Automatic Segmentation of Corneal Endothelium Images with Convolutional Neural Network

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Abstract. A fully-automatic segmentation of corneal endothelial images is addressed in this paper. It can find its application in the medicine removing the burden of manual annotations from the physicians allowing for faster patient diagnosis. The proposed system is based on pretrained convolutional neural network AlexNet and uses a transfer learning methodology to build a system for delineation of endothelial cells. The training is based on the classification of small patches of an image which represents cell body or cell border class. The validation set proved that 99% correct classification ratio accuracy and F1 score were achieved. Exploiting this network in a system configured for segmentation it proved very good detection of cell bodies and supported by best-fit skeletonization allowed to locate cell borders precisely.

Keywords: corneal endothelium images, convolutional neural network, segmentation, classification

1 Introduction

Vision is very important part of our life. Most of the people cannot imagine how they could exist without a possibility to observe its surrounding. While the younger generation seems to be addicted from modern devices, which all are based on the exploitation of this sense. The development of technical devices, which weary our sight, is also sought as one of the factor causing a higher number of eye defects. Those can be corrected using glasses (or more popular contact lenses) or with surgeries.

The application of lenses, surgeries performed on the eye influence a corneal endothelium, which is responsible for keeping the cornea clear by draining the water from it [1]. It is just one layer of cells of hexagonal shapes, which do not reproduce [11], therefore any damage diminishes the number of cells. When its density drops below 1000 $cells/mm^2$ the cornea has no longer the possibility to dehydrate and the endothelial insufficiency occurs [7].

The state of the corneal endothelium can be observed in vivo by specular microscopy. In a medical application, the state is usually recorded before and after any treatment. The comparison of changes in the number of cells, its shape,

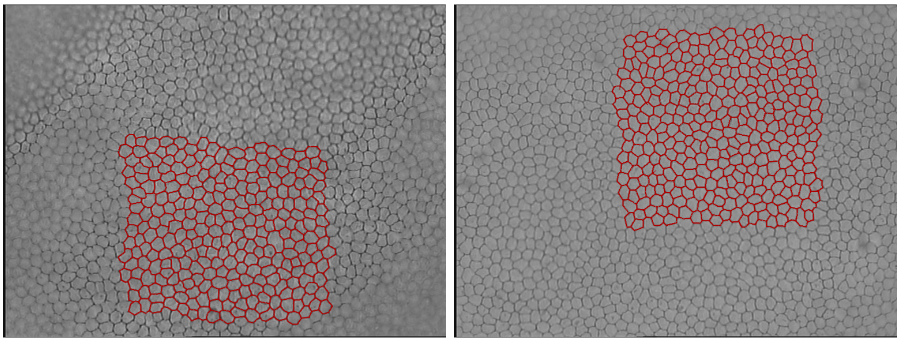


Fig. 1. Example of endothelial layer images with manually annotated cells in red color.

and distribution in the corneal endothelial layer make a foundation for a medical diagnosis. The manual annotation of the images (see Fig. 1) however is not difficult, is very tiresome and time-consuming, therefore from a long time a fully-automated solution for exact cell delineation is searched. As a response to the described needs, the paper presents a system, which enables fully-automatic annotation of data.

In the literature, a problem of automatic segmentation of cells on the images presenting endothelial layer has been addressed for three decades, yet it still remains unsolved. First approaches were simple and concentrated on noise removal followed with thresholding [12] or watershed methods [19]. Later, the solutions become more complex where various stages of image processing were distinguished: preprocessing for noise removal, cell border segmentation, and final thinning. In case of the second stage, several approaches were investigated. For instance, [5] used a Bayesian framework to detect cell borders using the assumption of its hexagonal shape, [2, 3] applied balloon snakes for cell detection, while [9] exploited wavelets. On the other hand, the local sign calculation and statistical dominance algorithm [13] were introduced to deal with this problem. An artificial neural network was applied to classify each pixel, whether it represents a boundary or not [4, 17], while other suggested application of genetic algorithms for precise cell border segmentation [16]. However, many of this approaches seem to be very exact (see the comparison [15]), those performing the most accurately are semi-automatic.

