



An Image Processing System using Deep Learning CNN Model for Early Identification of Diabetic Retinopathy: A Review

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Abstract: Diabetic retinopathy (DR) is a disease which can be observed in patients who have diabetes. Due to this, causes slowly detriment to the retina and light-sensitive nerves i.e photoreceptors, used to identify light at back to eye. DR is not identified in its early stage as no direct symptoms found in early stage, but as the patient progresses, the patient may experience blurred vision or overall loss of vision. People with diabetes can be 25 times more blind than the average person. Identification at initial stage and treatment of diabetic retinopathy (DR) are extremely important in forestall to vision loss among individuals with diabetes. However, existing screening methods, which rely on manual evaluation of retinal images captured by non-mydratic fundus cameras, are time-intensive and error-prone. Our proposed methodology employs convolutional neural networks (CNNs) in juxtaposition with advanced preprocessing systems to mine life-threatening features from retinal images. To address challenges such as high dimensionality and computational complexity, the model integrates Linear Discriminant Analysis (LDA) and Principal Component Analysis (PCA) for feature optimization. The system classifies retinal images into five stages of DR—Normal, Mild Non-Proliferative, Moderate Non-Proliferative, Severe Non-Proliferative, and Proliferative—achieving robust multiclass classification. To overcome limitations of traditional deep learning models, such as vanishing gradients and prolonged training times, the CNN architecture leverages dense residual U-network that enable feature reuse and enhance model efficiency. By integrating low-level features from shallow layers with high-level dense features, the model significantly improves detection accuracy. This research may mark a significant advancement in diabetic retinopathy screening, addressing key challenges in clinical practice and contributing to improved patient outcomes.

Keywords: — PCA, LDA, Dense

1. Introduction

Diabetic retinopathy:

Diabetic retinopathy is a disease which can be served in patients who have diabetes. Due to this, causes gradual damage to the retina and light-sensitive nerves at the rear or back of the eye. Diabetic retinopathy is a dangerous related eye problem of diabetes. The capacity of the body to utilize and store sugar (glucose) is hampered by diabetes. The disease is defined as excessively high sugar in the blood, which can harm many body parts, along with the eyes. After long period, diabetes affects small blood vessels all over the body, including the retina. Diabetic retinopathy is the result of the leakage of blood and other fluids from these small vessels. This causes the retinal cells to enlarge, which impairs or causes blurred vision.

Typically, both eyes are affected. Diabetes retinopathy is highly possible to develop as a person's diabetes progresses. Diabetic retinopathy can be reason of blindness if untreated.

Diabetes is a disease that continues for a long time which may be deleterious for various parts of the body, including the retina. As the study says that in most of the developed countries the diabetic retinopathy is one of the



leading factor of vision loss. It also develops to one extent in almost all patients with chronic diabetes. Closely associated with diabetes, it causes structural changes in the retina and causes irreversible damage.

DR is not identified in its early stage as no direct symptoms found in early stage, but as the patient progresses, the patient may experience blurred vision or overall loss of vision. People with diabetes can be 25 times more blind than the average person.

Corona virus disease (COVID19) pandemic resulted inexpressive death and illness, with 133,552,775 cases worldwide and 2,894,296 deaths as of April 2021. At the public health level, the effects of this epidemic, especially outside of control and trade ,are beginning to manifest themselves in diseases such as diabetic retinopathy. Diagnosed in about one-third of diabetics, DR is among the most frequent causes of vision loss globally[1].

Diabetic retinopathy is a diabetic complicity that involves enlargement of retinal veins and arteries as well as fluid and blood leaks.[18]. DR can cause vision loss if it is in high stage. Globally, DR causes 2.6% of vision loss [19]. Likelihood of DR being present is increased in diabetics who have been suffering from this disease for a long time. Normal retinal vetting is useful for early findings and remedy to keep away from the high possibilities of blindness in diabetics [20].

The emergence of distinct types of lesions on the retinal picture distinguishes diabetic retinopathy. Microaneurysms, haemorrhage, and soft and hard exudates are examples of these lesions (EX). [16, 20, 21].

The first sign of DR is microaneurysms, which are tiny pink spherical spots on the retina caused by a weak area in the vessel walls. There are sharp margins and the length is less than 125 μ m [22]. AOSLO reflectance and classic fluoresce in imaging have both revealed microaneurysms of this type.

