# Distilling a Pipeline of Retinal Image Analysis Tools Into a Single CNN

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## Abstract

A convolutional neural network (CNN) was constructed to distill a pipeline of unsupervised image analysis methods for the extraction of retinal biomarkers predictive of several diseases, including diabetes. Intraclass correlation between the predictions of the CNN and the results of the pipeline showed good agreement. The distilled network is fast and sensitive to key structures in the retina and will be used for disease classifications tasks.

## 1 Introduction

Retinal fundus imaging enables detailed visualization of the microvascular structure in the retina of the human eye. Geometrical properties of the retinal vessels have been identified as potential biomarkers for a variety of diseases, (e.g. systemic diseases such as diabetes (1) , eye diseases such as diabetic retinopathy (2) and neurological diseases such as Alzheimer's (3)). Early detection might improve the outcome for these patients.

Unsupervised image analysis methods for extraction of biomarkers predictive of these diseases have been developed, related to vessel caliber (4), tortuosity (5) and bifurcation features (6). A pipeline that combines the validated algorithms has been assembled for the RetinaCheck project, a large-scale diabetes screening program in China (7). The current pipeline is computationally expensive and could benefit from advances in machine learning techniques to speed up the biomarker extraction substantially.

This paper is a proof-of-principle for the distillation of a part of the pipeline of retinal image analysis models into a single convolutional neural network (CNN). The network is used to reproduce multiple biomarkers using a straightforward hard parameter sharing multi-target learning approach. The network is fast, flexible and can be easily adapted to include the biomarkers of choice.

**Related work** Distillation is described by Hinton et al. (8). The authors show that an ensemble of networks can be distilled into a single neural network. We extend this concept for an ensemble of geometrical models. CNNs have been applied to color fundus images by Poplin et al. (9) to predict cardiovascular risk factors. Multiple targets, including age, BMI and systolic blood pressure, were predicted with a single model

## 2 Materials and methods

The color fundus images used for this research originate from the Maastricht Study,[1] an extensive observational study that focuses on the etiology, complications and comorbidities of Type 2 Diabetes

[1] https://www.demaastrichtstudie.nl/

1st Conference on Medical Imaging with Deep Learning (MIDL 2018), Amsterdam, The Netherlands.

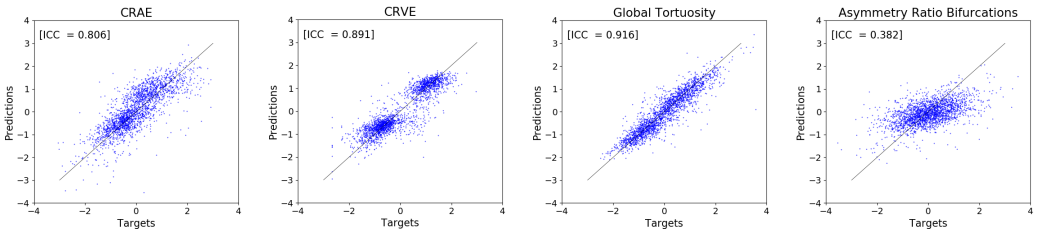


Figure 1: Comparing predicted values of the biomarkers with the labels. The $y = x$ line represent perfect correlation. The Intraclass Correlation Coefficient is shown for each biomarker.

Mellitus. The study comprises subjects that live in the southern part of the Netherlands and aims to include 10,000 participants. Each subject receives a full examination, including laboratory measurements, physical examination, interviews and extensive imaging (10).

All presented experiments were conducted using a subset of 10668 images from 2782 subjects from the Maastricht study. The subset comprises images of left and right eyes and are centered either on the fovea or on the optic disc. The images were resized to 384 by 384 pixels before further processing.

A selection of four biomarkers was chosen from an extensive list of features that were automatically calculated by the pipeline of methods described by (7). The biomarkers were chosen such that they represent the key vessel geometries: Central Retinal Arteriolar Equivalent (CRAE), Central Retinal Venular Equivalent (CRVE), Global tortuosity and Asymmetry ratio of bifurcations.

The asymmetry ratio values for 35 images were missing and therefore replaced with the mean of the other asymmetry ratio values. All labels are scaled to have zero mean and unit standard deviation, based on the statistics of the labels from the training set.

### 2.1 CNN model and experiments

The 10668 images are split into sets for training (N = 6352 [60%]), validation (N = 2130 [20%]) and testing (N = 2186 [20%]). All images of a single patient are assigned to the same set. A neural network is implemented in TensorFlow consisting of 6 convolutional layers with 32 filters (5 by 5) with stride 1. Each convolutional layer is followed by a batch-normalization layer and, a ReLu-nonlinearity and a 2 by 2 max-pooling layer. The last max-pooling layer is followed by two densely connected layer (128 nodes). The output layer consists of 4 nodes corresponding to the 4 biomarkers. The loss function is defined as the sum of L2 losses for each biomarker. Xavier initialization is used for setting the weights and biases are set to 0.1. Batches consist of 20 randomly sampled and augmented images. The augmentation includes translation (<30 pixels), full rotation, horizontal and vertical reflection, intensity shift, color shift and contrast shift. Training is continued for 75,000 iteration ($\approx$236 epochs) and weights are optimized using Adam optimization, with an initial learning rate of 0.0001.

For each biomarker, the performance of the model is evaluated on the test set by calculating the intraclass correlation coefficient between the labels and the predictions. At test time, the same augmentation settings are used to repeat the predictions for each image 30 times, which are then averaged for the final predictions.

## 3 Results and discussion

The prediction of the 4 four biomarkers for all test images took 146 minutes on a single GPU (Geforce GTX 1070), corresponding to a total analysis time of 4 seconds per image. The predictions show a quite strong correlation with the targeted values (Figure 1). Intraclass correlation coefficients indicate strong relations for CRAE (ICC = 0.81), CRVE (ICC = 0.89) and global tortuosity (ICC = 0.92), while the correlation for the asymmetry ratio of bifurcations is considered moderate (ICC = 0.38). If only 1 augmentation is used at test time, the analysis time was 0.1 seconds per image and the intraclass correlations decreased with 0.01-0.02.

Key biomarkers, originally extracted with a pipeline of unsupervised geometrical models, can be reproduced fairly well with the predictions of a single CNN. The distilled network is fast and flexible and can easily be trained on different, or more biomarkers. Validation on an external retinal fundus dataset could benefit the deployability.

The chosen biomarkers represent the main retinal microvascular structures. The distilled model is thus sensitive to features of the retina that have been related to several diseases. The distilled model can be considered pretrained for related classification tasks. A potential application of the pretrained network could be to improve the classification of diabetes Type 2 and prediabetes directly from fundus images (11), since both diseases are associated with microvascular dysfunction (12).

## 4 Acknowledgements

This research is financially supported by the STW Perspectief program and Philips Research.

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