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Diabetic retinopathy detection and classification based on deep learning: A review

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Abstract

Diabetic retinopathy can be defined as an eye disease that occurs specifically in diabetic patients and results in damaging the small blood vessels of the retina because of high and low blood sugar. Delayed detection and treatment often lead to blindness, so one of the most significant issues is early detection of this disease, which is necessary for successful treatment. Many deep learning methods have been suggested for diabetic retinopathy detection and classification. Manual inspection of the fundus images to check diabetic retinopathy is highly tedious and time-consuming work. Thus, an automatic method for early diabetic retinopathy diagnosis utilizing the fundus images is very useful tool that helps experts. In this review paper, several deep learning models that are widely used in literature investigated diabetic retinopathy classification will be presented and discussed. In addition, a comparative analysis for classification performance accuracy of diabetic retinopathy using these deep learning models will be reviewed comprehensively. Thus, an automatic approach for early diabetic retinopathy diagnosis utilizing the fundus images is a very useful tool that helps the experts.

Keywords: Diabetic retinopathy, Deep learning, Fundus images, CNN, Accuracy metrics
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1 Introduction

Diabetes represents a very serious and general health problem that happens in the case where the pancreas fails to secrete a sufficient amount of the insulin or the body is not capable of processing it, causing damage too many body organs. At least 33% of diabetics also experience the negative effects of an eye disease associated with diabetes, known as diabetic retinopathy [21]. High sugar in blood harms the blood vessels that feed the retina. Accordingly, eye develops new blood vessels, also different lesions appear on the eye that could lead to blindness in case of not being detected early. Prevention of the blindness from the diabetic retinopathy is a result of the early detection followed by the appropriate treatment [18]. The early diagnoses have been based upon the fundus image. Fundus photography can be defined as a rapid, non-invasive, widely available approach , which represents the most utilized approaches for the assessment of DR extent. Manual detection and determination of DR from images of the fundus requires large workload, high degree of experience and knowledge by ophthalmologists and Due to an increase in numbers of the people who have diabetes in comparison with the ratio of doctors that is 1 doctor to 10,000 patients, the manual

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method is considered uneconomical and sometimes the results are inaccurate, this made the research community look for computer-based systems to assist specialists in the early detection and determination of the degree of disease, that leads to reducing the time, cost and efforts by using the latest advancements in the area of Artificial Intelligence (AI) and an increase of the computational sources and abilities had resulted in the creation of the opportunity for developing applications of Deep Learning (DL) [38] in the rest of the sections of this article, Section 2 includes the introductory information regarding Diabetic Retinopathy, Section 3 will present a series of related works, in section 4 we present different datasets used for detect and classified DR, Section 5 we will present preprocessing technique, section 6 we will present deep learning methods Finally, we conclude this article.

2 Related Work

Many researchers suggested the automatic detection system for features of DR which is useful for the disease early detection and give the appropriate treatment. Researchers attempted to solve this problem using deep learning that have completely transformed the field of computer vision, and recent research had made significant progresses in working on the DR fundus image classifications. Priya and Aruna [33] have proposed using color fundus images a computer-vision-based method for the detection of the stages of the diabetic retinopathy. On a testing set of 250 images, they have made the attempt to extract the features from the raw image with the use of the methods of image processing and fed them to SVM for the binary classifications, reaching a 98% sensitivity, 96% specificity, and 97.60% accuracy. Sanskruti Patel [30] pre-trained CNN models VGG16 and MobileNet-V1 on publically available data-set of retinal fundus images on the kaggle, The accuracy of the test that has been achieved by the VGG-16 was 89.51% and MobileNet-V1 was 89.77%. Li et al. [28] proposes deep transfer learning approach utilizing Inception-v3 network and achieve accuracy of 93.49%, with a 96.93% sensitivity, while the AUC was up to 0.9905.

3 Diabetic Retinopathy

DR happen in half diabetes people when the levels of sugar in the blood high with high blood pressure and high cholesterol levels. Variation in blood sugar results in damaging the small blood vessels in the eyes and may, block them completely. Which makes the eye work to develop new minute blood vessels, but sometimes they are very thin may leak fluid into the retina this leads to appear different lesions types on the image of the retina [37].

