Predict Diabetic Retinopathy in Early-Stages: A Novel Ensemble Model using Efficient nets and an Automated System to Detect the Disease

Siddhartha Malladi, S. Suguna Mallika, Krishna Sai Prahlad M, Sai Madhav Reddy Nomula, Aadesh Pandiri

Abstract*: Diabetic Retinopathy is eye condition caused by high sugar levels inside the blood, which is the origin of excessive pressure inside blood vessels inside the eye, with the smallest vessels being the most vulnerable. This condition does not appear suddenly; rather, it develops gradually over time. After the disease progress, it can show symptoms like blurry vision, changes in vision from blurry to clear, and vice versa, blackspots or dark areas in the vision, poor night vision, fading out of colours, etc. Therefore, pre-emptive identification of disease is one of the beneficial tactics to prevent or get cured of this disease. This technique is also susceptible to human misjudgement, which exists in many clinical diagnoses. An Image Classification Model can accelerate the process of blindness detection in patients. We accomplish this by constructing a classifier using transfer learning that can extract key features from pictures and categorise them into separate stages. This work focused on making an efficient classifier with high accuracy and providing the patient with advance notice of their disease using an easy-to-use mobile application. Our model gave a 0.907 quadratic weighted kappa (QWK) score on independent test dataset and 93.2% accuracy on test time augmented data in multi-class classification. Furthermore, providing the necessary use cases with which the patient can track the diabetic retinopathy screening diagnosis

Keywords: Convolutional Neural Network, Deep Learning, Diabetic Retinopathy, Efficient Nets, Fundus Camera, Medical Image Analysis,

I. INTRODUCTION

In the world, the major reason of blindness amongst working-age adults is diabetic retinopathy [18]. Additionally, taking example of Hispanic American.

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These people of 50 years or above age have high chance of developing DR, and 19% of Hispanic Americans in the age group of 75 and above have suffered with DR [20]. Diabetic retinopathy in the initial stages does not pose any symptoms, which is why DR gets unnoticed in patients at the starting stages. However, after the disease progresses, it can show symptoms like blurry vision, changes in vision from blurry to clear and vice versa, blackspots or dark areas in the eye, poor night vision, fading out of colours, etc. The increasing sugar content has an impact on the vessels within the retinal tissues. Diabetic retinopathy may lead to complete blindness. People prone to this disease might have abnormalities in blood glucose, urinary proteins, high blood pressure, and long-term diabetes. Raised fats (triglycerides) in the blood can drive this disease and can be caused by irregular blood vessel development in the retina as the newly grown blood vessels can bleed into the vitreous—tiny amounts of bleeding impact the vision of the person as black spots. Increased bleeding can lead to permanent blindness. Two critical Diabetic Retinopathy stages are:

1. Non-Proliferative DR (NPDR) – The beginning stage primarily seen in people with diabetes. NPDR leads to tiny blood vessels leaking, retinal swelling, and blood vessels inside the retina can close off, so eyesight becomes blurry [21].
2. Proliferative DR(PDR) – The most severe stage of Diabetic Retinopathy, also known as neovascularization, is brought on by the development of new blood vessels in the retina. [21].

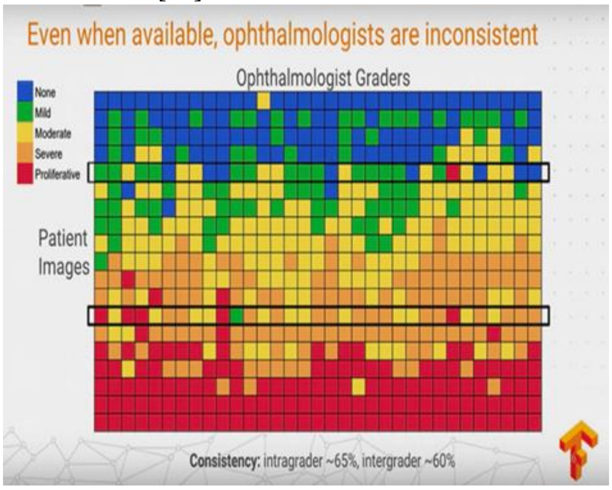

Fig. 1 google.com shows that ophthalmologists' diagnosis differs for the same fundus picture

A complication of diabetic retinopathy that affects the macula is called Diabetic Macular Edema (DME), which is located at centre of retina and responsible for central vision. The macula helps you see colour, minute details, and distant objects. It sends information to the brain that gets interpreted into images. It's needed for everything from recognizing faces to reading. DR causes DME when the retina can no longer absorb the fluids from those leaky blood vessels. That, in turn, causes the macula to thicken and swell. DME causes blurry vision, colours appearing dull, and trouble with facial recognition [36]. In DR screening centres, ophthalmologists first scan our dilated pupils and extract retinal images from both eyes to estimate the level of diabetic retinopathy. Unfortunately, human graders are sometimes inconsistent, as shown in Fig. 1. Hence, an efficient and accurate grader is required to give a judgement on a particular issue. Apart from the inconsistent grading, the above-said process involves a lot of time, as examining the retina and generating the report takes at least half a day. Manual diagnosis of these retinal images is a time-consuming job that necessitates the need for specialised experts with a strong background in identifying this eye condition using scans and other factors. Due to human limitations, the diagnosis is therefore expensive and can only treat a fixed number of patients at once. The procedure is also susceptible to human error, which can occasionally happen when doctors do several diagnostic tests for patients.

