Ensemble learning based method for severity detection of Age-Related Macular Degeneration

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Abstract

Age-related macular degeneration (AMD) is a leading cause of vision impairment and blindness among elderly people. AMD disease has different severity grades requiring different treatment procedures. Many studies proposed automated methods grading AMD using color fundus images, but none achieved optimal performance.

In this study we aim to develop an automated method to detect the severity of AMD from color fundus images. The main contribution consists of a stacking ensemble learning approach, which combines the knowledge of five CNN models in order to perform accurate AMD severity grading. Experimental results show that the ensemble method achieves a classification accuracy of 95.2%, a precision of 95.27, a sensitivity of 95.25%, a specificity of 96.68% and an F1-score of 95.11% which outperforms several existing methods.

Keywords: AMD, ensemble learning, deep learning, fundus images.

I. Introduction

Age-related macular degeneration (AMD) is a significant cause of vision impairment and blindness, particularly among the elderly population [1], [2]. AMD primarily affects the macula, the central part of the retina responsible for daily life tasks such as reading and driving. The disease manifests in two forms: dry AMD, characterized by gradual thinning of the macula, and wet AMD, which involves the growth of abnormal blood vessels that leak fluid, causing rapid and severe vision loss.

Early diagnosis of AMD is crucial as different stages of the disease require different treatments [3]. Early-stage AMD can be managed through lifestyle modifications, such as dietary changes and smoking cessation, which can slow its progression. In contrast, advanced stages require intensive treatments, including supplements and injections. Some treatments might be less effective depending on how far the disease progressed [4]. Therefore, accurate grading of AMD severity is essential to ensure appropriate and timely interventions at each stage of the disease. For that, different modalities [5] are used. Color fundus photography (CFP) is a common modality for AMD diagnosis due to its simplicity, non-invasiveness, and effectiveness in highlighting early signs such as drusen and pigmentary changes [5].

Many studies suggested methods to automate the process of detecting AMD from fundus images using machine learning and deep learning. Methods targeting the detection the detection of AMD has shown good performance. However, existing methods focusing on grading AMD severity failed to achieve higher performance due to the small nuances in symptoms in the retina.

In this study, we propose an advanced automated method for classifying different stages of AMD using ensemble learning techniques for color fundus images. Our approach involves the use of multiple CNN models as descriptors, having different convolutional processing principles. Their feature vectors are through a stacking ensemble model [6] in order to leverage the strengths of individual classifiers.

The paper is organized as follows. Section 2 presents a literature review of existing methods. The proposed method is detailed in section 3. The experimental evaluation is presented in section 4, followed by the conclusion in the last section.

II. Literature Review

Age-related macular degeneration (AMD) manifests in different types and stages with distinct symptoms [2]. The existing automated methods vary in terms of preprocessing principles and objectives, either for AMD detection or grading.

Several studies targeting the AMD detection achieved optimal performances. For instance, the method proposed in [7] developed a CNN for classifying fundus images into healthy and AMD-positive images. The approach included preprocessing phase based on the use of Gaussian Blur and Contrast Limited Adaptive Histogram Equalization (CLAHE) for noise removal and contrast enhancement. Then, the use of morphology and contour-based techniques, along with Canny edge detection to locate drusen lesions. Accuracy values of 95.24% on the ARIA dataset and 96.47% on the STARE have been achieved. Another study referenced in [8] combined deep learning feature extraction using VGG16 with handcrafted features such as Discrete Wavelet Transform (DWT), Local Binary Patterns (LBP), and Pyramid Histogram of Oriented Gradients (PHOG) descriptors. This hybrid approach achieved 97.08% accuracy. A study referenced in [9] developed a lightweight CNN with batch normalization and dropout along with basic preprocessing consisting of only noise removal. This method achieved 97.39% accuracy on the STARE dataset and 98.97% on the RFMiD dataset. A study referenced in [10] used a SVM classifier and focused more on applying preprocessing techniques like CLAHE for contrast enhancement and extracting lesions within the image. This approach achieved an accuracy of 88.23% detecting AMD. In summary, it is safe to say that methods based on deep learning achieved optimal performances for detecting AMD.

