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Multi-Scale Feature Pyramid for Detection of Red Lesions in Fundus Images

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Abstract**:** ***Diabetic retinopathy (DR) is increasing rapidly around the world, but there is a shortage of experienced ophthalmologists. Therefore, computer-based diagnosis of the fundus images is essential to screening of referable DR. Automated detection of red lesions is very important for screening of DR. This paper deals with a novel method for automatic detection of red lesion. The main contribution is developing a deep learning based detection framework to handle severe class imbalance and imbalance in sizes of red lesions. The multi-scale features are extracted using the feature pyramid network. A pyramid of features is generated with strong semantics. The proposed network is end-to-end trainable in image level with several scales and works for a wide range of red lesions with acceptable performance. Sensitivity of the proposed method is 0.76 with six false-positive per image on test set of publicly available DIARECTDB1 database and outperforms state-of-the-art approaches. A potential benefit with deep learning based detection framework could be used in screening programs of referable DR.***

Keywords: Diabetic Retinopathy, Fundus Images, Red Lesions Detection, Feature Pyramid Network, Focal loss

I. INTRODUCTION

In the United States, blindness is caused mainly due to DR [1]. Early diagnosis of DR is the only way to avoid blindness caused by DR [1][23]. About 77 million people are suffering from diabetes in India, and 18% of them are suffering from DR. DR may lead to blindness if treatment does not start in time [2]. There is a need for regular screening of diabetic patients for early detection of DR because DR is asymptomatic in the early stage. Microaneurysms and hemorrhages (Fig. 1) are called red lesions. Microaneurysms are the early sign of DR, and haemorrhages indicate the severity of DR [2]. Several challenges for detection of red lesion are poor image contrast, non-uniform illumination and wide variety of red lesions in terms of shapes and lead to missing of red lesions. In India, screening for DR is conducted by means of eye camps, where fundus evaluation is performed for diabetic patients attending the camps.

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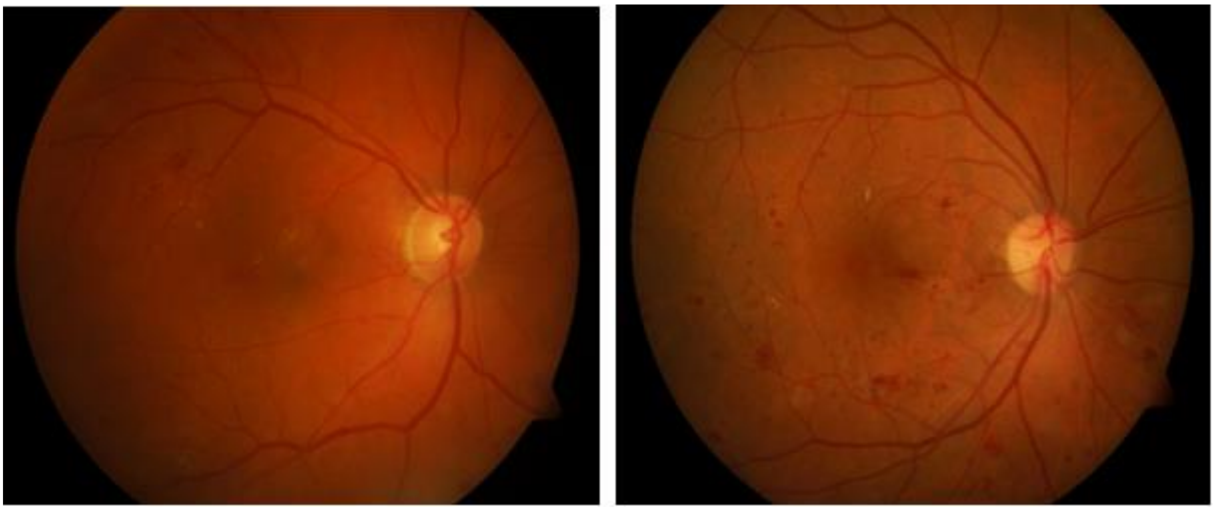
The digital retinal images are analyzed by experts and referable DR cases are segregated for further treatment. The healthy subjects are suggested to attend the next eye camps for follow-up Automated detection of red lesions is affected by low image contrast, non-uniform illumination, and very small structures of microaneurysms. The junction of blood vessels has similarity with red lesions and cause false positives. In classical image analysis, Mathematical morphology [3], template matching [4], cross-section profiles analysis [5], and multiscale filtering [6] were explored for red lesion detection.