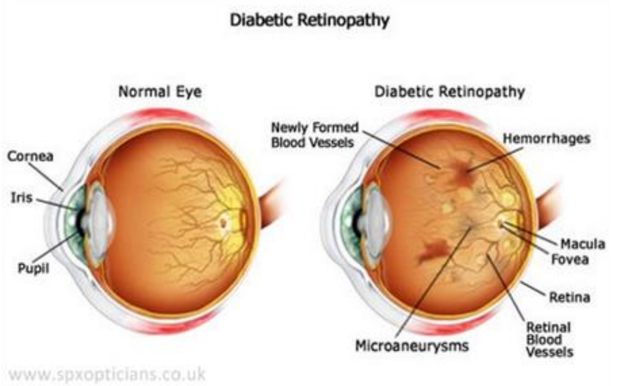

Fig. 2 Anatomy of the eye about diabetes and features of Diabetic Retinopathy decease [17]

Deep learning aids the present case and helps to provide the diabetic retinopathy diagnosis results accurately and instantly with minimal effort. Deep Learning has gained popularity in a variety of fields by portraying the universe as a hierarchical tree of concepts, with each notion determined by its link to simpler ones [24]. Additionally, to overcome these challenges, deep learning is a popular approach for computer-aided smart Diabetic Retinopathy diagnosis, and it also made some headway in biomedical image processing [43]. In this work, we will try out some of the popular convolutional neural networks (CNN) and some custom ensemble neural networks. Also, fine-tune it using the hyperparameters and train it with various open-source datasets which are available on the internet. We would like to train the model so that it produces the most accurate results possible. Most of the work available currently is based on training a single model and providing accuracy. The current implementations lack full-scale integration between the patient and the diabetic retinopathy model. Additionally, most people overlook the extremely valuable hand-crafted elements that could help to a more reliable estimation. CNN's can be used to automatically identify DR cases, however they come with time-consuming labelling tasks and data privacy concerns [41]. To tackle this issue, we use secure cloud storage to dump all the image and diagnostic data. This work concentrates on comprehensive integration, from hand-crafting the hyperparameters of the ensemble model with maximal accuracy and QWK score to testing the patient to see if he has the disease or not, and then describing the disease severity level. We use a mobile application and a fundus camera to eliminate the need for a physical grader. The mobile application has the functionality to get input from the fundus camera and process it in the embedded ML model in the application. It provides a report on the current patient situation and stores it in a database.

II. LITERATURE REVIEW

We will examine recent advancements in this area. A work is based on the APTOS Blindness Dataset using retinal images and projects an accuracy of 96.15%, a sensitivity of 79%, and a precision of 89% [11]. In 2011, research work from the Indian Institute of Sciences, Bangalore, explained the classification and detection of this disease from retinal images in IEEE [8]. The research concluded, "Random Forests are better to use for predicting and classifying DR with an accuracy of 90% for standard cases and 87.5% when it is a severe case" [8]. A Multi-layer Perceptron algorithm was used to classify fundus images as normal and abnormal by using features such as DCT and nine other statistical parameters with an average accuracy of 100% [13]. With single Colour Fundus photograph (CFP) and they applied a Dense Net encoder to construct a visual embedding [23]. Moreover, the Convolutional Block Attention Module for Bi-categorization Task Accuracy is 94%, and the network shown good competency for severity grading with QWK of 0.88 and accuracy 82%, indicating that it is promising for autonomous diagnosis [23]. An altered Xception network [25] is used by adding feature maps from various convolutional layers and a Multi-layer Perceptron as the classification head [24]. The Eye PACS dataset was used and implemented a two Dense Net's [14], Xception Network [51], ResNet50 [37], and InceptionV3 which are credible architectures with an ensemble stacking to improve the feature maps which yielded noteworthy results [26]. This research is done using APTOS dataset and they applied EfficientNet-B3 architecture for both multi and binary categorization and implemented a function for lesion detection and fact checked by exploiting the DIARETDB11 dataset [27]. Whereas for DR detection [32], employed a feature engineering process and then used Support Vector Machine [32] to grade the Diabetic Retinopathy level. To segment the micro-aneurysms, hemorrhages, and exudates, a 10-layer CNN was employed which gave a sensitivity and specificity of 0.8758 and 0.7158 and they mentioned that DR systems could help graders as an initial screening tool to distinguish between eyes with and without referable DR, allowing eye specialists to focus just on patients with referable DR [9].

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A novel unsupervised classification model is developed by adopting a muti-model domain method and combined with a weight mechanism to obtain a classification model that measures the importance of each domain and weighted pseudo-labelling strategy that attaches the source features while training [41]. This work deployed an automated estimation of microaneurysm (MA) turnover tool which aligns the fundus photos from numerous encounters of the person. It localizes and performs dynamic analysis on MA to assess new, disappeared, and persistent lesion maps and predicts the microaneurysm turnover rates. This tool is evaluated on Eye PACS dataset with 40,542 fundus images of 5084 patients and produced a 63.2 specificity and 90% sensitivity [10]. Most diabetic Retinopathy classifiers have high sensitivity (87.0- 95.2) but lower specificity (49.6–68.8) percentages [49]. The screening region should be acceptable for the examination procedures, and the Retinopathy detection systems should be used consistently and systematically. Also said that seven-field retinal imaging is preferable for Diabetic Retinopathy screening, but two-field imaging is sufficient. Furthermore, guidelines of referable DR must be defined beforehand, technology infrastructure, experienced and qualified staff should be present at screening to ensure t retinal images are stored securely to protect patient information [46]. Regardless of their success, Machine learning algorithms needs individualized experience and domain specific knowledge to locate the most appropriate features. In [35], for lung cancer detection, the authors utilized an optimized deep learning approach showing it is effective in image classification. The networks that employed hand-crafted configurations outperformed the models that did not use them and even exceeded the stated baselines and designs [50]. In [12], for those who require close monitoring and/or therapy. At Temple University Hospital, a diabetic telemedicine study was conducted with the goal of improving affordable access to eye care. It said that an excellent quality retina image, patient participation, and timely follow-up are essential components of a diabetic retinopathy telemedicine screening programme. To prevent blindness in a systematic way, a successful and timely telemedicine screening programme must include reasonable healthcare costs, patient comfort, and appropriate time to treatment. A comparison of DR severity between human retina specialists' gradings and AI based screening system which is approved by FDA [48]. They took the ultra-widefield (UWF) color images and concluded that like [9] that AI system demonstrates adequate accuracy in recognizing asymptomatic diabetic persons with referable Diabetic Retinopathy compared to fundus image seen by medical professionals. Thus, offering an appropriate method for the disease screening. As the statistics show, machine learning and deep learning algorithms are better at predicting and classifying diabetic retinopathy.

