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A Systematic Literature Review on Diabetic Retinopathy Stage Diagnosis Using Deep Learning Approach

Vishwanath K R[1], Amrutha A[2], Amogh B M[3], Yajat S Murthy[4], Dr. Vinutha D C[5]

[1]*Vishwanath K R, Computer Science Engineering (Artificial Intelligence and Machine Learning), Vidyavardhaka College of Engineering*
[2]*Amrutha A, Computer Science Engineering (Artificial Intelligence and Machine Learning), Vidyavardhaka College of Engineering*
[3]*Amogh B M, Computer Science Engineering (Artificial Intelligence and Machine Learning), Vidyavardhaka College of Engineering*
[4]*Yajat S Murthy, Computer Science Engineering (Artificial Intelligence and Machine Learning), Vidyavardhaka College of Engineering*
[5]*Dr. Vinutha D C, Computer Science Engineering (Artificial Intelligence and Machine Learning), Vidyavardhaka College of Engineering*

Abstract - Diabetic retinopathy is a medical condition that occurs due to diabetic mellitus causing blindness in the later stages. As the name says it is caused for people with the diabetes of type 1 and type 2 for a period of 20 years or more. However, early diagnosis and proper treatment at the initial stages could reduce aggressive forms of threatening retinopathy by up to 90%. According to the 2019 census from the ninth edition of the IDF Diabetes Atlas, India is put in the second slot right up to 2045 with people who are aged between 20-79 years. In 2019, India had 77 diabetic patients. In the recent survey of 2022 by the Union Health Ministry of India, almost 17% of the Indian population has diabetic retinopathy of which 3.6% is sight threatening. Specific to the rural population, 10.4% had diabetes of which 10.3% were diabetic retinopathy affected. From the WHO survey, it is estimated that by 2030, diabetics with retinopathy will increase by 50%. Without proper treatment, the individual is more likely to lose his vision. So, to prevent it, early detection of diabetic retinopathy and its stage is necessary.

***Key Words*:** Diabetic retinopathy, fundus, proliferative and non-proliferative, deep learning.

1.INTRODUCTION

Ophthalmology, a specialized field in medicine, is dedicated to researching, diagnosing, and treating various eye disorders. Historically, eye problems were diagnosed manually, requiring significant time. Diabetes, a chronic illness impacting our body's ability to process food, disrupts the usual breakdown of foods into glucose, leading to elevated blood sugar levels. In diabetes, the body either produces insufficient insulin or doesn't use it effectively, resulting in higher blood glucose levels. Complications of diabetes encompass issues like diabetic retinopathy-(damage to the eyes), neuropathy, (nerve damage), nephropathy (kidney disease), cardiomyopathy-(heart problems), gastroparesis, and skin problems.[8] Notably, eye problems rank as a primary cause of blindness in elderly populations. The World Health Organization ((WHO) predicts a rise in patients with ocular disorders as the global population ages. Consequently, there is growing interest in utilizing artificial intelligence (AI) to enhance ocular treatment and reduce healthcare costs, particularly with the integration of telemedicine. Despite the abundance of medical facilities, the prevalence of eye diseases remains high. Common causes of visual impairment include diabetic retinopathy, age-related macular degeneration, and glaucoma. Other issues affecting the eyes range from cataracts and macular edema to neovascularization of the choroids (CNV), retinal detachment, refractive errors, amblyopia, and strabismus, all of which may contribute to a compromised visual prognosis.

With the use of Artificial-Intelligence (AI) in real-world problems it is possible to reduce human invention. The count of ophthalmologists in India is 11 per million. So, for a country with approximately 1.428 billion, we could expect 130 ophthalmologists whereas India is home to 77 million diabetic patients.[8] So, with the help of new technologies-like Artificial intelligence (AI), advanced Machine Learning (ML), and Deep learning (DL) we can detect the presence of-diabetic retinopathy-in patients by analyzing the retinal scanned images.

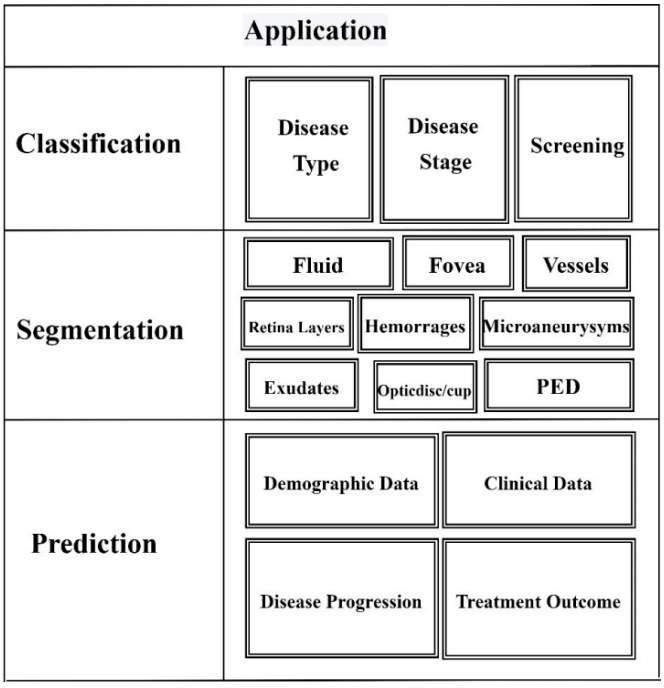

Fig -1: Application of AI in retinal imaging.