The micro-aneurysms were extracted from other dot-like structures using Watershed transform [7]. The hemorrhages of several shapes were taken care by template matching [4]. The circular red lesions were detected by Radon Cliff operator [8]. Wang et al. [5] performed singular spectrum analysis of cross-sections profiles of microaneurysms. Wavelet transform [9] and curvelet-based method [10] were also explored for red lesion detection.

Deep learning methods are very popular and mostly explored for the detection of objects in natural images. The region-based convolutional neural network (R-CNN) [11] and the spatial pyramid pooling (SPP) [12] networks are examples of two stage detectors. Faster R-CNN [14] uses a region proposal network and is an improvement over Fast R-CNN [13]. The deep features extracted by using a region proposal network is utilized to suggest approximate objects and finally bounding box are detected. It is a single and unified network and end-to-end trainable and shares computations across all proposals rather than doing the calculations for each proposal independently. The last convolutional layer is used to predict the class scores and corresponding bounding boxes.

The single shot detector (SSD) [15] and you only look once (YOLO) [16] are examples of single stage detectors, where detection is performed over a dense sampling. The performance of SSD is not good for small objects. Object detection in YOLO is considered as a regression problem and has better generalization for new domains. The main improvement is the use batch normalization, higher resolution inputs, convolution layer with anchors, dimensionality clustering and fine-grained features.

Deep neural network is taught to recognize pathological lesions from retinal fundus images for diagnosis of DR. Grinsven et al. [17] applied CNN to detect hemorrhages based on patch classification, where the negative patches are extracted from images without hemorrhages and positive patches are extracted only from hemorrhages location. The training was made faster by dynamically selecting misclassified negative samples. This method works on the patch level and is not trainable in end-to-end.



(a) **(b)**

Fig. 1: (a) and (b) Sample Relational Fundus Images from DIARECTDB1 [20] with Non-Uniform Illumination

We present a single-stage detection framework, which works on image level and end-to-end trainable. The architecture combines a backbone for generating feature map and feature pyramid network (FPN) [19][24][25][26] with skip connections for effectively combining the features of lower resolution with features of the higher resolution images. Finally, classification and regression heads are integrated to recognize the red lesions with their locations. The FPN take care several limitations of the previous architectures and creates feature pyramid with strong semantics at several scales. The proposed network is could be trained in image level in all possible scales and works for a wide range of red lesions.

II. METHODS

Object detection at a wide range of scales is a fundamental challenge, and feature pyramid is used as a neck in the architecture with classification and regression head. The feature extracted by convolutional networks is used to create feature pyramid. The pyramids are scale-invariant the model is able to detect objects of different shapes. The proposed network consists of a top-down and a bottom-up architecture with skip connections for generating better semantic features. Non-uniform illumination and poor contrast are observed in fundus images. Therefore, a preprocessing method is developed to improve image contrast so that red lesions are visible in preprocessed images.

A. Preprocessing

The maximum illumination in fundus image is observed near the optic disc and boundary region has less illumination. Therefore, illumination equalization is very important as a preprocessing step. The fundus portion is extracted from the big-size fundus images using template matching and then the images are resized to 512×512 to make the process faster. A contrast enhancement is performed as follows.

$$I'(x, y; \sigma) = \alpha I(x, y) - \beta G(x, y; \sigma) * I(x, y) + \gamma \quad (1)$$

