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An overview of deep learning techniques, datasets, architectures, and assessment metrics for automated diabetic retinopathy detection and grading systems

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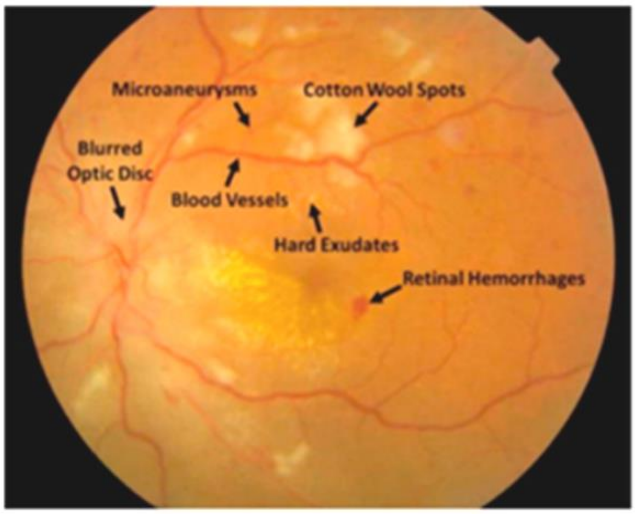
Abstract : Damaged blood vessels in the retina, a light-sensitive tissue located at the back of the eye, cause diabetic retinopathy, an ophthalmological disorder that damages the eyes. The blood must keep entering the eye's retina. The tiny blood arteries provide the retina with blood. High blood sugar levels might cause damage to the retinal blood vessels. Weak, readily bleeding blood vessels that were formed from scar tissue on damaged blood vessels are the cause of diabetic retinopathy. Diabetic Retinopathy (DR) may initially result in mild visual impairments or no symptoms at all. If diabetic retinopathy patients wait longer, they will lose their vision. Vision loss can be prevented by identifying and treating the problem early. Proliferative and non-proliferative are the two primary stages of this sickness that an ophthalmologist can identify. Non-proliferative diabetes comes in three stages: mild, moderate, and severe. Because diabetic retinopathy is asymptomatic, it necessitates thorough and systematic examination of the retina. Optimized DR stage grading is provided by Deep Learning models employing retinal fundus images, which aids ophthalmologists in their work. Deep learning techniques, datasets, evaluation metrics, and DR detection and grading systems are all covered in this overview.

***IndexTerms*—Diabetic Retinopathy, Deep Learning, classification**

1. INTRODUCTION

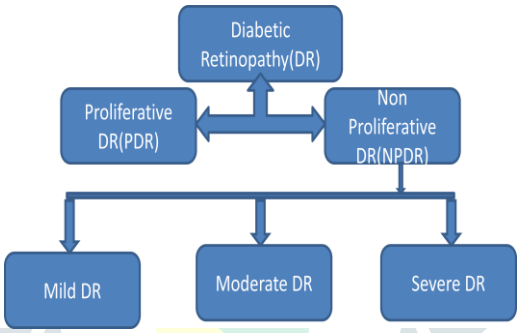
Diabetic Retinopathy (DR)[1] is a medical condition which effects the eyes and can be triggered by damaged blood vessels in the retina. Diabetic retinopathy (DR) begins through low blurred vision or no symptoms at all. If the eyes are affected prolong the period with DR, it will lead to blindness.A world wide survey[2] projected that approximately 600 million people will have diabetes by 2040 and one third of them may have vision loss. National Diabetic Retinopathy Rapid Assessment of Avoidable Blindness (RAAB) Survey 2015–2019, under the aegis of the Ministry of Health and Family Welfare, Government of India[3] says that the prevalence of DR among diabetics reasonably high figure as 16.9%.Continuous scanning of retina is vital for treating the DR at the earlier stage which reduces chances of the vision loss [4]. A non- invasive technology, helps the ophthalmologist to determine DR severity levels is 'fundus imaging'[5]. Taking Images of eye retina by using the fundus camera is known as 'fundus imaging'. DR detection[6] using computer technologies are more effective than the traditional diagnoses[7] of DR using fundus images. Especially the Deep Learning approaches gives promising results on DR detection and grading. The deep learning models are developed to detect lesions on the fundus images of eye retina. On the Deep Learning DR detection approaches, the detection of Lesions such as microaneurysms (MA), hemorrhages (HM), and hard and soft exudates (EX) are considered for grading the severity of the DR and shown by the following Figure1.

