Deep Learning for Diabetic Retinopathy In Fundus Images

Keyvan Rahimi, Rituraj Rituraj and Diana Ecker

November 16, 2022

Deep Learning For Diabetic Retinopathy In Fundus Images

Keyvan Rahimi
Computer Engineering, Faculty of Art and Engineering, Islamic Azad University, Science and Research Branch, Tehran, Iran
k1r.rahimi@gmail.com

Rituraj Rituraj
Doctoral School of Applied Informatics and Applied Mathematics, Obuda University, Budapest, Hungary
rituraj88@stud.uni-obuda.hu

Diana Ecker
Independent Researcher
Budapest, Hungary
Ecker.k.m.diana@gmail.com

***Abstract*— Clinically, using fundus pictures for predicting and detecting blind illnesses such as diabetic retinopathy (DR) is crucial. Deep learning (DL) is becoming a more common and promising technique in the different applications of DR, such as prediction, detection, classification, and disease diagnosis. Developing a review paper to analyze the DL techniques and their performance in the field is essential. We prepared a standard systematic review database including 341 publications. Accordingly, the main aim of the present review work is to present a systematic state-of-the-art by relying on PRISMA guidelines for the performance analysis of the DL in DR applications. The study has been shown in three main steps. The first step is to collect the database, the second step is to analyze the databases, and the last step is to conclude the study's main findings. According to the results, most studies employed accuracy as the most reliable and general evaluation metric for analyzing the DL techniques in different DR applications. Also, CNN has the most share of applications compared to other DL techniques. On the other hand, the best performance is related to the ensemble and advanced DL techniques. We'll also publish and regularly update the most recent discoveries in future studies to stay up with the quick technological improvements.**

Keywords*— Diabetic Retinopathy, Deep Learning, Systematic Review, PRISMA, Machine Learning

I. Introduction

A chronic disease called diabetic retinopathy (DR) can impair eyesight if it is not caught in time [1, 2]. The challenge of routinely diagnosing and identifying DRs is difficult and may need many exams. Most individuals worldwide are affected by diabetic retinopathy (DR), a concern for diabetes patients and one of the main causes of blindness [3]. The prevention or postponement of visual loss may be possible with early detection of DR [4]. These conditions can be efficiently detected with early examination of retinal fundus pictures, which includes optic disc and optic cup identification and segmentation of the retinal blood vessels [5]. The current techniques vary in performance and efficacy, cannot distinguish between distinct parts of the fundus picture, and are easily influenced by diseased areas [6, 7].

Expert manual visual inspection, which involved meticulously studying high-resolution color fundus photographs, was formerly the only method to diagnose these disorders. This method was expensive, time-consuming, and labor-intensive [8]. Recently, the use of Artificial intelligence (AI) based techniques has been significantly raised for different applications in different fields of the area [9-11]. Deep learning (DL), a subset of AI networks, has demonstrated excellent promise for illness prediction [12]. The literature review analysis reveals that DL methods can successfully assist in DR detection utilizing retinal pictures [13].

DL is a form of machine learning and AI that mimics how people study specific subjects. In data science, which also encompasses statistics and predictive modeling, DL plays a significant role [14-16]. Review studies in a specialist field can assist in evaluating a particular policy's benefits and drawbacks and offer further recommendations [17, 18]. Accordingly, we developed a short review paper for comparing the performance of the DL techniques applied for diabetic retinopathy in fundus images. We also explored similar conducted review works for detecting five primary eye diseases—diabetic retinopathy, glaucoma, age-related macular degeneration, cataract, and retinopathy of prematurity. Goutam et al. (2022) gives a thorough analysis of the various deep learning techniques used recently. This article is structured along the lines of the deep learning implementation process pipeline. Common datasets, evaluation metrics, image pre-processing methods, and deep learning backbone models are first illustrated, and then a thorough analysis of various approaches for each of the five retinal diseases mentioned is provided [19]. Jeong et al. (2022) presented a state-of-the-art piece using a color fundus image from one of the imaging modalities utilized in ophthalmology. Investigations focus on automated screening and diagnosis approaches using DL for glaucoma, age-related macular degeneration, and DR [20]. Shekar et al. (2021) presented a review paper intending to examine numerous pieces of existing literature that present various techniques for recognizing DR using DL and machine learning (ML) techniques, as well as to address the challenges associated with the various datasets that DR uses [21]. There are different review studies for considering DL in DR applications. But, a systematic review study for analyzing the performance of the DL techniques for DR is lost from the literature. Accordingly, the main aim of the present review work is to present a systematic state-of-the-art by relying on PRISMA guidelines for the performance analysis of the DL in DR applications. The study has been shown in three main steps. The first step is to collect the database, the second step is to analyze the databases, and the last step is to conclude the study's main findings.

