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ORIGINAL PAPER

Algorithms for the Automated Detection of Diabetic Retinopathy Using Digital Fundus Images: A Review

Oliver Faust · Rajendra Acharya U. · E. Y. K. Ng · Kwan-Hoong Ng · Jasjit S. Suri

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Abstract Diabetes is a chronic end organ disease that occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. Over time, diabetes affects the circulatory system, including that of the retina. Diabetic retinopathy is a medical condition where the retina is damaged because fluid leaks from blood vessels into the retina. Ophthalmologists recognize diabetic retinopathy based on features, such as blood vessel area, exudes, hemorrhages, microaneurysms and texture. In this paper we review algorithms used for the extraction of these features from digital fundus images. Furthermore, we discuss systems that use these features to classify individual fundus images. The classifications efficiency of different DR systems is discussed. Most of the reported systems are highly optimized with respect to the analyzed fundus images, therefore a generalization of individual results is difficult. However, this review shows that the classification results improved has improved recently, and it is getting closer to the classification capabilities of human ophthalmologists.

Keywords Diabetic retinopathy · Fundus images · Automated detection · Blood vessel area · Exudes · Hemorrhages · Microaneurysms · Maculopathy

O. Faust (✉) · R. Acharya U.
Department of Electronics and Computer Engineering,
Ngee Ann Polytechnic,
535 Clementi Road,
Singapore, Singapore 599489
e-mail: fol2@np.edu.sg

E. Y. K. Ng
School of Mechanical and Aerospace Engineering,
College of Engineering, Nanyang Technological University,
50 Nanyang Avenue, Singapore 639798

K.-H. Ng
Department of Biomedical Imaging, University of Malaya,
Kuala Lumpur, Malaysia

J. S. Suri
Biomedical Technologies,
Denver, CO, USA

J. S. Suri
University of Idaho,
Moscow, ID, USA

Introduction

The fast progression of diabetes is one of the main challenges of current health care. The number of people afflicted with the disease continues to grow at an alarming rate. The World Health Organization expects the number of people with diabetics to increase from 130 million to 350 million over the next 25 years [76]. The situation is made worse by the fact that only one half of the patients are aware of the disease. And in the medical perspective, diabetes leads to severe late complications. These complications include macro and micro vascular changes which result in heart disease, renal problems and retinopathy. For example, studies in the United States show that diabetes is the fifth-deadliest disease, and still there is no cure. In the United States, the total annual economic cost of diabetes in 2002 was estimated to be $132 billion, this translates to one out of every 10 health care dollars spent [14].

Diabetic retinopathy (DR) is a common complication of diabetes. Indeed, it is so common that it is the leading cause of blindness in the working population of western countries [54] The rate of diabetes is increasing, not only in developed countries, but in underdeveloped countries as well. Unfortunately, most developing countries lack basic recoding of DR cases [40]. It is estimated that 75% of people with diabetic

retinopathy live in developing countries [55]. The situation in developing countries is especially bad, because there is inadequate treatment. Regardless of the health care situation in their country of origin, people with diabetes are 25 times more likely to develop blindness when compared with individuals who do not suffer from this disease [74]. DR is a silent disease, because it may only be recognized by the patient when the changes in the retina have progressed to a level where treatment is complicated and nearly impossible. The prevalence of retinopathy varies with the age of onset of diabetes and the duration of the disease.

So far, the most effective treatment for DR can be administered only in the first stages of the disease. Therefore, early detection through regular screening is of paramount importance. To lower the cost of such screenings, digital image capturing technology must be used, because this technology enables us to employ state-of-the-art image processing techniques which automate the detection of abnormalities in retinal images.

This paper reviews automated detection systems for DR. This review is structured as follows: First we discuss the underlying disease, i.e. diabetes, in terms of its causes and effects on the human body. Following the goals of this paper, we focus on the effects of diabetes on the eye. These effects lead to features, such as blood vessel area, exudes, hemorrhages, microaneurysms and textures [5]. These features are used for the automatic detection of DR. In the automatic detection of DR stages section we reviewed different automated detection systems which have been reported in scientific literature. In the discussion section we discussed the advantages and disadvantages of different methods. The last section of this paper presents conclusions and outlines further work.

Diabetes

Diabetes mellitus (DM) is the name of a chronic, systemic, life-threatening disease. It occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. This results in an abnormal increase in the glucose level in the blood. Over time this high level of glucose causes damage to blood vessels. This damage affects both eyes and nervous system, as well as heart, kidneys and other organs [8].

In general there are two types of diabetes. Diabetes type 1 results from a failure of the human body to produce insulin. Type 1 diabetes is less common than type 2 diabetes. People with type 1 diabetes take insulin injections.

It is estimated that 90-95% of Americans, who are diagnosed with diabetes, have type 2 diabetes [1]. This form of diabetes usually develops in adults age 40 and older and is most common in the age group over age 55. About 80% of people with type 2 diabetes are overweight. It was reported that type 2 diabetes is often part of a metabolic syndrome that includes obesity, elevated blood pressure, and high levels of blood lipids [61].

