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Recent Automated Hard Exudates Detection Systems in Diabetic Retinopathy

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Abstract

Diabetic Retinopathy (DR) is the complexity arises because of raise in glucose level in the blood that causes retinal damage in diabetic patient's eye and leads to vision loss if not early detected and treated. Due to DR, retinal blood vessels get damaged and accumulation of lipoprotein forms Hard Exudates (HE). The early detection of HE in fundus photographs with the use of computer assisted tools helps Ophthalmologists to analyze and prevent vision impairment. Therefore many computer assisted systems were developed using image processing, supervised and unsupervised machine learning and deep learning. In this review, an analysis of latest development of such systems to detect hard exudates is presented. The objective of this paper is to define that systems which uses deep learning algorithms for efficient detection of bright lesions as HEs.

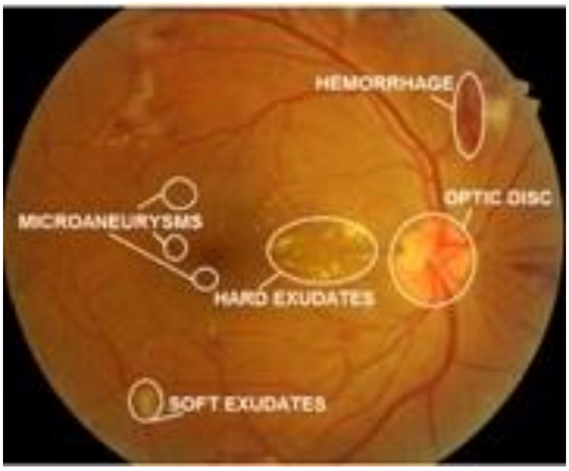
Keywords: Diabetic Retinopathy, fundus images, hard exudates, image processing, learning algorithms

Introduction

In medical system, Diabetic Retinopathy is the significant topic in the medical image processing to detect the affected region and exudates. Over 438 million people with diabetes will be found worldwide by 2030 as per the World Diabetes Foundation (Elbalaoui et al., 2019). According to (Gilbert et al., 2020), 65 million adults are affected by diabetic mellitus only in India and is expected to rise count to 130 million by 2045. Diabetic mellitus is triggered by insulin resistance or its deficiency. Insulin resistance results in rise in the ratio of sugar in the blood that causes vascular and neuropathic complications. DR is one of the leading complication of diabetic mellitus patients that causes loss of vision if not detected and timely treated (Kauppi et al., 2006). DR is a sight-threatening, chronic disease and causes irreversible blindness. The different lesions were caused due to retinopathy in form of red lesions and white lesions. Microaneurysms and hemorrhages referred as red lesions, while hard and soft exudates are white lesions.

A retinal digital fundus image gives photographic sight of the inner surface of the eye (Ward et al., 1989). In regular case, this retinal image has optic disc, macula, fovea and blood vessels. Diabetic retinopathy images includes microaneurysms, hemorrhages, soft and hard exudates and neovascularisation (Borsos et al., 2019). DR can be of two stages (Butt at al., 2019), one is nonproliferative DR, the early stage of the disease where tiny lumps formed in blood vessels of retina and/ or leaks of blood and second stage is proliferative DR, new unusual blood vessels formed and results into the translucent gel of the retina. Figure 1 shows digital fundus image with different features. As per severity scale of International Clinical Diabetic Retinopathy (Wilkinson et al., 2003), diabetic retinopathy consists of five stages: normal fundus (no abnormalities), minor NPDR (microaneurysms), modest NPDR (microaneurysms, hemorrhages, exudates), severe NPDR (vitreous hemorrhages, venous beading) and PDR (neovascularization, retinal detachment).

Figure 1: Retinal fundus image showing examples of the lesions *Image Source: (Borsos et al., 2019)*



Hard Exudates

Microaneurysms are tiny bulges of blood on the retina results in leakage from the blood vessels. As the disease grows, it develops hemorrhages deep inside the retina and with further advances fatty acid outflow from the blood vessels that form as hard exudates (HE). HE are waxy yellowish deposits with sharp margins having different shapes and size within the retina (C. Prateebha et al., 2009). The central vision is due to macula and fovea and may get affected if the exudates formed at these places. The automatic detection of HE from fundus color images plays an significant role in monitoring the progress of treatment to potentially reduce the risk of blindness of diabetic patient (Kauppi et al., 2006; Abramoff et al., 2008]. Manual detection of HE is time consuming as well demands high professional skills and expensive equipment and also when chemical used on patient’s eye to enlarge pupil irritation/side effects may be face by patient (Dixit et al., 2019; Wang et al., 2020; Liu et al., 1997).

