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# Detection of Retinal Changes from Illumination Normalized Fundus Images using Convolutional Neural Networks

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## ABSTRACT

Automated detection and quantification of spatio-temporal retinal changes is an important step to objectively assess disease progression and treatment effects for dynamic retinal diseases such as diabetic retinopathy (DR). However, detecting retinal changes caused by early DR lesions such as microaneurysms and dot hemorrhages from longitudinal pairs of fundus images is challenging due to intra and inter-image illumination variation between fundus images. This paper explores a method for automated detection of retinal changes from illumination normalized fundus images using a deep convolutional neural network (CNN), and compares its performance with two other CNNs trained separately on color and green channel fundus images. Illumination variation was addressed by correcting for the variability in the luminosity and contrast estimated from a large scale retinal regions. The CNN models were trained and evaluated on image patches extracted from a registered fundus image set collected from 51 diabetic eyes that were screened at two different time-points. The results show that using normalized images yield better performance than color and green channel images, suggesting that illumination normalization greatly facilitates CNNs to quickly and correctly learn distinctive local image features of DR related retinal changes.

**Keywords:** Microaneurysms, Hemorrhages, Fundus Images, Diabetic Retinopathy, Convolutional Neural Network, Longitudinal DR Screening

## 1. INTRODUCTION

Diabetic retinopathy (DR) is a complication of diabetes mellitus, which progressively damages retinal blood vessels and results in vision loss and even blindness if not diagnosed and treated adequately. Regular eye examination is necessary for the detection and treatment of DR at an early stage.[1] The current eye care practice for regular DR screening involves manual examination of multiple fundus photos and is resource demanding, subjective, and does not exploit images from previous retinal exam for progression assessment. Automated detection of longitudinal DR related changes provides an objective measure of retinal abnormalities over time and enables clinicians to objectively assess DR progression.

DR progression is accompanied by retinal changes due to appearance and disappearance of lesions such as microaneurysms, hemorrhages, exudates, and cotton wool spots. In addition to the number of these lesions at the time of examination, the dynamics of lesions such as the lesion turnover rate can provide more insight into the disease activities over time.[2,3] Therefore, automated detection and quantification of longitudinal retinal changes can be an important addition to regular DR screening.

Automated detection of longitudinal retinal changes due to microaneurysms and dot hemorrhages from a series of fundus images is challenging due to intra and inter-image illumination variation between fundus images captured at different retinal checkups (Fig.1b). A previous approach for longitudinal fundus image analysis excluded retinal regions around the borders of fundus images due to illumination variation and analyzed the remaining regions to identify change locations.[4] Retinal changes are then detected using hand crafted features extracted from each of the images.[4,5] Recently, deep convolutional neural networks (CNNs) are shown to be successful in automatically learning local image features for object detection and classification.[6,7] Deep CNNs can learn local object features in a hierarchical fashion using kernels that are limited to a small neighborhood.

