A Review on Methods for Automated Detection of Diabetic Retinopathy in Retinal Images

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Abstract— **Diabetic retinopathy is a condition that can lead to blindness due to fluctuation in sugar levels causing blockage to the blood vessels and ceasing blood supply. Early screening of diabetic retinopathy is based on features like micro-aneurysms, hemorrhage, hard exudates, neovascularization and macular edema which assist the ophthalmologist in detecting vitreous hemorrhage, retinal detachment, glaucoma, and blindness. In this paper, we review various algorithms used to extract these features from retinal images and portrays a comparison of performance metrics such as Accuracy (Acc), Sensitivity (SN), Specificity (SP) evaluated on retinal images. Manual detection is a tedious and time-consuming task, so automated algorithms are utilized for the attainment of task correctly. However, the paper is intended to give the user a framework for existing algorithms, discussing current problems and future scope.**

Keywords— Diabetic retinopathy, micro-aneurysms, exudates, retinal images, hemorrhage, macular edema.

I. INTRODUCTION

Diabetic retinopathy holds a major concern if left untreated over the years may lead to blindness. The occurrence of diabetic retinopathy is 80% in diabetic patients suffering for 20 years. The researches forecast that diabetes among individuals will hike up to 366 million in 2030 [1]. Diabetic retinopathy eventuates in both type-1 and type-2 diabetes and damages both the eyes. Diabetic retinopathy is a problem that occurs when the blood vessels of light-sensitive tissues are damaged at the back of the retina. As the condition worsens the symptoms that come into the acknowledge are blurred visions, impaired color vision, dark or empty areas in the vision, vision loss and eye floaters. The risk factor of diabetic retinopathy is enormously high in case of high blood pressure, high cholesterol, diabetic kidney diseases, genetically procured diabetes or fluctuations in sugar blood level.

Causes:

Variation in sugar level over the years may lead to the blockage of tiny vessels by cutting off its blood supply. Mainly diabetic retinopathy is of two types; proliferative (PDR) and non-proliferative (NPDR) [2].

- Proliferative Diabetic Retinopathy is dreadful such that it intimidates the vision. When there is less blood supply to the retina, it encourages the formation of new vessels which bud at the center of the eye. The new vessels are abnormal and fragile that it leaks out the fluid and bleeds assisting the formation of scar tissues, causing complications such as vitreous hemorrhage and retinal detachment.
- In Non-proliferative Diabetic retinopathy [3], the walls become thin and swell out configuring micro-aneurysm which leaks out some fluid and blood into the retina. Blood vessels may then begin to distort and blocks the area to starve oxygen and nutrients.

Complications:

Diabetic retinopathy can lead to many serious complications if left untreated over time. The complications are:

- Vitreous hemorrhage [4] occurs when the blood exudes around the areas of vitreous humor (which is a jelly in between the lens and retina) of the eye leading to several conditions such as floaters and impaired visions.
- In Retinal detachment, the retina is separated out from the back of the eye due to the germination of scar tissue. Symptoms include floaters, flashes of light and vision loss.
- Glaucoma [5] is a disease in which if the fluid pressure within the eye is left untreated, increases causing damage to the optic nerve and may lead the patient to severe vision loss.
- Blindness is caused by both diabetic retinopathy and glaucoma.

Feature-based Detection methods:

Diabetic retinopathy can be detected based on some features such as micro-aneurysms, hemorrhages, hard exudates, neovascularization. Early screening is a predominant step for the detection of diabetic retinopathy and conducting the treatment. Manual detection is a tedious task and the occurrence of erroneous results increases, so automated methods are taken in account to carry out the treatment process.

