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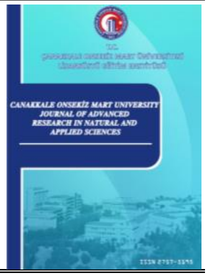

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lood Vessel Segmentation and Classification of Diabetic Retinopathy with Machine Learning-Based Ensemble Model

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Abstract − The incidence of diabetes has increased in recent times due to factors such as obesity and genetic predisposition. Diabetes wears out the eye vessels over time. Diabetic retinopathy (DR) is a serious disease that leads to vision problems. DR can be diagnosed by specialists who examine the fundus images of the eye at regular intervals. With 537 million diabetics in 2021, this method can be time-consuming, costly and inadequate. Artificial intelligence algorithms can provide fast and cost-effective solutions for DR diagnosis. In this study, the noise of blood vessels in fundus images was eliminated using the LinkNet-RCB7 model, and diabetic retinopathy was categorized into five classes using a machine learning-based ensemble model. Artificial intelligence-based classification training using images as input takes a long time and requires high resource requirements such as Random Access Memory (RAM) and Graphics Processing Unit (GPU). By using Gray Level Cooccurrence Matrix (GLCM) attributes in the classification phase, a lower resource requirement was aimed for. A Dice coefficient of 85.95% was achieved for the segmentation of blood vessels in the Stare dataset, in addition to 97.46% accuracy for binary classification and 96.10% accuracy for classifying DR into five classes in the dataset APTOS 2019.

Keywords − *Diabetic retinopathy, ensemble learning, classification, segmentation, information systems*

1. Introduction

Diabetes occurs in high glucose levels because of insufficient secretion or ineffective use of the hormone insulin. Nowadays, the incidence of diabetes is increasing due to factors such as obesity, lack of exercise, and genetic predisposition. In 2021, there will be around 537 million diabetics in all countries. According to forecasts, it will be 783 million by 2045 [1].

Diabetes affects many different organs in the human body via the bloodstream. If the amount of glucose in the blood transported to these organs increases, the organs can be damaged. One of the organs affected by diabetes is the eye. Diabetic retinopathy (DR) develops in the eye due to diabetes. In DR, the blood vessels are damaged by the effects of glucose. As a result, patients may experience visual impairment and blindness. In view of this situation, it is necessary to detect this disease at an early stage [2].

For the diagnosis of DR, patients' fundus images should be regularly examined by experts. The fundus image is an imaging technique that can display and archive the condition of the fundus structures, such as the optic nerve, macula, retina, blood vessels, and vitreous in color. There are around 40 thousand ophthalmologists in China. Compared to the number of diabetes patients, there is one specialist for every 3,000 patients. Moreover,

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diagnosis in this way is time-consuming and costly [3]. There are two approaches to classification in the literature. These are non-proliferative DR (NPDR) and proliferative DR (PDR). NPDR stands for phases of DR in which it is relatively benign. It is divided into three stages: mild, moderate, and severe. PDR refers to the advanced stage of the disease. On this basis, it is divided into normal, mild, moderate, severe, and PDR [4].

Thanks to the development of computer-aided technologies, image-based rapid diagnosis is now possible. Information systems using these methods are used for noise removal, segmentation, and classification of images. Numerous studies can be found in the literature using these methods for DR. Removing blood vessel noise on fundus images is essential for diagnosing DR. Classification of images from which the blood vessel noise has been removed can be performed with higher accuracy. In addition, images from which the blood vessel noise has been removed can be more easily examined and diagnosed by experts. Considering the number of ophthalmologists per patient, the fact that success depends on the skills of the specialist, and the costly and lengthy diagnosis, the importance of computerized studies for the diagnosis of DR becomes clear. This study used LinkNet-RCB, which provides successful results in the segmentation of medical images. Unlike in the literature, the dataset APTOS 2019 was cleaned of blood vessel noise utilizing this model and segmented into five classes using the Xception-based Convolutional Neural Network (CNN) algorithm. This will contribute to the diagnostic process by presenting noise-free images of blood vessels to experts and categorizing the images into five classes.

