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Deep Learning for Retinal Disease Detection Surveys

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Abstract

Retinal image analysis is crucial for The classification of retinal diseases such as “Age Related Macular Degeneration (AMD)”, “Diabetic Retinopathy (DR)”, “Retinoblastoma”, “Macular Bunker”, “Retinitis Pigmentosa”, and “Retinal Detachment”. The early detection of such diseases is important insofar as it contributes in mitigating future implications. Many approaches have been developed in the literature for auto-detecting of retinal landmarks and pathologies. The current revolution in deep learning techniques has opened the horizon for researchers in the field of ophthalmology. This paper is a comprehensive review of the deep learning techniques applied for the classification of retinal images, pathology, retinal landmarks, and disease classification. This review is based on indicators such as sensitivity, Area under ROC curve, specificity, F score, and accuracy.

Keywords:
Machine Learning, Deep Learning, Retinal Disease, Disease Detection

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I. INTRODUCTION

In telemedicine, the classification of “*ophthalmologic diseases”* using retinal images has Growth in recent years. The previous approaches used a manual segmentation that consumes time, efforts, and special skills [1]. Figure 1 depicts two images one for healthy retina and the other one is not. The use of naked eyes in detecting a particular retina issue may not always accurate since many diseases include complex texture that is difficult to distinguish manually. However, the computer-based detection approaches are preferred since they are more feasible and does not need skilled clinicians [2]. In fact, the development of screening systems and real-time classification of retinal diseases have become more helpful and effective [3]. Many algorithms that are based on, for instance, edge or morphology have been proposed by researchers for auto-detection of retinal pathology and landmarks [4][5]. Besides, the detection of retinal images can also involve machine learning approaches (supervised or unsupervised neural networks). The supervised approaches such as SVM, ANN, decision trees, and MLP [6][7]8]. The unsupervised machine learning approaches such as matched filtering and model based approaches are also used in retinal abnormality detection[9].

Figure 1: The left image reflects a healthy retina, while the right reflects unhealthy one.

Most of the approaches in the literature need manual feature extraction using SIFT, SURF, and HOG techniques [10][11]12]. Practically, the resulting features using these approaches are not generalized. The deep learning techniques in visual recognition have attracted researchers to involve these techniques in ophthalmology. In retinal images, the automatic learning of features can be achieved using the deep learning techniques. Moreover, generalizing the high level of features extraction from raw images can be performed using "*supervised/unsupervised multi-layer Deep Neural Networks*" (DNN). The deep learning based techniques has the ability to outperform the traditional methods for "*2-D fundus*" and "*3-D Optical Coherence Tomography*" (OCT) images [13].

The accurate imaging of retinal tissues is crucial for the detectinon/treatment of retinal diseases. The direct inspection of retina was first developed by [14]. After that, many models were developed for the retinal anatomical structures. Fundus images is an effective way for early detection and screening of the main causes of blindness (e.g., glaucoma, macular degeneration, and DR). The two-dimensional (2-D) representation of retinal using the "*primary fundus cameras*" struggled the depth, which caused inaccurate detection process of specific retinal pathology, which can be addressed using "*Tomography*". On the other hand, *"Optical Coherence Tomography (OCT)"* is a technique that is able to capture "3-D cross sectional maps" of retina [15].

The literature includes a lot of surveys and reviews that consider retinal diseases such as detecting retinal landmark, pathology segmentation, and classification of retinal diseases [1][13]. The contribution of this work is to comprehensively review the deep learning techniques that are mainly used for retinal image analysis, which is a lack in the literature. The main focus of this review is to cover the "*2-D fundus*" and " *3-D OCT*" retinal images based on advanced deep learning approaches that are used for auto-identification of pathology, retinal landmarks, and classification. The metrics used in the analysis of the approaches are: sensitivity, specificity, area under ROC curve, and accuracy. Hence, the main objective of this work is present the state-of-the-art in ophthalmology based on the recent deep learning techniques.

The rest of this paper is organized as follows: Section 2 presents the principles of deep learning and the main concepts used for implementing deep learning approaches. Section 3 illustrates the approaches in deep learning that are used in retinal images analysis and the state-of-the-art in this specific field. Section 4 discusses the presented works in terms of providing general observations for researchers who work in this area. Finally, this paper is concluded in Section 5.