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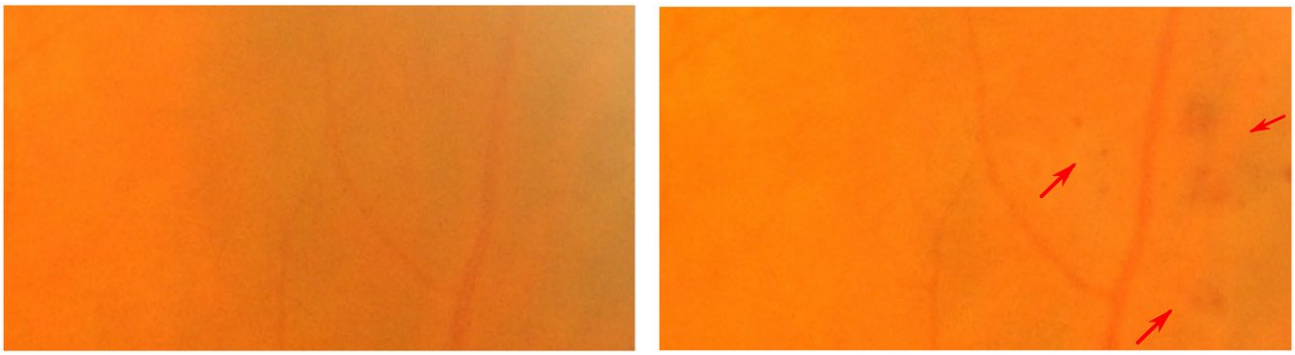
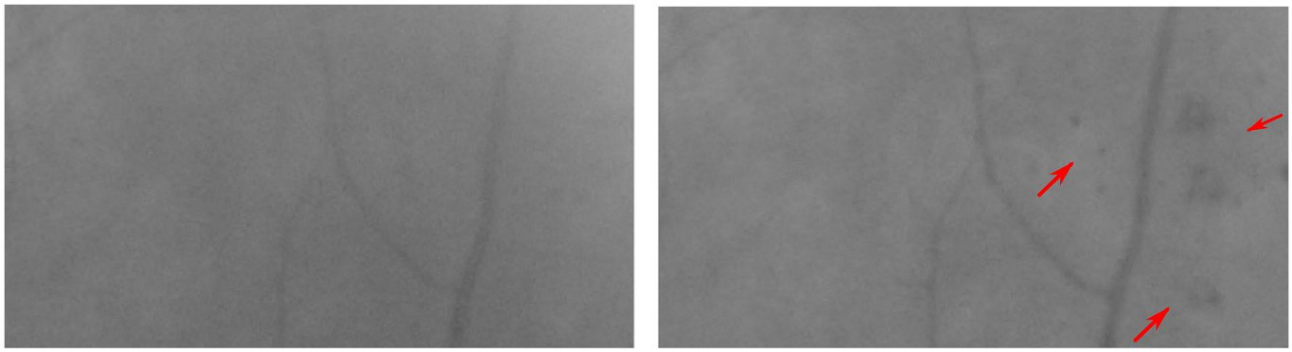
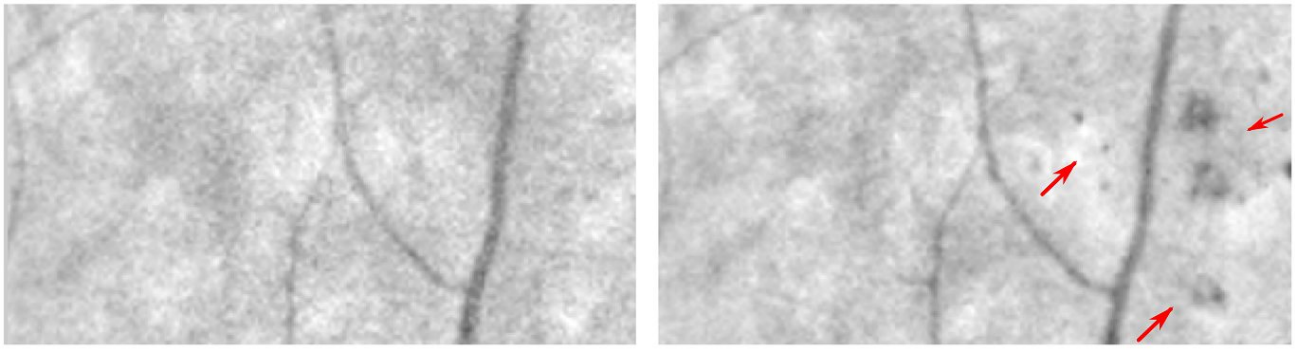


(a) Color fundus image patches.



(b) Gree channel fundus image patches.



(c) Normalized fundus image patches.

Figure 1: Examples of various fundus image patches showing retinal changes due to microaneurysms and hemorrhages (red arrows) between the baseline (left) and follow-up (right) DR checkups.

In this paper, we explore the performance of a CNN model for the detection of DR related retinal change in pairs of fundus images which are normalized for illumination variation and compare its performance with two other CNNs trained separately on color and green channel fundus images.

## 2. METHODOLOGY

### 2.1 Illumination Normalization and Registration

In color fundus images, the red and blue channels suffer from low contrast between the retinal features and the background. Because of its higher contrast, the green channel of the digital fundus images is commonly used in DR screeing by eye care experts as well as in automated fundus image analysis. However, the green channel images still show considerable variation in luminosity and contrast, both within and between images.

