and Hough transform to find its boundaries. For OD localization, we apply own approach which uses morphological operations and contrast adjustment based on [6].

In preprocessed images exudates can be localized. Walter *et al* [7] found exudates within the macular region using their high grey level variation and their contours by means of morphological reconstruction techniques using two threshold parameters. They worked in HSL color space and obtained mean sensitivity of 92.8 % and mean predictive value of 92.4 %. As a first step, they removed vessels and then they used local standard deviation to find candidates. The last step was finding candidates boundaries using morphological reconstruction. Other possible solution is to use median filter, process image block by block and then subtract the processed image from the original one. Hann *et al* [8] created algorithms using specific color channels and segmentation methods to separate diabetic retinopathy features with exudates identification 96.7 % sensitivity and 94.9 % specificity. They removed the optic disc and computed median. García *et al* [9] used combination of local and global thresholding to recognize exudates. They used also means of logistic regression (LR), radial basis function (RBF) neural network and post processing techniques. Their mean sensitivity was 92.1 % and mean positive predictive value 86.4 % in lesion-based criterion (pixel resolution). We applied the method of local and global thresholding to localize bright lesions.

In all described works, the specialist manually marked all bright lesions in the images for testing the method efficiency. Authors do not specify if the specialist marked these lesions pixel by pixel electronically with zooming (hand-labeled by computer's mouse), or if he marked them in the printed paper which could not be zoomed (hand-labeled with pen or pencil). Our specialist marked bright lesions pixel by pixel electronically with large zooming. The accuracy of marking bright lesions and the way of determination, whether the algorithm selected a lesion correctly or not can play crucial role in the process of results evaluation.

We had to find selected features of the region of interest and we assigned the image to the correct class according to the features. Features of localized bright lesions candidates were used as the input to the neural network classifier. We used 16 features and determined their parameters according to García *et al* in [9].

We classified found candidates described by 16 features using MLP neural network. The results of feature classification are presented.

2 BRIGHT LESIONS DETERMINATION

2.1 Fundus Images Preprocessing

Image preprocessing module has the role of luminance normalization, contrast enhancement and optic disk masking.

When we talk about medical images classification, we can find diverse images, which have the same common semantic features, but they are not exactly the same. This is the reason why it is relatively easy task for human with adequate education to determine the right diagnosis of

two differently colored images, but it comes more difficult for machine learning system without supervision. Because of that, all images are preprocessed in order to eliminate differences in color and brightness among them. Complete process of fundus image preprocessing is shown in Fig. 2.

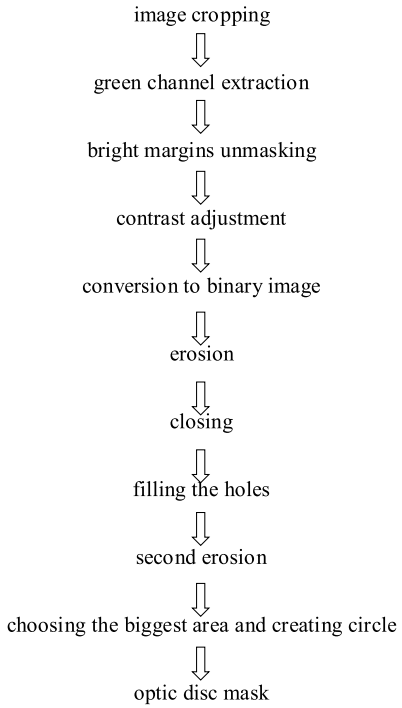


Fig. 2. The block diagram of preprocessing and optic disc masking

2.2 Localization of Bright Lesion Candidates and Feature Extraction

Feature extraction module includes two stages: (i) bright lesions candidates localization, followed by (ii) features extraction from localized candidates.

Bright lesions candidates localization — the main problem in bright lesions localization is that the brightness around the main vessels in the image is very close to the brightness of lesions. Application of basic thresholding results in finding many false positive candidates, mainly around the vessels.

We have created the optic disc mask before bright lesions localization was started, so we have been able to unmask the biggest bright area. We used the combination of global and local thresholding to obtain the candidates for bright lesions. Threshold was set to value, where histogram decreased to 10 % of the maximum. As a result of global thresholding we obtained the binary image. The local thresholding was applied on grey scaled image blocks of 100×100 px. The dimensions of one block were determined by several experiments and observations. Locally and globally thresholded images were combined by AND operation to gain only bright areas of image. Finally, the areas smaller than 2 px were removed as unimportant, because we worked with images in high resolution. To smooth the margins and connect the small gaps between areas, the closing operation with disc structural element of 10 px radius was applied. The procedure for a detection of bright lesions is based on [6] and [12]. The bright lesions localization is followed by features extraction and classification. The process of the detection of bright lesions is described in Fig. 3.

