Microaneurysms, Haemorrhages and Exudates based Diabetic Retinopathy: Automatic Early Detection Systems and the State of the Art

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Summary
One of the comorbidities of Diabetes Mellitus is Diabetic Retinopathy. This ailment is one of the leading causes of blindness worldwide. The presence of microaneurysms, haemorrhages and exudates is one of the early symptoms of diabetic retinopathy. Research has shown that detection at an earlier stage and proper treatment can control the disease and, hence, prevents from blindness. Fundus images of retina inside the eye are utilized for screening purposes. These screenings can be done manually by a human expert or automated using advanced detection and classification algorithms. Due to scarcity of ophthalmologists worldwide, a need of advanced automated systems is sensed like never before. This paper presents a brief review of diabetic retinopathy and its associated knowledge. It then provides a comparison of recent state of the art approaches for the computer aided detection of microaneurysms, haemorrhages and exudates. The discussion and comparison of different latest algorithms is presented at the end.
Key words:
Diabetic Retinopathy, Microaneurysm, Early Detection, Fundus Images, Exudate, Haemorrhage.

1. Introduction

Diabetes Mellitus (DM), which is commonly referred as diabetes, is one of the most widespread illnesses across the world. As of 2015, it was estimated that there were 415 million people with diabetes between the ages of 20–79 years [1], which accounts for 8.8% of global adult population. Five million deaths occurred worldwide due to diabetes, and the total global health expenditure due to diabetes was estimated at 673 billion US dollars. Diabetes is responsible for 4.6% of all deaths in Saudi Arabia alone [2]. Among many comorbidities of diabetes is Diabetic Retinopathy (DR), which is a leading cause of blindness across the globe.
DR is a medical complication of the eye and is attributed to the blood vessels supplying nutrition and oxygen to the retina. Retina is a light sensitive tissue responsible for capturing the vision stimuli of color and brightness and converting them to neural signals. These signals are then sent to the brain for visual recognition and interpretation [3]. The high sugar levels, as a consequence of diabetes, cause the blood vessels in the retina to swell, leak or block. Thus, cutting and distorting the passage of life rich blood into and out of the retina. With the passage of time, the retinal cells dye due to different deficiencies, thus causing permanent and irreversible state of blindness.
Some of the most common and sufficient early signs of DR include the presence of microaneurysms, haemorrhages and exudates [4].
The presence of microaneurysms is the earliest clinically visible signs of retinopathy. It is referred to a condition when small local capillary dilates in the form of small red dots due to the presence of excess glucose over a period of time. These dots can also be in the form of clusters at times. Due to their development at a very early stage, their detection is the first step in order to stop the propagation of DR to the advanced stages. One of the most popular imaging used in detection of DR is the use of digital fundus images. A fundus image is the image of the interior surface of the eye which is opposite to the lens and includes the retina, optic disc, fovea, posterior pole and macula [5]. Figure 1 (a) presents a fundus image of a normal human eye. Figure 1 (b) shows the presence of different microaneurysms in a fundus image.
Presence of haemorrhages is another very important and early sign of DR. Due to blockages in some capillaries, new small and fragile blood vessels are formed. They are very much susceptible to damage and leakage, thus forming haemorrhages. Figure 1 (c) shows an example of such haemorrhages formed in a human eye.
Besides haemorrhages, exudates are another early symptom of DR related macular degeneration. Exudates are the presence of random yellow or white patches at different locations in a fundus image. They correspond to a variety of physiological deteriorations in the retina. Exudates can be further classified as hard exudates and soft exudates. Hard exudates mostly constitute of extracellular serum lipid which is discharged from abnormal retinal blood vessels as a result of damage of the capillaries due to higher glucose levels. With the prolonged presence of hard exudates, vision can be

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severely compromised. Soft exudates, which are also sometimes referred as ‘cotton wool spots’, are the small gray-white or yellow-white cotton-like lesions in the retina. Soft exudates seldom are attributed to the loss of vision unless they constitute the fovea. Figure 1 (d) demonstrates some of the regions of exudates in a fundus image.