II. Methodology

Data collection has been conducted using standard PRISMA guidelines [22]. The first phase of the PRISMA guidelines, the identification phase, identifies the needed records and prepares the database (Figure I, Phase I). In this phase, 489 records (about 95% of total records) were selected from the Thomson Reuters Web-of-Science (WoS), and Elsevier Scopus, whereas the rest which is 22 records (about 5% of total records) were selected from the other databases. The searching queries were {"diabetic retinopathy (DR)", "fundus image", "Gradient Descent (GD)", "Autoencoder", "Boltzmann Machines", "machine learning (ML)", "Self-

Organizing Map (SOM)", "Generative Adversarial Network (GAN)", "deep learning (DL)", "Convolutional neural network (CNN)", "LSTM", "Recurrent neural network (RNN)" and "Deep reinforcement learning (DRL)". Records in the second phase, the screening phase (Figure I, Phase II), were evaluated in terms of duplication and the chosen relevant cases. During duplication, around 10% of total records (53 records) were eliminated. Meanwhile, 48 records (about 9% of the total) were determined as redundant and deleted by analyzing the title and their abstracts. Hence 410 records (about 80% of total records) were selected to be studied through Phase III, the eligibility phase (See Figure I, Phase III). In the third phase, the authors studied the full text of the selected records, and the most relevant cases were chosen during monitoring eligibility. However, there were some limitations to have access to the full text of the records. Hence, almost 341 records (about 66% of total records) were chosen for the next evaluations. Despite what has been mentioned, there are still some conference articles in which their full text was not available so it would be inevitable not being eliminated. It is the exact moment to generate the main database to do qualitative and numerical analysis.

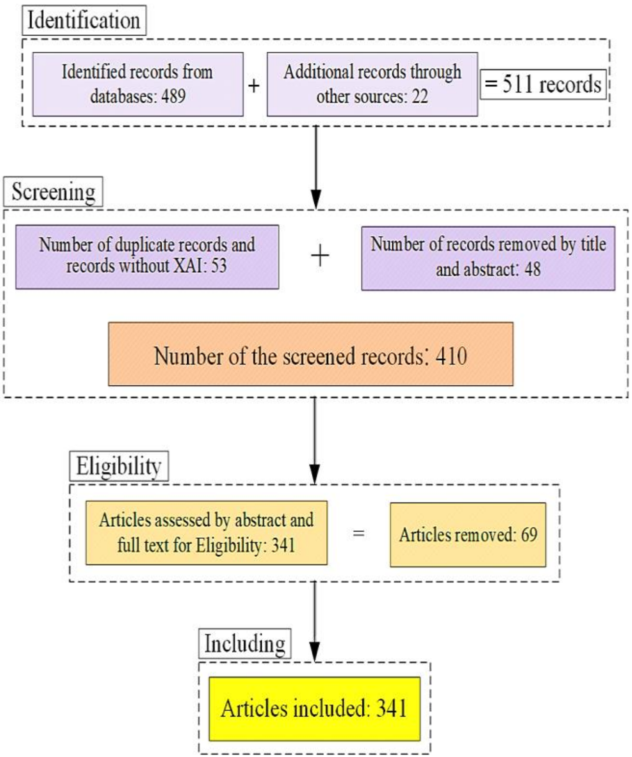

FIGURE I. PRISMA GUIDELINES

By analyzing the prepared database from the output of the PRISMA guideline, the published case trend has been presented in Figure II. As is clear, the trend of the published articles on the subject is rising significantly. This demonstrates that we are facing an attractive and popular topic. Figure III presents the type of published cases. According to Figure III, conference papers followed by articles have the highest share of the published cases (about 90%).