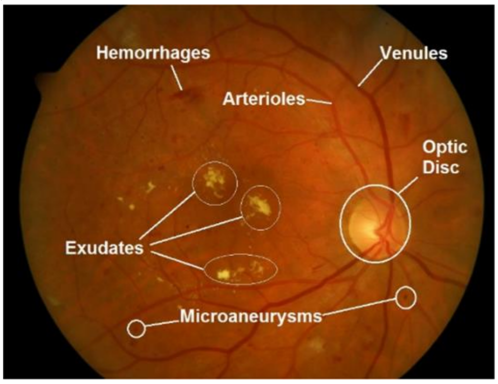

Figure 1. Different attributes of Diabetic Retinopathy

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Features of diabetic retinopathy:

- Micro-aneurysm [6] is the premature sign of diabetic retinopathy, is a small bulge manifested on the walls of vessels which may cut-off and lead to leakage around the areas.
- Hemorrhage [7] is a disease in which bleeding takes place in the retina, defined as blot or a dot.
- Hard exudates [8] are the accumulation of white or yellow leakage from the damaged capillaries, whereas the soft exudates are the cotton wool spots.
- Neovascularization [9] is the emergence of new blood vessels over the retina.
- Macular edema [10] is an acute condition, if left untreated may lead to vision loss. It occurs due to the leakage of blood vessels in the light-sensitive part.

The main aim of the paper is to review various algorithms used to extract these features from retinal images and portrays a comparison of performance metrics such as Accuracy (Acc), Sensitivity (SN), Specificity (SP) evaluated on retinal images. Organization of the paper is as follows: SECTION 2 reviews various detection methods. A detailed discussion based on various comparison metrics is presented in SECTION 3 followed by a conclusion in SECTION 4.

II. RELATED WORK

Shin et al. [11] proposed a computer-assisted automated method to macular drusen in fundus images, utilizing local thresholding and region-growing algorithm where the green channels are chosen to maximize contrast and preprocessing to reduce noise, contrast refining. Image analysis and statistical classification based algorithm is propound by M. Ege et al. [12], employing statistical classifier, a Bayesian and a Mahalanobis and a KNN classifier for which Mahalanobis outperforms best results in diagnosing micro-aneurysms, hemorrhage, exudates and cotton wool spots with a sensitivity of 69%, 83%, 99%, and 80%, respectively.

Walter et al. [13] bid a model to detect exudates and their contours by applying morphological reconstruction, whereas morphological filtering in combination with watershed transformation is then used to detect optic disc which is a requisite approach. The result evaluates a sensitivity of 92.8%. Sinthanayothin et al. [14] presented a system for automated screening of diabetic retinopathy incorporating multilayer perceptron neural network where the inputs are obtained from PCA (principal component analysis). Recursive region growing segmentation is used to detect hard exudates. The method measures 80.21% of sensitivity and 70.66% of specificity.

Gabor filters are employed to detect the abnormalities in diabetic retinopathy is proposed by Vallabha et al. [15]. The propound method categorizes the retinal image as mild or severe. D. Fleming et al. [16] put forward an automated technique using a watershed transform to obtain an area containing no lesion. Contrast normalization refines potentiality to classify micro-aneurysms and other dots which are managed by local vessel detection method, for which it measures 85.4% sensitivity and 83.1% specificity. Abramoff and Niemeijer [17] proposed a method to detect the position of the optic disc using KNN regression, originating a regression model. With the help of preceding segmented vessels, all other vessel pixels are explored using regression model in the optic disc. The outcome is blurred to handle noise and the point in the middle is chosen.

Walter et al. [18] presented an approach that uses diameter closing and kernel density estimation, ensuring no such features of diabetic retinopathy to be missed. The performance measures 88.5% sensitivity. Nayak et al. [19] propound an automated method to pinpoint diabetic retinopathy stages, which amalgamates morphological operations and texture analysis methods to perceive features like areas of heard exudates, blood vessels, and contrast which are then fed to the artificial neural network (ANN) as an input for classification. The proposed method outperforms an accuracy of 93%, sensitivity of 90% and specificity of 100%.

A new mechanism is described by Hatanaka et al. [20], which incorporates preprocessing and false-positive elimination. On combining hue saturation values (HSV) with a non-linear curve, the brightness is improved. The histograms of each red, green and blue-bit images are also expanded and with the help of density analysis the hemorrhage candidates are identified. The false-positive are then detached using a rule-based method and 3 Mahalanobis distance classifier which outperforms with a sensitivity of 80% and specificity of 80%.