Computer Aided Diagnostics (CAD) system provides services to analyse and segment retinal components and abnormal lesions within the colour fundus image for the ease of early screening of DR. These CAD systems reduces time, cost and manual analysis efforts of clinicians. CAD systems in DR is to differentiate anatomic elements from retinal lesions which includes detection, segmentation and classification of lesions in retinal images (Borsos et al., 2019; Abramoff et al., 2008 ; Shengchun et al.,2019]. Image processing, machine learning, deep learning and computer-vision based methods are extensively reported CAD systems for the early screening of DR using color retinal images. Several neural intelligent methods are implemented to detect the hard exudates in the diabetic retinopathy, because of complexity it has resulted in low detection rate. To evaluate the performance of these methods against ground truth various performance metrics are used.

2. Performance Metrics

The hard exudates are initial clinical signs in diabetic retinopathy. DR based automatic detection methods reduces time and efforts by ophthalmologists for manual notions of retinal features. To assess and examine the performance of these automatic detection methods, the performance metrics are used. Most common metrics used in referred papers are Accuracy (ACC), Sensitivity (SN), Specificity (SP), F-Score and Precision. The following terms are required to know about these metrics (Liu et al., 1997; Ward et al., 1989; Borsos et al., 2019 Abramoff et al., 2008; Liu et al., 1997]:

TP: True Positive, number of correctly classified DR lesions in the considered datasets

TN: True Negative, number of correctly found normal cases (non DR)

FP: False Positive, number of incorrectly classified DR lesions

FN: False Negative, number of incorrectly found normal cases

Accuracy is the ratio of correctly classified images to the total number of images.

$$ACC = (TP + TN) / (TP + TN + FP + FN) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

Sensitivity measures the ratio of correctly classified DR lesions. It is also called as true positive rate or recall.

$$SN = TP / (TP + FN) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

Specificity gives true negative rate that is the fraction of correctly classified non DR images

$$SP = TN / (TN + TP) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

Precision is positive predictive value describes the performance of diagnosis test whereas F-score combines precision and Sensitivity.

$$Precision = TP / (TP + FP) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4)$$

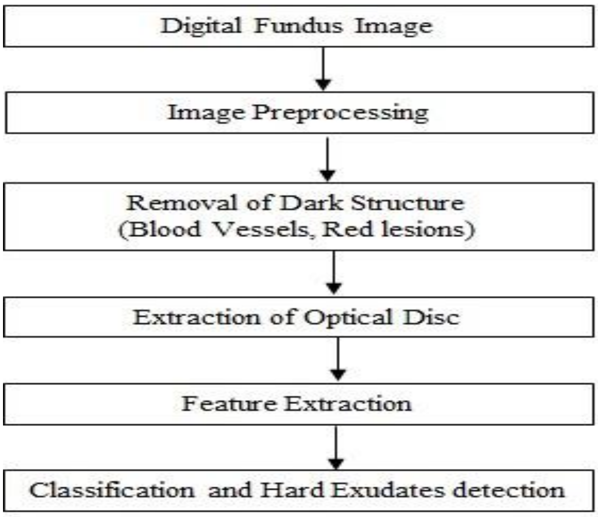
$$F\text{-}score = 2 \times (Precision \times SN) / (Precision + SN) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

The mean of recall and accuracy described the efficiency of the classifier. The objective of this review is to explore the current computerised HEs detection methods such as deep learning and traditional techniques. The review includes brief outline of detection methods and their results, any key gaps, conclusions and future trends in these topics.

