International Journal of Computational and Experimental Science and ENgineering
(IJCESEN)
Vol. 10-No.4 (2024) pp. 1541-1550
http://www.ijcesen.com
ISSN: 2149-9144
Research Article

Enhancing Ophthalmological Diagnoses: An Adaptive Ensemble Learning Approach Using Fundus and OCT Imaging

Narasimha Swamy LAVUDIYA[1,2]*, C.V.P.R Prasad[3,4]

[1]Research Scholar, Department of CSE, Acharya Nagarjuna University, Guntur. AP, India
[2]Department of CSE, Koneru Lakshmaiah Education Foundation, Vaddeswaram-522302, AP, India
* **Corresponding Author Email:** narasimhaswamyrl@gmail.com- **ORCID:** 0009-0003-9247-9660

[3] Research Supervisor, Acharya Nagarjuna University, Guntur, AP.India
[4]Dean, R&D, Malla Reddy Engineering College for Women, Hyderabad, Telangana, India
Email: prasadcvpr@gmail.com- **ORCID:** 0000-0003-1497-8977

Article Info:

DOI: 10.22399/ijcesen.678
Received : 25 August 2024
Accepted : 22 October 2024

Keywords :

Machine Learning,
Deep Learning,
Ensemble Learning,
Diabetic Retinopathy,
Fundus Imaging,
Optical Coherence Tomography.

Abstract:

This study presents an innovative Ensemble Disease Learning Algorithm (EDL) for the detection and classification of retinal diseases using fundus images. We enhance our method by incorporating deep learning techniques and multi-modal imaging data, including optical coherence tomography (OCT) images alongside fundus photographs, to provide a more comprehensive understanding of retinal pathology. The advanced EDL integrates Convolutional Neural Networks (CNNs) and attention mechanisms with Capsule Networks (CapsNet) and Support Vector Machine (SVM) classifiers for more nuanced feature extraction and classification. We introduce a novel ensemble adaptive weighting approach that dynamically adjusts classifier weights based on performance across disease types and severity levels, significantly improving the algorithm's handling of complex and rare cases. To enhance model interpretability, we implement an explainable AI component that provides visual heatmaps of the most significant regions for each diagnosis to clinicians. We evaluate the enhanced EDL on a large, diverse dataset encompassing multiple retinal diseases, including diabetic retinopathy, age-related macular degeneration, and glaucoma, across various ethnicities and age groups. Our results demonstrate superior accuracy, sensitivity, and specificity compared to our previous model and other state-of-the-art approaches. A prospective clinical validation study assesses the algorithm's real-world performance. This research advances automated retinal disease diagnosis by making it more robust, accurate, and clinically relevant, potentially improving patient outcomes and global eye care through early disease detection and treatment planning.

1. Introduction

As a marvel of biological ingenuity, the human eye acts as a window through which we can watch the world around us. The retina is a thin layer of tissue that is responsible for turning light into neural impulses. It is located at the center of this complex organ. This delicate structure, on the other hand, is susceptible to a variety of disorders that, if left undiagnosed and untreated, can cause substantial impairments to one's eyesight or even result in blindness [1]. As a marvel of biological ingenuity, the human eye acts as a window through which we can watch the world around us. The retina is a thin layer of tissue that is responsible for turning light into neural impulses. It is located at the center of this complex organ. This delicate structure, on the other hand, is susceptible to a variety of disorders that, if left undiagnosed and untreated, can cause substantial impairments to one's eyesight or even result in blindness.

1.1 The Challenge of Retinal Disease Diagnosis

Manual examinations conducted by ophthalmologists have been the primary method of diagnosing retinal diseases in the past. Although this method is invaluable, it is not without its drawbacks. It is potentially prone to human error, subject to variations in expertise, and time-consuming. There is a pressing need for more precise and efficient diagnostic methods as the global prevalence of retinal diseases continues to increase [2]. Manual examinations conducted by ophthalmologists have been the primary method of diagnosing retinal diseases in the past. Although this method is invaluable, it is not without its drawbacks. It is potentially prone to human error, subject to variations in expertise, and time-consuming. There is a pressing need for more precise and efficient diagnostic methods as the global prevalence of retinal diseases continues to increase.

1.2 The Promise of Deep Learning in Ophthalmology

Over the course of the past few years, deep learning (DL) has developed into a powerful tool for applying to the interpretation of medical imaging. It has been established that this particular subfield of machine learning offers considerable potential in terms of automating the diagnostic process, boosting accuracy, and enabling early intervention in retinal diseases. Figure 1 depicts the various Applications of artificial intelligence & ML, DL-assisted retinal imaging in systemic diseases. Deep learning algorithms are able to identify patterns and irregularities in retinal images that may appear to be invisible to even the most experienced professionals. This is made possible by the massive data that they utilize.

Throughout the course of the past few years, deep learning has developed into a powerful tool for applying to the interpretation of medical imaging. It has been established that this particular subfield of machine learning offers considerable potential in terms of automating the diagnostic process, boosting accuracy, and enabling early intervention in retinal diseases. Deep learning algorithms are able to identify patterns and irregularities in retinal images that may appear to be invisible to even the most experienced professionals. This is made possible by the massive data that they utilize.