Sopharak et al. [21] bid an automated method for the detection of exudates from the non-dilated pupil and low-contrast images using mathematical morphology. The result evaluates 80% of sensitivity and 99.5% of specificity.

Sanchez et al. [22] presented an algorithm using Fisher's linear discriminant analysis for the detecting exudates in the retinal images. The performance is evaluated on the basis of lesion-based criterion and image-based criterion, such that hard exudates are detected on the basis of lesion criterion utilizing statistical classification and Krisch operator with a sensitivity of 88% and accuracy is 100%. Li Yun et al. [23] put forward a three-layer Neural network to categorize different stages of diabetic retinopathy, where the extracted features are fed to the classifier for classification. The measured results are 91.7% sensitivity and 100% specificity.

Multiscale analysis and kernel-based anomaly detection are proposed by E. Freund et al. [24], so as to meet the difficulties in detecting and locating drusen. Fixed and the variable threshold is demonstrated by Reza et al. [25], incorporating a green bit of image for preprocessing like thresholding, filtering and contrast adjustment with morphological opening, maxima operator, minima imposition and watershed transformation. The proposed method yields 96.7% sensitivity and 100% specificity. Nayak et al. [26] propound an automated method for detecting glaucoma, utilizing morphological operations and thresholding. The features are bifurcated to distinguish between normal and glaucoma images utilizing neural network classifier. The performance measures 100% of sensitivity and 80% of specificity.

An approach to localize different features and lesions in fundus images is presented by Ravishankar et al. [27], introducing a new constraint to detect optic disk for which major blood vessels are first observed and then their intersection is utilized to delimit optic disc. The presented

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technique yields sensitivity and specificity of 95.7% and 94.2%, respectively for identification of exudate and 95.1% and 90.5%, respectively to observe micro-aneurysm/hemorrhage. Kande et al. [28] proposed a method for the detection of red lesions in the digital fundus images based on pixel classification and mathematical morphology. The algorithm measures 100% sensitivity and 91% specificity.

Arguto et al. [29] propound a multiscale AM-FM method to detect diabetic retinopathy. For global classification, an amalgamation of supervised and unsupervised methods are utilized. H-maxima transformation and multi-level thresholding are utilized by Saleh and Eswaran [30], a decision support system that extracts the main component of the retina and yields 89.47% of specificity and 95.65% specificity. Harangi et al. [31] came up with an active contour model and region-wise classification for automatic detection of exudates utilizes grayscale morphology for discovering the areas comprising exudates. Active contour model is then applied which is based on Chan-Vase energy to remove the frontier of the candidates and finally region-wise classifier is used to detach false candidates. The proposed method evaluates 75% sensitivity.

Hatanaka et al. [32] presented a model based on the double-ring filter and feature analysis to discern micro-aneurysms. Automatic extraction is utilized to detach false positive which are corresponding to blood vessels. Artificial neural network and rule-based method categorize candidate lesions into micro-aneurysm and false positives, evaluating the sensitivity of 68%. Tariq et al. [33] put forward a system to detect macula using vascular structure and optic disc location. The binary map is generated for exudate region utilizing filter banks to construct a complete feature vector for all regions. The Gaussian mixture model is also employed using macula coordinates and exudates feature set. The propound method measures 97.2% sensitivity, 98.32% specificity, and 97.89% accuracy.

The three-stage system is incorporated by U. Akram et al. [34] to detect micro-aneurysm timely utilizing filter banks. Candidate regions are separated in the first step, followed by classifying them into micro-aneurysm or non micro-aneurysm producing feature vector for each region. A hybrid classifier is presented in ensemble combining the Gaussian mixture model (GMM), the Support vector machine (SVM) and an augmentation of multi-model mediod based modeling approach to refine accuracy. The result evaluates a sensitivity of 98.64%, specificity of 99.69% and an accuracy of 99.40%.

Akram et al. [35] proposed a model utilizing a feature set and Gaussian mixture model (GMM) classifier. The ensemble of GMM and support vector machine to advance the diagnosis of exudate with the existence of bright lesions. The system evaluates the sensitivity of 97.3%, specificity of 95.9% and accuracy is 96.8%.