This paper is organized as follows. Section 2 explains some of the problems in conventional screening practices of DR and introduces the importance and use of automatic screening techniques. It then discusses some of the recent state of the art Microaneurysm, haemorrhages and exudates detection techniques and their brief comparison. Discussion is presented in section 3, whereas section 4 presents conclusion of this paper.

2. Automatic Detection of DR and State of the Art Techniques

Eye screening is one of the basic and essential step in diagnosis and early treatment of the diseases related to the eyes. Conventional screening of eyes involves the use of a fundus image examined by an expert ophthalmologist.

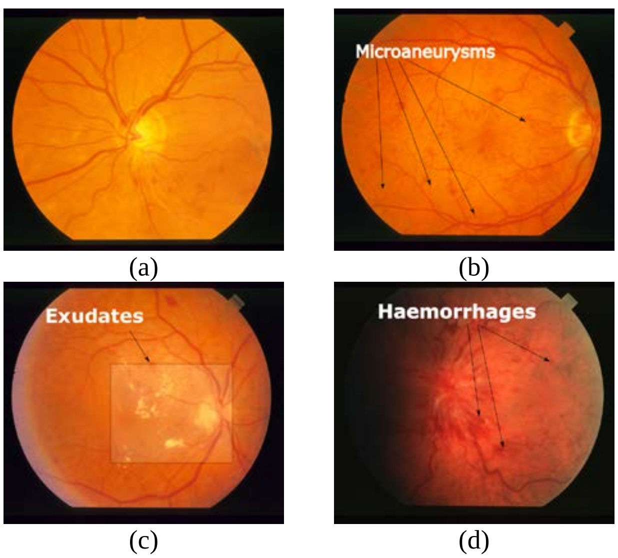

Fig. 1 Normal and abnormal fundus images according to the pathologies, (a) Normal image, (b) Microaneurysms present, (c) Exudates visible, and (d) Haemorrhages present.

Fundus images are captured by a special type of camera known as the fundus camera. A fundus image is the image of the inside surface of the eye which is parallel to the lens and includes the retina, optic disc, fovea, posterior pole and macula. Although a specialized camera is required for such a detailed image information, recently mobile phone cameras are also proposed to be used for the purpose[6]. A mobile phone with its built-in camera and flash light, and coupled with a condensing lens, can generate images of reasonable quality. This technique is a type of indirect ophthalmoscopy and has potential benefits of reducing the cost of screening test to a larger extent for the masses. Image processing techniques can be further applied to these low-cost solutions to remove noise and enhance the visible aspects of the images.

Albeit the low-cost solution development for the eye screening, the need of an expert ophthalmologist still exists. A large percentage of population around the globe has no access to proper medical facility. The availability of ophthalmologist is beyond that and very scarce. Therefore, it is highly judicious to take advantage and promote the automatic detection of ailments leading to DR. In the following subsections, we examine some of the state of the art algorithms proposed for automatic detection of DR which are based on micraaneurysms, haemorrhages and exudates.

2.1 Microaneurysm and Haemorrhages-based DR

Haemorrhages present in the blood vessels is a sign of DR. Diabetes sometimes causes blockage of small blood vessels. Due to this blockage of vessels, the retina tries to cope up with the supply of nutrition and oxygen by forming new blood vessels which are too weak and leak at times. This phenomenon is known as retinal haemorrhage. There are many algorithms for the detection of haemorrhages in the retina.

The existence of microaneurysms in the retina is the very first sign of DR. Therefore, its early detection is extremely important in order to prevent the disease. On the other hand, microaneurysms are also very difficult to be detected and accurately classified. There are many techniques proposed in literature which are based on automatic detection of microaneurysms. Some of the recent advanced techniques are discussed as follows.