3. Detection Methods of Hard Exudates

DR hard exudates detection criteria follows two levels: lesion based and image based (Shengchun et al., 2019; Chanda et al., 2019; Liu et al., 2016). Lesion level based detects lesions and their locations also checks correctly detected or rejected exudates per image. It involves lesion detection/ segmentation and lesion classification where detection phase produces possible region of interest and classification phase removes false positives. Image level based detection checks whether fundus image has presence of exudates or it is normal. It is useful especially for DR screening to evaluate DR signs. Figure 2 depicts the general framework of HE detection involves the steps of preprocessing, removal of dark lesions, extraction of optic disc (OD), feature extraction and classification methods. For automatic HE detection the published algorithm developed using some strategies: thresholding (Shengchun et al., 2019; Chanda et al., 2019), edge detection (Adem, 2018), mathematical morphological (Wang et al., 2020; Satyananda et al., 2020; Li et al., 2000; Maneerat et al., 2020), and region growing.

Figure 2: General Framework for HE detection



Using thresholding algorithm gives analysis of gray levels but due to uneven illumination automatic selection of threshold become difficult as it may ignore confined details of an image. Because of uneven exudates intensity and low contrast between retinal background and HE, global thresholding and edge detection method finds difficulty to achieve accurate result. Mathematical morphology based methods uses morphological operators to eliminate unwanted structures but selection of appropriate size of structuring element will be the problem and is highly sensitive to image contrast. Region growing based technique uses intensity homogeneity and spatial contiguity but suffers from seed point selection difficulties and is time consuming. Moreover, micro-aneurysms, hemorrhages, exudates, fluid loss, and blood pressure were the properties evaluating the deep learning algorithm effectively (Yang et al., 2021). In addition, pattern recognition in images was employed by a vital technique called feature fusion, extracted from the inner layer of deep neural network and handcrafted (i.e., manual) (Tavakoli et al., 2021). DL algorithms have been efficient in assessing various kinds of properties from images like fluid loss, micro-aneurysms, blood pressure, exudates etc.(Karthiyayini et al., 2021).

4. Literature Review

Based on the literature papers most of current methods to detect HE are based on Neural Network algorithms, Supervised and Unsupervised deep learning algorithms. The Supervised Learning (Predictive Models) predicts missing value using present values in the dataset. This algorithm has a set of input and output data and constructs a model to make representative predictions to new dataset. Supervised learning includes naive-Bayesian Method, Artificial Neural Network, KNN, Support Vector Machine and Random Forest Methods (Mujumdar et al., 2019). Unsupervised Learning (Descriptive models) have known set of inputs but output is unknown. These are mostly used on transactional data and includes clustering algorithms like k-Means clustering, Fuzzy C- means clustering.

Exudates are prime sign of DR to detect disease. Anatomical retinal standards such as Optic Disc leads to false positive indication in the automated HE detection. Therefore, Wang et al. (2020) employed an optimized morphological reconstruction-based segmentation (OMRBS) to distinguish HE candidates correctly. Initially, the fundus image was preprocessed by means of Canny Edge Detector and modification techniques of camera aperture for color normalization. Second, candidate regions matching to HEs were recognised in the preprocessed image using morphological construction and dynamic thresholding (used OMRBS). Third, from each region a centred patch was accumulated to find hand crafted features (Intensity, Geometric, Texture features) together with deep features (used DCNN & Class balanced Cross Entropy loss). Fourth, for every candidate the collective features were created according to multi-feature fusion strategy (use Ridge Regression). Finally, a Random Forest classifier was employed to classify the candidates. For unsupervised classification method (Kadan et al., 2019), first the OD was removed from the fundus image and the green channel represents all hard exudates better than the red and blue channels of the RGB color model. The features of HEs are extracted by morphological operations, entropy analysis, and standard deviation analysis. Finally, for hard exudates clustering an unsupervised k-mean classification technique was employed.