III. METHOD

A. Dataset:

Insufficient utilization of independent test datasets makes models more likely to overfit data and learn only the dataset-specific artefacts rather than underlying pathology and the genuine disease features [9]. These findings show that a stronger dataset is required in order to develop Deep Learning technologies that can be used in real-world clinical settings. Dataset labelling is costly yet important for present deep-learning-based diabetic retinopathy classification methods.

Table- I: Some of datasets available in open source

Dataset Name	Number of images	Resolution (in pixels)	Published Institution	Year
DDR Dataset [9]	13,673	128 × 128 to 1024 × 1024	Tao Li and Yingqi Gao *et al.*	2019
IDR iD [44]	516	4288×2848	Prasanna Porwal *et al.*	2018
Messidor and Messidor-2 [45]	1200 + 1748	440x960 to 2304x1536	Decencies, E *et al.*	2014, 2018
Eye PACS Dataset [6]	35,126	1396x1396 to 3168 x4752	Eye PACS, LLC	2015
APTOS DATASET [7]	3662 + 1928(test images)	1024x1024(resized)	Aravind Eye Hospital, India	2019

Table.1 above specifies some of the datasets that are available in the open-source and gives brief details about them. From 9598 patients, 13,673 fundus images are available in the DDR dataset. According to the DR level and image quality and, these photographs were categorized into six classes by seven graders. The category six indicates low quality retinal images. The Indian diabetic retinopathy image dataset (IDR iD) [44] contains nearly 500 fundus photographs taken at Indian health center by an ophthalmologist.

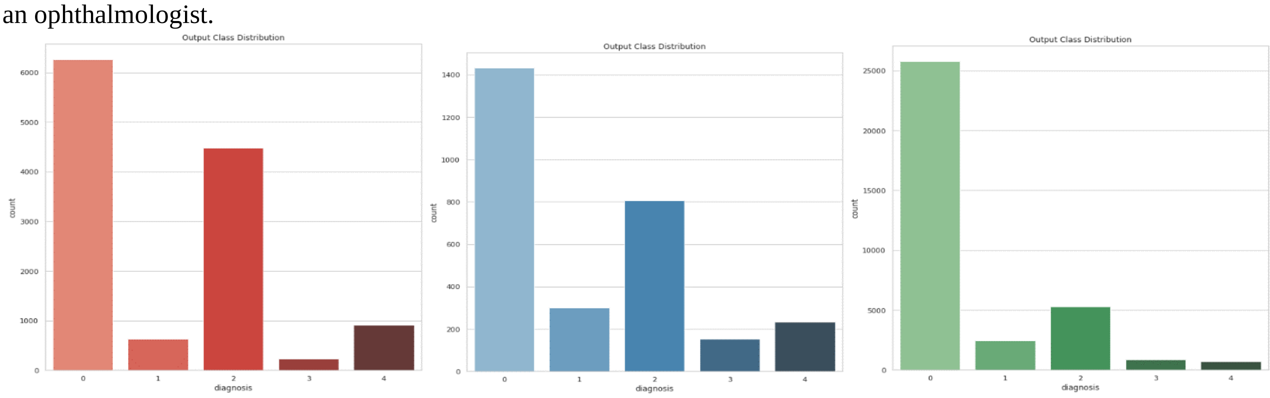

Fig. 3 (a) DRR dataset distribution, (b) APTOS dataset distribution, (c) Eye PACS dataset distribution

Further to substantially retain the combination of disease categories, 516 images were further separated into an 80% of train and 20% of test. It offers fundus images of sufficient quality, clinical relevance, and reality. The Messidor dataset [45] is an open-source dataset released by Messidor programme partners, consisting of 1,200 fundus photos. The Messidor-2 [45], an expansion of Messidor, has been widely used by academics worldwide for DR research projects involving analysis. It includes 1,748 retinal pictures from 874 exams. Despite the lack of official labels for this dataset, researchers can access third-party scores for 99% of 1,748 retinal images were judged by a three-member panel of eye specialists. We used the popular Eye PACS [6] 2015 dataset, which is hosted on Kaggle and consists of 35,126 labelled images, and each picture contains either a left or right eye. These fundus images are taken under different image settings. This data set includes five categories. Multiple fundus cameras were used to take the pictures at various clinics, and the resolutions are high as 3168 x 4752 pixels and low as 1396 x 1396 pixels. The Eye PACS dataset is used for pre-training models as there is a large amount of data for generalization. Another newer dataset consists of more resolution, and quality images called Asia-Pacific Tele-Ophthalmology Society Symposium also known as APTOS in 2019 [7]. The fundus images are collected by Aravind Eye Hospital, Chennai. The dataset contains 3662 labelled fundus images. In addition, 1,928 test images are not labelled and can be used for fine-tuning our model. The eye photographs provided in the dataset are captured from a color fundus camera. A fundus camera has a microscopic lens to photograph the eye's interior surface, including the retina and internal nerves. As mentioned in Fig. 3, Eye PACS and APTOS datasets have similar distributions of classes. There are imbalances in the data because of more cases of no DR level I.e., label 0.