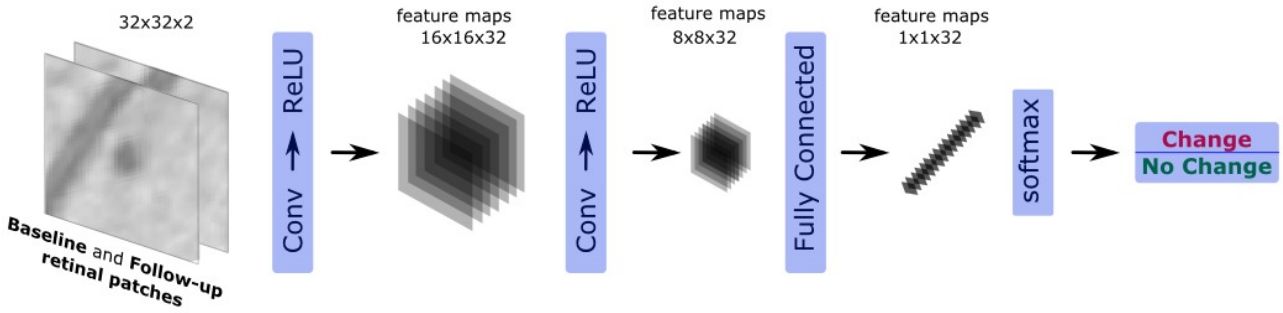



Figure 2: An overview of the convolutional neural network architecture.

This variability was normalized by estimating the luminosity and contrast from the local intensity distribution of the so-called background retina (i.e., the retina excluding features such as vessels, optic disc, and lesions) and subsequently correcting for their variation over the entire retinal image[8](Fig. 1c). Then, the intra- and intervisit fundus image series were aligned by a registration method that makes use of the normalized intensity as well as structural information of the retinal vasculature using a multiresolution matching strategy coupled with a hierarchical registration model.[8] The color and green channel fundus images were also registered into the same coordinate system as the normalized images using the final estimate of the transformation model parameters.

### 2.2 Data and Reference Annotation

Data for this study was obtained from the regular DR screening program at the Rotterdam Eye Hospital. Four field (macula-centered, optic nerve-centered, superior, and temporal regions) fundus image sets from 51 diabetic eyes who were examined for DR in 2012 and 2013 were included. For each eye, three expert graders independently inspected and annotated the registered color and normalized images for microaneurysm and hemmorrhage related retinal change between the two screening time-points. The experts annotated the center of each changed region. The reference annotation was defined as the union of all the annotations by the three graders. The estimated diameter of the annotated regions ranges from 3 to 16 pixels ($21\mu m$ to $112\mu m$).

### 2.3 Convolutional Neural Network Architecture

The CNN model consists of two convolutional layers and one fully connected layer (Fig. 2). In both convolutional layers, kernels of size $5 \times 5$ were applied to learn local image features. To progressively reduce the size of the spatial representation of the objects in the image and the amount of parameters, the kernels were applied with a stride of 2. A rectified linear unit (ReLU) activation function was employed after each convolutional layer. Then, 32 features maps were generated by the fully connected layer and fed into a softmax classifier to compute the probability that a *change* (or *no change*) has occured between the baseline and follow-up retinal regions. Note that in addition to the CNN shown in Fig. 2 with a specific configuration of the normalized input images ($32 \times 32 \times 2$), other CNNs consisting of different image types (color or green channel) and configuration (difference images) were also explored.

## 3. EXPERIMENTS AND RESULTS

A total of 531 retinal change locations were annotated on the 51 baseline ($I_B$) and follow-up ($I_F$) registered image pairs. A positive class, which represents the occurrences of a change, was formed by gathering image patch pairs of $32 \times 32$ pixels centered on each annotated change location. A negative class was created by randomly sampling 531 image patches of size $32 \times 32$ pixels from locations that were not marked by any of the experts. After splitting all the gathered patches as training (80%) and evaluation (20%) set, the sample size of each set was increased by applying data augmentation techniques such as Gaussian blurring, rotation, and flipping. In total, 7650 training and 1908 evaluation baseline and follow-up image patch pairs were gathered from each of the color, green channel and normalized fundus image types.

For each image type, the CNN model hyperparameters were optimized independently using a subset of samples from the training set. We explored two approaches to combine $I_B$ and $I_F$ and feed them into the CNNs.