Haemorrhages appear as big patches on the retina, measuring greater than 125 m in length and with an abnormal border. Flame (superficial) and blot (deeper) are main 2 parts of haemorrhages.

Hard exudates appear to be shiny-yellow spots on the retina ensuing from effusion of plasma. Their edges are razor-sharp and may be located within the retina's outside parts.

Soft exudates (additionally referred to as cotton wool) seem as white places at the retina attributable to the expansion of a neuron. The form is oval or spherical.

Diabetics are costly and time consuming as they have to undergo regular retinal health examinations. The main purpose of this study is to identify diabetic retinopathy, automatically evaluate and analyze retinal images using a deep learning CNN model, and help ophthalmologists treat and diagnose infected patients by using deep learning CNN model.

2. Proposed Work: Problem Formulation:

Regular eye checkup is necessary for detecting and treating diabetic retinopathy early. Regular eye checkup can help diagnose people with diabetes at an early stage, enabling fluctuations in blood pressure or blood glucose to be managed efficiently in order to slow the progression of diabetic retinopathy. This research is important because it will help to solve the present challenges in the diabetic retinopathy screening procedure.

Ophthalmologists currently employ non-mydratic fundus cameras to collect the retinal images for clinical analysis. The professional screening specialists will determine whether or not patients have any abnormalities based on the image obtained by the fundus camera (including diabetic retinopathy). Screeners manually examine any changes (abnormalities) on the retinal picture to determine the correct diagnosis. This procedure is both time-consuming and prone to mistake.

Various machine learning algorithms, like Adaboost, Random Wooded area, and SVM, had been applicable to improve the version of DR detection, according to the study. But, there's quite time to investigate additional important factors that contribute to the detection of DR images. This is done by employing feature selection algorithms to extract additional features and find associated qualities. Deep networks can aid in the diagnosis of chromatic diseases and the Coronary artery fragmentation. In latest years, deep neural networks have essentially relived arduous feature descent and selection phases; nevertheless, because fundus photographs generally have poor contrast and changing image rate, deep networks are also useful for image preparation for efficiency. Other deep networks can be employed instead of CNNs, which are the most commonly utilized by researchers. The process of building a solid picture database for deep network training is currently ongoing.

The emergence of distinct types of lesions on the retinal picture distinguishes diabetic retinopathy. Microaneurysms, haemorrhage, and soft and hard exudates are examples of these lesions (EX). [16, 20, 21].

Microaneurysms, which appear as little pink spherical spots on the retina due to a weak region in the vessel walls, are the initial indications of DR. There are sharp margins and the length is less than 125 μm . MA was classified into six categories by Michael [22]. AOSLO reflectance and classic fluorescein imaging have both revealed microaneurysms of this type.

Haemorrhages appear as big patches on the retina, measuring greater than 125 μm in length and with an unnatural border. Flame (superficial) and blot (deeper) are main 2 parts of haemorrhages.

Hard exudates appear to be shiny-yellow scars at the retina of the eye caused by plasma leakage. It creates the sharp edges and can be found in the outside layers of the retina.

Soft exudates (known as cotton wool) will be seen on the retina as white patches caused by nerve fibre swelling. Oval or spherical shapes are common.

As per the International Clinical Diabetic Retinopathy (ICDR), the Diabetic Retinopathy Severity Scale can classify as listed below: [4]

Severity Level 0: No obvious retinopathy Observation: No abnormalities

Severity Level 1: Mild NPDR Observation: Microaneurysms only

Severity Level 2: Moderate NPDR

Observation: Not only microaneurysms however less than intense NPDR

Severity Level 3: Excessive NPDR

Observation: One of the subsequent

In each of the four quadrants, there were more than 20 intraretinal haemorrhages.

Two or more quadrants of transparent venous beading

One or more quadrants have intraretinal microvascular abnormalities (IRMA).

There was no sign of proliferative retinopathy.

Severity Level 4: Proliferative diabetic retinopathy (PDR) Observation: One or both of the following are possible option i) Angiogenesis ii) Vitreous / Preretinal bleeding

Proposed Model will be implemented as the following way:

Input images from the Kaggle platform in its original format.

Conversion image to Grayscale.

Apply standardization & normalization on image

Apply Contrast Limited Adaptive Histogram Equalization

Apply the contrast enhancement mechanism (Edge-Preserving Guided Image Filtering)

Resized images to create proper data images.