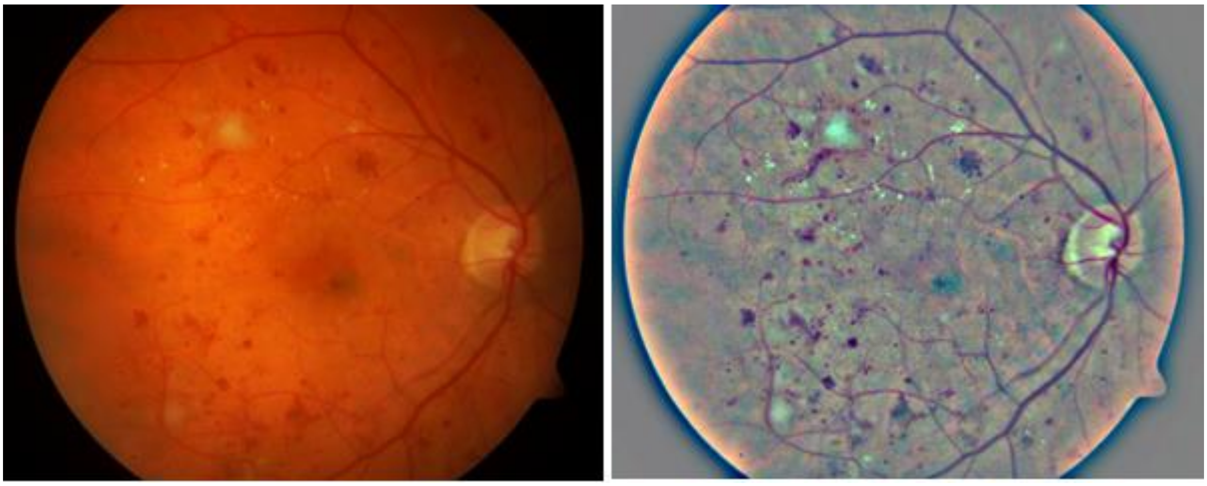


Fig. 2: Preprocessing Step: (a) Fundus Image and (b) Fundus Image After Preprocessing

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where, the convolution operation is performed with a Gaussian filter of scale σ. The values of the parameters are $\alpha = \beta = 4$, and $\gamma = 128$ for DIARECTDB1 database. The parameters are chosen empirically. The preprocessed image in Fig. 2(b) has high contrast with better visibility of red lesions for the low contrast input image in Fig. 2(a).

B. Network Architecture

The one-stage detectors are very popular because of their simpler design and acceptable performance. The proposed detection framework (Fig. 3) is one stage and has similarities with RetinaNet [18][22]. The network consists of a backbone for the extraction of features, the FPN, and the object detector head. The CNN is used to build the feature pyramid and throughout the pyramidal structure, high-level semantics is observed. The proposed method takes a preprocessed fundus image as input and creates feature map with several resolutions. The FPN helps to combine lower-resolution features with features of higher resolution. The FPN provides a semantically strong multi-scale feature map with all possible scales.

The bottom-up pathway computes a feature map with several resolutions and feature pyramid is generated. The top-down up-samples spatially coarser features, then combined with the feature pyramid via skip connections. The skip connection merges feature maps of the bottom-up path-way and the top-down pathway, where the same spatial size is considered during merging. The bottom-up feature map has the semantics of lower-level as it is sub-sampled fewer times. The top-down pyramid has high semantic information and it has fine resolutions. The classification and regression heads are similar to standard object detection methods.

The proposed network is end-to-end trainable with multiple scales and leads to detection of red lesions with wide range of shape and sizes. The focal loss [18] is considered for training of the network on hard examples as compared to easy negatives lesions or background.

The focal loss is an improvement of cross entropy by dynamically scaling the cross entropy loss so that little loss is assigned to well-classified examples and incurs high loss value for red lesion candidates, which are difficult to detect.

C. Anchor Box Tuning

Several detectors, such as Faster R-CNN [15], SSD [14], Retina Net [16], and YOLOv3 [18] use pre-defined boxes and could hamper the ability of generalizing detectors because they need tuning onmfresh detection tasks. In this work, suitable anchor boxes were generated adaptively based on the statistical analysis of sizes of red lesions on the test set of DIARECTDB1 [20] public dataset. In this application, anchor boxes are of three scales and four aspect ratios to detect red lesions large with imbalances in object sizes and shape variations as well as very small red lesions.

D. Network Training

The proposed method is implemented in PyTorch and training is performed using a workstation with 16 GB GPU and 64 GB RAM. The training is performed using the pre-processed fundus images of the training set of DIARECTDB1 [20] public dataset up to 150 epochs. The learning rate is 0.00001. Area of the regions of interest is very small as compared to size of image and could results severe class imbalance. Therefore, training is dominated by irrelevant background region and the easily classifiable background region lead to poor learning of the model. The focal loss could handle the class imbalance and the network is being trained using hard examples, i.e., red lesions which are difficult to detect as, compared to easy examples, i.e., red lesions which are easy to detect.