Blood vessel noise in fundus images can be removed using image processing algorithms. However, this solution has a low success rate, as an optimal threshold cannot be found for every image. Instead, the noise can be cleaned using deep learning with noise mask data and the results can be corrected with image processing. Cleaning up blood vessel noise in fundus images using deep learning methods involves some difficulties, such as the long duration of training, finding suitable datasets, and developing an effective model. In artificial intelligence-based approaches where the images are used as input during the classification phase, resources such as Graphics Processing Unit (GPU) and Random Access Memory (RAM) are used more, and the training time is extended. The relatively new LinkNetRCB7 model in this domain achieved high success rates in the segmentation phase to overcome these difficulties. A new ensemble learning approach based on machine learning was proposed in the classification phase. With this approach, successful results were achieved with fewer resources.

The purpose is explained in the introductory part of the study, and a literature study on this topic is carried out. In the second part, the phases of the study, the data sets, and the methods used are described in detail. The results are presented in the third part and commented on in the fourth part. Figure 1 shows the proposed approach. In summary, it can be said that in the study context.

1. The LinkNet-RCB7 model is used for blood vessel segmentation. Preprocessing was applied to input images. The prediction results were corrected with image processing.

2. Images cleared of blood vessel noise are divided into five and two classes with the proposed approach.

3. In order to consume less GPU, RAM, and Central Process Unit (CPU) resources, an ensemble method using Gray Level Cooccurrence Matrix (GLCM) features in the classification phase was proposed.

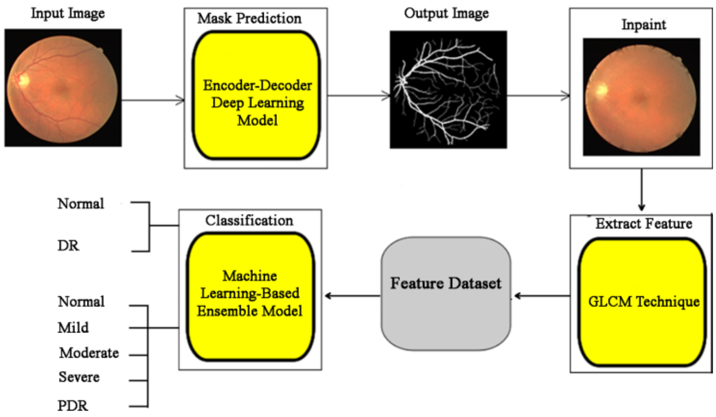

Figure 1. Proposed approach

Blood vessels must first be segmented to remove the noise of the blood vessels from the image. Masks and noise resulting from the segmentation can then be removed from the image using functions similar to inpaint. A literature review shows that blood vessel noise removal, optic disk segmentation, and DR classification play a role in the studies. Since the study focused on removing blood vessel noise and classification, the studies in this area were examined in the literature. In the vessel noise removal phase, the vessels in the images are segmented. Image segmentation algorithms from the literature can be used to segment the vessels. Some studies show that image processing or deep learning alone is used to segment the vessels. However, using these two methods together seems more advantageous as the accuracy can be increased by correcting the estimated masks. The images can also be preprocessed with image processing before being trained with deep learning. This way, the visibility of noise and areas on the image's increases.

There are studies in which the images are subjected to various preprocessing steps during the segmentation of blood vessels. The visibility of vein noise in the image varies depending on the channels in the Red-Green-Blue (RGB) color space. Tan et al. [5] show that the green color channel is more effective in determining blood vessel noise. In diagnosing DR with fundus images, the destruction of vessels causes noise in the image. Since the classification is performed with these images, the green color channel can be selected in the images that serve as input for deep learning training. The green channel has the highest contrast compared to the others. This situation was highlighted in the study by Long et al. [6], in which they attempted to detect microaneurysms. Tang et al. [7] used a new approach to remove blood vessel noise. In their study, image preprocessing was performed using the median filter. In this way, unnecessary background elements are removed from the grayscale image. Subsequently, each pixel of the image is classified as blood vessel noise or not, and the segmentation of the vessels is completed. The study favored the blue channel, where the vessel noise is most visible. The nearest neighbor algorithm is used to classify the pixels. This study's accuracy is 96.11% and 81.74% for the Digital Retinal Images for Vessel Extraction (DRIVE) and Structured Analysis of the Retina (STARE) databases, respectively.