П. Deep Learning Techniques

Generating self-thinking programs/machines has become one of the main goal of human beings. The advent of sophisticated software tools, techniques, and proficient programming languages, the focus has increased towards designing smart models that are able to overcome our everyday challenges. Deep learning is currently considered the most efficient way to apply Artificial Intelligence (AI) in our life. Deep learning can be applied using the " Deep Neural Networks.

DNN, which is a special form of Artificial Neural Network (ANN) has the ability to perform the following:

- Hierarchical feature extraction.

- Overcome input image pre-processing limitations.

Deep Neural Networks (DNN) contains three layers: input, hidden, and output. Using the DNN, features can be learned using the supervised or the unsupervised approaches and both can be used in detecting retina diseases. Figure 2 is plotted to clarify how a DNN detects retina diseases passing through network layers.

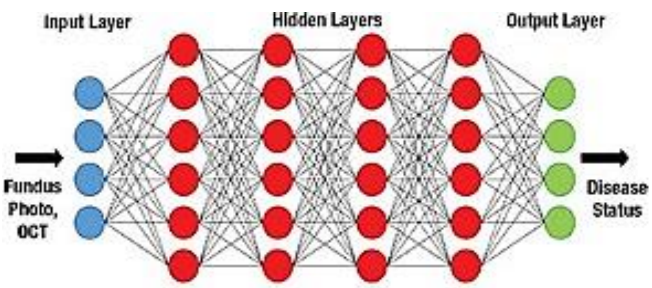

Figure 2: DNN in detecting retina diseases.

Datasets on retinal diseases images are available in many sources and can be listed below:

- **STARE**: image size of (700x605), 400 retinal images, 20 colored and 20 hand labeled images as "*Ground Truth*".
- **MESSIDOR**: image size of (1440 X 960, 2240 X 1488, 2304 X 1536), and 1200 eye fundus color images.
- **ARIA**: image size of (768 X 576), and 212 color fundus images where 92 are AMD, 59 are DR, and 61 are regular images.
- **EyePacs DR**: captured using different kinds of cameras including 35,126 images.
- **DRIONS**: with image size of (600 X 400) including 110 color digital retinal images.

In fact, the datasets are not limited to the above mentioned list, there are many datasets available for researchers such as Kaggle datasets [17].

II.I Supervised-Based Learning

By supplying labeled training data, it is possible to perform supervised learning using a DNN. After then, the network attempts to learn the labels using a specific approach. Typically, supervised learning is accomplished through the use of classification algorithms that deal with labeled data. On the other hand, a response can be made by CNNs' neurons to a particular area in the input image and is termed "receptive field", which is a region in the input image where neurons of the CNN respond to a particular portion of it. Several receptive fields are overlapping aiming to initiate the impact of the input image gliding across the receptive fields. An action is formed by convolution of a neuron's receptive field with a weight matrix. Each node of the input layer receives a patch of the input image, and the output is generated for the center pixel of the patch. It is also possible to construct output label maps for all pixels of the input image patch at the same time by employing the structured prediction method. Typically, CNNs have convolutional layers, pooling layers, and a terminating classification layer before they are considered complete. To reduce the dimensions of the feature vector, pooling layers are employed. Pooling layers are used to improve the computational performance of the system. Classification algorithms such as Softmax, Linear Support Vector Machine (LSVM), multi-class SVM, and random forest can be used to achieve the classification layer's goal. On the other hand, CNNs are available in a variety of configurations, for instance, it can be designed based on the number of layers, pooling, and classifier used.

II. II Unsupervised-Based Learning

Unsupervised learning approaches are widely involved in pattern recognition tasks. This kind of learning does not need labeled data during the learning process. The unsupervised DNNs also have the same three layers of the supervised approach and can be fully or partially tied. Usually, input images can be compressed in unsupervised DNN. Also, noise is introduced into the input images, and then a stacked de-noising auto-encoder is used to rebuild the original image from the compressed noisy image [17].

III. Deep Learning Challenges

Although deep learning is widely used in a variety of applications, it is still required to develop a concrete theoretical background for the tuning processes of parameters and performance evaluation of the features selected. Another challenge that struggle deep learning is the hardware resources required to perform the heavy computations of deep learning. Therefore, it is needed to adopt or develop efficient approaches that have the ability to deal with the aforementioned challenges [16].

IV. Detection of Retinal Diseases

Advances in the domains of image processing and machine learning have made it possible to totally automate the process of distinguishing between retinal illnesses and other health conditions. The advent of deep learning has opened a new path for the efficient and accurate diagnosis of retinal disorders just as old approaches for automatic classification of retinal diseases have reached their limit of effectiveness. Deep learning approaches have been used to automatically classify retinal illnesses in the literature. Both supervised and unsupervised algorithms have been developed for this purpose.