Kaur et al. [36] presented a supervised approach combining morphological operations and random forest-based classifiers to detect hemorrhages in the retinal images. The proposed algorithm achieves a sensitivity of 90.42% and specificity of 93.53%. Singh et al. [37] propound an automated detection of glaucoma using wavelet features. The bifurcated features of the optic disc are much more significant such that it results in 94.7% of accuracy.

A cuckoo search optimization algorithm is incorporated by Atlas and Parasuraman [38] to detect hemorrhage in retinal images, employing ANFIS classification to partition the affected and non-affected images and FCM-CS to bifurcate the affected images. The proposed method achieves 97.3% accuracy. Canche et al. [39] bid an Adaboost color algorithm which assists in maintaining the shape, color and increasing the division between the image background and the structure of the retina. Feature selection is acclaimed by utilizing scalar selection and vector selection. The presented method evaluates 83.51% sensitivity, 96.66% specificity, and 94.12% accuracy. Schlegl et al. [40] proposed a deep learning method to detect intra retinal cystoid fluid (IRC) and subretinal fluid (SRF) in OCT images, correctly evaluates the presence of fluid at a particular place.

III. DISCUSSION

The diabetes is a serious condition if left untreated for a longer period of time, may lead to the formation of micro-aneurysms, exudates, and hemorrhage which are features of diabetic retinopathy. These devastating features may also cause vision loss or even blindness. So, as to avoid such complication early screening is very necessary to detect the disease on time and accomplish the treatment. Manual detection is troublesome task and chances of errors increases, so automated methods are taken into account for detection at early stages resulting in more accuracy than the manual methods.

In the preceding section, we reviewed some automated methods which are utilized for detection of hard exudates, macular edema, tracing optic disc, hemorrhage, and glaucoma for grading diabetic retinopathy in retinal fundus images and based on that review a comparison of performance metrics using different detection methods is given in table1.

Table 1. Comparison of different detection methods

Author	Year	Methods	SN	SP	Acc	Section
M. Ege et al. [12]	2000	Statistical classification	99%	Not reported	Not reported	Supervised learning based classification
Sinthanayothin et al. [14]	2004	Multi-layer perceptron Neural Network	80.21%	70.66%	Not reported	
Vallabha et al. [15]	2005	Gabor filter	Not reported	Not reported	Not reported	
Abramoff and Niemeijer [17]	2006	K-NN regression	Not reported	Not reported	Not reported	
Walter et al. [18]	2007	Diameter closing and kernel density estimation	88.50%	Not reported	Not reported	
Nayak et al. [19]	2007	Morphological techniques and texture analysis method	90%	100%	93%	

Hatanaka et al. [20]	2008	Pre-processing and false positive elimination	80%	80%	Not reported	
Sanchez et al. [22]	2008	Statistical classification	88%	Not reported	100%	
Li Yun et al. [23]	2008	Three layer feed forward Neural network	91.70%	100%	Not reported	
E. Freund et al. [24]	2009	Multiscale analysis and kernel based anomaly detection	Not reported	Not reported	Not reported	
Hatanaka et al. [32]	2012	Double-ring filter and feature analysis	68%	Not reported	Not reported	
Tariq et al. [33]	2013	Gaussian mixture model	97.20%	98.32%	97.89%	
U. Akram et al. [34]	2013	Three stage system	98.64%	99.69%	99.40%	
Akram et al. [35]	2014	Hybrid classifier	97.30%	95.90%	96.80%	
Singh et al. [37]	2016	Wavelet features	Not reported	Not reported	94.70%	
Canche et al. [39]	2017	Adaboost color algorithm	83.51%	96.66%	94.12%	
Shin et al. [11]	1999	Local thresholding and region growing algorithm	Not reported	Not reported	Not reported	Unsupervised learning based classification
Walter et al. [13]	2002	Morphological operations	92.80%	Not reported	Not reported	
D. Fleming et al. [16]	2006	Watershed transform	85.40%	83.10%	Not reported	
Sopharak et al. [21]	2008	Mathematical morphology	80%	99.50%	Not reported	
Reza et al. [25]	2009	Fixed and variable thresholds	96.70%	100%	Not reported	
Nayak et al. [26]	2009	Morphological operations and thresholding	100%	80%	Not reported	
Ravishankar et al. [27]	2009	Features localization	95.70%	94.20%	Not reported	
Kande et al. [28]	2010	Pixel classification and mathematical morphology	100%	91%	Not reported	
Agurto et al. [29]	2010	Multiscale AM-FM	Not reported	Not reported	Not reported	
Saleh and Eswaran [30]	2012	h-maxima transformation and multi-level thresholding	89.47%	95.65%	Not reported	
Harangi et al. [31]	2012	Active contour model and regionwise classifier	75%	Not reported	Not reported	
Atlas and Parasuraman [38]	2017	Cuckoo search optimization algorithm	Not reported	Not reported	97.30%	
Schlegl et al. [40]	2018	Deep learning	Not reported	Not reported	Not reported	
Kaur et al. [36]	2016	Combination of Morphological operations and random forest based classifiers	90.42%	93.53%	Not reported	Combined Classification(both)