Causes

The recent increase in diabetes can be attributed to an aging population and increasing prevalence of obesity as well as sedentary life habits. Genetic inheritance plays a role in both, type 1 and type 2 diabetes. But it appears that type 1 diabetes is also triggered by some (mainly viral) infections. There is also a genetic element in individual susceptibility to some of these triggers which has been traced to particular human leukocyte antigen genotypes. However, even in those who have inherited the susceptibility, type 1 DM seems to require an environmental trigger. Some evidence indicates that the B4 virus might be such a trigger.

Effects

Diabetes affects the kidney, eyes, nerves and heart. In the following sections, we have discussed these affects briefly.

Diabetic nephropathy

Diabetic nephropathy is the main cause of end-stage renal diseases. When the body digests protein it contaminates the blood with waste products. The kidneys filter out these waste products. A large number of small blood vessels (capillaries) are an essential component of this filter. After 20-30 years, they start to leak and useful protein is lost in the urine [12].

It was stated that interruption of the renin–angiotensin system slows the progression of renal diseases in patients with type 1 diabetes, but similar data are not available for patients with type 2 [80].

Diabetic cardiomyopathy

Patients with both diabetes and ischemic heart disease seem to have an enhanced myocardial dysfunction leading to accelerated heart failure (diabetic cardiomyopathy). Thus, patients with diabetes are prone to congestive heart failure [62].

Diabetic neuropathy

Diabetic neuropathy results in a gradual loss of nerve function which limits the amount of sensation on the plantar aspects of the feet [83]. This diminished sensation disables individuals from being able to feel the onset or occurrence of a foot injury. As a result, patients with this disease are more inclined to experience plantar ulceration [83].

People with DM can develop nerve problems at any time, but the longer a person has diabetes, the greater the risk. Acharya et al. state that abnormal plantar pressures play a major role in the pathologies of neuropathic ulcers in the diabetic foot [6].

Diabetic retinopathy

Diabetes mellitus often results in diabetic retinopathy which is caused by pathological changes of the blood vessels which nourish the retina. DR is the main cause of new cases of blindness among adults aged 20–74 years. During the first 20 years of the disease, nearly all patients with type 1 diabetes and >60% of patients with type 2 diabetes have retinopathy. In the Wisconsin Epidemiologic Study of DR, 3.6% of younger-onset patients (type 1 diabetes) and 1.6% of older-onset patients (type 2 diabetes) were legally blind [38]. In the younger-onset group, 86% of blindness was attributable to DR. In the older-onset group, in which other eye diseases were common, one-third of the cases of legal blindness were due to DR. Figure 1 shows the different features of the typical DR image.

DR occurs when the increased glucose level in the blood damages the capillaries, which nourish the retina. As a result of this damage, the capillaries leak blood and fluid on the retina [24]. The visual effects of this leakage are features, such as microaneurysms, hemorrhages, hard exudates, cotton wool spots or venous loops, of DR [6, 84].

Types of diabetic retinopathy DR can be broadly classified as nonproliferative DR (NPDR) and proliferative DR (PDR). Depending on the presence of specific DR features, the stages can be identified [6, 17]. The following list describes three subclasses of NPDR as well as PDR:

- Mild NPDR: at least one microaneurysm with or without the presence of retinal haemorrhages, hard exudates, cotton wool spots or venous loops (Fig. 2(b)). Approximately 40% of people with diabetes have at least mild signs of diabetic retinopathy [48].
- Moderate NPDR: numerous microaneurysms and retinal haemorrhages are present. A limited amount and cotton wool spots of venous beading can also be seen (Fig. 2(c)). 16% of the patients with moderate NPDR will develop PDR within 1 year [33].
- Severe NPDR: is characterized by any one of the following (4-2-1 rule) characteristics: (1) numerous haemorrhages and microaneurysms in 4 quadrants of the retina (2) venous beading in 2 or more quadrants (3) Intraretinal microvascular abnormalities in at least 1 quadrant (Fig. 2(d)). Severe NPDR carries a 50% chance of progression to PDR within 1 year [33].
- PDR: is the advanced stage; signals, sent by the retina for nourishment, trigger the growth of new blood vessels. These blood vessels do not cause symptoms or vision loss. But, their walls are thin and fragile, this leads to a high risk that they leak blood (Fig. 2(e)). This leaked blood contaminates the vitreous gel and this causes severe vision loss and even blindness. About 3% of people, with this condition, may experience severe visual loss [16].

Detection methods

Early detection of DR is important, because treatment methods can slow down the progression of the disease. Most treatment methods are based on laser technology.