To boost data density, create [48*48] dimensional dapples via randomly picking their facilities within the unique retinal image (Data Augmentation).

Do sampling on image data 60% for training and 40% for testing.

Make a network of DRU-net

Apply feature extraction through train DRU-net using training dataset.

Apply a dimension reduction of features using Principal Component Analysis and Linear Discriminant Analysis (LDA)

Use of Softmax Function for testing the network using testing dataset, recognize images after evaluation process,

Classification of Diabetic Retinopathy symptoms.

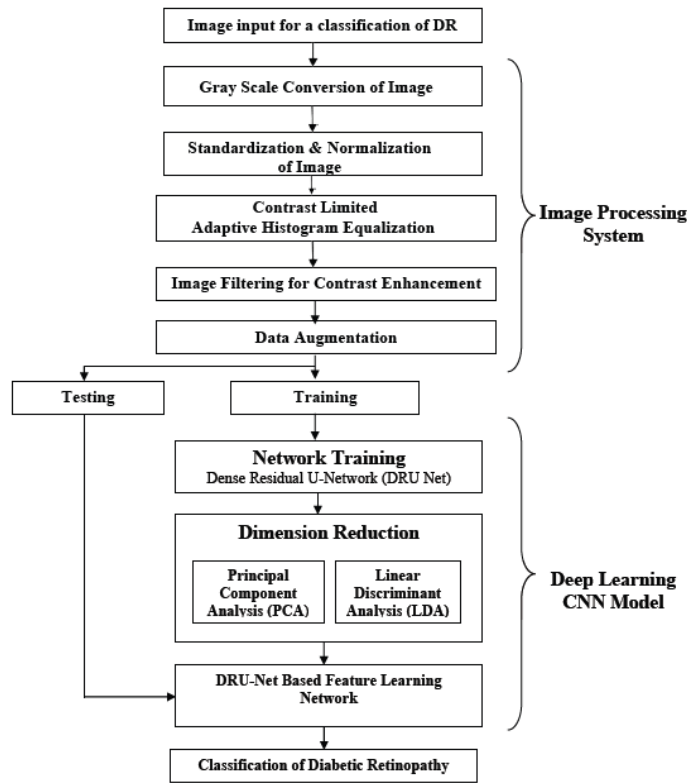


Figure 1: Architecture of a proposed model

Data Acquisition Phase:

The Kaggle images have a wide range of high-decision fundus images retrieved in various imaging conditions. A clinician (a trained pathologist) evaluated the dataset on a scale of 0 to 4 agreeing diabetic retinopathy is a classify in each image. [9] “[0- No DR, 1- Mild, 2- Moderate, 3- Severe, 4- Proliferative DR]”

Feature selection:

The technique of automatically picking characteristics in a predictor variable or data that contribute the most to the desired result is called as feature selection. Selection of features are used to identify and remove undesired, irrelevant, or excess attributes from data that do not contribute to classifier precision or have the potential to reduce model accuracy [9].