Figure IV presents the share of the frequently used keywords in the field, which has been extracted from the output of the systematic review section. According to Figure IV, computer science (about 62%) followed by Engineering and medicine are the three most frequently used keywords compared to others in the field.

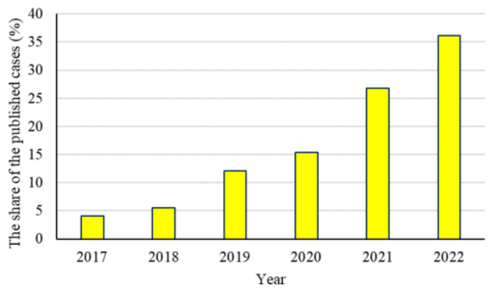

FIGURE II. THE TREND OF THE PUBLISHED CASES

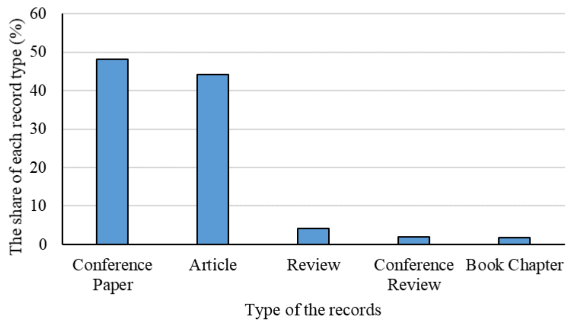

FIGURE III. THE SHARE OF THE DIFFERENT TYPES OF THE PUBLISHED CASES

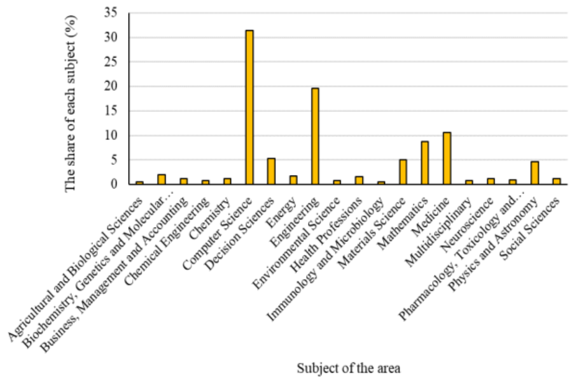

FIGURE IV. THE SHARE OF EACH FREQUENTLY USED KEYWORDS

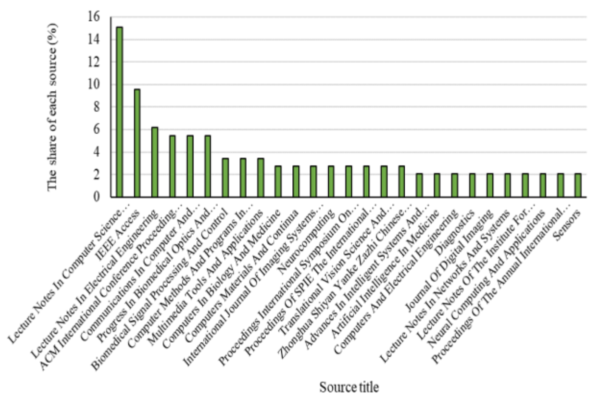

FIGURE V. THE SHARE OF EACH SOURCES

Figure V presents the share of the sources published the most cases in the field of the study. Accordingly, Lecture notes in computer science followed by IEEE and Lecture notes in electrical engineering have owned the most share of the publications (about 30%). Table 1 presents the notable technical studies conducted for DL in DR applications in 2022. Table 1 has six columns for references, year of publication, description, method type, dataset description and application type.