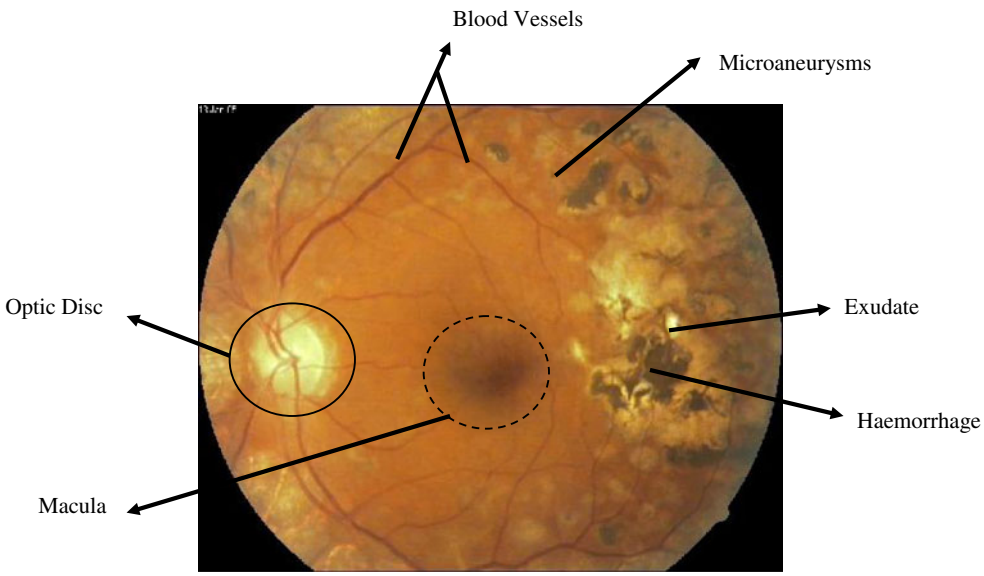

Fig. 1 Different features in a DR image

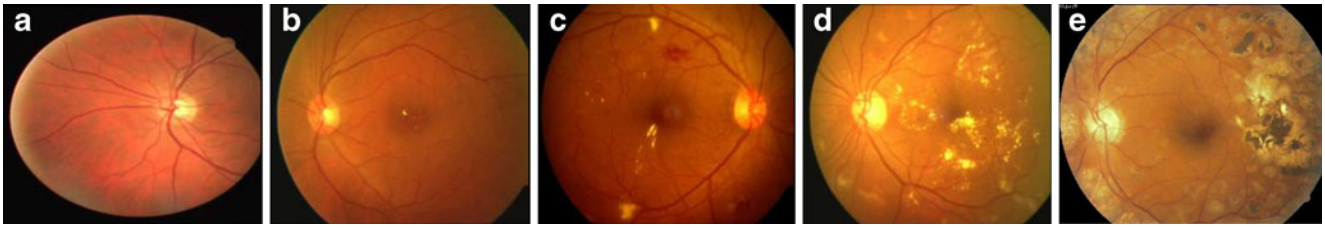

Fig. 2 Typical fundus images: (**a**) normal (**b**) mild DR (**c**) moderate DR (**d**) severe DR (**e**) prolific DR

Laser photocoagulation cauterizes ocular blood vessels, which effectively stops their leakage. The focal laser treatment method reduces retinal thickening. This may prevent worsening of retinal swelling. To be specific, this treatment reduces the risk of vision loss by 50%. For a small number of cases, with total vision loss, improvement is possible [64].

Fundus images

Medical image analysis is a research area that currently attracts lots of interest from both scientists and physicians. The objective of this field is to develop computational tools which will assist quantification and visualization of interesting pathology and anatomical structures. These tools work with digital fundus images of the eye. The procedure of taking fundus images starts by dilating the pupil with pharmaceutical eye drops. After that the patient is asked to stare at a fixation device in order to steady the eyes. While taking the pictures, the patient will see a series of bright flashes. The entire process takes about five to ten minutes. To ensure that DR treatment is received on time, the eye fundus images of diabetic patients must be examined at least once a year [22].

Feature extraction methods and analysis

Image processing can do both reduce the workload of screeners and play a central role in quality assurance tasks. Therefore, there has been an increase in the application of digital image processing techniques for automatic detection of DR [63]. For example, color features on Bayesian statistical classifier were used to classify each pixel into lesion or non-lesion classes [73].

The following sections describe blood vessels, exudes, hemorrhages, microaneurysms and maculopathy detection techniques. These detection techniques yield most of the features which are used in automated DR detection systems.

Blood vessels

Digital fundus photography from the human eye gives clear images of the blood vessels in the retina. This method provides an excellent window to the health of a patient affected by DR. Figure 3 shows an example of blood vessel detection from different types of DR [4]. The blood vessel structure was obtained by subjecting the green component of the RGB fundus image to a number of image processing algorithms [4].

Blood vessels were detected using two-dimensional matched filters [13]. Gray-level profile of cross section of blood vessel approximated by Gaussian shaped curve. The concept of matched filter detection of signals was used to detect piecewise linear segments of blood vessels after the vessel approximation.

Vessel points in a cross section are found with a fuzzy C-means classifier [31]. They have located and outlined blood vessels in images by the use of a novel method to segment blood vessels that compliments local vessel attributes with region-based attributes of the network structure.

Hayashi et al. have developed a computer aided diagnosis system to assist physicians in detecting abnormalities associated with fundus images of the retina [29]. Their proposed system can detect blood vessel intersections and it can identify abnormal widths in blood vessels.

Computerized system for both extraction and quantitative description of the main vascular diagnostic signs from

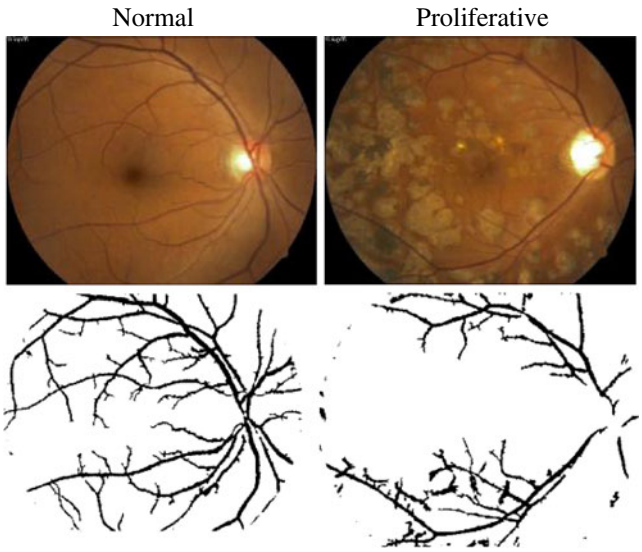

Fig. 3 Results of blood vessel detection for normal and PDR [4]

fundus images in hypertensive retinopathy was presented [23]. The features they have taken into account are vessel tortuosity, generalized and focal vessel narrowing, presence of Gunn or Salus signs.