Figure 1. Representation of a various lesions on fundus retinal image.



Leaks of blood or fluid on the retina cause Microaneurysms (MA), which are the first clinical signs of diabetic retinopathy disease. On the retina, they are the little red spots[8]. They would be less than 125 µm and have strong borders surrounding them. Hemorrhages (HM) are defined as patches on the retina that have an irregular border and can measure up to 125 µm in diameter. HM can be divided into two categories: blot (deep HM) and flames (superficial HM).Hard exudates (EX) are bright yellow patches on the eye, while soft exudates (cotton wool) are white spots caused by swelling of the nerve fibers. There are two types of depression research: Proliferative (PDR) and Non-Proliferative (NPDR). Additionally, as Figure 2 illustrates, NPDR is categorized as mild, moderate, and severe.

Figure 2: Various levels of DR



The mild stage of DR mostly contains MA. The moderate DR caused by HM and the severe stage of DR consists of Exudates[9]. The following **Table 1** shows the levels of DR according the lesions present in them.

Table 1: Different states of DR accordance with lesions

Level of DR	**Lesion presents/Existence of abnormalities**
No DR	Lack of lesions
Mild Non Proliferative DR	It only has MA.
Moderate Non Proliferative DR	More than only MA and DR, which are not serious
Severe Non Proliferative DR	Any of the following combinations: more than 20 intra-retinal HM. abnormalities in the four quadrants of the retina.
Proliferative DR	Any one of the following: Vitreous HM The creation of new blood vessels with all the defects of the retina.

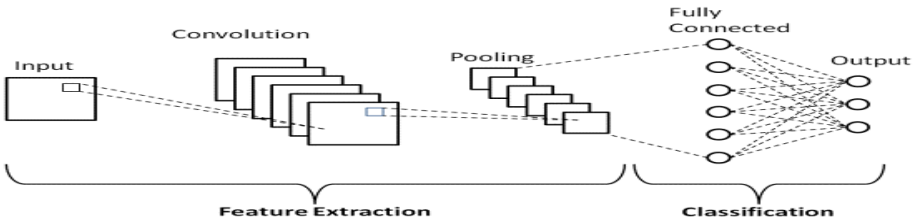
In most developing and industrialized countries, especially among working communities have the visual impairment because of DR[10]. The presence and the severity of the DR through a visual assessment by direct examination and evaluation of the eye retinal images (fundus image) by the Ophthalmologists which is expensive and time consuming process[11]. So cost effective computerized technologies are urgently needed to diagnosis DR with it's severity grading. In order to assist ophthalmologists in identifying DR as swiftly is feasible, researchers are developing an automated diagnosis and grading system for DR using digital image processing, artificial intelligence, machine learning, and deep learning.

2. Deep Learning Approaches for DR Detection:

Deep Learning (DL) is one of the computer-aided medical diagnosis method[12] and its various applications are classification, segmentation, detection, retrieval, and registration of the images. It is a branch of Machine Learning which includes hierarchical layers of non-linear processing of unsupervised features learning and classifying patterns[13].

DL is frequently used in the detection and categorization of DR. Effective feature learning of input data is achieved by DL models, even when numerous heterogeneous sources are combined [14] during training. Auto encoder, sparse coding [15], restricted Boltzmann Machines and convolutional neural networks (CNNs) are mostly used DL- based methods. In medical image analysis[16], CNNs are widely used more than the other DL-methods especially in DR detection and grading. ConvNet or Convolutional Neural Network[17] (CNN) is a special type of DL algorithm developed for the functions that are needed for object recognition, including image classification, detection, and segmentation. This feature of CNN makes it as N efficient neural network for medical diagnosis. The following Figure 3 shows basic architecture[18] of CNN.