In the work of Guo et al. [8], the vessel noise was removed using an Fully Convolutional Network (FCN)-based deep learning algorithm. In the segmentation performed with deep learning, an f1 score of 82.49% was achieved using only the rigid dataset. In another study [9] on blood vessel segmentation, the Clahe and Bottom Hat techniques were used with deep learning. These methods are used to increase the visibility of noise. A UNet-based model was proposed using driving data, and a training accuracy of 98.19% was achieved using this model. Laibacher et al. [10] proposed a UNet-based model called M2UNet. This model uses the residual blocks (RB) used in Residual Network (ResNet). The image size is kept the same at the inputs and outputs of the RBs. With this model, a cube accuracy of 80.91% was achieved in the Drive dataset and 80.06% in the Retinal Vessel Reference Dataset (Chase_DB1) dataset for the segmentation of blood vessels. Aurangzeb et al. [11] proposed a new algorithm called Anam-Net based on the decoder architecture. This model achieved a training accuracy of 96.60%, 97.28%, and 97.46% in Chase_DB1, Drive, and Stare. Diabetic retinopathy is a preventable disease if detected early. Experts can diagnose DR by examining images. However, there are many challenges in observing diabetic retinopathy, such as expertise, contrast differences, image noise, and financial constraints [12]. In the study by Sikder et al. [13], the images were categorized into five classes using the Extra Tree algorithm (a type of decision tree method) and a training accuracy of 91.07%, a prediction accuracy of 90.40%, and a sensitivity accuracy of 89.54% were achieved for the dataset The Asia Pacific Tele-Ophthalmology Society 2019 (APTOS 2019).

EfficientNet is a model offered by Google and has different types. Although the long training time is considered a disadvantage, it is a model with great accuracy. An example of the use of this algorithm is provided by Liu et al. [14]. In the study, DR was categorized into five classes using EfficientNetB5. As a result of the training, the study achieved a training accuracy of 84.88%. Majumder et al. [15] proposed a study on the classification of fundus images (five classes). They used the datasets APTOS and EyePACS for their research. They used SEDenseNet, a modified Dense Convolutional Network (DenseNet) algorithm. The training accuracy, sensitivity, and F1-score values were 85%, 70%, and 72%, respectively.

Modi and Kumar [16] divided the images of DR into two classes. They used random forest in their study. The accuracy rate of binary classification is 89.64% with the Messidor dataset. Wang et al. [17] presented a model based on InceptionV3 and achieved a training accuracy of 63.23% when students were categorized into five classes. In another study, using the Visual Geometry Group 16 (VGG16) model and CNN, a training accuracy of 73.83% was achieved for the DRISTHI dataset. The images were categorized into five classes in the study by Nagaraj et al. [18]. Wu et al. [19] presented a classification model called CF-DRNET based on CNN. They observed an accuracy of 86.61% with the Kaggle dataset.

By extracting the GLCM features of the images, DR classification can be performed, which provides faster results than classification with images. An example is the study by Rahman et al. [20]. In this study, binary classification was performed using the GLCM features (mean, energy, contrast, similarity, maximum, homogeneity, entropy). Binary classification using Support Vector Machine (SVM) achieved an accuracy of 94.59%. Sikder et al. [21] classified DR into five classes using GLCM features. In the study using the XGBoost method, an accuracy value of 94.20% was achieved with the dataset APTOS. The images were cropped to better display the relevant area. The images were sharpened, and the contrast was increased. In the study presented by Ishtiaq et al., the eyePACS dataset was divided into five classes with a hybrid model using DR CNN and ResNET50 models as an ensemble. An accuracy value of 98.85% was observed in the study. It was performed on the Kaggle EyePACS dataset; a five-fold classification of DR was performed by extracting the features of the images. LBP was used to extract the features. Classification with SVM yielded an accuracy of 98.63%, sensitivity of 98.628, prediction of 98.67, specificity of 99.656, and F1 value of 98.622 [22]. DR was separated into two classes using GLCM features and SVM by Foeady et al. [23]. Energy, entropy, homogeneity, contrast, and correlation values were selected as features in the images that underwent preprocessing steps, such as histogram equalization and optic disc elimination. When classified as PDR and NPDR, 92.86% accuracy, 100% sensitivity, and 91.67% specificity were achieved with 0 degrees GLCM. Ensemble models can provide more successful results than self-contained models.