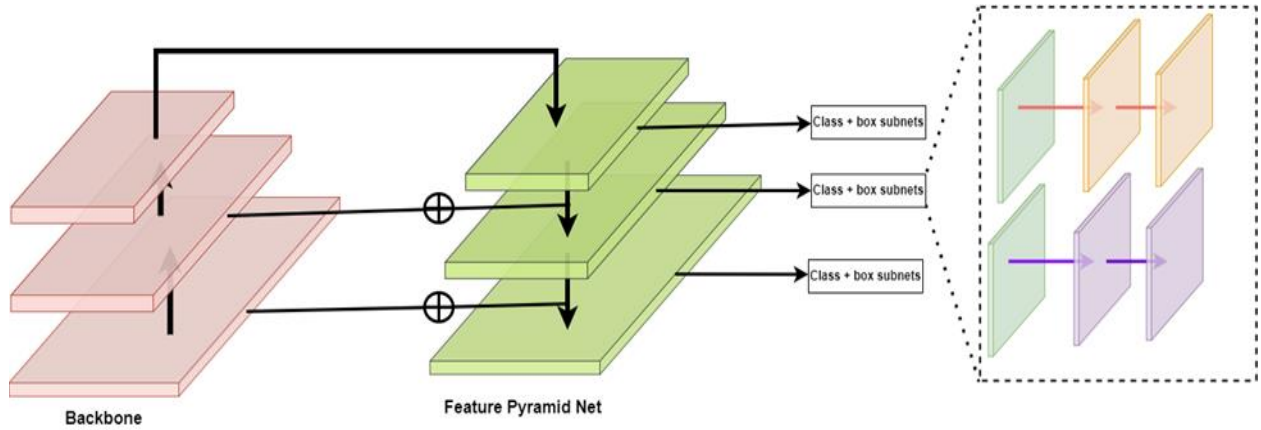

Fig. 3: Multi-Scale Feature Pyramid with Classification and Regression Head for Red Lesion Detection

III. RESULTS AND DISCUSSIONS

The proposed method is compared with method of Seoud et. al. [21] and the methods are evaluated on the publicly available DIARETDB1 dataset [20]. Total 89 fundus images are available in the database and the images are taken using 50-degree field of view. Out of 89 images, 84 images are mild or non-proliferative DR and 5 images are normal. Four expert ophthalmologists annotated several diabetic fundus lesions such as soft exudates, hard exudates, microanneurysm, and hemorrhages and the ground truths are at coarse level. The detection algorithms are evaluated on using those annotations. In this dataset, detection of red lesions is really challenging because of variation in imaging conditions which includes saturation, lighting condition, and different types of blurs. In this experiment, the lesions annotated in fundus image by at least one ophthalmologist is considered as ground truth. The methods have been evaluated on per-lesion basis, where a delineation of all the lesions was provided. The test set of DIARETDB1 dataset [20] is used for the evaluation of methods.

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The performance is analyzed on every single lesion by means of free-response receiver operating characteristic (FROC). In the per-lesion evaluation strategy, sensitivities are plotted with respect to the average number of false positives per image for several operating points. The FROC plot of the proposed method and the method of Seoud et. al. [21] is shown in Fig.4. The results depict that the proposed method outperforms the competing methods. The proposed network is end-to-end trainable at image level with all possible scales and achieves a sensitivity of 0.76 with six false-positive per image on the test set of publicly available DIARECTDB1 database and outperforms the method of Seoud et. al. [21]. Visuals result of the proposed method is shown in Fig.5 and it is observed that red lesions with a wide range of shapes are detected. The performance of detection is better for hemorrhages as compared to microaneurysm. A few vessel-junction has similarity with red lesion and appears as false positives. The method has been evaluated with and without preprocessing, and it is observed that preprocessing has a significant role in performance of red lesion detection.

