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Automated arteriole and venule classification using deep learning for retinal images from the UK Biobank cohort

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ABSTRACT

The morphometric characteristics of the retinal vasculature are associated with future risk of many systemic and vascular diseases. However, analysis of data from large population based studies is needed to help resolve uncertainties in some of these associations. This requires automated systems that extract quantitative measures of vessel morphology from large numbers of retinal images. Associations between retinal vessel morphology and disease precursors/outcomes may be similar or opposing for arterioles and venules. Therefore, the accurate detection of the vessel type is an important element in such automated systems. This paper presents a deep learning approach for the automatic classification of arterioles and venules across the entire retinal image, including vessels located at the optic disc. This comprises of a convolutional neural network whose architecture contains six learned layers: three convolutional and three fully-connected. Complex patterns are automatically learnt from the data, which avoids the use of hand crafted features. The method is developed and evaluated using 835,914 centreline pixels derived from 100 retinal images selected from the 135,867 retinal images obtained at the UK Biobank (large population-based cohort study of middle aged and older adults) baseline examination. This is a challenging dataset in respect to image quality and hence arteriole/venule classification is required to be highly robust. The method achieves a significant increase in accuracy of 8.1% when compared to the baseline method, resulting in an arteriole/venule classification accuracy of 86.97% (per pixel basis) over the entire retinal image.

1. Introduction

Inspection of the retinal blood vessels enables a direct and non-invasive view of the blood circulatory system, with images being easily captured using fundus photography. There has been considerable interest in using retinal vessel size and shape as a marker of vascular health status. The morphology of retinal vessels has been prospectively associated with cardiovascular and systemic diseases [1–4]. Associations between retinal vessel morphology and disease precursors/outcomes may be similar or opposing for arterioles and venules. For example, hypertension and atherosclerosis may have different effects in retinal arterioles and venules resulting in a decreased arteriole to venule width (AVR) [5]. Automated systems (e.g. QUARTZ [6,7] and VAMPIRE [8–10]) that extract quantitative measures of vessel morphology from large numbers of retinal images are needed to power these biomarker discovery studies, in which the automated classification of arterioles and venules is an essential element.

The appearance of arterioles and venules in retinal images are very similar. However, they can be differentiated in general using the following features as documented by Kondermann [11]:

- Arterioles are brighter than venules.
- Arterioles are thinner then neighbouring venules.
- The central reflex (the light reflex of the inner parts of the vessels) is wider in arterioles and smaller in venules.

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- Arterioles and venules usually alternate near the optic disc before branching out; that means near the optic disc one arteriole is usually next to two venules and the other way round.

There are challenges in building a robust vessel classification system. There is intra-image and inter-image variance in respect to colour, contrast and luminosity. The size and colour of vessels changes as they move away from the optic disc due to changes in levels of oxygenation. In the periphery (far away from the optic disc) vessels become so thin that are almost indistinguishable.

A number of automated methods have been reported in retinal arteriole/venule (a/v) classification. These can be divided into two broad categories; feature based and graph based methods. The majority of methods start with the segmentation of the vasculature followed by the creation of the vessel centrelines and then the removal of bifurcation and crossover points to create vessel segments. The centreline pixels are classified as arteriole or venule, and this information is then used to award the whole vessel segment as either arteriole or venule. Alternatively, some methods avoid pixel classification and make a direct decision on the a/v status of a vessel segment.

The most popular approaches are feature based methods. Kondermann [11] addressed intra-image variability by approximating the background and removing this from the image. Classification of the centreline pixels was then achieved using colour features from a square region centred on the target pixel and a neural network with one hidden layer of 40 neurons. Grisan [12] divided the image into four quadrants with the assumption that each quadrant had at least one arteriole and one venule. Within a quadrant, centreline pixels were classified using fuzzy clustering based on RGB (red, green, blue) and HSL (hue, saturation, lightness) features measured from a local circular region centred on the pixel. The use of quadrants exploited the local nature of a/v classification and thereby addressed the issue of intra and inter-image variability. Saez [13] and Vazquez [14] rotated the four quadrants in steps of 20° with the aim of fulfilling the assumption that each quadrant should contain at least one arteriole and one venule. Both performed K-means clustering based on vessel profiles and their RGB and HSL colour information. Vazquez [14] improved performance with the use of a tracking procedure to connect segments that belong to the same vessel based on finding the path of minimal cost between two points using image information.