In the realm of retinal-image analysis, classification plays a pivotal role, typically involving binary or multi-class

categorization for tasks like automated screenings or determining the disease stage. Machine learning (ML) and deep-learning (DL) methodologies find application based on factors-such as the desired level of interpretability or the scale of the available dataset. [2,8]

On the other hand, segmentation-oriented strategies aim to partition objects within an image. These approaches focus on dissecting morphological–features or extracting significant patterns from snapshots, such as delineating borders in 2D-or 3D imaging. Specifically, the segmentation of pigment epithelial-detachment (PED) serves as a diagnostic tool for chorioretinal diseases.

In the–domain of prediction, the emphasis often lies in foreseeing disease progression, anticipating treatment outcomes based on image analysis, and similar scenarios. Additionally, prediction methodologies can be employed to delineate local retention regions, adding another layer of sophistication to the analytical framework.

People with–diabetes- can be affected by an eye disease called diabetic–retinopathy. This is when- high blood sugar levels cause damage to blood–vessels in the retina. These blood vessels can swell and sometimes leak or close by stopping blood from passing through. Also, any abnormal and new blood vessel growth on the retina can cause visual impairment or complete visual loss leading to blindness. There are two main stages of diabetic retinopathy – NPDR (Non-proliferative diabetic retinopathy) and PDR (Proliferative Diabetic Retinopathy).

(a) Normal view (b) View observed due to DR

Fig -2: Normal vision and DR vision.

NPDR is the early stage of diabetic retinopathy which includes tiny blood vessel leaks, making the retina swell. The most common reason why people with diabetes lose vision is macular edema which is basically when the macula swells. If the blood vessels in the retina close off it is called macular ischemia causing blockage for blood vessels to reach the macula. Also, the formation of exudates (tiny particles) in the retina affects the vision. With NPDR, the patient is expected to have blurry vision.

PDR is the later stage of diabetic retinopathy which is the more advanced stage that can cause both central and peripheral vision.[3] This is when new blood vessels start growing in the retinal region referred to as neovascularization. These new blood vessels which are fragile often bleed into vitreous (jelly-like fluid that is filled in the middle of the eye). If the bleeding is little, one can see floaters but if the bleeding is more, it can block complete vision. These developed new blood vessels may form scar tissue which can cause macula problems or can lead to detached retina.

The identification of diverse lesions on the ocular surface stands as a diagnostic modality for discerning diabetic retinopathy (DR) images, as depicted in Figure 3. These lesions encompass microaneurysms (MA), hemorrhages (HM), and both hard and soft exudates (EX).

Microaneurysms (MA): These early clinical manifestations of DR, observable in fundus imagery, induce retinal dysfunction through the leakage of blood/fluid onto the retinal surface. Manifesting as diminutive red spots on the retina, microaneurysms may be delineated by a yellow lipid ring or adjacent hard exudates. Characterized by well-defined borders, these lesions typically exhibit dimensions below 125 µm.[8] The endothelial dysfunction inherent in microaneurysms precipitates leakage and retinal edema, culminating in compromised visual acuity. The discernment of microaneurysms is optimally achieved through fluorescein angiography–(FA), wherein their morphologies encompass focal bulge, saccular, fusiform, mixed, pedunculated, and irregular configurations.

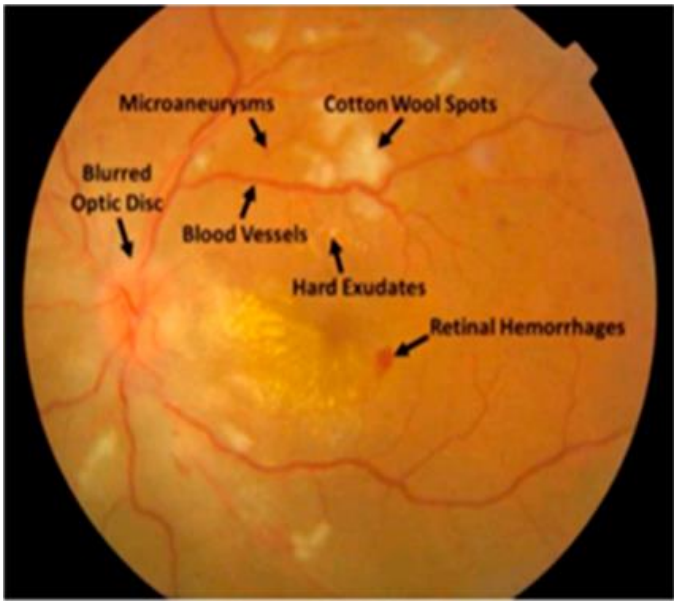

Fig -3: Representation of a fundus image with the lesion annotations.

Hemorrhages (HM) manifest as discernible patches on the retina, characterized by a potential diameter of 125 µm and an irregular border, falling into two categories: flames (superficial HM) and-blot (deep HM).

