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ENHANCING DIABETIC RETINOPATHY DETECTION USING CNN ENSEMBLES AND GRAD-CAM ON RETINAL FUNDUS IMAGES

***ARAOLUWA SIMILEOLU FILANI; *OLASUPO MODUPE ADEGOKE; **ABIMBOLA ABOSEDE JOSEPH; & *ADEMOLA TOLUWASE AMUDIPE**

*Department of Computer Science, Joseph Ayo Babalola University, Ikeji-Arakeji, Nigeria. **Department of Computer science, College of Science and Technology, Kaduna Polytechnic, 44 Polytechnic Road, Tudun Wada, Kaduna, Kaduna State, Nigeria

Corresponding Author: asfilani@jabu.edu.ng

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ABSTRACT

Diabetic Retinopathy (DR) is a progressive eye disease and a leading cause of blindness among individuals with diabetes. Early detection is critical for preventing irreversible vision loss. In this paper, we propose an automated DR detection system using deep learning and ensemble methods to improve classification accuracy across five DR severity levels. The system was trained on the APTOS 2019 Blindness Detection dataset

INTRODUCTION

In recent decades, the burden of non-communicable diseases such as diabetes mellitus has increased significantly across the globe, driven by sedentary lifestyles, urbanization, and poor dietary habits. According to the International Diabetes Federation (IDF), more than 537 million adults were living with diabetes in 2021, and this number is projected to rise to 783 million by 2045 [1]. One of the most devastating complications of diabetes is Diabetic Retinopathy (DR), a microvascular disorder that affects the blood vessels in the retina and remains a leading cause of irreversible vision impairment and blindness among the working-age population [2]. DR progresses silently and often asymptomatically in its early stages, which makes timely screening and detection vital to preserving visual function and reducing the risk of blindness.

comprising 3,662 retinal fundus images. Three convolutional neural network (CNN) models-ResNet18, ResNet50, and EfficientNetB3-were implemented individually and then combined using ensemble techniques: majority voting, weighted voting, and stacked ensemble with a random forest meta-classifier. Image preprocessing techniques such as LAB color conversion, CLAHE, denoising, and data augmentation were used to enhance diagnostic features. The ensemble models significantly outperformed the individual CNNs, with the stacked ensemble achieving the best results: 85.27% accuracy, 0.933 ROC AUC, and 0.7352 PR AUC. The system's interpretability was improved using Grad-CAM, providing visual heatmaps of model decision regions. These results demonstrate that ensemble learning, coupled with interpretable AI, offers a robust and clinically relevant approach to DR detection.

Keywords: diabetic retinopathy, deep learning, convolutional neural networks, ensemble learning, image classification, medical imaging, interpretability, Grad-CAM

Traditionally, DR diagnosis involves manual assessment of retinal fundus images by trained ophthalmologists or retina specialists who visually inspect the retina for clinical signs such as microaneurysms, hemorrhages, exudates, and neovascularization. While effective, this manual process is time-consuming, prone to human error, and highly dependent on the availability and expertise of healthcare professionals. In regions with limited access to ophthalmic care, particularly in low-income or rural communities, these limitations contribute to underdiagnosis and delayed treatment of DR, worsening patient outcomes. As such, there is a growing demand for automated DR detection systems that are accurate, scalable, and capable of supporting mass screening initiatives.

The advancement of artificial intelligence (AI) and deep learning (DL) has revolutionized medical image analysis by enabling machines to learn complex patterns from large-scale datasets without explicit programming. In particular, Convolutional Neural Networks (CNNs) have demonstrated exceptional performance in image classification tasks, including disease detection from medical imaging modalities such as X-rays, MRIs, CT scans, and retinal fundus images [3]. CNNs are capable of automatically extracting high-level abstract features from raw input images, allowing for end-to-end learning of classification pipelines without relying on handcrafted features. Several studies have validated the effectiveness of CNN-based models in DR detection, often achieving performance levels comparable to human experts [4–6].

Transfer learning has emerged as a pivotal technique in the training of CNNs for medical imaging, particularly when datasets are relatively small. It involves leveraging knowledge from pre-trained models trained on large general-purpose datasets such as ImageNet, and fine-tuning them on domain-specific datasets. This approach significantly reduces the computational resources and training time required while maintaining high classification accuracy. Notable CNN architectures such as ResNet18, ResNet50, VGG16, InceptionV3, and EfficientNet have been successfully employed in various DR classification tasks with commendable results [7–9].

Despite the progress, deep learning models often suffer from issues such as overfitting, high variance, and instability, especially when trained on imbalanced datasets with variable image quality. These shortcomings have motivated the adoption of ensemble learning techniques, which aim to improve model performance by combining the outputs of multiple classifiers. Ensemble methods such as majority voting, weighted voting, bagging, and stacking enable the aggregation of diverse model predictions, thereby reducing generalization error and improving overall accuracy and reliability [10–12]. Recent studies have shown that ensemble models outperform individual classifiers in DR detection, especially in multiclass classification scenarios where intra-class variability is high.

Another crucial aspect of deploying AI systems in the medical field is interpretability. Clinical professionals are often hesitant to adopt black-box models without understanding the rationale behind the predictions. To bridge this gap, visualization techniques such as Gradient-weighted Class Activation Mapping (Grad-CAM) have been employed to generate heatmaps that highlight important regions in an image contributing to a model's decision. These explainability tools increase trust in AI systems and provide valuable insights to clinicians, making them essential for real-world implementation [13,14].