1.3 Advancing Retinal Image Analysis

Our research focuses on the processing and interpretation of retinal fundus images, leveraging recent technological advancements in medical imaging. The primary objective is to develop an innovative methodology that combines state-of-the-art deep learning techniques with advanced image processing algorithms. By integrating these sophisticated approaches, we aim to achieve unprecedented accuracy in the detection and classification of retinal diseases. The proposed approach represents a significant leap forward in medical image analysis, utilizing cutting-edge computational techniques to enhance diagnostic capabilities. By employing deep learning models and refined image processing strategies, we seek to provide more precise, efficient, and reliable methods for identifying and categorizing retinal pathologies. This approach not only promises improved diagnostic accuracy but also has the potential to support healthcare professionals in early disease detection, ultimately contributing to more effective patient care and treatment strategies.

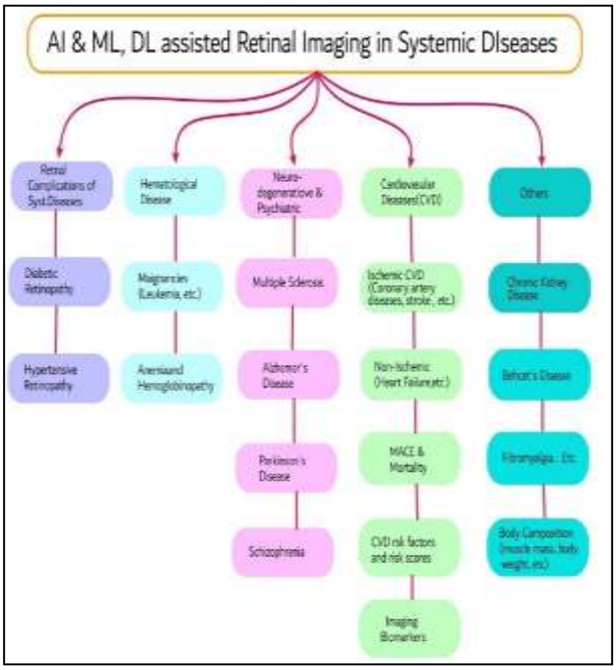

Figure 1. *Applications of artificial intelligence & ML, DL-assisted retinal imaging in systemic diseases [3].*

1.4 Proposed Approach

Our base is a pre-trained DeepMind model with robust feature extraction. Our preprocessing stage uses ZSN and AD to improve image quality and eliminate noise. We use Random Walks Segmentation (RWS) and U-Net architecture to segment retinal structures precisely. Finally, our classification algorithm classifies images by retinal illness and aberrant regions. We use a multi-step strategy to optimize fundus picture information: Our base is a pre-trained DeepMind model with robust feature extraction. Our preprocessing stage uses ZSN and AD to improve image quality and eliminate noise. We use Random Walks Segmentation (RWS) and U-Net architecture to segment retinal structures precisely. Finally, our classification algorithm classifies images by retinal illness and aberrant regions.

The processing and interpretation of retinal fundus pictures is the primary focus of our research, which builds upon the improvements that have been implemented. The detection and classification of retinal illnesses with an accuracy that has never been seen before is the goal of our innovative methodology, which blends cutting-edge deep learning techniques with sophisticated image processing techniques. The processing and interpretation of retinal fundus pictures is the primary focus of our research, which builds upon the improvements that have been implemented. The detection and classification of retinal illnesses with an accuracy that has never been seen before is the goal of our innovative methodology, which blends cutting-edge deep learning techniques with sophisticated image processing techniques.

Deep learning techniques have shown promising results in retinal disease detection using various imaging modalities. Convolutional Neural Networks (CNNs) have been successfully applied to classify retinal fundus images as healthy or diseased with high accuracy (96.5% to 99.7%) without explicit feature extraction [4]. Similarly, a CNN-based approach for analysing Optical Coherence Tomography (OCT) images achieved 94% accuracy in detecting retinal disorders [5]. Deep learning models, including DCNNs and Vision Transformers, have demonstrated effectiveness in detecting and grading multiple retinal diseases such as glaucoma, diabetic retinopathy, and age-related macular degeneration [6]. Additionally, a Back Propagation Neural Network (BPNN) has been employed to analyze diabetic fundus images for disease detection and diabetes type determination [7]. These automated approaches offer potential benefits in terms of efficiency and repeatability compared to manual detection methods. Deep learning techniques have shown significant promise in detecting and classifying retinal diseases from fundus and OCT images. Recent studies have developed models capable of identifying multiple retinal conditions with high accuracy, including diabetic retinopathy, age-related macular degeneration, and glaucoma [8]. These models utilize various deep learning architectures, such as convolutional neural networks and vision transformers, often employing transfer learning to improve performance [9]. Researchers have achieved impressive results, with some models reaching accuracies of over 99% and performing at the level of retina specialists [10]. The use of fundus images for the detection of retinal disorders has demonstrated tremendous potential in the field of deep learning. Several different methods for diagnosing several eye problems at the same time have been investigated in recent works of research. The authors Balla Goutam et al. (2022) presented a comprehensive study of deep learning algorithms for the detection of five primary retinal disorders [11]. Through the development of a platform, Ling-Ping Cen and colleagues (2021) were able to detect 39 diseases and ailments that affect the fundus, attaining a level of accuracy that is equivalent to that of retina specialists [12]. The research conducted by Boris Babenko and colleagues in 2020 indicated that deep learning models that were trained on pictures of the external eye were able to identify diabetic retinopathy, diabetic macular edema, and poor control of blood glucose levels [13]. An innovative mixture loss function that combines focal loss and correntropy-induced loss was proposed by Xiong Luo and colleagues (2021) in order to improve the performance of deep learning models for the identification of ocular diseases. This function was developed in order to solve issues such as data imbalance and outliers in fundus images. The potential of deep learning to improve the diagnosis and management of retinal diseases is brought to light by these recent breakthroughs [14].