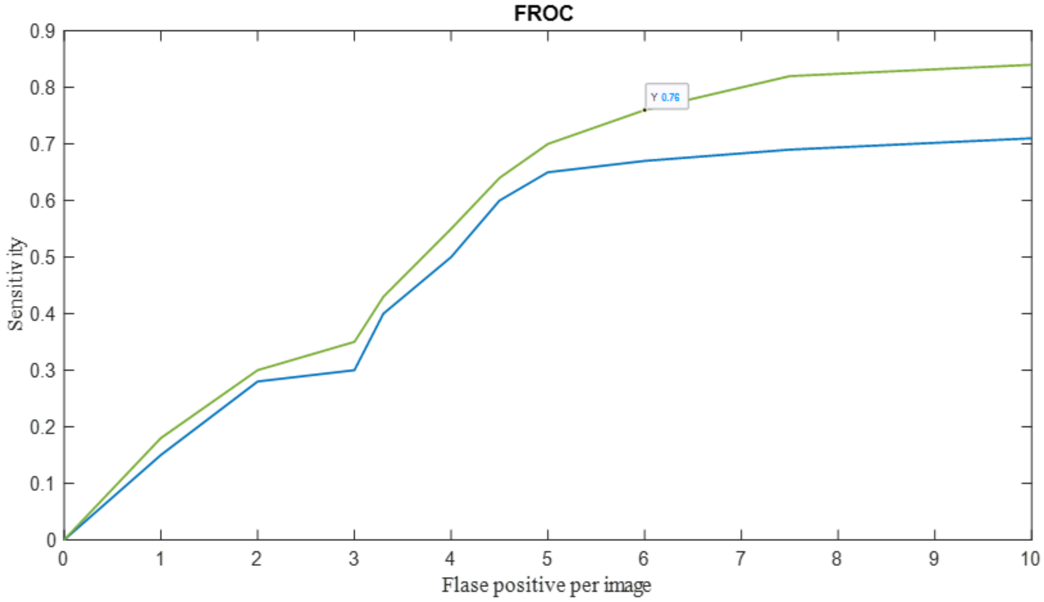

Fig. 4: FROC for the Test Set of DIARECTDB1 Database with the False Positive Per Case Along X-Axis and Sensitivity Along Y-Axis.

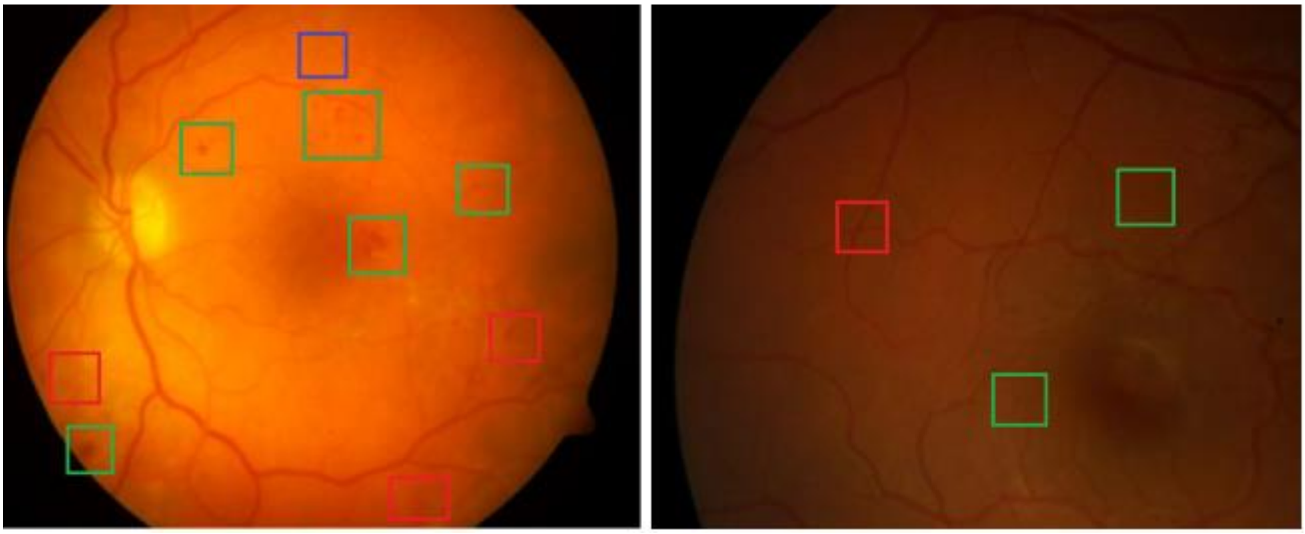

Fig. 5: Visual Results for a Few Test Images of DIARECTDB1 Database, Where True Positives, False Positives, and False Negatives are Marked with Green, red and Blue Boxes.

IV. CONCULSION

Early detection of red lesions in fundus images has immense potential in clinical practice and screening programs. Computer-aided screening of DR is very essential in handling a large number of patients who needs fundus examination. The improved performance of the methods for red lesion detection could improve the screening performance. The proposed network detects red lesions with a fewer number of false-negative and could be a part of DR screening tool. More work is needed to focus on developing red lesion detection methods with a minimum number of false-negative and false-positive and developing robust methods for grading the fundus images for diagnosis of DR. The preprocessing technique could be improved for better visualization of small pathologies in fundus images.

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DECLARATION STATEMENT

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Authors Contributions	All authors have equal participation in this article.

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