In this study, we propose an automated DR detection framework utilizing deep learning and ensemble learning techniques. Specifically, we compare the performance of three widely adopted CNN architectures-ResNet18, ResNet50, and EfficientNetB3-on the APTOS 2019 Blindness Detection dataset. Each model is trained independently, followed by the implementation of three ensemble strategies: majority voting, weighted voting, and stacked ensemble using a random forest meta-classifier. The dataset is preprocessed using advanced image enhancement techniques including contrast-limited adaptive histogram equalization (CLAHE), LAB color space conversion, denoising, resizing, and augmentation. Furthermore, Grad-CAM is employed to provide model interpretability by visualizing class-discriminative regions in the retinal images.

The objectives of this research are threefold: (1) to evaluate the individual performance of selected CNN architectures in DR classification; (2) to assess the effectiveness of ensemble methods in improving diagnostic accuracy and robustness; and (3) to enhance clinical applicability through the use of interpretable visual explanations.

Related Works

The detection of Diabetic Retinopathy (DR) has been a primary area of interest within medical image analysis, particularly due to the disease's widespread prevalence and the risk of irreversible vision loss if not diagnosed in its early stages. In recent years, deep learning (DL) methods, especially Convolutional Neural Networks (CNNs), have gained considerable attention as powerful tools for automating the classification of retinal fundus images. Researchers have explored several CNN architectures and training methodologies, which have yielded promising outcomes across multiple DR detection challenges.

Gulshan et al. [1] conducted a pioneering study that implemented a deep CNN to detect referable DR in retinal fundus images. Their model achieved sensitivity and specificity values comparable to those of ophthalmologists, establishing CNNs as viable tools for mass DR screening. Similarly, Pratt et al. [2] employed a custom CNN consisting of five convolutional layers and three fully connected layers, demonstrating high classification accuracy on a DR dataset. The architectural variations of CNNs have since been widely explored to optimize accuracy, precision, and computational efficiency.

Transfer learning has also become a standard approach in DR detection research. Zhang et al. [3] fine-tuned VGG16 and InceptionV3 on the Kaggle DR dataset, demonstrating that pre-trained models significantly reduce training time and improve generalization. Zuluaga et al. [4] explored the use of ResNet and EfficientNet architectures on the APTOS and Messidor datasets, achieving enhanced performance in distinguishing between different DR severity levels. These findings confirm the role of transfer learning in facilitating effective model training on limited medical datasets.

Image preprocessing has consistently been shown to play a vital role in improving DR classification accuracy. Common preprocessing steps include LAB color space conversion, Gaussian filtering, contrast-limited adaptive histogram equalization (CLAHE), and noise reduction. Rajalakshmi et al. [5] reported substantial improvements in lesion visibility and classification accuracy after applying CLAHE and Gaussian blurring techniques to their retinal images. Moreover, data augmentation strategies such as rotation, flipping, and brightness adjustments have been frequently adopted to address class imbalance and enhance model robustness.

Several studies have focused on the use of ensemble learning strategies to improve diagnostic reliability. Gonzalez et al. [6] developed an ensemble combining DenseNet, InceptionV3, and ResNet classifiers through majority voting. This configuration achieved higher stability and accuracy when compared to individual models. Similarly, Islam et al. [7] implemented an ensemble of MobileNetV2 and ResNet50 using weighted voting, reporting improved sensitivity, specificity, and reduced false positive rates.

Stacked ensembles, a more complex form of ensembling, have also been explored. These models involve training multiple base CNNs and combining their predictions through a meta-learner such as a Random Forest or Gradient Boosting classifier. Zhang et al. [8] demonstrated that stacked ensembles outperform conventional ensemble techniques by capturing deeper relationships among model predictions. Such frameworks not only improve predictive performance but also add flexibility in integrating heterogeneous architectures.

Explainable Artificial Intelligence (XAI) has also become increasingly relevant in DR research, particularly through methods like Gradient-weighted Class Activation Mapping (Grad-CAM). Grad-CAM allows visualization of key image regions that influence the model's prediction, thus improving clinical trust and model transparency. Selvaraju et al. [9] introduced Grad-CAM as a general XAI tool for CNN-based models, while Bhatia et al. [10] and Prabhu et al. [11] successfully implemented it in DR detection pipelines, providing meaningful insights into model decision pathways.

Despite progress, DR detection research continues to face several challenges. These include high inter-class similarity, poor visibility in low-quality images, and skewed class distributions that hinder accurate classification of underrepresented DR stages. Several studies have proposed solutions such as synthetic data generation, focal loss functions, and class balancing techniques. Nevertheless, the need for comprehensive ensemble evaluations across varied CNN architectures remains largely unexplored.

To address this gap, the present study evaluates three popular CNN architectures-ResNet18, ResNet50, and EfficientNetB3-on the APTOS 2019 Blindness Detection dataset. Each model is first trained independently, then combined using three ensemble strategies: majority voting, weighted voting, and stacked ensembling with a Random Forest meta-learner. Standardized preprocessing is applied across all experiments, and Grad-CAM is used to provide interpretability to the classification outcomes. This comparative study aims to deliver a holistic view of CNN and ensemble performance in DR detection, offering valuable guidance for future work in AI-assisted ophthalmology.

Methodology

The proposed system is designed to detect and classify the severity of Diabetic Retinopathy (DR) in retinal fundus images using a deep learning-based approach. The system framework integrates three convolutional neural network (CNN) architectures-ResNet18, ResNet50, and EfficientNetB3-trained individually and subsequently combined using multiple ensemble techniques. The goal is to improve diagnostic accuracy, minimize misclassification of critical DR stages, and enable model interpretability through visualization tools. This section outlines the methods used for data preprocessing, model training, ensemble construction, and evaluation, following a structured and reproducible experimental pipeline.

