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Deep Learning of Diabetic Retinopathy Classification in Fundus Images

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ABSTRACT

Diabetic retinopathy is an eye disease in diabetic patients due to damage to the small blood vessels in the retina due to high and low blood sugar levels. Accurate detection and classification of Diabetic Retinopathy is an important task in computer-aided diagnosis, especially when planning for diabetic retinopathy surgery. Therefore, this study aims to design an automated model based on deep learning, which helps ophthalmologists detect and classify diabetic retinopathy severity through fundus images. In this work, a deep convolutional neural network (CNN) with transfer learning and fine tunes has been proposed by using pre-trained networks known as Residual Network-50 (ResNet-50). The overall framework of the proposed classification model is divided into three major phases, including pre-processing, training the Resnet-50 network, and classification with evaluation. In the first phase, pre-processing techniques are applied to the APTOS2019 fundus images dataset to find the best features and highlight some fine details of these images. The resnet-50 network was trained in the second phase using the training set and saved the best model obtained that gives high accuracy during the training process. Finally, this saved model has been implemented on the testing dataset for classification DR grades. The proposed model shows good and best classification performance, which was obtained with an accuracy of 98.3%, a precision of 98.4%, an F1-Score of 98.5 % and the recall of 98.4%.

Keywords: Diabetic Retinopathy, Fundus Images, Pre-Processing, ResNet-50, Accuracy

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التعلم العميق لتصنيف اعتلال الشبكية السكري في صور قاع العين

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الخلاصة

اعتلال الشبكية السكري هو مرض يصيب العين لدى مرضى السكري نتيجة لتلف الأوعية الدموية الصغيرة في شبكية العين الذي يحصل بسبب ارتفاع وانخفاض مستويات السكر في الدم. يعد الكشف الدقيق عن اعتلال الشبكية السكري وتصنيفه بمساعدة الكمبيوتر مهم في التشخيص واعطاء العلاج المناسب وخاصة في المراحل المبكرة . لذلك ، تهدف هذه الدراسة إلى تصميم نموذج آلي بالاعتماد على التعلم العميق لمساعد أطباء العيون ودعمهم في الكشف عن مدى شدة اعتلال الشبكية السكري وتصنيفها من خلال صور قاع العين . في هذا العمل ، تم اقتراح شبكة عصبية تلافيفيه عميقة (CNN) مع نقل التعلم والضبط الدقيق باستخدام شبكة مدربة مسبقًا تُعرف باسم Residual Network-50 (ResNet-50). ينقسم الإطار العام لنموذج التصنيف المقترح إلى ثلاث مراحل رئيسية تشمل : المعالجة المسبقة ، تدريب شبكة Resnet-50 ,والتصنيف مع التقييم . في المرحلة الأولى ، يتم تطبيق تقنيات المعالجة المسبقة على صور قاع العين باستخدام مجموعة بيانات APTOS2019 للحصول على أفضل الميزات وتسليط الضوء على بعض التفاصيل الدقيقة في صور قاع العين . تم تدريب شبكة Resnet-50 في المرحلة الثانية باستخدام مجموعة التدريب و حفظ أفضل نموذج حُصل عليه أثناء عملية التدريب والذي اعطى اعلى دقة. أخيرًا ، يتم تنفيذ هذا النموذج المحفوظ لغرض اختبار مجموعة البيانات وتصنيف درجات اعتلال الشبكية السكري. اظهر النموذج المقترح افضل أداء تصنيف بدقة 98.3٪, و دقة ضبط 98.4٪ ولقيمة (F1-Score) تعادل 98.5%، ولدقة استعادة 98.4%.

الكلمات المفتاحية : اعتلال الشبكية السكري , صور قاع العين , المعالجة المسبقة , شبكة (ResNet-50) , الدقة .

1. INTRODUCTION

Diabetes is a severe public health issue that develops when the pancreas fails to secrete enough insulin, or the body cannot process it, which causes harm to numerous bodily organs, including the eyes **(Nasser and Dawood, 2021; Hameed, 2021).** At least 33% of diabetics have an eye Complication known as diabetic retinopathy (DR**).** There is no symptom in the early stages of DR, but some patients have vision changes, such as difficulty reading or seeing faraway objects **(Jenkins et al., 2015)**. Variation in blood sugar damages the small blood vessels in the eyes and may block them altogether. Thus, the eye works to develop new blood vessels, but sometimes these blood vessels are thin and cause a leak of fluid into the retina; this leads to many lesion types appearing in the retina **(Ali et al., 2022; Chaturvedi et al ., 2020).** DR lesions and retinal damage begin with small saccular dilations of the capillaries known as Micro aneurysms (Mas). Another type of lesion known as Hemorrhage (HM) is a wide accumulation of blood in the retina. When the lipoproteins leak from plasma, the Hard exudates (EX) or yellow spots on the retina appear., and as a result of the nerve fiber swelling, Soft exudates appear like white spots on the retina **(Asiri et al., 2019; Kwasigroch et al., 2018).** According to the presence of the lesions on the retina, DR is divided into two