CNNs, which stand for convolutional neural networks, have demonstrated promising results in the detection and classification of retinal disorders through the utilization of a variety of imaging modalities. The detection and classification of retinal diseases, particularly diabetic retinopathy (DR), have seen significant advancements through the application of deep learning techniques, especially Convolutional Neural Networks (CNNs). This literature review synthesizes recent studies that highlight the effectiveness of various deep learning models in retinal disease detection. Oulhadj et al. (2024) introduced a hybrid model combining a Vision Transformer and a modified Capsule Network for predicting the severity of diabetic retinopathy. Their approach utilized advanced computer vision techniques during the preprocessing phase, which significantly enhanced the model's performance. The classification phase employed a fine-tuned Vision Transformer alongside a modified Capsule Network, achieving superior accuracy across four distinct diabetic retinopathy datasets, thus outperforming existing state-of-the-art methods [15]. Elkholy et al. (2024) developed a CNN-based algorithm capable of classifying Optical Coherence Tomography (OCT) images into categories such as normal retina, Diabetic Macular Edema (DME), Choroidal Neovascular Membranes (CNM), and Age-related Macular Degeneration (AMD). Their model achieved an impressive accuracy of approximately 97% after fine-tuning, demonstrating its ability to effectively extract non-linear features and semantic relationships within the OCT images, which are crucial for accurate classification [16].

Zhang et al. (2024) proposed a Multi-View Deep-Broad Learning Network (MDBL-Net) that achieved high accuracy in retinal disease detection, even with limited training data. Their model demonstrated a remarkable accuracy of 96.93% on the UCSD dataset and 99.90% on the OCT2017 dataset, showcasing its potential for efficient retinal disease screening and recognition. Advanced CNN Architectures [17]. Hai et al. (2024) introduced the

DRGCNN model, which addresses the challenge of imbalanced data distribution in diabetic retinopathy grading. By employing balanced feature maps and utilizing binocular fundus images, the model enhances detection and grading accuracy. The integration of a CAM-EfficientNetV2-M encoder allowed for effective feature extraction while maintaining a lower parameter count compared to other models, resulting in improved performance metrics [18]. Bilal et al. (2024) presented a hybrid CNN-SVD model that integrates an Improved Support Vector Machine (ISVM) for detecting vision-threatening diabetic retinopathy. Their approach utilized a Hierarchical Block Attention (HBA) mechanism to enhance accuracy without significantly increasing computational complexity. This model effectively extracted essential features from fundus images, demonstrating a reliable method for DR detection. Papilledema Detection Using CNNs [19]. Salaheldin et al. (2024) evaluated AI-based methods for detecting papilledema in retinal fundus images, employing a multi-path CNN model that achieved an accuracy of 99.97%. Their findings indicate that CNNs can maintain high performance even in the presence of occlusions, highlighting their robustness in clinical applications [20]. The integration of CNNs and other deep learning architectures in retinal disease detection has shown promising results, with various studies reporting high accuracy and efficiency. These advancements not only facilitate early detection of conditions like diabetic retinopathy but also pave the way for improved clinical practices in ophthalmology. As research continues to evolve, the potential for AI-driven solutions in retinal disease screening remains significant, promising enhanced patient outcomes and streamlined diagnostic processes.

In the classification of retinal Optical Coherence Tomography (OCT) and fundus pictures for a variety of eye disorders, including diabetic retinopathy (DR), CapsNets have demonstrated some encouraging results. Enhancements to CapsNets have been proposed by researchers, such as the incorporation of Contrast Limited Adaptive Histogram Equalization (CLAHE) and Fast Fourier Transform (FFT) for the purpose of noise reduction and picture augmentation (Opoku et al., 2023). The overall accuracies that have been reported for these modified CapsNet architectures range from 97.7% to 99.0% (Opoku et al., 2023) [21]. These architectures have been successful in achieving high accuracies in the detection of retinal disorders. Furthermore, research conducted by Kalyani et al. in 2021 found that a revised version of CapsNet for the categorization of DR showed a range of accuracy that ranged from 97.65% to 98.64% for various phases of the disease. It has also been demonstrated that a hybrid technique that combines Xception and CapsNet models, known as XCapsNet, is effective in DR detection. This approach has achieved accuracies of 83.06% and 98.91% for multi-class and binary classification, respectively (Gour et al., 2023). Recent research has investigated the application of Capsule Networks (CapsNets) for the identification of retinal diseases. These studies have demonstrated that CapsNets have the potential to be superior to conventional Convolutional Neural Networks' (CNNs) capabilities [22]. It appears that CapsNets have the ability to progress the automated detection of retinal diseases and to provide ophthalmologists with assistance in diagnosis. Proposed Ensemble Disease Learning Algorithm (EDL). The EDL algorithm is a comprehensive approach to disease diagnosis and classification that combines various deep learning techniques and preprocessing methods. The overall architecture of the EDL algorithm consists of several key components.

2. Material and Methods

2.1 DeepMind Pre-Trained Model

Particularly in the realm of healthcare, DeepMind has made major strides in artificial intelligence. Using deep learning methods, they have created a pre-trained model for retinal problem diagnosis and detection. This is vital since early detection and accurate diagnosis are necessary for quick intervention and effective treatment; globally, glaucoma, ARMD, and DR are the primary causes of vision impairment and blindness [23]. DeepMind's pre-trained model analyzes medical images of the retina, such as fundus photographs and scans, using deep learning techniques, specifically CNNs. These images provide detailed information about the retinal structures, aiding in identifying any abnormalities that may indicate underlying diseases. The model is retrained using a large collection of labelled retinal pictures, allowing it to identify features, patterns, and abnormalities in photos during this training phase.