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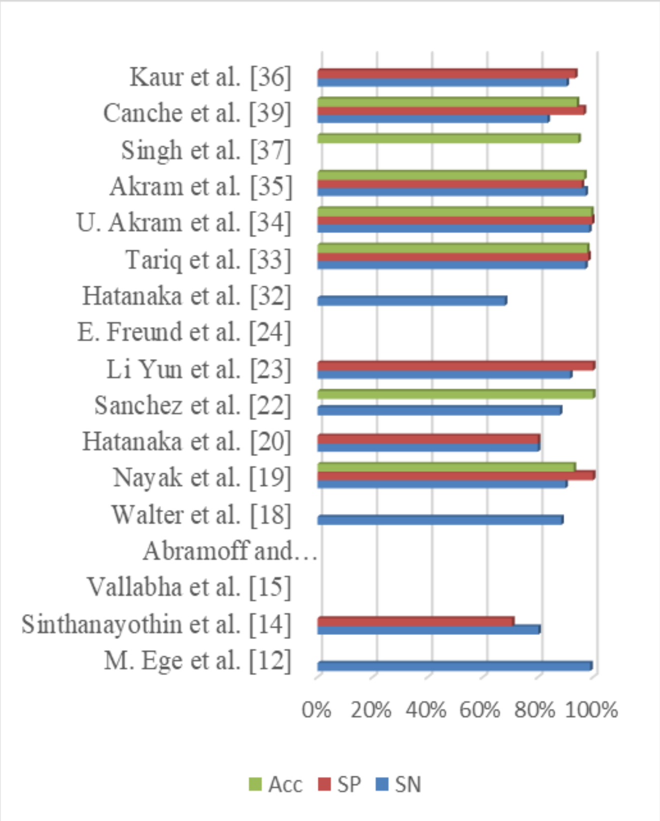

Figure2. Comparison of SN, SP, and Acc in Supervised learning-based classification