main stages: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) **(Wilkinson et al., 2003).** The manual method for detecting and classifying DR is considered uneconomical. The results can be inaccurate because the number of patients with diabetes is increasing compared to the ratio of doctors (1 doctor to 10,000 patients). This motivated the research community to develop deep learning methods that help specialists in early detection and classification **(Abdulhakeem Albayati, 2020)**. DL is a branch of machine learning that analyses data using a layered framework. Data is transferred through a stack of layers comprising a neural network. Each layer draws on the output of the layer before it produces its results. These layers employ mathematical operations to convert raw input data into valuable output **(Hssayni and Ettaouil, 2021; LeCun, 2016; Qusay et al., 2020).** Automatic feature extraction is a deep learning advantage and has been achieved promising in various computer vision and automatic fundus image analysis applications **(Ali et al., 2021).** Convolutional neural networks (CNN) have been used to identify and categorize Convolutions, pooling, and fully connected layers are among the layers that make up a CNN in most cases. Activation or a feature map is the output of each layer and can be used as an input for another layer **(Ahmed and Mohammed, 2022; Altaf et al., 2019).** Many researches have been proposed to detect and classify DR automatically depending on deep learning, and most of these used fundus images. **(Islam et al., 2020) (** developed a DL model with transfer learning from the VGG16 model followed by a pre-processing technique implemented to APTOS 2019 Blindness Detection Kaggle data sets divided differently into two subsets, one for training procedure and the second for testing. This provided an average accuracy of 0.9132683**. (Ghosh et al., 2017)** proposed an automated DR screening method using colour fundus retinal photography as input. Using CNN, the training dataset on Kaggle consists of 30,000 fundus images. On around 3,000 validation images, this system achieved approximately 95% accuracy for the two-class classifications and about 85% for the five-class classifications. **(Wan et al., 2018)** proposed convolutional neural networks (CNNs) for DR detection by adopting AlexNet, ResNet, GoogleNet, and VggNet, and analysed how these models are trained using Kaggle resources open to the public. **(Salvi et al., 2021)** examines the result of various CNN architectures using transfer learning for the DR Classification function. The focus of this study is The ResNet-50 V2, VGG16. ResNet-50 V2 architecture, which has an accuracy of 93% and 95%, was achieved with Transfer Learning on the VGG16 Model. **(Elswah et al., 2020)** proposed automatic system for early identification and grading of DR using fundus images known as (the Indian Diabetic Retinopathy Image Dataset)(IDRiD) that achieves an accuracy of 95.73%, specificity of 98.5%, and sensitivity of 95.73%, depending on the AlexNet model and a pixel-wise NN classifier.
This study aims to detect and classify DR grading automatically depending on severity to help ophthalmologists predict if a patient has DR.

2. MATERIALS AND METHODS

The overall framework utilized for the proposed model of diabetes retinopathy detection and classification based on deep learning includes three major phases, as shown in **Fig 1.** The first phase is applied for pre-processing on fundus images, which consists of five main steps: resizing, converting color images to greyscale, using median filter, applying CLAHE for contrast enhancement, and then applying circular crop to extract retina region of interest (ROI). In the second phase, the training dataset was trained using a pre-trained Resnet-50 network and saved the best-trained model. Finally, the saved trained model is applied to the testing dataset to find output predictions. The result of the classification procedure will be evaluated using (accuracy, precision, F1-score, and recall).