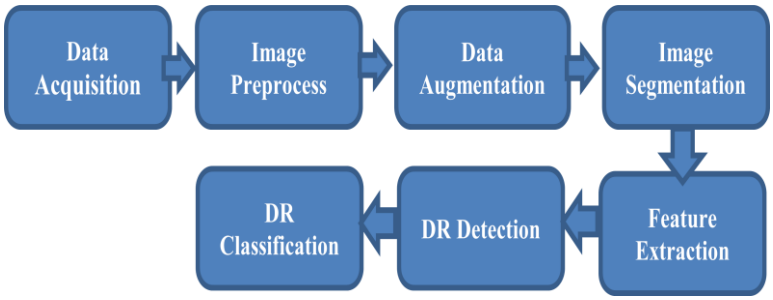
Figure 3: Convolutional Neural Network with it's layers



Convolutional, pooling, and fully linked layers make up CNN's three layers. The first layer that is utilized to extract various data from the input images is the convolutional layer. It carries out the convolutional mathematical operation between the input picture and a filter with a specific size of MxM. The dot product between the filter and the portions of the input image with regard to the filter's size (MxM) is calculated by swiping the filter over the image. This layer produces a feature map, which is supplied to subsequent layers so they can extract additional features from the input image. The pooling layer[19] is the next layer in the convolution layer, and its purpose is to minimize the feature map's size in order to lower computing costs. On the Fully Connected Layer, the classification process starts using the output image from the earlier pooling layers. The activation function is one of the CNN model's most crucial parameters. They determine whether an input to the work is significant enough to predict using mathematical operations, and they are used to learn and estimate any form of continuous and complicated relationship between variables in the network. Selected activation function influences the learning rate and accuracy of a DL Model[20]. SoftMax, Swish, Mish, Tanh, Sigmoid, Relu, LRelu, ELU, SELU, Logsin, Sinc, Wave Rootsig and Logsigm are different activation functions used by researcher for DR detection DL Models.

Typically, gathering the dataset and doing the required preprocess steps to sharpen and enhance the photos is the first stage in the process of utilizing DL to detect and grade DR images. Subsequently, as illustrated in Figure 4, these preprocessed images are fed into the DL technique to extract the features and categorize DR.

Figure 4: Processing Steps of DL Model on DR Detection & Classification



3. Data Sets:

The performance of CNN increases when the number of training data increase [21] due to the increase in the learned features. Public and private DR image data sources to train DL model are available on online. Below Table2 shows public dataset and Table3 shows private datasets.

3.1. Public Dataset:

Table 2: Public DR dataset with number of fundus images.

Sl. No.	Name of the Dataset	Number of Fundus Images available in the Dataset
1	Kaggle	88702
2	E-Ophtha	463
3	Retinopathy Online Challenge (ROC)	100
4	DIARETDB1	89
5	STARE	400
6	DRIVE	40
7	Messidor-2	1784
8	CHASE-DB1	28
9	FAZ (Foveal Avascular Zone)	60
10	ARIA	143
11	DR2	520
12	DR1	234
13	DRiDB	50
14	DIARETDB0	130

3.4 Private Datasets:

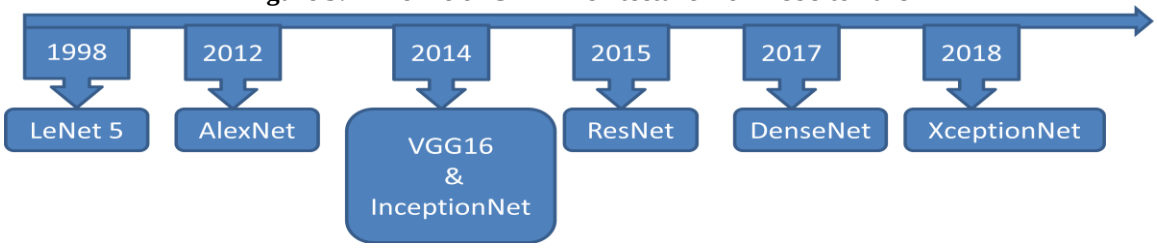
Table 3: Private DR dataset with number of fundus images.