An example is the study presented by Deepa et al. [24]. The study uses a separate data set. Two inception and two Xception models were used together. SVM was preferred for the final estimation. The study has four classes: pedunculated, mild, moderate, and PDR. An accuracy value of 96.20% was achieved.

In successful models in the literature, more successful results can be obtained by changing parameters such as activation function and number of layers. Kiliçarslan presented an example of this. The HardSReLUE activation function proposed in the study achieved 1.13% higher success with the VGG19 model than the standard Rectified Linear Unit (ReLU) [25]. Different combinations of activation and optimizer can offer different success values. ReLU activation function and AdaMax optimizer showed the highest value for glaucoma diagnosis in the study of Kılıçarslan [26]. This duo was also preferred in our research.

2. Materials and Methods

There are two phases in the study. These are blood vessel segmentation and DR classification. In the first phase, the model was run at 500 epochs. The hyper-parameters used in the training phase are shown in Table 1. For the classification phase, default parameters that belong to models were used. The datasets used in the study were divided into 80% training and 20% test.

Table 1. Hyper-parameters

Parameter	Blood vessel segmentation
Batch size	8
Weight decay	0.025
Epoch number	500
Input size	256x256
Optimizer	AdamW
Loss function	MSE+dice loss
Output function	Sigmoid
Learning rate	0.0001

2.1. Datasets and Image Preprocessing

For the segmentation phase, the data sets stare (20 images – 700 x 605) [27] and drive (20 images - 584 x 565) [28] were combined and used. This data set is referred to as the blood vessel data set (BVDS – 40 images and ground truth of the blood vessels). The green color channel is preferred as it increases the visibility of the vessel noise. The green color channel selection, grayscale conversion, normalization, Clahe filter, and Gaussian filter were applied to this dataset. Clahe is used to improve the contrast between the background and the vessels. The dataset APTOS 2019 [29] for DR classification was preferred in the training phase. The noise of the blood vessels in the dataset APTOS is adjusted by training. APTOS 2019 training dataset was split into 80% training and 20% test. The data distribution of APTOS 2019 can be seen in Table 2. All datasets used in this study are publicly available.

Table 2. APTOS 2019 distribution for two classes

Dataset	Class	Count	New Classes	Train (80%)	Test (20%)
APTOS 2019	Normal	1805	Normal	1444	361
	Soft	370	DR	1485	372
	Mild	999			
	Moderate	193			
	PDR	295			
TOTAL		3662		2929	733

2.2. Blood Vessel Segmentation Model

The LinkNet-RCB7 model, which showed high accuracy in image segmentation, was preferred at this phase. This model uses the EfficientNetB7 algorithm in coding blocks [30] (Figure 2). LinkNet-RB7 is a modified version of LinkNet-B7 [31]. Before the last layer, the ResNetC model was added. ResNetC is a more successful parallel model than ResNet [32]. The architecture of ResNetC can be seen in Figure 3. LinkNet-RCB7 is a model based on an encoder-decoder architecture. The encoder-decoder architecture is widely used in the literature due to its successful results in medical image segmentation. LinkNet-RCB7 has four encoder and decoder blocks. The decoder block is identical to the original LinkNet model. The encoder block contains different layers of EfficientNetB7. In this way, the number of extracted features is increased. Using ResNetC, LinkNet-RCB7 shows higher accuracy [30]. In this phase, the input images were divided into 36 layers with a resolution of 256x256. In this way, the input images could be used as 1024x1024. In this way, pixel losses that occur when images are resized are reduced. Morphological operations corrected the prediction results.