In a previous study (Sariera et al., 2019), 89 colour fundus images size 1500x1152 with 24 bits per pixel resolution employed for feature extraction using thresholding and features selection using Grey Wolf Optimization techniques and KNN algorithm used for HE classification. Shengchun et al. (Shengchun et al., 2019) developed an algorithm to detect HE by means of dynamic threshold and Fuzzy C-means clustering along with SVM for classification. Here, the assessment criteria to identify HE presented at pixel level and image level. In Kom et al.(2019), OD of the fundus image is identified using brightness and variance features using Circular Hough Transformation and masked then the bright patches are segmented based on thresholding and morphological reconstruction techniques. For classification, color, size, and texture features are taken from segmented candidate regions and are categorised with the use of multilayered perceptron neural network (MLP). In Benzamin et al. (2018) for preprocessing histogram expansion and median filter was applied, then variance between the filtered image and its inverse produced to the enhanced image. To suppress blood vessels, closing operation applied on the enhanced image followed by the segmentation of exudates and optic disk by Entropy Maximization Thresholding. Based on size, OD was removed and region remains with exudates. To enhance automatic HE detection, Adem K.(2018) used Canny edge detection algorithm and circular Hough transformation for extraction of OD. Then images obtained were trained with

CNN and the binary classification. From 54 fundus images two sets were created (Hussian et al., 2019); training set (40 images) and testing set (14 images). Generated 200000 image patches of dimension 32×32, the pixel at centre belongs to either exudate class or background class. From each image 2500 HE patches and 2500 background patches were extracted. For detection, they developed an 8 layer CNN to predict the central pixel belongs to HE or background class. Table 1 gives overview of literature papers highlighting the methods applied, dataset used and result of their performance metrics. Figure 3 gives some of automated results.

Table 1: HE detection methods and their performance metrics result in the literature

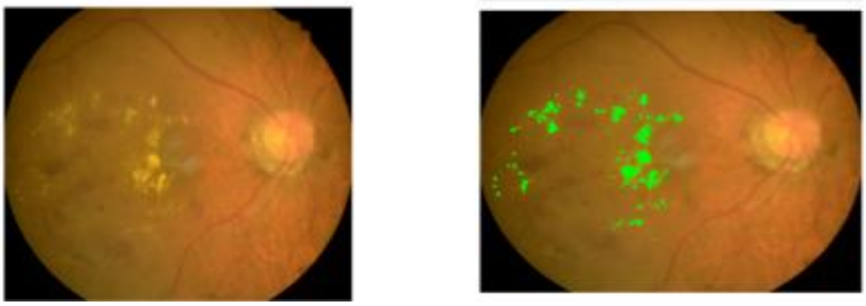
Author	Year	Method Used to	Database Used	Accuracy	Sensitivity	Specificity	Precision	F-Score
Wang H. et al.	2020	Random Forest	HEI-MED	93.23%	94.77%		91.79%	93.26%
Maneerat N. et al.	2020	k-mean algorithm	e-optha	96.44%	89.9%		88.68%	89.29%
			DIARECTDB1 DIARECTDB0	73%	70%	97%		
Kadan A. B. et al	2019	KNN	DRIVE, DIARECTDB1	99.73%	99.42%	99.87%		
Prateebha N. et al.	2019	Random Forest	DIARECTDB1 DIARECTDB0	99.89%	92%	99.9%	100%	
Borsos B. et al.	2019	ANN	IDRiD	94%	68.98%	99.01%		60.52%
Shengehun L. et al	2019	Fuzzy C-Means clustering	DIARECTDB1 (image level) e-Optha (Pixel level)	97.7% 76.5%	97.50% 76.60%	97.80% 94.8%	82.7%	76.7%
Al Sariera et al.	2019	Multilayered Perceptron NN	DIARECTDB1	93%	86.90%	94.80%		
Kom G.H. et al.	2019	Entropy Maximization	DIARECTDB1		95.27%	99.63%		

Table 1: HE detection methods and their performance metrics result in the literature (*continued*)