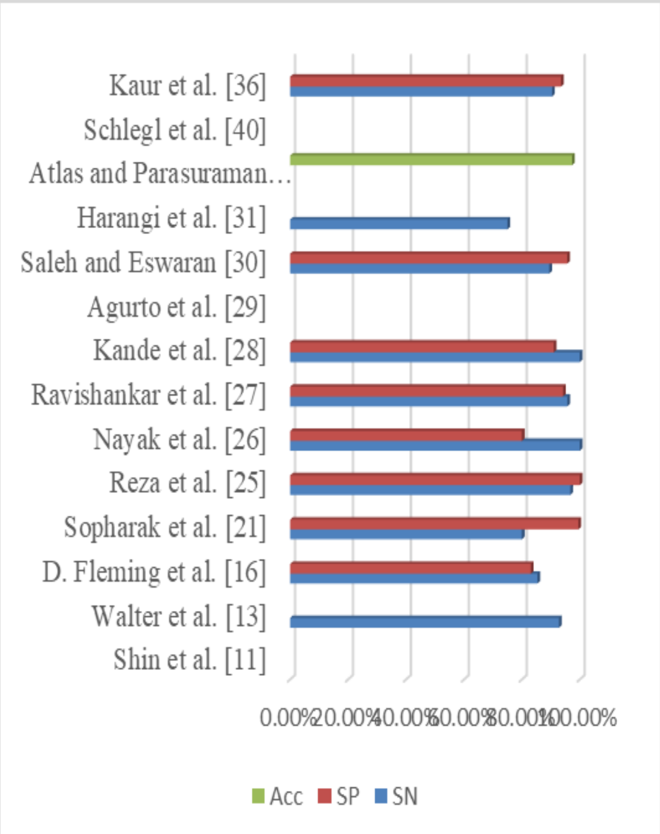

Figure3. Comparison of SN, SP, and Acc in Unsupervised learning-based classification

IV. CONCLUSION

Diabetic retinopathy is mainly seen in diabetic patients and can happen in people with both type 1 and type 2 diabetes which may lead to damage both the eyes. If it is left untreated over time, it may lead to severe vision loss or even blindness. The early detection of the eye disease is very necessary, so the ophthalmologist can begin with the treatment in time to prevent the major complications such as vitreous hemorrhage, retinal detachment, glaucoma, and even blindness. An automated method is used for early detection based on some features such as; micro-aneurysm, hard and soft exudates, neovascularization, macular edema, and hemorrhage. And so regular screening for a diabetic patient is compulsory to prevent diabetic retinopathy, because if neglected it may lead to costly treatment which not only is affordable by everyone but also does not guarantee for complete recovery. Thereby automated screening of diabetic retinopathy is less expensive. Some of the articles are reviewed and are compared based on their performance metrics and are closed enough to achieve diabetic retinopathy identification in clinical practice.

V. REFERENCES

[1] S. Wild, G. Roglic, A. Green, R. Sicree, and H. King, “Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030,” *Diabetes Care*, vol. 27, no. 5, pp. 1047–1053, May 2004.

[2] O. Faust, R. Acharya U., E. Y. K. Ng, K. H. Ng, and J. S. Suri, “Algorithms for the automated detection of diabetic retinopathy using digital fundus images: A review,” *J. Med. Syst.*, vol. 36, no. 1, pp. 145–157, 2012.

[3] U. M. Akram and S. A. Khan, “Automated Detection of Dark and Bright Lesions in Retinal Images for Early Detection of Diabetic Retinopathy,” *J. Med. Syst.*, vol. 36, no. 5, pp. 3151–3162, Oct. 2012.

[4] L. Seoud, T. Faucon, T. Hurtut, J. Chelbi, F. Cheriet, and J. M. P. Langlois, “Automatic detection of microaneurysms and haemorrhages in fundus images using dynamic shape features,” in *2014 IEEE 11th International Symposium on Biomedical Imaging (ISBI)*, 2014, pp. 101–104.

[5] M. R. K. Mookiah, U. Rajendra Acharya, C. M. Lim, A. Petznick, and J. S. Suri, “Data mining technique for automated diagnosis of glaucoma using higher order spectra and wavelet energy features,” *Knowledge-Based Syst.*, vol. 33, pp. 73–82, Sep. 2012.

[6] B. Zhang, F. Karray, Q. Li, and L. Zhang, “Sparse Representation Classifier for microaneurysm detection and retinal blood vessel extraction,” *Inf. Sci. (Ny).*, vol. 200, pp. 78–90, Oct. 2012.

[7] P. Jitpakdee, P. Aimmanee, and B. Uyyanonvara, “A survey on hemorrhage detection in diabetic retinopathy retinal images,” in *2012 9th International Conference on Electrical Engineering/Electronics, Computer, Telecommunications and Information Technology*, 2012, pp. 1–4.

[8] D. Youssef and N. H. Solouma, “Accurate detection of blood vessels improves the detection of exudates in color fundus images,” *Comput. Methods Programs Biomed.*, vol. 108, no. 3, pp. 1052–1061, Dec. 2012.

[9] S. S. A. Hassan, D. B. L. Bong, and M. Premsenthil, “Detection of Neovascularization in Diabetic Retinopathy,” *J. Digit. Imaging*, vol. 25, no. 3, pp. 437–444, Jun. 2012.