B. Evaluation Metrics

The International Clinical Diabetic Retinopathy (ICDR) classifies the disease into five stages: normal, mild, moderate, severe, and proliferative. [42]. Performance metrics currently used for this work are quadratic weighted kappa (QWK) scores to evaluate the outcome predictors. It is a score measuring the agreement between 2 ratings.

The score is determined between the actual tested results and the model-predicted scores as shown in (1). QWK score typically ranges from zero (random agreement between raters) to one. (Complete agreement between raters) and rarely it may drop below 0 if the raters' agreement is lower than would be predicted by chance [19].

$$k = 1 - \frac{\sum_{i=1}^{k}\sum_{j=1}^{k} w_{ij}\, o_{ij}}{\sum_{i=1}^{k}\sum_{j=1}^{k} w_{ij} e_{ij}} \qquad (1)$$

$$w_{ij} = (i-j)^2/(n-1)^2 \qquad (2)$$

Where n= number of labels

The models are evaluated based on the QWK score because of this unique feature. I.e., if there are different ratings from two raters, the ratio of kappa will be affected excessively as the difference between scores matters in calculating the ratio. Therefore, the QWK score is a volatile metric for analysing the statistical models. However, the QWK score being the primary metric, the secondary metrics such as accuracy and F_1 score (4) can be calculated.

$$Sensitivity = \frac{TP}{TP+FN} \qquad (3)$$

$$F_1\ Score = 2 \times \frac{precison \times recall}{precision + recall} = \frac{TP}{TP + \frac{1}{2}(FP+FN)} \qquad (4)$$

C. Approach

1) Data exploration and analysis

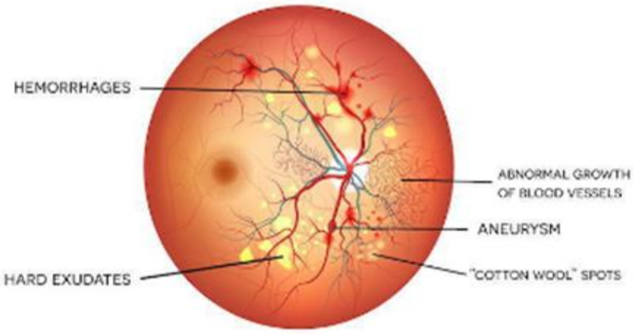

Fig. 4 Many serious problems impacting the blood vessels that nourish the retina can be caused by diabetic retinopathy [16]

Retinopathy in retinal Images is detected by features like abnormal growth of blood vessels, hard lipids, cotton wool spots, and spots of thick blood vessels in the retinal section. A network of blood vessels, the optic disc and macula can be seen in a healthy retinal photograph. [13].

In some fundus images, it is difficult to find the DR features like in Fig. 4. Fundus photography involves the flashlight focusing on the eye, where there are chances of change in the colour of the images taken from the fundus camera, which impacts the balance of light and brightness of the picture. As we tried zooming to see the details (using a real-size image), we observed some abnormalities, which signifies the image size attribute impacts the model performance.

The t-distributed Stochastic Neighbour Embedding (t-SNE) method to visualise the data in lower dimensions based on diagnosis levels like zero. t-SNE helps to separate this class from the other classes (1–4), which are levels of severity, as illustrated in Fig. 5. As a result, separating 1-4 severity levels is challenging.

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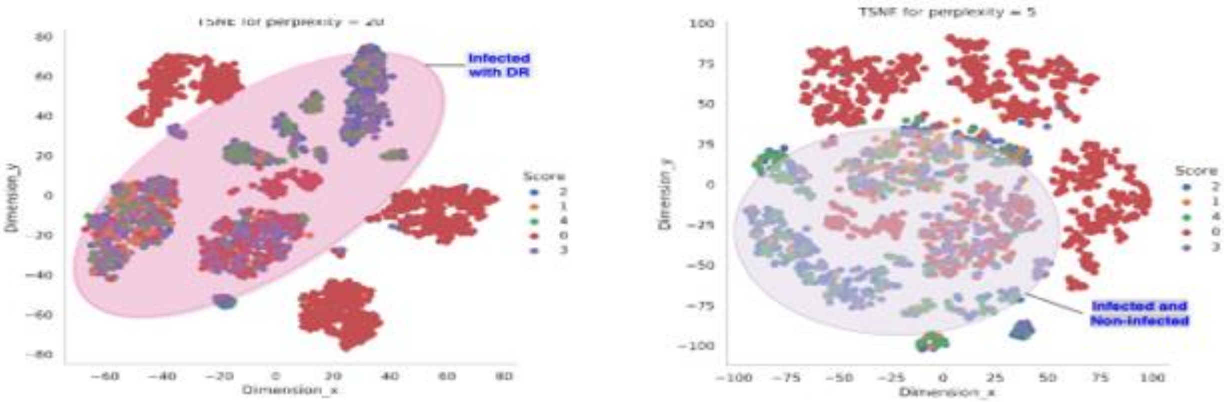

