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RESEARCH ARTICLE

A review on computer-aided recent developments for automatic detection of diabetic retinopathy

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ABSTRACT

Diabetic retinopathy is a serious microvascular disorder that might result in loss of vision and blindness. It seriously damages the retinal blood vessels and reduces the light-sensitive inner layer of the eye. Due to the manual inspection of retinal fundus images on diabetic retinopathy to detect the morphological abnormalities in Microaneurysms (MAs), Exudates (EXs), Haemorrhages (HMs), and Inter retinal microvascular abnormalities (IRMA) is very difficult and time consuming process. In order to avoid this, the regular follow-up screening process, and early automatic Diabetic Retinopathy detection are necessary. This paper discusses various methods of analysing automatic retinopathy detection and classification of different grading based on the severity levels. In addition, retinal blood vessel detection techniques are also discussed for the ultimate detection and diagnostic procedure of proliferative diabetic retinopathy. Furthermore, the paper elaborately discussed the systematic review accessed by authors on various publicly available databases collected from different medical sources. In the survey, meta-analysis of several methods for diabetic feature extraction, segmentation and various types of classifiers have been used to evaluate the system performance metrics for the diagnosis of DR. This survey will be helpful for the technical persons and researchers who want to focus on enhancing the diagnosis of a system that would be more powerful in real life.

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KEYWORDS
Diabetic retinopathy; classification; microaneurysm; exudate; machine learning; haemorrhage

1. Introduction

Diabetes is formed by the malfunctioning of sugar metabolism and is known to be the raising amount of glucose content within the blood. This sudden change in the increasing levels can damage the retinal blood vessels which supply blood to normally activate the essential organs in our body [1–7]. Diabetic Retinopathy (DR) is the consequential complicated condition of diabetes disease for which the retinal vasculature severely affects with progressive damages of the retina region that can cause legal impairment of vision and blindness [13–15,52–55,60,61,93]. Among the working age population, it is the most commonly recognised cause of blindness. DR is the progressive disease with the result of long-term diabetes, but it has not treated promptly at the initial stage because of the patients with DR indicate almost no signs of vision impairment [8,10,81,83]. Due to this kind of reason, one out of ten suffers from its severe vision threatening forms [9,91]. DR can be managed most effectively, only if the potentially sight-threatening diseases have been diagnosed using available treatment at an early stage [80,82,84]. With the available treatment of DR screening, retinal image analysis in which eye fundus examination plays a major role in monitoring any changes in the retinal region and early diagnosis of DR for all diabetic patients and even it ensures that the effective DR treatment is time-honoured [62–72]. There are impacts in information system [92] it is asymptomatic in the disease process and still it is diagnosed at an early stage, visual impairment from macular oedema can be effectively prevented using laser photocoagulation process [12,14,88].

Human retina comprises of different components namely fovea, macula [73,78], blood vessels [79] and Optic Disc (OD). DR is categorised into two different stages namely: Non Proliferative Diabetic Retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) [11,13,15,16]. On one hand, NPDR forms with the damage of blood vessels inside the retina and thereby causes the retina become more swollen and wet due

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to the leakage of fluids onto the retina region. Different signs of retinopathy lesions can occur in the NPDR stage: Microaneurysms (MAs) [58], Exudates (EXs), Haemorrhages (HMs) and Inter retinal microvascular abnormalities (IRMA) [17–27]. On the other hand, the severity of blindness occurs with the development of new blood vessels along the various region of the retina is termed as the advanced stage of PDR.

The first sign of DR is the MA which is formed by the leakage of tiny blood vessels present in the retina, and they are smaller in size, circular tiny red spots onto the retina. It is more visible to an ophthalmologist [28,30,31,33,36]. After the wall of MAs rupture, the next sign of DR called haemorrhages occurs with the form of dot and blot haemorrhage spots [29,32,34,35]. It is likely that the bright red dots and large Red Lesions (RLs) form dot as well as blot haemorrhages respectively [37–40]. Over a great expanse of time, the creation of yellow spots arises by the drip of blood contents like lipids and proteins onto the retinal region known as EXs. Due to the acquisition of lipids on or surrounding the macula region, they cause a high degree of blindness [42,44–47]. Finally, the abnormalities of blood vessels in the retina cause IRMA [41,43,46,48]. The ophthalmologist [85,86] normally classifies the diagnosis of NPDR based on the lesions being found and developed in the location of the retina into three different grades: i.e., mild, modest and severe [49–51,87–90]. As a consequence of early detection and diagnosis of various stages in DR, the vision of diabetes patients can be saved.

Figure 1 illustrates the overall process of the computer aided automatic DR screening system. In the off-line process, the retinal fundus image training database was pre-processed to extract the features using image processing techniques [74–77]. Further, the filtering or wrapper method selects the significant features from the extracted feature model in order to train the off-line classifier based on the available ground truth values. The training parameters obtained from the classifier and the calculated significant features follow the on-line classification process and perform the severity level classification of disease as normal, slight, modest, severe non-proliferative DR or proliferative DR [19,56–59].