A new system is proposed for the automatic extraction of the vascular structure in retinal images, based on a sparse tracking technique was proposed [28]. Blood vessel points in a cross section are found by means of a fuzzy c-means classifier. After tracking the vessels, identified segments were connected using greedy connection algorithm. Finally bifurcations and crossings were identified analyzing vessel end points with respect to the vessel structure.

Blood vessel tracker algorithm was developed to determine the retinal vascular network captured using a digital camera [19]. The tracker algorithm detects optic disk, bright lesions such as cotton wools spots, and dark lesions such as haemorrhages. This algorithm identifies arteries and veins with an accuracy of 78.4% and 66.5% respectively.

Vallabha et al. have proposed a method for automated detection and classification of vascular abnormalities in diabetic retinopathy [70]. They detected vascular abnormalities using scale and orientation selective Gabor filter banks. The proposed method classifies retinal images as either mild or severe cases based on the Gabor filter outputs.

The microaneurysms in retinal fluorescien angiograms was identified by first locating the fovea by sub-sampling image by factor of four in each dimension [15]. Subsequently, the image was subjected to median filtering with a 5 by 5 mask to reduce high-frequency components. Then the image was correlated with a two-dimensional circularly symmetric triangular function with modelled gross shading of the macula.

Blood-vessel detection algorithm based on the regional recursive hierarchical decomposition using quadtrees and post-filtration of edges to extract blood vessels was studied [37]. This method was able to reduce false dismissals of predominately significant edges and faster in comparison to the existing approach with reduced storage requirements for the edge map.

Li et al. have used the arteriolar-to-venular diameter ratio of retinal blood vessels as an indicator of disease related changes in the retinal blood vessel tree [45]. Their experimental results indicate a 97.1% success rate in the identification of vessel starting points, and a 99.2% success rate in the tracking of retinal vessels.

A new method of texture based vessel segmentation to overcome this problem was proposed [10]. The Fuzzy C-Means (FCM) clustering algorithm was used to classify the feature vectors into vessel or non-vessel based on the texture properties. They compared their method with hand-labeled ground truth segmentation for five images and achieved 84.37% sensitivity and 99.61% specificity.

Exudates

Exudates are accumulations of lipid and protein in the retina. Typically they are bright, reflective, white or cream colored lesions seen on the retina. They indicate increased vessel permeability and an associated risk of retinal edema. Although, not sight threatening in themselves, they are a marker of fluid accumulation in the retina. However, if they appear close to the macula center they are considered sight threatening lesions. Most of the time they are seen together with microaneurysms. These microaneurysms indicate themselves increased leakage, therefore the classical lesion is a circular ring of exudates with several microaneurysms at its center. Figure 4 shows an example exudates detection from different types of DR [4]. In the result pictures, black indicates no exudates and white indicates the area where exudates were detected. An important step in the extraction process is removing prominent structures of the retina, such as blood vessel tree and optic disc. After these structures have been removed, the exudates were detected using a sequence of image processing algorithms [4].

A novel approach which combines brightness adjustment procedure with statistical classification method and local-window-based verification strategy was proposed [73]. Their results indicate that they were able to achieve 100% accuracy in terms of identifying all the retinal images with exudates while maintaining a 70% accuracy in correctly classifying the truly normal retinal images as normal.

Hunter et al. have studied neural network based exudates detection [32]. They introduced a hierarchical feature selection algorithm, based on sensitivity analysis to

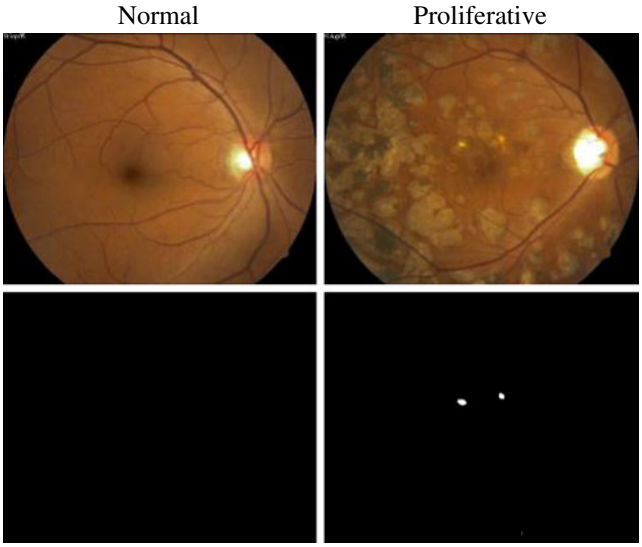

Fig. 4 Results of exudates detection for normal, PDR

distinguish the most relevant features. The final architecture achieved 91% lesion-based performance using a relatively small number of images.