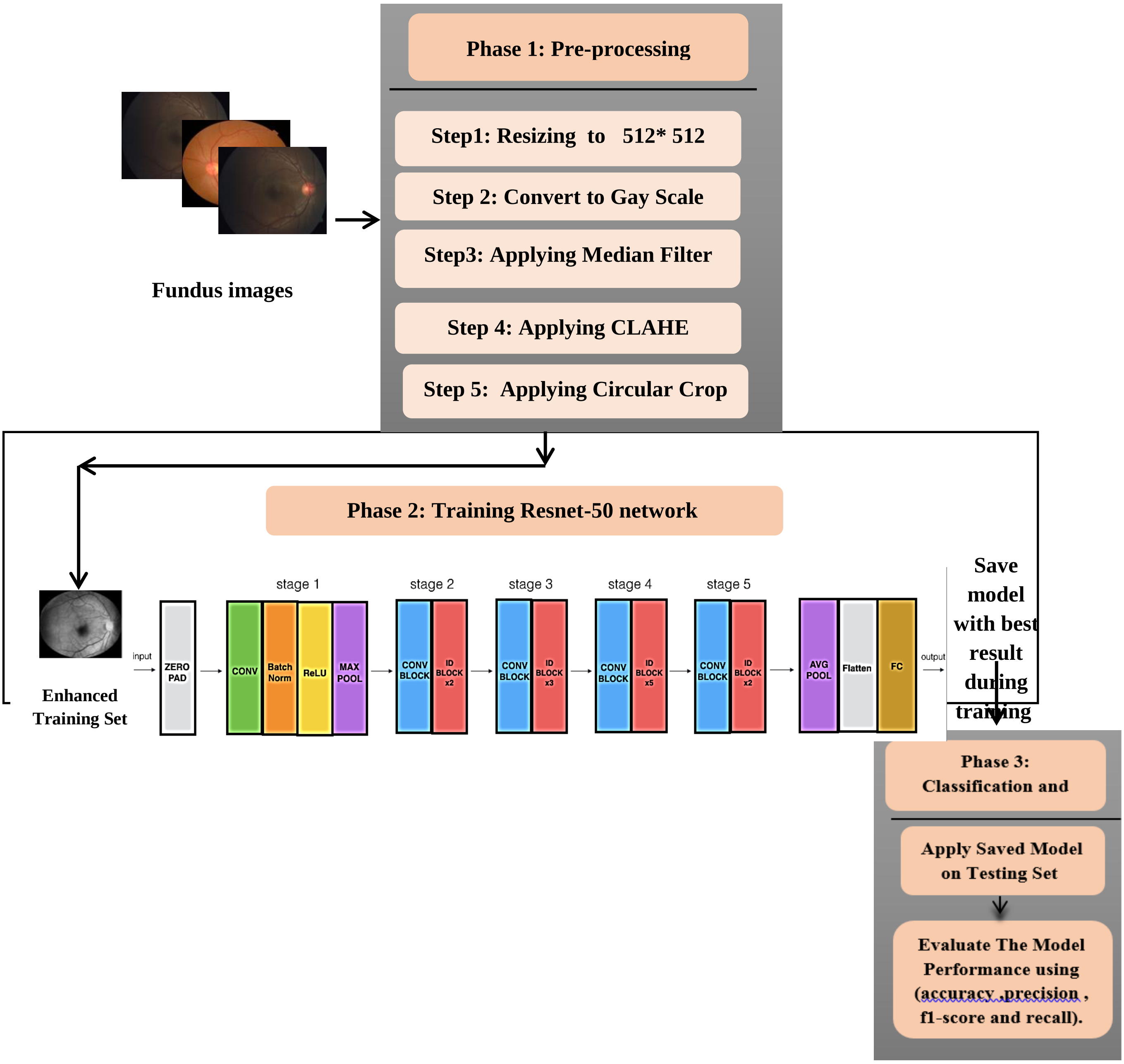
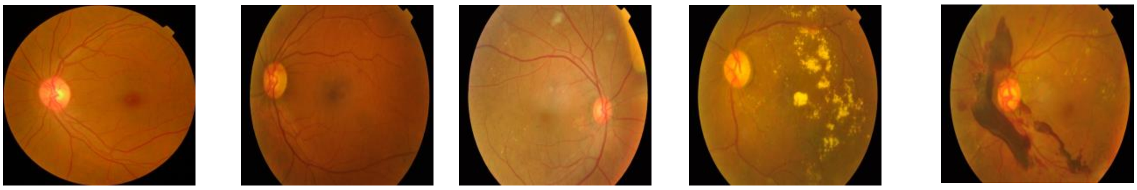


Figure 1. The overall Framework of the proposed model to Classify DR.

2.1 Dataset

This study uses the Asia Pacific Tele-Ophthalmology Society (APTOS 2019) obtained from Kaagle and collected by (Aravind Eye Hospital in India's rural area) using a Digital fundus camera. APTOS 2019 consists of 5590 images that are divided into two groups. The first group is for test images, which consist of (1929) images. The second group is for train images, which consist of (3662) images. As shown in **Fig. 2**, fundus images are divided into five grades (normal, mild, moderate, severe, and proliferative). These data sets differ in the image's actual time, location, equipment, and operator. Thus, size, color, and brightness are also different. One of its drawbacks is the significant class imbalance, primarily for the severe NPDR class, which includes only 193 images **(Ali et al., 2022)**.