3.1 Type of lesions

- Micro aneurysms (Mas) The earliest clinical DR signs and retinal damage. It is small saccular dilations of the capillaries which appear as round dark red spots that have sharp edges in retina background, micro aneurysms reduce vision as a result of the local loss of the functions of the endothelial barrier, which causes leakage and retinal edema [4].
- Hemorrhages (HM) wide accumulations of the blood in the retina, its size greater than 125 micrometer The retina's superficial layers are where hemorrhages begin [4].
- Hard exudates (EX) (yellow spots on retina) when the lipoproteins leakage from plasma. Their margins are sharp and they may be found in outer layers of retina [4].
- Soft exudates (which are referred to as the cotton wool as well) appear like white spots on retina, as a result from the nerve fiber swelling and when an arteriole is closed [4].
- Glaucoma new blood vessels can appear in the iris and start interfering with the normal gradient of fluid outside the eye, putting pressure on the eye. This pressure damages the optic nerve, which is responsible for the transmission of the images from eye to brain and finally blindness [44].

There are 2 main stages of DR, and those are: NPDR (non-proliferative diabetic retinopathy) and PDR (proliferative diabetic retinopathy) based upon presence of the features on retina [41] and these stage are divided into five level (Mild non-proliferative, moderate non-proliferative, Severe non-proliferative, Proliferative diabetic retinopathy) depending on severity. Table 1 shows DR stages and features appears in each stage. Figure 1. The fundus photography images from APTOS2019 Kaggle data-set explain the Normal, Mild, Moderate, Severe, and Proliferative DR stages [43]. Finally symptoms of DR may include (difficult in reading, spots appearance in your vision, shadow in the line of sight, Pain or pressure in the eyes and color perception difficulties) [37].

Table 1: Severity Scale of the Diabetic Retinopathy Disease [37]

Retinopathy level	**Findings Observable**
0= NO DR	No abnormalities
1=Mild DR	Only Micro-aneurysms
2=Moderate DR	More than MAs but less than the severe NPDR
3=Sever DR	Any of the below: • Over 20 intra-retinal hemorrhages in every one of the four quadrants • Prominent micro-vascular intra-retinal abnormalities in one quadrant And no proliferative retinopathy signs • definite venous beading in 2 quadrants
4= Proliferative DR	One or more of: • hemorrhage • Neo-vascularization, vitreous/preretinal

Figure 1: The stage of DR

4 Publicly Available Datasets

The dataset is the foundation of any model used to automated detection, based on DL or ML, or multi-model-based. Most researches use Fundus image for detections and classifications of the DR, these fundus images are taken by specialized fundus cameras to photograph the back of an eye, also referred to as fundus. The peripheral and central retina, optic disc, and macula represent the main structures that are visible on a fundus photograph. This section displays the available fundus images.

4.1 Messidor 1,2

Messidor 1 is made up of 1,200 retina fundus images that have been obtained between 2005 and 2006 [8]. Messidor 2 includes 1058 images from original Messidor data-set, in addition to 690 more images that have been collected in the dept. of Ophthalmology in Brest Univ. Hospital in France between 2009 and 2010 [19]. These datasets are very high quality, with no noise. And each image has an image-level medical diagnosis indicating the severity of Diabetic Retinopathy. On the other hand, their system of custom grading has been incompatible with ICDRS protocol, limiting its applicability and validity.

4.2 Kaggle EyePACS

Which represents the largest and most used public data-set for classification of Diabetic Retinopathy, which contains over 88702 fundus images and has been provided by platform EyePACS for competition of DR Detection that California Health-care has been sponsored it, its format was JPEG with a variety of the resolutions that range between 433×289 pixels and 5184×3456 pixels, which have been collected from a variety of the cameras [15].

4.3 E-ophtha

It is publicly available data-set includes 463 images divided into 148 images with MA, 47 exudates and 268 is normal images. It's mostly utilized in literature for the development of segmentation algorithms, not for the classification. As a result of a small number of the images that are contained in this data-set [7].

4.4 ODIR-2019

It is a public dataset includes 8000 images of the retina fundus that have been collected by using Fundus camera (Canon), Fundus camera (Kowa) and Fundus camera (ZEISS), in chine and its format is JPEG [11].