Hard Exudates: Distinguished by their manifestation as bright yellow regions on the ocular surface, hard exudates result from hemolysis. Typically situated in the peripheral areas of the eye, they exhibit clear demarcations. [2,8]

Soft Exudates: - White lesions on-the eye, originating from nerve–fiber swelling, are denoted as soft exudates or cotton wool spots. These lesions assume ovular or–circular configurations. Soft or-hard exudates represent distinct white lesions, while microaneurysms (MA) and hemorrhages (HM) manifest as red growths (EX). Figure 4 provides an illustrative representation of diverse stages of diabetic-retinopathy (DR). DR is categorized into non-proliferative DR–(NPDR) and proliferative DR—(PDR). Moreover, NPDR is further subclassified—into mild, moderate and severe stages.

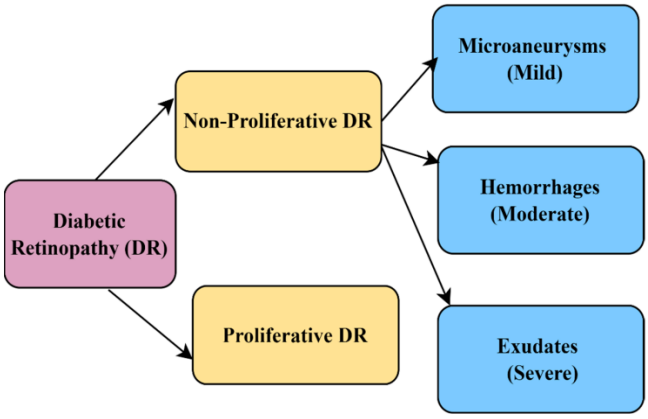

Fig -4: Stages-of DR.

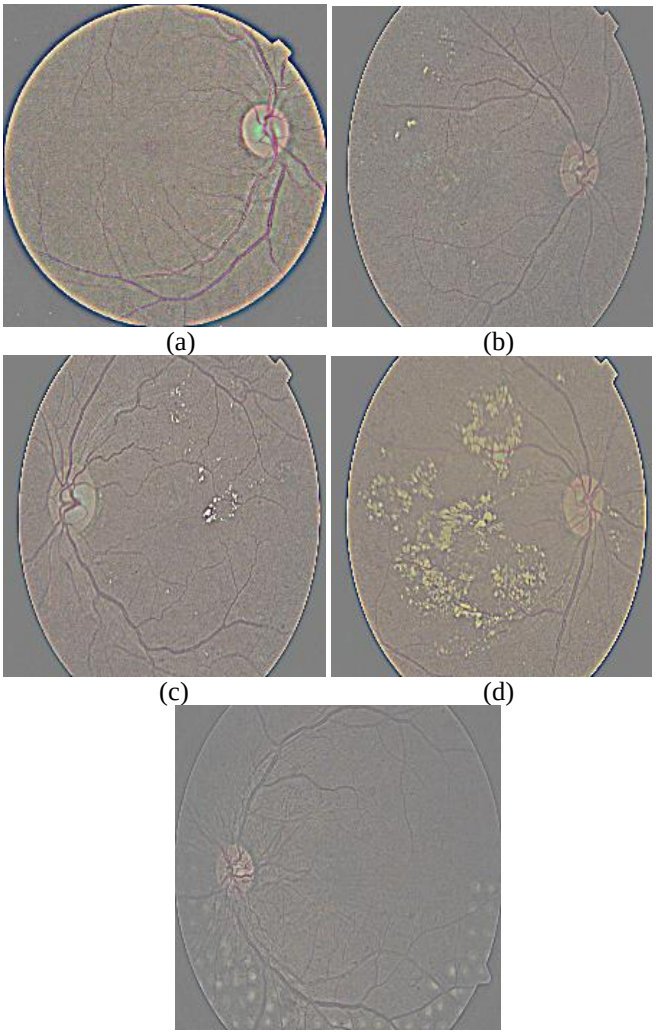

Fig -5: Classification–of Diabetic Retinopathy (Gaussian filtered fundus images of different stages). (a) No DR, (b) Mild, (c) Moderate, (d) Severe and (e) Proliferate DR

This paper delineates several salient focal points:

- Within the domain of diabetic retinopathy (DR) detection, there is widespread online accessibility to datastores, coupled with the presence of diverse DR datasets.
- A comprehensive survey is conducted, delving into the intricate landscape of machine learning-(ML) and deep learning–(DL) methodologies that are prevalently employed in the context of DR detection.
- The discourse extends to encompass an in-depth exploration of the intricacies surrounding feature extraction and classification techniques that find application in the realm of DR.
- The narrative extends its purview to articulate prospective avenues for research, notably delving into the realms of domain–adaptation, multitask learning, and the integration of explainable-artificial intelligence (AI) methodologies within the framework of DR detection.

2. Body of Paper

2.1 Dataset

Dataset plays an important role in training the models for analyzing the stages in the multi stage classification and the presence of diabetic retinopathy in the binary classification. Every researcher has used different datasets based on their aim of research. The diversity of dataset includes, raw fundus images, processed fundus images, different stages of diabetic retinopathy images - mild, moderate, severe, Non-PDR, PDR. Some research also includes a dataset which is region-based classification.