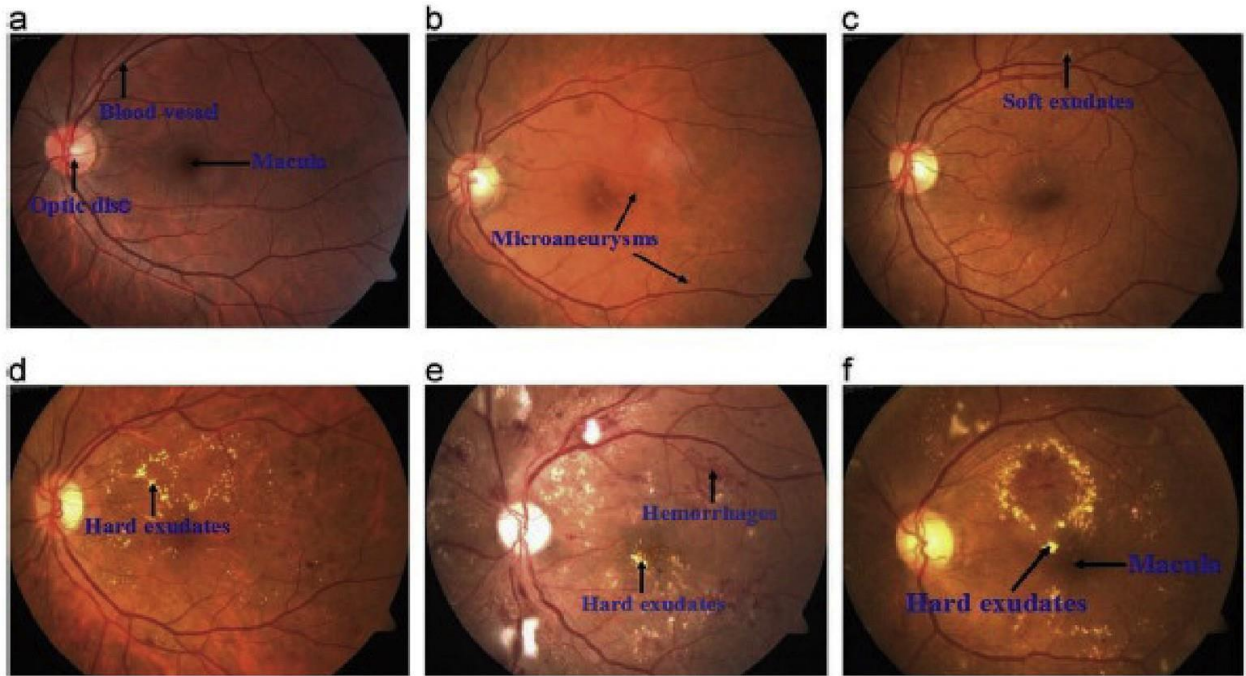


Fig. 2. The DR stages: (a) Normal (b) Mild (c) Moderate (d) Severe (e) Proliferative (f) Macular edema

Table 1: An overview of various feature extracted from retinal fundus images [9]

Features	Scientific importance and the reasons for their inclusion/exclusion
Optical separation	The part of the eye, often known as the distance, the region in the retina wherein the segments of the visual cortex go away the retina. The normal human eye's optic disc carries roughly from the optic nerve to the brain, there seemed to be 1 million neurons [38]. As a result, the quality to consider is excellent..
Fovea	The pyramidal cells in this region are connected to the ganglion cells and give foveal visual acuity, which is the sharpest central visual acuity in the retina [39]. However, this trait was not chosen since it was not included in earlier literature.
artery of plasma	Subconjunctival bleeding occurs when little fragile arteries of blood rupture beneath the tissue that covers the white of the eye (conjunctiva), causing redness [40]. The blood vessel area within the normal picture is 37230.56, which reduces with diabetic retinopathy owing to contraction. Diabetes destroys the retina's blood vessels. Diabetic retinopathy can lead to blindness if left untreated [30] [31].
Blood vessels are blotted.	They are ophthalmic and universal sickness markers, not disease manifestations in itself [40]. Hemorrhages are detected using the same detection technique. As a result, it is a crucial characteristic to think about. If they are tiny, they seem to be microaneurysms; they manifest as MA distortion in the retina's interior layers, including the outer area of natural and interior nuclear layers. Red lesions are another name for haemorrhages.
Number of respiratory secretions	Any fluid that filters into lesions or regions of inflammation from the circulatory system is called an exudate. Serum, fibrin, and white blood cells make up the fluid. Cuts, infection, and inflammation can all cause exudates [38]. However, there was no discernible change in the quantity of exudates between average and DR-affected picture.
Swelling	The formation of liquids within the macula, the area of the retina responsible for detailed central vision. the centre area of the retina, is specify as macular edoema. The macula is a region of the retina that is mainly accountable for eyesight that is clear and direct [41]. The retina is the light-sensitive and delicate tissue behind the