4.5 APTOS 2019(Asia Pacific Tele-Ophthalmology Society)

It represents the 3rd largest dataset, it consists of 5590 images which had been divided into train datasets and testing data sets, which have been collected by the aravind Eye Hospital in India's rural area using a digital fundus camera. One of its drawbacks is a large class imbalance, particularly for the Severe NPDR class that only includes 193 images in the PNG format [4].

4.6 FGADR

The FGADR data-set contains 1842 images with pixel-level DR-related lesion annotations in addition to 1000 images with the image-level labels. The suggested data-set allows for the extensive study of the DR diagnoses and is only available for the non-commercial research purposes. The majority of images in FGADR data base was collected from some UAE hospitals and is a characteristic of the Inception Institute of AI, Abu Dhabi, and UAE [26].

4.7 DRiDB (Diabetic retinopathy image database)

This database includes 50 fundus images as well as annotations of the structure of retina's vessels and optic disc, any present pathology cases, neo-vascularizations and disease grading. It has been obtained by the university hospital in Zagreb [32].

4.8 DDR

Contains 12522 images, and it is the 2nd largest data-set when considering the task of classification, however, it's a relatively new data set that hasn't been widely utilized yet. The information was gathered from 147 hospitals in China between 2016 and 2018. However, there is a significant disparity between the DR classes [26].

Table 2: Retina Fundus image details

Name	Number of images	Resolution	Format	Tasks
MESSIDOR 1 [8]	1200	1440×960	TIFF	DR and DME grading
MESSIDOR 2 [19]	1748	varying	TIFF	DR and DME grading
KaggleEyePACS [15]	88702	varying	JPEG	DR grading
E-ophtha [7]	463	varying	JPEG	Lesion detection
ODIR-2019 [11]	8000	varying	JPEG	DR, HT, AMD and Glaucoma
APTOS 2019 [4]	5590	varying	PNG	DR grading
FGADR [26]	1842		JPEG	DR and DME grading
DRiDB [32]	50	768×584	BMP files	DR grading
DDR [26]	12522	varying	JPEG	DR grading and lesion segmentation

5 Preprocessing Technique

The step of the pre-processing is a highly important step in the processing of the medical images. The goal of this study is examining literature in prior process of the digital imaging, in fundus image analysis area for the extraction of the pathologic and normal retinal features within a DR context. Due to the difference in the size of the images used to train the models, most researchers have resized the fundus image datasets used in their research and Exclusion of the background pixels and processing of only fundus pixels by using fundus mask (i.e. a binary image of one fundus image resolution whose positive pixels are corresponding to foreground area), as in ref [9, 13, 14]. In some works, such as [42] RGB images converted to greyscale. Histogram equalization and contrast Limited Adaptive Histogram Equalization (CLAHE) have been utilized for highlighting foreground from background [2, 25]. The image smoothing approach has been presented for the purpose of suppressing the noise or any other small fluctuations. M. Anto Bennet et al. [5] have utilized a median filter for removal of the salt and pepper noise. Feng Li, et al. [28]. Exudates appear brighter in the green layer in comparison to blue and red channels in the fundus image. To eliminate high frequency components from image, Gaussian filtering was applied separately to the red, green, and blue components in RGB images. Data augmentation methods have been used so as to improve model's robustness and accuracy as a result of a lack of balanced and rich data-sets. Such methods can include image rotation, rescaling, shearing, shifting, and flipping, as well as color and brightness enhancement [1, 34, 40].

6 Deep Learning Models

Deep learning (DL) represents a subset of AI, it employs multiple layers for the extraction of the higher-level features from inputs, picture examination, characterization, classification, and identification. DL was recently widely utilized in the DR detection and classification [22]. The term "deep" typically indicates the number of the stored layers in a CNN. Because the conventional NNs only have 3 layers: 1 input layer, 1 hidden layer, and one final output layer, they have been referred to as Shallow (or Feed-Forward) NNs when the network content more than one layer known as deep neural network. CNN are one of the most widely utilized networks in majority of DL techniques for detection and classification of the diabetic retinopathy [42]. Inspired by human vision, they mainly include 3 types of the layers, which are: convolutional, pooling and fully connected (FC). The convolutional layer performs the extraction of image features, the result of which is given to pooling layer, where the number of the feature extraction is computed. The fully connected layer has been categorized as DL algorithm which unlike feed forward neural networks accepts 2D arrays as their input; it can have upwards of 150 layers so CNN utilizes the convolutional layers which extract the features from the picture naturally [2]. This section presents an overview of convolution neural network types that were used in detection and classification of the diabetic retinopathy.