A new approach to automatically extract the main features in color fundus images was proposed [44]. Optic disk was localized by the principal component analysis (PCA) and its shape was detected by a modified active shape model (ASM). Exudates were extracted by the combined region growing and edge detection. Their results show 99%, 94%, and 100% for disk localization, disk boundary detection, and fovea localization respectively. The sensitivity and specificity for exudate detection were 100% and 71%.

Osareh et al. have presented results for fundus image based exudes classification [56]. Their method evaluated different learning algorithms, such as neural network and support vector machine. The neural network based approach performs marginally better than the support vector machine based approach, the latter is more flexible given boundary conditions such as control of sensitivity and specificity rates. The neural network results were: accuracy = 93.4%, sensitivity = 93.0%, specificity = 94.1%.

Exudates are found using their high grey level variation, and their contours were determined by means of morphological reconstruction techniques [72]. The optic disc was detected by means of morphological filtering techniques and the watershed transformation. Their results show a mean sensitivity of 92.8% and a mean predictive value of 92.4%.

Local contrast enhancement fuzzy C-means and support vector machine was used to detect and classify bright lesions [77]. Their classification results are as follows:

- Classification between bright lesions and bright non-lesion: sensitivity = 97%, specificity = 96%.
- Classification between exudates and cotton wool spots: sensitivity = 88%, specificity = 84%.

Fuzzy C-means clustering and morphological reconstruction was used to detect exudates detection on low-contrast images taken from non-dilated pupils [67]. The sensitivity and specificity for the exudates detection are 86% and 99% respectively.

Flemming et al. have used multi-scale morphological algorithms to obtain what they call candidate exudates [21]. The final classification was done by determining the background (drusen) of the candidates. Exudates were detected with sensitivity 95.0% and specificity 84.6% in a test set of 13219 images of which 300 contained exudates.

Automated system capable of detecting exudates and cotton-wool spots and differentiating them from drusen in color images obtained in community based diabetic patients has been developed [52]. The machine learning can be further improved with additional training data sets, and can be useful for detecting clinically important bright lesions, enhancing early diagnosis, and reducing visual loss in patients with diabetes.

A set of optimally adjusted morphological operators were used for the detection of exudate in diabetic retinopathy patients' non-dilated pupil and low-contrast images [68]. They used these operators to design an exudes detection system. This system achieved sensitivity and specificity of 80% and 99.5%, respectively.

Microaneurysms detection

Microaneurysms detection is very important, because these structures constitute the earliest recognizable feature of DR. The first reports which link these structures to DR date back to 1879 [11]. More recently, Jalli et al. have analyzed the appearance and disappearance of microaneurysms in different phases of fluorescein angiography [34]. In a similar study both formation rate and disappearance of microaneurysms in early DR were analyzed [30]. The microaneurysms turnover were computed reliabibly from color fundus images [9]. They used a new method called MA-tracker to count microaneurysms. They showed that the microaneurysms remain stable over time, but only 29% remain at the same place.

Figure 5 shows the results of microaneurysms detection for normal and PDR [4]. In example the green component, of the RGB fundus image, was chosen to obtain the microaneurysms. Similar to the exudates detection algorithm, first the prominent structures within retina images, such as blood vessel tree and optic disc are to be removed. After that a sophisticated sequence of image processing algorithms was used to determine the areas within the fundus images to get microaneurysms [4].

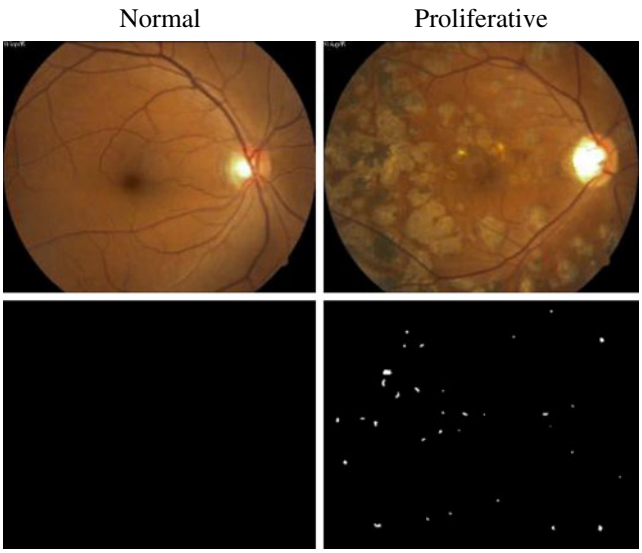

Fig. 5 Results of microaneurysms detection for normal, PDR [4]

The automated identification of diabetic retinopathy based on the presence of microaneurysms was studied [35]. The optometrists achieved 97 per cent sensitivity at 88 per cent specificity and the automated retinopathy detector achieved 85 per cent sensitivity at 90 per cent specificity.

Hemorrhages

As the degree of DR advances retinal hemorrhages become evident. They indicate an increased ischemia (loss of oxygen) retina. As their numbers increase the retinal vessels become more damaged and leaky this leads to exudation of fluid, lipid and proteins. Figure 6 shows the result of hemorrhage detection [4]. The white patches indicates the hemorrhages in the image. There are two parts in haemorrhages detection:

i) Detection of blood vessels;
ii) Detection of blood vessels with haemorrhages.