1.Normal (1805) images 2. Mild (370) images 3. Moderate (999) images 4. Severe (193) images 5. Proliferative (295) images

Figure 2. Examples of APTOS 2019 fundus images Grades

2.2 Pre-Processing

The APTOS-2019 fundus images use various hardware devices under different environmental conditions during capturing. Thus, this process leads to adding noise to the final image. To reduce such noise, which ultimately affects the performance of the classification model, five main pre-processing steps are applied below to find the features in the dataset, highlight some fine details of the images, and get very good results for our model.

- **Image resizing:** Deep learning systems train quicker on smaller images in general. The dataset used has varying image sizes. We resize fundus images to the size (256*256 pixels) to form a standardized dataset, optimize the execution time, and reduce the amount of computer memory required during the learning process **(Doshi et al., 2016).**
- **Convert Color Images to Greyscale:** This study's APTOS 2019 dataset is color; we applied the luminosity method to convert the color images to grey because blood vessels and haemorrhages appear darker in the grey image. This conversion is easy and effective, used For making images more informative and their computations in the later stages less intensive and to extract features from the retinal fundus image. The luminosity method creates a weighted average to consider human vision, which is more sensitive to green than other hues, giving the most weight to green **(Pradhan et al., 2020).**
- **Median Filter:** this is a very common and widely applied filter used to solve many image issues because of its ability to preserve the edges and minimize noise **(Balafar, 2012)**. This research used a median filter with a size (of 3×3 pixels).
- **Contrast Adaptive Histogram Equalization CLAHE**: For low-contrast images, we used is common pre-processing technique. It is mainly utilized for highlighting the foreground from the background in which the brighter sections in the entire image are flattened. This tends to enhance the dark region and avoid overexposing **(Wu et al., 2017).** The local contrast enhancement in the homogeneous areas can be restricted to prevent over-enhancement of noise and lessen the edge-shadowing effects in the enhanced image. The CLAHE controls the quality of the enhanced image by two essential parameters: the Clip Limit (CL) and Block Size (BS). A higher value of the CL parameter leads to a brightness increase in the input image due to the low-intensity level of the input image. On the other hand, a higher value of the BS parameter expands the image intensity's dynamic range

and increases its contrast level. This work set the CL and BZ to 2 and (8×8), respectively **(Reza, 2004)**.

- **Circular Crop:** Finally, the last stage of circular cropped is applied to extract the retina region of interest from fundus images to run the model on the retina and avoid background pixel interference. To get more exact information from circular images, photographs are cropped into a circular shape.

Fig. 3 shows an enhanced fundus image after applying the pre-processing steps on the original fundus image with differences in histogram distribution.

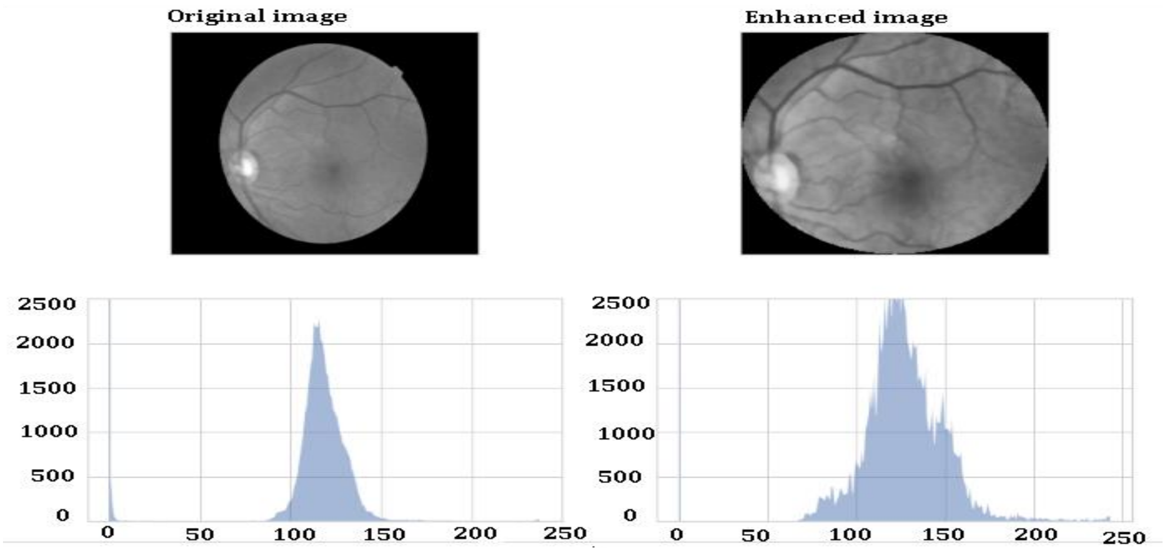


Figure 3. An example of the original fundus image before and after enhancement using pre-processing

2.3 Transfer Learning and ResNet-50

Sometimes, developing accurate and dependable models for medical problems may be challenging since deep neural network training demands a lot of computing power and data. Like individuals using their existing knowledge to comprehend and solve problems, deep neural networks are trained and tested on datasets such as ImageNet. They then transfer the learned information to other different models, even if the application area is separate. This means it improves the learning in one task by transferring knowledge from another task that is already learned)this process is transfer learning.