In this paper, we have reviewed various techniques based on classification and image processing of DR for the exposure of the signs of DR lesions such as MAs, HMs, EXs and IRMA. Additionally, the detection of IRMA having received lesser attention among the researchers is also discussed in this review paper. Here, we discussed the fully automated accurate and fast computer aided DR screening and grading systems that can be used for the accurate diagnosis of DR stages and treatment prioritisation. With the aid of digital retinal fundus images obtained from different databases, the classification of severity levels in NPDR and PDR can be performed effectively. Finally, the performance metrics of existing methods are comprehensively reported and the results obtained are encouraging.

The organisation of this paper is as follows: Section 1 focuses the synopsis of DR disease and the architecture of automatic DR detection and classification of disease severities on retinal images. Section 2 presents the chronological and methodological reviews on early detection of DR. Modalities and retinal abnormalities detection have investigated in Section 3. A preliminary feature extraction and machine learning methods are

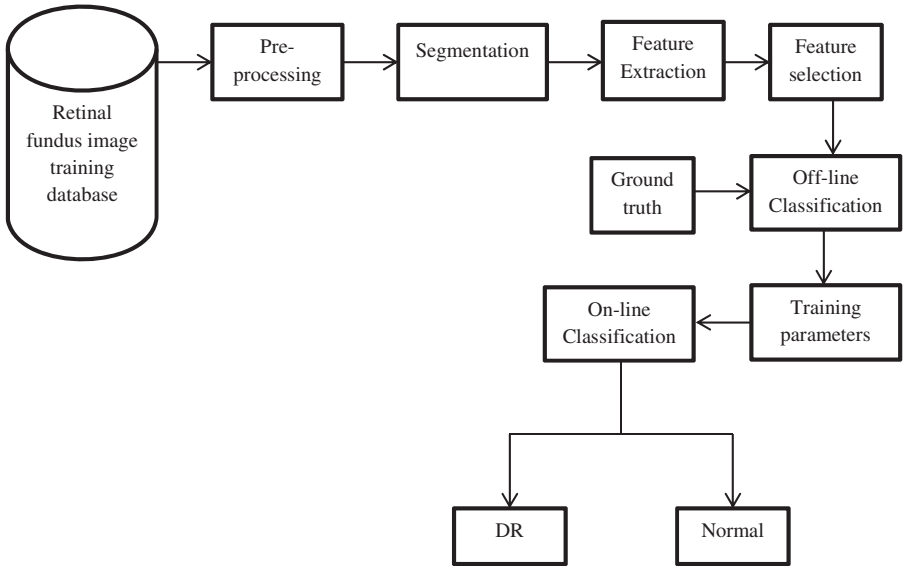

Figure 1. Architecture of the computation process in automated DR diagnosis.

clearly discussed in Section 4. As for improving the performance of DR diagnosis, the review outcomes are reported in Section 5. Finally, the concluding remarks are described in Section 6 of this paper.

2. Review on early detection of diabetic retinopathy

2.1. Chronological review

Nowadays, DR is the most significant causes of retinal vision impairment and becoming a global wide-spread dreadful disease. According to the WHO global report of DR in 2016, there was approximately 8.5% increase of the world's adult population has in possession of DR compared to early periods. The problem is drastically increasing in its scale particularly in poor resource countries with the consumption of less nutritious food, poorly-controlled diabetes, elevated blood cholesterol level, chronic diabetes, sedentary lifestyles results in obesity. Various research studies have shown that DR on sight-threatening in diabetes patients has a recognisable early detection stage. In this chronological review, we have highlighted the percentage of contributions on early detection of DR using Figure 2. The review period has been considered from 2006 to 2016 from which the contributions on DR has been acquired. The research interest is getting increased every year, and at 2016, 19% of the DR detection methods have been reported. This ensures that the percentage contribution of DR detection for the recent years is high enough. The sharp slope of the graph shows that the percentage contribution is strictly improved for the years of 2012 to 2014 and it is yet to be increased in the coming years.

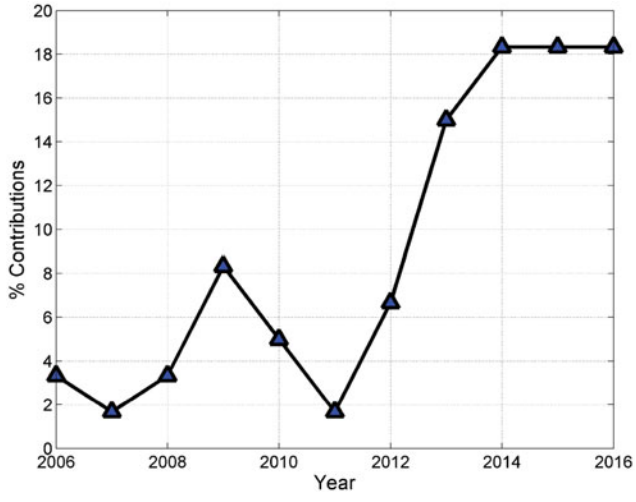

Figure 2. Chronological review of DR detection.