Fig. 5 t-SNE visualization applied on APTOS Dataset images with perplexity (a)5 and (b)20

2) Pre-processing

When gathering dataset, the variations in light conditions and camera configurations will result in significant data discrepancy. The following process will convert the raw input in Fig 6(a) to a processed state through which the model can quickly identify the DR features based on the exploratory data analysis. The processed image will exhibit the DR symptoms like abnormal growth of blood vessels and hemorrhages more precisely than the raw image.

$$F(x) = (1 - \alpha) * x^0 + \alpha * x^1 + \gamma \qquad (5)$$

$$G(x, y) = \frac{1}{2\pi\sigma^2} e^{-(x^2+y^2)/2\sigma^2} \qquad (6)$$

We start by resizing the image, as processing a raw image that may have higher or lower resolution can lead to inconsistent processing time. Then we remove the blackout edges by converting them into grayscale and fixing a threshold that would crop the borders. The image is then converted into an ideal circle image by performing a circle crop (Fig 6(b)). To achieve it, find the largest circle radius that could fit in the current picture, create a dummy blank image of the exact resolution as the original, insert a circle of radius, and mask the dummy image using the original. Another image is generated using gaussian blur on the above image, i.e., circle cropped. Now, image blending is applied to the gaussian blur image referred to as x^1 and the circle crop image referred to as x^0 in (5) to improve lighting conditions. The blended value is maintained to set the level of brightness of the image in such a way that it observes the patterns for DR symptoms, as shown in Fig. 6. (c). Then, follow one round of circle cropping and resizing to get the final image. So as seen, the model tends to focus on essential features, i.e., eyeball, which is the centre of the picture. Finally, the image is resized based on the requirement of the certain model. As we have numerous models requesting different image sizes.

Fig. 6 Fundus image showing pre-processing steps: (a) Raw Image (b) Circle cropped Image (c) Processed Image

3) Data Augmentation

The augmented data is also used to decide the problem of class disparity in the classification tasks [11]. The Image Data Generator method from the Keras, an open-source library, is used to augment the current dataset. Also, the dataset includes a class imbalance in the output class distribution.

The augmentation techniques applied on images include:

- Zooming of the image
- Horizontal flip
- Width shift
- Height shifts
- Vertical flip
- Random rotation of 0-90 degrees

During the training of the neural network, each image is randomly augmented. For ease of computation, each image's pixel values are converted into the binary values 0 and 1 by dividing them by 255. It influences the activation function's efficacy also [11]. Image augmentation is extremely helpful for these datasets to make models more robust and would also have a higher ability to generalise well.

4) Preparation of Dataset

As the problem is a multiclass classification problem, the target is changed to a multilabel problem instead of predicting a single label. I.e., if the target is a certain class, it encompasses all the classes before it (ordinal classification). For example, the encoding of level 4 would usually be ` [0, 0, 0, 1, 0] `, but in this case predicted output is ` [1, 1, 1, 1, 0] ` [5].

This encoding will affect the QWK score drastically, i.e., if a two-label is predicted instead of a three, the penalty would be way less than if it predicted a 0 label. A regression analysis that predicts an ordinal variable is known as ordinal regression [1]. An Ordinal variable whose value exists on an arbitrary scale where only the relative ordering between different values is significant [3]. The training and testing split of 0.15 is followed.

D. Model

1) Network Architecture

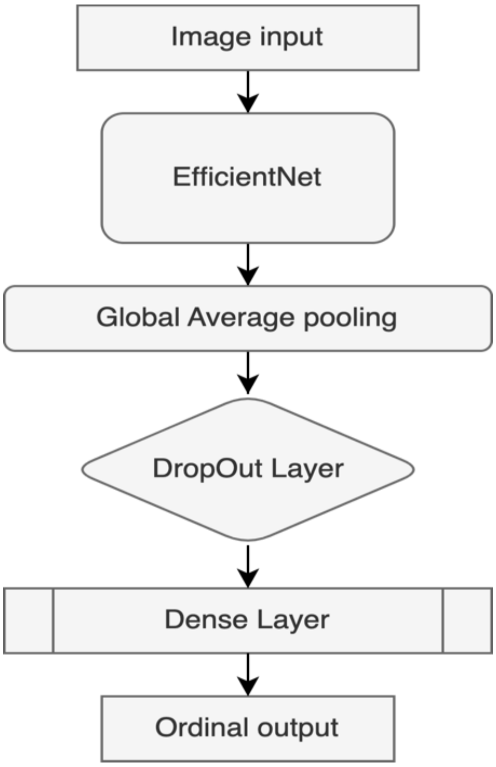

Fig. 7 Flow Diagram of Single Classifier. The Efficient Net is attached to more 3-layer for providing better classification