The architecture of the system is divided into five core stages: data acquisition, image preprocessing, individual model training, ensemble generation, and interpretability integration. Figure 1 illustrates the general workflow of the system, showing how data flows from the raw image dataset to final classification through both individual and ensemble modeling approaches.

The dataset used for training and evaluation is the APTOS 2019 Blindness Detection dataset, sourced from a Kaggle-hosted competition by the Asia Pacific Tele-Ophthalmology Society (APTOS). The dataset consists of 3,662 high-resolution retinal fundus images labeled according to five DR severity levels [15]: Class 0 (No DR), Class 1 (Mild), Class 2 (Moderate), Class 3 (Severe), and Class 4 (Proliferative DR). Each image is in JPEG format with varying resolution and lighting conditions. Due to differences in illumination, contrast, and image quality across the dataset, significant preprocessing steps were required before model training. Furthermore, the dataset suffers from class imbalance, with a disproportionate number of samples in Class 0, while Classes 3 and 4 are underrepresented. To mitigate the effect of imbalance, a combination of oversampling and augmentation was applied.

The primary objective of this study is to comparatively evaluate the classification performance of three CNN models and three ensemble strategies in detecting and differentiating DR stages. Specifically, the research aims to: (1) Train and evaluate individual CNN architectures (ResNet18, ResNet50, EfficientNetB3) on preprocessed retinal images; (2) Construct ensemble classifiers using majority voting, weighted voting, and stacking with a meta-learner; (3) Use Grad-CAM for model interpretability, generating heatmaps of image regions influencing the model's decision; and (4) Compare the performance of all models using standard classification metrics.

The choice of CNN architectures is motivated by their established effectiveness in medical image classification. ResNet18 is a lightweight deep residual network with fewer

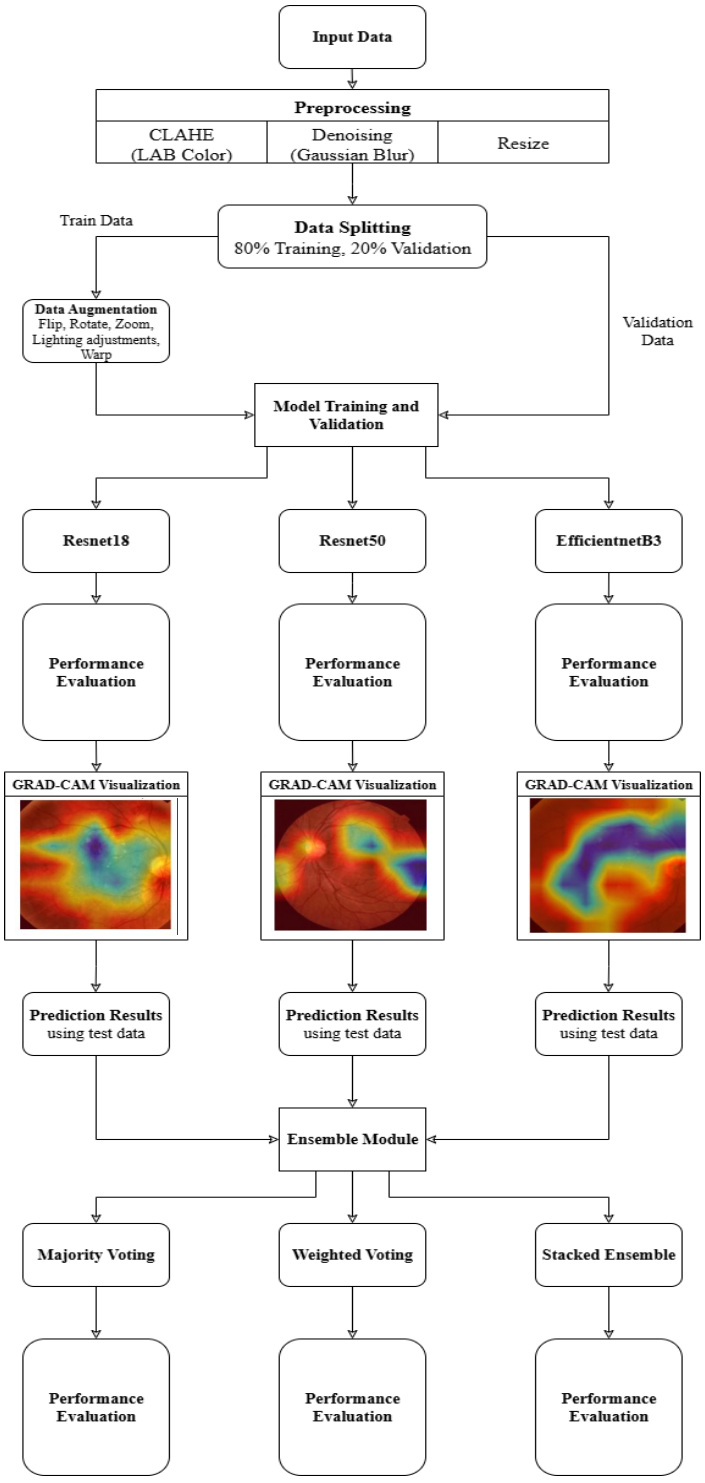
parameters, suitable for rapid deployment in resource-constrained environments. ResNet50, a deeper variant, allows more complex feature learning, enhancing performance on subtle DR cases. EfficientNetB3 is a state-of-the-art model known for its optimized accuracy-to-parameter ratio, making it ideal for applications requiring both performance and scalability. These architectures were chosen to allow comparative evaluation across different model sizes, depths, and design philosophies.