TABLE I. NOTABLE DL TECHNIQUES FOR DIABETIC RETINOPATHY IN FUNDUS IMAGES IN 2022

References	**Year**	**Description**	**Method**	**Dataset**	**Application**
[23]	2022	To analyze diabetic and hypertensive retinopathy	CNN	Digital retinal images for vessel extraction,	Detection
[24]	2022	Early detection of diabetic retinopathy	CNN	APTOS 2019 dataset	Detection
[25]	2022	To detect several retinal pathologies	CNN-LSTM	DIARETDB0, DIARETDB1, CHASE-DB1, IDRiD and STARE	Detection
[26]	2022	To segment and classify the segment the retinal vessels	CNN-U-nets	the public DRIVE and HRF datasets	Classification
[27]	2022	To classify the Diabetic Retinopathy	CNN	Clinical dataset	Classification
[28]	2022	To diagnosis the lesions bears for the detection of diabetic retinopathy	RNN	Clinical dataset	Detection
[29]	2022	To develop a red lesion detection algorithm	RNN	ROC challenge, e-ophtha, DiaretDB1, and Messidor	Detection
[30]	2022	To detect and classify the diabetic retinopathy	LSTM-RFO	MESSIDOR, STARE, and DRIVE datasets	Detection/classification
[13]	2022	To identify the diabetic retinopathy	stochastic gradient descent	Clinical dataset	Identification
[31]	2022	To identify the diabetic retinopathy in the presence of the Fundus Images	CNN-LSTM	Kaggle retina image	Identification
[3]	2022	To classify a certain set of fundus images	RNN-LSTM	2000 fundus images	Classification
[32]	2022	Early diagnosis of diabetic retinopathy	deep belief network	Clinical dataset	Classification
[33]	2022	To classify the severity level of diabetic retinopathy	Autoencoder	DIARETDB0 and DIARETDB1 databases	Classification

Accordingly, analyzing the conducted technical studies can help us prepare the study's main taxonomy. Figure VI presents the primary taxonomy of the work.

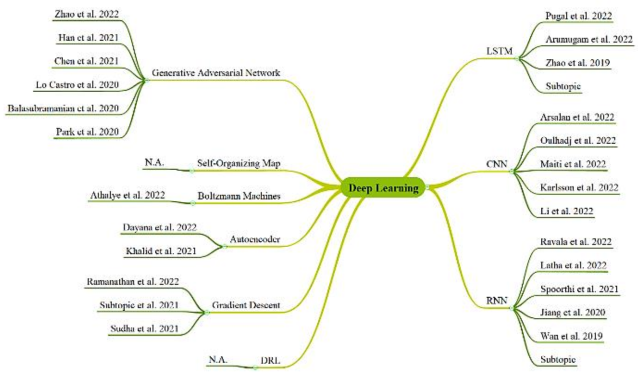

FIGURE VI. THE TAXONOMY OF THE STUDY

The study's taxonomy served to categorize numerous DL technique types used in various DR-related applications. The primary taxonomy of the terms used in the search queries is shown in Figure VII, along with links between them. Additionally, it shows the relationships between the frequently used taxonomy terms connected to DL in the current study. According to this figure, the size of keyword indicators directly correlates to how often they are used. The VOSviewer program created this map based on data retrieved from the Scopus and WoS databases. Network visualization is another name for this procedure. Items are represented in the network by their label and, by default, a circle. An object's weight determines the circle's size and labels for that item. The label and circle of the object are larger when the item's weight is higher. The label may not be visible for some items. In order to prevent overlapping labels, this is done. The cluster to which an item belongs determines the hue of the object. Lines between objects show links.

The text mining feature of the VOSviewer was employed to extract keywords from the titles, abstracts, and citation contexts. This program generates a two-dimensional map showing the co-occurrence network of keywords (adjectives and nouns). If two terms appear in the same title/abstract or citation context, they are called to co-occur. The similarity (relatedness in terms of co-occurrence) of two keywords (two nodes) is roughly inversely proportional to their distance. As a result, keywords having a greater co-occurrence rate are frequently seen together. The VOSviewer has a clustering feature that allocates keywords to clusters depending on how frequently they occur together.

