G Model
ARTMED-1587; No. of Pages 13

ARTICLE IN PRESS

Artificial Intelligence in Medicine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Artificial Intelligence in Medicine

journal homepage: www.elsevier.com/locate/aiim

Segmentation of corneal endothelium images using a U-Net-based convolutional neural network

Anna Fabijańska

Institute of Applied Computer Science, Lodz University of Technology, 18/22 Stefanowskiego Str., 90-924 Lodz, Poland

ARTICLE INFO

Article history:
Received 23 January 2018
Received in revised form 5 April 2018
Accepted 10 April 2018

MSC:
68-U10
68-T10
68-T45

Keywords:
Corneal endothelial cells
Image segmentation
Convolutional neural network
U-Net

ABSTRACT

Diagnostic information regarding the health status of the corneal endothelium may be obtained by analyzing the size and the shape of the endothelial cells in specular microscopy images. Prior to the analysis, the endothelial cells need to be extracted from the image. Up to today, this has been performed manually or semi-automatically. Several approaches to automatic segmentation of endothelial cells exist; however, none of them is perfect. Therefore this paper proposes to perform cell segmentation using a U-Net-based convolutional neural network. Particularly, the network is trained to discriminate pixels located at the borders between cells. The edge probability map outputted by the network is next binarized and skeletonized in order to obtain one-pixel wide edges. The proposed solution was tested on a dataset consisting of 30 corneal endothelial images presenting cells of different sizes, achieving an AUROC level of 0.92. The resulting DICE is on average equal to 0.86, which is a good result, regarding the thickness of the compared edges. The corresponding mean absolute percentage error of cell number is at the level of 4.5% which confirms the high accuracy of the proposed approach. The resulting cell edges are well aligned to the ground truths and require a limited number of manual corrections. This also results in accurate values of the cell morphometric parameters. The corresponding errors range from 5.2% for endothelial cell density, through 6.2% for cell hexagonality to 11.93% for the coefficient of variation of the cell size.

1. Introduction

One of the challenges in recent ophthalmology is the development of methods for the automatic assessment of the corneal endothelium health status. The latter manifests itself by the structure of the organization of the endothelial cells. In a healthy cornea, the size of the endothelial cells is uniform and they exhibit regular, hexagonal shapes within the overall tissue structure similar to that of honeycomb. Different pathological conditions deteriorate this regularity causing damage of some cells and a resulting unpredictable elongation, thinning and an increase in the size of the other ones. Therefore, corneal endothelium condition is assessed by means of cell morphometric parameters and geometry, including cell density, the coefficient of variation and hexagonality [4]. These parameters are calculated by analyzing cells extracted from specular microscopy images of the corneal endothelium. Manual cell extraction by an ophthalmologist is very tedious and time-consuming since it requires manual delineation of the contours of multiple cells present in a field of view. Therefore, methods for an automatic and reliable segmentation of corneal endothelial cells need to be developed.

Various algorithms for the automatic segmentation of images of the corneal endothelium have been deployed over last 25 years. The early approaches involved thresholding cell edges followed by morphological processing [3,17,24]. However, these kinds of methods were very sensitive to low contrast and uneven illumination. Therefore, they yielded reasonable results only for high quality images where the cell edges were sharp and well defined.

The other group of approaches to the segmentation of corneal endothelium images based on hexagon detection by using directional filtering followed by binarization, pixel-wise logical operations and thinning [11,16]. The missing or false cell boundaries were then edited manually.

Many authors have also tried to apply a watershed algorithm to perform cell segmentation by drawing watershed damns along the cell edges. As a result, several modifications of the method have been proposed, e.g. segmentation driven by markers like in [28], performed on a distance map [2,5,9] or in a stochastic variant as proposed in [27]. A slightly different approach was proposed in [12] where multiple balloon snakes were evolved starting from the contours of the watershed regions. However, watershed based approaches are still prone to oversegmentation. Additionally, they may either require placing the seeds manually [2] or an extensive experimentation with the empirical parameters setting [10].

E-mail address: anna.fabijanska@p.lodz.pl

https://doi.org/10.1016/j.artmed.2018.04.004
0933-3657/

Please cite this article in press as: Fabijańska A. Segmentation of corneal endothelium images using a U-Net-based convolutional neural network. Artif Intell Med (2018), https://doi.org/10.1016/j.artmed.2018.04.004

There also exist some machine learning methods based on Bayesian framework [8] and support vector machines [20]. More recently, Scarpa and Ruggeri [26] used a genetic algorithm to segment endothelial cells, while Fabijańska [7] applied a feed-forward neural network with one hidden layer. However, none of the existing approaches is perfect and the image segmentation results often require (sometimes even extensive) manual editing. The results of the image segmentation also may be influenced by a set of handcrafted features considered in the machine-learning process. Additionally, various methods often yield different cells segmentation results and thus different values of the cell morphometric parameters [19].