This study addresses the problem of fully-automatic segmentation of endothelial images. We propose an application of convolutional neural networks, yet unlike the ideas presented in [8] a transfer learning for AlexNet [10] is suggested as the methodology. The details of experiment preparation are given in Section 2. Section 3 presents results of performed experiments. Finally, Sec. 4 concludes the work.

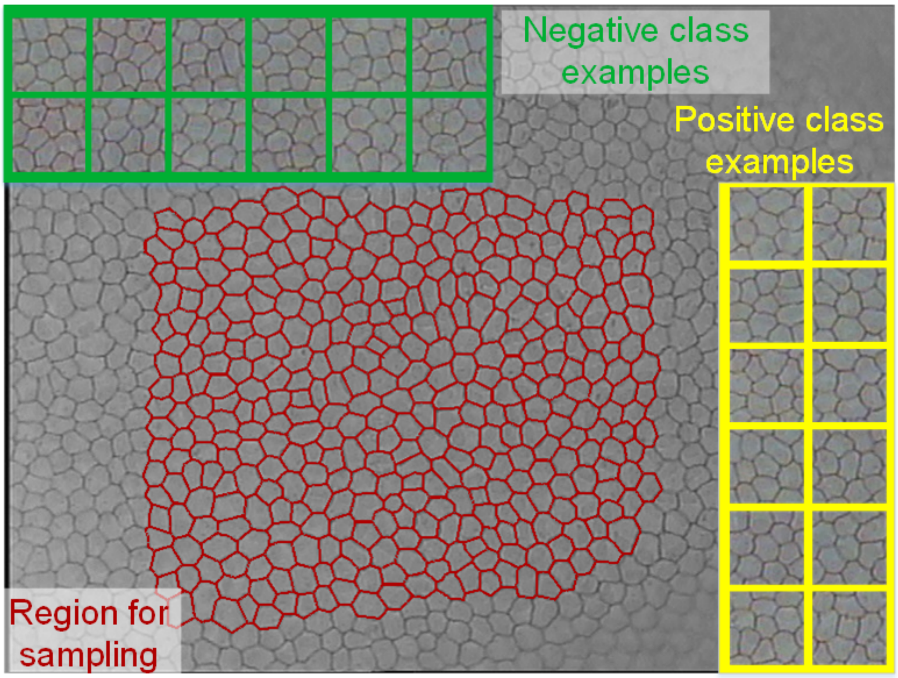


Fig. 2. Visualization of data sampling for training the convolutional neural network. The data was sampled inside the region denoted by manual annotation (red color). Yellow box collects examples presenting the cell body, while green box presents examples of cell border images.

2 Image Segmentation Approach

The idea of the system performing fully automatic localization of cell borders in the images of corneal endothelium assumes verification whether each pixel of the image represents the border or cell body. This information is achieved by classification of image patches with a convolutional neural network (CNN). The details of system preparation are presented below.

2.1 Database

The experimental dataset consists of 30 images presenting a corneal endothelium, which was taken from porcine eyes stained with alizarine. It should be pointed out, that the cell shape does not differ between this data and human corneal endothelium. The inverse phase contrast microscope (CK 40, Olympus) with 200× magnification and an analog camera (SSCDC50AP, Sony) were used for data acquisition [17]. The images are monochromatic with resolution 768×576 and were saved in JPEG format. They show a good contrast in the focus area and blurring on the edges. The manual segmentation was performed for this image part, which has good quality. In result, there are from 188 to 388 cells detected within images, with the average of 232. The cell average area is 272.76 pixels. Fig. 1 shows an example of the original image and the ground truth segmentation. This dataset is available at `http://bioimlab.dei.unipd.it`.

2.2 Data preprocessing

The training of CNN demands a large number of samples representative for cell body and border separately. In order to fulfill this constraint, the original images from the dataset were divided into smaller patches representing each class, which dimension was 64×64. The ground truth segmentation masks were exploited to generate appropriate training samples as depicted in Fig. 2. For cell body class (yellow color), the centroid of each cell was computed and its coefficients were taken as a middle of the patch which has been selected to train the system. Hence we had as many samples as there were cells detected in the original dataset. The patches created to describe border randomly chose points laying on the borders selected manually and used them as the central point of a patch representative for a border (green). In result, there were around 10 000 of images prepared for each class.