	eye. Edema does not induce diabetic retinopathy, according to the above research analysis.
The junction of two blood vessels	Bifurcation is the splitting of a blood vessel, creating two or more branches. Filtering methods that function by optimizing the responsiveness of a ship structure are used in the general class of ship segmentation procedures. As observed in [48], the average of normal fundus images is much higher than the average of diabetic images. As a result, it is a useful accent to be considered.
Entropy of Shannon	Shannon entropy is the anticipated arithmetic mean of a data provided from each transmission. Any flow of information can be used to simulate or display messages[42]. Diabetic retinopathy photos have a much lower entropy value than normal ones.
LBP entropy	LBP is a superior texture description operator that requires less computation and is light interference resistant. However, the characteristics chosen by LBP mostly include textual information about the input, not information about shape.
LBP energy	In glaucoma, LBP energy is much decreased, and alpha-LBP function is provided. This suggests that glaucoma has more structural alterations than other eye diseases [44].
Microaneurysm	Microaneurysms are seen in the retina of diabetics' eyes [45]. The existence of MA in the diabetic picture may be seen by detecting it and comparing it to the normal image. Patients with DR are usually asymptomatic in primary condition or situation; Patients may experience symptoms including distortion, floaters, and poor vision as the situation worsens. Microaneurysms are the most common early sign of diabetic retinopathy.
Exudates Area	Hard exudates are the yellow specks on the skin. They're lipid leakage residues from injured capillaries. Diabetes is the most prevalent cause of the aforementioned symptoms[46][41]. It may be found in all phases of the DR process. As a result, it must be regarded a significant characteristic.

Pre-processing:

In this we are going to use Preprocessing, feature ranking and segmentation are used to determine to an existence of diabetic retinopathy. For an assurance that the dataset is consistent and only displays important characteristics, preprocessing is necessary [9].

The Guided Image Filtering (edge-preserving filtering) [3]

Edge Preserving Guided Image Filtering (EGIF) is a contrast enhancement approach that is used to enhance sharp edges, aside from flattening low-gradient zones. Diabetic retinopathy results in progressive destruction to the retina's capillaries and arteries, leaving traces and lesions in the retinal tissue. These lesions show as boundaries, and when processing retinal pictures, the goal is to highlight these boundaries so that DR symptoms can be diagnosed more accurately. This is why it's important to take advantage of the advantages of guided picture filtering. Edge-save smoothing and filtering are performed on specific photos using guided filters, which are based on another image termed a guided image [13]. The guided image can be the original image, a modified or updated version of original image, or something entirely new. [14].

The Principal Component Analysis [3]

The Principal Component Analysis is a strong computer approach that transforms a set of associated features into a reduced set of characteristics are said to be principle elements using complex mathematical ideas. According to the typical image with integrated projections onto the subspace formed by the orthogonal axis approach, the data recorded in the dataset is recovered in reduced dimensions in PCA. Important data features are given with minimal data loss using dimensionally compressed computational information. Many applications benefit from this decrease, including picture compression and data representation. PCA is therefore employed in a variety of biological imaging applications. Pattern detection for high-dimensional data and emphasize extraction, image decomposition, image registration, image fusion, image segmentation, and image noise removal are examples of face recognition and picture compression. **Linear**

Discriminant Analysis (LDA)

A statistical, pattern recognition, and machine learning method for determining a linear combination of variables that classifies or separates two or more classes of objects or occurrences is Fisher's linear discriminant, which is expanded upon by discriminant function analysis, also known as normal discriminant analysis (NDA). Prior to further classification, the combined output is often utilized to reduce entropy. It may also be used as a linear classifier.

Data augmentation [3]

When the dataset contains just a little amount of training data, the data augmentation approach is critical in assisting the network in learning the required invariance and healthiness features. Data augmentation refers to a collection of techniques for increasing the amount and efficiency of data sets. Horizontal flipping, random crop, scale transformation, rotation, translation and noise disruption are some of the data augmentation techniques that may be used to enhance a dataset.

This research classifying the images of retina of diabetic patient into five labels numbered from 0 to 4 where each label named as Normal, Mild non-proliferative, Moderate non-proliferative, Severe non-proliferative and proliferative. To achieve the accuracy we are using image processing system to improve the input quality of image before extracting the features and deep learning CNN model will use in combination of Principal Component Analysis (PCA) and Linear Discriminant Analysis(LDA) for multi class classification and to get the accuracy in the result.

Scope of Research:

Regular eye checkup is necessary for detecting and treating diabetic retinopathy early. Regular eye checkup can help diagnose people with diabetes at an early stage, enabling fluctuations as a linear classifier or, more typically, to reduce dimensionality before further classification, the resulting combination can be utilized. This research is important because it will help to solve the present challenges in the diabetic retinopathy screening procedure.

Ophthalmologists currently employ non-mydratic fundus cameras to collect the retinal images for clinical analysis. The professional screening specialists will determine whether or not patients have any abnormalities based on the image obtained by the fundus camera (including diabetic retinopathy). Screeners manually examine any changes (abnormalities) on the retinal picture to determine the correct diagnosis. This procedure is both time-consuming and prone to mistake.