Before training the models, extensive image preprocessing was applied to standardize and enhance the retinal images. The preprocessing pipeline included: Color space conversion from RGB to LAB to separate luminance from chromaticity; CLAHE applied to the L-channel to enhance contrast and detail visibility [16]; Gaussian filtering for noise reduction; resizing all images to 224×224 pixels to match CNN input requirements; normalization of pixel values to [0, 1]; and extensive data augmentation including rotation, flipping, and brightness variation to combat class imbalance and promote generalization.

The dataset was split into 80% training and 20% validation sets. Stratified sampling ensured balanced class distribution across both sets. No separate test set was used due to the limited dataset size, and performance was evaluated using the validation set. All training and validation were conducted on Kaggle notebooks using GPU-accelerated runtime (NVIDIA Tesla T4), constrained by Kaggle's 30-hour weekly GPU quota.

Model training was carried out using the fastai library, which is built on PyTorch and provides high-level abstractions for rapid experimentation. All three CNN architectures were implemented using fastai's transfer learning pipeline [17]. Each model was initialized with ImageNet pre-trained weights, with the final classification layers replaced to match the five DR severity classes. Training was done using the Adam optimizer with discriminative learning rates, and categorical cross-entropy as the loss function. A batch size of 32 was used. Instead of training for a fixed number of epochs, training was conducted dynamically-each model was monitored for validation performance, and training was stopped early once performance plateaued [18]. In practice, none of the models were trained for more than 20 epochs, as early stopping consistently occurred beforehand due to the performance stabilizing.

The next subsection discusses the process of training individual CNN architectures and evaluating their performance using standard metrics.



Individual CNN Model Training

In this study, three well-established convolutional neural network (CNN) architectures-ResNet18, ResNet50, and EfficientNetB3-were selected and trained individually on the preprocessed APTOS 2019 Blindness Detection dataset. These models were chosen due to their proven effectiveness in image classification tasks and their varying levels of architectural complexity and parameter counts. This selection allows for a comparative evaluation of lightweight, mid-weight, and advanced CNN structures in the context of diabetic retinopathy (DR) classification.

All models were trained using the fastai library, built on top of PyTorch, within the Kaggle notebook environment using NVIDIA Tesla T4 GPUs. Fastai's high-level API provided efficient model initialization, data loading, transfer learning utilities, and training callbacks including early stopping and learning rate scheduling. Each

model was initialized with ImageNet pre-trained weights, and only the final classification layers were re-initialized and trained to adapt to the five DR severity classes.

ResNet18

ResNet18 is a relatively shallow residual network with 18 layers, characterized by its use of skip connections to prevent vanishing gradient problems. Its relatively low number of parameters (~11.7 million) makes it a good candidate for rapid training and deployment in environments with limited computational power. In this implementation, the final fully connected layer was replaced with a linear layer containing five output nodes, followed by a softmax activation function.

Due to its shallow depth, ResNet18 converged rapidly during training and demonstrated decent baseline performance. The training was conducted with a batch size of 32 using the Adam optimizer with default β parameters and a learning rate range test to select optimal learning rates. On average, ResNet18 models reached peak performance between 8–12 epochs, after which early stopping was triggered based on validation loss plateau.

ResNet50

ResNet50 is a deeper and more expressive architecture, with 50 layers and approximately 25 million parameters. Its depth enables it to learn more complex hierarchical features, which is particularly useful for distinguishing between DR stages with subtle visual differences. Like ResNet18, the final layer was modified to suit the five-class DR problem. ResNet50 required slightly more training time and computational resources compared to ResNet18. However, it demonstrated improved performance in detecting mid-stage DR classes (Classes 2 and 3), which are commonly misclassified in simpler models. Fastai's differential learning rate technique was applied, assigning lower learning rates to the earlier layers and higher rates to the newly initialized layers. Most ResNet50 training runs converged optimally between 10–15 epochs.

EfficientNetB3

EfficientNetB3 is a more recent architecture designed with neural architecture search principles to optimize performance-to-complexity tradeoffs. It balances depth, width, and resolution using compound scaling. EfficientNetB3 contains roughly 12 million parameters but achieves higher accuracy per parameter compared to traditional models. Due to its internal squeeze-and-excitation blocks and swish activations, it tends to generalize well on medical datasets.

EfficientNetB3 was implemented using the cnn_learner function from fastai with a custom architecture import. Pre-trained ImageNet weights were loaded, and the classifier head was replaced with a batch-normalized linear block leading to a five-class softmax output. To avoid overfitting, dropout was enabled in the final layers. EfficientNetB3 showed the most promising results in early experimentation, particularly in detecting minority class instances (e.g., severe and proliferative DR). However, it also required more careful learning rate tuning due to its sensitivity to parameter updates.

Training was again guided by fastai's learning rate finder. In practice, the learning rate was set between 1e-4 and 3e-4, with one-cycle learning rate scheduling used to improve convergence. On average, EfficientNetB3 reached its best performance within 6–10 epochs, with validation loss decreasing steadily until early stopping was activated.

