

MADeep-Automatic Microaneurysms Detection on Retinal Fundus by using region growing and deep neural networks

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Summary

Detection of microaneurysms (MAs) is required by ophthalmologists as a part of eye screening process. It is difficult for them to detect and count MAs through the existing system due to its complex structure. If MAs lesions are automatically detected then it can definitely release the workload on experts. Therefore in this paper, the competition region growing algorithm (CRGA) and variants of deep neural networks (DNNs) techniques are used to automatically detect microaneurysms (MAs) lesions. This new proposed system is known as MADeep that contains three main phases such as localization of MAs regions through a CRGA, segmentation of candidate regions of red lesions by the region-based convolutional neural network (R-CNN) and detection of MAs regions by stack-based autoencoders (SAEs). The MADeep system is tested and evaluated on a set of 600 retinal images that contains 1024 MAs, which are obtained from three different online sources. On average, the MADeep achieved sensitivity (SE) of 92%, specificity (SP) of 95%, true positive rate (TPR) of 93%, false positive rate (FPR) of 65% and area under ROC curve (AUC) of 0.94. The experimental results indicate that the proposed MADeep system is better than other state-of-the-art systems.

Key words:

Microaneurysms, Diabetic retinopathy, Retinal fundus images, Deep neural network, Region-based convolutional neural network, Autoencoders, region growing.

1. Introduction

The diabetic retinopathy (DR) is increasing rapidly at an alarming rate throughout the worldwide. The Diabetes is the fourth leading cause of death [1] especially among adults. According to estimation, the diabetes among adults [2] will be 6.4%, affecting 285 million adults. In year of 2010, the effect of this disease will increase more to 7.7% and 439 million adults by 2030. If DR is detected at an early stage [3] then the incidence of disability or death is definitely decreased. In general, the diabetes effect on the visibility of human and if detected at an early stage then it can be 90% cured. Digital fundus camera and automatic methods are widely utilized by clinical experts to detect diabetic retinopathy. To detect DR, this eye screening processing is costly, time-consuming, and often inaccurate due to the complex structure of many lesions of DR [4].

These DR-lesions are generated through an effect of microaneurysms (MAs) [5], hemorrhages, hard exudates, cotton wool spots or venous loops of DR. Among many DR-lesions, the detection of MAs lesions is a complicated task for ophthalmologists during screening process. For screening process of patients during diagnosis of DR, the basic process is to detect the lesions such as microaneurysms (MAs), hemorrhages, hard exudates, cotton wool spots or venous loops from color fundus images. If there are more MAs lesions are presented then there are more chances of diabetes. Therefore, the detection of MAs red lesions is a necessary step. The microaneurysms (MAs) example is visually shown in Fig. 1 (b) from region-of-interest (ROI) image.

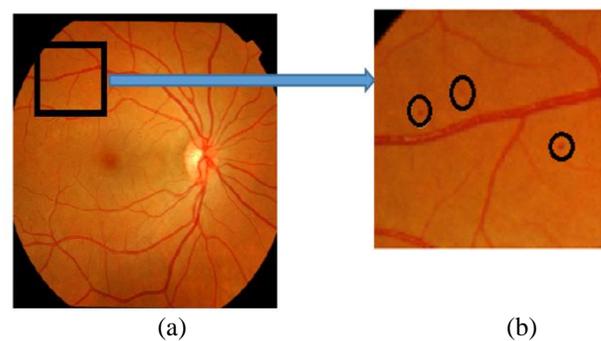


Fig. 1 An example of manual microaneurysms (MAs) defined by an expert ophthalmologist in retinal fundus image (b) from the original input region-of-interest (ROI) image (a).

In particular, the MAs feature appears as small reddish isolated points, which cause vascular failure in the affected capillaries. Due to its small size and lack of contrast against the background of the image, the manual detection process is a slow even for the experienced Ophthalmologist. The first clinically observable sign of DR is the presence of MAs that is also the major cause of blindness. The initial appearance of MAs in the vasculature of the retina are not noticed by the patient, until DR evolves and new symptoms appear, such as macular edema that causes blurred vision or even blindness shadows. In these situations, at which, patients generally decide to visit an ophthalmologist. To perform early

diagnose of diabetic retinopathy, the patients have to do eye screening. Since, this procedure is very costly, time-consuming and inaccurate at many times. Even though in rural areas, the situation is even worse because it is difficult to find an expert ophthalmologists. As a result, the researchers are trying to develop an automatic computerize solution for detection of DR. In the subsequent paragraph, the past computerize systems are described in brief.