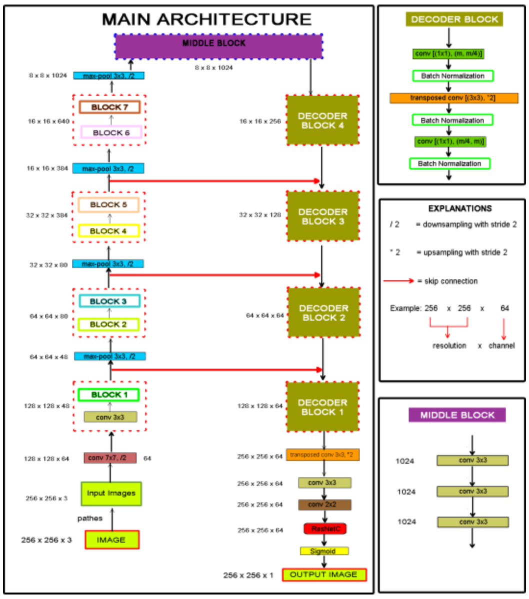

Figure 2. LinkNet-RCB7 architecture [30]

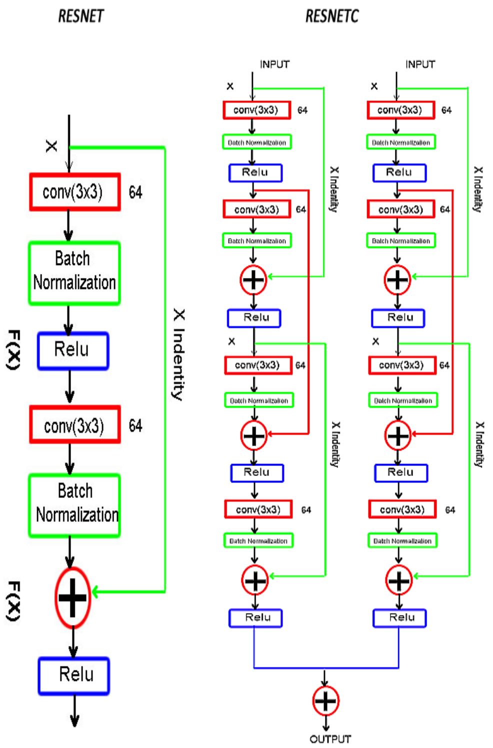

Figure 3. ResNetC architecture [32]

2.3. DR Classification Model

At this phase, the DR was classified into two and five classes. The binary classification has two classes: normal and DR. Normal, mild, moderate, severe, and PDR were used to classify DR into five classes. The number of data given in Table 2 was used for classification in binary classification. In classifying DR into five classes, the number of images was balanced by smote data balancing. Table 3 shows the dataset used for the five classes.

Table 3. APTOS 2019 distribution for five classes

Dataset	Class	Count	Balanced Train (80%)	Test (20%)
APTOS 2019	Normal	1805	1454	351
	Soft	370	1454	68
	Mild	999	1454	213
	Moderate	193	1454	36
	PDR	295	1454	65
TOTAL		3662	7270	733

An ensemble learning-based method was used for classification. This method uses stacking and includes base classifiers and meta-classifiers. Each base classifier produces a prediction result. Then, the meta classifier selects the best result by voting. The stacking classifiers in the Sklearn library were used for the final prediction. Decision Tree, K nearest neighbor (KNN), Random Forest, and SVM were selected as base classifiers based on their success in classification. XGBoost is a metaclassifier. It provides parallel tree boosting. Figure 4 shows the proposed approach.

The features that belong to images were achieved using GLCM. The images were resized to 256x256. The dissimilarity, energy, correlation, homogeneity, contrast, and Angular Second Moment (ASM) features were used at 0, 45, 90, and 135 degrees. The training dataset, therefore contained a total of 30 features.