This work focuses on classifying each fundus image accurately. A deep neural network should be constructed and trained to obtain the image's features and output the disease's severity as shown in Fig. 7. Classifiers like SVM and deep neural networks have a vast history concerning biosystems [19]. But, training a raw deep Conv Net with randomised weights with a small dataset is difficult. Alex Net [34] is a CNN that is 8 layers deep. More than hundred thousand photos from the ImageNet repository are used to train the neural networks, which is accessible as a pretrained models. Furthermore, there are many algorithms such as Dense Net [14], and InceptionV3 [47] but in the study, Efficient Net scored better compared to others. Efficient Net is a unique CNN architecture and scaling method that evenly scales all depth, width, and resolution dimensions using a compound coefficient [2]. Table. 1 from [2] shows how the Efficient Net layers are structured. With considerably fewer parameters, the family of models is efficient and provides better results. Pre-trained weights will be used where the model is trained on the ImageNet repository. This is a massive dataset with over 14 million records [4]. The convolutional neural networks achieve better performance on ImageNet [34] compared to previous state-of-the-art models [34]. Transfer learning is used to save time and get better performance. Transfer learning involves passing on the learned features of one application's model to another. When there isn't enough input data to train the Neural network, transfer learning is helpful [38] [39] [40]. The acquired features of the model from one system are applied to a new set of input data using this technique, which uses pre-trained models like Res Net [37], VGG, Alex Net [34], etc. Accuracy can be increased by freezing different layers in pre-trained CNN's. Though Efficient Nets perform well on ImageNet, to be most helpful, they could be transferred to other datasets [2]. Hence, the standard architecture of Efficient Net with transfer learning is applied. Here, Efficient Net will predict the ordinal vector. If an image falls into level X, it automatically falls into all levels from 0 to X-1. After experimenting with the Efficient Net models like B1, B2, and B7, models B3 and B5 turned out to be the best fits for the problem statement. B7 turned out to be more memory-consuming and heavy to train. As the final classification targets, the mobile, B3 and B5 are well balanced. This work uses four models, i.e., three Efficient Net B5 and one EfficientNetB3. Then we ensembled it all as a single classifier. Our algorithm is implemented in TensorFlow [29], which is an open-source framework.

E. Training Procedure

The process involves training at multiple stages with parameters and datasets. The Eye PACS and APTOS dataset's images looked different, but the native features remained the same irrespective of the dataset. Eye PACS dataset is used to train two models, and additional datasets are integrated as part of the data integration phase from several fundus machines. Training the model with this knowledge will enhance its performance in general and elevates the significance of natural diabetic retinopathy features through the depreciation of sensitivity to instrumental noise.

Pre-processing is not applied to reduce the risk of overfitting a particular class. Training begins by initializing with ImageNet weights, followed by training the model for 15 epochs with Eye PACS data. The primary training is carried out on the APTOS dataset, with each model using different settings. The pre-trained weights are taken for two model weights and ImageNet weights for the other two. Different settings are used for the model to generalize well with different datasets or real-time usage. The networks use 5-class sigmoid activation to label the classes. We set the training for 15 epochs. In each epoch, the QWK score is computed, and the model with the best QWK is saved. Adam optimizer [30] and binary cross entropy [31] are used as optimization and loss functions. Learning rate reduction and early stopping are also utilized on validation loss with a factor of 0.25 and patience of 10. During the training process, Grad-CAM visualization [22] is applied to see if the input's essential features (e.g., cotton wool, blood vessels, scabs) are captured by the CNN, as shown below in Fig. 8.

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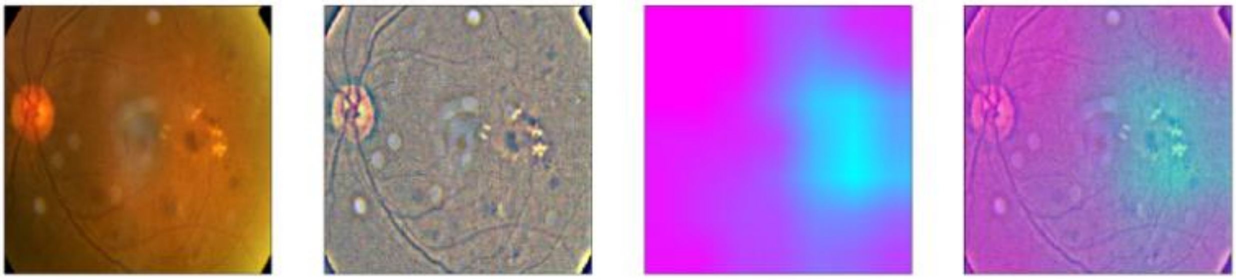

Fig. 8 Grad-CAM visualisation of Sample Image fundus images showing how the CNN is detecting the features. Best viewed in colour

1) Ensembling

Ensembling is for more generalization, aiming to show as much data variance to models as possible. Ensembling often yields significant advancements in accuracy, though with an increase in complexity and computational cost. The EfficientNetB5 model that we are using has nearly 28 million trainable parameters. Adding weak networks to an ensemble can improve performance [15]. To achieve this, all the models are combined by using different resolutions for each model, as listed: EfficientNet-B3 (300x300), EfficientNet-B5 (456x456), EfficientNet-B5(380x380), EfficientNet-B5(456x456). After the Efficient Net models, a global average pooling layer is concatenated to the network. Additionally, a dropout layer [28] is attached for generalization with a probability of 0.5. Finally, a fully connected layer receives the feature vector.

Furthermore, the feature vector varies from ninety thousand to two million features for the different model configurations we are using and is passed on to four classifiers. The following hyperparameters were set Adam optimizer, binary cross-entropy loss, initial learning rate of 0.5*10-4, and sigmoid activation function. Additionally, the learning rate is reduced automatically when validation-loss with patience of 3 is applied, and the reduced factor is set to 0.25. The TensorFlow framework and the Keras library are used to build the algorithms. Models are trained on Kaggle notebooks with GPU support, which have a Tesla P100 GPU, 16GB of RAM, and an Intel Xeon CPU with a clock speed of 2.2GHz. The machine took 8.8 hours to train the models. The four models' outputs are taken, the statistical mode is calculated, and this is the final output of the ensemble model, as depicted in Fig. 9. Based on the experiment results, the ensemble model gave one of the best in terms of Cohen kappa score and Accuracy.