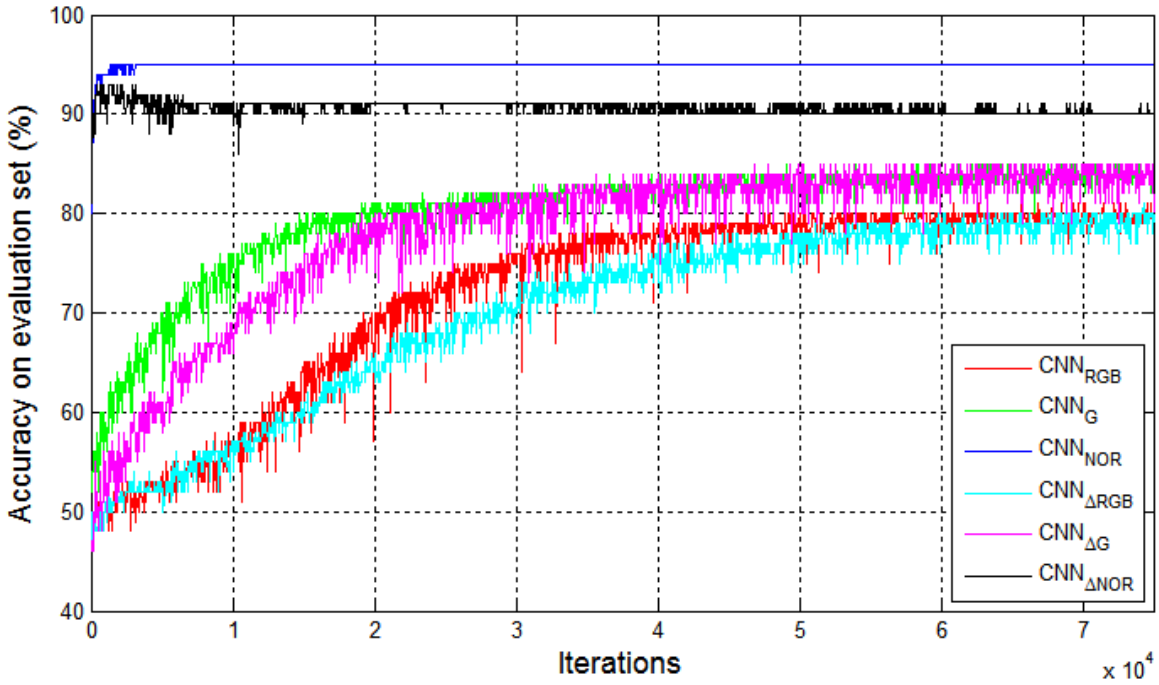


Figure 3: Accuracy on the evaluation set after each iteration.

In the first approach, both $I_B$ and $I_F$ were directly fed into the CNN models as separate channels (Fig. 2). In the second approach, the absolute difference between the two images, $|I_B - I_F|$, was used as input to the CNNs. The performance evaluation metrics were the sensitivity and the specificity, which are computed as

$$Sensitivity = \frac{TP}{TP + FN} \tag{1}$$

$$Specificity = \frac{TN}{TN + FP}, \tag{2}$$

where $TP$ is the number of true positives, $FN$ is the number of false negatives, $TN$ is the number of true negatives and $FP$ is the number of false positives. The results are summarized using receiver operating characteristics (ROC) curves. All the experiments were done using TensorFlow.[9]

The results show that in both approaches the accuracy of the CNNs trained on the normalized images was higher than the accuracy of the CNNs trained on either the color or the green channel images (Fig. 3). In addition, the results suggest that illumination normalization helps the CNN to quickly learn distinctive local image features of DR related retinal changes and thus converge fast. The ROC curves in Fig. 4 show that a higher sensitivity and specificity was achieved for the CNN that is trained on the normalized images than on the color or green channel images. For both the normalized and green channel images, a slight increase in performance was observed when directly using the $I_B$ and $I_F$ input image patches as separate channels than combining them as $|I_B - I_F|$. For the color and green changel images, the performance does not reach the same level as for the normalized images even after many iterations. This may be due to the normalization operating on a larger scale ($151 \times 151$ pixels) than the kernel size of the CNN ($5 \times 5$ pixels).