2.2. Methodological review

There is some evidence for the efficiency of available treatment of DR screening have been provided by numerous related studies on the early DR detection and the preliminary treatment of DR reports.

In 2006, a report from the early diagnosis and treatment of DR study had presented the Bayesian and Image structure clustering techniques that substantially reduced the risk factors of vision loss. In 2007, the three-layer based feed forward neural network have proposed for the classification of four groups of DR eye diseases that successfully concluded that screening of sight-threatening on DR was merely cost effective.

In 2008, authors noted that mathematical morphology with embedded feature extraction methods and linear Support Vector Machine (SVM) classifiers were employed for the early detection and recommend proper treatment for the control of eye with high risky characteristics of DR.

In 2009, few investigations identified the region of DR using various algorithms for segmentation such as genetic algorithm, information fusion of multiple CAD algorithms, fuzzy c-means clustering and several classifiers like multilayer neural network, modified matched filter.

In 2010, much of the published research works for the discovery of RLs like MAs, and HMs in the digitally retinal colour fundus DR images were developed based on the use of different types of Neural Network (NN) classifiers. Moreover, feature extraction techniques such as morphological, Circular Hough Transform, edge detection, multi-scale FM methods also have developed.

With respect to the early detection of DR, a successive Clutter-Rejection approach from retinal colour fundus images was solely introduced in 2011 for the automatic diagnosis and treatment of MA.

In 2012, the authors estimated the automated retinal fundus image classification of DR using multiple-instant learning framework, ensemble-based framework embed with the combination of pre-processing and candidate extractors, and they have also suggested different simple segmentation methods such as inverse segmentation, geometric based threshold and criteria before to detect the candidate.

In 2013, computer-aided screening system gained the significance of feasibility on early detection and classification of various stages involved in DR. The authors used many algorithmic methods based on the segmentation techniques such as mathematic morphology and naive Bayes classifier for coarse segmentation as well as fine segmentation of DR stages. For the DR classification

in retinal images, machine learning techniques like Evolutionary algorithm based Probabilistic Neural Network classifier parameter tuning, fuzzy logic, Non-invasive method, Combined form of SVM, GMM and an advanced modelling of multimodal mediod approaches have used. Likewise, multi-overlapping windows and RT, Local maxima, and naive Bayes classification methods also successfully developed.

In 2014, the research community developed an automated system for diagnosing and classifying DR on human retinal colour fundus images. Respective image processing methods like standard/modified line operator for Vessel segmentation, High grey-level variations, artificial neural network classifier, Curvelet Transform segmentation, Two-scale exudate candidates segmentation methods have developed. Classifier approaches such as support vector machine classifier, Extension of the m-Mediods based modelling approach, Gaussian Mixture Model (GMM) for reducing the noise, Levenberg–Marquardt algorithm, Multilayer perceptron neural network, Back propagation algorithm, Automatic vessel extraction method and fuzzy classification, Ensemble-based methods were developed.

The study of the development of automatic telemedicine system for computer aided diagnosing and grading of DR was reported in 2015. For the detection of DR lesions, most of the research works have projected various methods using feature selection based Genetic algorithm combined with dual SVM classifier.

Recently in 2016, researchers have developed an automated diagnosing computer aided system in order to assist the ophthalmologists to shorten the time-consuming screening process. In order to detect and classify the abnormal DR features of human retina, various image processing and classification techniques such as Gabor filter texture edge detection based segmentation algorithm, Two-field fundus photography, Convolutional Neural Network approach, Artificial Neural Network, Deep Neural Networks and Anatomical Landmark Detection Fusion, Extreme Learning Machine (ELM), Principal Component Analysis and Fuzzy SLIQ decision tree algorithm based Modified Gini Index, automated DR grading assessment systems, Mathematical morphology on different planes of RGB, HSI and YCbCr colour models, Fuzzy conditional entropy and Differential Evolution algorithm were presented.

3. Review on diagnostic aids

3.1. Modalities for lesion detection

In 2006, all digital retinal images were obtained from the DR screening and treatment programme conducted in Netherland using three types of camera: the Canon CR5-45NM, the Topcon NW 200 and the Topcon NW 100. As for effectively evaluating the two stages of DR, the records of clinical data images have taken from the Centre for Sight in New York using a TOPCON TRC 50IA retinal fundus camera.

In 2007, the digital fundus retinal images for grading the DR were taken using Ziess Visucam fundus camera and the details had been acquired from the National University Hospital, Singapore.

In 2008, the number of photographic digital retinal images was obtained from Thammasat University Hospital using KOWA-7 non-mydriatic retinal camera for the detection of exudate in patients with non-dilated pupils.