Training Strategy

Across all models, the same training pipeline was followed for consistency and fair comparison:

(i) **Loss Function**: Categorical Cross-Entropy
(ii) **Optimizer**: Adam
(iii) **Batch Size**: 32
(iv) **Metric Monitored**: Validation Accuracy and Validation Loss
(v) **Early Stopping**: Applied with patience of 3 epochs
(vi) **Learning Rate**: Selected using fastai's built-in learning rate finder
(vii) **Augmentation**: Enabled during training (rotation, flipping, brightness)

Each model was trained on **80% of the dataset,** with the remaining **20% used for validation.** Since the APTOS dataset is inherently imbalanced, data augmentation helped expose the models to underrepresented classes more frequently. No fixed number of epochs was predefined; instead, training continued until the model performance stabilized or began to degrade, ensuring each model received adequate training without unnecessary overfitting.

After training, the individual model outputs (class probabilities) were stored and later used in ensemble constructions. The confusion matrix, class-wise accuracy, and ROC curves were generated for each model to support comparative analysis

Ensemble Techniques

Ensemble learning has become an essential technique in deep learning research and applications [19], particularly in scenarios where individual models exhibit limitations in

generalization or robustness. The fundamental concept behind ensemble learning is that combining the outputs of multiple models can lead to improved predictive performance compared to relying on a single model. This is achieved by leveraging the diversity in the learned representations of each model, effectively reducing variance and error propagation. In the context of diabetic retinopathy (DR) classification, ensemble methods are particularly valuable due to the complexity and variability of retinal fundus images, which can lead to inconsistent performance across different CNN architectures.

This study implements and evaluates three distinct ensemble strategies: majority voting, weighted voting, and stacked generalization (stacking). Each method aggregates the outputs of three independently trained CNN architectures-ResNet18, ResNet50, and EfficientNetB3-to generate a single prediction per input image. The goal of employing multiple ensemble techniques was not only to boost performance but also to compare their strengths and limitations in handling the five-class classification task of DR severity.

Majority Voting Ensemble

The majority voting strategy is a non-parametric and intuitive ensemble method. Each of the three base models independently predicts a class label for a given image. The final predicted label is determined by a simple vote-counting process: the class that receives the most votes is selected as the ensemble's prediction. In cases where all three models predict different classes (i.e., a tie), a predefined priority order was applied based on class frequency observed in the training set, favoring the more prevalent classes to mitigate misclassification of common conditions.

Despite its simplicity, majority voting can be effective when the individual models make different types of errors or when they exhibit complementary strengths. In this study, majority voting provided a significant improvement in stability, particularly for commonly occurring classes such as "No DR" (Class 0) and "Moderate DR" (Class 2). However, the method does not account for model confidence or individual performance variance, which may reduce its effectiveness in classifying rarer DR stages such as "Severe" (Class 3) or "Proliferative DR" (Class 4). Since this method assigns equal weight to all models regardless of their validation accuracy, its utility is mainly tied to the presence of diversity among the base classifiers.

Weighted Voting Ensemble

To address the limitation of equal weighting in majority voting, the weighted voting ensemble approach was implemented. This method improves upon majority voting by assigning a confidence-based weight to each model's prediction [20]. These weights were

calculated based on each model's overall validation accuracy, allowing models with higher predictive performance to exert greater influence on the final decision. Specifically, the softmax output vectors from each model were multiplied by their respective weights, and the resulting vectors were summed element-wise. The final predicted class was selected based on the index with the highest aggregated score.

The weight assignment was proportional to the validation accuracy observed during individual model evaluation. For instance, EfficientNetB3, which demonstrated the best accuracy and F1-score on the validation set, received the highest weight, followed by ResNet50 and ResNet18. This strategy allowed the ensemble to capitalize on the strengths of stronger models while still retaining the diversity of the ensemble structure. In practice, the weighted voting ensemble showed noticeable improvements in minority class sensitivity and macro-averaged F1-score, especially for Class 3 and Class 4 predictions, where the base models individually struggled due to limited training samples. Another advantage of weighted voting lies in its implementation simplicity and computational efficiency, as it does not require additional model training. The weighted aggregation of probabilities can be computed in a vectorized form during inference, making this method suitable for real-time or resource-constrained deployment environments.

Stacked Generalization (Stacking)

Stacking, also known as stacked generalization, is a more sophisticated ensemble technique that involves training a second-level model (meta-learner) to combine the predictions of base models. Unlike majority and weighted voting, stacking treats the outputs of the base models as features for a new classifier, which learns to correct the base models' errors by identifying correlations and dependencies between their predictions.

In this study, stacking was implemented using the softmax probability outputs from ResNet18, ResNet50, and EfficientNetB3. For each input image, the predicted probabilities from all three models (each outputting a 5-element vector) were concatenated to form a single 15-dimensional feature vector. These feature vectors, along with the corresponding ground truth labels, were then used to train a Random Forest classifier as the meta-learner [21]. The Random Forest algorithm was chosen for its robustness, interpretability, and ability to handle small input dimensionality while capturing non-linear decision boundaries.

The meta-classifier was trained using the validation set predictions from the base models, with 5-fold cross-validation applied to reduce overfitting risk. During training,

hyperparameters such as the number of trees (set to 100), maximum tree depth, and minimum samples per leaf were tuned using grid search. To ensure fairness and avoid data leakage, the validation set used for training the meta-learner was kept separate from the training data of the base CNNs.

Stacking demonstrated the highest overall performance across all evaluated metrics. It consistently outperformed both majority and weighted voting methods in terms of accuracy, macro-F1, and balanced accuracy. Additionally, the stacking approach showed better generalization on underrepresented classes due to the meta-learner's ability to exploit inter-model agreement patterns and inconsistencies. However, the increased complexity of this method introduces computational overhead and latency during inference, as it requires both base model predictions and an additional inference step through the meta-classifier.