There are several studies that focused on grading AMD severity. For instance, a study referenced in [11] used OverFeat along with SVM classifier with a preprocessing phase consisting of cropping the image to the boundaries of the retina. This method scored 79.4% and 81.5% accuracy values for 4-class and 3-class severity scale classifications, respectively. Another study referenced in [12] leveraged an ensemble of deep learning models using a Random Forrest classifier along with a light preprocessing to remove noise and data augmentation. Their model scored 63.3% accuracy on the AREDS data targeting 13 classes excluding patients over 55 years of age and using the KORA dataset, and 84.2% accuracy for classifying early or late AMD images. Similarly, the referenced study [13] built a Random Forrest ensemble of two different deep learning architectures and used progressive resizing techniques. An accuracy of 82.55% has been achieved for 4-class AMD classification. We also see this trend of using ensemble learning to tackle a multiclassification problem in the two iteration of the same study referenced in [14] and [15], which focused on classifying fundus images into 4-class severity scale using single model and then using an ensemble of couple deep learning models namely Inception-ResNet-V2 and Xception in the second study which saw an increase in performance achieving an accuracy of 86.13% compared to 83.0% using the single VGG16 model. An unsupervised learning method, proposed by the study referenced in [16] scored 65% and 25% accuracy values for the 4-class and the 12-class AMD severity classification respectively. However, it did not perform as good as supervised deep learning approaches and performs significantly worse for higher number of classes.

In summary, existing automated methods for detecting and classifying different stages of AMD still fall short in terms of achieved performance, with deep learning performing better than machine learning approaches even when using ensemble methods. Additionally, some reported metrics may be misleading due to potential overfitting and insufficient dataset diversity as small or biased datasets likely overestimate model performance as these data may underrepresent the different stages of the disease.

III. Ensemble Learning Method for AMD Classification

The core objective of our study is to detect and classify different stages of AMD from color fundus images. The main contribution of this study is to leverage the power of stacking ensemble learning to enhance the performance of severity scales grading of the disease. The proposed method consists firstly to preprocessing input image and data augmentation, secondly train each of the deep learning models individually and assess their performance, then build an ensemble using the most optimal meta classifier trained the stacked features from the base models.

A. *Data preprocessing & augmentation*

Fundus images in publicly available datasets are inconsistent as they are collected from different sources and captured using different supports. For that, we need to standardise and enhance these images as shown in Fig. 1. The very first needed step is to resize all the image to a standard input size that would fit all the input of the different DL models that we will implement, in our case 299 x 299 sized images would fit. To further reduce the noise caused by unrelated features, we are keeping only the green channel of the image which showcases the drusen deposits and pigmentations more clearly as drusen appears as a yellow deposit [17]. The collected images have varying contrast which is caused by the variation in lighting conditions in which the images were taken. For that, we normalized the light intensity across all images and applied Contrast Limited Adaptive Histogram Equalization (CLAHE) to enhance the contrast of the images without amplifying noise [18]. Finally, we applied a Top-Hat filter which enhances bright spots on an image on a darker background, in our case making the drusen and pigmentations pop more.

Publicly available datasets are often unbalanced, with healthy images being much more prevalent. To address this issue, we apply data augmentation to artificially generate images for the underrepresented classes especially AMD positive fundus images. For each image we apply a combination of transformations including horizontal and vertical flips, random rotations up to 40°, and random adjustments in brightness and contrast up to 0.2. The number of generated images for each original image is set depending on how underrepresented a class is. Samples of images result after the transformations are shown in Fig 2.

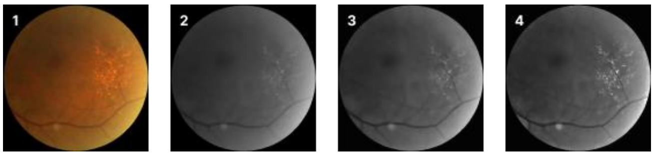

Fig. 1. (A) Preprocessing pipeline: (1) Original image, (2) Extracted green channel and noise removal, (3) Application of CLAHE filter, (4) Application of Tophat filter.