Kangrok et. al. in [1] have used the Ultra-wide fundus images (UWF images) of DR patients. The device used for capturing the images is Optos Daytona UWF retinal imaging system. From that system the image size produced is of 3073 x 3900 pixels. The dataset includes 11,374 and 1537 UWF (Ultra-wide fundus) photographs of DR patients and also from healthy subjects. Total number of patients examined was 1308. The average patient's age was found to be 50.76 where patients' ages ranged from 8 to 89 years. The statistics of patients with respect to their age is found to be- age 40 to 70 is 72.1%, the male population to the total population was found to be 50.75%. This proposed methodology was to classify DR and healthy patients. The grading of the images is performed by ophthalmologists with ten or more years of experience-and also the certified grader with two years of experience graded the images independently. The validation of the images was done from Catholic Kwandong–University–-International St. Mary's Hospital, South Korea.

Gothane et. al. in [2] have used the dataset available in Kaggle consists of fundus images. The image of fundus was taken from the back side of the retina and the pupil is dilated. The fundus images include mild, moderate, severe, Proliferate DR and No DR. All the images are taken from professional technicians.

Ling Dai et. al. in [3] says that within the SIM cohort, comprising 173,346 subjects denoted as the local dataset in this study, a deliberate partitioning strategy was employed. Specifically, 121,342 subjects, constituting 70% of the cohort, were randomly selected to form the training set, while the remaining 52,004 subjects, accounting for 30%, comprised the local validation set. It is noteworthy that each subject within the SIM cohort was uniquely identified by a resident ID, ensuring unequivocal data separation between the training and local validation datasets. The prevalence—of diabetic retinopathy (DR) within the study cohorts is elucidated by the following statistics. In the training dataset, encompassing a total of 12.85% of images, instances of DR were identified, with 27.94% of these cases classified as mild non-proliferative diabetic retinopathy (NPDR). In parallel, the local validation dataset, comprising 200,136 images, exhibited a DR prevalence of 12.99%, with 27.30% of cases falling under the category of

mild NPDR. These meticulously curated datasets, characterized by unique subject identifiers, lay the foundation for robust training and–validation processes in the study's exploration of diabetic-retinopathy.

Kanagasingam Y et. al. in [4] The AI system for spotting diabetic retinopathy (DR) relied on a dataset with 30,000 color fundus images. These images come from different databases like DiaRetDB1, Kaggle13 (EyePACS), and an Australian Tele-eye care DR database. Researchers manually sorted the images into two groups: those showing DR and those without.

Bellemo V et al., in their clinical validation study [5], utilized a dataset sourced from a diabetic retinopathy screening program conducted by the Community Eye Service Programme in collaboration with Kitwe Central Hospital Eye Unit (Zambia), Konkola Copper Mines, and Frimley Park Hospital Eye Department (UK). This initiative, which marked Zambia's inaugural mobile diabetic retinopathy program, aimed to raise awareness among diabetic individuals and promptly refer those with vision-threatening diabetic retinopathy to tertiary eye-care services for early intervention. Identification of patients with either type 1 or type 2 diabetes was facilitated through diabetes or pharmacy registries, and they were invited for screening through diverse channels including local advertising, radio and TV broadcasts, as well as church congregations. Nearly 70% of patients had unspecified diabetes types. The screening procedure entailed capturing two-field retinal fundus photographs for each eye using the Digital Retinopathy System fundus camera. For cases of low quality or uncertain diagnosis, multiple images, sometimes exceeding two per eye, were saved in JPEG format with dimensions of 2592 × 1944 pixels. The dataset encompassed patient demographics, risk factors (such as age, sex, duration of diabetes, type of diabetes, HbA1c, body mass index, and blood pressure), and had previously received approval from the Tropical Diseases Research Centre in Zambia and the Centralized Institutional Review Board of Sing Health, Singapore, in adherence to the Declaration of Helsinki.

Ali et al. [6] the hybrid deep–learning–approach for Diabetic Retinopathy classification was evaluated using three datasets: APTOS-2019, Messidor-2, and a local public Diabetic Retinopathy dataset. These datasets provided a diverse set of images for training and testing the model. The inclusion of multiple datasets enhances the robustness and generalizability of the model, as it is exposed to a variety of image characteristics and conditions, ensuring that the proposed method's effectiveness is validated across different sources and image types.

The APTOS 2019 [7] blindness detection dataset (30) was selected in this research to be experimented with by the different deep transfer learning models. This dataset was released in the second quarter of 2019 by the Asia Pacific Tele-Ophthalmology Society. The dataset contains 3662 images and consists of 5 classes.

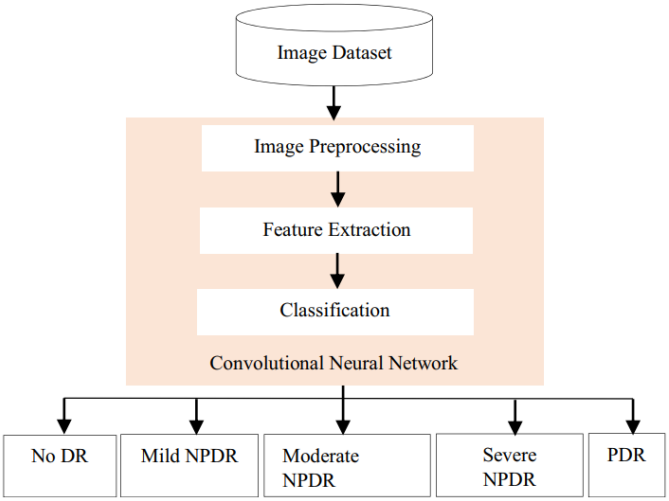

Fig -6: Flow of image acquisition used in reference [9].