This study employed an image processing-based methodology. The goal of adopting this strategy is to identify specific traits that are responsible for diabetic retinopathy. It has been discovered that using deep learning CNN model-based classifiers to extract features from raw photos results in more accurate predictions.

The scope of this research classifying the images of retina of diabetic patient into five labels numbered from 0 to 4 where each label named as Normal, Mild non-proliferative, Moderate non-proliferative, Severe non-proliferative and proliferative. To achieve the accuracy we are using image processing system to improve the input quality of image before extracting the features and deep learning CNN model will use in combination of Principal Component Analysis (PCA) and Linear Discriminant Analysis(LDA) for multi class classification and to get the accuracy in the result.

About Proposed Model:

In our proposed model consist of a useful convolutional neural network architecture. First Preprocessing is to be done on retinal images provided to the model [3]. Deep supervised learning designs provide significantly high efficiency and realization in real-world use, in addition to traditional supervised and unsupervised strategies. This proposed research uses image processing system using deep learning CNN model to influenced neural networks and incorporates the rest of the feedback connections to enable low-level feature migration and reuse. There are many issues associated with training very deep neural networks. Due to the potential for the gradient to disappear, the forward current is often reduced and the training period can be cruelly delayed [3]. To overcome these problems, it was introduced to reuse the low-level properties of the shallow layer to take advantage of the prosperity of deep CNNs in recent years. Skipping the remaining links is an efficient and comprehensive classification procedure that uses a bearing design that integrates high-stage functions of dense layers and coffee-degree features of sparse layers [3].

This proposed model can achieve the classification accuracy to efficiently identify diabetic retinopathy in early stage