In 2009, the retinal images were collected from the screening programme conducted by different databases like STARE, the Bristol Eye Hospital, Instituto de Oftalmobiologia Aplicada (IORA) under the Valladolid University, Spain. In order to test and train the database, the fundus images were acquired from the TopCon TRV-50 camera, a Cannon non-mydriatic CR6-45NM, TopCon TRC-50IX mydriatic retinal camera, TopCon TRC-NW6S non-mydriatic retinal camera, the Topcon NW 100, the Topcon NW 200, canon D30 cameras and the Canon CR5-45NM.

In 2010, for testing the significance of developed methods, MESSIDOR, ETDRS based clinical DR database with variable colour, quality and brightness were selected. Various retinal images were acquired from a high-quality TopCon TRC-NW6S non-mydriatic and TopCon TRC-50IX mydriatic retinal camera.

In 2011, for the purpose of analysing the patient profile with DR, three commonly available databases were considered namely, CRIAS, ROCd, and DIARETDB1 acquired from the screening programme conducted across multiple sites. These databases consist of retinal images which were captured from the high contrast digital fundus camera.

In 2012, the eye fundus photographs were collected from the most commonly available Messidor database, University Malaya Medical Centre (UMMC), and the private database. In order to test the accuracy of classification and grading performance, the digital fundus images were captured with either TopCon TRC-NW7SF Non-Mydriatic/Mydriatic or CR-DGi Retinal Camera.

For evaluating and testing of automated medical diagnostic systems, all high quality digital retinal images were acquired and certified from the Department of Ophthalmology. Thammasat University Hospital obtained the retinal images using the KOWA-7 non-mydriatic retinal camera with the

patient's non-dilated pupil. MUMS-DB and publicly available DR datasets like DIARETDB1 and DIARETDB0 acquired from the Kuopio University Hospital were captured using Canon TRC-50EX Mydriatic Retinal Camera and digital fundus cameras and private dataset provided by the Moorefields Eye Hospital, UK in 2013.

In 2014, some publicly available benchmark databases were taken for an automated screening and classification of DR stages. They have used the four commonly available databases such as STARE, DRIVE, MESSIDOR, and DIARETDB. With the aid of CanonCR5 Non-Mydriatic Retinal Camera, a digital fundus camera, and Top Con TRV-50 fundus camera the high-quality fundus losslessly compressed images were taken.

In 2015, the experimental detection and classification of automated DR diagnosis systems were tested on different standard benchmark databases: MESSIDOR, DRIVE, and STARE. The selected colour fundus images were acquired from the TopConTRV-50 retinal fundus camera, Canon CR DGi non-mydriatic, Topcon TRC NW6 non-mydriatic retinograph and Zeiss camera devices.

In 2016, depending on the client, experiments were carried out on digital fundus images of research resources like MESSIDOR, DRIVE, DIARETDB0, DIARETDB1 and STARE databases. The retinal images were captured from various models of retinal camera devices like Topcon TRC-50DX mydriatic fundus camera, Nikon D90 DSLR camera, fundus camera model KOWA nonmyd α-DIII at general hospital of North-eastern Thailand, Canon CR5 non-mydriatic 3-CCD camera from diabetic retinopathy screening programme conducted in the Netherland. For the research of medical diagnosis on medical retinal digital fundus images, the availability of widely accessible image acquisition modalities are shown in Table 1.

3.2. Retinal abnormalities detection

Depending on the occurrence of different features, DR can be categorised as four different stages namely Mas, HMs, EXs and IRMAs which are determined by several research works and the brief description is tabulated in Table 2.

Figure 3 shows a clear change of the non-proliferative stages of DR are characterised by retinal vascular related abnormalities namely MAs, HMs, EXs and IRMA with an increase of diagnostic DR stages from 2006 to 2016. We review the literature that deals with severe forms of DR stages by various early diagnostic procedures. It is also evident from the results that the IRMA in 2006 achieved 12% with MA of 2%, HM of 3% and EX of 2.5% compared to the absence of IRMA and EX stages of DR in 2007 respectively. These values are according to the observed study of research papers published in 2006 to 2007. The percentage

Table 1. Acquisition modalities of retinal fundus images.