This study used pre-trained networks known as ResNet-50, available in the Keras library **(Abuqadumah et al., 2020).** ResNet-50 is a type of deep learning algorithm consisting of 50 weighted layers over 25.6 million parameters created by **(He et al., 2016)**. ResNet model has an advantage in that the performance does not suffer when the design becomes more complex; ResNet can reach up to 152 layers by using the concept of shortcut connections, which is also known as a residual block that skips over 3 convolution layers such as shown in **Fig 4.** This process made the training of the networks more effective, and the computation was lighter **(Elswah et al., 2020; Thenmozhi and Reddy, 2019).**

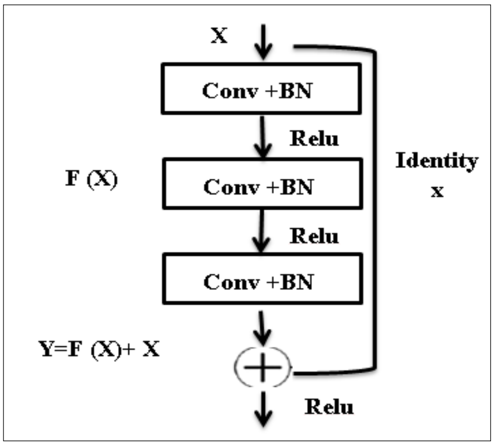


Figure 4. The Residual Connection in Resnet-50 **(He et al., 2016)**

As shown in **Fig. 5**, Res-Net50 architecture (is a deep network with 50 layers. These layers are divided into five stages, as explained below :

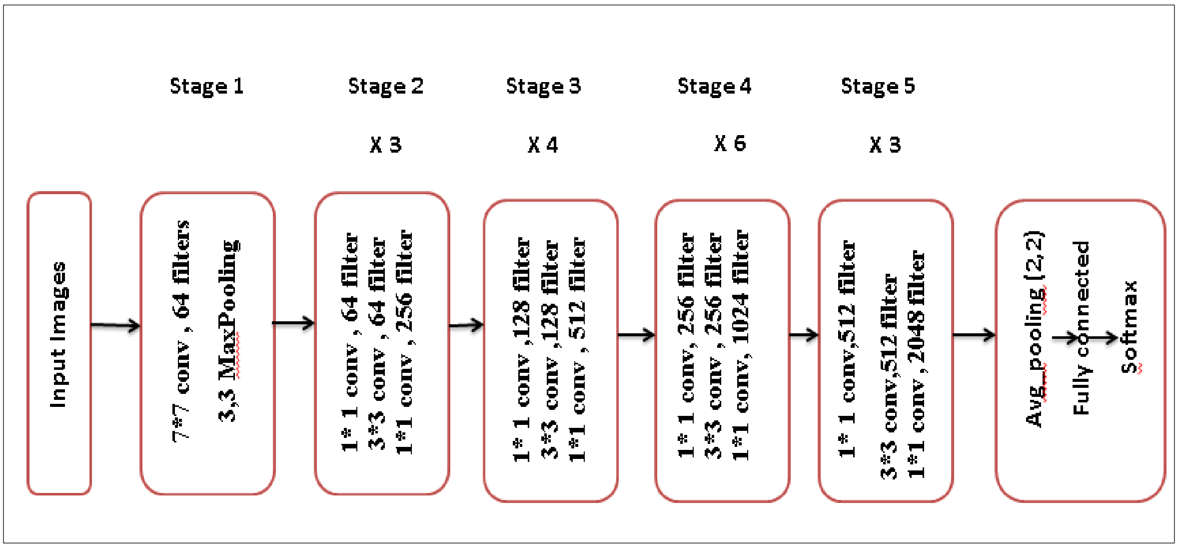


Figure 5. ResNet-50 network Architecture **(Salvi et al., 2021).**

- Stage 1 consists of 2 layers: the convolution layer and max-pooling layer.
- Stage 2 consists of 3 residual blocks, each with three convolution layers.
- Stage 3 consists of 4 residual blocks, each with three convolution layers.
- Stage 4 consists of 6 residual blocks, each with three convolution layers.
- Stage 5 consists of 3 residual blocks, each with three layers.