References

1. I. Liu, T.Y.A. The Impact of COVID-19 on Diabetic Retinopathy Monitoring and Treatment. *Curr Diab Rep* 21, 40 (2021), Springer Nature.
2. JDiabetic retinopathy detection through deep learning techniques: A review Wejdan L. Alyoubi *, Wafaa M. Shalash, Maysoon F. Abulkhair, *Informatics in Medicine Unlocked* Volume 20, 2020.
3. A New Early Stage Diabetic Retinopathy Diagnosis Model Using Deep Convolutional Neural Networks and Principal Component Analysis Mali Mohammed hasan*, *Harun Uğuz Traitement du Signal*, Vol.37, No.5, 2020.
4. A critical review on diagnosis of diabetic retinopathy using machine learning and deep learning Dolly Das, Saroj Kr. Biswas, Sivaji Bandyopadhyay National Institute of Technology Silchar, Cachar, Assam, India *Multimedia Tools and Applications* <https://doi.org/10.1007/s11042-022-12642-4>
5. Automated microaneurysms detection for early diagnosis of diabetic retinopathy: A Comprehensive review Veena Mayya , Sowmya Kamath S, Uma Kulkarni *Computer Methods and Programs in Biomedicine Update* <https://doi.org/10.1016/j.cmpbup.2021.100013>
6. Diabetic Retinopathy: Present and Past Ankita Gupta, Rita Chhikara published in *Procedia Computer Science* Volume 132, 2018, Pages 1432-1440 <https://doi.org/10.1016/j.procs.2018.05.074>
7. 7. Diabetic Retinopathy Detection Using Semantic Segmentation And Optic Disc Localization swathy K.P a and Dr. D.Vimal Kumar DOI: <https://doi.org/10.18280/ts.370503>
8. Presentation of a Segmentation Method for a Diabetic Retinopathy Patient's Fundus Region Detection Using a Convolution Neural Network Amin Valizadeh , Saeid Jafarzadeh Ghouschi, Ramin Ranjbarzadeh, and Yaghoub Pourasad Hindawi *Computational Intelligence and Neuroscience* Volume 2021, Article ID 7714351, 14 pages <https://doi.org/10.1155/2021/7714351>
9. Diabetic Retinal Fundus Images: Preprocessing and Feature Extraction For Early Detection of Diabetic Retinopathy DILIP SINGH SISODIA, SHRUTI NAIR and POOJA KHOBRAGADE National Institute of Technology Raipur, India. <http://dx.doi.org/10.13005/bpj/1148>
10. Ensemble of multi-stage deep convolutional neural networks for automated grading of diabetic retinopathy using image patches V. Deepa a, C. Sathish Kumar, Thomas Cherian *Computer and Information Sciences* <https://doi.org/10.1016/j.jksuci.2021.05.009> 1319-1578/ 2021
11. Ibrahim Kandel, Mauro Castelli. Transfer Learning with Convolutional Neural Networks for Diabetic Retinopathy Image Classification. *A Review Appl. Sci.* 2020, 10, 2021; doi:10.3390/app10062021
12. Automated Detection and Diagnosis of Diabetic Retinopathy: A Comprehensive Survey asudevan Lakshminarayanan 1,* , Hoda Kheradfallah 1, Arya Sarkar 2 and Janarthanam Jothi Balaji J. *Imaging* 2021, 7, 165. <https://doi.org/10.3390/jimaging7090165>
13. He, K., Sun, J., Tang, X. (2010). Guided Image Filtering. In: Daniilidis K., Maragos P., Paragios N. (eds) *Computer Vision – ECCV 2010*. ECCV 2010. Lecture Notes in Computer Science, vol 6311. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-15549-9_1
14. Paris, S., Kornprobst, P., Tumblin, J., Durand, F. (2008). Bilateral filtering: Theory and applications. *Foundations and Trends in Computer Graphics and Vision*, 4(1): 1-73. <https://doi.org/10.1561/06000000020>
15. M. R. K. Mookiah, U. R. Acharya, R. J. Martis, C. K. Chua, C. M. Lim, E. Y. K. Ng, and A. Laude, "Evolutionary algorithm based classifier parameter tuning for automatic diabetic retinopathy grading: A hybrid feature extraction approach," in *Knowledge-Based Systems*, 39: pp. 9–22 (2013).
16. Taylor R, Batey D. *Handbook of retinal screening in diabetes: diagnosis and management*. second ed. John Wiley & Sons, Ltd Wiley-Blackwell; 2012.
17. International diabetes federation - what is diabetes [Online]. Available, <https://www.idf.org/aboutdiabetes/what-is-diabetes.html>.
18. American academy of ophthalmology-what is diabetic retinopathy? [Online]. Available, <https://www.aao.org/eye-health/diseases/what-is-diabetic-retinopathy>.
19. Bourne RR, et al. Causes of vision loss worldwide, 1990-2010: a systematic analysis. *Lancet Global Health* 2013;1(6):339–49.
20. Harper CA, Keeffe JE. Diabetic retinopathy management guidelines. *Expet Rev Ophthalmol* 2012;7(5):417–39.
21. E. T. D. R. S. R. GROUP. Grading diabetic retinopathy from stereoscopic color fundus photographs- an extension of the modified Airlie House classification. *Ophthalmology* 1991;98(5):786–806.
22. Scanlon PH, Wilkinson CP, Aldington SJ, Matthews DR. *A Practical manual of diabetic retinopathy management*. first ed. Wiley-Blackwell; 2009.
23. Dubow M, et al. Classification of human retinal microaneurysms using adaptive optics scanning light ophthalmoscope fluorescein angiography. *Investig Ophthalmol Vis Sci* 2014;55(3):1299–309.
24. deng Li. A tutorial survey of architectures, algorithms, and applications for deep learning. *APSIPA Trans. Signal Inf Process* 2014;3(2):1–29.
25. V Vasilakos A, Tang Y, Yao Y. Neural networks for computer-aided diagnosis in medicine : a review. *Neurocomputing* 2016;216:700–8.
26. Wilkinson CP, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Am Acad Ophthalmol* 2003;110(9): 1677–82.