Existing commercial software for an automatic quantitative analysis of corneal endothelium images also has limited capabilities since, as reported by some authors [13], they yield a modest to very substantial overestimation. Therefore, even in the most recent studies, corneal endothelial cells are still being segmented manually [18]. The reason is the low quality of specular microscopy corneal endothelial images which manifests itself in an inhomogeneous illumination, low contrast and focus loss.

Keeping in mind the above-mentioned limitations of the existing approaches as well as the recent advances in machine learning this paper proposes to segment the corneal endothelial cells from the specular microscopy images using a convolutional neural network (CNN, ConvNet). ConvNets have recently demonstrated exceptional performance in various machine learning approaches, in some of these surpassing the human level [23]. They are especially good in identifying, learning and recognizing patterns. Therefore in this paper, a CNN is adapted to recognize and learn the features related to the borders of the endothelial cells and then use this knowledge to perform cells segmentation by edge delineation.

Although ConvNets have recently become popular and been more and more often used in many pattern recognition problems, their application in the field of corneal endothelium image segmentation is not common. To the best of author's knowledge, the approach proposed in this paper is one of the two works which consider segmentation of corneal endothelial cells with the use of CNN and the first one which performs patch-to-patch processing (i.e., uses the architecture with the contracting and the expanding path) instead of patch-to-pixel application (i.e., the architecture with the contacting path only) as in the other approach proposed by Katafuchi and Yoshimura [14]. The latter method has also some limitations related to the training (e.g., the length of the training and a large amount of training data required) and the patch-to-pixel application in a sliding window setup (causing a loss of information at the image borders). The approach proposed in this paper is a remedy to these drawbacks. This is achieved by applying a reduced U-Net, i.e. a CNN of the architecture based on the U-Net framework [21] but adapted to the considered application via shallowing, shrinking and network hyper-parameters setting. The learning of the network and the segmentation of the cells are performed without user interaction. Additionally, the training and prediction are applied in the patches-to-image framework, instead of the image-to-image framework used commonly in other applications of the U-Net. In the opposite to the other methods dedicated to the segmentation of corneal endothelium images, the new approach was extensively tested and assessed not only visually, but numerically as well. The comparison with the previous CNN-based method is provided and proves the superiority of the new approach. To facilitate the comparison with future methods the results on the publicity available dataset of corneal endothelium images are shown and are made available for download.[1] The assessment against the clinical objectives (i.e., by means of the parameters derived from the size and the shape of the segmented cells) was also performed and shows that the proposed approach can successfully be used in ophthalmology to assess the health status of cornea and aid the diagnosis.

The following part of this paper is structured as follows. Firstly, in Section 2 the dataset of the corneal endothelium images used in this study is described. This is followed in Section 3 by a detailed description of the proposed approach. The obtained results are presented in Section 4 and discussed in Section 5. Finally, Section 6 concludes the paper.

2. Input data

A dataset of 30 images of the corneal endothelium was used. The original specular microscopy image together with the corresponding ground truth segmentation was provided in each case. The original data was stored as 8-bit grey scale images with a spatial resolution of 152 × 388 pixels. The images presented endothelial cells of various sizes (from small to large), ranging from 27 to 191 cells within the field of view. The ground truths were binary images representing the contours of the cells drawn manually by an expert ophthalmologist. The dataset was originally provided by Gavet and Pinoli in [10].[2]

The dataset was divided into two subsets, each containing 15 images (having odd and even ID numbers respectively). The first subset was used for the training. The trained CNN was next tested on the second subset. Next, the purpose of the subsets was interchanged and the training/testing procedure was repeated based upon the new subsets. In the training procedure, the ground truth segmentations were used to train the network to recognize the cell borders.

The ground truths included in the testing set were used for the evaluation of the network performance.

3. The proposed approach

3.1. Network architecture

The architecture of the CNN used for the segmentation of the corneal endothelium images is presented in Fig. 1. It was derived from the U-Net network presented in [21]. The U-Net exhibits the encoder-decoder architecture where the encoder gradually reduces the input data spatial dimension, while the decoder gradually recovers it. As a result, it produces a pixel-wise probability map instead of classifying an input image as a whole. The U-Net in opposition to other CNN architectures does not require a huge amount of training samples and can be effectively trained with only a few images. This was also in the case of the dataset considered in this study.

Compared to the original architecture, some important modifications were introduced in the CNN used in this work. First, the network was downscaled. Particularly, the depth of the network was reduced by removing two (out of five) levels of pooling/upsampling operations with the corresponding convolutions. Additionally, the number of feature vectors at each level was halved. As a result, the number of filters varies from 32 at the input to 128 in the lowest resolution. The downscaling was performed since shallower architecture allowed to obtain equivalent results as the original U-Net, but the training became easier and its time was significantly reduced (see Section 4.2). The final number of layers and their configuration were selected via experimentation

[1] http://an-fab.kis.p.lodz.pl/cornea.

[2] Distributed under the Creative Commons Attribution License, https://creativecommons.org/licenses/by/3.0/.

Please cite this article in press as: Fabijańska A. Segmentation of corneal endothelium images using a U-Net-based convolutional neural network. Artif Intell Med (2018), https://doi.org/10.1016/j.artmed.2018.04.004