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Diabetic Retinopathy Classification with Deep Learning via Fundus Images

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Abstract - Diabetic retinopathy (DR) is a micro vascular disease that is associated with diabetes mellitus. DR can cause irreversible vision loss and low vision. DR classification, that is, early DR diagnosis and accurate DR grading, is critical for vision protection and immediate treatment. Deep learning-based automated systems led to significant expectations for DR classification based on fundus images with advantages. In the past several years, many outstanding studies in this area have been conducted and several review articles have been published. However, the new trends and the future directions are need to furtherly analyzed. Thus, we carefully included and read 94 related articles published from 2018 to 2023 through Web of Science, PubMed, Scopus, and IEEE Xplore. From this review, we found that transfer learning has been used as an outstanding strategy for overcoming the issue of the limited data resources to support DR analysis. CNN models of ResNet and VGGNet with layers of tens or even hundreds are the most popular frameworks used for DR classification. The APTOS 2019 and EyePACS are the most widely used datasets for DR classification. In addition, some lightweight DL architectures like Squeeze Net and MobileNet have been proposed for DR classification tasks, especially for limited data resources and computational capabilities. Although deep learning has achieved or surpassed human-level accuracy in DR classification, there is still a long way to go in real clinical workflows. Further improvements in model interpretability. This work introduces an automated system for identifying these conditions using image processing and machine learning. Our methodology includes image acquisition, pre-processing to enhance quality, and the extraction of key features relevant to glaucoma (optic disc) and DR (microaneurysms, exudates). A trained classifier then accurately identifies the presence of these diseases. This automated approach offers a rapid, objective tool for early detection and diagnosis, enabling timely interventions to potentially prevent vision loss. The development of such a system holds substantial potential for improving healthcare accessibility and patient outcomes in ophthalmology.

Key Words: Authentication, data security, distributed ledger, online voting, privacy, verification

1. INTRODUCTION

Diabetic retinopathy (DR), one of the most feared microvascular complications of diabetes mellitus (DM), is a major cause of irreversible vision impairment and low vision among working adults. Approximately 30% of people with DM have signs of DR, of which 30% have vision-threatening DR . According to the reports by the International Diabetes Federation, there are approximately 537 million diabetes in 2021 worldwide. This number will exceed 700 million by 2045 and nearly 30% of them, that is, more than 200 million people will suffer from DR. It is known that DR is a progressive disease with the resulting from long-term diabetes, the risk of incurable vision loss and low vision can be largely reduced by early DR diagnosis and accurate DR grading. A fundus image is a projection of the fundus captured by a monocular camera on a 2D plane. Unlike optical coherence tomography images and angiographs, fundus images can be acquired in a rapid, non-invasive and cost-effective way, making them more suitable for large-scale screening. Besides, many important biomarkers can be seen in the fundus image, such as optic disc, macula, fovea, blood vessel, and some DR related lesions. Traditionally, DR classification is mainly performed by analyzing lesion features in fundus images obtained from digital fundus photography. However, the interpretation of fundus images requires specialized knowledge and experienced ophthalmologists, and it is time-consuming, labor-intensive, and prone to human errors. Thus, the increased global prevalence of DR and limited availability of professional ophthalmologists have motivated an urgent need to develop fast, cost-effective, and accurate automated systems to assist DR classification. With the increase in computing power and availability of large amounts of labeled data, the deep learning (DL) technique shows excellent performance in automatic analysis and evaluation of image-related data through the combination of large amounts of data with intelligent algorithms. DL is designed using a multilayer data representation architecture that can automatically extract low- level and high-level features without human interference. Many DL-based algorithms (such as convolution neural networks (CNNs), autoencoders (AE), recurrent neural

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networks (RNNs), deep belief networks (DBN) and transfer learning) have been designed and applied to fundus images.