Acquisition modalities	Citations
KOWA-7 non-mydriatic retinal camera	[1]
Topcon TRC NW6 fundus 3CCD camera	[2,5,23]
Canon CR5 Non-Mydriatic retinal camera	[3]
TOPCON non-mydriatic retinal camera of model TRC-NW200	[4,40]
Fundus image	[5,37,42,44,52,53]
Digital fundus camera	[6,8–11,16,18,20,24,25,31,32,34,36,38,39,56,58,59]
non-mydriatic digital colour fundus cameras	[12]
Cannon nonmydriatic CR6-45NM camera	[13]
TOPCON TRC 50IA fundus camera	[14]
TopCon TRV-50 fundus camera	[15,35]
Topcon TRC-50DX mydriatic fundus camera with Nikon D90 DSLR camera	[17]
In-house designed device with three chip CCD camera and two D65 fluorescent tubes placed symmetrically around the camera	[17]
Zeiss, Topcon and Canon digital fundus camera	[21]
fundus camera model KOWA nonmyd α-DIII	[22]
Infrared camera	[27]
Ziess Visucam fundus	[29]
Topcon NW 100 and Canon CR5-45NM	[40]
Canon CR5 non-mydriatic 3CCD camera	[28,43,47]
Canon TRC-50EX Mydriatic retinal camera	[46]
TopCon TRC-50IX mydriatic digital retinal camera and TopCon TRC-NW6S non-mydriatic digital retinal camera	[48,51]
TopCon TRC-NW7SF Mydriatic/Non-Mydriatic Dual type retinal camera	[49]
high resolution retinal fundus camera	[50]
Topcon NW 100 Camera	[54]
Canon fundus camera	[55]
Topcon TRC NW6 non-mydriatic retinograph	[57]
Canon CR-1 fundus camera	[43]
Canon CR DGi nonmydriatic retinal camera	[33]

Table 2. Different stages of DR.

Authors	Microaneurysm	Haemorrhage	Exudates	Inter-retinal microvascular abnormalities
Akara Sopharak et al. [1]	✓			
R.A. Welikala et al. [2]	✓	✓		
M. UsmanAkram et al. [3]	✓	✓		
M.R.K. Mookiah et al. [4]	✓	✓	✓	
R.A. Welikala et al. [5]	✓	✓	✓	
Gwenole Quellec et al. [6]	✓	✓	✓	✓
Sohini Roychowdhury et al. [7]	✓	✓	✓	
N.G. Ranamuka and R.G.N. Meegama [8]	✓	✓		
Keerthi Ram et al. [9]	✓			
Priyadarshini Patil et al. [10]			✓	
Deepthi K Prasad et al. [11]	✓		✓	
Sundararaj Wilfred Franklin and Samuelnadar Edward Rajan [12]	✓	✓		
Alireza Osareh et al. [13]	✓	✓	✓	
Harihar Narasimha-Iyer et al. [14]	✓	✓	✓	✓
Lei Zhang et al. [15]				✓
Balint Antal and Andras Hajdu [16]	✓	✓		✓
Sharath Kumar P N et al. [17]	✓	✓	✓	
Harry Pratt et al. [18]	✓	✓	✓	
Bob Zhang et al. [19]	✓	✓	✓	
Carla Agurto et al. [20]	✓	✓	✓	✓
Lama Seoud et al. [21]	✓	✓		
Weeagul Pratumgul and Worawat Sa-ngiamvibool [22]	✓		✓	
G. Mahendran and R. Dhanasekaran [23]	✓	✓	✓	
Pavle Prentasic and Sven Loncaric [24]			✓	
Elaheh Imani et al. [25]	✓	✓	✓	
Joao Dallyson Sousa de Almeida et al. [27]				✓
Chengzhang Zhu et al. [28]	✓		✓	
Wong Li Yun et al. [29]	✓	✓		
Cemal Kose et al. [30]	✓	✓	✓	
Kamadi V.S.R.P. Varma et al. [31]				✓
Akara Sopharak et al. [32]	✓	✓	✓	
Andrew Hunter et al. [33]			✓	
M. Kavitha and S. Palani [34]			✓	
Ahmed H. Asad et al. [35]			✓	
Dawn A. Sim et al. [36]	✓	✓		
W. Mimi Diyana W. Zaki et al. [37]	✓	✓	✓	
Xiwei Zhang et al. [38]	✓	✓	✓	
M. UsmanAkram et al. [39]	✓			
Meindert Niemeijer et al. [40]				✓
Baek Hwan Cho et al. [41]				✓
S. Wilfred Franklin and S. Edward Rajan [42]				✓
Jyoti Prakash Medhi and Samarendra Dandapat [43]	✓	✓	✓	✓
Eysteinn Mar Sigurosson et al. [44]				✓
Francesco Saverio Sorrentino et al. [45]				✓
MeysamTavakoli et al. [46]				✓
RobertoVega et al. [47]				✓
María García et al. [48]	✓	✓		
Marwan D. Saleh and C. Eswaran [49]	✓	✓		
P.V.Rao et al. [50]				✓
María García et al. [51]			✓	
Balint Antal and Andras Hajdu [52]	✓	✓	✓	✓
Sudeshna Sil Kar and Santi P. Maity [53]			✓	
Meindert Niemeijer et al. [54]	✓	✓	✓	
David J Taylor et al. [55]	✓		✓	
Malay Kishore Dutta et al. [56]	✓		✓	
Arturo Aquino et al. [57]			✓	
Istvan Lazar and Andras Hajdu [58]	✓			
Bob Zhang et al. [19]	✓		✓	✓
Balazs Harangi and Andras Hajdu [59]			✓	

contributions of diagnostic method in 2008 showed the EX of 2.5%, MA of 2% and HM of 3% in the early detection of DR. It can also be seen from the figure that, the percentage contribution of HM, EX and IRMA stages of DR are zero in 2011 indicating the absence of these stages. In 2016, we have observed the maximum percentage contribution of EX is 28% than other previous year papers. Furthermore, studies showed that the HM stage exerts maximum 19% for 2014 papers. In the year 2013, if the percentage contribution of MA value obtained is 20% higher than other three stages, then the screening and diagnosing of DR are considered to be better. Moreover, the percentage contributions of MA, HM, EX and IRMA in the year 2012 are 10.3%, 14%, 5% and 11% respectively.