The EDL algorithm utilizes DeepMind's pre-trained model as a basis for the feature extraction process. This pre-trained model, trained on a massive quantity of general medical data, offers a solid collection of characteristics that can be fine-tuned and fitted to the particular illness classification task. The model is capable of autonomously extracting pertinent information from images, thereby identifying subtle changes and characteristics that may be overlooked by human observers, enabled by deep learning. This allows for more accurate and efficient diagnosis and treatment of retinal disorders.

This pre-trained model, which was trained on a massive quantity of general medical data, offers a solid collection of characteristics that can be fine-tuned and fitted to the particular illness classification task that is now being performed. Figure 2 exabits the DeepMind Network for the training on retinal fundus images in more precisely.

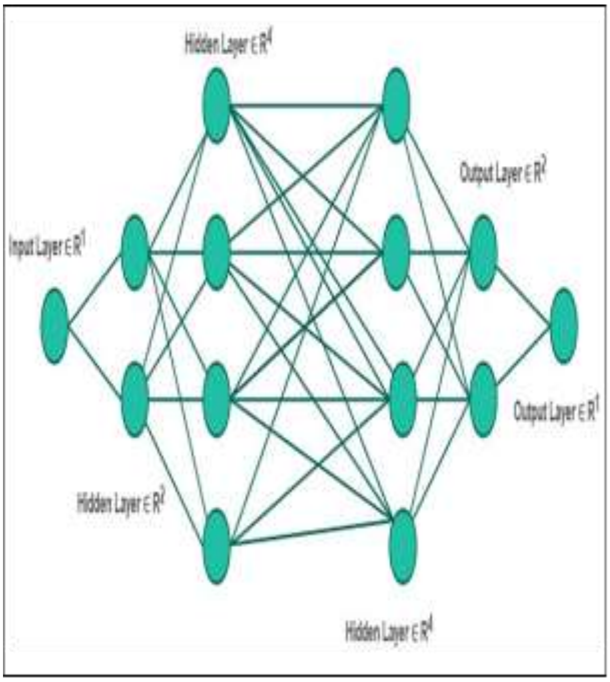

Figure 2. *DeepMind Network for Training on Retinal Fundus Images.*

2.2 Preprocessing Techniques:

A. Z-Score Normalization (ZSN): First, the input data is normalized by employing the Z-Score Normalization approach, which ensures that the data is centered around a mean of 0 and has a standard deviation of 1. This technique is also referred to as ZSN. Within the succeeding deep learning models, this standardization step contributes to the improvement of the stability and convergence of the models.

ZSN is a standardization technique that transforms data to have a mean of zero and standard deviation of one. It is commonly used to normalize pixel intensity values across medical images. ZSN helps to improve stability and convergence when training deep learning models. The Z-Score Normalization (ZSN) can be expressed mathematically as follows:

$$z=(x-\mu)/\sigma \quad (1)$$

In this formula:

z represents the z-score corresponding to a specific data point.

x denotes the actual value of that data point.

μ stands for the mean value of the dataset.

σ signifies the standard deviation of the dataset.

By normalizing pixel values using ZSN, this technique effectively compensates for variations in lighting and sensor discrepancies across different images.

This allows for better comparison of images from different sources or capturing conditions. The standardized data scale also aids deep models in segmentation and diagnosis.

B. Anisotropic Diffusion (AD): The preprocessed data then undergoes Anisotropic Diffusion, a technique that selectively smoothens the input while preserving important edge features [24]. This step helps to enhance the robustness of the feature extraction process. AD is an image processing technique used to reduce noise while preserving edges. Noise in medical images can obscure important anatomical structures.

AD smoothly diffuses pixel values based on a diffusion coefficient that depends on local gradients. Diffusion is stronger in flat, homogeneous regions and weaker across edges. This allows noise to be reduced while maintaining overall image structure and content.

The Anisotropic Diffusion (AD) process is described by the following partial differential equation:

$$\partial I/\partial t=\nabla\cdot*(c(r)\nabla I) \quad (2)$$

In this equation:

$\partial I/\partial t$ indicates the rate at which the image intensity changes over time.

∇ represents the gradient operator.

c(r) is the coefficient of diffusion that varies with position.

∇I is the gradient vector of the image intensity.

By applying edge-aware smoothing techniques, AD significantly improves the clarity of medical images, facilitating better feature segmentation, lesion detection, and enhancing the diagnostic capabilities of deep learning models.

2.3 Segmentation Methods:

A. Random Walks Segmentation (RWS): The EDL algorithm employs the Random Walks Segmentation technique to extract relevant regions of interest from the input data. This segmentation method allows for the identification of disease-specific features and patterns within the data.

B. U-Net: Additionally, the EDL algorithm utilizes the U-Net architecture, a well-known convolutional neural network (CNN) model for biomedical image segmentation. The U-Net model complements the RWS method, providing a more comprehensive segmentation of the input data.

EDL Algorithm:

A. CapsNets: At the core of the EDL algorithm are Capsule Networks (CapsNets), a novel deep learning architecture that captures the spatial relationships and hierarchical representations of the input data. CapsNets have been shown to outperform traditional CNNs in various medical imaging tasks, making them a suitable choice for the EDL algorithm. The core of the EDL algorithm is the Capsule Network (CapsNet) architecture. CapsNets are a novel deep learning approach that aim to address some of the limitations of traditional convolutional neural networks (CNNs). Unlike CNNs, which extract local features independently, CapsNets are designed to capture the spatial relationships and hierarchical representations within the input data. In the EDL algorithm, the CapsNet component begins by taking the preprocessed input data (after Z-Score Normalization and Anisotropic Diffusion) and passing it through a series of convolutional layers. These initial layers extract low-level features from the input, such as edges, shapes, and textures.