2. Research Background

In the literature, many studies conducted to automatically detect microaneurysms (MAs) from retinal fundus images. Although, the review of these systems suggested that there are lots of false positives wrongly diagnosed patients [6]. It is usually happened due to the fact that color fundus image is composed of different objects such as an optic disc, fovea or microaneurysms (MAs) in which the MAs lesions have low brightness compared to other objects and vascular network of blood vessels have always interference in this detection process [7]. Therefore, the accurate methods for detection of diabetic retinopathy are always required [8].

The Zhou et al. [9] detected MAs through the multi-features and dictionary learning methods. They have tested the system on ROC dataset and compared with an average sensitivity compared to the other systems developed in the past studies. Whereas Srivastava et al. [10] detected the red lesions known as microaneurysms (MAs) from blood vessels through the Multiple Kernel Learning technique. They performed experiments on a data set of 143 retinograph digital images and achieved the areas under receiver operating characteristic curve (AUC) of 0.97 for detection of MAs. Despite these methods, the Adal et al. [11] suggested a computerize system for detection of microaneurysm (MAs) from digital retinograph images. The Adal et al system is trying to detect region-of-interest through scale-adapted region descriptors. In Hatanaka et al [12] study, the authors presented an automated MAs detection system by finding eigenvalues from retinograph images and then utilized a Hessian matrix technique. Then, they extracted 126 features and classified using artificial neural networks (ANN). The authors reported a 73% of the true positive rate (TPR) per image. Also in Akram et al. study [13], the accurate detection of microaneurysms (MAs) is performed by using a feature vector and a hybrid classifier. The authors developed this system by using GMM model, SVM, and multi-model model.

In Fleming et al. study [14], they suggested that it is very vital to detect MAs lesions because MAs red lesions displayed the early sign of retinopathy. Therefore, it is very vital to develop automatic methods for MA detection. The authors utilized contrast normalization technique to

improve red lesions MAs compare to background of retinograph images. The authors have also done comparisons with other contrast normalization technique. In that paper, the authors also applied watershed transform technique to detect regions that contains no contains no vessels or other lesions in retinograph image. They reported on a limited dataset with sensitivity (SE) of 85.4% and specificity (SP) of 83.1%.

In Walter et al. study [15], a pre-processing step is first performed to do image enhancement, shade correction, and normalization of the green channel. Next, the features are extracted to automatically classify candidate regions into real MAs as a post-processing step. A dataset of 21 annotated images was used and achieved a sensitivity of 88.5% for detection of MAs. Whereas in [16], a hybrid approach was developed to detect MAs from retinal fundus images. In that system, the authors first detected candidate objects through feature set and a k-nearest neighbor classifier. The authors reported that a sensitivity of 100% at a specificity of 87% for detection of red lesions. Also in Niemeijer et al. study [17], an automatic method to detect microaneurysms by locally matching a lesion template in subbands of wavelet transformed images and followed by a genetic algorithm on a dataset of 120 retinal images. They achieved a SE of 89.62% and a positive predictive value (PPV) of 89.50%.

In the past studies, many researchers developed automatic system for detection of MAs from retinal digital images. Since, those studies focused more on pre- or post-processing step and defining some expert to classify MAs. In this work, deep neural networks (DNNs) based learning technique is developed by combining region-based convolutional neural networks (R-CNN) and Stack-based autoencoders (SAEs). So, there is no need to perform image processing based complex steps to extract and select features. Moreover, the proposed MADeep system detect MAs from retinal fundus images independent of vessel structures, the optic disc, and the fovea. Hence extraction or detection of these features is not required.

3. Proposed Architecture

The proposed MADeep system contains three main phases such as segmentation of regions, Deep candidate regions and detection of microaneurysms (MAs). The systematic flow diagram of the proposed MADeep system is visually represented in Fig.2. Instead of using complex image processing algorithms, the deep neural networks (DNNs) model is performed to get effective MAs detection results. The DNNs algorithms are used [21] because it has been utilized in many automatic applications such as Computer