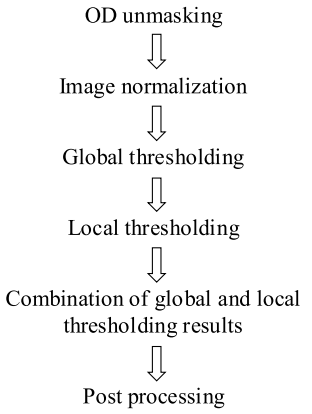


Fig. 3. The process of bright lesions localization

Feature extraction from candidates — it is necessary to extract several features from bright lesions candidates to be able to use neural network classifier effectively. Candidates for bright lesions had been used as a mask for areas which can possibly be the bright lesions. We obtained features from red, green and blue channel of image. Our feature selection was inspired by [9] and we have selected 16 different features:

1. μ_R	5. μ_G	9. μ_B	13. a
2. σ_R	6. σ_G	10. σ_B	14. $Ecct$
3. C_R	7. C_G	11. C_B	15. P_Ω
4. H_R	8. H_G	12. H_B	16. C

Features μ, σ, C and H have indices R, G, B that correspond to color channels used for computation. The color of region is one of the most significant features, furthermore the shape is also important, since hard exudates have sharp margins and soft exudates have soft margins.

We use features definitions as follows:

Region size a is the sum of pixels inside the bright lesion candidate region Ω.

RGB mean values and standard deviations features were defined for all three channels of the RGB color image where Ω is the related region of pixels and a is the region size

$$\mu_R = \frac{\sum_{j\in\Omega} R(j)}{a}\,,\ \mu_G = \frac{\sum_{j\in\Omega} G(j)}{a}\,,\ \mu_B = \frac{\sum_{j\in\Omega} B(j)}{a}\,, \tag{1}$$

$$\sigma_R = \frac{\sqrt{\sum_{j\in\Omega}(R(j)-\mu_R)^2}}{a}\,,\quad \sigma_G = \frac{\sqrt{\sum_{j\in\Omega}(G(j)-\mu_G)^2}}{a}\,,\quad \sigma_B = \frac{\sqrt{\sum_{j\in\Omega}(B(j)-\mu_B)^2}}{a}\,, \tag{2}$$

RGB values of the region center. It is the value of intensity of the pixel in the center of the bright lesion candidate region.

Homogeneity of the region. Entropy as the measure of the amount of information describes the uncertainty of single color level occurrence in the region. Entropy symbolizes statistical measure of randomness which can be used to describe the image texture. It can be interpreted as homogeneity measure. It is calculated for each color channel

$$\begin{aligned} H_R &= -\sum_{i=0}^{L_R-1} P(b_{Ri}) \ln\left[P(b_{Ri})\right], \\ H_G &= -\sum_{i=0}^{L_G-1} P(b_{Gi}) \ln\left[P(b_{Gi})\right], \\ H_B &= -\sum_{i=0}^{L_B-1} P(b_{Bi}) \ln\left[P(b_{Bi})\right], \end{aligned} \tag{3}$$

where L_R, L_G, L_B are numbers of R, G and B levels inside the region, respectively, and $P(b_{Ri})$, $P(b_{Gi})$, $P(b_{Bi})$ are probabilities of levels inside the region

$$\begin{aligned} P(b_{Ri}) &= \frac{N(b_{Ri})}{a},\ j = 0, \ldots, L_R - 1, \\ P(b_{Gi}) &= \frac{N(b_{Gi})}{a},\ j = 0, \ldots, L_G - 1, \\ P(b_{Bi}) &= \frac{N(b_{Bi})}{a},\ j = 0, \ldots, L_B - 1, \end{aligned} \tag{4}$$

$N(b_{Ri})$, $N(b_{Gi})$, $N(b_{Bi})$, are numbers of pixels in the region with intensity equal to single R_i,,G_i, B_i levels b_{Ri}, b_{Gi}, b_{Bi}, for red, green and blue color channels, respectively.

Eccentricity of the region, $Ecct$, is the scalar which defines eccentricity of the ellipse with the same second moment of the region.

Perimeter of the region is P_Ω, which is scalar.

Region compactness C describes a region in a term of the region edge smoothness. Perimeter of the region P_Ω, included in the above equation is $C = \frac{P_\Omega^2}{a}$. Mentioned 16 features were extracted from each bright lesion candidate localized in previous step.

2.3 Neural network classification

We used neural network — multilayer perceptron (MLP) [13] classifier to identify real bright lesions. Network classification is based on 16 features described in Part 2.2 of this article. Candidates are classified into two classes: (i) Candidate is bright lesion, (ii) Candidate is not bright lesion.