4. Feature extraction and machine learning methods

4.1. Feature extraction

For classifying the DR, each digital fundus image is represented by a vector of visual features called signature. We found that MAs, HMs, EXs and IRMAs appear with various significant vectors of visual features or signatures such as size, shape, colour, intensity, texture, etc., they consider. Depending on either normal or DR condition, the size of DR lesions achieves a value of 20% as against 35% for shape and 43.33% for colour. For the digital fundus retinal image detection, the feature extraction of statistics and edge strength are 5% and 8.33% respectively. Prior to the characteristics of common features, the classification of DR image regions was simplified by describing new vessels containing a number of vessel pixels, the number of vessel segments which are closely spaced with a multiple number of vessel orientations, blood vessel area, and vessel density. In order to determine local features based on the morphology of vasculature, the number of vessel segments, vessel pixels, vessel orientations and vessel density values achieve 6.7%, 6.7%, 8.33% and 6.7% respectively. Thus we observe that for DR classification, the most important features of intensity, contrast, texture and blood vessel area have the achievable percentage of 20%, 5%, 25% and 5% respectively. Finally, by examining the best combination from all features, the colour feature of 43.33% significantly improves the requirement for feature extraction than the other selected feature groups. Table 3 summarises the salient features required for the extraction of DR stages.

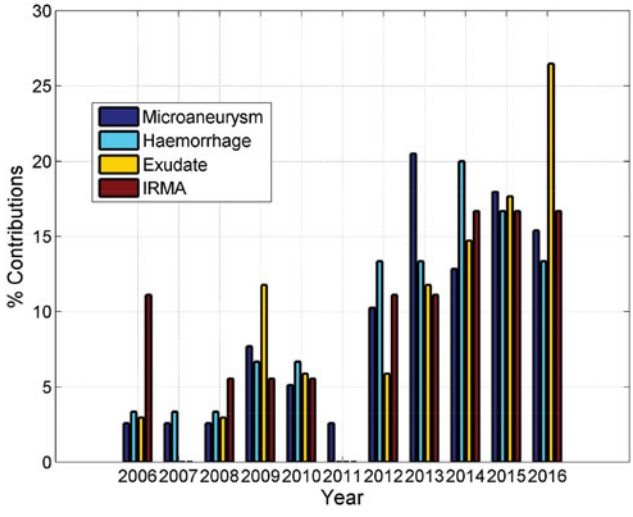

Figure 3. Review of Retinal Abnormalities detection.

4.2. Machine learning methods

A diagnosis of DR lesions is also concluded from the detected feature selection and its pathologies using a machine learning methods. We model the MAs, EXs, HMs and IRMAs of DR classes using machine learning collective of the state-of-the-art classifiers involving SVM, an extension of multimodal m-Mediod based modelling scheme, GMM. For machine learning based One Rule Classifier (ORC), classification of the retinal fundus image is performed by generating a single rule of target class and distinguishing it with the maximum accuracy from the samples belongs to all other classes. Besides, with the effective classification of DR, a simple and robust probabilistic classifier called Naive Bayes (NB) classifier has been introduced that assumes individual features to be independent. In order to provide high flexibility for different databases, an ensemble based framework has been developed for selecting the best grading performance of MA detector. In 2016, a supervised approach of extreme ELM based segmentation method has inspected to learn the model of segmenting the vessels with the aid of manually segmented training images called gold standard.

Since the blood vessel properties are mostly subjective, their accurate extraction and classification with various metrics become very difficult through mathematical solutions. This has been suggested the use of

Table 3. Salient features of different methods.

Features	Citations
Size	[1,3,12,13,22,34,38,42,46,49,53,58]
Shape	[1,3,6,11,12,16,21,22,23,24,39,43,44,46,48,49,51,54,57,58,59]
Color	[1,3,6,9,11,12,13,14,19,21,23,24,32,33,34,39,43,44,47,48,51,54,55,56,57]
Number of vessel pixels	[2,5,15,35]
Amount of vessel segments	[2,5,15,35]
Number of vessel orientations	[2,5,7,15,35]
Vessel density	[2,5,15,35]
Intensity	[8,27,28,32,33,39,43,44,47,52,56,59]
Statistics	[9,39,41]
Blood vessel area	[4,7,18]
Texture	[4,6,10,11,12,13,18,19,20,23,25,30,34,52]
Edge strength	[8,10,13,33,34]
Contrast	[17,32,60]

Table 4. Machine learning methods for the diagnosis of DR.