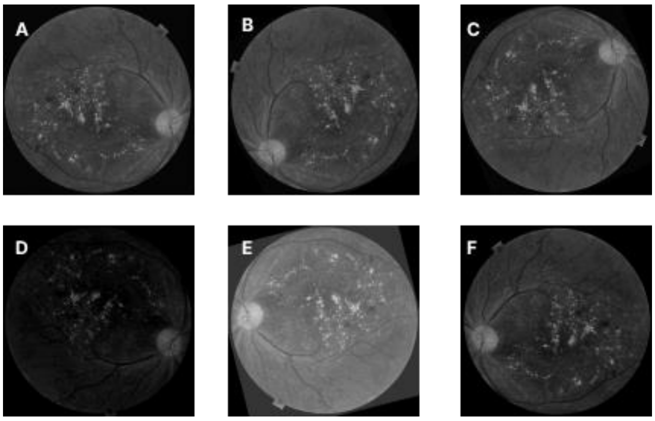

Fig. 2. (A) original image, (B) horizontal flip and random rotation, (C) Vertical flip and random rotation (D, E, F) Random brightness contrast and rotation

B. Deep learning models selection

An important step in our approach involves selecting a set of deep learning models as feature extractors for the ensemble. According to Ganaie et al. [19], the success of ensemble learning relies heavily on the diversity of its base classifiers. This diversity can be achieved through methods [6] such as bagging, which creates varied base classifiers by generating multiple datasets from the original data, or by using different architectures in the case of stacking. The fundamental principle is that varying outputs from base classifiers enhance the ensemble's overall performance compared to individual models.

Based on this principle, we utilize models with varying complexities. Deeper networks excel at identifying complex patterns, making them suitable for distinguishing similar image classes, but they are prone to overfitting [20]. In the other hand, shallower networks with fewer layers and parameters focus on more general features, reducing the risk of overfitting. This blend ensures that the ensemble is neither too simplistic nor overly tailored to the training data, allowing it to perform effectively across different severities of AMD. For example, if a deeper model misclassifies an image due to overfitting, a shallower model might still correctly identify it based on simpler features and if a shallower model misclassifies an image with small features, such as tiny drusen pigmentations, the deeper model might correctly identify it as early-stage AMD.

For the shallow networks, we selected Xception and ResNet50V2, models known for their high top-5 accuracy and fewer layers, as provided by Keras [21]. For deeper models, we chose EfficientNetB5, which offers a balance between efficiency and performance, unlike EfficientNetB6 or EfficientNetB7, which, despite slightly better performance in the ImageNet challenge [22], are more prone to overfitting on smaller datasets. InceptionV3 is another popular choice, as its use of different kernel sizes in the same layer allows it to capture information at various scales, making it effective for identifying both large simple features and complex ones [23].

C. Transfer learning and fine-tuning

Transfer learning leverages pre-trained deep learning models, which have already learned features from large datasets, and fine-tunes them on smaller, domain-specific datasets. This approach is helpful when dealing with smaller set of data, as in our case, as it mitigates the risk of overfitting and reduces the computational resources and time required for training from scratch [24]. For that matter all the five deep learning models come pre-initialized with the ImageNet weights [25].

For each base classifier, we added three layers for feature extraction and one for classification, which we later remove when creating an ensemble as we are using the features extracted by each model instead of the final prediction. The first layer is a 2D pooling layer that simplifies the data by transforming the output of the base model into a 2D feature vector, followed by a dropout layer which takes the simplified feature vector and randomly set some neurons to zero during training to help prevent overfitting, for that we set the probability value to 0.2 based on experimenting with different values. Following this is a dense layer outputs a 1D vector of size 1024, with a ReLU activation function which allows faster training and less errors during backpropagation. The activation function is shown in Equation 1.

For individual models, we add an extra dense layer with a SoftMax activation function producing a probability distribution for the 3 targeted classes, in our case: healthy, early and late AMD based on the feature vector outputted by the previous layer. The activation function is shown in Equation 2. Later when building the ensemble we discard it and train the meta classifier using the stacked features. The values of the hyperparameters used in the training of each of the base models is summarised in TABLE I. For each parameter we picked the values that yields the best result.

$$f(x) = \max(0, x) \tag{1}$$

$$\sigma(\vec{z}) = \frac{e^{z_i}}{\sum_{j=1}^{K} e^{z_j}} \tag{2}$$

D. Ensemble learning framework

A stacking ensemble learning framework combines the predictions of different base classifiers in order to make a more accurate final prediction [6]. For our experiment, we selected 6 different meta-classifiers namely SVC, Random Forrest, KNN, Gradient Boosting classifier, XGBoost and MLP to make predictions based on the stacked features extracted from the base classifiers then optimized and validated each of the ensembles using grid search method [26] to find the best parameters. Our main purpose of an ensemble is to outperform the base classifiers while being able to generalize better and overfit less compared to the single model solution. Fig. 3 showcases the overall architecture of the ensemble.