Implementation Considerations and Evaluation Consistency

To ensure a fair and reproducible comparison of ensemble methods, all predictions used in the ensemble calculations were extracted and stored during the initial evaluation of each base CNN model. This ensured that the same validation samples and model outputs were used across all ensemble experiments, eliminating variability due to randomness or batch effects. Furthermore, class distributions in the validation set were preserved using stratified sampling.

The ensemble methods were implemented using Python with support from libraries including NumPy, Scikit-learn, and Pandas. All performance metrics were computed numerically, including overall accuracy, class-wise precision, recall, F1-score, and area under the ROC curve (AUC). Confusion matrices were also generated for visual assessment of true and false classifications across classes, though they were not used as quantitative evaluation metrics. Precision-recall curves further highlighted the performance of each ensemble, particularly the enhanced detection of minority classes under the weighted and stacked configurations.

Comparative Insights

The comparative analysis of the three ensemble methods revealed a spectrum of trade-offs between simplicity, performance, and computational cost. Majority voting offered the most lightweight solution with fast inference and no parameter tuning but struggled in low-representation class detection. Weighted voting introduced confidence-driven balancing and showed improvements in F1-score for challenging classes. Stacking, although the most resource-intensive, delivered the best overall classification

performance and interpretability through feature importance analysis within the Random Forest.

This comparative evaluation highlights that the optimal ensemble method depends on the deployment context. For clinical applications requiring high accuracy and reliability-especially in distinguishing advanced DR stages-stacking emerges as the most effective technique. In contrast, for lightweight deployment in mobile or edge devices, majority or weighted voting may offer sufficient performance with lower overhead.

The next section presents the evaluation metrics used to benchmark all models and ensemble strategies.

Evaluation Metrics

To evaluate the performance of the diabetic retinopathy (DR) classification models, several evaluation metrics were used. These metrics provide a balanced view of the models' effectiveness, especially in the context of a multi-class, imbalanced dataset.

All models and ensemble strategies were evaluated using the same 80/20 train-validation split from the APTOS 2019 dataset. Metrics were computed using Python libraries including Scikit-learn, NumPy, and fastai.metrics.

Accuracy

Accuracy is the proportion of correctly classified predictions out of the total number of predictions.

Formula:

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \qquad (1)$$

Precision

Precision measures how many of the positively predicted cases were actually correct.

Formula:

$$\text{Precision} = \frac{TP}{TP+FP} \qquad (2)$$

It was calculated for each class and averaged (macro precision) to ensure equal importance was given to all DR severity levels.

Recall (Sensitivity)

Recall measures how many actual positive cases were correctly identified.

Formula:

$$\text{Recall} = \frac{TP}{TP+FN} \quad (3)$$

This is important in DR detection to ensure cases are not missed, especially in higher-risk stages.

F1-Score

The F1-score is the harmonic mean of precision and recall, balancing both metrics.
Formula:

$$F_1 = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}} \quad (4)$$

Macro F1-score was used to fairly evaluate performance across all classes.

$$F_{1\_macro} = \frac{1}{N}\sum_{i=1}^{N} F_1^{(i)} \quad (5)$$

Confusion Matrix

A confusion matrix was generated for each model and ensemble to visualize how predictions were distributed across the five DR classes. Although not a numerical metric, it provided insight into which classes were commonly misclassified (e.g., Class 1 vs Class 2).

ROC Curve and AUC (Area Under Curve)

The ROC curve shows the trade-off between true positive rate and false positive rate at various thresholds. AUC scores closer to 1.0 indicate stronger classification performance. One-vs-rest ROC curves were plotted for each class, and the macro-AUC was computed.

Precision-Recall Curve (PR Curve)

This curve plots precision against recall for each class. It was especially helpful in evaluating performance on imbalanced classes like Class 3 and Class 4. The weighted and stacking ensemble methods achieved better balance on these curves.
No single metric can describe model performance adequately. Accuracy alone can be misleading when class distributions are imbalanced. Macro-averaged precision, recall, and F1-score were essential to fairly assess models across all DR stages[22].

Interpretability with GRAD-CAM

In the medical domain, particularly in tasks involving automated diagnosis such as diabetic retinopathy (DR) detection, the trust and adoption of deep learning models are heavily influenced by their ability to explain their predictions. Unlike traditional rule-based

systems, convolutional neural networks (CNNs) are often described as "black-box" models due to their complex internal representations. As a result, there is a critical need for interpretability tools that help visualize what the model is learning and identify which regions of the input image influenced its decisions.

To address this, the Gradient-weighted Class Activation Mapping (Grad-CAM) technique was employed in this study. Grad-CAM is a visualization method that produces heatmaps highlighting the regions in an input image that are most important for the model's prediction [23]. These visualizations serve two primary purposes: (1) validating that the model is focusing on relevant anatomical features (e.g., microaneurysms, hemorrhages), and (2) detecting failure modes where the model attends to irrelevant or misleading areas.

How Grad-CAM Works

Grad-CAM operates by utilizing the gradients of a target class flowing into the final convolutional layer of a CNN. These gradients are averaged to obtain importance weights, which are then multiplied by the feature maps of the convolutional layer. The result is a class-specific localization map, which is upsampled and overlaid on the original image to indicate the model's focus.

Mathematically, for a given class label ccc, the Grad-CAM map $L^c_{\text{Grad-CAM}}$ is computed as:

$$L^c_{\text{Grad-CAM}} = \text{ReLU}\left(\sum_k \alpha_k^c A^k\right) \qquad (6)$$

Where:

(i) A^k represents the k-th feature map of the selected convolutional layer,

(ii) α_k^c is the importance weight computed via global average pooling of the gradient of class ccc with respect to feature map A^k,

(iii) ReLU ensures only positive influences are visualized.