Since the image quality varies spatially, three approaches to work with the data were investigated. The network was fed with:

- original data;
- enhanced data where histogram stretching was applied – that aimed in better border visualization by contrast improvement;
- blurred data with a Gaussian filter – that deteriorated the training data in order to better correspond to this part of images, where the contrast is lower.

2.3 Convolutional Neural Network

The CNN is a type of an artificial neural network which learns patterns from data using also the information about its spatial extent. This network represents the deep neural network paradigm, where the more layers, the better performance can be achieved. There are several types of neural layers which can be a part of such network. Its choice, parameters, and order correspond to final efficacy.

Each convolutional layer consists of a set of filters, which weights are trained automatically in the process of learning. Each filter generates an activation map which is later processed by a non-linear layer; usually, it is the ReLU (Rectifier Linear Unit). Next, the pooling layer is used to choose the most important data and if necessary the spatial dimension of data is reduced. This process is repeated several times before the fully connected layer or other layers (eg. softmax) for final data analysis and generation of class probability are applied.

Designing own network is a very complex task, as there are many parameters influencing the final performance. On the other hand, the number of prepared data, although seem large, still is rather small when talking about deep learning. Therefore, in presented research, it was decided to exploit already trained network (in our case it is the AlexNet [10]) and use the transfer learning methodology to train it.

The AlexNet is a CNN which consists of 5 convolutional layers which are followed by three fully connected layers. It accepts colorful images of 227×227 resolution as an input. Since the prepared samples are smaller it was decided to create an empty image and paste the data in the top right corner of the first channel. Moreover, originally this network is prepared for classification between 1000 classes, hence the last layer was also changed to return only two responses.

The network was trained using 90% of prepared data, the rest was used for validation. The best scores were obtained for learning rate equal to 0.001, the mini-batch size was set to 64, and the network run 20 epochs. When the network was applied for segmentation, the input images were analyzed pixel by pixel, sending the 64×64 neighborhood for classification. The authors are aware that this is not a very optimal solution, as each pixel in the input is analyzed 4096 times and probably much better time performance would be achieved using a semantic neural network. Yet due to the lack of a large amount of data, it was decided that this approach, however not free from defects allows verifying whether it is at all reasonable to use deep learning for the problem of corneal endothelium segmentation.

2.4 Data postprocessing

The borders segmented with an application of CNN are thick, therefore further processing is necessary. As presented in [15] it is not a trivial problem and standard skeletonization approaches are not satisfactory. Recently a Best-Fit (BF) method has been introduced [14] for automatic delineation of binary images. It proved to be very accurate so it is exploited for final cell border location.

3 Results

In this section, the results of performed experiments are presented. Firstly, the general classification performance recorded for the validation set is given. It is calculated with accuracy and F1 score, which is given by the formula:

$$F1 = 2 \cdot \frac{precision \cdot recall}{precision + recall}, \tag{1}$$

$$precision = \frac{TP}{TP + FP}, \tag{2}$$

$$recall = \frac{TP}{TP + FN}, \tag{3}$$

where TP stands for true positive, FP for false positive, and FN false negative. Next, experiments concerning the segmentation problem are addressed.

Table 1. Verification of correct classification ratio of the CNN networks trained for segmentation.

CNN Input	F1 Score [%]	Accuracy [%]
Original	99.19	99.18
Contrast enhancement	99.00	98.99
Blurred	99.29	99.28