In [9] the Diabetic Retinopathy Feature Extraction and Classification (DRFEC) methodology, the model evaluation is conducted using a substantial fundus image dataset obtained from Kaggle's EyePACS. This dataset, characterized by its notable disproportionality, comprises a total of 35,126 fundus images. For training and validation purposes, 27,446 and 7,680 images, respectively, are utilized. The dataset provides a comprehensive representation of diverse ocular conditions and characteristics, enhancing the model's ability to discern patterns across varied scenarios. The images are not detailed individually, but they include both left and right eye images, each corresponding to different stages-of diabetic retinopathy (DR), such as no DR, mild-DR, moderate-DR, severe DR, and proliferative DR (PDR). The EyePACS dataset encompasses images captured by different cameras, featuring varied fields of view (FOV) and a resolution of 1440 × 960, all provided in jpeg format. These fundus images have undergone meticulous grading by multiple experts, ensuring the dataset's reliability and accuracy for the assessment of diabetic-retinopathy.

2.2 Approach

The methods used to train the obtained dataset changes from research to research based on their desired outcome. A few images need pre-processing while others–are processed images used for training.

2.2.1 Pre-processing technique

The methodology for the classification of Diabetic Retinopathy comprises two phases in the DR model [6]. In the initial phase, the dataset, consisting of 57,625 DR images obtained from-various sources, is divided into training (80%) and validation (20%) sets. These images are labeled as DR positive or negative by experts. The convolutional neural network-based DR model is then trained and validated using this dataset.

For the testing phase, a separate dataset is created using real-time DR data obtained from patients at Sindh Institute of Ophthalmology & Visual Sciences (SIOVS) in Hyderabad, Pakistan, captured through image-capturing devices. The DR model employs convolutional and pooling layers to extract features and reduce activation map size. Various pooling techniques are applied, and the output is

obtained in the form of DR-Positive and DR-Negative results through fully connected layers.

In the second phase, real-time DR data collected over five weeks is evaluated for image quality by an intelligent model. Unacceptable images are rejected and recaptured, while accepted images are classified into DR-Positive or DR-Negative using the trained model. Clinical experts review and compare the performance of the trained models based on the classified images.

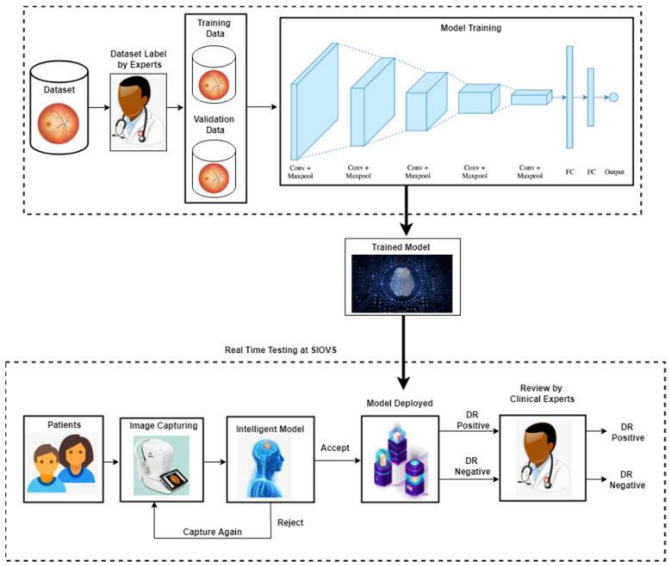

Fig -7: The diagram depicts an automated–diabetic retinopathy (DR) detection system utilizing a convolutional neural network (CNN) trained on labeled fundus images. Expert-labeled training data enables the CNN to learn DR-associated features, facilitating the classification of new fundus images as DR-positive or DR-negative. A feedback loop involving clinical experts allows refinement of the CNN's accuracy, and the real-time system is tailored for smartphone-based image capture in settings like telemedicine clinics, providing swift classifications for review by healthcare professionals.

In [7] the models proposed relied on deep transfer learning CNN architectures to transfer learning weights, thereby reducing training time, mathematical computations, and the consumption of hardware resources. While some studies have attempted to create custom architectures for specific problems, these architectures may not be suitable for the data presented in this paper. The deep transfer learning CNN models investigated in this research include AlexNet, ResNet18, SqueezeNet, GoogleNet, VGG16, and VGG19. Notably, these CNN models have a relatively small number of layers compared to larger counterparts like Xception, DenseNet, and InceptionResNet, which have 71, 201, and 164 layers, respectively. The choice of these models is aimed at reducing training time and computational complexity.

In the preceding CNN models, customization was applied to the last fully connected layer to align with the number of classes in the APTOS–2019 dataset, which consists of 5 classes.