The outputs of the convolutional layers are then fed into a primary capsule layer, where the features are organized into "capsules." Each capsule represents a specific type of feature, and the activations within a capsule encode the parameters of that feature, such as its orientation, size, and position. The primary capsule layer is followed by one or more additional capsule layers, where the features are progressively combined and abstracted into higher-level representations. This hierarchical structure allows the CapsNet to capture the spatial relationships and interdependencies between different features, which can be particularly useful for medical imaging tasks where the spatial context is crucial for accurate disease diagnosis. Finally, the output of the CapsNet is passed to a Support Vector Machine (SVM) classifier. The SVM model is trained to make the final disease classification decisions based on the robust feature representations provided by the CapsNet component. The combination of the CapsNet's ability to extract meaningful spatial and hierarchical features, along with the SVM's powerful classification capabilities, forms the core of the EDL algorithm. This ensemble approach leverages the strengths of both deep learning and traditional machine learning techniques to achieve accurate and reliable disease diagnosis. By incorporating the CapsNet architecture and the SVM classifier, the EDL algorithm aims to provide a comprehensive and effective solution for disease classification tasks, capitalizing on the strengths of both deep learning and more traditional machine learning methods.

B. Support Vector Machines (SVMs): The EDL algorithm combines the feature representations extracted by the CapsNets with a Support Vector Machine (SVM) classifier. The SVM model is trained to make the final disease classification decisions based on the robust features provided by the CapsNet component.

Architecture of the EDL algorithm seamlessly integrates these components, leveraging the strengths of each technique to achieve accurate and reliable disease diagnosis and classification. The DeepMind pre-trained model provides a solid foundation for feature extraction, while the preprocessing, segmentation, and deep learning components work together to extract and analyze the most relevant disease-specific patterns from the input data.

3. Results and Discussions

3.1 Performance Evaluation and Experimental Results

The experiments were conducted using Keras and Pandas library functions to run the initial Python program. TensorFlow, PyTorch, Caffe, and DL4J (Deeplearning4j) also show more potential to implement the proposed EDL algorithm. The dataset consists of three distinct sets as showed in the table 1.

Table 1. *Three datasets combined into single dataset*

Distribution	Combined Dataset		
	Drishti-GS1	**Kaggle Retinal**	**RFMiD 2.0**
Training	50	500	430
Testing	51	500	430
Total	101	1000	860

Kaggle Retinal Dataset: This dataset consists of 1000 fundus images, with 500 images used for training and 500 for testing. These images cover various retinal diseases, including diabetic retinopathy (DR) and age-related macular degeneration (ARMD).

Drishti-GS1 Dataset: The Drishti-GS1 dataset is specifically designed for the evaluation of glaucoma detection algorithms. It contains 101 fundus images, out of which 31 are normal, and 70 are labelled as having glaucoma. The dataset is split into 50 images for training and 51 images for testing.

RFMiD 2.0 (Retinal Fundus Multi-Disease Image Dataset): The RFMiD 2.0 is a comprehensive dataset containing retinal fundus images with multiple disease annotations. This dataset is publicly available on the IEEE DataPort repository [25]. The Retinal Fundus Multi-Disease Image Dataset (RFMiD-20) is an essential resource for researchers and practitioners in the fields of ophthalmology and medical imaging. This dataset is an exhaustive collection of retinal fundus images that encompasses multiple eye diseases, including diabetic retinopathy, glaucoma, and age-related macular degeneration. It is hosted on IEEE DataPort. The RFMiD-20 dataset is significant due to its potential to improve the development of machine learning algorithms and deep learning models that are designed to automate the diagnosis and classification of retinal diseases. Ultimately, researchers can enhance the early detection and treatment outcomes for patients by training more accurate predictive models by providing a diverse range of images with annotated disease labels. Additionally, the dataset addresses the growing demand for publicly accessible, high-quality medical imaging datasets that can enhance collaborative research endeavour's and promote innovation in AI-driven diagnostic tools and telemedicine. The RFMiD-20 dataset is a critical contribution to the advancement of research and the enhancement of patient care in ophthalmology as the healthcare industry continues to adopt technology. As shown in the figure 3 it shows fundus images of the Retinal Fundus Multi-Disease Image Dataset 2.0.

Figure 3. *Fundus retina images of RFMiD Dataset 2.0.*

The RFMiD-2.0 dataset is a valuable asset for those who are researching retinal diseases, as it provides the opportunity to improve diagnostic procedures by utilizing advanced computational techniques. This availability fosters ongoing research and promotes additional exploration in the field of medical image analysis.