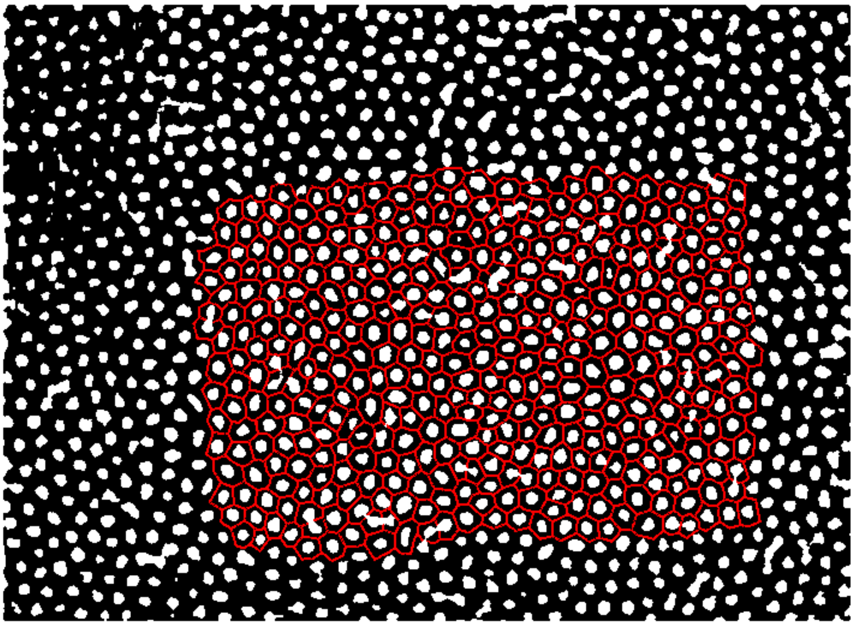
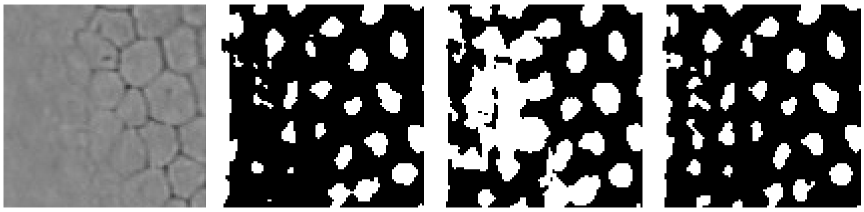


Fig. 3. Images segmented with CNN trained with original images. White color denotes cell centers and black stands for cell boundaries. For better visualization an original mask is marked with red color.

3.1 Cell Body vs. Cell Border Classification

Before the segmentation can take place, the CNN network accuracy was verified. Table 1 collects achieved results for three presented approaches of data training, which were validated on 10% of the original dataset. In all cases, the correct recognition between classes is very high and reaches around 99% accuracy with the F1 score is above 99%. This almost perfect classification ratio should also be visible in the segmentation process.



(a) Original (b) CNN for orginal (c) CNN for enhanced (d) CNN for Blurred

Fig. 4. Visualization of segmentation problems when the input is blurred. the exemplary image is half blurred (left) and with good contrast (right). Cases b-d show segmentation performance for CNN trained with original, enhanced, and blurred images respectively.

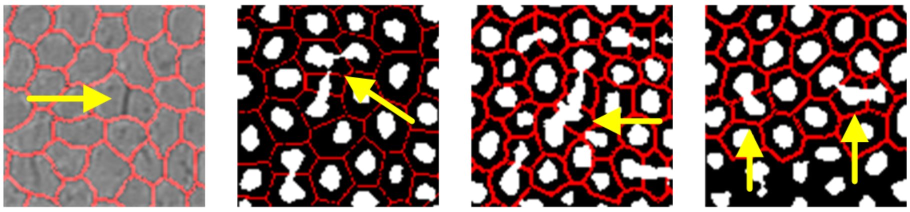


Fig. 5. Examples of merged cell bodies. On the left in original data and as a result of automatic segmentation.

3.2 Image Segmentation with CNN

The automatic segmentation results for CNN trained with the original images are depicted in Fig. 3. For all images transformed with CNN a median filter with mask 3×3 was applied to smooth the outcome and remove outliers. The white spots correspond to regions classified as the cell bodies, while the black color refers to cell border class. Additionally, the originally segmented cell borders are denoted with red color. As it is seen, the proposed methodology enabled very good segmentation of the image. The cell centers overlap well with manual annotations. Of course, this region of the image was also used for training, so very good results are sought. Yet, one can also see that this segmentation works very well on the whole image, which was unknown data for the system. Similar performance is observable for networks trained with enhanced or blurred images.