Finally, the network has an Average Pooling layer followed by a fully connected layer having 2048 neurons with softmax activation function) **(Salvi et al., 2021**).

2.4. Performance Evaluation of the Classification Model

This study calculates image enhancement evaluation using PSNR, MSE, and SSIM values **(Swathi et al., 2017)**.

- **MSE (Mean Square Error)** is used to assess the ratio of the difference between the actual value and the value that the filter implied by using Eq. (1)

$$MSE = \frac{\sum_{i=1}^{M}\sum_{J=1}^{N}[X(I,J)-Y(I,J)^2]}{M*N} \tag{1}$$

where
X(I, J) represents an input image with an index *i* and *j*, having *M * N* pixels,
Y(I, J) denotes the resultant enhanced image at location (*I, J*).

- **PSNR (Peak Signal to Noise Ratio)** is used to Find the ratio of the most significant value of enhanced images to the noises that impact the image, so the best filter is one with a higher PSNR value by using Eq . (2)

$$PSNR = 10\ LOG\ 10\ \left[\frac{(Peak\ value)^2}{MSE}\right] \tag{2}$$

The Peak value is the maximum difference between an original image value and MSE.

- **SSIM (Structural Similarity Index)** measures the loss of image quality brought on by processing. It is a complete reference measurement that uses two images, the original image and the enhanced image, by using Eq. (3)

$$SSIM(X,Y) = [I(X,Y)].^{\alpha}\ [c(X,Y)].\beta[s.(X,Y)]^2 \tag{3}$$

where X and Y refer to two images with the same dimensions as the original and enhanced image; $\alpha > 0$, $\beta > 0$, $y > 0$ refer to constant exponents used here as weight parameters; and *l, s, c* represent luminance, structure, and contrast components respectively. In this work, the performance for the classification task used different metrics of accuracy that refer to the ratio of correctly predicted observations to the total observations (**Alfarhany and Abdullah, 2023)**. It is calculated as:

$$Accuracy = \frac{TP+TN}{TP+FP+FN+TN} \tag{4}$$

Precision refers to predicted positive observations corrected ratio to the total positive observations evaluated by:-

$$precision = \frac{TP}{TP+FP} \tag{5}$$

Recall (Sensitivity) refers to the ratio of predicted positive observations corrected to observations in actual classifies calculated using Eq. (6).

$$Recall = \frac{TP}{TP+FN} \tag{6}$$

The *F1- Score* is the ratio of balance and compatibility between the precision and the recall using Eq. (7) as the confusion matrix **(Ghadi and Salman, 2022; Alfarhany and Abdullah, 2023)**.

$$F1 - score = 2 \cdot \frac{Precision \cdot Recall}{Precision \cdot Recall} \quad (7)$$

where,
TP is the True Positive number of images of diseases classified as a disease,
TN is the True negative number of normal images classified as normal,
FP is the False Positive number of normal images classified as a disease, and false negative FN is the number of diseases of the images classified as usual.
A positive result in any one of the classification tests with a high specificity range is sufficient to make decisions in any disease type **(Rawat and Suryakant, 2019; Mateen et al., 2020).**

3. IMPLEMENTATION OF RESNET-50

The ResNet-50 Model is imported from the Keres library in Python with model weights available in the Keras package. Then, fine-tune ResNet-50 by adding Average Pooling with Dropout (0.5) and Dense with 2048 nodes and Dropout (0.5) on the top layer of ResNet-50. The original layer of ResNet-50 is prevented from training, but the layers added on the top layer of ResNet-50 are trained first to ensure that the added layers are working correctly and to know the accuracy obtained when training only the upper layers. After that, all ResNet-50 models with added layers and pre-trained weights are trained five times to warm up the model with a warmup learning rate (1e-4). After the warmup model trained for 20 epochs with batch size 8, the model propagates 366 times during the training process (2929 images/ 8=366) and the warmup learning rate (1e-4). As explained above, different hyper-parameters were used to modify the model's performance before training ResNet-50, which can be presented in **Table 1.**

Table 1. The hyper-parameters with the best values obtained ResNet-50 model.