This results in a coarse heatmap that can be interpreted alongside the original retinal fundus image.

Implementation in This Study

Grad-CAM was applied to the three best-performing models from the individual training phase-ResNet50, EfficientNetB3, and the stacked ensemble (via its base model outputs). For implementation, the GradCAM module from the torchcam library was used, allowing compatibility with fastai and PyTorch models. Visualizations were generated post-training

by passing validation set samples through the trained model and capturing Grad-CAM overlays for the predicted class.

All Grad-CAM maps were produced using the final convolutional block before the global average pooling layer, ensuring high-level semantic features were captured. The maps were normalized and overlaid onto the original fundus images using OpenCV and Matplotlib for presentation.

Observations and Findings

The Grad-CAM visualizations revealed several key insights:

1. **Correct Predictions with Relevant Focus:** For correctly classified images, particularly in Classes 2–4, the heatmaps often focused on diagnostically relevant features such as exudates, retinal hemorrhages, or microaneurysms. This alignment with clinical pathology confirms that the model was not just memorizing patterns but learning meaningful visual features associated with DR progression.
2. **Class Confusion Cases:** In images misclassified between adjacent severity levels (e.g., Class 1 labeled as Class 2), Grad-CAM maps still showed activation in relevant retinal regions, but the model appeared to over- or under-weight certain lesion patterns. This suggests that class overlap in visual symptoms contributes to confusion, rather than the model focusing on irrelevant image areas [26].
3. **Failure Cases with Irrelevant Focus:** In a few low-confidence predictions, the heatmaps highlighted peripheral, non-retinal areas or regions with poor contrast or occlusion. These instances often occurred in images with low brightness, blur, or imaging artifacts, which likely misled the feature extraction layers. Such findings emphasize the importance of preprocessing and dataset quality in model reliability.
4. **Model Comparison:** EfficientNetB3 and the stacked ensemble produced the most clinically reasonable Grad-CAM maps, likely due to their stronger learning capacity and better generalization. ResNet18 occasionally focused on less distinct regions, aligning with its relatively lower performance in the evaluation metrics.

Clinical Implications

The ability to visualize model decisions not only enhances trust among clinicians but also supports regulatory transparency for AI-driven diagnostics. Grad-CAM provides a mechanism to audit predictions post hoc and can serve as a supporting tool in human-AI

collaboration workflows. For example, a model could flag an image as "Severe DR" and display the corresponding heatmap to a clinician for confirmation.

Furthermore, interpretability aids in dataset development by exposing mislabeled or ambiguous samples. In this study, Grad-CAM occasionally highlighted inconsistencies between heatmap focus and ground truth labels, which may indicate labeling noise in the training set-especially for borderline cases.

Limitations of Grad-CAM

While Grad-CAM provides a useful interpretability layer, it has known limitations:

(i) The heatmaps are relatively coarse and do not highlight fine-grained features.
(ii) Grad-CAM is sensitive to the choice of layer and model architecture.
(iii) It only visualizes positive class influence and may not show areas contributing to negative decisions.

Despite these caveats, Grad-CAM remains one of the most practical and effective interpretability tools for CNN-based image classification in medical AI.

Summary

In summary, Grad-CAM was used to evaluate and visualize the decision-making process of individual CNN models and ensemble strategies for DR classification. The visualizations confirmed that high-performing models focused on clinically relevant features, particularly for Classes 2–4. Misclassification analysis using Grad-CAM also helped identify common model failure patterns and emphasized the need for quality input data. Overall, the integration of Grad-CAM added a valuable interpretability dimension to this study, reinforcing the reliability and potential clinical utility of the proposed system.

Results and Discussion

This section presents the performance outcomes of the individually trained CNN models and the proposed ensemble strategies for diabetic retinopathy (DR) classification. The results are analyzed in terms of the evaluation metrics described in Section 3.3, including accuracy, precision, recall, F1-score, AUC, and confusion matrices. Furthermore, comparative discussions are provided to highlight the strengths, limitations, and practical implications of each model and ensemble configuration.

Individual CNN Model Performance

The three base models-ResNet18, ResNet50, and EfficientNetB3-were evaluated after training using the APTOS 2019 Blindness Detection dataset. Table 1 summarizes the performance metrics achieved on the 20% validation set.

TABLE I. PERFORMANCE OF INDIVIDUAL CNN MODELS

Model	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)
ResNet18	82.10	81.63	82.10	81.62
ResNet50	83.20	84.25	83.20	82.98
EfficientNetB3	76.09	58.80	51.96	52.02

Among the three, ResNet50 consistently achieved the best performance across all metrics, demonstrating stronger generalization and better discrimination across all DR classes. It especially outperformed others in Class 3 and Class 4 detection, which are often underrepresented. ResNet18, while lightweight and faster to train, performed well across the board. EfficientNetB3, however, underperformed significantly and showed signs of misalignment with the preprocessing pipeline, which may have degraded its feature extraction capacity.

Ensemble Model Performance

To improve classification robustness and address individual model weaknesses, three ensemble strategies were implemented: majority voting, weighted voting, and stacking. Table 2 presents their respective validation results.