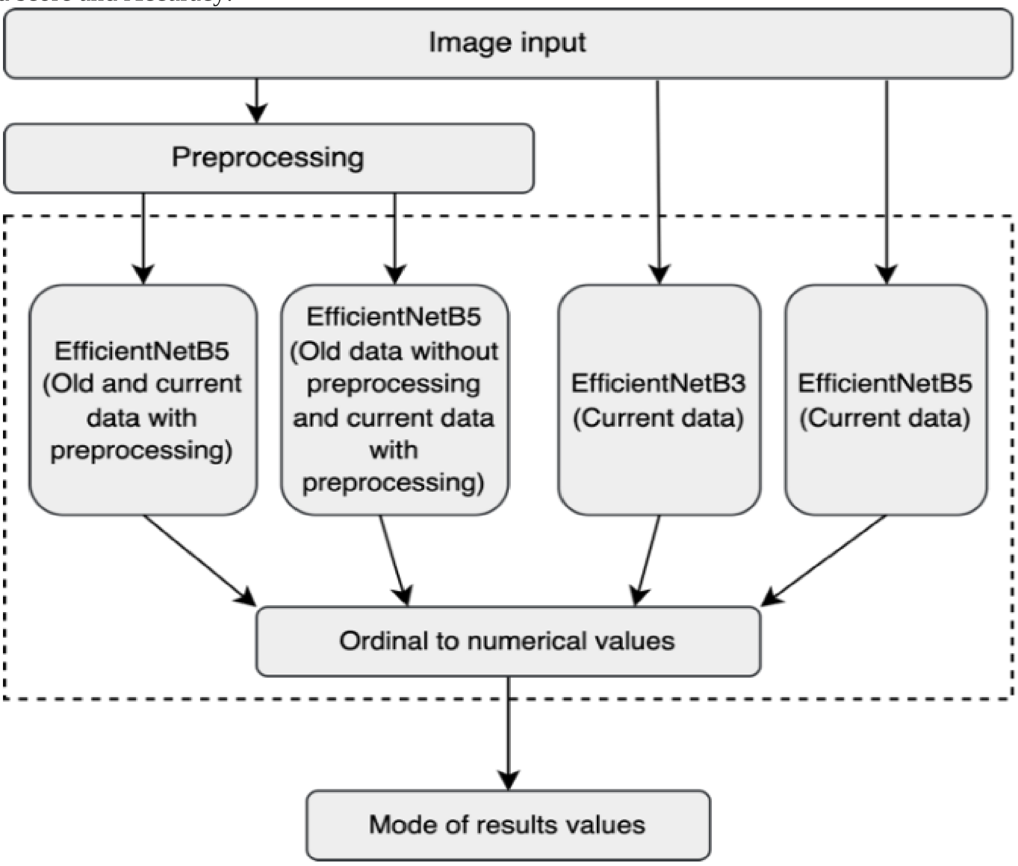

Fig. 9 Ensemble Model of four Efficient Net Models where three Efficient Net B5 and one Efficient Net B3 models. These output the ordinal vector which is further converted to diagnosis level.

IV. RESULTS

Table II A Brief Overview of The Latest Research Works/Publications About Diabetic Retinopathy Prediction Via the Fundus Images Taken from The Patients, Open-Source Datasets, And Comparison of Those Results.

Reference	Method	Dataset	Result	Published Year
Kanika Verma et al. [8]	Random Forests	STARE Database	Normal cases- 90% and severe NPDP- 87.5 Accuracy	2011
Bhatkar et al. [13]	Multi-layer Perceptron Classifier	DIARETDB0	100% Accuracy for normal and abnormal	2015
Malavika Bhaskaranand et al. [53]	Custom MA turnover estimation tool aligns	EyePACS	90% sensitivity and 63.2% specificity	2016
Jen Hong, et al. [52]	Custom 10-layer Convolution Neural Network	CLEOPATRA database	sensitivity of 0.8758	2017
Qummar et al. [26]	Ensemble model	EyePACS	AUC, precision, recall individually calculated	2019
N. Firke et al.[11]	Convolutional Neural Network	APTOS	96.15% Accuracy	2021
Sugeno ,et al. [27]	EfficientNetB3	APTOS	specificity and sensitivity values ≳ 0.98	2021
Gharaibeh, et al. [32]	Support vector Machines	DIARETDB0, DIARETDB1	96.8 % accuracy	2021
Farag, et al. [23]	DenseNet169 with convolutional Block Attention Module	APTOS	82% accuracy - 0.888 (QWK)	2022

Table. II shows a comparison of the study with recent research articles. The hybrid feature vector and SVM classifiers had the highest average accuracy in binary classification (97.8%) and multiclass classification (89.29%), respectively. The final ensemble model gave a quadratic weighted kappa score of 0.907 in the hidden test set from Kaggle website. While for the local test set, TTA (Test time augmentation) is applied with an accuracy score of 93.2% in multi-class classification, which asserts that the model is generalised on new data. As shown in Fig. 10, the model performs poorly in classifying severe DR, i.e., level 3, but it provides greater than 80% confidence in all other levels. An image is classified (pre-processing, inference, averaging) in 1.9 seconds on an ensemble, meaning real-time feedback for the patient is possible.