Sl. No.	Name of the Dataset	Number of Fundus Images available in the Dataset
1	HUPM, Spain	250
2	KMCM, India	340
3	LECHC, India	122
4	SNDRSP, Singapore	197085
5	JMU	9939
6	CLEOPATRA	298
7	Moorfields Hospital, London	21536
8	TMUMDH	414

4. CNN architectures:

Different CNN architectures have different number of layers and different activation function. The **Figure5** shows the timeline from 1998 to 2018 for different CNN architecture.

Figure 5: Timeline of CNN Architecture from 1998 to 2018



LeNet architecture was developed by Yann LeCun[22] in the year 1998. This CNN architecture has 5 layers with learnable parameters. So named as LeNet 5. This CNN has 3 set of convolution layers with a combination of average pooling layers. Using 32X32 grayscale images, using Gradient Based Learning, it classifies the images in to respective classes.

After a sequence of investigations and studies, Yunlei Sun[23] et al. choose LeNet-5 as their basic model as it is a most classic and earliest model, it can be used in small data sets and it is more suitable for one Dimensional data. Their model achieve a training accuracy of 99.85% and a testing accuracy of 97.56%. To automatically extract features of DR, K Priyanka[24] et al. used the convolutional neural networks (CNN) model, or Lenet-5 architecture. DR Detection Model preprocessing involves applying edge detection, thresholding, and data augmentation to the model. With an average accuracy of 97%, recall of 22%, and f1-score of 65%, their suggested model performs well.

AlexNet[25] CNN architecture was developed by Alex Krizhevsky in 2012, It contains 5 convolutional layers, 3 max-pooling layers, 2 normalization layers, 2 fully connected layers and 1 softmax layer. Input images size of this architecture is 227 X 227 X 3.

An algorithm proposed by T. Shanthi and R.S. Sabeenian [26] was verified with the Messidor database. Their work focuses on combining AlexNet with appropriate Pooling, Softmax, and ReLU layers to classify DR fundus photos based on the disease's severity in order to achieve a high degree of accuracy. With their suggested model, classification accuracy of 96.6% and 96.2%, 95.6% and 96.6% was achieved for DR pictures of diabetic retinopathy's stage 1, stage 2, and stage 3.

Oxford University researchers A. Zisserman and K. Simonyan created the VGG16[27] architecture. It supports up to 16 layers and can categorize images into 1000 different object categories, such as mice, keyboards, animals, and pencils. The input image size of this architecture is 224X224. This CNN architecture was submitted in IVSVRC - 2014(ImageNet Large Scale Visual Recognition Challenge in the year 2014).

In Inception[28] a total of 27 deep layers in the CNN architecture. This network's GoogLeNet variant achieved breakthrough results in the ImageNet Large Scale Visual Recognition Challenge 2014 (ILSVRC14) computer vision classification task. The Inception V1, V2, V3, and V4 versions are the most often used.

ResNet, an acronym for residual networks, was first proposed by He and colleagues in 2015 [29]. With 18 deep levels, ResNet18 has a 72-layer architecture. Gao Huang and colleagues created DenseNet[30] in 2017. CNN layers are extensively connected in it. Each layer's output is coupled to every layer that comes after it in a dense block. in order for the layers to form with dense connection. That gave rise to its name. The network parameters are greatly lowered by this CNN.