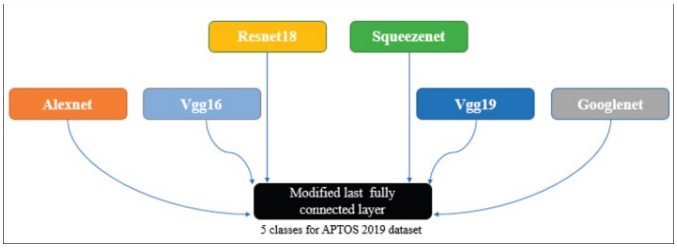

Fig -8: The diagram illustrates a modified last fully connected layer in a convolutional neural network (CNN) tailored for medical image classification, particularly on fundus images from the APTOS 2019 dataset. Trained on labeled fundus images, the CNN employs architectures like AlexNet, VGG16, VGG19, GoogLeNet, and ResNet18, with a specialized last fully connected layer. This modification enhances the CNN's accuracy in categorizing fundus images into five classes for diabetic retinopathy detection, ranging from Normal to Proliferative diabetic retinopathy, by learning distinctive features associated with each class, such as hemorrhages or microaneurysms.

The data augmentation techniques used to mitigate overfitting, a widely employed technique involves expanding the training dataset by applying label-preserving transformations. In this study, data augmentation–strategies were implemented on the training set to enhance the model's invariance to various transformations and noise. The augmentation techniques utilized include reflection around the X-axis, reflection around the Y-axis, and reflection around the X-Y axis. Through these augmentation techniques, the number of images in the dataset increased fourfold compared to the original, resulting in a dataset of 14,648 images used for training and testing. This substantial increase is anticipated to significantly enhance CNN testing accuracy, as detailed in the following section. Furthermore, this approach enhances the resilience of the proposed methods by preventing the model from memorizing the data, thereby rendering it more robust and accountable during the testing phase.

In [3] the below preprocessing technique is followed to train the model.

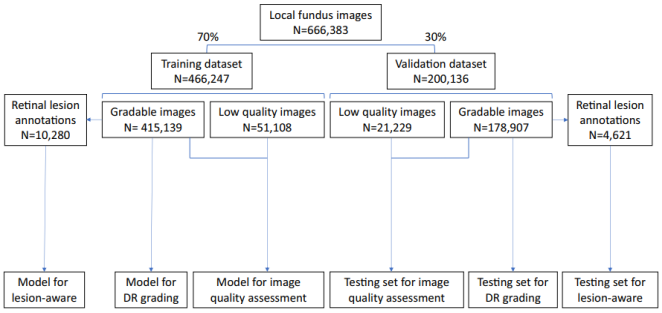

Fig -9: The SIM cohort's local dataset for the DeepDR system involved random division, with 466,247 images dedicated to training the image quality sub-network, 10,280 for lesion detection, and 415,139 for DR grading. In the validation phase, 200,136 images were used for testing the image quality sub-network, while 178,907 were employed for assessing the DR-grading sub-network. The evaluation of the lesion-detection sub-network utilized 4621 images specifically labeled for retinal lesions, ensuring a meticulous and comprehensive assessment of the DeepDR system's efficacy in diabetic retinopathy diagnosis.

2.2.2 Multi stage classification

Ling Dai et. al. in [3] says they employed ResNet and Mask-RCNN to create the lesion detection and lesion segmentation modules, respectively. The pre-trained DR base network was then transferred to the lesion detection module by initializing its feature extractor with the pre-trained DR base network's feature extractor. Subsequently, we fine-tuned the lesion detection module. Following this, we initialized the feature extractor of the lesion segmentation module by utilizing the feature extractor of the lesion detection module. The feature extractor layers of the lesion segmentation module were kept constant, and the remaining layers were updated during training. In the lesion segmentation sub-module, non-maximum suppression was applied to choose the bounding box with the highest objectiveness score among multiple predicted bounding boxes. This process involved selecting the bounding box with the highest objectiveness score initially and then comparing its Intersection over Union (IoU) with other bounding boxes, eliminating those with IoU greater than 0.5.

Kanagasingam Y et. al. in [4] says the system used a smart approach called transfer learning, tweaking a pre-trained Inception-v3 model for DR detection. They trained and tested the model with a split of 80% for training and 20% for testing, making sure both groups were fairly represented. The AI system can also identify specific issues like microaneurysms, exudates, and classify DR severity. It works with various retinal cameras like Canon, Zeiss, and DRS cameras, making it versatile for different setups.