It is obvious that the number of papers on fundus images and DL for DR classification is increasing year by year. Recently, several review articles have been published in this topic. In 2019, Asiri et al. published a review of DL techniques applied to DR detection and classification of lesions in fundus images. In 2020, Alyoubi et al. reviewed and analyzed the significant research on DL for DR detection. In 2023, Sebastian et al. presented a review of DL developments in the domain of DR classification including detection and grading based on fundus images. Although these comments cover a lot of work regarding DR lesion detection and classification, a detailed account of the preprocessing methods and the specific DL methods or structures in recent studies has not been included. Image preprocessing is necessary to reduce the heterogeneity resulting from various imaging conditions. Identifying the specific DL structures in recent research can provide new advances on this topic. Therefore, the objective of this paper is to provide a more comprehensive review that analyzes the new trends and highlights the future directions for the DR classification of deep learning in fundus images. In contrast to previous works, the major contributions of this work be summarized as follows. First, a novel holistic overview is provided by presenting the detailed data prepro- cessing pipelines and latest studies within the past three years in the field of DR classification using DL approaches. Second, the databases, DL models and the performance of reported techniques in two classification tasks, i.e., binary classification for DR diagnosis and multi-classification for DR grading are discussed. Third, the limitation and future evolution of the application of DL for DR classification is addressed. Thus, we believe that a more detailed and integrated review is more comprehensive to provide inspiring ideas for researchers in this active area. The review adopts the PRISMA approach for articles searching and selection. We searched for 345 related papers published from 2018 to 2023 through Web of Science, PubMed, Scopus, and IEEE Xplore using the terms ‘‘artificial intelligence’’, ‘‘deep learning’’, ‘‘diabetic retinopathy’’, ‘‘classification’’, ‘‘detection’’, and ‘‘grading’’. After removing and determining the specific DL tasks for DR, final 94 articles were carefully included. This paper is organized as follows. In a back- ground of DR and related biomarkers on fundus images for DR classification are provided. In the publicly available DR datasets are described. In data preprocessing methods and pipelines are introduced. commonly used DL architectures for DR classification are discussed. In recent research for DR classification by DL techniques is reviewed and discussed. Some of challenges and potential future directions are provided. In the conclusion is summarized.

2. RELATED WORKS

In this section, an overview of DR and the related biomarkers on a fundus image as shown in Figure 3 are provided

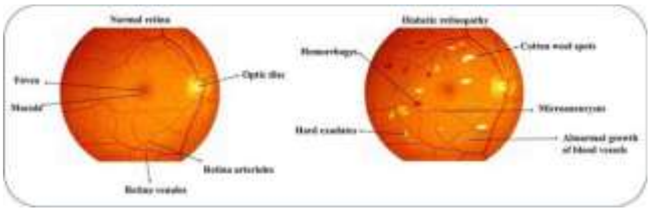

Figure 1. Normal retina and diabetic retinopathy on a fundus image

Including blood vessels, optic disc, DR lesions, stages and severity grading of DR

A. Blood vessels and optic disc

Blood vessel assessments, including assessments of vascular thickness, diameter, length, arteriovenous ratio, bifurcations, and curvature have been proven to be closely related to DR occurrence and its severity, especially in the proliferative stage of DR (PDR). The growth of new tiny pathogenic blood vessels in PDR makes accurate segmentation and evaluation of the retinal vasculature much more important. The optic disc (OD), that is, the optic nerve head (ONH), is the brightest region in fundus images, which is oval-shaped with clear boundaries and located exactly 3 mm nasally (medially) to the macula lutea. The optic disc is also called a ‘‘low vision spot’’ of the eye, because it is the only area on the retina without any photoreceptors. During fundus image analysis, the optic disc needs to be removed to avoid the misclassification of OD, because the OD has a similar appearance of pixels to the bright exudates in the fundus image.