Xiaoliang Wang[31] et al. used InceptionV3, VGG16, and AlexNet for their DR detection model; InceptionNet V3 yielded data with higher precision. AlexNet obtains 37.43%, VGG16 achieves 50.03%, and InceptionNet V3 achieves 63.23% using the Kaggle dataset that they used.

5. Evaluation Measures

Evaluation Measures are important to evaluate the DL Model's accuracy. Here are a few of them:

False Positive Rate (FPR):

The proportion of cases in which the segmentation of retinal images yields positive results instead of negative ones. It is going to be:

$$FPR = \frac{FP}{TN + FP}$$

False Negative Rate (FNR):

It is the proportion of cases in which the segmentation of retinal images yields negative results instead of positive ones. It is going to be:

$$FNR = \frac{FN}{TP + FN}$$

Accuracy (A):

It is the proportion of numerous blood vessel pixels to appropriately allocated pixels in the segmented retinal image. It is going to be:

$$A = \frac{TN + TP}{TN + FN + FP + TP}$$

Specificity (Spec):

Specificity quantifies the percentage of True Negative (No DR) data that the model accurately detects. It goes by the name True Negative Rate (TNR) as well. The increased Specificity of the model suggests that the majority of the negative (No DR) the results have been correctly identified by the model. That's going to be

$$Spec = \frac{TN}{FP + TN}$$

Sensitivity (Sen) /Recall Rate:

Sensitivity measures how well a DL model can detect positive instances (other than No DR). In other words, it measures how likely you will get a positive result when you test for something. It comes by the term True Positive Rate or Recall as well. It is going to be:

$$Sen = \frac{\mathrm{TP}}{\mathrm{FN} + \mathrm{TP}}$$

F-Score:

Test accuracy is measured by the F-score. The ratio of legitimate positive findings to the number of positive outcomes is calculated.

$$F - Score = 2X\frac{Recall + Precision}{Recall + Precision}$$

ROC:

It is a graph that depicts the performance of the classifier at every possible threshold. The graph shows the positive rate on the Y-axis and the false positive rate on the X-axis.

Area Under Curve (AUC):

AUC measures a deep learning model's capacity to distinguish between classes during classification.

Confusion Matrix:

To determine the successes and failures of our DL Model, we employ a confusion matrix. It is a matrix that is used to assess how well a classification model performs with a certain test set. It can only be ascertained if the testing data's initial values are known. Since the model's performance defects are shown as a matrix, it is sometimes referred to as an error matrix [32].

Positive Predictive Value (PPV):

It can be determined by the probability of precisely segmented fundus images.

Negative Predictive Value (NPV):

It can be determined by the probability of fundus images that are incorrectly segmented.

False Discovery Rate (FDR):

The rate of an expected portion of errors is known as the false positive rate.

Researches on Diabetic Retinopathy Diagnosis using DL can be categories as following:

Binary Classification, Multilevel Classification, and Lesion localization.

In above foresaid categories feature extraction algorithms play a vital role. Researchers are contributed lots of DL Models using Feature Extraction. Following sections describes all the above categories of research on DR Diagnosis.

6. Binary Classification

This section elaborates the proper statistical/econometric/financial models which are being used to forward the study from data towards inferences. The detail of methodology is given as follows.

Binary Classification DL Models diagnosis DR in to two classes: DR and NoDR. This section reviews the DR detection models using Binary Classification.

The proposal of Quellec et al. [33] uses Kaggle dataset with 88,702 images, DiaretDB1 dataset with 89 images and E-Ophtha private dataset with 107,799 images. They resized and cropped the images as 448x448 pixels images in processing. On the Alexnet CNN architecture they classified them as referable DR and Non – referable DR using MA, HM, soft and hard EX detection on CNN. That proposal of has ROC curve of 0.954 in Kaggle dataset and 0.949 in E-Ophtha private dataset.