The image with blood vessel alone was subtracted from image with blood vessel and haemorrhages to get the image with haemorrhages [4].

Ege et al. have developed a tool which provides automatic analysis of digital fundus images [18]. In their study, a Bayesian, a Mahalanobis, and a k nearest neighbor classifier were used on 134 retinal images. The Mahalanobis classifier showed the best results: microaneurysms, haemorrhages, exudates, and cotton wool spots were detected with a sensitivity of 69%, 83%, 99%, and 80%, respectively.

Fully automated computer algorithms were able to detect hard exudates and haemorrhages and microaneurysms (HMA) using of a new technique, termed a 'Moat Operator', was proposed [65, 66]. The sensitivity and specificity for exudates detection were 88.5% and 99.7%, respectively and algorithm achieved a sensitivity of 77.5% and specificity of 88.7% for detection of HMA.

Larsen et al. have used image processing for the detection of both hemorrhages and microaneurysms [41]. Their algorithm demonstrated a specificity of 71.4% and a sensitivity of 96.7%.

The robust detection of red lesions in digital color fundus photographs is a critical step in the development of automated screening systems for diabetic retinopathy [53]. Their method achieved a sensitivity of 100% at a specificity of 87% in detecting the red lesions.

Bottom-up and top-down strategies were applied to cope with difficulties in lesions detection, such as inhomogeneous illumination [78]. After the application of appropriate strategy, they used local contrast enhancement, fuzzy C-means and hierarchical support vector machine to classify bright non-lesion areas, exudates and cotton wool spots.

Distance of exudates from fovea

In diabetic maculopathy, fluid rich in fat and cholesterol, leaks out of damaged blood vessels. If fluid and cholesterol accumulates near the center of the retina (the macula) it can cause distortion and permanent loss of central vision. There are the two types of maculopathy eye disease:

- Non-Clinically Significant Macular Edema (NCSME). Figure 7(a) shows a fundus image of NCSME, in this stage the patient will not realize that he is affected, because there are no visible symptoms. Exudates start to leak, and the retina becomes boggy like a sponge. But, the patient's vision is not seriously affected, because the locations of the exudates are far away from the fovea.
- In the Clinically Significant Macular Edema (CSME) stage, most of the retinal blood vessels are damaged and the leakage area becomes bigger. The exudates leak out and this liquid concentrates very close to the fovea. The visibility is greatly affected, because the detected image cannot be focused on the macula properly. Figure 7(b) shows a CSME fundus image.

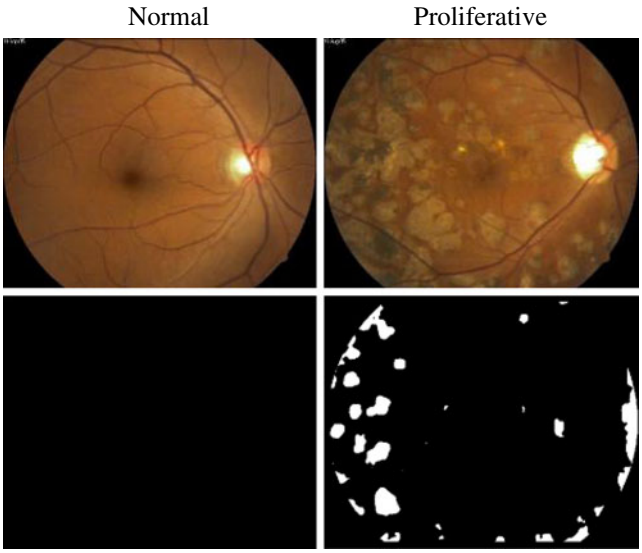

Fig. 6 Results of hemorrhages detection for normal, PDR [4]

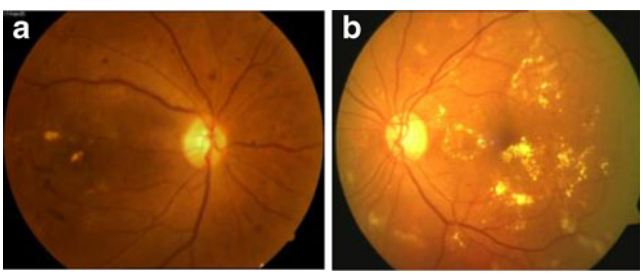

Fig. 7 Fundus images: (**a**) NCSME (**b**) CSME

Philips et al. have studied diabetic maculopathy and detection of exudates on fundus images [58, 59].

Nayak et al. have present a computer- based system for the identification of CSME, non-CSME and normal fundus eye images [49]. Features are extracted from raw fundus images which are then fed to an artificial neural network classifier. They demonstrated a sensitivity of more than 95% for these classifiers with a specificity of 100%.

Texture

Texture is a measure of properties, such as smoothness, coarseness, and regularity of pixels, in an image [26]. One way to define texture is: a mutual relationship among intensity values of neighboring pixels repeated over an area larger than the size of the relationship [39]. Conventional texture recognition systems can be grouped into three classes: structural, statistical and spectral [27, 47]. Textures can be defied using statistical approaches, this yields characterizations such as smooth, coarse, grainy and so on. Statistical algorithms are based on the relationship between intensity values of pixels; measures include entropy, contrast, and correlation based on the gray level co-occurrence matrix [60]. Different texture parameters can be used for the detection of DR stages [69].