Zhang et al.[7] proposed a technique based on multiscale correlation filtering and dynamic thresholding for Microaneurysm detection. They evaluated their developed algorithm on two publicly available datasets known as ROC (Retinopathy Online Challenge) [8] and DIARETDB1 [9].

Sopharak et al. [10] presented a technique for detection of microaneurysm from dilated pupils. They used coarse segmentation by utilizing mathematical morphology in addition to fine segmentation based on naïve Bayes classifier. They used a dataset of 80 retinal images. From these, a set of 40 images were used as the training set, while from the remaining 40 are used as a testing set. These testing set images consisted of 10 normal images and 30 images with the presence of microaneurysms.

Aravind et al. [11] proposed a microaneurysm detection algorithm based on morphological operations and a support vector machines (SVM) based classifier.

Tamilarasi and Duraiswamy [12] proposed a microaneurysms detection algorithm which is wavelet-based and Gaussian mixture model and microstructure texture feature extraction. Firstly, gamma correction and bottom-hat filtering are applied to separate out the green channel of the digital colored fundus image. Next, they extracted Gaussian profiles in wavelet domain in order to obtain multiscale Gaussian kernels to extract histogram-based features. At the end, they have applied the Markov Chain Monte Carlo method to classify the microaneurysms using the optimal feature set. There are two datasets used in their experimentation, namely, DIARETDB0 [13] and DIARETDB1 [9].

Dai et al. [14] proposed a scheme based on gradient vector analysis and class imbalance classification. Their proposed technique is comprised of two stages. The first stage consists of the candidate microaneurysm extraction from the fundus image. They analyze the gradient field of an image and compute multi0scale log condition number for vessel removal. Second order directional derivatives are then computed to localize he microaneurysms in different directions. In the second stage, they classify the candidate microaneurysm based on a set of features that include the geometry of the candidate, edges, contrast, intensity value, texture, region descriptors etc.

Zhou et al. [15] propose a novel MA detection approach named multi-feature fusion dictionary learning (MFFDL).

Their method consists of four basic steps which includes preprocessing candidate microaneurysm extraction, multi-feature dictionary learning, and classification. The novelty in their algorithm comes from the idea of incorporation of the semantic relationships among multi-features and dictionary learning into a unified framework for automatic detection of microaneurysms.

Srivastava et al. [16] proposed an automatic scheme for the detection of haemorrhages. They proposed a set of novel filters that can differentiate between blood vessels and red lesions. They base their assumption on the fact that lesion is usually circular and blob-like in nature. While, vessels are mostly elongated. Instead of filtering the whole image, they apply their designed filter on patches of different sizes. These patches are obtained by dividing the original image using a grid size that determines the patch size. By doing so, the problem of varying sizes of lesions is resolved. Lesion detection results for these grid sizes were combined using Multiple Kernel Learning.

Table 1: Comparison of Microaneurysms and Haemorrhages based detection techniques

Techniques	***Database***	***Method***
Zhang et al. [7], 2010	ROC microaneurysm and DIARETDB1	multiscale correlation filtering and dynamic thresholding
Sopharak et al. [10], 2013	80 dilated retinal images. 40 for training and 40 for testing.	mathematical morphology and naïve Bayes classifier
Arvind et al. [11], 2013	-	morphological operations and SVM
Tamilarasi and Duraiswamy [12], 2015	DIARETDB0 [13]	wavelet-based Gaussian mixture model
	DIARETDB1	
Dai et al. [14], 2016	ROC DiaRetDB1 V2.1	Gradient vector analysis and class imbalance classification
Zhou et al. [15], 2017	ROC	multifeature fusion dictionary learning (MFFDL)
Srivastava et al. [16]. 2017	DIARETDB1 and MESSIDOR [17]	Novel filter based on Frangi filters

2.2 Exudates-based DR

Exudates present in the retina is another sign of DR. Diabetes sometimes causes macular degeneration. Due to this blockage of vessels, the retina tries to cope up with the supply of nutrition and oxygen by forming new blood vessels which are too weak and leak at times. This phenomenon is known as retinal haemorrhage. There are many algorithms for the detection of haemorrhages in the retina.