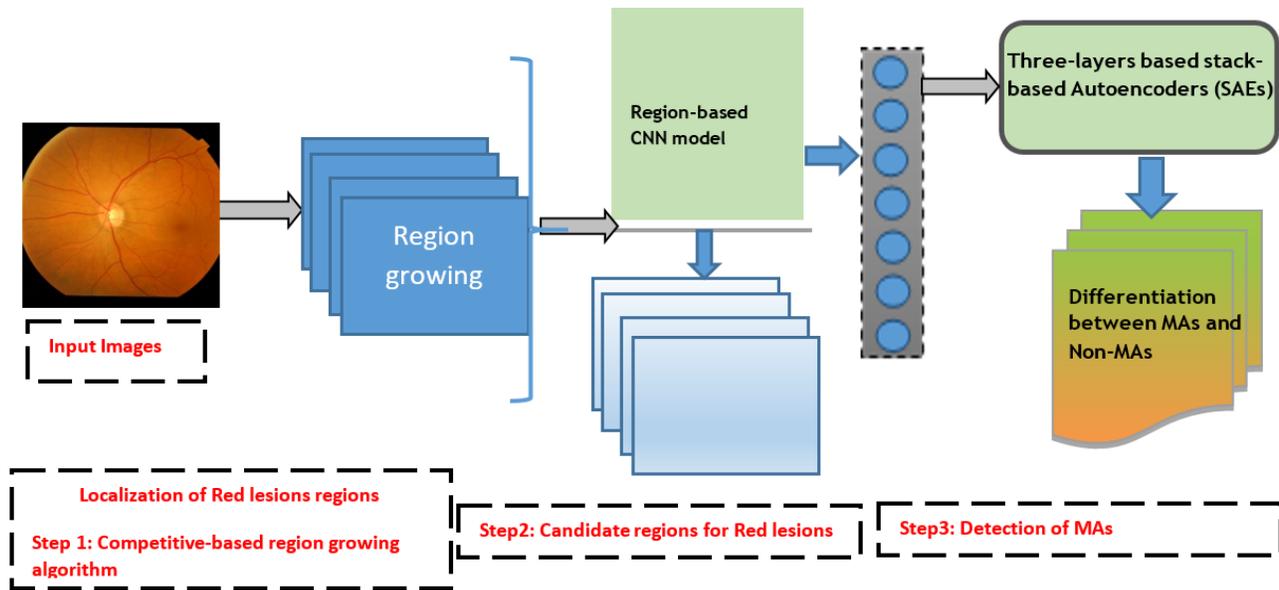


Fig. 2 A systematic diagram of the proposed detection system for microaneurysms (MADeep) when diagnosis through diabetic retinopathy..

Vision, Data Mining, Biomedical Image and Signal processing, Bioinformatics and video tracking. To segment regions from retinal images, competition-based region growing algorithm [22] (CRGA) modified to segment only red lesions instead of blood vessels lines. To detect deep candidate regions (DCRs), the unsupervised region-based convolutional neural networks (R-CNN) model [23] is used and afterward, the stack-based autoencoders (SAEs) [24] is utilized to finally select MAs from DCRs candidate regions. These steps are explained in the following subsections.

3.1 Utilization of Dataset

The MADeep is evaluated by using three publicly available data sources such as retinopathy online challenge (ROC) [18], Diaretdb1v2 [19] and Messidor [20]. In ROC dataset, there are 50 retinal images selected that contain 210 MAs in total. In many past studies, the ROC dataset is widely used for competition to detect MAs. Whereas in the Diaretdb1v2 dataset, the 90 images are selected that contains 184 MAs in total. In the case of Messidor dataset, there are 460 images selected among 1200 images contains 630 MAs. In total, there are 600 retinal images used in this experiment that contains 1024 MAs. An expert ophthalmologist is requested to draw the manual border on MAs and Non-MAs red lesions contours to test and compare the proposed MADeep system.

3.2 Localization of MAs regions

Retinal fundus images contained different objects such as MA, blood vessels, OD and CUP areas, and noises. Therefore, the detection of MAs or red lesions is a complicated task. A simple region growing algorithm (RGA) [22] is used to do initial segmentation for detecting of different regions that are presented in the retinal fundus images. The RGA algorithm is modified in this study to segment only red lesions instead of blood vessels through competition technique known as CRGA algorithm. In CRGA technique, neighboring pixels are grouped together and examined if they belong to same class. If adjacent regions are captured then it groups together by region merging algorithm to dissolve the weak edges. In addition to this property, the CRGA algorithm is very effective to detect different regions from image compared to noise. In general, the CRGA algorithm is working based on pixel-based image segmentation and it is important to provide initial seed points. Based on these initial seed points, the CRGA algorithm is then trying to check neighboring pixels and determines whether the pixel neighbors should be added to the region. This CRGA region growing algorithm is also based on iteration. During each iteration, the CRGA algorithm is performing same operation as a clustering technique.