Automatic detection of DR stages

Over the last two decades there was a rapid development of Computer-aided diagnosis (CAD) [25]. The idea of using computers to help in medical image diagnosis is in more practice. However, the quality of these CAD systems increased with more accurate sensor data, more processing power and better understanding of the underlying disease. Recently, Lee et al. have concluded that the performance of their computer vision system in diagnosing early retinal lesions is comparable with that of human experts [42]. In the next section we have reviewed different classification methods.

Classification methods

Colour features were used on Bayesian statistical classifier classify each pixel into lesion or non-lesion classes [73]. They have achieved 100% accuracy in identifying all the retinal images with exudates, and 70% accuracy in classifying *normal* retinal images as *normal*.

DR and normal retina were classified automatically using image processing and multilayer perceptron neural network [65] The system yielded a sensitivity of 80.21% and a specificity of 70.66%. Automated diagnosis of NPDR, based on three lesions: hemorrhages and microaneurysms, hard exudates, and cotton wool spots, was studied [80]. The method was able to identify the NPDR stage correctly with an accuracy of 81.7%.

Exudates, haemorrhages, and microaneurysms were used for screening of DR subjects [81]. The sensitivity and specificity of their software was 74.8% and 82.7%, respectively in differentiating DR and normal subjects correctly.

Early detection of DR (presence of microaneurysms) was proposed based on decision support system by Kahai et al. [36]. Bayes optimality criteria was used to detect microaneurysms. Their method was able to identify the early stage of DR with a sensitivity of 100% and specificity of 67%.

Normal, mild, moderate, severe and prolific DR stages were automatically classified using both area and perimeter of the RGB components of the blood vessels together with a feedforward neural network [75]. System average classification efficiency was 84% and sensitivity, specificity were 90% and 100% respectively. Nayak et al. have used exudates and blood vessel area along with texture parameters coupled with neural network to classify fundus images into normal, NPDR and PDR [48]. They obtained a detection accuracy of 93%, sensitivity and specificity of 90% and 100% respectively. Recently, bispectral invariant features were used as features for the support vector machine classifier to classify the fundus image in to normal, mild, moderate, severe and prolific DR classes by Acharya et al. [7]. They have demonstrated an average accuracy of 82% and sensitivity, specificity of 82% and 88% respectively. Normal, mild, moderate, severe and prolific classes of DR were classified automatically based on haemorrhages, microaneurysms, exudates and blood vessel areas with a support vector machine classifier [4]. The system was able to identify the unknown class accurately with an efficiency of more than 85% and a sensitivity of more than 82% and a specificity of 86%.

Nicolai et al. have designed an automated lesion system, which identified 90.1% of patients with DR and 81.3% of patients without DR, when applied in a screening population comprising of patients with untreated DR [51]. The automated system demonstrated a sensitivity of 93.1% and a specificity of 71.6%.

Usher et al. have designed a support system for DR screenings [82]. Their system showed a maximum sensitivity for the detection of any retinopathy on a per patient basis of 95.1%, accompanied by a specificity of 46.3%. The specificity could be increased as far as 78.9%, but this increase was accompanied by a fall in sensitivity to 70.8%. At a setting with 94.8% sensitivity and 52.8% specificity, no cases of sight threatening retinopathy were missed.

Neubauer et al. have investigated both photography and optic disc topography mode of the retinal thickness

analyzer [50]. The system yielded a mean 93% sensitivity for PDR together with 100% specificity for DR cases.

A software to grade the severity of 3 types of early lesions, hemorrhages and microaneurysms, hard exudates and cotton wool spots of DR was proposed to classify NPDR [43]. They were able to identify 82.6%, 82.6%, and 88.3% using the 430 images and 85.3%, 87.5%, and 93.1% using the 361 images, respectively, for hemorrhages and microaneurysms, hard exudates, and cotton wool spots.

Philip et al. have assessed the efficiency of automated "disease/no disease" grading for DR within a systematic screening programme [57]. Detection of retinopathy was achieved by automated grading with 90.5% sensitivity and 67.4% specificity.

A system, designed by Estabridis et al., has detected features such as fovea, blood vessel network, optic disk, bright and dark lesions, which are associated with DR successfully [20]. It has achieved a classification accuracy of 90%.

Li et al. have proposed a method for screening DR and distinguishing PDR from NPDR automatically using color retinal images [46]. Their method showed a sensitivity 80.5%, positive predictive value 90.8%, true positive ratio 95.8%, false positive ratio 16.7% in detecting PDR and NPDR accurately.

Abràmoff et al. have evaluated the performance of a system for automated detection of DR in digital retinal fundus images [2]. The system was constructed entirely from published algorithms and it was tested in a large, representative, screening population. They achieved a sensitivity of 84% and a specificity of 64%.

Higher order spectra features were used as input to a support vector machine classifier in order to classify fundus images into normal, mild DR, moderate DR, severe DR and PDR classes with an accuracy of 82% [3].

Vujosevic et al. have determined single lesions to grade clinical levels of DR and diabetic macular edema using both 1 and 3 nonmydriatic digital color retinal images [71].