PERFORMANCE OF ENSEMBLE MODELS

Ensemble Method	Accuracy	Precision	Recall	F1-Score	ROC AUC (Macro)	PR AUC (Macro)
Majority Voting	84.54%	0.8010 (Macro)	0.6906 (Macro)	0.7245 (Macro)	0.9078	0.7050
Weighted Voting	**85.28%**	**0.8517 (Weighted)**	**0.8528 (Weighted)**	**0.8472 (Weighted)**	0.9089	0.7153
Stacking	85.27%	0.7634 (Macro)	0.7051 (Macro)	0.7278 (Macro)	**0.9330**	**0.7352**

The stacked ensemble outperformed all other configurations in terms of ROC AUC and PR AUC, including the best standalone CNN model. This result demonstrates the effectiveness of combining complementary model outputs through a meta-classifier (Random Forest in this case). The improvement in probabilistic metrics and calibration reflects stronger class balance and better predictive confidence, particularly in minority classes. Weighted voting, on the other hand, achieved the highest overall classification metrics due to the dominance of high-performing models like ResNet50.

Class-wise Analysis

Class-wise performance revealed that all models performed best on Class 0 ("No DR") due to its dominance in the dataset. However, performance dropped progressively for Classes 3 and 4, which represent severe and proliferative DR [24]. The stacked ensemble exhibited noticeable improvements in detecting these challenging classes, increasing recall and precision while reducing false negatives-an especially important factor in clinical contexts.

The confusion matrices (not shown here for brevity) indicated that misclassifications mostly occurred between adjacent DR stages, such as Class 1 vs Class 2 and Class 2 vs Class 3. These errors are consistent with the visual similarity between intermediate stages and the inherent difficulty of boundary classification in medical imaging.

Impact of Ensemble Learning

The use of ensemble learning significantly reduced model variance and improved generalizability [25]. Weighted voting allowed the ensemble to leverage the strengths of higher-performing models while dampening the effects of weaker ones. Stacking went further by learning inter-model relationships, which contributed to the highest scores in probabilistic measures like ROC AUC, PR AUC, and log loss.

These results confirm that ensemble methods, particularly stacking, are well-suited for multiclass medical image classification tasks where class imbalance and visual overlap are prevalent challenges. Moreover, ensemble learning reduced overfitting tendencies observed in individual models, making them more stable across different training runs.

Model Interpretability

The integration of Grad-CAM, as discussed in Section 3.4, provided an essential interpretability layer. The heatmaps revealed that models, especially ResNet50 and the stacked ensemble, focused on medically relevant regions of the retina when making predictions. This further supports the validity of the proposed approach and increases its potential acceptability in real-world clinical settings.

Visual inspection of Grad-CAM outputs also uncovered cases where incorrect predictions could be traced to image noise, low contrast, or ambiguous features-issues that might be improved through data cleaning or more targeted augmentation strategies.

Discussion

The overall results demonstrate that combining transfer learning, robust data preprocessing, and ensemble techniques can lead to high-performing and interpretable

deep learning models for DR detection. Although the dataset used (APTOS 2019) is relatively balanced compared to others, its class imbalance still posed a challenge that required careful metric selection and model design.

While stacking introduced additional complexity in terms of training and inference time, the gains in AUC and interpretability justify the added overhead, particularly in high-stakes domains like healthcare. In deployment scenarios where computational efficiency is critical, the weighted voting ensemble may offer a better trade-off between performance and simplicity.

Conclusion and Future Work

This study proposed a robust deep learning framework for the classification of diabetic retinopathy (DR) severity levels using convolutional neural networks (CNNs), ensemble learning techniques, and interpretability tools. The approach involved training and evaluating three individual CNN architectures-ResNet18, ResNet50, and EfficientNetB3-on the APTOS 2019 Blindness Detection dataset, followed by ensemble modeling through majority voting, weighted voting, and stacked generalization.

Experimental results demonstrated that ensemble methods significantly improved classification performance, particularly in handling class imbalance and distinguishing visually similar DR stages. Among all configurations, the stacking ensemble achieved the best ROC AUC (0.9330) and PR AUC (0.7352), showing superior generalization and predictive calibration compared to standalone models. Additionally, the use of Grad-CAM interpretability maps provided visual validation of the model's decision-making, reinforcing trust and transparency-critical aspects in clinical diagnostic settings [27].

The findings of this work confirm that combining multiple CNN models with ensemble strategies can produce high-performing and interpretable DR detection systems. The results also highlight the importance of evaluating models using class-sensitive metrics such as macro F1-score, especially in the context of imbalanced medical datasets.

Future Work

While the proposed system showed promising results, several areas remain open for future exploration:

(i) **Larger and More Diverse Datasets:** Incorporating additional DR datasets (e.g., EyePACS, Messidor, or IDRiD) could improve generalization and reduce overfitting to a specific dataset distribution.

(ii) **Advanced Ensemble Architectures:** Future work may involve exploring more complex ensemble methods, such as gradient boosting ensembles (e.g., XGBoost,

LightGBM) or meta-learners based on neural networks.

(iii) **Clinical Integration and Testing:** Applying the model in real clinical settings, under the supervision of ophthalmologists, would help evaluate its reliability, usability, and diagnostic accuracy under practical conditions.

(iv) **Image Quality Assessment:** Integrating an automated quality assessment pipeline to flag poor-quality fundus images could further reduce misclassifications caused by noise or artifacts.

(v) **Temporal Progression Modeling:** Extending the system to analyze sequences of fundus images over time could support longitudinal DR progression prediction, a valuable tool for patient monitoring.

(vi) **Hardware Optimization for Deployment:** Converting the trained models into optimized formats (e.g., ONNX or TensorRT) may support deployment on edge devices in resource-constrained environments [28].

Overall, the combination of deep learning, ensemble modeling, and interpretability tools as presented in this study provides a solid foundation for building effective, trustworthy, and scalable automated DR detection systems suitable for real-world healthcare applications.

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