Google NET The accuracy of the model may be enhanced by increasing its complexity. On the other hand, a large number of parameters that cause overfitting will significantly increase amount of computing required. Which requires a massive increase in the number of parameters with increasing the sparsity of CNN structures Google net maintains computational performance, trained the model with efficient memory, low computational to perform makes fast diagnosis and correct detection for a patient [38].

UNet Due to its capability for the preservation of the image structural integrity, UNet is better suited for segmentation than traditional CNNs. UNet architecture has fewer parameters and it's faster when compared to the conventional CNNs because it processes an image in a single pass. And it requires significantly less data compared to the conventional CNNs which is critical in the medical image analyses, where the number of the available images was limited [17].

AlexNet Proposed by Alex Krizhevsky in 2012. Which is one of the most CNN models use to significantly improve ImageNet accuracy when compared to standard approaches? It represents the base of today's deep CNN because of its historical importance. Whereas the AlexNet utilizes the GPUs in order to accelerate the computation, the authors have made their CUDA code for the training of the CNNs on GPU that is available for download. AlexNet is comprised of 60 million parameters, 630 million connections, and 650,000 neurons. It has 5 convolutional layers, the first three of which are followed by the second three [35].

VGGNet Can be defined as a deep CNN that has been developed by the Univ. of Oxford Vision Geometry Group and Google DeepMind to investigate correlation between depth of a CNN and its efficiency. It can construct a convolution that consists of 16–19 deep layers NN through continuously stacking 3×3 small convolutional kernels and 2×2 max pooling layers. In comparison with the earlier state-of-art network architecture, the VGGNet had achieved a considerable reduction of the error rate, as well as 2nd place in ILSVRC 2014 competition category and 1st place in positioning project. The 3×3 convolutional kernels and 2×2 pooling cores are used in all VGGNet's articles for the improvement of the performance through the continuous deepening of the network structure. A list of resources is provided below [24].

ResNet (Residual Neural Network). It trained 152 DNNs to win ILSVRC 2015 championship and achieve 3.57 percent error rate classification for top-five classes using the Residual Unit, which is have parameters less than the number of parameters in VGGNet. Highway Nets, at the heart of ResNet, utilizes skip connection in order to arbitrarily allow some input into (skip) layer for the purpose of integrating information flow while avoiding information loss and gradient vanishing problems (also suppressing generation of some noise). Furthermore, suppressing noise necessitates model averaging, which keeps the model's balance between generalization and training accuracy. The most prosperous [36].

A comparative analysis for classification performance accuracy of diabetic retinopathy using most common DL models that have been utilized in the literatures that were investigated will be summarizes and reviewed comprehensively in the following Table 3:

Table 3: comparative of different methods for detecting DR

Researcher Name	Dataset	Pre-Process Method	Feature Extraction Method	Classifier	Performance Accuracy
Michael David Abràmoff et al. [17]	Messidor2 1748 images	–	Lesions detection	CNN	Sensitivity=96.80% Specificity= 87% AUC= 0.98
Piotr Chudzik et al. [6]	E-Ophtha ROC (100) DIARETDB1	Extraction of fundus image green plane, generation of a mask for the pixels outside FOV, Noisy areas are eliminated by morphological operations and the image is cropped to size to 130	MA only	CNN	AUC=0.562 AUC=0.193 AUC=0.392
Wei Zhang et al. [42]	Their Own dataset (13767)	Rwmove black background, convert to gray, enhance pixels, AHE and Augmentation	Lesions detection	CNN Xception, ResNet50, InceptionV3, DenseNets and InceptionResNetV2	Accuracy=96.50% Sensitivity =98.10% Specificity= 98.90%
Yi-Peng Liu et al. [29]	Their Own dataset (60,000), and STARE (131)	Augmentation Resizing to 299×299	–	CNN, ResNet, SeNet and DenseNet	ACU=0.9823% Accuracy=94.23% Sensitivity=90.9% Specificity=95.7% STARE ACU=0.951% Accuracy=90.84
X. Li et al. [27]	Messidor IDRiD	–	–	CNN (ResNet50)	Messidor ACU=96.3% Accuracy=92.6% Sensitivity=92% IDRId Accuracy=65.10%
Rishab Gargeya, Theodore Leng et al. [12]	75,137 publicly available images of the fundus	resizing images to 512×512, cropping inner retinal circle and padding it to square and Augmentation	Lesions detection	deep convolutional neural networks	AUC=0.97% Sensitivity=94% Specificity=98
Dutta, Suvajit et al. [10]	Fundus images from kaggle 2000 images	Convert to gray scale, apply different filter to enhance the image	–	DNN, CNN (VGGNET architecture), BNN	Accuracy BNN =42% DNN= 86.30% CNN=78.30%