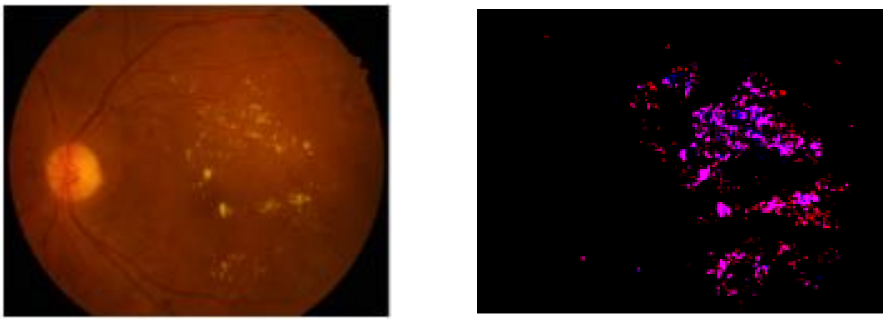
F-Score							76%				

Author	Year	Method Used to detect HE	Database Used	Accuracy	Sensitivity	Specificity	Precision
Husssian M.A. et al.	2019	ANN	DIARECTDB1	98.5%	98.70%	97.50%	
Elbalaoui A. et al.	2019	Maximum entropy	DIARECTDB1, DIARECTDB0	93.34%	92.70%	95.60%	
Adem K.	2018	CNN	DIARECTDB1, DIARECTDB0	99.18%	99.20%	97.97%	
Poonkasem. et al	2019	CNN	DIARECTDB1	AUC: 0.95			
Benzamin A. et al.	2019	Cross Entropy	IDRiD	98.6%	98.30%	41.30%	
Zhou W. et al.	2017	Superpixel Multifeature	DIARECTDB1, e-optha	AUC: 0.96	88%	95%	
Liu Q. et al.	2017	Location –to-Segmentation	DIARECTDB1 Lesion Level		76%		75%
			e-optha Image Level	79%	83%	75%	
Sopharak A. et al.	2010	SVM and navie Bayes	Local data set	*Navie Bayes:* 98.05%	93.40%	98.10%	47.51%
				SVM Classifier: 98.4%	92.30%	98.50%	53.10%

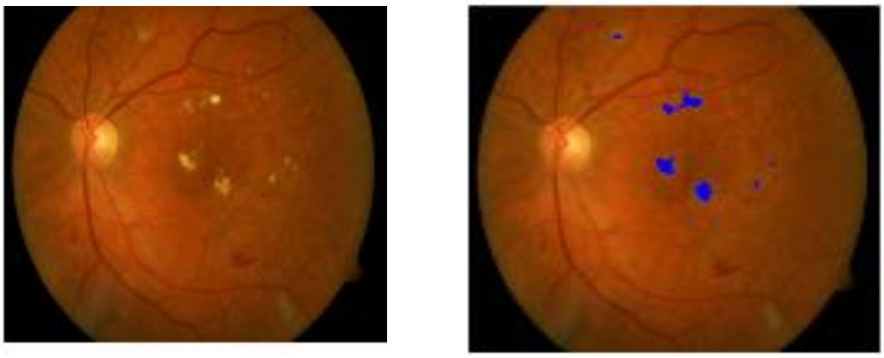
Figure 3: Fundus images (Left Side represents original image and Right Side as HE detected image).



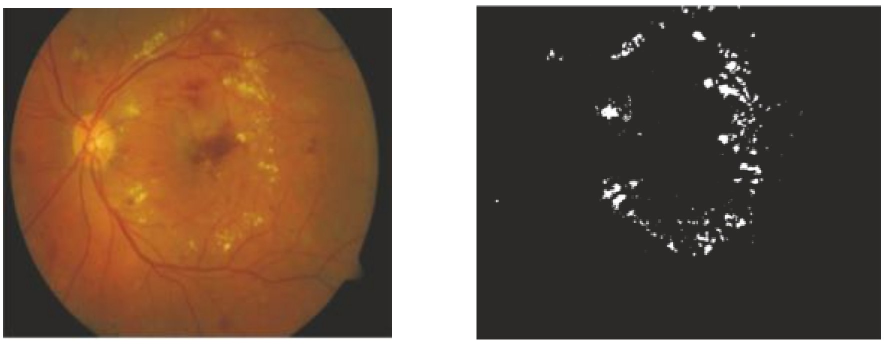
Using Random Forest with 93.23& Accuracy (Wang et al., 2020)



Using ANN with 94% Accuracy (Boros et al., 2019)



Using Entropy Maximization with 95.27% Sensitivity (Benzamin et al., 2018)



Using SVM Classification with 97.7% Accuracy (Shengchun et al., 2019)