Hyper-Parameters	Values	Hyper-Parameters	Values
Optimization Method	Adam	Learning Rate	1e-4
Activation Function	Softmax	Total No. of Epochs	20
Weight-decay of	0.0005	Image Size	(512×512)
DECAY_DROP	0.5	Early Stop Patience	5
Batch Size	8		

ResNet-50 was trained using a training set from APTOS 2019, which consists of 2929 fundus images. Each fundus image is attached with labels provided by the dataset. A validation set assessed the model during the training with 733 fundus images. During training, enhanced training and validation datasets were augmented by applying vertical and horizontal flip Rotation (0°-360°) to reduce overfitting and increase the model's accuracy. Finally, all pixels of fundus images are rescaled to (1./255) using Keras "ImageDatgenerator," in this step, if the training accuracy is increased or decreased five times, the model's training is stopped. The activation for all layers except the last layer was ReLU set to Adam optimizer because it is faster than the other optimizers at convergent, reaching the global minimum. At last, after training, the model with the most training and the lowest error rate on the validation set should be chosen and saved. The following steps have been used and clarified in the proposed training model by using the ResNet-50 network:

- Step 1: Split the training set into two sets, 20% for validation and 80% for training.
- Step 2: Set the initial value of hyper-parameters

- Step 3: Train the network using the hyper-parameters that were set previously.
- Step 4: Validation sets are used to assess the network performance during the learning procedure.
- Step 5: Repeat steps 3 and 4 for 20 iterations.
- Step 6: selecting the model with the best training that has the lowest error rate on the validation set
- Step 7: Use the testing set to determine the trained model's performance.

4. EXPERIMENTAL RESULTS

The proposed classification model has been designed and implemented using the programming python in Keras library in Google Collab notebook on 64-bit Windows 10 OS. The Pre-processing phase is implemented on APTOS 2019 fundus images, and then ResNet-50 is used to classify diabetic retinopathy using the enhanced APTOS 2019 fundus images datasets. The outcomes of using ResNet-50 for distinguishing between no DR and DR refer to excellent results of network capabilities. The model can classify 98.3% of the testing set cases with a Precision of 98.4%, an F1-Score of 98.5 %, and a recall of 98.4%. Image enhancement results are evaluated using three common metrics (RMSE, PSNR, and SSIM), as explained in **Table 2**. The results of the pre-processing steps are explained in **Fig. 6**.

Table 2. The performances Evaluation of Fundus Images Enhancement

Pre-processing Step	RMSE	PSNR	SSIM
Median Filter	1.98	139.69	0.96
CLAHE	18.44	95.68	0.71
Median Filter + CLAHE	16.52	96.64	0.8

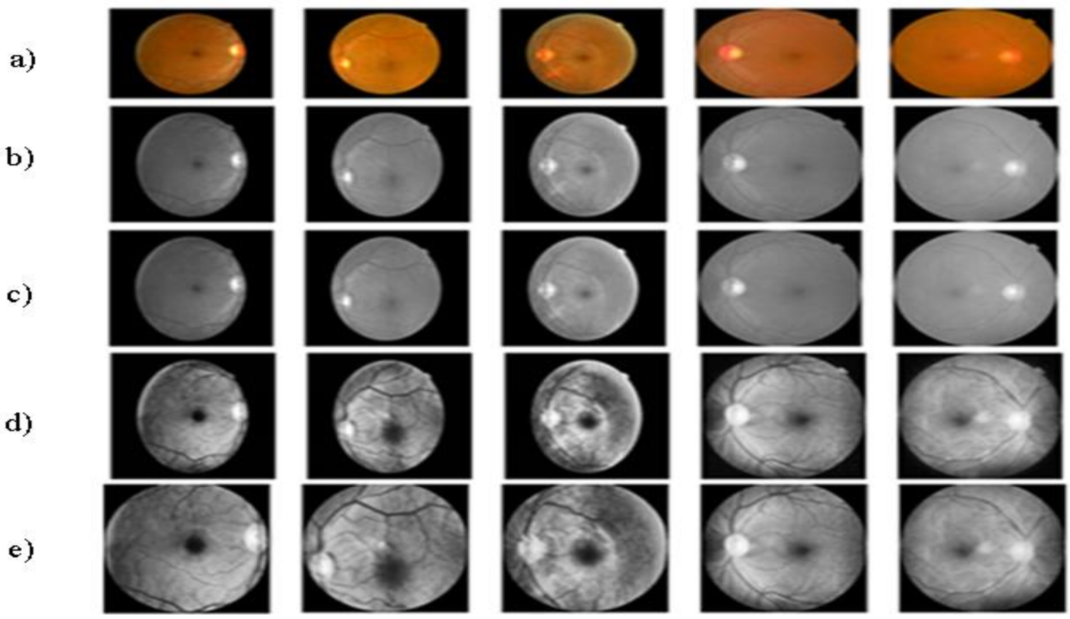


Figure 6 The output of the pre-processing method applied on APTOS 2019 for fundus: a)original images, b) images after converting to greyscale, c) images after the applied median filter, d) images after applying median filter and CLAHE, and e) images after circular cropped.