The next step is to obtain the only MA candidates regions without the vascular tree, the determination of the initial seed, obtained by performing thresholding attach to it without the vascular tree. In this process that the selection

at most, candidate regions 1000 to seed MAs. This number of candidate regions has been experimentally calculated so that even regions representing MA with low contrast in the image are included in the selection of seeds. To accomplish this, the process begins the process started with a threshold value is 0.1 and if the resulting regions are more than 1000, then increases the threshold at 0.01 and repeats the process. When we get a number of regions below 1000, the thresholding process stops, and the pixel with greater intensity in each region is considered as a candidate for MAs seed.

In order to reduce the number of candidates for seed pixels, each of them applies the calculation of statistical Tail Ratio [14], which provides information about the intensity distribution in the histogram of a window centered at pixel under study. Once we have the definitive set of seeds, we proceed to perform a region growing from each image. Moreover, the regions with an area greater than 35 pixels are discarded, since this is the value, as our resolve to work, to the maximum area that can have a MAs. The initial segmentation step through the region-growing algorithm is visually represented in Fig.3.

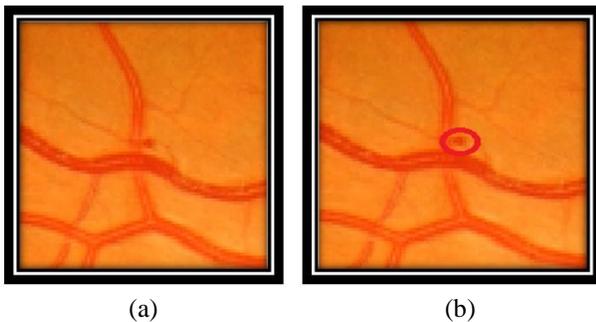


Fig. 3 Detection of Microaneurysm (b) through region-based convolutional neural network and stack-based autoencoders (SAEs) on example region-of-interest (ROI) image (a).

3.3 Candidate regions of red lesions

To accurately detect candidate regions of MAs, the region-based convolution neural networks (R-CNNs) [23] is utilized and modified to detect regions of MAs from retinal fundus images. In R-CNNs model, the regions of the pixel are classified as MAs or Non-MAs. The basic model of R-CNN is based on the region proposals were created through selective search technique. In the modified version of R-CNN, the localization of MAs regions are used as an input to R-CNN model. In this paper, regions are segmented through the previous step (localization of MAs) and in the second step, the activation features are extracted from all the MAs. Finally, the trained stack-based

autoencoders (SAEs) is integrated to evaluate the regions as MAs or non-MAs. This step is explained in the subsequent subsection. The R-CNN mode is effectively utilized in this paper to find out the different regions in an image based on variety of windows sizes. In fact, the R-CNN model is always trying to make a group of adjacent pixels based on the format of color, texture on intensity-level. Therefore in this paper, the R-CNN model is to detect candidate regions for red lesion objects.

3.4. Detection of microaneurysms

The stack-based autoencoders (SAEs) [24] model is integrated into this study to correctly evaluate the MAs regions compared to Non-MAs regions. The SAEs have used the features, which are extracted from the previous steps to form a deep neural network (DNN). The stack-based autoencoders (SAEs) is trying to contrast different layers through training of denoising autoencoders. After construction of these pre-trained layers, the network is then utilized for fine-tuning step.

On a supervised SAEs, the fine-tuning is used to minimize the prediction error. This fine-tuning step is implemented by using softmax linear classifier that is added to the top layer of the network. The entire network is trained through a multilayer perceptron. Currently, the encoding parts are considered of each Autoencoder. This stage is supervised since now the target class is utilized during training.

4. Experimental Results

The proposed MADeep system for detection of Microaneurysms (MAs) is implemented in MATLAB 2016 and is evaluated by using three publicly available data sources such as retinopathy online challenge (ROC) [18], Diaretdb1v2 [19] and Messidor [20]. In total, there are 600 retinal images that contain 1024 red MAs lesions. An expert ophthalmologist is requested to draw the manual border on MAs to test and compare the proposed MADeep system. The detection of MAs decision is performed by combining the integration of region-based convolutional neural networks (R-CNN) and stack-based autoencoders (SAEs). In all these 760 retinal fundus images, the 30% lesions are used to train the proposed deep learning classifier and 70% are used to test this classifier.