The research Model of M.T. Esafahan et al. [34] classifies the images into two classes as normal and DR on the 35000 images of Kaggle using ResNet34 Architecture. They preprocessed the images with set of preprocessing techniques which includes Gaussain filter, weighted addition and normalization to improve quality of the images with 512x512 pixels. They achieved an accuracy of 85% and sensitivity of 86% on their proposed model.

The CNN Model proposed by R. Pires et al. [35] determined referable DR and Non referable DR. Their CNN Model contains 16 layers allows 512x512 pixel images on trainng. It uses dropout and L2 regularization to reduce overfitting. Kaggle Dataset used to train the model and tested by Messidor-2 and DR2 dataset. Data augmentation was used to balance the classes of training dataset. That Model have an area under ROC curve of 98.2% when testing the Messidor-2.

H. Jiang et al.[36] built a CNN model which integrated three pretrained CNN models, Inception V3, Inception-Resnet-V2 and Resnet152. These pretrained model's weights are updated by using Adam optimizer. The proposed Model classify the 30,244 images of their own dataset as referable DR and Non referable DR. The images were enhanced, augmented and resized as 520x520 pixel images. The accuracy of 88.21 and area under curve(AUC) of 0.946 was obtained by this model.

A weighted paths CNN (WP-CNN) model was developed by Y.Liu et al. [37] for detecting referable DR and Non referable DR images over 60,000 labelled images of their own dataset. The normalized and resized 299x299 pixel images were fed in to WP-CNN with different weighted paths that merged in averaging. This WP-CNN contains 105 layers and achieves 94.23% of accuracy on their own dataset and 90.84% in the STARE dataset.

7. Multilevel Classification

The DR Detection Models which diagnosis DR with more than two classes fall under this category. M. Abramoff and his team members[38] takes Messidor-2 dataset with 1748 retinal images and proposed a DR detection model which classify DR using Random Forest Classifier. Their model detect DR with 3 stages: No DR, referable DR and vision threatening DR. This proposed model considered images of mild DR as No DR and five stages of DR are not considered. This model has sensitivity of 96.8% and specificity of 87.0%.

W. Zhang et al.[39] proposed DR diagnosis model with their own dataset which contains 13,767 images. Their model grouped the images in to four classes. The images were cropped and improved the images by a contrast stretching algorithm. They applied pretrained CNN architectures: ResNet50, InceptionV3, InceptionResNetV2, Xception and DenseNet to detect the DR. This model obtain the specificity of 98.9% and sensitivity 98.1% and achieves the accuracy of 96.5%.

Using AlexNet, VGG-16 and SqueezeNet architecture and MESSIDOR dataset of 1200 images Mobeen-ur-Rehman et al.[40] designed a DR classifying model. Their model classify DR with four stages. MESSIDOR dataset images were cropped and resized with 244X244 fixed sized pixels. They achieved the model accuracy of 98.15%, specificity of 97.87% and sensitivity of 98.94%.

With kaggle dataset H. Pratt et al.[41] proposed model to classify the DR images with five DR stages. Their CNN Model contains 10 convolutional layers, 8 max pooling layers and 3 fully connected layers. The proposed model produce the accuracy as 75 %, specificity as 95% sensitivity as 30%.

Using public IDRiD dataset and Messidor Dataset X.Li et al.[42] proposed a DR classification model which classifyies DR with five stages. The dataset images were argumented, normalized, resized and then feed in the model with ResNet50 CNN architecture. Their model achieves semsitivity of 92% and accuracy of 92.6% for Messidor and accuracy of 65.1% for IDRiD dataset.