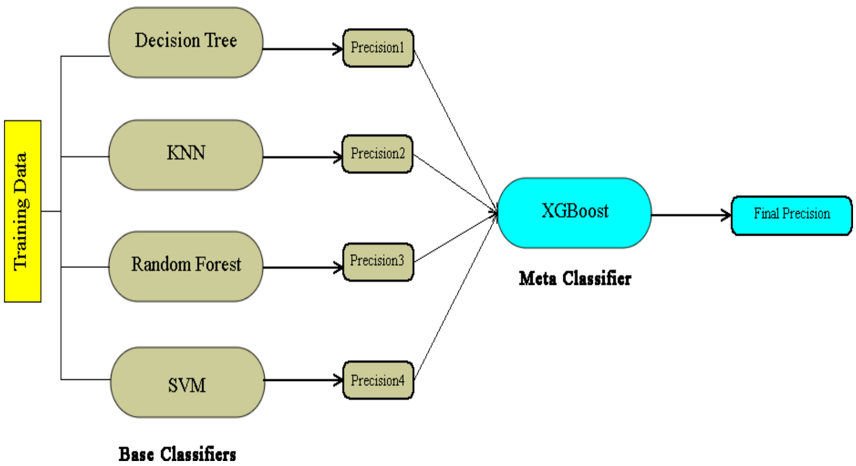

Figure 4. The architecture of the classification approach

3. Results and Discussion

The results obtained in the segmentation of the blood vessels are shown in Table 4. At this phase, the noise in the estimated masks was corrected by morphological operations, median filters, and the removal of independent segments from the image. Figure 5 shows example results. Table 5 shows the results of the study trained on different datasets.

Table 4. Blood vessel segmentation

Study	Model	Acc (%)	DA (%)	F1-Score (%)	Dataset
[7]	KNN	96.11	-	-	Drive
[8]	FCN	-	-	82.49	Rigid
[9]	UNET	98.19	-	-	Drive
[10]	M2UNET	-	80.91	-	Drive
[11]	Anam-NET	96.60	-	-	Drive
[30]	LinkNet-RCB7	98.50	85.75	86.50	Stare
Proposed Model	LinkNet-RCB7	98.56	85.95	86.54	Stare
Proposed Model	LinkNet-RCB7	98.10	85.48	86.33	Drive
Proposed Model	LinkNet-RCB7	98.08	85.65	85.96	BVDS

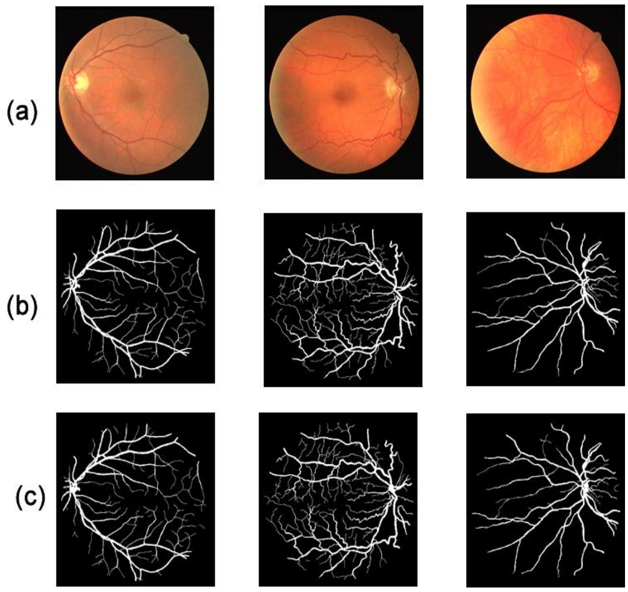

Figure 5. Sample results of blood vessel segmentation

The results obtained in the classification phase are presented in Table 4 in comparison with other studies based on the datasets. The results show that the study succeeded in classifying DR into two and five classes. We have used "accuracy_score(y_pred,y_test):0.2f}" with the training dataset for results.