Bellemo V et al. in [5] highlight the difference between ResNet and sequential network architectures like VGGNet. Unlike VGGNet, ResNet utilizes network-in-network architectures composed of micro-architecture modules. Residual networks enable the training of deep networks by incorporating skip connections and feature-heavy batch normalization, which improves model convergence. This design allows ResNet to accommodate more layers and consider more features in images while maintaining lower network complexity compared to VGGNet. ResNet operates as a multiple binary classifier, generating probabilities for four disease classifications: mild NPDR or worse (p_0), moderate NPDR or worse (p_1), severe NPDR or worse (p_2), and proliferative DR (p_3).

$$p_1 + \Sigma 4i=0\ i \cdot score(i)$$

The determination of the final score for referable diabetic retinopathy classification is primarily based on p_1, excluding mild cases. To achieve this, the ensemble model combines the probability output scores of both VGGNet and ResNet, summing their probabilities for referable diabetic retinopathy. The ultimate classification is then decided by applying thresholds to the output scores to meet the desired sensitivity and specificity performance. Specifically, for a predetermined optimal sensitivity of at least 90%, which is suitable for the screening use case, specific thresholds were established: 0.70 for VGGNet, 0.13 for ResNet, and 0.43 for the ensemble. This multi-stage classification approach significantly enhances the accuracy and performance of the AI system in diagnosing diabetic retinopathy.

In [9] Diabetic Retinopathy Feature Extraction and Classification (DRFEC) methodology addressed the inefficiencies of manual examination in detecting diabetic retinopathy (DR) by leveraging machine learning techniques, particularly deep learning (DL). Acknowledging the impracticality of manual processes for early DR detection, the system employed a range of state-of-the-art DL models, such as VGG-19, VGG-16, Xception, InceptionV3, MobileNet, MobileNetV2, EfficientNet B0-B7, DenseNet121, DenseNet169, DenseNet201, ResNet50, ResNet50V2, ResNet101, ResNet101V2, ResNet152, ResNet152V2, NASNetLarge, NASNetMobile, and InceptionResNetV2. These models, pretrained-on the ImageNet dataset, facilitated feature–extraction and image classification. The DRFEC methodology incorporated inbuilt preprocessing and downsampling of input data acquired from the Kaggle DR Detection dataset sourced from EyePACS. The system systematically evaluated each DL model's performance, computing training and validation/test accuracy values to assess for overfitting and generalization. The selection of the best DL architecture for deep DR feature-extraction and image classification was determined based-on the performance and inferences drawn from each individual DL CNN model. The entire process was illustrated in a flowchart, demonstrating the iterative selection and evaluation of DL models to optimize DR detection efficiency. The implementation was carried out using Keras from TensorFlow, Python 3.8, TensorFlow version 2.4, on a 64-bit operating system with a ×64-based processor, Windows 10 Pro, 64GB RAM, and an Intel(R) Xeon(R) W-2155 CPU @ 3.30GHz.

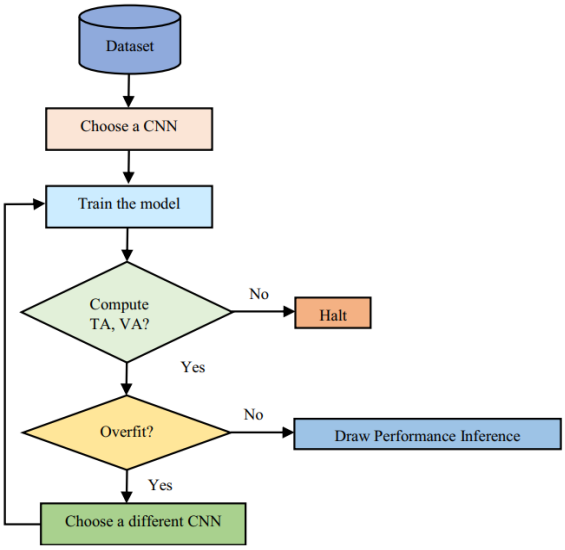

Fig -10: Flow chart of working of feature extraction and classification.

2.2.3 Binary classification

In [1] diabetic retinopathy (DR) detection system involves a multi-step process for improved accuracy. The initial step focuses on automatic segmentation of the Early–Treatment Diabetic Retinopathy Study Seven Standard Fields (ETDRS 7SF). This segmentation aims to eliminate unwanted components, such as eyelashes and skin, from the region of interest (ROI). Subsequently, the–segmented–ROI image is utilized in conjunction with a deep learning architecture, specifically the Residual-Network-with 34 layers (ResNet-34) model, which serves as a classifier for the DR detection-task.

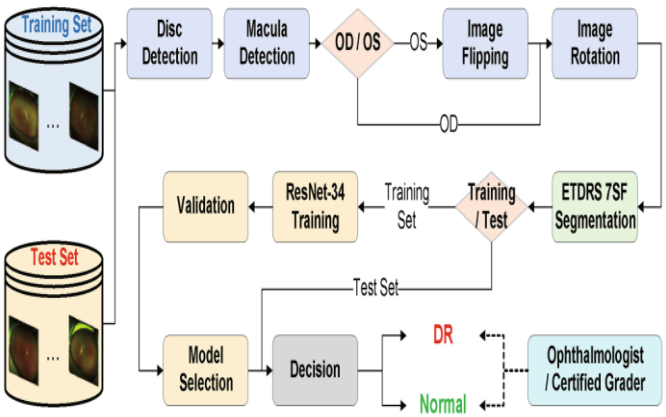

Fig -11: Overview of DR detection system.

The overall structure of the proposed DR detection system is depicted in Figure 9, providing a visual representation of the system's components and their interconnections. To assess the performance of the DR detection system, a comprehensive evaluation is conducted by comparing its results with an alternative system. The alternative system relies on the region of interest composed solely of ETDRS Field 1 and Field 2 (F1–F2). This comparison is carried out using several metrics to ensure a robust assessment of the system's efficacy.