B. DR lesions

In diabetes, large amounts of glucose in the blood can damage retinal blood vessels, resulting in vascular swelling, leakage, and even abnormal growth of new vessels. Various pathological changes in the retina have been observed. Microa- neurysms are the earliest symptoms of DR. Possible reasons for micro aneurysm formation include vasoproliferative factor release, capillary wall weakness, and increased intraluminal pressure. Microaneurysms present slight widening of the capillary walls and are defined as deep red dots (25 - 100 μm) with sharp margins on the fundus images. Hemorrhages occur when the weak capillaries break. Hemorrhages Hemorrhages are identified as red spots similar to microaneurysms. Unlike microaneurysms, hemorrhages are usually larger than 125 μm and have irregular edges. Hard exudates are mainly lipoproteins that leak from the damaged capillaries. They often appear as small white or white-yellow individual dots or continuous flaky spots with sharp margins. Soft exudates or cotton wool spots are lesions of the retinal nerve fiber layer caused by small-artery occlusion. Small-artery occlusion reduces blood flow to the retina, which causes ischemia of the retinal nerve fiber layer and accumulation of axoplasmic debris in retinal ganglion cell axons. This accumulated debris appears slightly raised, with small gray-white cloud-like shapes in the superficial layer of the retina. Neovascularization refers to the abnormal formation of new

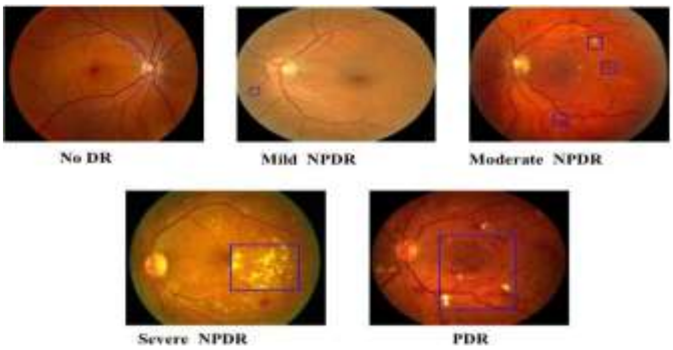

Figure 2. The dr grading according to icdrss (npdr: non-proliferative diabetic retinopathy; pdr: proliferative diabetic retinopathy

blood vessels on the retinal inner surface, which is a hallmark of PDR. The release of vasoactive factors in ischemic retina can provoke the growth of new vessel, which may lead to vitreous hemorrhages that block vision. Macular edema occurs when vascular permeability increases and abnormal blood vessels leak into the surroundings of the macula, which causes macular swelling and retinal thickening, and even threatens central vision.

C. DR grading

DR grading evaluates vascular changes and identifies DR severity levels. At present, there are various DR grading protocols, including the Early Treatment Diabetic Retinopathy Study (ETDRS) classification, International Clinical Diabetic Retinopathy Severity Scale (ICDRSS) ,Inter- national Clinical Diabetic Macular Edema Severity Scale (ICDMESS) , and Scottish DR grading protocol . Although the ETDRS grading scheme is the gold standard, its multiple levels and complex implementation make daily clinical and large-scale grading difficult. Owing to its con-venience and ease of adoption, the ICDRSS proposed by the Global Diabetic Retinopathy Project Group has attracted much more attention in clinical practice and computer-aided diagnosis (CAD) settings worldwide. According to ICDRSS, DR can be classified into five severity levels, that is, No DR, mild NPDR, moderate NPDR, severe NPDR, and PDR

3. CLASSIFICATION

The main aims of DR classification can be divided into binary classification for DR diagnosis and multi-class classification for DR grading. In this section, we provide a short review of recent literature on published DL models used in DR classification tasks. And three standard metrics, i.e., accuracy sensitivity, and specificity are used to evaluate the performance of DL models in these studies

A. Binary Classification For Diagnosis

Binary classification is primarily used to differentiate between healthy and diseased individuals. Any DR is defined as the presence of NPDR, PDR, DME, or a combination thereof. Most models have been trained for binary classification tasks, such as the presence or absence of any DR, referable DR (RDR) or non-referable cases, and severe DR or non-severe DR. summarizes the major DL models for binary DR classification.