## 4. CONCLUSION

In this paper, we presented an approach for the automated detection of longitudinal retinal changes from a series of fundus images. The approach employed a deep CNN trained on normalized fundus images that are corrected for intra- and inter-visit illumination variations, thereby enabling the CNN to correctly learn highly representative local image features of DR related retinal changes. Evaluation showed that the CNN network

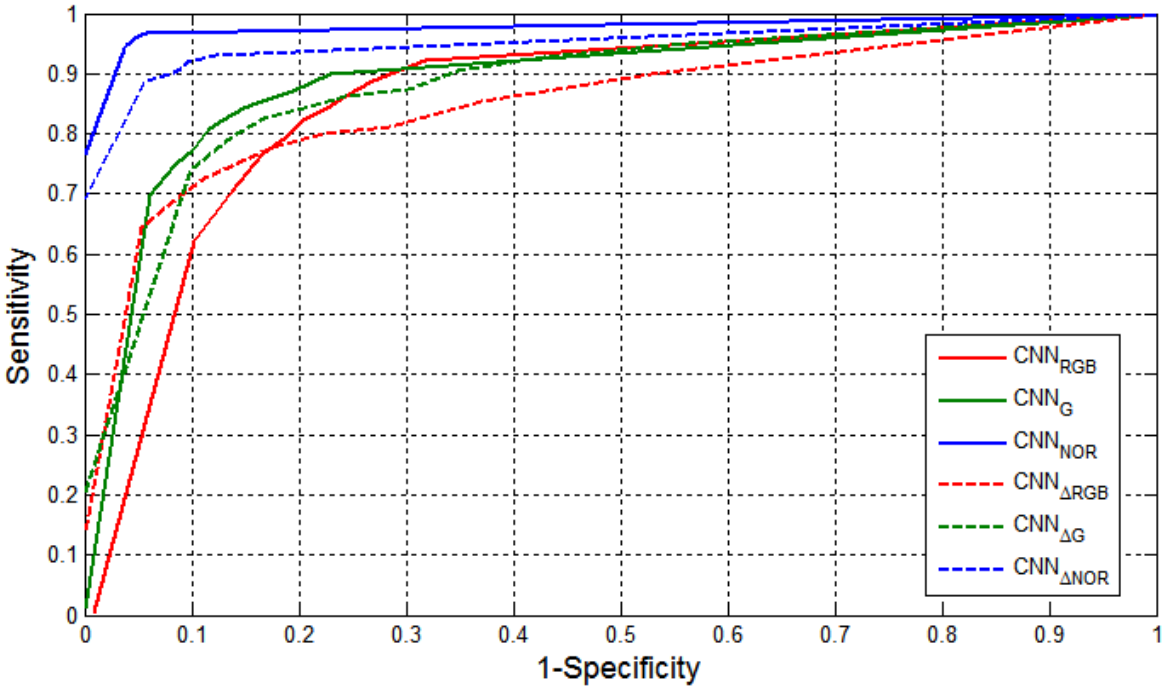



Figure 4: ROC curves of CNN models trained on color (RGB), green channel (G), and normalized (NOR) fundus images for the detection of retinal changes due to DR lesions. For each image type, the CNNs that are trained directly on $I_B$ and $I_F$ are indicated by $\text{CNN}_*$ and those networks trained on $|I_B - I_F|$ are indicated by $\text{CNN}_{\triangle *}$.

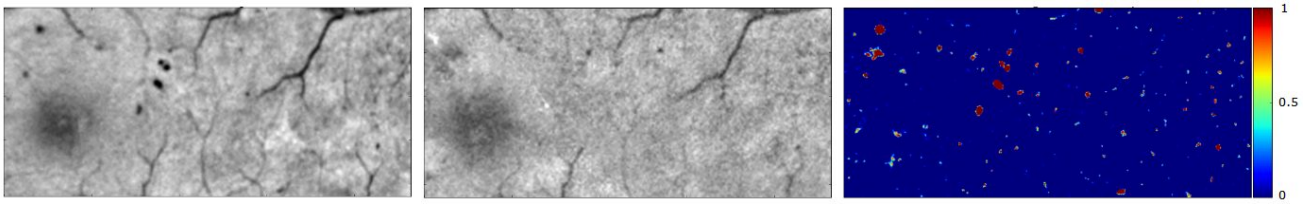



Figure 5: An example of baseline (left) and follow-up (middle) retinal regions on which a CNN trained on normalized images was applied to produce pixelwise probability map (right) for DR related retinal changes.

trained on normalized fundus images outperforms two other CNNs trained separately on color and green-channel images. The detected DR related changes may be used for objective assessment of DR progression as well as for more efficient human grading by highlighting DR related changes since the previous visit (Fig. 5). Future work includes incorporating contextual information between neighboring pixels using fully CNNs and incorporating postprocessing methods to remove regions that are less likely to be clinically relevant from the pixelwise probability map.

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