27. Chen XW, Lin X. Big data deep learning: challenges and perspectives. *IEEE Access* 2014;2:514–25.
28. Guo Y, Liu Y, Oerlemans A, Lao S, Wu S, Lew MS. Deep learning for visual understanding: a review. *Neurocomputing* 2016;187:27–48.
29. Deng L, Yu D. Deep learning: methods and applications. *Found Trends® Signal Process* 2014;7(3–4):197–387.
30. Bakator M, Radosav D. Deep learning and medical diagnosis: a review of literature. *Multimodal Technol Interact* 2018;2(3):47.
31. Mookiah M, Acharya UR, Kuang C, Min C, Ng EYK, Laude A. Computer-aided diagnosis of diabetic retinopathy : a review. *Comput Biol Med* 2013;43:2136–55.
32. Krizhevsky A, Sutskever I, Hinton GE. ImageNet classification with deep convolutional neural networks. *Commun ACM* 2017;60(6). [20] Szegedy C, Vanhoucke V, Ioffe S, Shlens J, Wojna Z. Rethinking the inception architecture for computer vision. In: *IEEE Conference on computer Vision and pattern recognition*; 2016. p. 2818–26.
33. He K, Zhang X, Ren S, Sun J. Deep residual learning for image recognition. In: *IEEE Conference on computer Vision and pattern recognition*; 2016. p. 770–8.
34. Esfahani MT, Ghaderi M, Kafiye R. Classification of diabetic and normal fundus images using new deep learning method. *Leonardo Electron J Pract Technol* 2018; 17(32):233–48.
35. Li T, Gao Y, Wang K, Guo S, Liu H, Kang H. Diagnostic assessment of deep learning algorithms for diabetic retinopathy screening. *Inf Sci* 2019;501:511–22.
36. Abramoff MD, Garvin MK, Sonka M. Retinal imaging and image analysis. *IEEE Rev Biomed Eng* 2010;3:169–208.
37. Kauppi T, et al. The DIARETDB1 diabetic retinopathy database and evaluation protocol. In: *Proceedings of the British machine vision conference* 2007; 2007. p. 1–10.
38. S. J. H. Yancopoulos, G. D., Davis, S, Gale, N. W., Rudge, J. S., Wiegand, “Vascular-specific growth factors and blood vessel formation,” *Nature*, (2000).
39. G. Bergers and S. Song, “The role of pericytes in blood-vessel formation and maintenance.,” *Neuro. Oncol.*, 7(4): pp. 452–464 (2005).
40. C. I. Sánchez, R. Hornero, M. I. López, M. Aboy, J. Poza, and D. Abásolo, “A novel automatic image processing algorithm for detection of hard exudates based on retinal image analysis.,” *Med. Eng. Phys.*, 30(3): pp. 350–7 (2008).
41. L. Giancardo, F. Meriaudeau, T. P. Karnowski, Y. Li, S. Garg, K. W. Tobin, and E. Chaum, “Exudate-based diabetic macular edema detection in fundus images using publicly available datasets,” *Med. Image Anal.*, 16(1): pp. 216–226 (2012).
42. J. Lin, “Divergence measures based on the Shannon entropy,” *IEEE Trans. Inf. theory*, 37(1): pp. 145–151 (1991).
43. M. Kaufman, U. Zurcher, and P. S. Sung, “Entropy of electromyography time series,” *Phys. A Stat. Mech. its Appl.*, 386(2): pp. 698–707 (2007).
44. R. Szeliski, R. Zabih, D. Scharstein, O. Veksler, V. Kolmogorov, A. Agarwala, M. Tappen, and C. Rother, “A Comparative Study of Energy Minimization Methods for Markov Random Fields A Comparative Study of Energy Minimization Methods for MRF’s,” *Part II LNCS*, 3952, pp. 16–29 (2006).
45. M. Niemeijer, B. Van Ginneken, M. J. Cree, S. Member, A. Mizutani, B. Zhang, R. H. Member, M. Lamard, C. Muramatsu, X. Wu, G. C. Member, J. You, Q. Li, Y. Hatanaka, C. Roux, and F. Karray, “Retinopathy Online Challenge/ : Automatic Detection of Microaneurysms in Digital Color Fundus Photographs,” 1: pp. 185– 195 (2010).
46. T. Walter, J.-C. Klein, P. Massin, and A. Erginay, “A contribution of image processing to the diagnosis of diabetic retinopathy—detection of exudates in color fundus images of the human retina.,” *IEEE Trans. Med. Imaging*, 21(10): pp. 1236– 1243 (2002).
47. “MBW:Optimum Design Of Blood Vessel Bifurcation.” [Online]. Available:https://mathbio.colorado.edu/index.php/MBW:Optimum_Design_of_Blood_Vessel_Bifurcation.
48. J. Lachure, A. V. Deorankar, S. Lachure, S. Gupta, and R. Jadhav, “Diabetic Retinopathy using morphological operations and machine learning,” in *Souvenir of the 2015 IEEE International Advance Computing Conference, IACC 2015*, pp. 617–622 (2015).
49. “Kaggle Diabetic Retinopathy Detection,” 2015.[Online]. Available: <https://www.kaggle.com/c/diabetic-retinopathy-detection>.