8. Lesion localization

Lesion Localization based DL Models detect the lesion on the fundus image and localize the lesions on the retinal images. The proposed Research work of Waleed M. Gondal[43] classifies diseased and healthy images with AUC of 0.954 on the DiaretDB1. They uses weakly supervised object localization method to localize the lesions on the retina. They adopted CNN Architecture of Antony and Braggymann. Their model has sensitivity of 97.6%. They used two publically available dataset Kaggle Diabetic Retinopathy Dataset and DiartDB1. On Kaggle Dataset they used 80% images for training and 20% images for validation. DiaretDB1 dataset is used to validate the lesion level detection. They applied Batch Normalization in each convolutional layer during the training process to achieve faster training convergence with higher learning rates. They also applied regularization within their Network to avoid overfitting.

Gabriel TozattoZagoet et. al.[44] designed a Deep Network patch based Model to detect DR using Red Leision localization Method. They trained a Model on Standard Diabetic Retinopathy Database calibration level1 (DIARETDB1) and is tested on several database, especially on Messidor. It produces AUC as 0.912 and sensitivity of 0.940. Most of the researches use CNN globally on the images without any detection of regions, but the author and his team split the retinal images in to patches which to constitute the input to the network. That patches extracted from an image that are used to provide a DR Diagnosis.

Wejdan L. Alyoubiet et. al.[45] Proposed Deep Learning Model which classifies DR stages in to five:NoDR, mild DR, Moderate DR, Severe DR and Proliferative DR and also localizes the leision on the retinal surface. This team developed two models CNN512 and YOLOV3. They uses CNN512 to classify the five stages of DR and YOLOV3 architecture used to localize the DR lesions as a proposed model. This proposed model has an accuracy of 89%, sensitivity of 89%and specificity of 97.3%. They used DDR and APTOS Kaggle 2019 public dataset.

Using VGG16, ResNet-50, InceptionV3 and Inception ResNetV2 Samuel ofosu Mensah, Bubacarr bah, and Willie Brink proposed a DR detection CNN model[46] towards localization of lesions in retinal images. They used the post-attention technique called Gradient – Weighted Class Activation Mapping(Grad-CAM) in their model. They found out InceptionV3 obtain the high classification accuracy as 96.07% and localize lesions faster and better.

9. Challenges

Due to the poor quality of retinal images, extracting the DR features for image analysis process is challenging one. Low contrast, uneven illumination, presence of noise and color variation affects the prominent detection of DR and its classification. For the better detection[47] of DR lesions such EX, MA, HM on the retinal images, the image preprocessing techniques are required which raises the computational cost. For high performance and high accuracy the training phase of DL model development requires Big data which are in high volume, high velocity, high variety and high veracity. Handling the Big data is another big challenge. Data taken from a single repository is not enough for efficient training so Big data taken from different repositories like kaggle, MESSIDOR, APTOS etc., are raw fundus images that requires efficient preprocessing will raise the computational cost. Single classifier based DL Model may have low bias and high variance in making predictions. So Multiple classifier based predictions are prominent in DR detection and classification. Multiple classifier engaged DL models require high computational memory and high cost. High computational memory devices such as Graphical Processing Unit(GPU) required for high performance DL model with bigger sized neural network architecture, evolutionary feature extraction algorithms, feature concatenation techniques, optimization techniques and large ensemble network will leads to high cost.

10. Conclusion

DR is a significant medical disorder rooting to blindness which is of absolute concern, and DL techniques can have be a valuable role in its early finding using conventional techniques. This article discusses a variety of DL techniques used to detect DR lesions. Various methodologies are considered and reviewed for early finding of DR. Even when the number of feature and data increases, some of the DL techniques are scalable and some of them are not. On the training phase, DL model requires huge amount of data for it's accurate prediction. Accuracy of the prediction of DR may vary on DL models because of different data acquisition, data pre processing and deep feature extraction techniques of different CNN architectures. The some of the challenges faced on to design DL Model are reducing the bias in the data set, data drift, dimensionality reduction in data set, balancing the underfitting and overfitting of DL model. This article reviewed various researchers' DL models with their suitable solutions leads to design a DL model with accurate detection of DR. Thus this review article useful for today's engaged aspiring researchers those who are interested in the field of medical imaging, DL and automated DR detection.

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