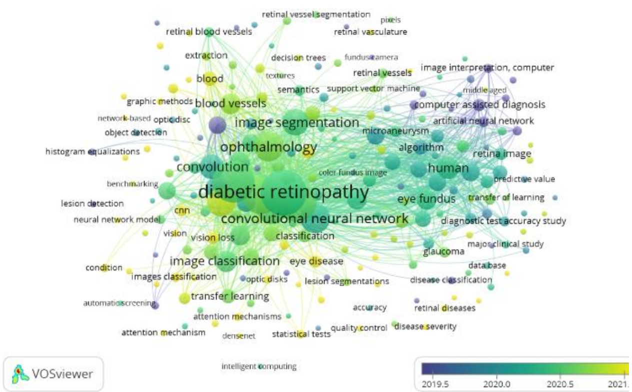

FIGURE VII. THE FREQUENTLY USED KEYWORDS

Researchers might choose the exercise model with the highest performance criterion compared to other models during the evaluation phase. To evaluate the DL approaches in various applications of DR, different evaluation criteria have been conceived in the current survey. A statistical comparison of several evaluation metrics supplied by surveyed studies and taken from Table 1 and the prepared database from the PRISMA output is shown in Figure VIII. As is clear from Figure VIII, the accuracy can be called the frequently used evaluation criteria for analyzing and checking the DL in the different applications of the DR.

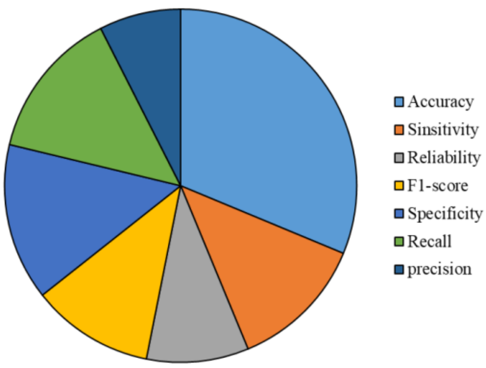

FIGURE VIII. THE FREQUENTLY USED EVALUATION CRITERIA

Figure VIII shows that accuracy has the most share, followed by specificity, recall, and sensitivity (approximately 31.25, 14.37, 13.75, and 12.5%, respectively). Below are the mathematical formulas for Accuracy (Eq. 1), Precision (Eq. 2), Recall (Eq. 3), and F1-score (Eq. 4). [34].

$$Accuracy = \frac{T_p + T_n}{T_p + T_n + F_p + F_n} \quad (1)$$

$$Recall = \frac{T_p}{T_p + F_n} \quad (2)$$

$$Precision = \frac{T_p}{T_p + F_p} \quad (3)$$

$$F1 - score = \frac{T_p}{T_p + \frac{1}{2}(F_p + F_n)} = 2(\frac{Precision \times Recall}{Precision + Recall}) \quad (4)$$

Tp refers to the True positive, Tn refers to the True negative, Fp refers to the False positive, and Fn refers to the False-negative.

III. RESULTS AND DISCUSSION

This section presents the study's main findings (see table 2). Table 2 has five columns, including the references, year of the publication, method type, results, and pros. and cons. of the DL techniques in DR. it should be noted that Table 2 only presents the findings of the notable studies in 2022.

TABLE II. RESULTS OF THE NOTABLE DL TECHNIQUES FOR DIABETIC RETINOPATHY IN FUNDUS IMAGES IN 2022

References	**Year**	**Method**	**Findings**	**Pros. and Cons.**
[23]	2022	CNN	Sensitivity of 82.69, specificity of 98.17, accuracy of 96.82, and area under the curve of 98.35	Automatic vessel detection for diagnosis purposes
[24]	2022	CNN	Accuracy of 85.28%	fine-tuning
[25]	2022	CNN-LSTM	Accuracy of 99.44%.	Automatic screening of fundus images
[26]	2022	CNN-U-nets	F1-score of 0.952	Automated retinal vessel segmentation
[27]	2022	CNN	Accuracy	automatic screening and accurate diagnosis
[28]	2022	RNN	Accuracy	The proposed technique improves the feature selection
[29]	2022	RNN	Accuracy of 95.48, Recall (Sensitivity) of 84.54, Precision of 97.3, F1 score of 90.47, Specificity of 86.81, and AUC of 93.43%	Reduced the false negative values
[30]	2022	LSTM-RFO	98.45% specificity, 96.78% sensitivity, 97.92% precision, 96.89% recall, and 97.93% F-score	The proposed technique successfully copes with the task
[13]	2022	stochastic gradient descent	Accuracy of about 95%	To increase the system reliability

[31]	2022	CNN-LSTM	Accuracy	The proposed approach is more reliable than the existence systems
[3]	2022	RNN-LSTM	Accuracy	automatically detects all the stages
[32]	2022	Deep belief network	Specificity of 90.757%, sensitivity of 92.225%, and accuracy of 92.122%	better theoretical error bounds
[33]	2022	Autoencoder	F1-Score of 95.9%	Effective an robust solution

According to Table 2, it can be claimed that DL techniques could successfully cope with the task in different applications of the DR. as the accuracy was the frequent and general evaluation criteria, we decided to present the accuracy values for the notable studies in Figure IX. According to Figure IX, the advanced hybrid CNN followed by the single CNN techniques for applying DR provided the highest accuracy values.