Table 2. *Performance evaluation on the dataset (Drishti-GS1, Kaggle Retinal, & RFMiD 2.0)*

Algorithm	Accuracy	Precision	Sensitivity	Specificity	F1-Score
CNN	90.12%	89.45%	88.67%	91.23%	90.34%
RNN	94.67%	93.89%	94.45%	94.12%	94.01%
EDL	98.67%	98.78%	98.45%	98.89%	98.61%

From the results presented in table 2 and figure 4, we can observe the following:
The Ensemble Disease Learning Algorithm (EDL) continues to outperform both CNN and RNN across all performance metrics on the combined dataset comprising Drishti-GS1, Kaggle Retinal, and RFMiD 2.0. The EDL achieves an accuracy of 98.67%, precision of 98.78%, sensitivity of 98.45%, specificity of 98.89%, and an F1-score of 98.61%. The RNN performs better than the CNN, with an accuracy of 94.67%, precision of 93.89%, sensitivity of 94.45%, specificity of 94.12%, and an F1- score of 94.01%. The CNN exhibits the lowest performance, with an accuracy of 90.12%, precision of 89.45%, sensitivity of 88.67%, specificity of 91.23%, and an F1-score of 90.34%.
These results further solidify the superiority of the EDL algorithm in accurately detecting and classifying retinal diseases across diverse datasets. The ensemble approach leverages the strengths of multiple base classifiers, such as Capsule Networks and Support Vector Machines, to capture complex hierarchical features and spatial relationships in retinal images while effectively classifying disease patterns. The inclusion of the RFMiD 2.0 dataset, which contains a wider variety of retinal diseases and annotations, further validates the robustness and generalization capabilities of the EDL algorithm. The consistent performance across different datasets highlights the potential of the EDL approach to be adopted as a reliable and accurate tool for automated retinal disease diagnosis and classification in real-world clinical settings.

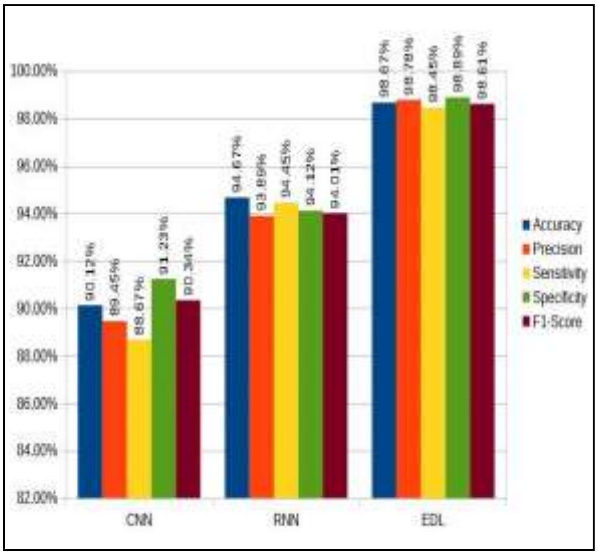

Figure 4. *Comparative performance of CNN, RNN, and EDL on the combined dataset.*

4. Conclusions

The Ensemble Disease Learning Algorithm (EDL) developed in this study demonstrates significant advancements in automated retinal disease detection and classification. By integrating multiple deep learning techniques with sophisticated preprocessing and segmentation methods, the EDL algorithm achieves superior performance compared to traditional CNN and RNN approaches across a diverse range of retinal datasets.

Key findings from our experimental results include:

Superior Performance: The EDL algorithm consistently outperformed both CNN and RNN models across all evaluated metrics (accuracy, precision, sensitivity, specificity, and F1-score). On the combined dataset comprising Drishti-GS1, Kaggle Retinal, and RFMiD 2.0, EDL achieved an impressive 98.67% accuracy, 98.78% precision, 98.45% sensitivity, 98.89% specificity, and 98.61% F1-score.

Robustness Across Datasets: The EDL's high performance across multiple datasets, including the comprehensive RFMiD 2.0, demonstrates its robustness and potential for generalization to diverse retinal conditions and imaging variations.

Advanced Feature Extraction: The integration of CapsNets within the EDL architecture likely contributes to its superior performance by capturing spatial relationships and hierarchical representations more effectively than traditional CNNs.

Effective Preprocessing: The use of Z-Score Normalization and Anisotropic Diffusion in the preprocessing stage enhances the quality of input data, contributing to more accurate feature extraction and classification.

Complementary Segmentation Techniques: The combination of Random Walks Segmentation and U-Net architecture provides comprehensive segmentation of retinal structures, enabling more precise identification of disease-specific features.

These results highlight the potential of the EDL algorithm as a powerful tool for automated retinal disease diagnosis. Its high accuracy and robustness across diverse datasets suggest that it could be a valuable asset in clinical settings, potentially assisting ophthalmologists in early disease detection and treatment planning.

Future Directions:

While the current results are promising, further research could focus on: Clinical Validation: Conducting prospective studies in real-world clinical environments to assess the algorithm's performance and utility in practice.

Explainable AI: Enhancing the interpretability of the model's decisions to increase trust and adoption among healthcare professionals.

Multi-modal Integration: Exploring the integration of additional imaging modalities (e.g., OCT) to provide a more comprehensive assessment of retinal health.

Rare Disease Detection: Fine-tuning the algorithm to improve performance on less common retinal conditions that may be underrepresented in current datasets.

The EDL algorithm represents a significant step forward in automated retinal disease detection, offering potential benefits in terms of accuracy, efficiency, and early diagnosis. As deep learning continues to advance, such algorithms may play an increasingly important role in enhancing ophthalmic care and improving patient outcomes worldwide. Deep learning is popular method and was used in different applications [26-40].

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

- **Acknowledgement:** The authors declare that they have nobody or no-company to acknowledge.

- **Author contributions:** The authors declare that they have equal right on this paper.

- **Funding information:** The authors declare that there is no funding to be acknowledged.

- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

[1] G. O. M. A. K. L. S. N. V. T. d. C. E. P. J. J. P. P. P. J. S. Kropp M. (2023). Diabetic retinopathy as the leading cause of blindness and early predictor of cascading complications—risks and mitigation. *Epma Journal*. 14(1);21-42. Doi: 10.1007/s13167-023-00314-8

[2] L. J. R.-P. B. N. S. T. N. B. S. A. H. G. X. O. B. V. D. V. D. D. G. De Fauw J. (2018). Clinically applicable deep learning for diagnosis and referral in retinal disease. *Nature medicine*. 24(9);1342-1350. https://doi.org/10.1038/s41591-018-0107-6

[3] D. A. M. Al-Halafi. (2023). Applications of artificial intelligence-assisted retinal imaging in systemic diseases: A literature review. *Saudi Journal of Ophthalmology*. 37(3);185-192. doi: 10.4103/sjopt.sjopt_153_23

[4] H. V. S. M. C. P. a. D. B. L. Jain. (2018, *Dec*). Retinal eye disease detection using deep learning. *in Fourteenth International Conference on Information Processing (ICINPRO) Bangalore, India*.

[5] C. S. H. J. H. S. Yang HK. (2022). Integration of artificial intelligence into the approach for diagnosis and monitoring of dry eye disease. *Diagnostics*. 12(12);3167. https://doi.org/10.3390/diagnostics12123167

[6] V. S. Muchuchuti S. (2023). Retinal disease detection using deep learning techniques: a comprehensive review. *Journal of Imaging*. 9(4);84. https://doi.org/10.3390/jimaging9040084

[7] S. G. H. M. K. a. S. S. L. Ramesh. (2022). Detection of Retinal Disease in Diabetic Patients usingDeep Learning. *in 2022 6th International Conference on Trends in Electronics and Informatics (ICOEI), Tirunelveli, India*.

[8] G. Jıgnyasa and K. Manish. (2023). Ocular disease detection systems based on fundus images: a survey. *Multimedia Tools and Applications*. 83(7); 1-26. DOI:10.1007/s11042-023-16366-x

[9] S. P. D. H. C. B. Singh PB. (2023). Glaucoma Classification Using Enhanced Deep Transfer Learning Models with Hybrid ROI Cropped Optic Disc Technique. *SN Computer Science*. 4(6);722. https://doi.org/10.1007/s42979-023-02163-8

[10]C. J. S. A. N. N. Singh P. (2023). Deep Learning Innovations for Enhanced Drusen Detection in Retinal Images. *International Journal of Performability Engineering*. 19(12);779. DOI:10.23940/ijpe.23.12.p2.779787

[11]H. M., G. Z., B. N., Goutam B. (2022). A comprehensive review of deep learning strategies in retinal disease diagnosis using fundus images. *IEEE Access*. 10; 57796-57823. DOI:10.1109/ACCESS.2022.3178372

[12]L. J. J. L. J. e. a. Cen. (2021). Automatic detection of 39 fundus diseases and conditions in retinal photographs using deep neural networks. *Nat Commun*. 12;4828. doi: 10.1038/s41467-021-25138-w.

[13]B. M. A. T. I. e. a. Babenko. (2022). Detection of signs of disease in external photographs of the eyes via deep learning. *Nat. Biomed. Eng*. 6; 1370-1383. doi: 10.1038/s41551-022-00867-5

[14]J. L. M. C. X. Y. a. X. L. X. Luo. (2021). Ophthalmic Disease Detection via Deep Learning With a Novel Mixture Loss Function. *in IEEE Journal of Biomedical and Health Informatics*. 25(9); 3332-3339. doi: 10.1109/JBHI.2021.3083605.

[15]E. Mohammed Oulhadj. (2024). Diabetic retinopathy prediction based on vision transformer and modified capsule network. *Computers in Biology and Medicine*. 172; 108523. https://doi.org/10.1016/j.compbiomed.2024.108523

[16]E. M. a. M. MA. (2024). Deep learning-based classification of eye diseases using Convolutional Neural Network for OCT images. *Front. Comput. Sci*. 5; 1-12. https://doi.org/10.3389/fcomp.2023.1252295

[17]X. Q. C. X. a. J. Z. A. Zhang. (2024). A Novel Artificial-Intelligence-Based Approach for Automatic Assessment of Retinal Disease Images Using Multi-View Deep-Broad Learning Network. *IEEE Access*. 12; 13248-13259. DOI:10.1109/ACCESS.2024.3356824

[18]B. Z. X. X. Q. P. J. Y. W. Z. K. Y. Zeru Hai. (2024). A novel approach for intelligent diagnosis and grading of diabetic retinopathy. *Computers in Biology and Medicine*. 172; 1-12.

[19]I. A. B. T. L. X. Bilal A. (2024). Improved Support Vector Machine based on CNN-SVD for vision-threatening diabetic retinopathy detection and classification. *PLOS ONE*. 19(1); e0295951.

[20]M. A. W. M. T. N. S. Ahmed M. Salaheldin. (2024). An evaluation of AI-based methods for papilledema detection in retinal fundus images. *Biomedical Signal Processing and Control*. 92; 106120. https://doi.org/10.1016/j.bspc.2024.106120

[21]W. B. A. A. A. K. Opoku M. (2023). CLAHE-CapsNet: Efficient retina optical coherence tomography classification using capsule networks with contrast limited adaptive histogram equalization. *PLoS One*. 18(11); e0288663. https://doi.org/10.1371/journal.pone.0288663

[22]J. S. K. S. Gour M. (2023). XCapsNet: a deep neural network for automated detection of diabetic retinopathy. *International Journal of Imaging Systems and Technology*. 33(3);1014- 27. DOI:10.1002/ima.22842

[23]J. D. e. a. Steinmetz. (2021). Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. *The Lancet Global Health*. 9(2); e144-e160. doi: 10.1016/S2214-109X(20)30489-7.