Zhang et al. [18] proposed a scheme which emphasizes on preprocessing before the detection of MA. These preprocessing methods also detect the reflections and artifacts in the fundus image in addition to denoising and normalization tasks. Candidate exudates are segmented based on mathematical morphology. They utilize contextual features as well as classical features in a random forest learning algorithm to detect the true exudates among the candidates.

Pereira et al. [19] presents an exudates segmentation scheme based on Ant Colony Optimization (ACO). ACO is an optimization technique inspired by natural ants and their behavior of following a pheromone trail and optimizing the path to the trail. They have used the HEI-ME data set for their experimentation.

Table 2: Comparison of exudates-based detection techniques

Techniques	***Database***	***Method***
Zhang et al.[18], 2014	Messidor [17], DiaRetDB1v2 and HEI-MED [20]	candidates segmentation method
Pereira et al. [19], 2015	HEI-MED dataset	Ant-colony optimization
Imani and Pourreza [21], 2016	DiaRetDB1	Morphological Component Analysis (MCA) algorithm
Prentašic and Loncaric´[22], 2016	DRiDB [23]	deep convolutional neural networks
Liu et al. [24], 2017	e-ophtha EX dataset [25]	Location-to-segmentation algorithm

Imani and Pourreza [21] presented a novel algorithm by utilizing Morphological Component Analysis (MCA) to isolate lesions from normal retina structures in order to accelerate the exudate detection process. First, they separate out the lesions from the vessels using the MCA algorithm using suitable dictionaries. Next, they utilize the lesion area of the fundus image for the detection of exudates. Finally, exudate map is created by using dynamic thresholding technique and mathematical morphologies.
Prentašic and Loncaric [22] presented an algorithm based on deep convolutional neural networks for exudate detection. Output of the vessel detection system and the optic disc detection procedures are combined with conventional neural network. This inculcates the high level anatomical information regarding the potential exudates location.
Recently, Liu et al. [24] proposed a scheme for automatic exudates segmentation which they call location-to-segmentation scheme. Their scheme is designed for color retinal fundus images and comprises of tree stages, namely, anatomic structure removal, exudate location, and exudate segmentation. In the first stage, they propose a matched filter based main vessel segmentation method and a saliency-based optic disk segmentation method. The optic disk and the main vessel are next removed. In the second stage, a random forest classifier is used to classify the patches into two classes: exudate patches and non-exudate patches. They used the DIARETDB1 [9] fundus images database for the experimentation results.

3. Results and Discussion

Table 1 shows a brief comparison of some of the microaneurysms and haemorrhages based techniques which are then used for the diagnosis of DR. The first column in the table corresponds to the algorithm presented in literature along with the year presented. Due to the limited space, we have included some of the best techniques from past several years. In the second column of the table, the dataset on which the corresponding algorithms are applied is mentioned. Some of the most popular datasets present in literature includes DIARETDB0 [13], DIARETDB1 [9], MESSIDOR [17], ROC [8], HEI-MED [20], e-ophtha [25] and DriDb [23]. It is to be noted that these datasets are prepared by different institutes and organizations from around the globe and vary upon the number and types of samples, their permission for usage and the main focused ailment. The last column in table 1 presents the type of algorithm applied by each of the research contribution.
Table 2 presents a comparison of different techniques for the detection of exudates. Again, the first column corresponds to the research contribution in the past recent years. The second column constitutes the name of the data sets used by these research contributions. Here, two new datasets, e-ophtha [25] and DriDB [23] are also utilized as compared to the algorithms presented in table1. The last column presents the algorithm applied to achieve the results. It is to be noted that some of these results are reported from [4].
In order to evaluate and compare the performance of the detection process, there are several metrics proposed in literature. These also include two very widely and frequently used metrics which are sensitivity and specificity. Sensitivity, which is also referred to as true positive rate (TPR), measures the proportion of actual positives that are correctly detected as positives. Specificity, which is also referred to as true negative rate (TNR), measures the proportion of actual negatives that are correctly detected as negatives.
The expression for sensitivity is given as:

$$Sensitivity = TPR = TP / (TP + FN) \quad (1)$$

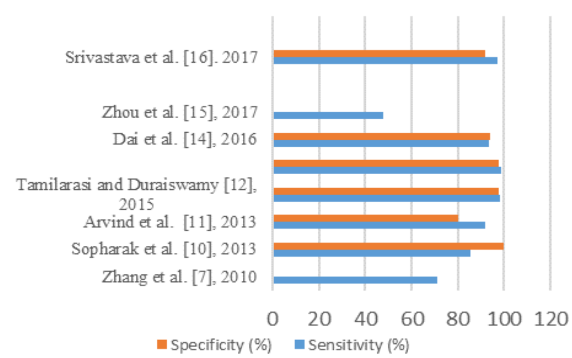

Fig. 2 Specificity and sensitivity measures for different techniques in literature based on Microaneurysms and Haemorrhages

And the expression for specificity is given as:

$$Specificity = TNR = TN / (TN + FP) \quad (2)$$

Figure 2 presents a bar diagram of the comparison between the recently presented techniques for the detection of microaneurysms and haemorrhages in terms of specificity and sensitivity. An overview of these techniques is already presented in section 2.1 and are outlined in table 1.

Figure 3 presents the comparison in terms of specificity and sensitivity of recent algorithms proposed for the segmentation and detection of exudates. These algorithms are also discussed is section 2.2 and presented in table 2. It is to be noted that the difference in performance, both in figures 2 and 3, is attributed to the goodness and efficiency of the algorithm, as well as the type of dataset used to test it. Some of these datasets are advanced and quite challenging. Therefore, using a better technique could be, in comparison to the one using a simple dataset, not that promising in the presence of a challenging dataset.

The image capturing technique of the fundus camera also plays a vital role in the detection of these pathologies in the retinal images. The best and standard retinal image capturing method is known as Fundus Fluorescein Angiography (FFA). It gives a very good quality of retinal image and is best suited for accurate detection of different pathologies. Nevertheless, FFA is an invasive process and requires an injection that can cause and complicate many other health issues for the patients. Therefore, it is not recommended in practice. On the contrary, color-filtered fundus images suffer from a variety of issues such as varying low contrast and noise.

Therefore, as can be seen in figures 2 and 3, there is some margin of improvement still remaining in even some of the recent state of the art techniques. Future research should focus on removing these gaps in the detection of microaneurysms, haemorrhages and exudates by exploiting other random local search techniques which are quite effective in other domains. These include evolutionary computation, deep learning and other nature inspired techniques.

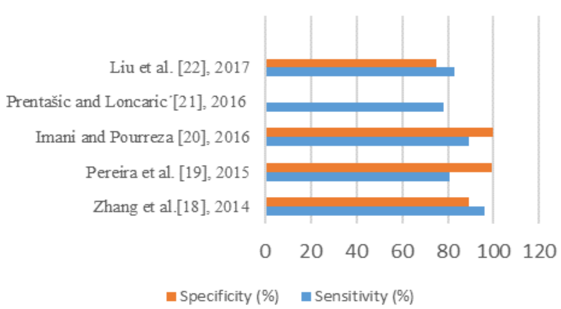

Fig. 3 Specificity and sensitivity measures for different techniques in literature based on Exudates detection

4. Conclusion

This work presents a comparison of different state of the art techniques present in recent literature for computer aided early detection of diabetic retinopathy. The presence of microaneurysms, haemorrhages and exudates are considered one of the earliest signs in the human retina which leads to diabetic retinopathy, and hence, permanent blindness. Therefore, the detection of these disorders at an earlier stage is of prime importance. This paper discusses and compares recent literature based on microaneurysms, haemorrhages and exudates separately. In the end, specificity and sensitivity measures are presented on standard datasets.

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