[10] R. J. Qureshi, L. Kovacs, B. Harangi, B. Nagy, T. Peto, and A. Hajdu, “Combining algorithms for automatic detection of optic disc and macula in fundus images,” *Comput. Vis. Image Underst.*, vol. 116, no. 1, pp. 138–145, Jan. 2012.

[11] D. S. Shin, N. B. Javornik, and J. W. Berger, “Computer-assisted, interactive fundus image processing for macular drusen quantitation11The authors have no proprietary interest in any aspect of this study.,” *Ophthalmology*, vol. 106, no. 6, pp. 1119–1125, Jun. 1999.

[12] B. M. Ege *et al.*, "Screening for diabetic retinopathy using computer based image analysis and statistical classification," *Comput. Methods Programs Biomed.*, vol. 62, no. 3, pp. 165–175, Jul. 2000.

[13] T. Walter, J. 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*, vol. 21, no. 10, pp. 1236–1243, Oct. 2002.

[14] C. Sinthanayothin, V. Kongbunkiat, S. Phoojaruenchanachai, and A. Singalavanija, "Automated screening system for diabetic retinopathy," in *3rd International Symposium on Image and Signal Processing and Analysis, 2003. ISPA 2003. Proceedings of the*, 2004, vol. 2, pp. 915–920.

[15] D. Vallabha, R. Dorairaj, K. Namuduri, and H. Thompson, "Automated detection and classification of vascular abnormalities in diabetic retinopathy," in *Conference Record of the Thirty-Eighth Asilomar Conference on Signals, Systems and Computers, 2004.*, 2005, vol. 2, pp. 1625–1629.

[16] A. D. Fleming, S. Philip, K. A. Goatman, J. A. Olson, and P. F. Sharp, "Automated microaneurysm detection using local contrast normalization and local vessel detection," *IEEE Trans. Med. Imaging*, vol. 25, no. 9, pp. 1223–1232, Sep. 2006.

[17] M. D. Abramoff and M. Niemeijer, "The automatic detection of the optic disc location in retinal images using optic disc location regression," in *2006 International Conference of the IEEE Engineering in Medicine and Biology Society*, 2006, pp. 4432–4435.

[18] T. Walter, P. Massin, A. Erginay, R. Ordonez, C. Jeulin, and J.-C. Klein, "Automatic detection of microaneurysms in color fundus images," *Med. Image Anal.*, vol. 11, no. 6, pp. 555–566, Dec. 2007.

[19] J. Nayak, P. S. Bhat, R. Acharya U, C. M. Lim, and M. Kagathi, "Automated Identification of Diabetic Retinopathy Stages Using Digital Fundus Images," *J. Med. Syst.*, vol. 32, no. 2, pp. 107–115, Apr. 2008.

[20] Y. Hatanaka, T. Nakagawa, Y. Hayashi, T. Hara, and H. Fujita, "Improvement of automated detection method of hemorrhages in fundus images," in *2008 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2008, vol. 2008, pp. 5429–5432.

[21] A. Sopharak, B. Uyyanonvara, S. Barman, and T. H. Williamson, "Automatic detection of diabetic retinopathy exudates from non-dilated retinal images using mathematical morphology methods," *Comput. Med. Imaging Graph.*, vol. 32, no. 8, pp. 720–727, Dec. 2008.

[22] 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.*, vol. 30, no. 3, pp. 350–357, Apr. 2008.

[23] W. L. Yun, U. Rajendra Acharya, Y. V. Venkatesh, C. Chee, L. C. Min, and E. Y. K. Ng, "Identification of different stages of diabetic retinopathy using retinal optical images," *Inf. Sci. (Ny).*, vol. 178, no. 1, pp. 106–121, Jan. 2008.

[24] D. E. Freund, N. Bressler, and P. Burlina, "Automated detection of drusen in the macula," in *2009 IEEE International Symposium on Biomedical Imaging: From Nano to Macro*, 2009, pp. 61–64.