5. Discussion

Automated screening programs are able to do fast classification of DR lesions using fundus images. To find optimum HE lesions, some challenges are associated with automatic detection methods such as huge variations in the intensity of images across fundus image databases, reflection noise similar in intensity, color and contrast of HE and some anatomical structures like OD, vessels reflections share similar texture or illumination information to exudates. However some published paper overcome this uneven illumination for every image variable threshold can be selected that ensures the system is independent of the nature of the image. The studies listed in this survey use Supervised and Unsupervised learning algorithms. However, most of researcher used supervised learning methods that learn the classification rules from training set. Several studies conveyed that among different supervised methods, KNN, CNN and SVM algorithms performs better classification than Random Forest classifier. Neural networks retinal screening is popular because of classification ability with high sensitivity and specificity. For DR detection it has been established that deep learning performed better even though there are fewer levels (Lam, et al. 2018).

Most of the researchers used accuracy, sensitivity, specificity and precision to estimate the efficiency of the classifiers. The critical challenge in learning algorithms is to acquire valued features to be used as inputs to the algorithm for creating a classification manner. Most of the researcher used features like shape, color, texture and text, to test the classification efficiency. For HE extraction most commonly, shape feature is employed as it gives the outline and structure of retinal image.

6. Research Gaps and Scope

This review of HE detection and classification methods exposes that deep learning is simplified to design superior techniques for DR finding but it invites more research. These learning based models are sort of unknown box that do not offer clarifications of outcomes. The studies have mostly used neural network prototypes to plan multi-layer architectures for exudates detection. For designing robust learning algorithm, the acquisition of large volume of retinal image with image level and pixel level observations is required that is time consuming and involves the services of expert ophthalmologists. Therefore to design learning algorithms a scarce dataset of retinal fundus images is required. But deep learning software demands a significant training data to capture all image artifacts. Thus using enhancing approaches such as flipping, rotating, cropping and color casting on existing image database, the methods can be skilled with additional distinct features. Also for robustness of deep learning methods it is required to perform across different datasets. The outline of retina is nearly sphere which obstructs the light incident to reflect evenly and also the images are captures under various illumination conditions like camera resolution, etc. To tackle these problems, preprocessing stage can be added in learning methods.

7. Conclusion

Diabetic Retinopathy is due to increase of glucose level in the body that affects retina which causes vision defects. To avoid vision defects, detection of DR at early stage is important. This paper provided a knowledge of automatic hard exudates detection and analysis using supervised and unsupervised deep learning algorithms. The main articles are collected from various Bio Medical journals, IEEE journals and Scopus scientific repositories. Initially, an overview of different DR lesions and then performance metrics used for assessment is presented. After that different traditional HE detection methods and their limitations are summarised. After providing necessary background, deep learning based methods for HE classification is reviewed and discussed about their overall performance. Each research is addressed from specific aspects including DL-based classifications, databases and performance metrics. In DL systems, most of the readings revealed that deep neural networks gives enhanced classification results followed by SVM and Random Forest classifiers. For performance assessment many investigators used accuracy, sensitivity, specificity and precision as indicators. This review offered research challenges in deep learning based HE detection and classification.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

References

Abramoff M., Niemeijer M., Maria S. (2008). Evaluation of a system for automatic detection of diabetic retinopathy from color fundus photographs in a large. *Diabetes Care, 31(2), 193-198.* https://doi.org/10.2337/dc07-1312.M.D.A.

Adem, K. (2018). Exudate detection for diabetic retinopathy with Circular Hough transformation and convolutional neural networks. *Expert Systems with Applications*, 114, 289-295. https://doi.org/10.1016/j.eswa.2018.07.053

Al Sariera, T. M., Rangarajan, L., & Amarnath, R. (2019). Detection and classification of hard exudates in retinal images. *Journal of Intelligent & Fuzzy Systems*, 38(2), 1943-1949. https://doi.org/10.3233/jifs-190492

Akara Sopharak, Matthew N. Dailey, Bunyarit Uyyanonvara, Sarah Barman, Tom Williamson, Khine Thet Nwe & Yin Aye Moe (2010). Machine learning approach to automatic exudate detection in retinal images from diabetic patients, *Journal of Modern Optics*, 57(2), 124-135, https://doi.org/10.1080/09500340903118517