Although many cell bodies ware segmented correctly, a few problems were noticed. First of all, this approach did not work well for data of very low contrast. Figure 4 presents an image patch where the contrast changes from left to right (from very low to good one) and segmentation results achieved by all suggested networks. The CNN fed with original data seems to have a problem with correct detection of cells in blurred regions, better outcomes are noticeable when data

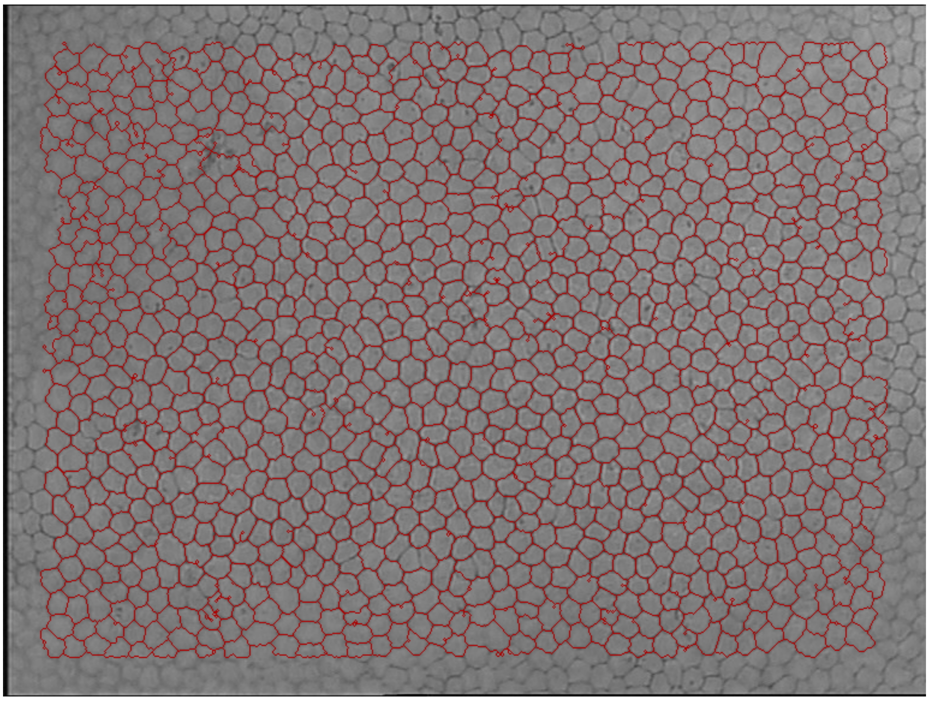


Fig. 6. Cell borders obtained with a Best-Fit approach.

is smoothed before classification. The worst case is when the enhanced approach for image preprocessing is used. This result is not surprising since in the training only data of good contrast was applied. Therefore, in case of image enhancement approach, the CNN was trained with nice borders, which does not exist in the patches prepared from data of very blurred origin. On the other hand, using smoothed images in learning process made the system prone to such problems in real world and therefore the results are outperforming others in this case. Moreover, it can be noticed that when the input data is blurred the cell bodies are getting smaller or even disappear in segmentation.

Another issue which needs further addressing is merged cell bodies. One can easily spot cell bodies which overlap through adjoining cells (see examples in Fig. 5), yet it is a rare problem. Moreover, similar issue occurred in the manual segmentation, too.

Next, the obtained segmentation is not sufficient for medical analysis and further thinning of the cell border is necessary. In the presented approach the BF method was exploited, and the obtained outcome is presented in Fig. 6. The last visualization proves that it is possible to automatically segment endothelial image with very high accuracy. While in Fig. 7 a comparison between the cell borders obtained by presented fully automatic approach (green color) and those manually localized (pink color) is depicted. The black color of contour corre-