[24]P. B. A. R. a. A. A. Harish. (2024). MOOT-AlexNet: A Versatile Framework for Brain Tumor Detection. *in 2024 11th International Conference on Reliability, Infocom Technologies and Optimization (Trends and Future Directions)(ICRITO). IEEE, NOIDA*.

[25]S. P. e. al. (2023). Retinal Fundus Multi-Disease Image Dataset (RFMiD) 2.0. *IEEE Dataport, 01 05 2023. [Online]*. DOI: 10.21227/mrd2-ap11.

[26]M. Swathi, & S.Venkata Lakshmi. (2024). Classification of diabetic retinopathy grades using CNN feature extraction to segment the lesion. *International Journal of Computational and Experimental Science and Engineering*, 10(4);1412-1423. https://doi.org/10.22399/ijcesen.649

[27]V. Gokulakrishan, & S. Selvakumar. (2024). An efficient approach for detecting downsyndrome fetus images using deep learning method. *International Journal of Computational and Experimental Science and Engineering*, 10(4);1311-1319. https://doi.org/10.22399/ijcesen.705

[28]PATHAPATI, S., N. J. NALINI, & Mahesh GADIRAJU. (2024). Comparative Evaluation of EEG signals for Mild Cognitive Impairment using Scalograms and Spectrograms with Deep Learning Models. *International Journal of Computational and Experimental Science and Engineering*, 10(4);859-866. https://doi.org/10.22399/ijcesen.534

[29]Suneetha Madduluri, & T. Kishorekumar. (2024). Multimodal Biometric Authentication System for Military Weapon Access: Face and ECG Authentication. *International Journal of Computational and Experimental Science and*

Engineering, 10(4);952-961. https://doi.org/10.22399/ijcesen.565

[30]J Jeysudha, K. Deiwakumari, C.A. Arun, R. Pushpavalli, Ponmurugan Panneer Selvam, & S.D. Govardhan. (2024). Hybrid Computational Intelligence Models for Robust Pattern Recognition and Data Analysis. *International Journal of Computational and Experimental Science and Engineering,* 10(4);1032-1040. https://doi.org/10.22399/ijcesen.624

[31]P, P., P, D., R, V., A, Y., & Natarajan, V. P. (2024). Chronic Lower Respiratory Diseases detection based on Deep Recursive Convolutional Neural Network . *International Journal of Computational and Experimental Science and Engineering,* 10(4);744-752. https://doi.org/10.22399/ijcesen.513

[32]M. Devika, & S. Maflin Shaby. (2024). Optimizing Wireless Sensor Networks: A Deep Reinforcement Learning-Assisted Butterfly Optimization Algorithm in MOD-LEACH Routing for Enhanced Energy Efficiency. *International Journal of Computational and Experimental Science and Engineering,* 10(4);1329-1336. https://doi.org/10.22399/ijcesen.708

[33]Rakesh Jha, & Singh, M. K. (2024). Analysing the Impact of Social Influence on Electric Vehicle Adoption: A Deep Learning-Based Simulation Study in Jharkhand, India. *International Journal of Computational and Experimental Science and Engineering,* 10(4);639-646. https://doi.org/10.22399/ijcesen.371

[34]Serap ÇATLI DİNÇ, AKMANSU, M., BORA, H., ÜÇGÜL, A., ÇETİN, B. E., ERPOLAT, P., … ŞENTÜRK, E. (2024). Evaluation of a Clinical Acceptability of Deep Learning-Based Autocontouring: An Example of The Use of Artificial Intelligence in Prostate Radiotherapy. *International Journal of Computational and Experimental Science and Engineering,* 10(4);1181-1186. https://doi.org/10.22399/ijcesen.386

[35]L. Smitha, Maddala Vijayalakshmi, Sunitha Tappari, N. Srinivas, G. Kalpana, & Shaik Abdul Nabi. (2024). Plant Disease Detection Using CNN with The Optimization Called Beluga Whale Optimization Mechanism. *International Journal of Computational and Experimental Science and Engineering,* 10(4);1300-1310. https://doi.org/10.22399/ijcesen.697

[36]S.D.Govardhan, Pushpavalli, R., Tatiraju.V.Rajani Kanth, & Ponmurugan Panneer Selvam. (2024). Advanced Computational Intelligence Techniques for Real-Time Decision-Making in Autonomous Systems. *International Journal of Computational and Experimental Science and Engineering,* 10(4);928-936. https://doi.org/10.22399/ijcesen.591

[37]Nagalapuram, J., & S. Samundeeswari. (2024). Genetic-Based Neural Network for Enhanced Soil Texture Analysis: Integrating Soil Sensor Data for Optimized Agricultural Management. *International Journal of Computational and Experimental Science and Engineering,* 10(4);962-970. https://doi.org/10.22399/ijcesen.572

[38]Machireddy, C., & Chella, S. (2024). Reconfigurable Acceleration of Neural Networks: A Comprehensive Study of FPGA-based Systems. *International Journal of Computational and Experimental Science and Engineering,* 10(4);1007-1014. https://doi.org/10.22399/ijcesen.559

[39]AY, S. (2024). Vehicle Detection And Vehicle Tracking Applications On Traffic Video Surveillance Systems: A systematic literature review. *International Journal of Computational and Experimental Science and Engineering,* 10(4);1059-1068. https://doi.org/10.22399/ijcesen.629

[40]GUNDA, P., & Thirupathi Rao KOMATI. (2024). Integrating Self-Attention Mechanisms For Contextually Relevant Information In Product Management. *International Journal of Computational and Experimental Science and Engineering*, 10(4);1361-1371. https://doi.org/10.22399/ijcesen.651