The best value obtained using the pre-trained networks ResNet-50 on the enhanced testing fundus images is the confusion matrix used to evaluate the model's accuracy, as explained in **Fig. 7**.

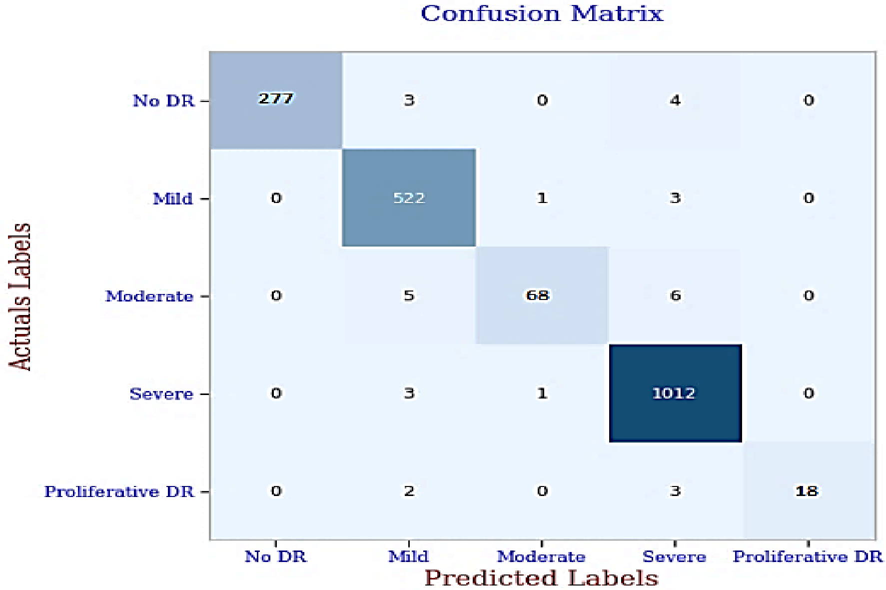


Figure 7. The confusion matrix with the accuracy rates of correctly classified samples per class in the testing set.

The proposed deep learning model's experimental results are evaluated using three common metrics (Precision, recall, and F1-score) as explained in **Table 3.**

Table 3. Result from testing fundus images

DR Class	Accuracy	Precision	Recall	F1-score
0	1.00	1.00	0.98	0.99
1	0.95	0.98	0.99	0.98
2	0.99	0.97	0.86	0.91
3	0.91	0.98	1.00	0.99
4	0.96	1.00	0.78	0.88

The comparative analysis of the proposed model for DR classification with and without applying image enhancement by different approaches is presented in **Table 4.**

Table 4. The comparative analysis of the proposed model for DR classification with and without applying image enhancement using different approaches

Approach	Accuracy	Precision	F1-Score	Recall
Using Original Images	79.91	80.32	81.13	80.32
Median Filter	84.76	84.11	84.91	85.71
CLAHE Circular crop	93.53	91.84	93.26	94.74
Median Filter + CLAHE + Circular Crop	98.39	98.4	98.5	98.4

As noticed in **Table 3**, the results which give a high accuracy of the proposed model for DR classification is when using the approaches of median filter and CLAHE with the circular crop with 98.39% accuracy, 98.4% precision, F1-score of 98.5% and Recall 98.4%.

5. CONCLUSIONS

This study proposed an automatic DR detection and classification model based on a deep-learning convolution neural network with transfer learning. Three main phases have been implemented to classify DR grades, including pre-processing, training the Resnet-50 network, and classification with evaluation. APTOS 2019 fundus images obtained from Kaggle have been used for training and testing in the proposed model. Five pre-processing steps enhance these images: resizing, grey scaling, noise removal, CLAHE, and cropping. Then, the Resnet-50 Network was applied to enhance the fundus images dataset using 5590 fundus images. Three metrics were used to evaluate the classification performance: accuracy, precision, and F1-score. The experimental results of applying an enhanced Resnet-50 network for classification DR grades showed excellent network capabilities. The model was able to classify DR with 98.39% accuracy, 98.4% precision, 98.5% F1-score, and a Recall of 98.4% for all used cases.

NOMENCLATURE

Symbol	Description	Symbol	Description
FN	The number of diseases of the images classified as usual.	SSIM	Structural Similarity Index
FP	The False Positive number of normal images classified as a disease, and false negative	*TP*	The True Positive number of images of diseases classified as a disease,
MSE	Mean Square Error	*TN*	The True negative number of normal images classified as normal,
PSNR	Peak Signal to Noise Ratio		

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