Other feature based methods include the following. Fraz [15] avoided the computational expense of the quadrant based approach and addressed intra and inter-image variability using shade correction and image normalization. Classification of the centreline pixels was performed using the ensemble classifier of bagged decision trees and pixel based, profile based and segment based features from both RGB and HSI (hue, saturation, intensity) colour spaces. Relan [16] developed a method with a feature vector based on colour information calculated from a circular neighbour around the target pixel. Classification was performed using a Least Square Support Vector Machine, and showed that the method performed well using a small training dataset. This is the latest method to be incorporated into the VAMPIRE software [8–10]. Niemeijer [17] proposed methodology that labelled centreline pixels using a 27-D feature vector and the linear discriminant classifier. Pixel and vessel profile based features were used based on RGB and HSI colour information. Performance was improved using the prior knowledge that arterioles and venules usually come in pairs, thus an iterative approach was used to match arteriole venule pairs. Xu [18] proposed novel features for a/v classification which included first and second order texture features measured from the vessel profile and an image patch around the target pixel. A k-nearest neighbour was used for classification.

Graph based approaches make up a smaller section of the literature. Rothaus [19] and Dashtbozorg [20] used the centreline of the vasculature to produce a planar graph, in which each link corresponded to a vessel segment and the nodes represented the branches or crossings of the vessel segments. Using information on the node (e.g. number of links connected to the node, orientation of each link etc.), the node type was determined. Once all nodes on the graph had been identified then all links that belong to a particular vessel could be identified. Rothaus [19] required a few manually labelled vessel segments and then this rule based method was used to propagate vessel labels through the vascular graph. Dashtbozorg [20] separately performed a/v classification for every centreline pixel using a 30-D feature vector based on colour information and a linear discriminant analysis classifier; this was combined with the graph based labelling to achieve the final classification. Estrada [21] did not use a rule based method to determine the type of nodes of the planar graph. Instead the method took an optimization based approach where it determined the most likely set of a/v labels by efficiently searching through the space of possible a/v labelled trees. A global likelihood model that used the features of local growth, overlap and colour was used to determine the quality of each directed tree (a/v labelled tree).

There are many other notable a/v classification methods [22–25]. Existing methods can heavily rely on hand crafted features and thereby can be limited to what humans perceive as interpretable differences between arterioles and venules. Graph based approaches can struggle when sections of the vasculature cannot be segmented, resulting in unreliability when linking vessel segments. Therefore, there is scope for improvement in a/v classification.

In the past few years there has been a shift towards methods employing deep learning approaches across a variety of fields. Deep learning is a subfield of machine learning concerned with algorithms inspired by the structure and function of the brain called artificial neural networks. Deep referring to the number of layers in the network. The driving force behind deep learning is that we now have fast enough computers and large enough datasets to actually train large neural networks. Neural network results get better with more data and larger models, but in turn require more computation to train. In addition to scalability, another benefit of deep learning models is their ability to perform automatic feature extraction from raw data, also called feature learning. Automatically learning features at multiple levels of abstraction allow a system to learn complex functions mapping the input to the output directly from data, without depending completely on human-crafted features. A convolutional neural network (CNN) is a powerful deep learning technique whose architectures make the explicit assumption that the inputs are images. Since winning the ImageNet [26] competition in 2012 with AlexNet [27], CNNs have gained wide popularity in computer vision. The highest performing algorithms in the recent Kaggle competition [28], which completed in July 2015, all used CNNs to identify signs of Diabetic retinopathy in retinal images. The application of CNNs on retinal images continues to grow with multiple recent studies [29–36]. To the best of our knowledge deep learning has yet to be applied to tackle a/v classification.

In this paper, we present a convolutional neural network architecture designed for the automated classification of arterioles and venules in retinal images. Implementing deep learning enabled complex patterns to automatically be learnt from the data; thus, avoiding the use of hand crafted features. The classification was performed across the entire vasculature in the retinal images and not simply concentric areas centred on the optic disc or a limited number of pre-specified retinal vessel locations. The method has been developed and evaluated using retinal images from UK Biobank which is a large population-based cohort study. The proposed method will replace the current a/v classification method [15] in QUARTZ (QUantitative Analysis of Retinal vessel Topology and siZe) [6,7]. QUARTZ is a retinal image analysis system developed by our research group, capable of processing large numbers of retinal images and obtains quantitative measures of vessel morphology to be used in epidemiological studies [37].

2. Materials

UK Biobank [38] contains a very large retinal image repository (135,867 images from 68,549 participants at baseline examination) in a