Many significant studies present from 2018 to 2020 VGG16 was proposed for DR identification using the loss function of binary cross entropy. They compared two experiments, that is, the VGG16 combined with a linear SVM and VGG16 combined with a softmax function as an output fully-connected layer, and a higher sensitivity of 93% and specificity of 85% were achieved by the former. Using the same EyePACS dataset, Liu et al designed a CNN model by applying multiple weighted paths into a convolutional neural network, named WP-CNN (weighted paths-CNN), for referable and non-referable DR identification. This binary classification experiment finally obtained an accuracy of 91.05%, sensitivity of 89.3%, and specificity of 90.89%. Chalakkal et al. developed a simplified approach for screening clinically significant macular edema (CSME) using a combination of pre-trained DCNNs and a meta-heuristic feature selection approach. The results indicate that Inception-ResNet-v2 yielded the best performance. Gangwar and Ravi used transfer learning on pre-trained Inception-ResNet-v2, and a custom block of CNN layers was added on top to design a hybrid model to detect DR. The performance of this model was evaluated on the MESSIDOR-1 and ATOS 2019 datasets, and a high accuracy of 82.18% was achieved for the latter one. In 2022, a large number of related research in DR classification using DL method has emerged, Inception V3 was adopted to identify severe DR and non-severe cases based on the recognition of DR lesions. Owing to the large imbalance between cases of severe DR and non-severe DR, a weighted random sampling strategy was used to balance the positive and negative cases in the training set. The Kaggle public dataset for DR grading was used, and a sensitivity of 92.5% and specificity of 90.7% were achieved. Padmanayana and Anoop designed a CNN architecture to classify images of DR or non- DR, and different optimizers, such as Adagrad, Adam, and RMSPROP with momentum, were used to compare the performance of the model. Testing on the APTOS 2019 dataset, the highest accuracy of 94.6%, the sensitivity of 86%, and the specificity of 96% were respectively obtained. An additional private hospital dataset was also used for testing, an accuracy of 94.6%, sensitivity of 88% and specificity of 97% were obtained. Macsik et al. proposed a new local binary convolutional neural network (LBCNN) deterministic filter generation approach, in which fewer learnable parameters and less memory were useful for enhancing the performance of the standard CNN. These experiments were evaluated on the EyePACS and APTOS datasets, and the performance of the LBCNN with 24 fixed filters outperformed that of all the other DL models in this study. Farag et al proposed a model by combing DenseNet169's encoder to construct a visual embedding and convolutional block attention module (CBAM) to enhance its discriminative power. They applied their algorithm to APTOS dataset for binary and multi-class classification tasks. On the binary classification for DR or No DR, accuracy of 97%, sensitivity of 97% and specificity of 98.3% were achieved. Moreover, this network also showed high accuracy of 82% for severity grading.