We used multilayer perceptron with one hidden layer, which had 16 inputs, 10 neurons in hidden layer and 2 output neurons. Network was trained using scaled conjugate gradient. As a result of classification, we obtained marked image with green colored bright lesions (soft and hard exudates together).

3 EXPERIMENTAL PART

3.1 Image database

We used fundus images from Messidor database. The Messidor fundus images database was created as a part of TECHNO-VISION project which was donated by French government in 2004. It contains 1200 color fundus images gained by 3CCD fundus camera Topcon TRC NW6 with 45° visual field from three ophthalmologic departments. The images are of 8 bits color depth and 1440×960, 2240×1488, 2304×1536 resolutions [10].

3.2 Marking Images by an Ophthalmologist

Bright lesions in fundus images were marked pixel-by-pixel by our ophthalmologist. It was allowed to use zooming tool to distinguish also small features, as during standard fundus examination on the slit lamp. The doctor marked (with computer mouse) hard exudates with 100% green color and soft exudates (cotton wool spots) with 100% blue color manually. The marking tool was variable pixel sized pencil tool.

3.3 Multilayer Perceptron Classifier

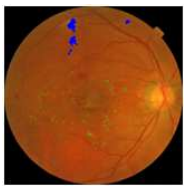
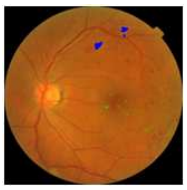
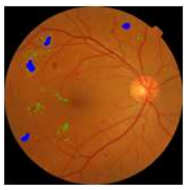
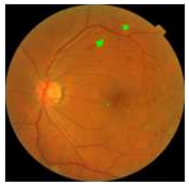
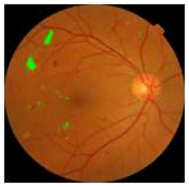
Testing and results — system was tested on 8 images, which were marked by the doctor (the ophtalmologist). As a first step we divided these 8 images into 2 sets of 5 and 3 images. The first set of 5 images was used as a training set and the second set of 3 images one was for testing. It means that network was trained and tested on completely different (disjunctive) sets of images. As a programming tool, we used MATLAB [11].

Network training — training set which contains 3562 candidates for bright lesions, was divided randomly into the following 3 subsets: training set (70%), testing set (15%), and validation set (15%). Table 1 shows classification results for individual data sets. Results are evaluated by means of classification accuracy that expresses percentage of samples that were classified by neural network correctly.

Table 1. Classification results

Data set	Number of bright lesions in set	Classification accuracy (%)
Training set	2138	90.97 %
Test set	712	91.01 %
Validation set	712	89.33 %

Table 2. Neural network testing results: A – fundus image marked by doctor, B – fundus image marked by neural network, C – number of candidates, D – neural network classification accuracy, E – number of bright lesions marked by doctor compared to bright lesions marked by neural network (in percent). In A, green color means hard exudates, blue color means soft exudates. In B, all bright lesions are marked with green color.

	1	2	3
A			
B			
C	1365	461	1156
D	93.11%	95.01%	93.43%
E	60.00%	45.45%	49.46%

Network testing — we tested our neural network on set of 3 test images. We compared results of bright lesions classification obtained by our proposed method to bright lesions marked by the doctor.

When bright lesion detected by our neural network overlaps the lesion manually marked by the doctor at least in one pixel, such situation is considered as the match. It means that size of a bright lesion is not taken into account. Obtained results and marked images are shown in Tab. 2.

From Tab. 2 we can see that in three test images not included in the training set our proposed method is able to find 93.85 % real lesions from the set of all candidates.

This means that the neural network system for classification of candidates is powerful enough to find sufficient number of lesions. On the contrary, if we take into account number of candidates found in bright lesions localization step and compare them to bright lesions marked by doctor, the classification accuracy on three test images is 51.64 % on average. This comparison clearly leads to the need of more efficient bright lesions localization procedure. Nevertheless even in this stage of research this method can be used as the part of the ophthalmology screening program. Such program helps the doctor to extract and focus on possible diabetic retinopathy patients.

4 DISCUSSION

Proposed neural network classifier achieves good results; therefore we conclude that we can find more real bright lesions by raising the number of right candidates for bright lesions.

It should be noted that data gained from doctor were very precise. To obtain this marked data, the doctor had to enlarge the picture on a computer, because the standard fundus examination on a slit lamp is made by using the magnification lens with which also many very small bright lesions are visible.

In some cases the algorithm marked some objects which were not bright lesions. This could be caused by inappropriate OD mask, which does not cover the whole OD area. This failure could be resolved by increasing and customizing OD mask size. It is also difficult to distinguish between bright areas around vessels from bright lesions especially in young individuals, where these bright-looking areas could be physiologic or they could be artifacts because of nerve fibers reflectivity along blood vessels.