Machine learning methods	Citations	
naive Bayes classifier	[1,58]	
support vector machine classifier	[2,5,23,39,41,48]	
m-Mediods approach	[3,39]	
one rule classifier	[11]	
Bayesian algorithms	[14]	
An ensemble-based framework	[16]	
ELM	[28]	
Support Vector Regression	[27]	
fuzzy	[8,44,52]	
	[13]	c-means clustering
	[31]	Modified Gini index SLIQ decision tree
	[53]	conditional entropy
Neural Network classifier	[51]	
	[4,23]	Probabilistic
	[11,42,50]	Back propagation
	[12,22,33]	artificial
	[13]	multilayer
	[18]	Convolutional
	[24]	Deep
	[29]	Feedforward
	[34]	Levenberg–Marquardt algorithm
	[36]	Joslin Vision Network
	[42,48,50]	Multilayer perceptron
	[47]	Lattice with Dendritic Processing
	[48]	radial basis function

linguistic descriptor called fuzzy based approaches like C-means clustering, Modified Gini Index SLIQ decision tree, conditional entropy methods as used in image segmentation using multiple thresholds.

In addition to the conferred approaches, the detection and classification of DR lesions with different classes in retinal fundus images using NNs have also been exploited. In order to classify the retinal fundus images into normal, non-proliferative retinopathy and proliferative retinopathy, various features were entered as inputs to NN. The vast majority of research on various NN classification based on Probabilistic (PNN), Artificial Neural Network (ANN), Convolutional Neural Network (CNN) have been carried out for the better early detection and classification of DR diagnosis. A brief summary of Machine learning methods suggested by many authors for the detection of DR is depicted in Table 4.

5. Performance and review outcome

5.1. Performance study

In order to evaluate the performance of such differently exploited approaches and machine learning algorithms, it is the common practice of estimating the most publicly available performance metrics of sensitivity, specificity, precision, accuracy and Area Under the Curve (AUC). Here, sensitivity and specificity are the pixel level accuracy measurement of algorithms. Accuracy is referred to be the overall success rate of the classifier. False Positive rate (FP), True Positive rate (TP) and other similar parameters are chosen as the pixel based evaluation. M. Usman Akram et al. [3] reported the sensitivity of 97.39%, specificity of 98.02%, accuracy of 98.52% and area under the curve of 98.10% respectively. Nayomi Geethanjali Ranamuka and Ravinda Gayan N. Meegama [8] have managed to detect the exudates with specificity, sensitivity, and accuracy of 100%, 81.75% and 99.84% respectively. The overall mean values of sensitivity and precision were reported to be 58.43% and 90.17%, respectively. Akara Sopharak et al. [1] have achieved a high efficiency of 99.99% accuracy. In the evaluation part, Maria Garcia et al. [51] have obtained the maximum sensitivity, specificity and accuracy values of 100%, 92.59% and 97.01% respectively, and hence we state that the screening method is considered to be better. Moreover, Sudeshna Sil Kar and Santi P. Maity [53] illustrated an accuracy including 2.60% FP and 72.82% TP for the extraction of retinal blood vessels at the pixel level of retinal images. The summary of performance measures of DR detection methods are given in Table 5.

5.2. Research gaps and challenges

During image acquisition, most of the standard field stereoscopic colour photography of retinal images are noisy and non-uniformly illuminated due to inappropriate focussing of light and thus practicing DR screening is quite impractical. This makes the accuracy of extracting the thin, narrow and small retinal blood vessels become difficult, since small blood vessels are

Table 5. Performance metrics of DR diagnostic methods.