IV. EXPERIMENTS AND RESULTS

A. Dataset

The collected images are selected from the publicly available RFMiD dataset [27] totaling to 1135 images including 669 healthy fundus images and 466 diagnosed with age-related macular degeneration out of which 402 images account for the eark AMD and 64 representing late-stage AMD.

In the case of this dataset and many other publicly available datasets, data augmentation is important to make sure the models do not turn out to be biased towards a certain class as the healthy images account for more than half the total data. To address such issue, we used an open source tool named Albumentations [28] to artificially generate new images by applying transformations to the original images.

TABLE I: Hyperparameters of training DL models

Parameter	**Value**
Optimizer	Adam
Batch size	8
Learning rate	0.0001
Epochs	40
Early stopping patience	3
Start from epoch	3
Activation function	SoftMax
Loss function	Categorical cross-entropy
Dropout	0.2

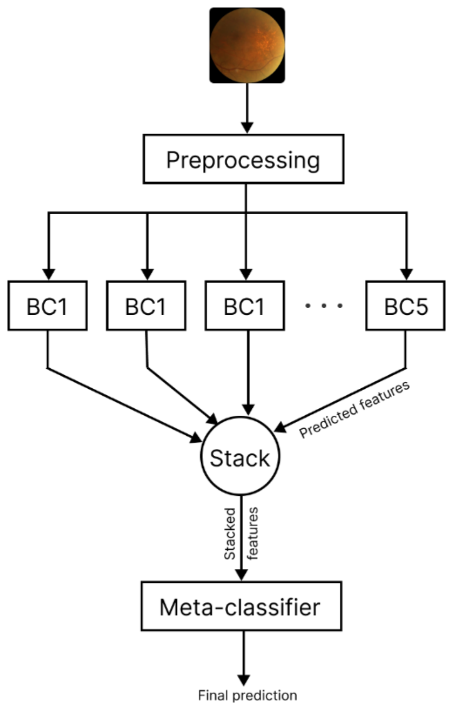

Fig. 3. Pipeline for ensemble method for AMD classification

The total count of images for each class before and after augmentation is shown in TABLE II. To further evaluate the generalizability of the models and the ensemble, we split the data into five subsets. One subset is designated for testing, another for validation, and the remaining three for training. We performed a four-fold cross-validation experiment, with the subsets assigned differently for each fold, to thoroughly see how well our model performs for different unseen data as shown in Fig. 4.

B. Evaluation metrics

The training and testing experiments are conducted using a combination of different tools, notably Keras and SciKit-Learn which provide a variety of metrics to evaluate the performance of our models such as accuracy, sensitivity, precision, specificity and f1-score. The different metrics are calculated from the confusion values as shown in the equations 3,4,5,6 and 7.

TABLE II. Image count before and after data augmentation

Total original images		
Healthy	**Early**	**Late**
535	321	51
Total images after augmentation		
Healthy	**Early**	**Late**
535	642	459

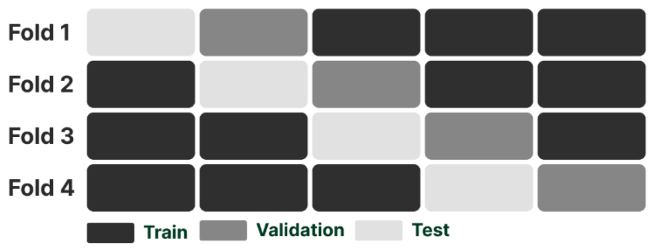

Fig. 4. Data splitting for each of the four folds

$$\text{Accuracy} = \frac{TP + TN}{TP + FP + TN + FN} \quad (3)$$

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (4)$$

$$\text{Precision} = \frac{TP}{TP + FP} \quad (5)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (6)$$

$$F1 = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}} \quad (7)$$

C. Ensemble method evaluation and results

Each base classifier is trained and validated first for optimization and later for comparison with EL method. We then used the five trained models for feature extraction to create a new dataset consisting of stacked features and their corresponding true labels. This new dataset is used in six sperate experiments each time with a different meta-classifier. Each time, the selected meta-classifier is trained, validated and optimized using the grid search method [26].