Table 5. DR classification

Study	Model	Acc (%)	Recall (%)	Precision (%)	F1	Dataset/Number of classes
[13]	Extra Tree	91.07	89.54	90.40	89.97	APTOS/five classes
[14]	EfficientNetB5	86.34		90.94	93.90	APTOS + Kaggle + EyePACS/five classes
[15]	DenseNet	85.00	70.00	75.00	72.00	EyePACS/five classes
[16]	Random Forest	89.64	-	-	90.41	Messidor/ two classes
[17]	InceptionV3	63.23	-	-	-	EyePACS/five classes
[18]	VGG16	73.83	-	-	-	DRISTHI/five classes
[19]	CNN-Based	86.61	-	-	-	Kaggle/five classes
[20]	GLCM+SVM	94.59	-	-	-	APTOS/ five classes
[21]	GLCM+XGBoost	94.34	92.69	-	-	EyePACS/ five classes
[22]	GLCM+ Hybrid Model	98.63	-	99.65	98.62	EYEPACS/five classes
[23]	GLCM+SVM	92.86	-	91.67	-	Special (44 images-10 normal and 34 DR) /two classes
[24]	Ensemble Model	96.20	-	-	-	Special / four classes
Proposed Ensemble Model		**97.46**	**97.00**	**96.00**	**97.00**	**APTOS/two classes**
Proposed Ensemble Model		**96.10**	**94.80**	**95.90**	**96.00**	**APTOS/five classes**

Table 6 shows the cross-validation results obtained by selecting the k value as 5. We have used cross-validation from the sklearn library for binary and multi-classifications. With cross-validation, the data set was divided into 5 parts, and one was selected as validation in each training, while the remaining ones were used as the training set. The purpose is to measure the model's effectiveness on data it has never seen.

Table 6. Cross-validation results

Model	Fold	Acc (%)	Recall (%)	Precision (%)	F1	Dataset/Number of classes
Proposed Ensemble Model	1	91.807	90.25	92.37	91.30	APTOS/two classes
Proposed Ensemble Model	2	94.10	91.56	95.00	93.25	APTOS/two classes
Proposed Ensemble Model	**3**	**94.25**	**95.57**	**94.12**	**93.34**	**APTOS/two classes**
Proposed Ensemble Model	4	93.07	92.90	92.00	92.45	APTOS/two classes
Proposed Ensemble Model	5	92.57	94.25	91.54	92.87	APTOS/two classes
Proposed Ensemble Model	1	86.58	85.50	87.60	86.00	APTOS/five classes
Proposed Ensemble Model	2	88.13	86.00	89.00	88.70	APTOS/five classes
Proposed Ensemble Model	3	88.83	87.72	89.40	89.20	APTOS/five classes
Proposed Ensemble Model	4	88.18	88.00	89.32	89.10	APTOS/five classes
Proposed Ensemble Model	**5**	**90.38**	**89.90**	**90.00**	**90.00**	**APTOS/five classes**

4. Conclusion

In this study, the noise of the blood vessels in fundus images was eliminated, and the images were classified into two and five classes. Examination of the results obtained shows that the study presented has high accuracy values. Especially in the classification phase, the accuracy distribution between the classes is balanced. This can be seen in Table 4.

In the blood vessel segmentation phase, it is important to pre-treat the images by image processing and correct the estimated masks before inputting them into the system. The image was divided into 36 layers to reduce pixel loss. These processes are effective in achieving high accuracy with LinkNet-RCB7.

This study divides DR into two and five classes using ensemble learning. This is to help decision-makers in the diagnosis phase of DR. In the ensemble learning approach proposed in the study, SVM, Random Forest, Decision Tree, and KNN were used as base classifiers and XGBoost as meta-classifiers. The accuracy values achieved were 97.46% in two classes and 96.10% in five. In future studies, comparisons can be made with different datasets by performing cross-training. The fact that other datasets from the literature were not used in the study can be considered a limitation.

As a result, the existing LinknetRCB7 model was used in the grain noise removal stage by dividing the input images into 36 slices instead of 16. At this stage, increasing the total resolution of the images taken as input greatly improved success. In the classification stage, the main goal was determined as achieving similar success with less resource use rather than achieving higher success than existing studies, and this goal was achieved. In addition, hybridizing existing machine learning methods with an ensemble model in the classification stage has been observed to give successful results. In future studies, success can be increased with parameters and models such as different activation functions and optimizers.

Author Contributions

The first author conducted the experiments, analyzed the results, and wrote the article. The second author planned for the tables, graphs, and figures used in the study. The second author also contributed to the creation of the methods used in the study. All authors read and approved the final version of the paper. This paper is derived from the first author's master's thesis, supervised by the second author.

Conflicts of Interest

All the authors declare no conflict of interest.

Ethical Review and Approval

No approval from the Board of Ethics is required.

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