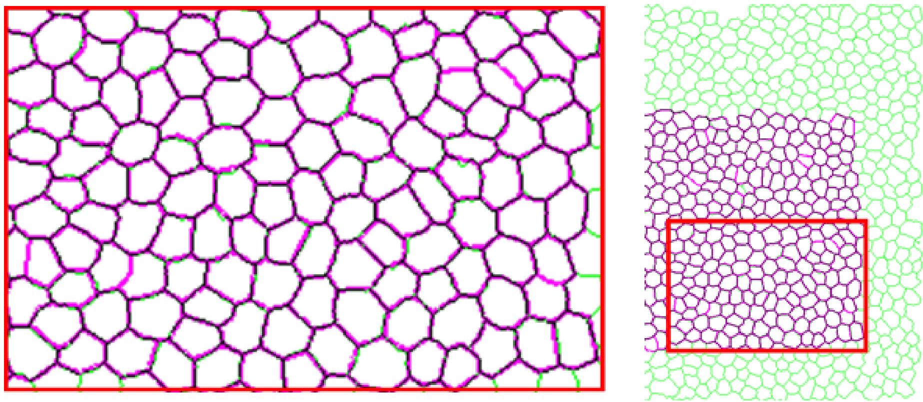


Fig. 7. Repeatability in cell border detection. On the right the half of the original image, while on the left zoomed region marked by rectangle. Black line depicts overlapping borders between the original masks and automatically computed. Pink color corresponds to original borders which were not detected, green is for automatically detected borders.

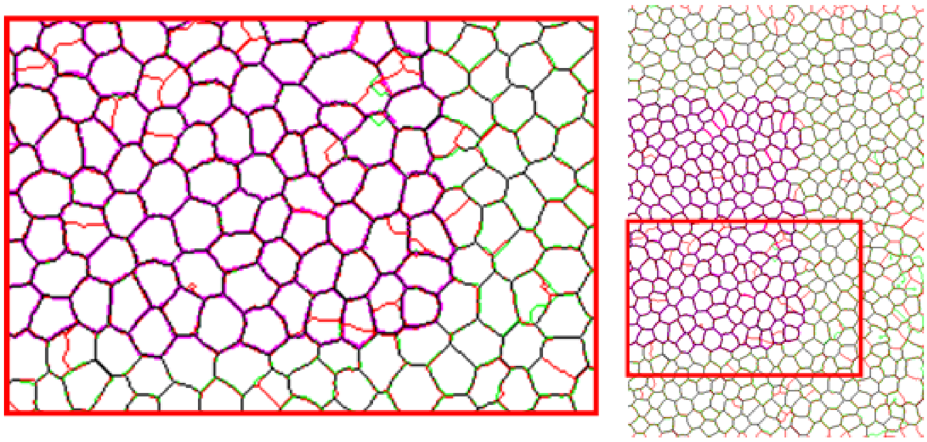


Fig. 8. Repeatability in cell border detection. On the right the half of the original image, while on the left zoomed region marked by rectangle. Black line depicts overlapping borders between the original masks, presented solution, and KH method. Pink color corresponds to original borders which were not detected, green is for presented method, while red shows the KH performance.

sponds to overlapping solutions delivered by the ground truth and automatic solution. As it is presented, the borders annotated automatically cover those prepared manually.

Finally, the achieved segmentation is compared with other (KH) automatic approach described in [6]. Figure 8 similarly as the previous one, presents on one image, the manually annotated mask in pink colour, use green to show the delineation generated by proposed approach and red colour for the KH method. In case all methods overlap the black colour is used. As one can see, the proposed system is more accurate moreover no over-segmentation is introduced.

4 Conclusions

This work addresses the problem of fully-automatic segmentation of corneal endothelial images. It is suggested to exploit already existing convolutional neural network (the AlexNet) and train it using the transfer learning approach. For training small patches of the original image, or its enhanced version, or blurred one are used. The validation of this three network proved in all cases 99% of accuracy. In case of segmentation very good results were achieved for all of them. Yet in case of regions with very low contrast, better performance was noticed for networks using blurred or original input. Application of Best-Fit algorithm allowed for precise skeletonization of segmented cell borders.

In further work, the design of CNN tailored for this problem seems necessary in order to reduce the computational overload existing in these regions of AlexNet weights which are not used due to a smaller size of training patches. Our methodology might be applied to color images by simply exploiting the luminance component obtained using a color space transform [18] or extended by incorporating additional color features like hue. Next, removal of the post-processing step by more precise border segmentation is sought. It is also considered to use class prediction value instead of binary classification outcomes to improve the border segmentation.

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