B. Multi-Class Classification For Grading

Multi-class classification is commonly defined as assigning a fundus image to different disease stages according to the most severe grade in both eyes of each patient. As described in DR is graded according to a five-level protocol: no DR, mild NPDR, moderate NPDR, severe NPDR, and PDR. In this section, we present research regarding published DL models for multi-class classification of DR. summarizes the major DL models for multi-class DR classification. In 2018, Wan et al adopted transfer learning and hyper parameter tuning on the pre-trained models of AlexNet, VGGNet, GoogleNet, and ResNet for DR classification. The models were fine-tuned using the EyePACS dataset. The best results, with an accuracy of 95.68%, sensitivity of 86.47%, and specificity of 97.43% were obtained from the pre-trained VGGNet. In 2019, Hagos and Kant used a small subset of the EyePACS dataset to train Inception V3 for 5-class clas- sification. The inception modules in this model enabled different-sized feature extraction from the input images in one of the convolution layers. A high accuracy of 90.9% was achieved. Qummar et al. trained an ensemble architecture of five deep CNN models (ResNet50, Inception V3, Xception, Dense121, and Dense169) to classify the DR stages. This ensemble architecture can encode rich features to improve classification performance. The experimental results show that the proposed model can effectively identify five stages of DR, and its performance outperforms that of other common models trained on the same Kaggle dataset. Zhang et al built an automatic grading system to evaluate the DR severity using two strategies. The first strategy consisted of two phases. In the first phase, a binary classification was performed to identify abnormal and normal images via Xception, and in the second phase, a ternary classification was used to evaluate DR severity based on the above abnormal images using ResNet50. The other strategy was a four-class model based on all fundus images using ResNet50 and DenseNet. A high sensitivity of 98.1% and specificity of 98.9% were achieved by the DenseNet. Harangi et al. graded DR stages by combining hand-crafted features with AlexNet. The Kaggle dataset was used for training and the IDRiD dataset was used for testing. Classification accuracies of 90.07% and 96.85% were achieved for the 5-class DR and the 3-class DME tasks, respectively. In 2020, Tymchenko et al.applied a multistage approach to transfer learning to detect the stages of DR. They built a deep ensemble CNN architecture by combining 3 CNN architectures (EfficientNet-B4, EfficientNet-B5, and SE-ResNeXt50) and transfer learning. To train the encoder based on a small amount of training data, ImageNet- pre-trained CNNs were used for the initialization. The training process was performed on the APTOS 2019, IDRiD, and MESSIDOR datasets and the model was tested on the EyePACS dataset with a sensitivity of 99.3% and specificity of 99.3% too. Mishra et al. used a pre-trained DenseNet with quadratic weighted kappa (QWK) on the APTOS 2019 dataset to automatically detect the DR stage and finally got an accuracy of 96.1%. Comparing the accuracy of 73.26% from VGG16 architectures trained without QWK and ImageNet, the QWK can significantly enhance the accuracy of DenseNet architecture. Tu et al. proposed a feature separation and union network (SUNet) for simultaneous DR and DME grading. SUNet contained a feature-blending block with two parts: feature separation and feature union. In the feature-separation part, task-specific features for lesion detection and DR/DME grading can be learned, whereas in the feature-union part, these features can be aggregated. Thus, irrelevant features can be extracted and used for related tasks to improve the performance of each task. Experiments on the IDRiD dataset demonstrate that SUNet significantly outperformed some existing models, such as VGG19 and ResNet34, for both DR and DME grading.

4. PROPOSED SYSTEM

The proposed system aims to address the limitations of the existing methods by developing an automated, objective, and efficient tool for the identification of glaucoma and diabetic retinopathy from retinal fundus images using advanced image processing and deep learning techniques.

The core idea is to leverage the power of Convolutional Neural Networks (CNNs) to automatically learn discriminative features from retinal images and accurately classify them into categories such as normal, glaucomatous, and indicative of diabetic retinopathy.

5. MODULES

5.1 Image Acquisition Module:

This module assumes the availability of a digital retinal fundus image dataset. In a real-world scenario, this would involve capturing retinal images using standard fundus cameras.

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5.2 Image Pre-processing Module:

This module will focus on enhancing the quality of the input retinal images and reducing noise to improve the performance of the subsequent analysis.

5.3 Noise Reduction:

Applying filters (e.g., median filter, Gaussian filter) to reduce random noise while preserving important image details.

5.4 Contrast Enhancement:

Utilizing techniques like histogram equalization or adaptive histogram equalization to improve the visibility of subtle retinal features.

5.5 Image Normalization:

Standardizing the pixel intensity values across the dataset to ensure consistent input to the deep learning model.

5.6 Image Resizing and Cropping:

Resizing the images to a consistent input size required by the CNN architecture and potentially cropping the region of interest (e.g., centered on the optic disc or macula).

5.7 Deep Learning Model (CNN) for Feature Extraction and Classification:

This is the core of the proposed system. A suitable Convolutional Neural Network (CNN) architecture will be selected or designed. This could involve adapting well-established architectures like ResNet, Inception, or Efficient Net, which have demonstrated excellent performance in image classification tasks. The CNN will consist of multiple convolutional layers, pooling layers, and fully connected layers.

5.8 Automatic Feature Learning

The convolutional layers will automatically learn hierarchical features from the pre-processed retinal images, capturing patterns and structures relevant to glaucoma (e.g., optic disc cupping, changes in blood vessel curvature) and DR (e.g., presence of lesions, vascular abnormalities).