The metrics used in evaluating the approaches can be summarized as follows [13]:

- **Sensitivity**: It is the ratio of the classified “True Positive” to the actual “True Positive” in the ground truth, and sometimes termed as “True Positive Rate TPR”.
- **Specificity**: Similar to the previous but for “True Negative” and usually termed as “False Positive Rate FPR”.
- **Accuracy**: reflects the accuracy of the detection process.
- **Area under the curve**: The area that is covered by the characteristic curve when achieving optimally.

IV. I Supervised Approaches

A supervised deep learning method for DR classification, together with an automated screening algorithm, is suggested by [17]. To this end, they designed a DNN approach. This method is run through Kaggle's DR Detection dataset to check if it's working properly. The dataset consists of 5000 patient photos taken from over 10,000 photographs. As seen in Table 1, the algorithm had an AUC of 94.6%, sensitivity of 96.2%, and 66.6% as determined.

The authors in [18] proposed a neural network to identify and classify all kinds of DR into four categories: “*mild, moderate, severe, and proliferative”*. They performed mining deep features from retinal images, and then applied these features to categorization. The proposed network consists of 10 convolutional layers, each with an intermediate max pooling layer, two fully connected layers, and a Softmax classification layer. L2 normalization was used for weights and biases, and each layer had leaky ReLU activation unit. The final result was to balance out all the extraneous variances in the images. Batch normalization was applied to each weight matrix after each layer. Node dropout method was used to avoid overfitting. The methods used were “stochastic gradient descent”, “Nestrov”, and training using stochastic gradient descent. Network training was augmented with real-time image patches prior to initial training. To help improving the localization of the system. The validation of the algorithm was assessed by analyzing the Kaggle dataset. It was reported that this strategy provided a sensitivity of 95% and an accuracy of 75% as shown in Table 1.

Another study performed Abramoff et al. [19] suggested an updated version of their prior work, using deep learning for categorization of both DR and ME. An improved statistical method was developed to automate the process of identifying and classifying DR into moderate, severe non proliferative DR (NPDR), PDR, and ME. The “*IDX-DR*

X2.1" automated system was involved. The "EyeCheck" project dataset was used to train the device. To evaluate the system, the Messidor-2 dataset was used. Table 1 presents the statistical findings of the approach. Gulshan et al. [20] developed an approach to identify diabetic macular edema (DME) and diabetic retinopathy (DR) using fundus images. They involved DNN v3 architecture based on Inception V3. Training and testing were performed on the EyePACS-1 and MESSIDOR-2 datasets. The ImageNet dataset was utilized to set the initial weights of the network. Distributed stochastic gradient learning methods and batch normalization were both utilized in learning the weights, which resulted in an efficient training and Table 1 presents the obtained results.

Furthermore, a visualization heatmap could assist clinicians in grading DR. The study of Gargeya and Leng [21] suggested an automated CNN-based model for DR grading. This method enabled clinicians to easily discover abnormalities using a heatmap. The network was composed of convolutional blocks with 4, 6, 8, and 10 layers. Each layer contained batch normalization and units of ReLU activation. Softmax classification was the final layer, followed by an average pooling layer and a visualization layer. The heatmap was created using a visualization layer that performed similarly to a convolutional layer. The model was trained using the EyePACS dataset. To eliminate unnecessarily changing brightness and contrast the input images, they were normalized, reduced, and augmented. To normalize the effect of environmental variables, some meta-data pertaining to the original image was appended to the feature vector. The algorithm achieved an AUC of 97 percent, with sensitivity and specificity of 94 percent and 98 percent, respectively, for the EyePACS dataset. The algorithm's generalizability was evaluated using the MESSIDOR-2 and E-OPTHA datasets. Table 1 summarizes the findings. Retinopathy of Prematurity (ROP) is a leading preventable cause of childhood blindness. Thus, early detection of ROP is critical for preventing childhood visual loss. Worrall et al. [22] advocate for the use of a deep CNN to detect ROP. They were the first to propose an end-to-end system based on deep learning approach for the early detection of ROP. They optimized the pre-trained GoggleNet and employed it as a ROP detector. A Bayesian framework was involved aiming to improve the accuracy. Besides, they used pre-processing and enhancement of retinal images. A private database was used to train and test the network. As indicated in Table 1, the statistical performance evaluation resulted in sensitivity, specificity, and accuracy of 93.6 percent, 95.4 percent, and 94.7 percent, respectively. AMD diagnosis was critical. Due to the disease's silent character during the middle stage, asymptotic severity leads in full eyesight loss. The characteristics learned from pre-trained neural networks may aid in the effective diagnosis of AMD in its intermediate stage. Burlina et al. [23] evaluated the technique's suitability for AMD categorization. Overcome Features (OF) were extracted from pre-trained deep convolutional neural networks (CNNs) on the generic dataset ImageNet. The network was given resized images for the purpose of learning OF features. The central portion of the retina was the most critical and prognostic for AMD diagnosis. The data was derived by appending features to numerous concentric square grids. The LSVM classifier was trained using the retrieved characteristics. The model's efficiency was evaluated using the NIH AREDS dataset. The dataset was separated into two classes: EIPC (equal number of images in each class) and MIPC (equal number of images in each class) (maximum number of images per class). The performance of the algorithm was assessed on both kinds of datasets as shown in Table 1.