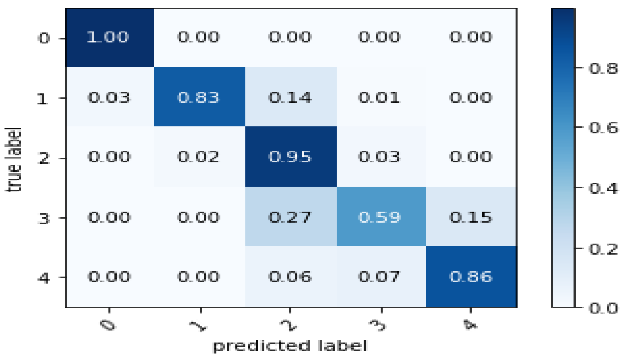

Fig. 10 Confusion Matrix of Ensemble model which is comparison between the predicted label and the true label

V. IMPLEMENTATION

For medical purposes, it is vital to translate observations into the most accurate model predictions. For usage on small devices, i.e., mobile phones, the model is converted to a light-model version that will occupy less space with TF Lite [29]. We experimented with mobile-friendly algorithms such as MobileNetV3 [28], but Efficient Net with TF Lite conversion yielded the best results.

Furthermore, it makes this model inference even faster by using quantisation on both weights and activations. Weights pruning is also done to increase inference speed further.

The primary step of this DR screening process is to dilate the patient's eye with Tropicamide and Phenylephrine ophthalmic solution for approximately three hours and capture the retinal images of dilated pupils using a mobile fundus. The retinal image is captured with the help of a third-party application that facilitates the feature of zooming range and enough focus and light, as demonstrated in Fig. 11. After capturing the retinal image, it is stored on the local device so that our mobile application can access it, and it is passed to the ensemble model to predict the DR severity. The mobile application is designed to coordinate with the fundus camera, and the user can maintain their profiles. In addition, it has a tracking history showing previous test trials and an option to shoot basic FAQs about DR. The history tracking uses the support of a database to maintain the user's test trials with their timestamps. In addition, it provides information such as dietary guidelines to be followed, precautions to be taken, and other necessary information. Mobile applications are built using the technology stack of cross-platform mobile applications, specifically the Flutter framework and Dart as the programming language.

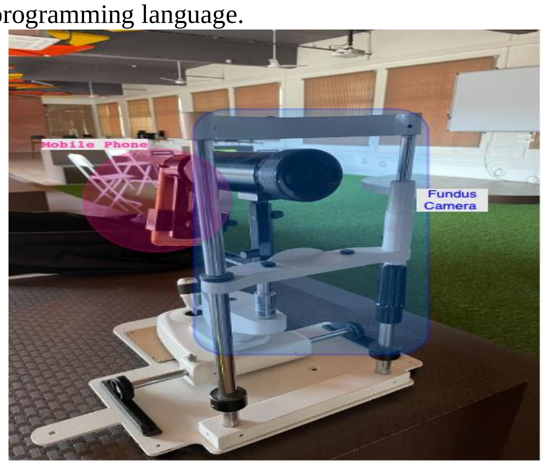

Fig. 11 Image of the mobile fundus camera setup to screen patients and provide the diagnosis level in mobile application

VI. DISCUSSION

This work aimed to dig out more interesting facts about health issues derived from retinal images and respective hemorrhage patterns. The plan is to acquire a much cleaner and well-balanced dataset that helps to a great extent by improving the classification accuracy. The latest datasets could help the network identify more features.

The sensitivity while classifying the mild, moderate, severe, and proliferate classes is not as accurate as the normal class, so these can be improved to a better extent by penalizing the weights. One of the concerns in this implementation is the inference time, which is approximately two seconds, which we could significantly reduce further by using hardware optimization techniques and changing the model hyperparameters appropriately.

A crowdsourcing model for getting images would be helpful. Enhancements such as data augmentation and the use of numerous pre-processing approaches will be carried out to improve the results synch, resulting in greater refining of the fundus images. We can take the application to the next stage by manually implementing a doctor-patient relationship where a patient can register with an ophthalmologist of their choice and get a prescription from the doctor based on the patient's current and previous DR screening on the application itself. It can be treated as a conversion from an automatic process to a patient-doctor relationship.

VII. CONCLUSION

Diabetic Retinopathy is a significant and low-monitored disease whose effects on vision are averse to the extent of complete blindness. Early detection and preventive measures for this diabetic retinopathy are always a good choice. The patient could get instant results and a quick diagnosis from the trained network.

Deep learning techniques will solve this issue through careful pattern extraction from previous testimonials of the retinal images. Through keen visualizations and various feature extraction experiments, Efficient Net, Convolution Neural Networks, and transfer learning algorithms like ResNet50 and Inception V3 exhibit higher accuracy in predicting the severity levels of DR. The quadratic weighted kappa score is 90.7%, and the test accuracy is 93.5% with the ensemble technique using Efficient Net models.

VIII. DECLARATIONS

A. Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

B. Conflict of interest

The authors declare no conflict of interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. No potential conflicts of interest exist for any of the authors with respect to this research and manuscript.

C. Consent for participate

Written informed consent was obtained from all participants prior to inclusion in the study.

D. Data and materials availability

The datasets generated during and/or analysed during the current study are available on the internet https://www.kaggle.com/c/aptos2019-blindness-detection, https://www.kaggle.com/c/diabetic-retinopathy-detection, https://github.com/nkicsl/DDR-dataset.

E. Code availability

All code and analyses which in python are available from the corresponding author upon request

F. Author Contributions

All authors contributed to the study's conception and design. The Diagrams and Datasets are acquired by M. Krishna Sai Prahlad and N. Sai Madhav Reddy. Siddhartha Malladi worked on the Machine learning section. Aadesh, Madhav built the flutter application from scratch.

Suguna Mallika is the backbone providing essential information on Machine learning and Diabetic Retinopathy. The first draft of the manuscript was written by Siddhartha Malladi and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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