A statistical analysis was also performed to evaluate the suitability of the proposed MADeep system for better eye screening program and to assist ophthalmologists. This statistical analysis was also used to compare the MADeep algorithm with two state-of-the-art methods. An area under the receiver operating curve (AUC) [55] is used along with three measures such as true positive rate (TPR), false

positive rate (FDR), sensitivity (SE), specificity (SP) and

Table 1: The average values of Sensitivity (SE), Specificity (SP), TPR: True positive rate, FPR: False positive rate and area under the receiver operating curve (AUC) of the MaDeep system on 1024 Microaneurysms (MAs).

No.	Category deection	SE	SP	TPR	FPR	AUC
1	Microaneurysms (MAs)	92%	95%	93%	65%	0.94
2	Non-Microaneurysms (Non-MAs)	94%	95%	96%	77%	0.95
SE : Sensitivity, SP: Specificity, TPR: True positive rate, FPR: False positive rate and AUC : area under the receiver operating curve						

Table 2 - The average values of the comparison of Sensitivity (SE), Specificity (SP), TPR: True positive rate, FPR: False positive rate and area under the receiver operating curve (AUC) of the MaDeep system on 1024 Microaneurysms (MAs).

No.	State-of-the-art	SE	SP	TPR	FPR	AUC
1	Adel-MAs [11]	78%	80%	70%	80%	0.79
2	Walter-MAs [15]	80%	83%	73%	74%	0.84
3	MADeep	93%	95%	94%	70%	0.96
SE : Sensitivity, SP: Specificity, TPR: True positive rate, FPR: False positive rate and AUC : area under the receiver operating curve						

comparisons are also performed with two state-of-the-art MAs detection systems such as Adel-MAs [11] and Walter-MAs [15] on this selected dataset.

For better representation of accuracy sensitivity and specificity at pixel level was used as measurement in this paper. These statistical metrics are used in this study same as mentioned in the paper [5]. The authors are requested to read the paper for further details [5]. Thus the global sensitivity (SE) and the global specificity (SP) and accuracy AC for each image are calculated to show the effectiveness of the proposed algorithm compared to state-of-the-art techniques.

The table 1 shows the achieved results of MADeep system on 1024 MAs extracted from retinal fundus images. From this table, it noticed that the proposed MADeep achieved SE of 92%, SP of 95%, TPR of 93%, FPR of 65% and AUC of 0.94 in the case of detection of Microaneurysms (MAs) red lesions. Moreover, in the case of Non-Microaneurysms (Non-MAs), the MADeep obtained SE of 94%, SP of 95%, TPR of 96%, FPR of 77% and AUC of 0.95. These results demonstrate the proposed MADeep is getting significantly high detection accuracy compared to other systems.

To evaluate the performance of MADeep system, the comparisons are also performed by MADeep with state-of-the-art systems such as Adel-MAs [11] and Walter-MAs [15]. These comparisons results have mentioned in Table 2. In this table, the Adel-MAs obtained very low significant results such as SE of 78%, SP of 80%, TPR of 70%, FPR

area under the receiver operating curve (AUC). The of 80% and AUC of 0.79. Whereas somewhat higher results achieved in the case of Walter-MAs system but low compare to propose MADeep system as SE of 80%, SP of 83%, TPR of 73%, FPR of 74% and AUC of 0.84. It is happened due to integrate R-CNNs and SAEs deep learning algorithms.

5. Conclusion

The two variants of deep neural networks (DNNs) algorithms are effectively used in this paper to automatically detect microaneurysms. A new proposed system (MADeep) contains three main steps such as localization of MAs, segmentation of candidate regions and detection of MAs. For localization of MAs, the competition-based region growing algorithm (CRGA) is developed. To segment candidate regions, the region-based convolutional neural network (R-CNN) is used to find out features and those features are classified through stack-based Autoencoders (SAEs) on a set of 1024 MAs obtained from different sources. The obtained results indicate that the propose MADeep system is better compared to state-of-the-art systems. Hence, the MADeep automatic system can be used to monitor the progress of DR at an early stage. To increase the accuracy of MADeep system, the training is performed by stack-based autoencoders (SAEs) that achieved state-of-the-art performance with the very low false positive rate on publicly available datasets. In this paper, a novel algorithm was developed for the automatic detection of microaneurysm (MAs). In the future work, the system will also be able to detect other objects such as OD/CUP area, Glaucoma that is presented in retinal fundus images. The detection of other objects helps to detect severity-level of diabetes.

Acknowledgment

The authors would like to express their cordial thanks to the department of Research and Development (R&D) of IMAM, university for research grant no: 360915.

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