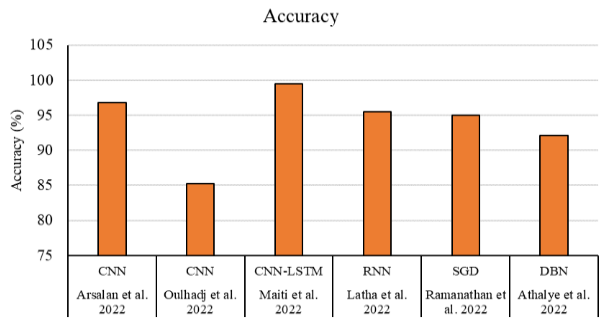

FIGURE IX. THE ACCURACY VALUES FOR THE NOTABLE STUDIES

In the following, we decided to present a general analysis of the database findings in the methodology section. Most publications claimed that the Ensemble techniques provided the highest score for different applications of DR followed by the Hybrid DL and CNN (See Table 3). Each of the methods has its advantages and disadvantages. This study can give us a general perspective for policymakers about the use of each DL technique in the desired DR application based on their performance score, advantages, and disadvantages. Figure X presents the share of DL techniques employed for the different DR applications. As the final suggestion, it is clear that CNN has the most share of the applications. But SOM and DRL are not employed in the field yet. These techniques can be proposed for future opportunities for completing this cycle.

TABLE III. Comparing the DL-based techniques

Method	Score	Advantages	Disadvantages
Ensemble	+++++	Strong learning ability	computationally expensive
Hybrid DL	+++++	Strong reliability	Complexity
CNN	++++	accurate at image recognition	fail to encode the position and orientation
RNN	+++	Processes inputs of any length	Training is difficult and time consuming
SGD	+++	Computationally fast	It requires more memory for loading
DBN	+++	Specific robustness in classification	Not suitable for high dimensional images
Autoencoder	+++	High reliability for homogeneous data	Not mutually exclusive architectures
GAN	++	Extracting details of data	Hard to train
DRL	NA.	To solve complex problems and to achieve long-term results	It is not suitable for simple problem
SOM	NA.	To reduce incredibly complex problems	it requires necessary data to develop meaningful clusters

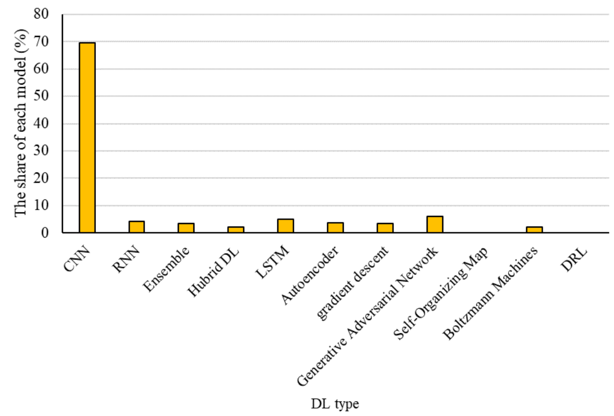

FIGURE X. THE SHARE OF DL TECHNIQUES FOR DIFFERENT APPLICATIONS OF DR

IV. CONCLUSION

The present study employed standard PRISMA guidelines for preparing a comprehensive database and analyzing the DL techniques used for DR applications. In this step, about 341 cases have been selected from the output of the PRISMA guidelines. In the following, the study analyzed the statistical results. According to the findings, we obtained the following marks:

- The most selected and relevant cases were related to conferences and articles publications. The frequently used keywords have combined three terms: computer science, engineering, and medicine
- The most share of the publications are related to Lecture notes in computer science, IEEE and Lecture notes in electrical engineering. The most shares of the studies employed accuracy as the most reliable and general evaluation metric for analyzing the DL techniques in different DR applications.
- CNN has the most share of applications compared to other DL techniques. Generally, the best performance is related to the ensemble and advanced DL techniques.