Burlina et al. [24] developed their previous work by identifying a subclass of AMD. No AMD was classified as *Class_1*, early AMD was classified as *Class_2*, intermediate AMD was classified as *Class_3*, and advanced AMD was classified as *Class_4*. They determined the severity score of AMD using OverFeat deep CNN. The algorithm's efficacy was evaluated using the NIH AREDS dataset. Table 1 summarizes the performance metrics acquired. The *"3-D OCT imaging"* is the most frequently used imaging modality in ophthalmology. The combination of OCT images and electronic medical records (EMR) created a large dataset for training DNNs. In the same context, Lee et al. [78] used the same methodology for AMD detection. They used OCT images to develop a VGG-16 DNN for effective AMD classification. Their network comprises of 21 layers, some of which were convolutional while the others were max pooling, each with a ReLU activation unit. OCT images extracted automatically and utilized to train and test the network. The Xavier algorithm [25] was used to establish the weights, and stochastic gradient descent was used to optimize them. After downscaling and histogram equalization, the input images were fed into the network. The results are summarized in Table 1. Choi et al. [26] used fundus images sourced from the STARE dataset to develop a deep CNN for the systematic diagnosis of numerous retinal disorders. The dataset was supplemented with 9 additional disorders, including baseline "DR, PDR, Dry AMD, Wet AMD, Retinal Vein Occlusion, Retinal Artery Occlusion, Hypertensive Retinopathy, Coat's disease, and Retinitis". Initially, random forest with VGG19 transfer learning was used to categorize the diseases. However, the accuracy was relatively low because of the large number of disorders. Later on, ensemble classifiers were developed to improve the accuracy of categorization for multiple diseases. The network showed an accuracy of 36.7 % for 9 retinal disorders.

In addition to the aforementioned studies, a recent study presented by Sarki et al. [32] in 2020 surveyed the literature considering a variety of datasets using variety of approaches such as image processing techniques and deep learning techniques. The study also presented different metrics to evaluate the techniques and came up with some recommendations. Similarly, the study of Attia et al. [33] reviewed the progress of the literature in using the deep learning techniques and the most popular datasets used for this purpose. The authors found that deep learning techniques are able to detect retinopathy diseases with high performance and high automatic identification. Another study proposed by Saba et al. [34] in 2021 suggested an approach that was based on deep learning techniques for detecting grades papilledema through U-Net and Dense-Net architectures. The findings showed interesting and promising results in terms of the metrics used (sensitivity, specificity, and accuracy). Muller et al. [35] in 2021 proposed a multi-disease detection approach for retinal images using the predictive capabilities of deep convolutional neural networks. Their approach contributes in obtaining high accuracy detection rate as well as high reliability compared to the available approaches in the literature.

IV. II Unsupervised Approaches

Unsupervised deep neural networks have been shown to be excellent at classifying retinal illnesses such as "AMD, DR, Macular Bunker, Retinoblastoma, Retinal Detachment, and Retinitis Pigmentosa". In the study of Arunkumar and Karthigaikumar [3], they proposed an approach for reducing the dimensions of the feature vectors using a Generalized Regression Neural Network (GRNN). This was performed aiming to improve the efficiency of computation. The model was capable of extracting detailed features due to the fact that its layers contain layered Restricted Boltzmann Machines (RBMs) [27]. Preprocessing of the input photos removes noise and adjusts contrast. The system's effectiveness was evaluated using the ARIA dataset. Table 1 summarizes the findings.