5.9 Classification Layer

The final fully connected layers will perform the classification, outputting the probability of the input image belonging to each of the predefined categories (e.g., normal, glaucoma, diabetic retinopathy). A Softmax activation function will be used in the output layer to obtain probability distributions over the classes.

5.10 Classification and Output Module

Based on the output probabilities from the deep learning model, this module will assign a final classification label to the input retinal image. The system will output the predicted class (e.g., "Normal," "Glaucoma," "Diabetic Retinopathy") along with a confidence score indicating the certainty of the prediction.

5.11 Performance Evaluation Module

This module will be used to evaluate the performance of the trained system on a separate test dataset. Key performance metrics such as accuracy, sensitivity, specificity, precision, F1-score, and Area Under the ROC Curve (AUC) will be calculated to assess the system's effectiveness in identifying glaucoma and DR.

6. RESULT

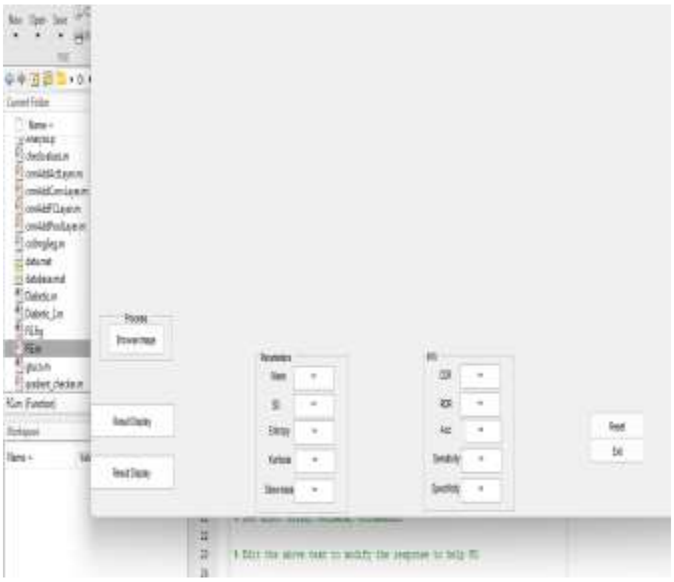

Figure 3: Fundus Diabetic Detection

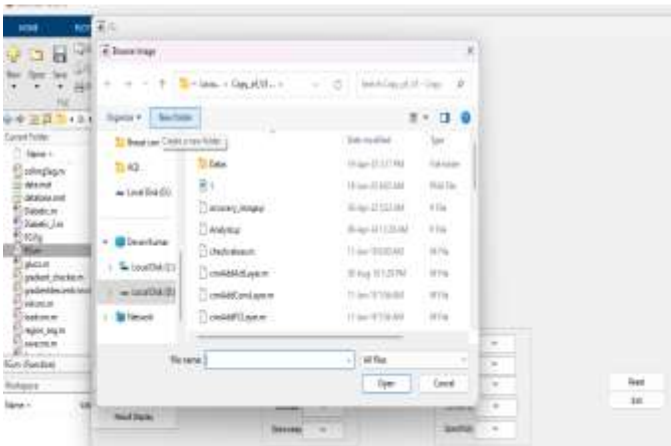

Figure 4: Browse Image

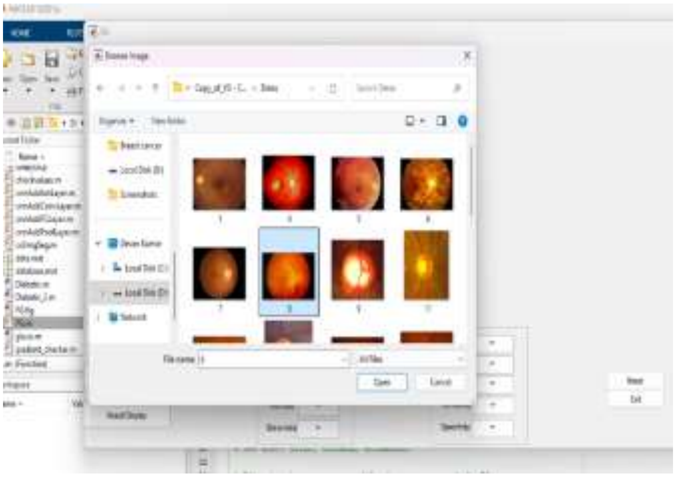

Figure 5: Fundus Image Selection

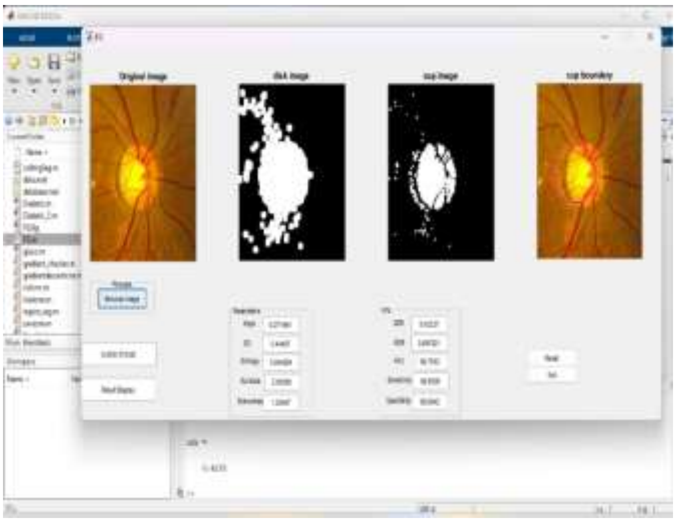

Figure 6: Calculating the diabetic level

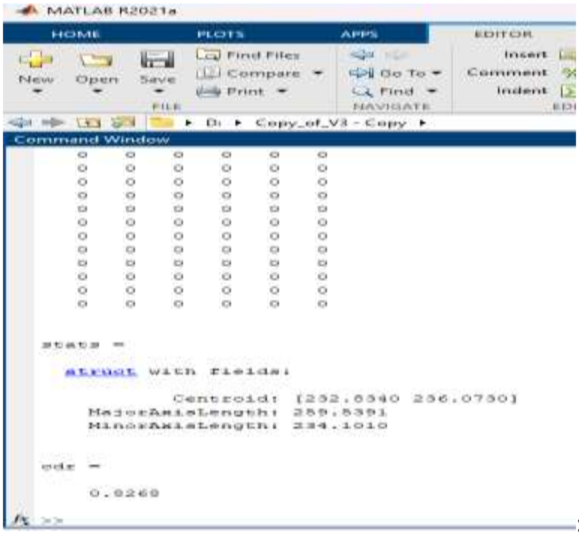

Figure 7: Diabetic Result Analytics

6. CONCLUSION

In this study, we provide a comprehensive review of recent advances in deep learning-based research on DR classification based on fundus images. Some key findings can be obtained. First, there is an obvious trend that transfer learning is an outstanding strategy for overcoming the issue of the limited data samples available during model training. With the help of transfer learning techniques, a number of pre-trained networks are accessible to support DR analysis. Both the training time and robustness of the model can be improved by training with parameters from the pre-trained model. Sec- ond, CNN models of ResNet and VGGNet are the most popular frameworks used for DR classification. The depth of the ResNet- and VGGNet-based networks can reach tens or even hundreds of layers, which can provide outstanding classification results. The APTOS 2019 and EyePACS are the most widely used datasets for DR classification. Third, some lightweight DL architectures like SqueezeNet and MobileNet have been proposed for DR classification tasks, especially for limited data resources and computational capabilities. These architectures can greatly reduce parameters while ensure model accuracy in the complicated image analysis. Although deep learning has achieved or surpassed human-level accuracy in DR diagnosis and grading, there is still a long way to go in real clinical workflows. Further improvements in model interpretability, trustworthiness from ophthalmologists, and cost-effective and reliable DR screening systems are needed.

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