According to the analysis and also reviewing of the databases, it is suggested that in the future, the following actions should be investigated to improve the methods presented in the field: The conducted techniques have a good potential for segmenting retinal lesions such as hemorrhage in retinal fundus color images. Improving the conducted studies need to be applied to reduce the time of disease diagnosis and, in the following, to reduce the cost. Also, to improve the diagnosis of diabetes, it is possible to use the hybrid advanced DL methods, which require a supercomputer.

REFERENCES

[1] J. Ramya, M. Rajakumar, and B. U. J. J. o. D. I. Maheswari, "Deep CNN with Hybrid Binary Local Search and Particle Swarm Optimizer for Exudates Classification from Fundus Images," vol. 35, no. 1, pp. 56-67, 2022.

[2] S. Das, S. K. J. M. T. Saha, and Applications, "Diabetic retinopathy detection and classification using CNN tuned by genetic algorithm," vol. 81, no. 6, pp. 8007-8020, 2022.

[3] K. Spoorthi and B. Rekha, "Diabetic Retinopathy Prediction using Deep learning," in *2021 IEEE International Conference on Computation System and Information Technology for Sustainable Solutions (CSITSS)*, 2021, pp. 1-6: IEEE.

[4] N. Ullah *et al.*, "Diabetic Retinopathy Detection Using Genetic Algorithm-Based CNN Features and Error Correction Output Code SVM Framework Classification Model," vol. 2022, 2022.

[5] Y. Jiang, F. Wang, J. Gao, and S. J. A. S. Cao, "Multi-path recurrent U-Net segmentation of retinal fundus image," vol. 10, no. 11, p. 3777, 2020.

[6] K.-K. Maninis, J. Pont-Tuset, P. Arbeláez, and L. V. Gool, "Deep retinal image understanding," in *International conference on medical image computing and computer-assisted intervention*, 2016, pp. 140-148: Springer.

[7] S. P. J. P. R. Rajan and I. Analysis, "Recognition of cardiovascular diseases through retinal images using optic cup to optic disc ratio," vol. 30, no. 2, pp. 256-263, 2020.

[8] M. Zhao and G. Hamarneh, "Retinal image classification via vasculature-guided sequential attention," in *Proceedings of the IEEE/CVF International Conference on Computer Vision Workshops*, 2019, pp. 0-0.

[9] M. Rezakazemi, et al., "ANFIS pattern for molecular membranes separation optimization," vol. 274, pp. 470-476, 2019.

[10] A. Sina, et al., "Systematic review of deep learning and machine learning for building energy," 2022.

[11] M. Dehghan Manshadi, M. Ghassemi, S. M. Mousavi, A. H. Mosavi, and L. J. E. Kovacs, "Predicting the Parameters of Vortex Bladeless Wind Turbine Using Deep Learning Method of Long Short-Term Memory," vol. 14, no. 16, p. 4867, 2021.

[12] S. S. Band *et al.*, "A Survey on Machine Learning and Internet of Medical Things-Based Approaches for Handling COVID-19: Meta-Analysis," vol. 10, 2022.

[13] T. T. Ramanathan, M. Hossen, M. Sayeed, J. J. I. J. o. E. E. Emerson Raja, and C. Science, "A deep learning approach based on stochastic gradient descent and least absolute shrinkage and selection operator for identifying diabetic retinopathy," vol. 25, no. 1, pp. 589-600, 2022.

[14] S. M. Mousavi, et al., "Deep learning for wave energy converter modeling using long short-term memory," vol. 9, no. 8, p. 871, 2021.

[15] S. Shamshirband, et al., "Prediction of significant wave height; comparison between nested grid numerical model, and machine learning models of artificial neural networks, extreme learning and support vector machines," vol. 14, no. 1, pp. 805-817, 2020.

[16] A. Mosavi, S. Ardabili, and A. R. Varkonyi-Koczy, "List of deep learning models," in *International Conference on Global Research and Education*, 2019, pp. 202-214: Springer.