It is important to highlight that the ETDRS-F1–F2 image is presented as an alternative to conventional single or two non-mydriatic 45-degree fundus photography. This alternative is particularly relevant in scenarios where ultra-widefield (UWF) and conventional–fundus images do not coexist, emphasizing the adaptability and applicability of the-proposed DR-detection-system across different imaging conditions.

2.2.4 Real-time image quality feedback

We utilized DeepDR to offer immediate feedback on image quality while conducting non-mydriatic retinal photography for 1294 elderly subjects from the NDSP cohorts, all aged over 65 years. Each eye underwent the capture of two retinal photographs—one centered on the macula and the other on the optic disc. In cases where DeepDR identified the initial image's quality as ungradable, a second image of the same field was taken. To prevent contracted pupils caused by the camera flash, only one additional photograph was captured for each field.

In the course of this procedure, a total of 5176 retinal images were initially acquired from 1294 patients. Among these, 1487 images (28.7%) exhibited issues related to artifacts, clarity, and/or field definition, classifying them as low-quality. In response to the feedback provided, a second photograph was taken for these identified patients. Out of the 1487 initially low-quality images, 1065 (71.6%) of the recaptured images were deemed to have satisfactory quality. Substituting the low-quality images with the recaptured ones resulted in an enhancement of the diagnostic accuracy for each stage of Diabetic Retinopathy (DR). Particularly noteworthy was the improvement in the Area Under the Curve (AUC) for mild Non-Proliferative Diabetic-–Retinopathy (NPDR), which increased from 0.880 (0.859–0.895) to 0.933 (0.918–0.950) ($P < 0.001$), accompanied by an elevation in sensitivity from 78.5% (72.7–83.4%) to 87.6% (83.2–92.3%).

2.3 Evaluating techniques

Various performance metrics are commonly employed in evaluating the effectiveness of Deep Learning (DL) methods for classification tasks. Key measurements include accuracy, sensitivity, specificity, and the area under the Receiver Operating Characteristic (ROC) curve (AUC). Sensitivity gauges the percentage of abnormal images correctly identified as abnormal, while specificity assesses the percentage of normal images correctly identified as normal. AUC is a graphical representation plotting sensitivity against specificity. Accuracy, on the other hand, represents the percentage of images correctly classified. The equations for each measurement are as follows:

$$\text{Specificity} = TN / (TN+FP)$$
$$\text{Sensitivity} = TP / (TP+FN)$$
$$\text{Accuracy} = (TN+TP) / (TN+TP+FN+FP)$$

Here, TP denotes true positive (number of disease images correctly classified), TN stands for true negative (number of normal images correctly classified), FP represents false positive (number of normal images incorrectly classified as disease), and FN indicates false negative (number of disease images incorrectly classified as normal). The percentage of these performance measures is commonly reported in studies related to the current work.

Statistical analyses

The efficacy of DeepDR in evaluating image quality, detecting retinal lesions, and grading Diabetic–Retinopathy (DR) was assessed through the Area–Under the Curve (AUC) of the receiver-operating characteristic-(ROC) curve. The ROC curve was generated by plotting sensitivity (true-positive rate) against 1-specificity (false-negative rate). The thresholds for sensitivity and specificity were determined using the Youden index. Statistical significance in AUC comparisons was determined through binormal model methods, with a two-sided P value less than 0.05 considered significant. Lesion detection AUC was calculated as a binary classification to ascertain whether a quadrant contained a specific type of lesion. The performance of lesion segmentation was evaluated using Intersection over Union (IoU) and F-score. For Cotton Wool Spots (CWS), hard exudates, and hemorrhages, IoU was employed to gauge the segmentation network's performance.

The IoU was calculated as follows: [IoU calculation formula]:

$$\text{IoU}(A,B) = |A \cap B| / |A \cup B|$$

where A and B were a set of pixels in the retinal images (e.g., A was the segmented lesion and B was the ground truth).

In the case of microaneurysms, the F-score was employed instead of the Intersection over Union (IoU) score. This decision was made due to the fact-that-the average diameter of microaneurysms in retinal images typically falls below 30 pixels. Consequently, even minor alterations in the predicted map could lead to significant fluctuations in the IoU score. The F-score, a measure that considers both precision and recall, was utilized for assessment:

$$F = 2 \cdot |tp| / (2 \cdot |tp| + |fp| + |fn|)$$

3. CONCLUSIONS

The pivotal role of datasets in model training for multi-stage classification, as well as binary classification assessing the presence of diabetic retinopathy, cannot be overstated. Researchers adopt varying datasets tailored to their specific research objectives. These datasets encompass a spectrum, ranging from raw to processed fundus images, and may span diverse stages of diabetic retinopathy, including mild, moderate, severe, Non-Proliferative Diabetic Retinopathy (Non-PDR), and Proliferative Diabetic Retinopathy (PDR). Certain investigations even delve into region-based classification datasets, reflecting the nuanced approach researchers take to address the intricacies of diabetic retinopathy in their studies.

The study includes classification of images based on presence as well as stages of DR where in some cases regions were included as well.

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