Benzamin, A., & Chakraborty, C. (2019). Detection of hard exudates in retinal fundus images using deep learning. *Joint 7th International Conference on Informatics, Electronics and Vision and 2nd International Conference on Imaging, Vision and Pattern Recognition, ICIEV-IVPR 2018*, 465–469. https://doi.org/10.1109/ICIEV.2018.8641016

Borsos, B., Nagy, L., Iclănzan, D., & Szilágyi, L. (2019) Automatic detection of hard and soft exudates from retinal fundus images. *Acta Universitatis Sapientiae, Informatica*, https://doi.org/10.2478/ausi-2019-0005

Butt, M. M., Latif, G., Iskandar, D. N. F. A., Alghazo, J., & Khan, A. H. (2019). Multi-channel convolutions neural network based diabetic retinopathy detection from Fundus Images. *Procedia Computer Science*, 163, 283-291. https://doi.org/10.1016/j.procs.2019.12.110

Chanda, K., Issac, A., & Dutta, M. K. (2019). An adaptive algorithm for detection of exudates based on localized properties of fundus images. *International Journal of E-Health and Medical Communications*, 10(1),18-37, https://doi.org/10.4018/IJEHMC.2019010102

C. Prateebha, N. Nirmal Singh.(2009). A novel approach for detection of hard exudates using random forest classifier. *Journal of Medical Systems*, 43(7), https://doi.org/10.1007/s10916-019-1310-9

Dixit, A. K., & Prabhakar, P. (2019). Hard exudate detection using linear brightness method. *4th IEEE International Conference on Recent Trends on Electronics, Information, Communication and Technology, RTEICT 2019 – Proceedings*, 980–984. https://doi.org/10.1109/RTEICT46194.2019.9016792

Elbalaoui, A., & Fakir, M. (2019). Exudates detection in fundus images using mean-shift segmentation and adaptive thresholding. *Computer Methods in Biomechanics and Biomedical Engineering: Imaging and Visualization*, 7(2), 145-153. https://doi.org/10.1080/21681163.2018.1463175

Gilbert, C., Gordon, I., Mukherjee, C. R., & Govindhari, V. (2020). Perspective guidelines for the prevention and management of diabetic retinopathy and diabetic eye disease in India : a synopsis, 63-66, https://doi.org/10.4103/ijo.IJO

Kauppi, T., Kalesnykiene, V., Kamarainen, J., Lensu, L., & Sorri, I. (2006). Diaretdb0 : Evaluation database and methodology for diabetic retinopathy algorithms. *Machine Vision and Pattern Recognition Research Group, Lappeenranta University of Technology, Finland*, 1–17. https://www.it.lut.fi/project/imageret/diaretdb0/doc/diaretdb0_techreport_v_1_1.pdf

Kadan, A. B., & Subbian, P. S. (2019). Detection of hard exudates using evolutionary feature selection in retinal fundus images. *Journal of Medical Systems*, 43(7), 209. https://doi.org/10.1007/s10916-019-1349-7

Kom, G. H., Wouantsa Tindo, B. C., Mboupda Pone, J. R., & Tiedeu, A. B. (2019). Automated exudates detection in retinal fundus image using morphological operator and entropy maximization thresholding. *Journal of Biomedical Science and Engineering*, 12(3), 212-224. https://doi.org/10.4236/jbise.2019.123015

Lam, C., Yu, C., Huang, L., & Rubin, D. (2018). Retinal lesion detection with dep learning using image patches. *Invest Opthalmol Vis Sci.2018;59:. 590-596.* https://doi.org/10.1167/iovs.17-22721.