Table 1 Comparison of different classification methods

Authors	No of classes	Method	Accuracy of classification	Sensitivity	Specificity
Wang et al. 2000 [73]	2	Minimum distance discriminant classifier	70%		
Sinthanayothin et al. 2003 [66]	2	Moat operator	Not reported	80%	71%
Usher et al. 2003 [82]	2	Lesions	Not reported	95%	53%
Singalavanija et al. 2005 [81]	2	Blood vessels, exudates, haemorrhages, microaneurysms	Not reported	75%	83%
Lee et al. 2005 [43]	3	Hemorrhages, microaneurysms, hard exudates, cotton wool spots	Max: 88%	Not reported	Not reported
Neubauer et al. 2005 [50]	2	Retinal thickness analyzer	Not reported	93%	100%
Kahai et al. 2006 [36]	2	Decision support system (DSS)	Not reported	100%	63%
Philip et al. 2007 [57]	2	Exudates	Not reported	91%	67%
Estabridis and Figueiredo 2007 [20]	2	Fovea, blood vessel network, optic disk, bright and dark lesions	90%	Not reported	Not reported
Li et al. 2008 [46]	2	Bright lesions, retinal vessel patterns	Not reported	81%	Not reported
Abràmoff et al. 2008 [2]	3	Optic disc, retinal vessels, hemorrhages, microaneurysms, vascular, abnormalities, exudates, cotton wool spots, drusen	Not reported	84%	64%
Wong et al. 2008 [75]	4	Area of blood vessel	84%	92%	100%
Nayak et al. 2008 [48]	3	Blood vessels, exudates and texture	94%	90%	100%
Acharya et al. 2008 [3]	5	Higher order spectra	82%	83%	89%
Acharya et al. 2009 [5]	5	Blood vessel, exudates, microaneurysms, haemorrhages	86%	82%	86%
Vujosevic et al. 2009 [71]	2	Single lesions	Not reported	82%	92%

Sensitivity and specificity for detecting referable levels of DR were 82% and 92%, respectively.

Table 1 summarizes the results of the 15 automated DR classification systems. The table entries are chronologically ordered and the percentage values for accuracy of classification, sensitivity and specificity are rounded to the nearest integer.

Discussion

The prolonged diabetes leads to the formation of microaneurysms and subsequently it leads to exudates as well as haemorrhages. These are the features of DR and they may lead to severe vision loss or even blindness. In order to avoid these complications, it is very important to detect DR early. This can be done by an accurate detection of microaneurysms.

It is very difficult to detect the exudates clearly, because they are tiny spots on the retina. Also, the detection of haemorrhages is very challenging. The texture of haemorrhages and macula is almost the same. So, we need to have robust algorithms which detect these features.

In the previous section we reviewed and compared 15 automated DR detection systems. The results were obtained by optimizing the algorithms for a specific set of fundus images.

In the earlier part of the research, authors have classified into two classes using fundus images based on two or three features. Then subsequently, more features were introduced to improve the classification efficiency. Also, the classification efficiency was improved further by using non-linear methods like higher order spectra [3]. The algorithms involving four features namely, area of blood vessel, exudates, haemorrhages and microaneurysms coupled with support vector machine were used to classify fundus images into five classes (normal, mild DR, moderate DR, severe DR and prolific DR) with an efficiency of 86%, sensitivity and specificity of 82% and 86% respectively [4].

Most of algorithms, discussed in the earlier section, have used only a few features like blood vessels, haemorrhages, exudates and microaneurysms etc. We predict that an algorithm involving all features namely, blood vessels, exudates, haemorrhages, microaneurysms, distance between exudates and macula, and texture parameters will be more robust. However, for this forecast to hold it is of paramount importance that the individual parameter extraction algorithms are also as robust as possible.

The design of good classifiers will increase the automatic detection rate. Huge diverse training data will significantly improve the classification efficiency. Also, fundus images taken under uniform good lighting conditions will improve the detection of DR. Furthermore, different texture parameters along with other DR features can improve the classification efficiency.

The accurate detection of macula, optic disc, microaneurysm and haemorrhages is challenging. But, we feel that, with recent advances in the medical imaging and data mining techniques as well as novel algorithms for the detection of these features, it may be possible.

Also, we feel that, the early detection of the DR (mild DR) by detecting the microaneurysm can save the progression of the disease and hence can save the loss of vision and improve the quality of life.

Conclusions

Prolonged diabetes leads to DR, where the retina is damaged due to fluid leaking from the blood vessels. Usually, the stage of DR is judged based on blood vessels, exudes, hemorrhages, microaneurysms and texture. In this paper, we have discussed different methods for features extraction and automatic DR stage detection. An ophthalmologist uses an ophthalmoscope to visualize the blood vessels and his or her brain to detect the DR stages. Recently digital imaging became available as a tool for DR screening. It provides high quality permanent records of the retinal appearance, which can be used for monitoring of progression or response to treatment, and which can be reviewed by an ophthalmologist, digital images have the potential to be processed by automatic analysis systems. A combination of both accurate and early diagnosis as well as correct application of treatment can prevent blindness caused by DR in more than 50% of all cases. Therefore, regular screenings for DR of patients with diabetes is important. The grading of the resultant fundus images is an important cost factor. Automated DR detection can reduce the grading cost and thereby make the whole screening process less expensive. Some of the algorithms and systems reviewed in this paper are close to achieve DR identification in clinical practice.

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