More objective results could be achieved by evaluating number of found pixels in all lesions instead of just number of bright lesions. As already mentioned, presented classification results were based on any overlapping of objects found by neural network and doctor (even one pixel overlapping was taken into account). For further work, we plan to work with number of pixels. It means, classification accuracy will be derived from the ratio of number of pixels in bright lesions chosen by the computer to number of pixels inside bright lesions marked by the doctor. This way of measuring could be more significant for medical practice because larger areas should mean more severe impairment of the retina.

5 CONCLUSION

In this work we presented proposal and implementation of a method for bright lesion detection and localization in fundus images using morphological operations and thresholding. The image contrast and illumination were normalized by the adaptive histogram equalization as a part of bright lesions extraction process. The candidates were found by combination of local and global thresholding. In order to classify bright lesions we extracted 16 features and use multilayer neural network classifier. Proposed system was tested on 3 testing images where we are able to find 93.85 % real lesions from the set of all candidates and we achieved 51.63 % accuracy from all manually marked bright lesions. More objective results can be achieved by computing percentage from number of pixels contained in bright lesions instead of number of bright lesions. This will be also a part of our future work.

At this stage the proposed method offers promising results in neural network classification. Multilayer perceptron is able to reach 93.85 % accuracy on average.

The proposed system needs some improvements in stage of finding candidates for bright lesions. We still work on removing blood vessels from the image before localization of candidates for bright lesions. It should improve candidates localization efficiency. We also plan to optimize the feature extraction stage by applying new features. Another improvement could be achieved using more sophisticated methods for illumination and contrast enhancement [7].

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References

[1] KAUPPI, T.: Eye Fundus Image Analysis for Automatic Detection of Diabetic Retinopathy, Thesis for the degree of Doctor of Science, Acta Universitatis Lappeenrantaensis 414, Nov 2010.

[2] ONG, G. L.—RIPLEY, L. G.—NEWSOM, R. S.—COOPER, M.—CASSWELL, A. G.: Screening for Sight-Threatening Diabetic Retinopathy: Comparison of Fundus Photography with Automated Color Contrast Threshold Test, Am. J. Ophthalmol. **137** No. 3 (2004), 445–452.

[3] CIULLA, T. A.—AMADOR, A. G.—ZINMAN, B.—: Diabetic Retinopathy and Diabetic Macular Edema, Diabetes Care **26** (2003), 2653–2664.

[4] RANGAYYANN, R. M.—ZHU, X.—AYRES, F. J.—ELLS, A. L.: Detection of the Optic Nerve Head in Fundus Images of the Retina with Gabor Filters and Phase Portrait Analysis, Journal of Digital Imaging **23** No. 4 (2010), 438–453.

[5] AQUINO, A.—GEGÚNDEZ-ARIAS, M. E.—MARÍN, D.: Detecting the Optic Disc Boundary in Digital Fundus Images Using Morphological, Edge Detection, and Feature Extraction Techniques, IEEE Transactions on Medical Imaging **29** No. 11 (2010), 1860–1869.

[6] BLAŠKO, R.—ORAVEC, M.—PAVLOVIČOVÁ, J.—HANÚSKOVÁ, V.—LEHOCKI, F.: Image Preprocessing for Diagnostics Support in Ophtalmology, EE časopis pre elektrotechniku a energetiku **17** (2011), 5–8. (Slovak)

[7] WALTER, T.—KLEIN, J-C.—MASSIN, P.—ERGINAY, A.: A Contribution of Image Processing to the Diagnosis of Diabetic Retinopathy-Detection of Exudates in Color Fundus Images of the Human Retina, IEEE Transactions on Medical Imaging **21** No. 10 (2002), 1236–1243.

[8] HANN, C. E.—REVIE, J. A.—HEWETT, D.—CHASE, J. G.—SHAW, G. M.: Screening for Diabetic Retinopathy Using Computer Vision and Physiological Markers, Journal of Diabetes Science and Technology **3** No. 4 (2009), 819–834.

[9] GARCÍA, M.—SÁNCHEZ, C. I.—POZA, J.—LÓPEZ, M. I.—HORNERO, R.: Detection of Hard Exudates in Retinal Images Using a Radial Basis Function Classifier, Annals of Biomedical Engineering **37** No. 7 (2009), 1448–1463.

[10] Messidor Techno-Vision Project,2008. http://messidor.crihan.fr/.

[11] The MathWorks, Inc. MATLAB Product Documentation. 2011. http://www.mathworks.com/help/techdoc/.

[12] FORACCHIA, M.—GRISAN, E.—RUGGERI, A.: Luminosity and Contrast Normalization in Retinal Images, Medical Image Analysis **9** (2004), 179–190.

[13] HAYKIN, S.: Neural Networks – A Comprehensive Foundation, Macmillan College Publishing Company, New York, 1994.

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