Table 1: Performance of retinal disease detection Approaches.

Reference	Dataset	Sensitivity	Specificity	Accuracy	Area Under the Curve	Approach	Application

[17]	Kaggle DR detection dataset	96.2 %	66.6 %	-	94.6 %	Supervised	DR Identification/ Classification
[18]	Kaggle DR detection dataset	95%	-	75%	-		
[19]	MESSIDOR-2	96.8 %	87%	-	98%		
[20]	EyePACS-1 MESSIDOR-2	90.3 % 87%	98.1 % 98.5 %	- -	- -		
[21]	MESSIDOR-2 E-OPTHA	93% 90%	87% 94%	- -	94% 95%		
[22]	Private dataset	93.6 %	95.4 %	94.7 %	-		ROP Identification
[23]	NIH AREDS	90.9 %–95.7 %	90.1 %–95.6 %	91.9 %–95%	-		AMD Identification/ Classification
[28]	3-D OCT images	92.64 %	93.69 %	93.45 %	97.45 %		
[24]	-	-	-	85%	-		
[26]	STARE	-	-	36.7 %	-		Multiple Retinal diseases classification
[33]	papilledema images	98.63 %	97.83 %	99.17 %	-		
[3]	ARIA	79.32 %	97.89 %	87.62 %	-	Unsupervised	
[29]	DRIVE	-	-	94.7 %	-		detection of blood vessels in fundus color images
[30]	DRIVE and STARE	78.19%	-	87.02%	-		Segmentation of Fundus images
[31]	DRIVE STARE	73.9 % 73.7 %	97.4 % 96.2 %	94.5 % 94%	-		Segmentation of Retinal images

V. Discussions

The field of retinal image analysis using DNNs is still in its infancy. Although research into the extraction of retinal diseases has been undertaken, the apex of this technology is going to grow. However, unsupervised learning-based DNNs is doing a minor progress in the analysis of retinal images. Moreover, there are no restrictions on the number of layers or design of neural networks; the network architecture is determined heuristically based on the domain of the problem. Deep Neural Network versions like as AlexNet, LSTM, VggNet, and GoogleNet can be used to extract retinal anatomical structures. Although Lee et al. [78] used “VGG-16 for 3-D OCT” retinal image analysis, there is no precedent for its usage with color fundus images. All of these networks are extremely dense, and they are capable of extracting significantly more complicated characteristics than standard approaches do, while also providing better performance metrics. This property enables DNN to be used in place of conventional ophthalmologic screening procedures.

VI. Conclusion and Future Works

Our review of DNNs for retinal image processing indicates that, on average, supervised learning approaches outperformed unsupervised learning methods, owing to the fact that supervised learning networks efficiently learn the mapping in the presence of ground truth data. Rather than manually detecting retinal landmarks one by one, DNNs can be utilized to simultaneously extract retinal landmarks from retinal images. DNNs have not been extensively investigated for the detection of retinal disease. Recent research has examined the use of supervised DNNs for concurrent segmentation of retinal diseases.

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طرق التعلم العميق في الكشف عن أمراض شبكية العين دراسة استقصائية

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ملخص

يعد تحليل صورة شبكية العين أمراً ضروريًا لتصنيف أمراض الشبكية مثل الضمور البقعي المرتبط بالعمر، واعتلال الشبكية السكري، واورام الشبكية ، والبقعة البقعية ، والتهاب الشبكية الصباغي ، وانفصال الشبكية. ان الاكتشاف المبكر لمثل هذه الأمراض مهم جداً كونه يساهم في التخفيف من الآثار المستقبلية لهذه الأمراض. قام العديد من الباحثين بتطوير العديد من الأساليب للكشف التلقائي عن معالم الشبكية وأمراضها. لقد فتحت الثورة الحالية في تقنيات التعلم العميق الأفق للباحثين في مجال طب العيون. هذه الورقة هي مراجعة شاملة لتقنيات التعلم العميق المطبقة لتصنيف صور الشبكية ، وعلم الأمراض ، وعلامات شبكية العين ، وتصنيف الأمراض. تستند هذه المراجعة إلى مؤشرات مثل الحساسية والمنطقة تحت منحنى *ROC* والنوعية ودرجة *F* والدقة.

الكلمات المفتاحية: تعلم الألة، التعلم العميق، امراض شبكية العين، تشخيص الامراض