[17] S. Ardabili, et al., "Deep Learning and Machine Learning Models in Biofuels Research: Systematic Review," 2020.

[18] A. Mosavi *et al.*, "Comprehensive review of deep reinforcement learning methods and applications in economics," vol. 8, no. 10, p. 1640, 2020.

[19] B. Goutam, M. F. Hashmi, Z. W. Geem, and N. D. J. I. A. Bokde, "A Comprehensive Review of Deep Learning Strategies in Retinal Disease Diagnosis Using Fundus Images," 2022.

[20] Y. Jeong, Y.-J. Hong, and J.-H. J. D. Han, "Review of Machine Learning Applications Using Retinal Fundus Images," vol. 12, no. 1, p. 134, 2022.

[21] S. Shekar, N. Satpute, and A. J. J. o. M. I. Gupta, "Review on diabetic retinopathy with deep learning methods," vol. 8, no. 6, p. 060901, 2021.

[22] P. S. Fleming, D. Koletsi, and N. J. P. O. Pandis, "Blinded by PRISMA: are systematic reviewers focusing on PRISMA and ignoring other guidelines?," vol. 9, no. 5, p. e96407, 2014.

[23] M. Arsalan, A. Haider, Y. W. Lee, and K. R. J. E. S. w. A. Park, "Detecting retinal vasculature as a key biomarker for deep Learning-based intelligent screening and analysis of diabetic and hypertensive retinopathy," vol. 200, p. 117009, 2022.

[24] M. Oulhadj *et al.*, "Diabetic retinopathy prediction based on deep learning and deformable registration," pp. 1-19, 2022.

[25] S. Maiti, D. Maji, A. K. Dhara, G. J. B. S. P. Sarkar, and Control, "Automatic detection and segmentation of optic disc using a modified convolution network," vol. 76, p. 103633, 2022.

[26] R. A. Karlsson, S. H. J. C. M. Hardarson, and P. i. Biomedicine, "Artery vein classification in fundus images using serially connected U-Nets," vol. 216, p. 106650, 2022.

[27] X. Li, H. Xia, and L. Lu, "ECA-CBAM: Classification of Diabetic Retinopathy: Classification of diabetic retinopathy by cross-combined attention mechanism," in *2022 the 6th International Conference on Innovation in Artificial Intelligence (ICIAI)*, 2022, pp. 78-82.

[28] L. Ravala and R. J. T. C. J. GK, "Automatic Diagnosis of Diabetic Retinopathy from Retinal Abnormalities: Improved Jaya-Based Feature Selection and Recurrent Neural Network," vol. 65, no. 7, pp. 1904-1922, 2022.

[29] D. Latha, T. B. Bell, C. J. M. T. Sheela, and Applications, "Red lesion in fundus image with hexagonal pattern feature and two-level segmentation," pp. 1-19, 2022.

[30] R. Pugal Priya, T. Saradadevi Sivarani, and A. J. I. J. f. N. M. i. B. E. Gnana Saravanan, "Deep long and short term memory based Red Fox optimization algorithm for diabetic retinopathy detection and classification," vol. 38, no. 3, p. e3560, 2022.

[31] S. R. Arumugam, E. A. Devi, V. Rajeshram, R. Balakrishna, S. G. Karuppasamy, and S. V. Kumar, "A Robust Approach based on CNN-LSTM Network for the identification of diabetic retinopathy from Fundus Images," in *2022 International Conference on Electronic Systems and Intelligent Computing (ICESIC)*, 2022, pp. 152-156: IEEE.

[32] S. S. Athalye, G. J. I. J. o. I. S. Vijay, and Technology, "Taylor series ‐ based deep belief network for automatic classification of diabetic retinopathy using retinal fundus images," vol. 32, no. 3, pp. 882-901, 2022.

[33] A. M. Dayana, W. J. M. T. Emmanuel, and Applications, "An enhanced swarm optimization-based deep neural network for diabetic retinopathy classification in fundus images," pp. 1-32, 2022.

[34] S. S. Band *et al.*, "When Smart Cities Get Smarter via Machine Learning: An In-depth Literature Review," 2022.