The metrics achieved by the different ensembles are presented in TABLE III. Both KNN and SVC performed better than every single individual model with KNN scoring the best metrics out of the six different ensembles achieving an accuracy of 95.25%, a precision of 95.27%, a sensitivity of 95.25%, a specificity of 96.68% and an F1-score of 95.11%. The cross-validation results for the KNN ensemble, as indicated in TABLE IV, demonstrate robust and reliable results, characterized by high accuracy, precision, sensitivity, specificity, and F1-score for all subsets of the data. Moreover, the deviation range of each metric is between ±0.76 ±1.01 indicating slight variability between the achieved metrics for each validation. This guarantees a consistent performance for any data used for training and testing. For a better analysis of the achieved result by the best meta-classifier, we illustrate it in box plots as shown in Fig. 5.

TABLE III. Evaluation metrics achieved by each of the meta-classifiers

Classifier	**ACC**	**PRE**	**SEN**	**SPE**	**F1**
XGB	93.53	93.41	93.53	95.75	93.34
GB	93.96	93.96	93.96	95.90	93.83
RF	94.39	94.59	94.39	96.18	93.96
MLP	93.96	94.18	93.96	95.84	93.54
SVC	94.82	94.76	94.82	96.52	94.70
KNN	95.25	95.27	95.25	96.68	95.11

TABLE IV. AMD classification performance for four-fold cross validation

Fold	**ACC**	**PRE**	**SEN**	**SPE**	**F1**
1	95.25	95.27	95.25	96.68	95.11
2	93.96	94.22	93.96	95.72	93.52
3	92.67	92.85	92.67	94.76	92.51
4	93.53	93.91	93.53	95.13	93.38

TABLE V. Performance comparison between the ensemble method and the base classifiers

Model	**ACC**	**PRE**	**SEN**	**SPE**	**F1**
EfficientNetB5	88.8	87.5	82.0	87.5	83.9
InceptionV3	90.1	89.0	82.3	89.0	85.1
Xception	91.4	92.1	85.2	92.1	88.1
ResNet50V2	91.8	94.9	91.2	94.9	92.7
DenseNet201	94.4	96.6	84.5	96.6	88.9
Ensemble	**95.2**	**95.2**	**95.2**	**96.6**	**95.1**

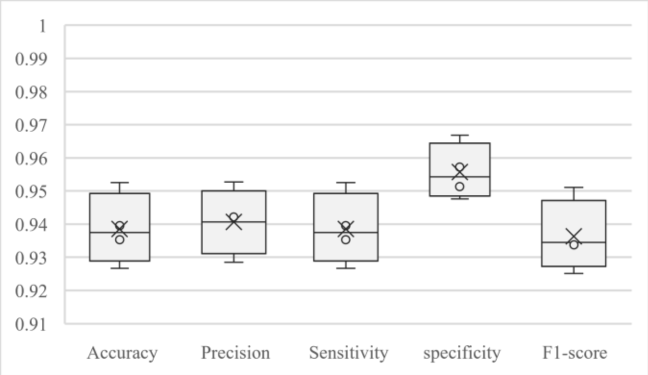

Fig. 5. Performance evaluation by the KNN ensemble method using box plots

D. Proposed method comparison with existing studies

Numerous studies have focused on classifying AMD into three or four severity steps. For example, Burlina et al. [11] achieved accuracies of 81.5% and 79.4% for the three step and four step severity scale respectively using SVM, as shown in Table VI. Domínguez et al. [13] and Govindaiah et al. [15] both utilized ensemble learning to classify images into 4 classes, achieving accuracies of 82.55% and 83.0% respectively. Similarly, Grassman et al. [12] employed an ensemble learning approach for the three step severity scale, reaching an accuracy of 84.2%. Yellapragada et al. [13] with their unsupervised learning method attained a lower accuracy of 65% on the four-step severity scale. In contrast, our study achieved a higher accuracy of 95.2% higher than the above results.

V. CONCLUSION

The stacking ensemble learning method utilizing a KNN classifier has demonstrated excellent performance on the RFMiD dataset. As highlighted in the results section, this ensemble method achieves a 95.25% accuracy in correctly classifying color fundus images, surpassing the base classifiers. It also consistently performs well across all data subsets, in contrast to single model approaches which fall short in terms of generalizability and effectiveness.

Table VI: Comparative analysis with existing methods

Study	Classes	Method	ACC
Yellapragada et al.[16]	4	NPID	65.0
Domínguez et al.[13]	4	EL	82.55
Govindaiah et al. [15]	4	EL	83.0
Burlina et al. [11]	4	LSVM	79.4
Burlina et al. [11]	3	LSVM	81.5
Grassman et al.[12]	3	EL	84.2
Our method	**3**	**EL**	**95.2**

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