7 Detection lesions of DR

Detection the features of diabetic retinopathy from fundus image are very significant in the automated detection of DR. Hu etal. [20] have proposed a CNN and CRF-based approach for the retinal vessel fragmentations. A multi-scale CNN has been utilized in the first segmentation step for the generation of probability map and gathering more information concerning the retinal vessels, whereas the CRFs have been utilized in the 2nd step for the final binary segmentation that is helpful in detecting cardio-vascular edges. Hatanaka etal. [16] have suggested an MA detector which merges 3 current detectors which include double-ring filter, shape index based upon Gabor filter and Hessian matrix. The proposed model has been made with 2-layer DCNN and 3-layer perceptron. In the 2-level DCNN, early DCNN is for the primary MA identification and secondary DCNN is for the reductions of FP. The approach has been conducted on DIARETDB-1 data-base and it was able to obtain a sensitivity of 84% of 8 FPs for each image. A unified method for computerized HEMs' identification from retinal images had been presented by Kaur etal. [23] This paper presented effective and adjustable approach for the identification of HEMs. The research includes studying 4,546 blobs from 50 images of the retina picks up from data-base. A united method of the morphological operation and RF-based classifications has been deployed. In [39], an approach for the enhancement and boosting of CNN training for the review of clinical images through energetically selecting the incorrectly classified negative samples throughout the training has been suggested. Weight values have been allocated to the training samples and valuable samples have been more possible to be involved in additional repetition of CNN training. The proposed method has been assessed and compared through the training of a CNN using a selective sampling approach. EXs system of identification has been proposed by Prentasic and Loncaric, [31] utilizing DCNN. In addition to that, the DL facilitates the architectural landmark identifications. The planned approach mainly identifies EXs from the images of retinal fundus. for incorporation of a high level of anatomical information concerning potential locations of exudate.

7.1 Performance Metric

The performance evaluation metrics that are well known, and utilized for the purpose of assessing the efficiency of the algorithms and classification are accuracy(percentage of the images that had been correctly classified), specificity(which represents percentage of the normal images that have been classified as normal), sensitivity (percentage of the abnormal images which had been classified as abnormal), and AUC (which represents a graph that has been created through the plotting of the sensitivity against the specificity). And these calculate by using these functions [3].

Table 4: Performance evaluation metric

1	Specificity $\frac{1}{4}TN/(TN\ FP)$	• True positive (TP) denotes the number of disease images that classified as disease • True negative (TN) represents number of the normal images which have been classified as normal, whereas the false positive (FP) represents number of normal images that have been classified as a disease.
2	Sensitivity $\frac{1}{4}TP/(TP\ FN)$	• False negative (FN) represents number of the disease images which have been classified as normal.
3	Accuracy $\frac{1}{4}TN\text{Þ}TP/(TN\text{Þ}FN\text{Þ}FP)$	

8 Conclusions

Diabetic retinopathy represents a serious complication of the patients who have diabetes mellitus that causes progressive retinal damages and even blindness. Automated DR detection systems are highly important in detecting DR early on, reducing the time that is needed for the determination of the diagnoses, saving money and time, and allowing patients to be treated faster. The type of lesions which occur on retina determines the stage of DR. This paper explain the common available datasets, preprocessing technique used to enhance the fundus images, the most recent DL-based automated methods for the detections of the diabetic retinopathy and performance metric.

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