Authors [Citation]	Sensitivity (%)	Specificity (%)	Precision (%)	Accuracy (%)	AUC (%)	FP (%)	TP (%)	Other features (%)
Akara Sopharak et al. [1]	85.68	99.99	83.34	99.99				
R.A. Welikala et al. [2]	100	90			96.32			
M. UsmanAkram et al. [3]	97.39	98.02		98.52	98.10			
M.R.K. Mookiah et al. [4]	96.27	96.08		96.15				
R.A. Welikala et al. [5]	91.38	96		94.54	96			
Gwenole Quellec et al. [6]						50		False negative rate- 4.70
Sohini Roychowdhury et al. [7]	100	53.16		99.70	90.40			
Nayomi Geethanjali Ranamuka and Ravinda Gayan N. Meegama [8]	81.75	100		99.84				
Keerthi Ram et al. [9]	90	90						
Priyadarshini Patil et al. [10]	87							
Deepthi K Prasad et al. [11]	93.30	95.23		93.80				
Sundararaj Wilfred Franklin and Samuelnadar Edward Rajan [12]	96.30	99.80		99.70				
Alireza Osareh et al. [13]	96.00	94.60		95.30				
Harihar Narasimha-Iyer et al. [14]			97	99.30		3		False alarm- 10
Lei Zhang et al. [15]				94.16		3.72	72.86	
Balint Antal and Andras Hajdu [16]	96	51		75				
Sharath Kumar P N et al. [17]	80	50		96				
Harry Pratt et al. [18]	95			75				
Bob Zhang et al. [19]				80.52				
Carla Agurto et al. [20]								Cumulative distribution function- 92
Lama Seoud et al. [21]								ROC- 89.90
Weeagul Pratumgul and Worawat Sa-ngiamvibool [22]	99.25	97.77		98.89				
G. Mahendran and R. Dhanasekaran [23]				97.89				
Pavle Prentasic and Sven Loncaric [24]	78							
Elaheh Imani et al. [25]	92.01	95.45						
Joao Dallyson Sousa de Almeida et al. [27]								Mean absolute error- 46
Chengzhang Zhu et al. [28]	71.40	98.68		96.07				
Wong Li Yun et al. [29]	90	100						
Cemal Kose et al. [30]	98.10	99.80		90				
Kamadi V.S.R.P. Varma et al. [31]				76.8				
Akara Sopharak et al. [32]	80	99.50						
Andrew Hunter et al. [33]	92	65						
M. Kavitha and S. Palani [34]				95.55				
Ahmed H. Asad et al. [35]	75.84	93.88		91.55				
Dawn A. Sim et al. [36]	93	78						
W. Mimi Diyana W. Zaki et al. [37]	82	86		85.90				
Xiwei Zhang et al. [38]	83				95			
M. UsmanAkram et al. [39]				99.50				
Meindert Niemeijer et al. [40]				97.40				
Baek Hwan Cho et al. [41]	97	82.2		83.9				
S. Wilfred Franklin and S. Edward Rajan [42]	69.70	98.30		95.03				
Jyoti Prakash Medhi and Samarendra Dandapat [43]	98.86	98.05		98.92				
Eysteinn Mar Sigurosson et al. [44]				95.19				
MeysamTavakoli et al. [46]	100	70						
RobertoVega et al. [47]	83.60	96.70		95.70				
María García et al. [48]	100	56.00		83.08				
Marwan D. Saleh and C. Eswaran [49]	87.53	95.08						Kappa coefficient- 74.91
P.V.Rao et al. [50]				90.60				
María García et al. [51]	100	92.59		97.01				
Balint Antal and Andras Hajdu [52]	90	91		90	98.90			
Sudeshna Sil Kar and Santi P. Maity [53]				96.16		2.60	72.82	
Meindert Niemeijer et al. [54]	87.30	60						

(*continued*)

Table 5. Continued.

Authors [Citation]	Sensitivity (%)	Specificity (%)	Precision (%)	Accuracy (%)	AUC (%)	FP (%)	TP (%)	Other features (%)
David J. Taylor et al. [55]	74	96						
Malay Kishore Dutta et al. [56]	90.75	84		90				
Arturo Aquino et al. [57]				99				
Istvan Lazar and Andras Hajdu [58]	61.5							
Bob Zhang et al. [19]	89.66	84.62		87.14				
Balazs Harangi and Andras Hajdu [59]	92	68		82				

most oftenly non-isolated from the background. This leads to the improper classification of DR disease. It is observed that the detection of different ophthalmologic disease symptoms found in many online databases as well as available standard DIARETDB1 [6], DRIVE [3], STARE [5] databases become a more challenging task. Existing research reports have exploited the vessel extraction algorithms with the contents, characteristics and the disease indication on the retinal images show enhanced performance on a specific database of related images than different databases. CNN is an impressive method for the application of medical image diagnosis in the interpretation and image analyses of DR. There exist two main issues. One is the desirable offset in specificity and sensitivity parameter of automated DR grading process. Another one is the over-fitting issue caused in the neural network from which large datasets are often massively skewed. In order to determine the efficient DR cruel stages, there is no complete study and any precise demonstration of the relationship of retinal vessel tortuosity.

6. Concluding remarks

The generalised framework in this paper presented a detailed review of several methods for diagnosing the DR with their feature segmentation and severity classification by employing techniques on image processing on the digitised retinal fundus photographs captured by the use of different fundus cameras obtained from the publicly available and private databases of hospitals. The robustness in automatic early detection of DR screening tool will effectively reduce the workload of ophthalmologists and patients bearing DR. The retinal images are analysed by the process involving series steps namely identification of anatomical structures, extraction of lesion features from the background images and then classification based on the severity levels. Furthermore, the individual steps of retinal image analysis showed the better achievements on screening and classification of DR. Even though by now some progress has been achieved in digital fundus images; there are still few more challenges for the direction of future research on obtaining higher accuracy of DR screening. For the early screening of DR in the retinal images, NN based research papers have achieved the classification successfully.

Disclosure statement

No potential conflict of interest was reported by the authors.

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