[25] A. W. Reza, C. Eswaran, and S. Hati, "Automatic tracing of optic disc and exudates from color fundus images using fixed and variable thresholds," *J. Med. Syst.*, vol. 33, no. 1, pp. 73–80, 2009.

[26] J. Nayak, R. Acharya U., P. S. Bhat, N. Shetty, and T. C. Lim, "Automated diagnosis of glaucoma using digital fundus images," *J. Med. Syst.*, vol. 33, no. 5, pp. 337–346, 2009.

[27] S. Ravishankar, A. Jain, and A. Mittal, "Automated feature extraction for early detection of diabetic retinopathy in fundus images," in *2009 IEEE Conference on Computer Vision and Pattern Recognition*, 2009, vol. 2009 IEEE, pp. 210–217.

[28] G. B. Kande, T. S. Savithri, and P. V. Subbaiah, "Automatic detection of microaneurysms and hemorrhages in digital fundus images," *J. Digit. Imaging*, vol. 23, no. 4, pp. 430–437, 2010.

[29] C. Agurto *et al.*, "Multiscale AM-FM Methods for Diabetic Retinopathy Lesion Detection," *IEEE Trans. Med. Imaging*, vol. 29, no. 2, pp. 502–512, Feb. 2010.

[30] M. D. Saleh and C. Eswaran, "An automated decision-support system for non-proliferative diabetic retinopathy disease based on MAs and HAs detection," *Comput. Methods Programs Biomed.*, vol. 108, no. 1, pp. 186–196, Oct. 2012.

[31] B. Harangi, I. Lazar, and A. Hajdu, "Automatic exudate detection using active contour model and regionwise classification," in *2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2012, pp. 5951–5954.

[32] Y. Hatanaka, T. Inoue, S. Okumura, C. Muramatsu, and H. Fujita, "Automated microaneurysm detection method based on double-ring filter and feature analysis in retinal fundus images," in *2012 25th IEEE International Symposium on Computer-Based Medical Systems (CBMS)*, 2012, vol. 7260, pp. 1–4.

[33] A. Tariq, M. U. Akram, A. Shaukat, and S. A. Khan, "Automated detection and grading of diabetic maculopathy in digital retinal images," *J. Digit. Imaging*, vol. 26, no. 4, pp. 803–812, 2013.

[34] M. U. Akram, S. Khalid, and S. A. Khan, "Identification and classification of microaneurysms for early detection of diabetic retinopathy," *Pattern Recognit.*, vol. 46, no. 1, pp. 107–116, Jan. 2013.

[35] M. U. Akram, A. Tariq, S. A. Khan, and M. Y. Javed, "Automated detection of exudates and macula for grading of diabetic macular edema," *Comput. Methods Programs Biomed.*, vol. 114, no. 2, pp. 141–152, Apr. 2014.

[36] N. Kaur, S. Chatterjee, M. Acharyya, J. Kaur, N. Kapoor, and S. Gupta, "A supervised approach for automated detection of hemorrhages in retinal fundus images," in *2016 5th International Conference on Wireless Networks and Embedded Systems (WECON)*, 2016, pp. 1–5.

[37] A. Singh, M. K. Dutta, M. ParthaSarathi, V. Uher, and R. Burget, "Image processing based automatic diagnosis of glaucoma using wavelet features of segmented optic disc from fundus image," *Comput. Methods Programs Biomed.*, vol. 124, pp. 108–120, Feb. 2016.

[38] L. G. Atlas and K. Parasuraman, "Detection of retinal hemorrhage in fundus images using ANFIS classification and FCM with cuckoo search optimization algorithm," in *2017 2nd International Conference on Communication and Electronics Systems (ICCES)*, 2017, no. Icces, pp. 35–39.

[39] M. Canche, O. Dalmau, and M. Garcia, "Automatic Detection of Hard Exudates in Retinal Images with Diabetic Retinopathy," in *2017 Sixteenth Mexican International Conference on Artificial Intelligence (MICAI)*, 2017, pp. 53–59.

[40] T. Schlegl *et al.*, "Fully Automated Detection and Quantification of Macular Fluid in OCT Using Deep Learning," *Ophthalmology*, vol. 125, no. 4, pp. 549–558, Apr. 2018.