Liu Z., C. Opas and S. M. Krishnan, (1997). Automatic image analysis of fundus photograph. *Proceedings of the 19th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. 'Magnificent Milestones and Emerging Opportunities in Medical Engineering' (Cat. No.97CH36136)*, 2,524-525. https://doi.org/10.1109/IEMBS.1997.757661

Li, H., & Chutatape, O. (2000). Fundus image features extraction, *Proceeding of 22nd Annual EMBS International Conference of IEEE Engineering in medicine and Biology Society*,4, 3071-3073. https://doi.org/10.1109/IEMBS.2000.901530

M.A.Hussian, S. Islam,Tiwana,U. Rehman, W. Qureshi. (2019). Detection and classification of hard exudates with fundus images complements and neural networks. *5th International Conference on Control, Automation and Robotics, ICCAR,206-211*, https://doi.org/10.1109/ICCAR.2019.8813469

Mujumdar, A., & Vaidehi, V. (2019). Diabetes Prediction using Machine Learning Algorithms. *Procedia Computer Science*,165,292-299. https://doi.org/10.1016/j.procs.2020.01.047

N. Maneerat, T. Thongpasri, A. Narkthewan and C. Kimpan. (2020). Detection of hard exudate for diabetic retinopathy using unsupervised classification method. *6th International Conference on Engineering, Applied Sciences and Technology (ICEAST), 1-4.* https://doi.org/10.1109/ICEAST50382.2020.9165498

Poonkasem, Nipon Theera-Umpon, Sansanee Auephanwiriyakul, Direk Patikulsila. (2019). Detection of hard exudates in fundus images using convolutional neural networks. *Proceedings - 2019 7th International Conference on Green and Human Information Technology, ICGHIT*, 77–81. https://doi.org/10.1109/ICGHIT.2019.00025

Qing Liu, Beiji Zou, Jie Chen, Wei Ke, Kejuan Yue, Zailiang Chen, Guoying Zhao (2017). A location-to-segmentation strategy for automatic exudate segmentation in colour retinal fundus images. *Computerized Medical Imaging and Graphics*, 55, 78-86. https://doi.org/10.1016/j.compmedimag.2016.09.001

R. Karthiyayini and N. Shenbagavadivu, (2021). Retinal image analysis for ocular disease prediction using rule mining algorithms, *Interdisciplinary Sciences: Computational Life Sciences,* 13, 451-462. https://doi.org/10.1007/s12539-020-00373-9

Satyananda, V., Narayanaswamy, K. V., & Karibasappa. (2020). Detection of exudates from fundus images. *Advances in Intelligent Systems and Computing*, 940, 988-997. https://doi.org/10.1007/978-3-030-16657-1_92

Shengchun Long , Xiaoxiao Huang ,Zhiqing Chen, Shahina Pardhan ,and Dingchang Zheng. (2019). Automatic detection of hard exudates in color retinal images using dynamic threshold and svm classification: algorithm development and evaluation. *BioMed Research International*, 1-13. https://doi.org/10.1155/2019/3926930

Tavakoli, M., Mehdizadeh, A., Aghayan, A., Shahri, R. P., Ellis, T., & Dehmeshki, J. (2021). Automated microaneurysms detection in retinal images using radon transform and supervised learning: application to mass screening of diabetic retinopathy. *IEEE Access*, *9*, 67302-67314. https://doi.org/10.1109/ACCESS.2021.3074458

Wang, H., Yuan, G., Zhao, X., Peng, L., Wang, Z., He, Y, Peng, Z. (2020). Hard exudate detection based on deep model learned information and multi-feature joint representation for diabetic retinopathy screening. *Computer Methods and Programs in Biomedicine. 191*, 105398. https://doi.org/10.1016/j.cmpb.2020.105398

Ward, N. P., Tomliivson, S., & Taylor, C. J. (1989). Image analysis of fundus photographs: the detection and measurement of exudates associated with diabetic retinopathy. *Ophthalmology*. 1989, https://doi.org/10.1016/S0161-6420(89)32925-3

Wilkinson, C. P., Ferris, F. L., Klein, R. E., Lee, P. P., Agardh, C. D., Davis, M. Lum, F. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology*. 2003, https://doi.org/10.1016/S0161-6420(03)00475-5

Yang, Yehui, et al. "Robust collaborative learning of patch-level and image-level annotations for diabetic retinopathy grading from fundus image." *IEEE Transactions on Cybernetics* (2021). https://doi.org/10.1109/TCYB.2021.3062638

Zhou, W., Wu, C., Yi, Y., & Du, W. (2017). Automatic Detection of Exudates in Digital Color Fundus Images Using Superpixel Multi-Feature Classification. *IEEE Access*, *5*(1), 17077–17088. https://doi.org/10.1109/ACCESS.2017.2740239